UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA



Dementia and Alzheimer's disease in Portugal: from illness progression to economic costs

Patrícia Vanessa Almeida Lindeza

Orientador(es): Prof. Doutor – Mário Miguel Rosa

Prof. Doutora – Maria Manuela Guerreiro

Doutora – Sónia Pereira (enterprise tutor)

Tese especialmente elaborada para a obtenção do grau de Doutor em Tecnologias da Saúde – Especialidade em Saúde Ambiental

2022

UNIVERSIDADE DE LISBOA

FACULDADE DE MEDICINA

Dementia and Alzheimer's disease in Portugal: from illness progression to economic costs

Patrícia Vanessa Almeida Lindeza

Orientador(es): Prof. Doutor – Mário Miguel Rosa
Prof. Doutora – Maria Manuela Guerreiro
Doutora – Sónia Pereira (enterprise tutor)

Tese especialmente elaborada para a obtenção do grau de Doutor em Tecnologias da Saúde – Especialidade em Saúde Ambiental

Júri:

- Doutor João Eurico Cortez Cabral da Fonseca, Professor Catedrático e Vice-Presidente do Conselho Científico da Faculdade de Medicina da Universidade de Lisboa (Presidente de Júri)
- Doutora Maria Isabel Jacinto Santana, Professora Catedrática da Faculdade de Medicina da Universidade de Coimbra;
- Doutor Manuel Maria dos Santos Matroco Gonçalves Pereira, Professor Auxiliar da Faculdade de Ciências Médicas da Universidade Nova de Lisboa;
- Doutor António Cândido Vaz Carneiro, Professor Catedrático Jubilado da Faculdade de Medicina da Universidade de Lisboa;
- Doutor Alexandre Valério de Mendonça, Professor Catedrático Convidado da Faculdade de Medicina da Universidade de Lisboa;
- Doutor João Nuno Marques Parracho Guerra da Costa, Professor Associado da Faculdade de Medicina da Universidade de Lisboa;
-Doutor Mário Miguel Coelho da Silva Rosa, Professor Auxiliar Convidado da Faculdade de Medicina da Universidade de Lisboa (Orientador)

Programa Doutoral do Centro Académico de Medicina de Lisboa – Programa Doutoral
FCT Saúde Ambiental – Envi&Health
FCT PhD fellowship Reference: PDE/BDE/120498/2016
2022

A impressão desta tese foi aprovada pelo Conselho Científico da Faculdade de Medicina de Lisboa em reunião de 21 de Setembro de 2021.

DECLARAÇÃO

Todas as opiniões expressas nesta publicação são da exclusiva responsabilidade do seu autor, não cabendo qualquer responsabilidade à Faculdade de Medicina de Lisboa pelos conteúdos apresentados.

Esta tese é dedicada aos meus amados pais

e a todas as pessoas com demência e seus familiares que me deram a honra de estar e aprender com elas

ACKNOWLEDGMENTS

The following section of this thesis will be addressed in Portuguese:

Esta tese foi realizada no âmbito do Programa Doutoral EnviHealth&Co, promovido pelo Instituto de Saúde Ambiental (ISAMB), da Faculdade de Medicina da Universidade de Lisboa. Deste modo, expresso a todos os envolvidos neste inovador Programa Doutoral o meu agradecimento e o meu reconhecimento pelo apoio e incentivos proporcionados durante o desenvolvimento deste estudo. Este agradecimento estende-se à Fundação para a Ciência e Tecnologia (FCT) e à Empresa parceira deste projeto, Merck Sharp & Dohme Portugal.

Agradeço aos meus orientadores, Professor Doutor Mário Miguel Rosa e Professora Doutora Maria Manuela Guerreiro, pela disponibilidade constante, orientação sábia, confiança depositada, e incentivo ao longo de todo o percurso do estudo. À Doutora Sónia Pereira, pela enorme disponibilidade, dedicação a este projeto e orientação ao longo do tempo.

Não posso deixar de agradecer aos demais companheiros de equipa que embarcaram nos vários estudos conduzidos neste projeto: Doutor Mário Rodrigues, Professor Doutor João Costa, Doutora Ana Virgolino, Professor Doutor Osvaldo Santos e Professora Doutora Lara Noronha Ferreira. A todos o meu muito obrigada.

Agradeço de forma muito especial à Professora Doutora Ana Verdelho, Professor Doutor Alexandre de Mendonça e Professor Doutor Frederico Simões do Couto pelo apoio incondicional neste projeto e forças mobilizadas na recolha da amostra. Agradeço a todas as pessoas com demência e familiares com quem me cruzei, assim como todas as pessoas que permitiram que este estudo fosse possível no Hospital de Santa Maria, nas instalações da Alzheimer Portugal, Rehabilitar Alzheimer ou Santa Casa da Misericórdia de Lisboa e do Fundão: foram um contributo essencial para este estudo, sem vocês não seria possível.

Aos membros do Comité de Tese pela orientação e disponibilidade ao longo do projeto: Professor Doutor Paulo Nogueira, Professor Doutor Luís Silva Miguel e Professor Doutor Carlos Gouveia Pinto.

Agradeço aos meus colegas e amigos desta jornada pela força que todos transmitimos uns aos outros nos momentos difíceis. À Liliane Morais, pelo apoio e carinho sempre demonstrados. Um agradecimento especial à Marta Salgado, Sara Madeira e Cátia

Reis pela enorme amizade e apoio incansável. É pelo sonho é que vamos! “E Setúbal é já ali!”, os grupos mais motivacionais de sempre!

À minha melhor amiga de sempre, Patrícia Oliveira, que muitas vezes estando fisicamente longe, foi determinante para me incentivar a dar sempre o melhor. Obrigada! Também distantes fisicamente, mas sempre presentes na minha vida, à Inês, ao Rui, à Benvinda e ao Luís por fazerem parte da minha vida há tanto tempo e viverem comigo todas as batalhas! À minha Celina Cruz, que tem um lugar especial para sempre no meu coração.

À minha grande família, por ser o melhor exemplo que poderia ter e por me lembrar todos os dias que nada, mas mesmo nada, é impossível. Se podemos pensar, podemos fazer. Agradeço por, em momento algum, duvidarem da minha capacidade para realizar este sonho. Foram o motor que me permitiu seguir sempre em frente neste longo caminho. À minha mãe que é a maior prova de força e amor deste planeta, incansável; ao meu pai pela grande determinação e exemplo que me passa diariamente; à minha irmã pelo enorme orgulho e amor que me transmite e pela equipa que somos – juntas podemos vencer todos os obstáculos que apareçam na vida; ao Samuel pela confiança e apoio e à Maria, o bebé pequenino, por me tornar melhor pessoa todos os dias e a cada sorriso!

Um especial agradecimento ao meu companheiro de vida, de sempre, Luís Miguel, por me acompanhar desde o início de tudo, e pela sua enorme envolvência pessoal neste projeto, como em tudo na vida. Obrigada por acreditares incondicionalmente em mim e me apoiares diariamente. O teu apoio e força foram fundamentais para superar os momentos mais difíceis. Foste e és a melhor pessoa que posso ter ao meu lado a vida toda! Obrigada pelo carinho e amor de sempre!

A todos, o meu profundo e verdadeiro agradecimento!

TABLE OF CONTENTS

ACKNOWLEDGMENTS I

TABLE OF CONTENTS III

ABSTRACT VII

RESUMO IX

THESIS MOTIVATION AND OUTLINE XIII

LIST OF ABBREVIATIONS XVII

LIST OF FIGURES XIX

LIST OF TABLES XXI

CHAPTER 1 1

GENERAL INTRODUCTION 3

1. THE PROCESS OF AGEING AND HEALTHY AGEING TRENDS 5

1.1. Demographic aspects of ageing in Portugal 8

1.2. Changes introduced by ageing 10

1.3. Dementia is not part of the normal ageing 13

1.4. "Ensure healthy lives and promote well-being for all at all ages" 16

2. DEMENTIA 17

2.1. Alzheimer's Disease 20

2.2. Other dementias 22

2.3. Disease progression and health-related quality of life 23

3. CARING FOR A PERSON WITH DEMENTIA 27

3.1. Informal care 28

3.2. Formal care 30

4. QUALITY OF LIFE AND FUNCTIONAL/COGNITIVE ABILITY ASSESSMENT IN DEMENTIA RESEARCH 31

4.1. QoL-AD 32

4.2. EQ-5D-3L 32

4.3. Blessed Dementia Rating Scale 32

4.4. Mini-Mental State Examination 33

5. PHYSICAL, EMOTIONAL AND SOCIAL BURDEN ASSESSMENT IN DEMENTIA RESEARCH 33

5.1. QASCI 33

6. AIMS 36

6.1. General aim 36

6.2. Specific aims 36

7. PROJECTS DEVELOPED 36

CHAPTER 2 ..... **38**

IMPACT OF DEMENTIA ON INFORMAL CARE: A SYSTEMATIC REVIEW OF FAMILY CAREGIVER'S PERCEPTIONS **40**

STUDY FRAMEWORK 42

IMPACT OF DEMENTIA ON INFORMAL CARE: A SYSTEMATIC REVIEW OF FAMILY CAREGIVER'S PERCEPTIONS 44

ABSTRACT 44

1. INTRODUCTION 45

2. MATERIALS AND METHODS 46

2.1. Search strategy and inclusion criteria *46*

2.2. Data extraction *49*

2.3. Quality appraisal *49*

2.4. Data Analysis *49*

3. RESULTS 50

3.1. Type and quality of the results *50*

3.2. Study quality *51*

3.3. Caregiver's perception of the effects of caring for a person with dementia *52*

4. DISCUSSION AND IMPLICATIONS 61

5. STRENGTHS AND LIMITATIONS 65

CHAPTER 3 ..... **68**

FACING COSTS WITH DEMENTIA: DAILY PERSPECTIVES FROM INFORMAL CAREGIVERS **70**

STUDY FRAMEWORK 72

FACING COSTS WITH DEMENTIA: DAILY LIVES PERSPECTIVES FROM INFORMAL CAREGIVERS 74

ABSTRACT 74

1. INTRODUCTION 75

2. METHODS 77

2.1. Design *77*

2.2. Focus groups composition and participants *77*

2.3. Sampling and recruitment process *78*

2.4. Data collection *78*

2.5. Data analysis *79*

2.6. Independent review board approval and consent to participate *79*

3. RESULTS 80

3.1. Description of the focus groups and participants *80*

3.2. Themes elicited from the content analysis *81*

3.3. Roadmap of factors affecting caregivers' daily life experiences and quality of life *90*

4. DISCUSSION 91

5. CONCLUSION 96

6. Strengths and limitations 96
7. Funding 97
8. Availability of data and materials 97
9. Ethics approval and consent to participate 97

CHAPTER 4 102

QUALITY OF LIFE AND FUNCTIONAL ABILITY OF OLDER ADULTS LIVING WITH DEMENTIA: OUTCOMES OF A PORTUGUESE SAMPLE 104

Study framework 106
Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample 108
Abstract 108
1. Introduction 109
2. Methods 111
2.1. Design 111
2.2. Participants and recruitment process 112
2.3. Independent review board approval and consent to participate 113
2.4. Tools 113
2.5. Data analysis 115
3. Results 117
3.1. Participants 117
3.2. Quality of life (proxy-report) 119
3.3. Functional ability (proxy-report) 124
3.4. Cognitive impairment 125
3.5. Correlations between QoL, functional ability and sociodemographic variables 126
3.6. Summary of collected data 129
3.7. Factors potentially associated with patients' QoL 132
4. Discussion 133
5. Strengths and Limitations 138
6. Conclusion 139

CHAPTER 5 141

DETERMINANTS OF BURDEN AND QUALITY OF LIFE AMONG INFORMAL CAREGIVERS OF INDIVIDUALS WITH DEMENTIA 143

Study framework 145
Determinants of burden and quality of life of informal caregivers of individuals with dementia 147
Abstract 147
1. Introduction 148
2. Methods 150

2.1. Design ... *150*
2.2. Participants and recruitment process ... *150*
2.3. Independent review board approval and consent to participate ... *151*
2.4. Tools ... *151*
2.5. Data analysis ... *153*
3. RESULTS ... 154
3.1. Participants ... *154*
3.2. Quality of life ... *155*
3.3. Informal caregiver burden ... *157*
3.4. Impact of dementia according to informal caregivers and PwD related factors ... *158*
3.5. Correlations between QoL, overall burden and sociodemographic variables of informal caregiver and their relatives with dementia ... *162*
3.6. Factors potentially associated with caregivers' QoL and overall burden ... *163*
4. DISCUSSION ... 164
5. STRENGTHS AND LIMITATIONS ... 170
6. CONCLUSION ... 170

CHAPTER 6 ... **173**

DISCUSSION AND CONCLUSIONS ... **175**

1. GENERAL DISCUSSION ... 177
2. STUDY LIMITATIONS ... 190
3. CONCLUSIONS ... 191
4. FUTURE PERSPECTIVES ... 192

CHAPTER 7 ... **193**

REFERENCES ... **195**

SUPPLEMENTARY MATERIAL ... **226**

ABSTRACT

Ageing of population is a worldwide reality and Portugal is one of the most ageing -leading countries. The prevalence of dementia increases with age, almost doubling every five years when over 60 years old. With the increase in human longevity, the global number of people with dementia is expected to grow significantly upon incoming years. Following increasing demographic ageing, the prevalence of dementia is particularly worrying in Portugal.

Dementia prevalence has undergone a vast increase in recent years, and it has become one of the greatest healthcare challenges of the 21st century due to the high demand for medical, social, and institutional care. Dementia is a clinical syndrome characterised by a cluster of symptoms manifested by impairment in higher brain functions such as memory, language and cognitive functions, changes in behaviours, entailing difficulties in activities of daily living (ADL). As a result, there is an increasing demand for informal care that play an important role for people with dementia (PwD), helping them in their daily activities, whose dependence increases as disease progresses.

The task of caregiving is complex and can lead to physical, mental, and financial stress for caregivers. Emotions such as guilt, resentment, sadness, and anticipated loss of the cared one can emerge. Therefore, informal caregivers significantly endure levels of psychological morbidity, depression, stress and burden. It is widely reported that dementia informal care affects the health, well-being and quality of life (QoL) of caregivers. Therefore, the burden experienced by caregivers might result in low capacity or mood to care for their relatives with dementia, affecting patient's well-being as well.

The studies of this thesis aimed to help characterize the daily impact of dementia in a Portuguese sample of PwD and their informal caregivers at the individual, familiar and social level. To measure the QoL and dependency level of the patients, while describing their living context and formal care services utilization. To describe, as disease progresses, how it is like to care for a PwD in a familial context and the costs involving dementia were also objectives of the work, as well as, to measure the QoL and physical, emotional and social burden of the informal caregivers and describe the main factors involved. This thesis is a synergy of qualitative and quantitative methods. The mixed use of these methodologies empowered caregivers, allowing a voice to better describe how is caring for a PwD and its impact on QoL. The quantitative part of this study allows data characterization of patient's QoL, cognitive and functional ability and, informal caregivers QoL and physical,

emotional and social burden, together with study of the influence of sociodemographic variables of the dyads that influenced PwD QoL, informal caregivers QoL and overall burden.

The work in this dissertation showed that our sample of Portuguese PwD were referred by their caregivers as having extreme low levels of QoL and high impairment on their functional and cognitive ability. Of note, dementia informal care included a wide range of experiences referred by the caregivers, as well as drastic changes introduced in their personal lives. Altogether, informal care resulted in high burden and low levels of QoL for the informal caregiver. Factors such as the PwD educational level, the changes in everyday life and habits were identified as potential explanatory factors of PwD HRQoL. Different explanatory factors were identified for caregivers QoL and burden, however, in both cases the familiar relationship with the PwD and PwD pain/discomfort were identified.

Planning to decrease the burden of dementia informal care and the impact on caregivers and patient's well-being, will likely mean that the articulation and cooperation of different public services (formal care services, neurology, psychiatric, psychology, social and financial support) should be re-thought. In the future, more studies are needed to further characterize the hurdles and needs of dementia care to further develop multicomplex interventions aimed to reduce the negative effects of dementia on patient's QoL, while promoting caregiver's QoL and decrease the overall burden.

Keywords: Dementia; Informal care; Quality of life; Functional ability; Costs.

RESUMO

O envelhecimento é uma realidade global e Portugal é um dos países com maior índice de envelhecimento. A prevalência da demência aumenta com a idade, duplicando a cada cinco anos após atingir os 60 anos de idade. Com o aumento da longevidade da vida humana, prevê-se que o número de pessoas com demência aumente significativamente num futuro próximo. Associada ao crescente envelhecimento, a prevalência de demência é particularmente preocupante em Portugal.

A demência é caracterizada por um conjunto de sintomas manifestados como dificuldades de memória, distúrbios de linguagem e em várias outras funções cognitivas, mudanças de comportamento e dificuldades nas atividades da vida diária. O tipo de demência mais comum é a doença de Alzheimer (DA), responsável por 50-70% dos casos de demência. A prevalência de DA sofreu um grande aumento nos últimos anos, tornando-se um dos maiores desafios da saúde do século XXI devido à elevada necessidade de cuidados médicos, sociais e formais. Como consequência, existe uma necessidade crescente de cuidados informais, assegurados por familiares da pessoa com demência (PcD), que desempenham um papel importante para estas pessoas, auxiliando-as nas suas atividades diárias.

A tarefa de cuidar é complexa e pode conduzir a problemas físicos, mentais e financeiros para os cuidadores. A prestação de cuidados é envolvida por muitas emoções como a culpa, ressentimento, tristeza, bem como sentimentos relacionados com a perda antecipada do familiar. Como resultado, os cuidadores informais sofrem níveis significativamente mais elevados de problemas psicológicos, depressão, stress e sobrecarga física, emocional e social. É amplamente descrito na literatura que a prestação de cuidados informais afeta o bem-estar e a qualidade de vida (QV) dos cuidadores. Este aspeto em conjunto com a sobrecarga física e psicológica do cuidador pode resultar na diminuição da capacidade e da disponibilidade para cuidar, afetando assim, também o bem-estar das PcD.

Os estudos realizados nesta tese tiveram como objetivo caracterizar o impacto diário da demência numa amostra Portuguesa de PcD e cuidadores informais ao nível individual, familiar e social, com foco na qualidade de vida e nível de dependência das PcD. São ainda objetivos deste estudo, descrever o contexto envolvente das PcD e o impacto da doença na QV, analisar o modo como os cuidadores lidam com a prestação de cuidados, entender os custos envolvidos na demência, assim como descrever os fatores

envolvidos na sobrecarga física, emocional e social e o impacto na QV dos cuidadores informais.

Esta tese reflete uma sinergia de métodos qualitativos e quantitativos. O uso misto destas metodologias permitirá dar uma voz aos cuidadores para descrever como é viver com uma PcD à medida que a doença progride e qual é o impacto na QV de ambos. A componente quantitativa permite a recolha de dados sobre a QV e a capacidade cognitiva e funcional da PcD, a QV de cuidadores informais e sua sobrecarga física, emocional e social, juntamente com o estudo da influência de variáveis sociodemográficas das díades que influenciam a QV e a sobrecarga física, emocional e social dos cuidadores informais.

De forma a cumprir estes objetivos, foram realizados quatro estudos:

Estudo 1) Com o objetivo de conhecer o que a literatura sobre o impacto da demência nos cuidadores informais, foi criada uma estratégia de pesquisa sistemática que permitiu selecionar 81 estudos qualitativos, entre 2685 estudos encontrados, a partir dos quais foram reunidas as perceções dos cuidadores sobre os aspetos positivos e negativos do ato de cuidar de uma PcD e os fatores que contribuíram de forma positiva ou negativa para essa tarefa. Os aspetos positivos de cuidar incluíram a realização pessoal e o fortalecimento de relacionamentos familiares, que foram aumentados na presença de um bom aconselhamento médico/apoio formal e apoio da família ou amigos. Os aspetos negativos incluíram, principalmente, as alterações emocionais e sociais que aumentaram com a ausência de apoio médico/formal, com a progressão da doença e os elevados custos associados à demência. Os resultados fornecem uma descrição holística sobre o ato de cuidar de uma PcD.

Estudo 2) Com o objetivo de caracterizar as experiências de vida diária de cuidadores informais de PcD e identificar as despesas relacionadas com a demência, recorreu-se a uma amostra Portuguesa de cuidadores informais. Os participantes identificaram, qualitativamente, os principais custos introduzidos pela doença e as alterações que sentiram na sua vida pessoal, familiar, profissional e social. Em resultado, os temas discutidos incluíram mudanças na rotina diária, utilização de serviços de cuidados formais, identificação de custos e alterações na QV. Em detalhe, as alterações que afetaram a QV do cuidador incluíram isolamento social, alterações na saúde física, como aparecimento de perturbações do sono ou cansaço e alterações na saúde psicológica como stress, descontrolo emocional ou solidão. Os custos introduzidos pela demência e que afetaram o orçamento financeiro geral da família incluíram despesas acrescidas na alimentação, produtos de higiene, eletricidade, medicamentos, custo dos serviços de

cuidados formais, entre outros. O último tema discutido incluiu o uso de serviços formais e as barreiras/dificuldades associadas.

Estudo 3) Com o objetivo de avaliar o impacto da demência na QV e a capacidade funcional e cognitiva de PcD foi desenvolvido um estudo descritivo, transversal, com uma amostra não probabilística e intencional de 187 PcD e os seus cuidadores informais. Foram usados os questionários EQ-5D-3L e Qualidade de Vida na Doença de Alzheimer (QoL-AD) para medir a QV de PcD. A Escala de Demência de Blessed (EDB) e a avaliação global do estado mental (Mini-Mental Examination Scale - MMSE), permitiram medir o comprometimento funcional e cognitivo da PcD, respetivamente. Todos os questionários foram respondidos em entrevistas semi-estruturadas, face a face, pelos cuidadores informais (sobre a PcD cuidada), com exceção do MMSE, aplicado ao doente, sempre que possível. A média para o questionário EQ-5D-3L foi de -0.005±0.31 (-0.536-0.766), para o EQ-VAS foi de 36.9±1.4 (5-90) e para o QoL-AD foi de 19.5±4.0 (15.5-23.5), revelando valores extremamente baixos para a QoL da PcD. A média do EDB foi de 15.8±4.8 (11.0-20.6) e do MMSE de 16.0±5.5 (10.5 to 21.5), indicando um elevado comprometimento físico e cognitivo. As dimensões mais afetadas no EQ-5D-3L foram a capacidade da PcD para realizar tarefas de cuidados pessoais, tarefas relacionadas com atividades diárias e a mobilidade. O modelo multivariado demonstrou associações significativas entre a QV das PcD e os anos de diagnóstico, utilizar centros de dia, anos de escolaridade das PcD e idade das PcD e dos cuidadores. Este estudo fornece uma importante descrição sobre a situação de vida da PcD, tentando preencher a lacuna que envolve o desconhecimento em Portugal sobre o impacto desta doença na QV e a sua relação com a capacidade funcional e cognitiva das PcD.

Estudo 4) Com o objetivo de avaliar o impacto da demência na QV e a sobrecarga física, emocional e social nos cuidadores informais de PcD foi desenvolvido um estudo descritivo, transversal, com uma amostra não probabilística e intencional de 187 cuidadores informais de PcD. Foram usados os questionários EQ-5D-3L e o Questionário de Avaliação da Sobrecarga do Cuidador Informal (QASCI), tendo os questionários sido respondidos em entrevistas semi-estruturadas, face a face, pelos cuidadores informais (sobre si mesmos). Os resultados obtidos mostram que a QV dos cuidadores informais apresentou valores relativamente baixos (0.375±0.28 (-1.11-1.00), indicando que os cuidadores informais tiveram alguns/muitos problemas em duas a três dimensões do EQ-5D-3L, nomeadamente, a capacidade para realizar tarefas habituais, dor/desconforto e ansiedade/depressão), enquanto a sobrecarga física, emocional e social sentida foi

moderada (53±14 (0-100), com as dimensões sobrecarga financeira, implicações na vida pessoal e sobrecarga emocional a serem as mais afetadas. Diferentes fatores explicativos foram identificados para QV e sobrecarga do cuidador informal, porém, em ambos os casos, a relação familiar com a PcD e a dor/desconforto da PcD foram identificados como potenciais fatores explicativos. Os resultados deste estudo apontam para que vários fatores estejam envolvidos na QV e sobrecarga do cuidador informal, sugerindo que a prestação de cuidados informais ocorre num ambiente complexo determinado por características das díades (PcD e cuidador informal) que podem resultar em maior ou menor impacto na vida e saúde do cuidador, mas também, na QV do próprio doente.

Em conclusão, esta tese enfatiza que o impacto da demência na amostra em estudo resultou em reduzida QV quer no doente quer no cuidador informal, assim como elevado comprometimento das capacidades funcionais e cognitivas da PcD e elevada sobrecarga física, emocional e social no cuidador. A prestação de cuidados informais na demência incluiu uma ampla gama de experiências e emoções descritas pelos cuidadores, bem como mudanças drásticas na sua vida pessoal, profissional, social e económica.

Para diminuir o impacto da demência nos cuidadores informais e nas PcD, a articulação e a cooperação de diferentes serviços públicos (serviços de cuidados formais, neurologia, psiquiatria, psicologia, apoios sociais e financeiros) deve ser repensada. No futuro, são necessários mais estudos que descrevam as necessidades dos cuidadores informais e dos seus familiares com demência de forma a ser possível desenvolver intervenções multidisciplinares que reduzam os efeitos negativos da demência na QV dos cuidadores e das PcD.

Palavras-chave: Demência; Cuidados informais; Qualidade de vida; Capacidade funcional; Custos.

THESIS MOTIVATION AND OUTLINE

This thesis was developed in the context of *EnviHealth&Co Doctoral Program* that is an innovator doctoral program due to its linkage to different companies in health sciences. This project was co-founded by *Merck Sharp & Dohme, Lda* due to its relevance to neuroscience field, particularly regarding dementia and its impact in Portugal. The general objective of this project was the description of a Portuguese sample of dementia patients and their family caregivers in terms of cognitive and functional ability of the persons with dementia (PwD), while describing the impact of disease on quality of life (QoL) trough quantitative and qualitative analysis in both PwD and their informal caregivers. The assessment of the physical, emotional and social burden of informal caregivers was also an aim of this study. Dementia is a progressive disease that causes dependence due to physical and cognitive impairment, exceeding what would be reasonably expected for normal ageing, and can be severe enough to compromise the individual's autonomy and self-care. The prevalence of dementia increases with age, almost doubling every five years after reaching 60 years old (Salthouse, 2004; I. Santana et al., 2015). With the increase in human life longevity, the global prevalence of dementia is expected to grow significantly in the near future (Åkerborg et al., 2016; Getsios et al., 2012). Prince and colleagues estimated that by 2030, 65.7 million people worldwide will live with dementia, increasing to 115.4 million in 2050 (Prince et al. 2013). Associated with the growing demographic ageing, the prevalence of dementia is particularly concerning in Portugal (Santana et al. 2015). Until recently, Portuguese authors resort to indirect methods to estimate the number of people with dementia in the Country. Despites the limitations of published community studies in Portugal, the findings support the urgent need for effective national policies in dementia care (M Gonçalves-Pereira et al., 2021).

In Portugal, few observational studies assessed the effects of dementia on patient's well-being and the impact of the act of caring for a PwD on informal caregivers. Since this community is not especially known, it is of major interest to characterize these patients to better know how they live with dementia as its progression. Additionally, the inclusion of informal caregivers was considered as essential, since they play a major role supporting the patient's daily needs before, the eventual, institutionalization (Alberdi et al., 2016; Stefanacci, 2011). There is significant literature revealing that dementia caregivers are exposed to high levels of stress, depression, physical and financial burden (Courtney Allyn Polenick & Martire, 2013; Tynan & Allen, 2002). This project includes the synergy of

qualitative and quantitative methods, that were considered the best approach to explore the holistic impact of dementia in terms of patient and the caregiver QoL and burden. The objective of the qualitative methodology was to give caregivers a voice to better describe how is living with dementia as its progresses and the critical aspects that, in their opinion, contributed positively and negatively to the dyad's (patient and caregiver) QoL. The quantitative part of this study aimed to collect data on patient's QoL, cognitive and functional ability, informal caregivers QoL and physical, emotional and social burden, while describing which sociodemographic features of both patients and caregivers were involved in the changes of QoL and burden.

This thesis is composed of six chapters. Chapter 1 correspond to a general introduction focusing the process of ageing, dementia and Alzheimer's Disease characterization, importance of informal and formal care, measurements on QoL, burden and functional/cognitive ability in dementia. Chapter 2, 3, 4 and 5 are composed of the full reproductions of the publications produced during the PhD work (published or submitted), being provided a brief rational of the study in the beginning of each chapter. Chapter 2 is composed of one systematic review that included more than twenty years of publications where the main positive and negative aspects of the holistic experience of informal care were established trough caregivers' perceptions. Chapter 3 is composed of one publication where we characterized a Portuguese sample of informal caregivers to identify, qualitatively, the main costs of living with dementia in a day-to-day basis. Topics included changes in daily lives, formal care services utilization, identification of economic costs and changes in QoL. Chapter 4 contains the publication where 187 Portuguese dementia dyads were objectively interviewed, allowing to determine the dementia patient's QoL and functional/cognitive ability. Chapter 5 includes the results on the assessment of informal caregivers QoL and physical, emotional and social burden.

Chapter 6 is composed of a general discussion of all the studies with conclusion remarks and future perspectives. All references used throughout the thesis are together in the last chapter, Chapter 7 called "References". The facsimiles of all the publications are presented at the end of the thesis in annex.

This thesis is based on the following published or submitted manuscripts:

- Lindeza, P, Rodrigues M, Costa J, Guerreiro M, Rosa MM. Impact of Dementia on informal care: a systematic review of family caregivers perceptions. BMJ Supportive & Palliative Care. Published Online First: 14 October 2020. doi: 10.1136/bmjspcare-2020-002242
- Lindeza, P, Virgolino A, Santos O, Guerreiro M, Rosa MM. Facing Costs With Dementia: Daily Lives Perspectives From Informal Caregivers. BMC Geriatrics, (under review)
- Lindeza P, Noronha L, Guerreiro M, Rosa MM. Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample. Ageing & Society, (submitted).
- Lindeza P, Noronha L, Guerreiro M, Rosa MM. Determinants of burden and quality of life among informal caregivers of individuals with dementia. Ageing & Society, (submitted).

During the time of the thesis, it was possible to be involved in the development of other publication:

- Costa J, Borges M, Encarnação R, Firmino H, Gonçalves-Pereira M, Lindeza P, Sampaio F, Santana I, Sousa R, Taipa R, Verdelho A, Silva-Miguel L. Custo e carga na doença de Alzheimer em Portugal, (in preparation).

LIST OF ABBREVIATIONS

AD: Alzheimer's disease

ADL: Activities of daily living

ADRDA: Alzheimer's Disease and Related Disorders Association

APOE: Apoliprotein E

BDRS: Blessed Dementia Rating Scale

CSF: Normal cerebrospinal fluid

CT: Computed tomography

CTA: CT angiogram

DSM: Diagnostic and Statistical Manual of Mental Disorders

ECG: Electrocardiogram

EEG: Electroencephalogram

FTD: Frontotemporal Dementia

HRQoL: Health-related QoL

INE: Instituto Nacional de Estatística

LBD: Lewy Body Dementia

MCI: Mild Cognitive Impairment

MMSE: Mini-Mental State Examination

MND: Mild Neurocognitive Disorder

MRA: Magnetic resonance angiogram

MRI: Magnetic resonance imaging

NINCDS: National Institute of Neurological and Communicative Disorders and Stroke

NMDA: N-methyl-D-aspartic acid

PET: Positron emission tomography

PwD: Person with dementia

QASCI: Informal Caregiver Burden Assessment Questionnaire

QoL: Quality of life

QoL-AD: Quality of Life in Alzheimer's Disease

VaD: Vascular dementia

VAS: Visual analogue scale

WHO: World Health Organization

YOD: Young-onset dementia

LIST OF FIGURES

Chapter 1

Figure 1. 1. Young people and older people as a percentage of global population: 1950-2050. Adapted from United Nations. World Population Prospects. The 2010 Revision. Adapted from: http://esa.un.org/unped/wpp, (Dobriansky, Suzman, and Hodes 2007)..... 6

Figure 1. 2. Elderly population comparisons between Portugal and European Countries, Total, % of population, 1990-2018. Adapted from: www.data.oecd.org 8

Figure 1. 3. People aged ≥55 years, by age class, 2019 and 2050 (% share of total population). Adapted from: 2020 edition of Ageing Europe Book "Looking at the lives of older people on the EU", (Comission, 2020). Note: all data as of 1 January. 9

Figure 1. 4. A. Percent distribution of resident population according to age groups by region, 2019; B. Ageing ratio by region, 2019. Adapted from: As pessoas/ The people, 2019, (INE 2019a). 10

Figure 1. 5. Difference between Alzheimer's and typical age-related changes. Adapted from: Alzheimer's Association Webpage, https://www.alz.org/alzheimers-dementia/10_signs (visited in 01/03/2021). 15

Figure 1. 6. The United Nations Sustainable Development 17 Goals. Adapted from: WHO Website, https://www.who.int/health-topics/sustainable-development-goals, visited in 06/03/2021)..... 16

Figure 1. 7. Clinical Evaluation of Suspected Dementia. Abbreviations: AD, Alzheimer disease; CT, computed tomography; CTA, CT angiogram; ECG, electrocardiogram; EEG, electroencephalogram; MRA, magnetic resonance angiogram; MRI, magnetic resonance imaging. Depending on the clinical presentation, consider blood tests (complete blood cell count, erythocyte sedimentation rate, glucose level, renal and liver function tests, folic acid level, and rapid plasma reagin test). Adapted from: Arvanitakis et al., 2019. 18

Figure 1. 8. A. Causes of dementia (≥65 years old). AD, Alzheimer's disease; VaD, Vascular dementia. B. Pooled prevalence of dementia by sex. Adapted from: Van Der Flier & Scheltens, 2005. ..... *19*

Figure 1. 9. Model of the clinical trajectory of Alzheimer's disease (AD). Adapted from Sperling et al., 2011. ..... *24*

Figure 1. 10. Manifestations of Dementia in Earlier and Later-Stages. Adapted from Arvanitakis et al., 2019 ..... *25*

Figure 1. 11. Impact-cost matrix along dementia progression. Adapted from Jönsson et al., 2017 ..... *26*

Figure 1. 12. Informal and formal care definitions. Adapted from EUROFAMCARE studies (Triantafillou. et al. 2010). *27*

Chapter 2

Box 2.1. Systematic review of literature: search terms, inclusion/exclusion criteria and information extraction *48*

Chapter 3

Figure 3. 1. Informal care impact to caregiver's quality of life 91

LIST OF TABLES

Chapter 1

Table 1. 1. Differentiating between common forms of dementia *23*

Chapter 2

Table 2.1. Examples of the studies including positive, negative or combined aspects of caregiving role (n=81) *52*
Table 2.2. Main positive and negative aspects and related factors influencing caregivers' role (n=81) *53*

Chapter 3

Table 3. 1. Background characteristics of participants (n=14) and their relatives with dementia *81*
Table 3. 2. Content analysis: categories, themes and sub-themes *82*

Chapter 4

Table 4. 1. Background characteristics of informal caregivers, (n=187) *117*
Table 4. 2. Background characteristics of PwD, (n=187) *119*
Table 4. 3. EQ-5D-3L and EQ-VAS univariate values, (n=187) *120*
Table 4. 4. Distribution of responses of the EQ-5D-3L index scores, (n=187) *122*
Table 4. 5. Five most common PwD EQ-5D-3L scores and health states, (n=187) *123*
Table 4. 6. Distribution of QoL-AD scores, (n=187) *124*
Table 4. 7. Distribution of BDRS scores by domain, (n=187) *125*
Table 4. 8. Distribution of MMSE scores, (n=43) *126*
Table 4. 9. Correlations with EQ-5D-3L, Qol-AD and BDRS scores with each other's and sociodemographic variables, (n=187) *128*
Table 4. 10. Summary of PwD and caregiver collected data per group, (n=187) *131*
Table 4. 11. Influence of PwD and informal caregivers' characteristics in PwD QoL (EQ-5D-3L) *132*

Chapter 5

Table 5. 1.Frequency distributions by EQ-5D-3L dimensions and means of EQ-5D-3L/EQ-VAS for the overall sample and by age group *157*

Table 5. 2. Distribution of responses of the QASCI score by domain, (n=187) *158*

Table 5.3. Distribution of responses of the EQ-5D-3L index score, EQ-VAS and QASCI score according to informal caregivers and PwD related factors……*161*

CHAPTER 1

GENERAL INTRODUCTION

1. The process of ageing and healthy ageing trends

Human ageing is a natural process that slowly reveals its mysteries and concerns since the dawn of humankind. According to World Health Organization (WHO), ageing is a course of biological reality which starts at conception and ends with death, with its own dynamics, much beyond human control. It has been a concern for physicians and researchers especially in the last decades, because of the worldwide demographic increase of the elderly population.

The book "*Evolutionary Biology of Aging"* presented, in 1991, the following definition of ageing that has been widely used: "a persistent decline in the age-specific fitness components of an organism due to internal physiological deterioration" (Rose, 1991). This definition was a modest generalization of a definition given by Alex Comfort in his book "*The Biology of Senescence"* (Comfort, 1979): "a progressive increase throughout life, or after a given stadium, in the likelihood that a given individual will die, during the next succeeding unit of time, from randomly distributed causes". Recently, biologists defined ageing as an age-dependent or age-progressive decline in intrinsic physiological function, that lead to an increase in age-specific mortality rate and an decrease in age-specific reproductive rate (Bronikowski & Flatt, 2010; Promislow, D. E. L., Bronikowski, 2006; Tatar, 2001).

The global ageing represents a success of medical, social, and economic advances over disease but, at the same time, it also represents a tremendous challenge demonstrating that population ageing matters and must be considered as a priority topic in health care policies (Dobriansky et al., 2007). The long-term fall in fertility rates and the increased life expectancy combined with advances in public health and medical technologies, increased the awareness of the benefits of a healthy lifestyle and improved living conditions, contributing to population ageing (European Comission, 2020).

Globally, there were 703 million elder people in 2019. Of that, 260 million were located in Eastern and South-Eastern Asia, being the largest number of the world's older population, followed by Europe and Northern America (over 200 million) (United Nations, 2019). A person is considered older/elderly when aged 65 or over. In Portugal, "elderly" is often associated with the retirement age (although, this is currently 66.5 years old), a factor that changes the role of individuals in society. Young children have always outnumbered elder people; however, for the first time in history elderly people will outnumber children

under age 5 (Figure 1.1). This trend is emerging around the globe and with increasing population ageing, the number of older people is expected to reach to 1.5 thousand millions worldwide in 2050, affecting mainly developing countries (Dobriansky et al., 2007). The differences, both within and across countries and the assumptions of geography of rural and urban communities, significantly affect the comparability of elderly population data (OECD, 2020). It is widely known that elderly people tend to live in few areas within each country, usually rural areas, which means that a small number of regions will have to face a number of specific social and economic challenges due to population ageing (OECD, 2020).

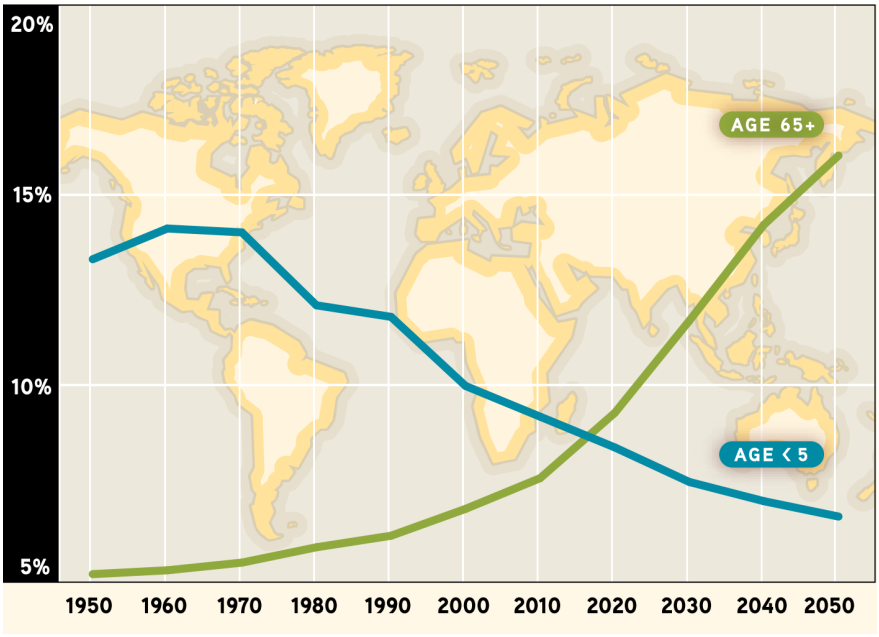


Figure 1. 1. *Young people and older people as a percentage of global population: 1950-2050. Adapted from United Nations. World Population Prospects. The 2010 Revision. Adapted from: http://esa.un.org/unped/wpp,* (Dobriansky et al., 2007).

Additionally, the growth of the elder is a global concern that imply not only an increase of chronic morbidity and disability rates, but also leads to the occurrence of multiple chronic conditions in the same person. As time passes, the comorbidity might cause decrease in functional abilities, as well as social and psychologic problems with huge impact on well-being and quality of life (QoL) (Ferrucci et al., 2008) (WHO, www.who.int, visited in 26/02/2021).

Altogether, considering the alarming of worldwide demographic and epidemiologic perspectives, significant changes in the structure and function of health systems and social protection should have been addressed, showing that we are unprepared to deal with the

enormous challenge of population ageing (Ferrucci et al., 2008). To overcome this reality, the WHO included in *"10 Facts on Ageing and Health*" (WHO, www.who.int, visited in 26/02/2021) envisaging that a comprehensive public health action is needed and that will require fundamental changes related to ageing and health, suggesting a realignment on health systems to better meet older populations needs. Another goal is making all health care services accessible to elderly people and people with disability, as well reduce unacceptable health inequalities. Additionally, it is remembered that healthy ageing might involve all levels and sectors of government to enhance the progress on healthy ageing, therefore a better understanding of age-related issues and healthy ageing trends is required (WHO, www.who.int, visited in 26/02/2021).

1.1. Demographic aspects of ageing in Portugal

In Europe, citizens are living longer than ever before. At the beginning of 2019, Europe had 90.5 million elder people among its population (20.3% of the total population) (Nations, 2019). As well as the worldwide trend, the number of older people in the Europe (27 countries) is projected to reach 129.8 million residents in 2050 (United Nations, 2019). This fast grow of population ageing will rapidly change the structure of society, affecting economic growth, trade, migration, disease patterns and prevalence, and fundamental assumptions about growing older (Dobriansky et al., 2007; United Nations, 2019).

In Portugal, "elderly" is often associated with the retirement age (although, this is currently 66.5 years old). However, the retirement age varies according to the occupation and function performed, the historical time, the country and its social system (Paúl, 1997). Data from Eurostat show that Portugal percentage of elderly population in 2018 was 21.67%, fairly above the European Union (28 countries) average of 19.85% (Figure 1.2). The countries such as Italy (Figure 1.2), Germany (21.47%) and Greece (21.89%), presented similar ratios of elderly populations comparatively to Portugal, while countries like France (19,84%) or Spain (Figure 1.2) presented lower percentages of elderly population.

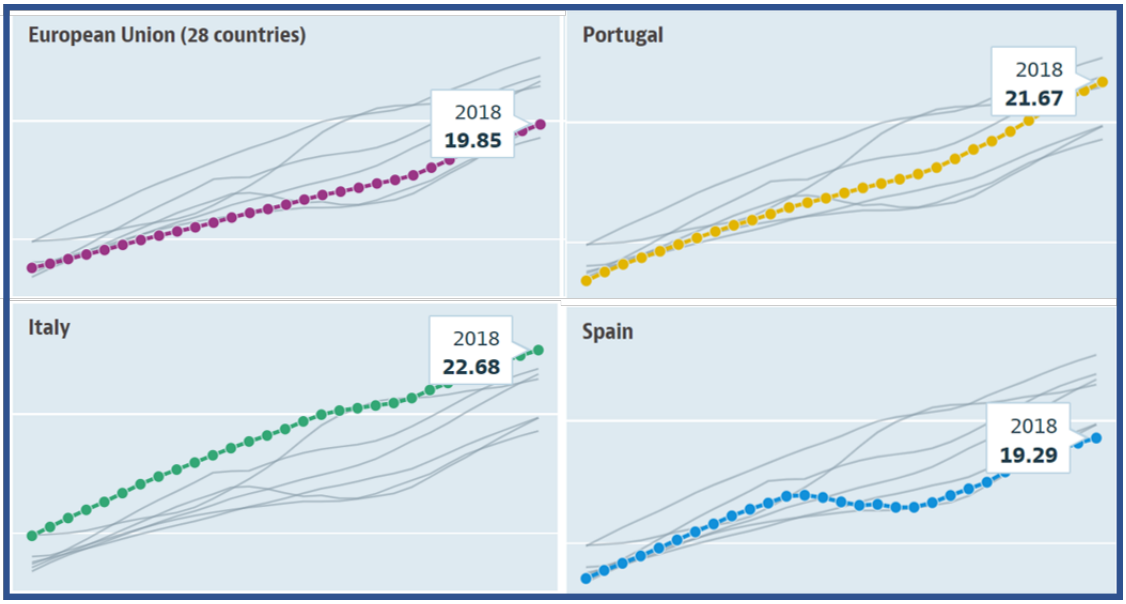


***Figure 1. 2**. Elderly population comparisons between Portugal and European Countries, Total, % of population, 1990-2018. Adapted from: www.data.oecd.org*

The 2020 edition of Ageing Europe Book *"Looking at the lives of older people on the EU"*, reported very important projections about the population (European Comission, 2020). The figure 1.3 present the people aged equal or over 55 years old expected growth until 2050. The group of very old (people aged 85 years or more) is growing faster than any other age group, deserving special attention (European Comission, 2020). Until 2050, the number of very old people in Europe (27 countries) is projected to more than double, reaching 26.8 million. In Portugal, the percentage of people aged 55 or more years is expected to reach more than 45% of total population until 2050, with more than 35% over 65 years old, again higher than the European mean (27 countries) (Figure 1.3) (European Comission, 2020).

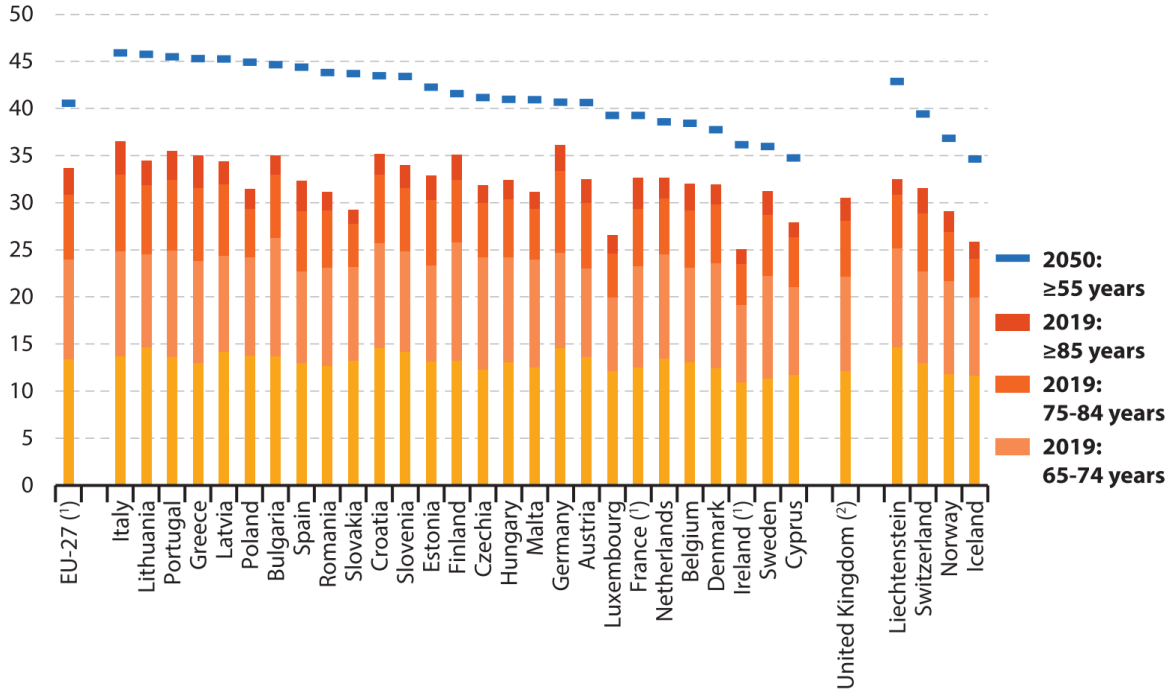


Figure 1. 3. *People aged ≥55 years, by age class, 2019 and 2050 (% share of total population). Adapted from: 2020 edition of Ageing Europe Book "Looking at the lives of older people on the EU", (Comission, 2020). Note: all data as of 1 January.*

1.1.1. Life expectancy, distribution of population and ageing ratio

According the Instituto Nacional de Estatística (INE) Mortality Tables for Portugal (INE, 2019b), the life expectancy reached 80.80 years at birth and 19.49 years at 65 years old, with 77.78 years for men and 83.43 years for women in the period 2016-2018. Within a decade, there was an increase of 2.06 years of life expectancy for the total population, 2.29 years for men and 1.62 years for women. In women this increase resulted mainly from

the reduction in mortality at the age of 60 years or over, in men this increase was mainly due to reduction in mortality at ages below 60 years. Data from INE regarding the year of 2019 reveals that the distribution of resident population according to age groups sightly varied by regions, demonstrating a quite similar distribution of Portuguese population across the country (Figure 1.4. A, left panel) (INE, 2019a).

Additionally, in 2019, the ageing ratio was 163.2 elderly per every 100 young people, increasing by 3.8 percentual points comparatively to the previous year, being particularly high in *Alentejo* and *Centro* (Figure 1.4.B, right panel). This ratio considers the number of elderly persons of an age when they are generally economically inactive (aged 65 and over) to the number of young persons (from 0 to 14 years old) (INE, 2019a).

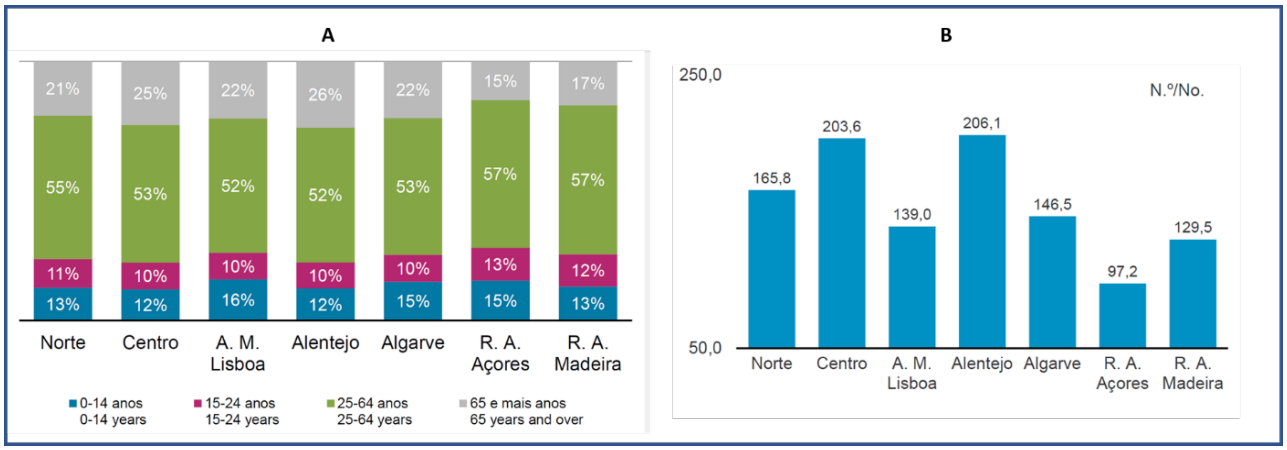


***Figure 1. 4**. **A.** Percent distribution of resident population according to age groups by region, 2019; **B.** Ageing ratio by region, 2019. Adapted from: As pessoas/ The people, 2019,* (INE, 2019a).

1.2. Changes introduced by ageing

Ageing, in most of its social representations, is often attributed to negative aspects, where the elderly person is frequently seen as a fragile, dependent, poor, childish and forgotten. These attributions are related to the fact that ageing overlap with steeper and gradual decline of many physical, psychological and neurological processes; however, this decline is not always age-related, varying from person to person (Aalami et al., 2003; Driscoll et al., 2003; Ihle-Hansen & Ihle-Hansen, 2018; Shilpa Amarya, Kalyani Singh, 2018).

1.2.1. Physiological changes

The physiological ageing process concerns the physical changes that reduce the effectiveness of the organism's functional and organic systems leading to a progressive decrease in the ability to maintain homeostatic balance (Netto MP, 2000). Through the accentuated physiological decline, the individual's functional capacity is affected, leading to a high or total degree of dependence, increasing the susceptibility to chronic diseases (Netto MP, 2000). Physiological changes include, among others, changes in nervous system (in detail in section 1.2.3.1), musculoskeletal system, respiratory system, body composition, immune system, bone structure and the cardiovascular system. The structural changes are mainly at the metabolic and cellular level while functional changes mainly concern the reduction of cells and physiological reserves (Aalami et al., 2003; Berger L, 1995). The physical inactivity associated with ageing leads to decreased muscle strength and, consequently, loss of muscle tissue. This factor can have consequences such as difficulty in motor ability, including mobility and is usually the cause of recurrent falls in older people (Bird et al., 2013; Sequeira, 2007).

1.2.2. Psychosocial changes

Social participation is an important criterion of QoL in old age and can be defined as socially oriented sharing of individual resources, being affected due to the changes in life cycle transitions (e.g., retirement, empty nest), and later due to the decline of individual capacities (physical and mental health) (Bukov et al., 2002). The individual role is largely modified, including the family, professional and occupational dimensions. The most common changes include affective and cognitive changes that, together with the consciousness of the approaching end of life and the stopping of professional activity, result in feelings of worthlessness and loneliness, as well as economic difficulties (S. Charles & Carstensen, 2010; S. T. Charles et al., 2009; Marchand, 2005). In short, the loss of the social role is one of the main losses that occur during ageing, contributing to the loss of life goals and purpose, friendship and social engagement, and leading to feelings of worthlessness and deep loneliness (S. T. Charles et al., 2009).

1.2.3. Psychological changes

According to WHO: “Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity.” (WHO, www.who.int, visited in 28/02/2021). An integral and essential component of health is mental health that is more than just the absence of mental disorders or disabilities. Mental health constitutes a state of well-being where the individual realizes his or her own abilities, being able to deal with normal difficulties of life and work productively (WHO, www.who.int, visited in 28/02/2021). Mental ageing is linked to a decrease in the perception of oneself and is not exactly related to the individual's age. Due to the changes introduced, ageing is seen as a “crisis situation” and a turning point in personal life, that due to the ineffective response of adaptation mechanisms and the appearance of health complications, result in worry and anxiety (S. T. Charles et al., 2009).

During the ageing process, the reduction of cognitive functions is considered normal, being present in more functional elderly persons. According to different studies, the effect of normal ageing on memory may result from the subtly changing environment within the brain (Cabeza & Moscovitch, 2013; Driscoll et al., 2003). However, the decrease in the cognitive function represents a strong threat to the well-being and self-esteem of the individuals. This decline is common from 50-60 years of age, with minimal expressions. It is important to refer that these types of cognitive dysfunctions are not considered a disease, but a result of normal physiological states from the ageing process. These changes include decreased conceptualization ability and attention, difficult to maintain the vocabulary and verbal reasoning, difficult to maintain the acquired knowledge, increased reaction time, slowness in the learning process, decreased short-term memory and difficulties in using stored information. Additionally, there are difficulties in solving problems, decreased creativity, rigidity of thoughts and a tendency to maintain old habits (Harada et al., 2013; Murman, 2015).

1.2.3.1. Neurological changes: the ageing brain

The ageing process involving normal brain can be characterized by a reduction in cognitive abilities, envisaging mainly three domains: executive function, processing speed, and episodic memory. It is still uncertain whether and how the cognitive decline is caused by the brain changes, however, both structural and functional changes in the central nerve

system are certainly linked to the decline. Functional changes in brain include structural changes involving the central nerve system, affecting particularly basic anatomy, physiology, synaptic plasticity and neuroplasticity (Ihle-Hansen and Ihle-Hansen, 2018).

It is assumed that normal healthy ageing is associated with numerous structural, chemical, gene expression and functional changes. However genetic and environmental factors represent, probably, a thin line distinguish normal ageing than pathology. Cognitive decline is thought to begin around the age of 50 allied to reductions in brain volume of approximately 0.5% every year, increasing in older ages (Ihle-Hansen & Ihle-Hansen, 2018).

1.3. Dementia is not part of the normal ageing

Dementia is not part of the normal ageing, contrarily it is a neurological disease characterized by an accumulation of protein waste products including amyloid protein that triggers inflammation and a loss of brain cells over several years. The signs of Alzheimer's disease (AD) and dementia differ from the typical age-related changes that occur in elderly people, some examples are presented in figure 1.5.

Degenerative dementia occurs mainly in adults aged 65 years or older, however, young-onset dementia (YOD) is defined as dementia with debut of symptoms before the age of 65 years. So, contrarily to what is commonly thought, degenerative dementia can appear at younger ages and not only in older people. In treatable dementias such as dementia due to lack of vitamins, early detection and prevention are currently the most efficient methods. In neurodegenerative dementias, for the time being incurable, there is little physiological benefit in early diagnosis, with prevention and genetic studies being the available resources in case, until a modifying treatment the course of the disease is effective. As subjective memory complaints are frequently reported by older people (Ginó et al., 2010; Jonker et al., 2000; Sataloff et al., 1994), many studies have focused on the subjective memory impairment of the elderly population. Memory changes can possibly correlate with subsequent global cerebral metabolic decline (Ercoli et al., 2006), and potentially predict the progression to objective memory impairment and dementia (Mitchell, 2008; Reid & MacLullich, 2006). Particularly, memory complaints including forgetting names of family members or friends plays an important role in the clinical setting (Pires et al., 2012).

With this in mind, there is great interest surrounding elderly people with memory or other cognitive complaints who are not demented, to better describe memory impairment and its eventual progression to effective memory problems (Blanchet S, et al., 2002). A review on Mild Cognitive Impairment (MCI) and its diagnosis settled that these patients appear to have a high probability to develop dementia, particularly, AD and the frontotemporal type, highlighting the need of studying neuroprotective compounds that, allied with early detection and treatment of elderly people with MCI might decrease or delay disease progression to dementia (Mendonça et al., 2004). Moreover, the benefit of exercise in terms of neuroplasticity and the ability of the brain to self-repair, is widely described in literature (Ihle-Hansen & Ihle-Hansen, 2018; Strollo et al., 2018; Winblad et al., 2016). It is postulated that aerobic exercise can increase synaptic strength and improve brain health due to the increase of blood flow, immune system and metabolism; also, physical exercise may also improve attention, executive function and episodic memory (Ihle-Hansen,b2018; Strollo et al. 2018; Winblad et al. 2016).

The multifactorial etiology of dementia rend uncertain the weight of its risk factors which are based on few studies. A systematic review found good support for the following risk factors for dementia development: depression, (midlife) hypertension, physical inactivity, diabetes, (midlife) obesity, hyperlipidemia, and smoking. Additionally, the coronary heart disease, renal dysfunction, diet, and cognitive activity were referred as in need of further investigations, but highly candidate risk factors for dementia (Deckers et al., 2015; Winblad et al., 2016). Moreover, genetic risk factors have been found in a small proportion of individuals with dementia that suffer from a familial form of dementia, caused by an autosomal dominant mutation (Van Der Flier & Scheltens, 2005). Despite that the largest proportion of AD cases is therefore ‘‘sporadic’’, mutations in several genes (including Aβ precursor protein, presenilin 1, and presenilin 2) account for less than 5% of all cases. As well, non-familial cases of AD seem to be, somehow, influenced by some genetic factors as well, being controlled by common DNA variants. These variants significantly increase the disease risk but are not necessary nor sufficient to cause a specific disorder. To date, only one genetic factor has been identified in AD: the apoliprotein E (APOE) gene that presents in three allelic forms (ϵ2, ϵ3, and ϵ4), of which the ϵ4 allele is a risk factor for AD, but APOE ϵ4 itself is neither necessary nor sufficient to cause AD. The presence of APOE ϵ4 is probably acting as a genetic risk modifier (i.e., interacting with vascular risk factors) (Van Der Flier & Scheltens, 2005). An interesting review included the most recent genetic risk factors included in genome-wide studies for

AD (CR1, BIN1, INPP5D, among other examples), however only the previously referred APOE reached significance for AD (Ferencz & Gerritsen, 2015). Still, CSF Aβ42, total tau (t-tau), and phosphorylated tau (p-tau) biomarkers and amyloid positron emission tomography (PET) have been widely studied (Arnerić et al., 2016; Chételat et al., 2013). In the past years, tau PET has shown promise as a fairly specific marker of tau deposits known as characteristic of AD (Morgeson et al., 2013; Ossenkoppele et al., 2016).

Signs of Alzheimer's and Dementia	Typical Age-Related Changes
Poor judgment and decision-making	Making a bad decision once in a while
Inability to manage a budget	Missing a monthly payment
Losing track of the date or the season	Forgetting which day it is and remembering it later
Difficulty having a conversation	Sometimes forgetting which word to use
Misplacing things and being unable to retrace steps to find them	Losing things from time to time

Figure 1. 5. *Difference between Alzheimer's and typical age-related changes. Adapted from: Alzheimer's Association Webpage, https://www.alz.org/alzheimers-dementia/10_signs (visited in 01/03/2021).*

1.4. "Ensure healthy lives and promote well-being for all at all ages"

The United Nations Sustainable Development Goals are 17 goals with 169 targets that all United Nations Member States have agreed to work towards achieving by the year 2030 (Figure 1.6). Among the seventeen goals, health has a central place in Goal 3 *"Ensure healthy lives and promote well-being for all at all ages"*. This aim is of major importance to all countries, from poor, rich and middle-income to promote prosperity. This aim has a strong focus on improving equity to meet the needs of all and, particularly, disadvantaged populations so that "no one is left behind". Objectively, the aim strives to reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well- being for all at all ages, by the year of 2030 (United Nations Website, https://sdgs.un.org/goals, WHO Website, https://www.who.int/health-topics/sustainable-development-goals, visited in 06/03/2021).

Efforts must be directed to the community initiatives that promote better QoL and mental health for all age individuals, while highlighting the advantages of the healthy ageing, and more than never, promote healthier lives and well-being for all, around the world.



Figure 1. 6. *The United Nations Sustainable Development 17 Goals. Adapted from: WHO Website, https://www.who.int/health-topics/sustainable-development-goals, visited in 06/03/2021).*

2. Dementia

Dementia, as discussed above, can be defined as a clinical syndrome generally characterised by a cluster of symptoms exhibited by difficulties in memory, disturbances in language and cognitive functions, changes in behaviours and impairments in activities of daily living (ADL). It includes a range of neurological disorders characterised mainly by memory loss and cognitive impairment (Bouchard, 2007; Hung et al., 2016; Winblad et al., 2016).

As population longevity increases, so does the prevalence of degenerative dementia, most with no effective treatment. The worldwide estimated number of people living with dementia in 2015 was 47.47 million, reaching 75.63 million in 2030 and 135.46 million in 2050 (Alzheimer's Disease International, 2013). Therefore, the worldwide prevalence of new dementia cases per year is 7.7 million, which means one new case in every 4.1 seconds. In Europe, this means new 2.3 million (31% of the world) cases per year, being expected to reach 14 million of persons with dementia (PwD), by 2029 (ADI, 2019; World Health Organization, 2018). Despite these alarming numbers, dementia is probably underdiagnosed, with an estimated half of primary care patients aged over 65 years not diagnosed by their primary care physicians (Qiu et al., 2009; Verbeek et al., 2012).

The conceptualization of dementia usually considers two distinct classifications: the "neurodegenerative" type ("irreversible") and non-neurodegenerative type (potentially "reversible"). However, this conceptualization is too simplified, since dementia can, and frequently do, have multiple causes which can be neurodegenerative (i.e., AD, dementia with Lewy bodies (LDB) and non-neurodegenerative (i.e., cerebrovascular disease, vitamin deficits or dementia with known ethology), that contribute together for the impairment (Schneider et al., 2007). Additionally, terms such as Mild Neurocognitive Disorder (MND) and MCI can be used to describe a disease that impairs cognition without leading to a decline in daily functioning, according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV-TR) and the most recent version (DSM-V) (American Psychiatric Association, 2000, 2013a). Regarding dementia diagnosis, the standard criteria widely used have been those of the DSM-III (American Psychiatric Association, 1987), DSM-IV (American Psychiatric Association, 1994) and more recently, DSM-IV-TR and DSM-V (American Psychiatric Association, 2000, 2013a). impairment of memory and at least one of the following domains (representing a significant decline from a previous level

of functioning that interferes with independence in everyday activities): language, praxis, gnosis, executive functioning; there is impairment of social or professional life compared to the previous level of functioning and the decline does not occur only during delirium and cannot be explained by any other medical, neurological or psychiatric condition.

No set of diagnostic criteria is perfect to describe dementia, due to all the spectrum of dementias and their differences (Bouchard, 2007). For example, neuropsychiatric symptoms, such as mood and behaviour changes or psychotic features are not included in the standard DSM criteria (M. P. Copeland et al., 2003). Additionally, the most recent DSM criteria, the fifth edition, no longer require the occurrence of memory impairment for the diagnosis of neurodegenerative dementia (American Psychiatric Association, 2013b; Calderon-Garcidueñas & Duyckaerts, 2018). This approach in DSM-5 is probably related to the absence of memory impairment in some dementia types and because, sometimes it is not an early symptom of dementia (Calderon-Garcidueñas & Duyckaerts, 2018). So, briefly, dementia diagnosis is based on a careful history with a semi-structured interview and a detailed medical and neurological examination and neuro-cognitive testing. The study of vascular comorbidities and depression, as well as, a physical examination and neuroimaging are relevant steps to increase diagnosis accuracy (de Moraes & Bertolucci, 2017). The clinical evaluation of suspected dementia including all steps in detail is presented in figure 1.7.

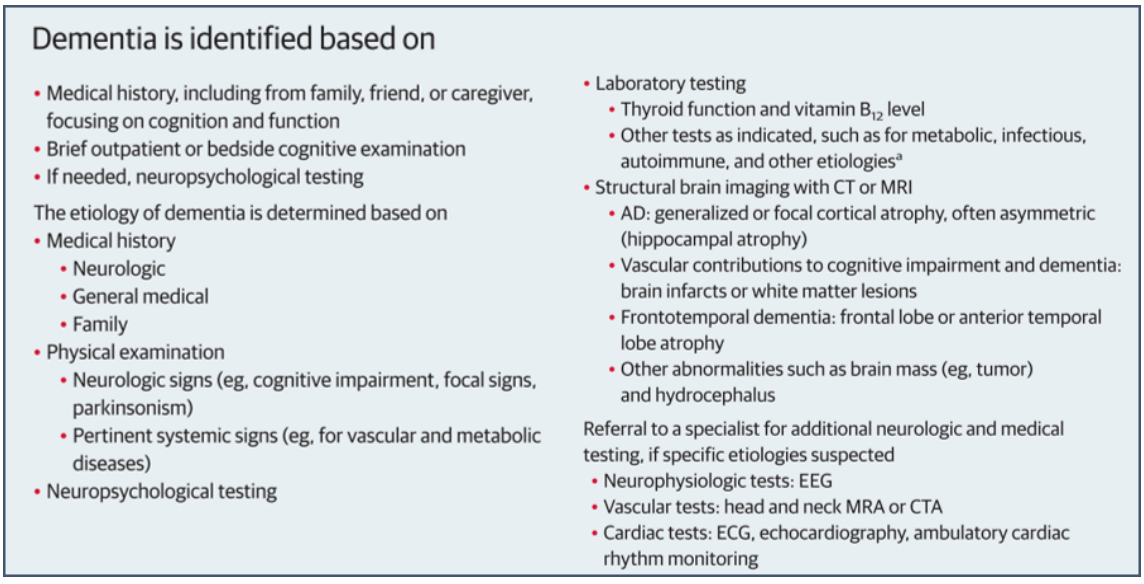


Figure 1. 7. *Clinical Evaluation of Suspected Dementia. Abbreviations: AD, Alzheimer disease; CT, computed tomography; CTA, CT angiogram; ECG, electrocardiogram; EEG, electroencephalogram; MRA, magnetic resonance angiogram; MRI, magnetic resonance imaging. Depending on the clinical presentation, consider blood tests (complete blood cell count, erythocyte sedimentation rate, glucose level, renal and liver function tests, folic acid level, and rapid plasma reagin test). Adapted from:* Arvanitakis et al., 2019.

The four most common types of dementia are AD, Vascular dementia (VaD) and Frontotemporal dementia (FTD) and LBD. Among these four types, AD is the most prevalent (34% before 65 years old, and 54% after 65 years), followed by VaD (18% before 65 years old, and 32% after 65 years) (M Prince, R Bryce, E Albanese, A Wimo, W Ribeiro, 2019; Van Der Flier & Scheltens, 2005).

A collaborative study of population-based European cohorts (Lobo et al., 2000), estimated the prevalence of dementia in the elderly (≥ 65 years) of 6.4%, being 54% for AD, and 16% for VaD (Figure 1.8.A, left panel). Additionally, dementia affected more women than men and the prevalence nearly doubled with every five years of increase in age (increase of 0.8% in the group age 65–69 years and 28.5% at age 90 years and older) (Figure 1.8.B, right panel).

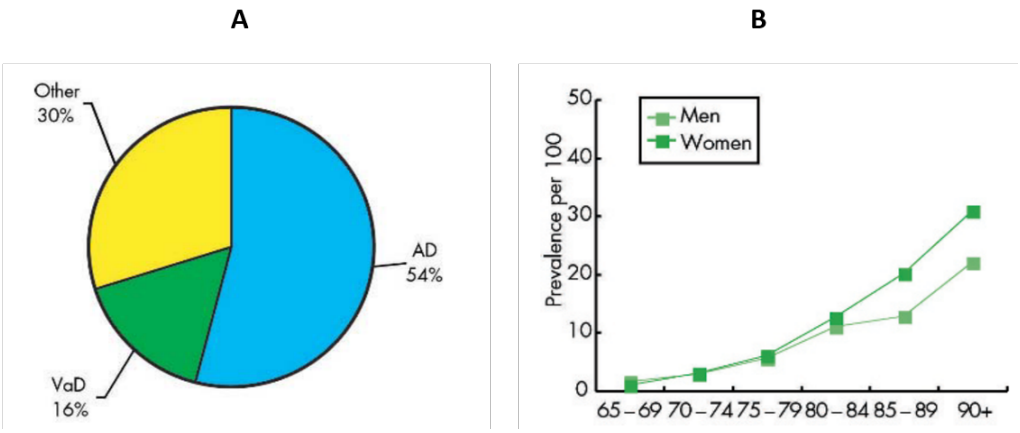


***Figure 1. 8. A**. Causes of dementia (≥65 years old). AD, Alzheimer's disease; VaD, Vascular dementia. **B**. Pooled prevalence of dementia by sex. Adapted from: Van Der Flier & Scheltens, 2005.*

The development of dementia symptoms before the age of 65 years, defined as YOD, and its impact in the persons who develop YOD and their families is still relatively unknown (Hvidsten, 2019). A study of Arai et al. did not find any significant differences between caregivers of persons with YOD or late onset dementia, but their findings did suggest that YOD caregivers experience greater difficulties in dealing with behavioral problems, demonstrating a need to raise awareness about the YOD as a public-health concern and to identify the unmet needs of these persons and their family caregivers (Arai et al., 2007).

In Portugal, epidemiological studies indicated that the prevalence of dementia varied from 2.4% to 9.23% depending on the methods and criteria applied (C. Garcia et al., 1994;

Manuel Gonçalves-Pereira et al., 2017; Gonçalves-Pereira et al., 2016; Hofman et al., 1991; Nunes et al., 2010; I. Santana et al., 2015). However, due to its publication date, the majority of these studies are probably outdated. A study of 2018 based in a population-based cohort from northern Portugal, assessed the prevalence for MCI (4.1%) and for dementia (1.3%), with VaD being the most prevalent type of dementia (52.8%), followed by AD (36.1%) (Ruano et al., 2019). Recently, in the Dementia in Europe Yearbook, the overall population data of Portugal is described as having a relevant decrease until 2050, however, the overall numbers of people with dementia will more than double reaching 346,905 (3.82%) by 2050 (Alzheimer Europe, 2019). Still, the estimate of dementia prevalence in Portugal exceed the broader European trend, probably due to the numbers of Portuguese people aged over 70 and over 85 that doubles until 2050 (Alzheimer Europe, 2019).

2.1. Alzheimer's Disease

The most common form of dementia, AD, account for 50%–70% of dementia cases, being a neurodegenerative disorder associated to progressive cognitive and functional impairment, due to accumulation of amyloid and tau protein depositions in the brain. Being the most common dementia, its prevalence has undergone a huge increase in recent years, becoming one of the greatest healthcare challenges of the 21st century due to the high demand for medical, social and institutional care (Brodaty & Green, 2002; Calderon-Garcidueñas & Duyckaerts, 2018; Ibarria et al., 2016).

The diagnosis of AD is based on clinical criteria, being classified as possible, probable, or definite (Van Der Flier & Scheltens, 2005). The Alzheimer's Association (Alzheimer's Association Webpage, https://www.alz.org/alzheimers-dementia/10_signs (visited in 01/03/2021)), distinguishes between age-related memory changes and those that warrant medical evaluation in a section named: "*10 Early Signs and Symptoms of Alzheimer's"*: 1) memory loss that disrupts daily life; 2) compromised planning and problem-solving; 3) difficulty with familiar tasks at home, work or leisure; 4) confusion with time or place; 5) trouble understanding visual images and spatial relationships; 6) new problems finding words in speaking or writing; 7) misplacing things and losing the ability to retrace steps; 8) decreased or poor judgment; 9) withdrawal from work or social activities and 10) changes in mood and personality.

Several sets of criteria are available for AD diagnosis, of which the criteria for probable AD of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA), dating from 1984, are the most generally used (Bouchard, 2007; McKhann G et al., 1984). Also, the standard criteria of the DSM-IV (now the DSM-V) for AD have been used for research and in clinical trials and are still recommended, as well (the same as the standard criteria for dementia together with the notion of insidious onset and progressive decline), since memory is a predominant symptom in AD (American Psychiatric Association, 1994, 2000; Bouchard, 2007). Additionally, the evaluation of mood, behavior disturbances and psychotic symptoms are recommended to increase the diagnosis accuracy, but not included in these criteria. Nevertheless, these criteria are mainly targeted to the pure AD patients, even if many of those AD patients have mixed pathologies and do not account to the very early stages of AD. The application of the DSM-IV-TR and DSM-V appears to be simpler for the clinician, but the NINCDS-ADRDA criteria are more suitable for research proposes and clinical trials (Alberdi et al., 2016; Arvanitakis et al., 2019; Bouchard, 2007; Emre, 2009; Van Der Flier & Scheltens, 2005).

In summary, AD diagnosis include dementia based on clinical examination and neuropsychological tests, deficits in two or more areas of cognition, progressive worsening of memory and other cognitive functions, with normal consciousness. Other features can include progressive deterioration of language, praxis and gnosis, impaired ADL and behavior, positive family history, normal cerebrospinal fluid (CSF), non-specific electroencephalography (EEG), and progressive cerebral atrophy with time on neuroimaging. Also, neuropsychiatric and extrapyramidal symptoms can appear. The computed tomography (CT) or (magnetic resonance imaging) MRI for age is usually normal. In the early stages of the disease, the volumetric measurement of the hippocampal region with MRI may show some atrophy. Some of these features are not part of the basic investigation for the diagnosis of dementia (e.g., CSF study, EEG recording) but are appropriate in the context of specific research studies and the development of future therapies. The high degree of accuracy of approximately 90% of the classic criteria widely contribute to their preferable application, being better than any clinical biomarker available at this date (Alberdi et al., 2016; Arvanitakis et al., 2019; Bouchard, 2007; Emre, 2009; Van Der Flier & Scheltens, 2005). The AD treatment should begin as early as possible to optimize therapeutic efficacy, which increased the interest in identifying useful biomarkers for initiating and evaluating treatment (Kusne et al., 2017). So, the investigation on

biomarkers such as CSF amyloid-β [Aβ]/tau, amyloid PET and hippocampal atrophy on MRI, is also recommended in certain cases, increasing the diagnostic certainty, probably earlier than other techniques (Bouchard, 2007).

The prevention and risk factors of AD is the same as dementia and the pharmacologic management approved by the United States Food and Drug Administration and EU include four agents: Acetylcholinesterase Inhibitors (Donepezil, Rivastigmine and Galantamine) and Memantine, an antagonist of receptor N-methyl-D-aspartic acid (NMDA). In some EU countries a fixed combination drug of Memantine and Donepezil is also available (Arvanitakis et al., 2019). Indeed, the majority of AD therapeutics in development focuses on either limiting the production of Aβ or accelerating its removal from the brain with modest symptomatic benefit for the cognitive symptoms (Arvanitakis et al., 2019; Mangialasche et al., 2010).

2.2. Other dementias

Many people worldwide is diagnosed with dementia, but dementia appears in many forms, but the AD is still the most common form (50-70%). Other dementias such as VaD, are known has an unpredictable progression pattern and usually appears abruptly. The LBD shares features of both AD and Parkinson's disease (PD) including fluctuating cognitive performance and visual hallucinations while the FTD is associated less with memory disorders and more with behavioral and language abnormalities. Of note, there are also the mixed dementia that covers those patients who do not have an apparent singular cause of dementia. Finally, pseudodementia is a dementia resulting from underlying causes and is reversible, unlike the previous mentioned dementias (Zanni & Wick, 2007). The examination of the course and clinical features of a patient's cognitive impairment can help differentiate between the various common subtypes (Table 1.1).

It is important to refer the MCI syndrome that describes cognitive decline that significantly exceeds age-related norms, allowing overall functioning and ADLs, and many researches consider MCI has prodromal for dementia (Zanni & Wick, 2007). The MCI prevalence is estimated at 3% to 19% for adults older than 65 years old. MCI's pathophysiology includes cholinergic dysfunction, white-matter lesions, cerebral infarctions, amyloid deposits, and neurofibrillary complications (Petersen, 2006).

Table 1. 1. Differentiating between common forms of dementia

	AD	VaD	DLB	PaD	FTD
Course	• Insidious onset and gradual progression[1]	• Presentation based on extent and location of cerebrovascular event (CVE)[1] • Often stepwise decline[2]	• Insidious onset and gradual progression[1]	• Insidious onset and gradual progression[1]	• Insidious onset and gradual progression[1]
Presentation	• Memory loss and impaired learning early in the disease[1] • Visuospatial and language deficits present in moderate to severe stage[1]	• Temporal relationship between CVE and onset of cognitive impairment[1] • Memory loss usually secondary to impairment in frontal/executive function[2]	• Fluctuating cognition with early changes in attention and executive function[1] • Detailed, recurrent visual hallucinations present early in the disease[1] • Cognitive symptoms start shortly before or concurrently with motor symptoms[1]	• Established Parkinson's disease of at least a year duration before onset of cognitive decline[1,2]	• Behavioral variant: Impaired social cognition and/or executive abilities with behavioral symptoms such as disinhibition, apathy, lack of empathy, compulsive behavior and hyperorality[1] • Language variant: Loss of word memory, including speech production, word finding and comprehension, and grammar[1] • Many present with both types[1]
Associated features	• Behavioral and psychological symptoms are common – Early: Depression, apathy[1] – Moderate to severe: psychotic features, agitation, wandering[1] – Late: Gait disturbance, dysphagia, incontinence, myoclonus, seizures[1]	• History of stroke and/or transient ischemic attacks[1] • Personality and mood changes[1] • May exhibit parkinsonian features such as psychomotor slowing, but not sufficient for Parkinson's diagnosis[1] • Slow, gradual progression often due to small vessel disease[1]	• Rapid eye movement sleep behavior disorder may be early sign[1] • Nearly 50% have severe neuroleptic sensitivity[1] • Falls, syncope and transient loss of consciousness are common1 • Autonomic dysfunction[1] • Often a history of delirium during illness or surgery[1]	• Apathy, anxious or depressed mood, hallucinations, delusions, personality changes, rapid eye movement sleep disorder and excessive daytime sleepiness[1]	• Extrapyramidal symptoms may be present[1] • Overlaps with other neurological conditions such as progressive supranuclear palsy, corticobasal degeneration and motor neuron disease[1] • Visual hallucinations may be present1 • Majority (3/4) present between the ages of 56 to 65[2]
Risk factors	• Age, genes, Down's, traumatic brain injury[1] • Family history of Alzheimer's disease in a first-degree relative doubles the risk[2]	• Hypertension, diabetes, smoking obesity, hypercholesterolemia, high homocysteine levels and other risk factors for atrial fibrillation and athero- and arteriosclerosis[1]	• Genetic risk identified but no family history in most cases[1,2]	• Exposure to herb- and pesticides, duration of disease[1]	• Up to 40% are familial[2] • Present in up to 10% of patients with motor neuron disease[2] • Brief cognitive assessments often normal[2]
Imaging	• Hippocampal and temporoparietal cortical atrophy[1]	• Infarcts and white hyperintensities[1]	• Lewy bodies found primarily in the cortex[1] • Medial temporal structures preserved[1]	• Lewy bodies found primarily in the basal ganglia[1] • Medial temporal structures preserved[3]	• Pattern of brain atrophy dependent on subtype[1]
Other	• Often occurs with VaD[1]	• Only 5-10% have pure VaD[2] • Often occurs with AD and/or DLB[1,2] • Depression is often present[2]	• Frequently coexists with AD and/or VaD[1]	• Distinguish from neuroleptic-induced parkinsonism, which may occur when dopamine-blocking drugs are prescribed for behavioral symptoms[1] • Often coexists with AD and VaD[1]	• May be mistaken for depression, bipolar disorder or schizophrenia[1]

1. American Psychiatric Association, American Psychiatric Association. Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed. Washington, D.C: American Psychiatric Association; 2013, (American Psychiatric Association, 2013a). *2. Budson AE, Solomon PR. Memory Loss: A Practical Guide for Clinicians. [Philadelphia]: Elsevier Saunders; 2011,* (Budson & Solomon, 2011). *This table can help inform a full dementia evaluation, but it is not a diagnostic tool. Primary care practitioners should consider seeking the opinion of a dementia expert in cases in which it is warranted. For more information on these and other types of dementia, visit alz.org/hcps. Adapted from: Alzheimers Association, 2013.*

2.3. Disease progression and health-related quality of life

The course of dementia can be very different in each case, being dependent on the type, general condition and comorbidities of those affected, with average survival time from initial diagnosis to death of approximately eight years. (Weichbold, 2015). Dementia

affects not only the individuals with the condition, who gradually lose their abilities, as well as their relatives, that care for them as their dependency and severity increases (Banerjee, 2013; Livingston et al., 2017; World Health Organization, 2012). Sperling et al., created a hypothetical model of the clinical trajectory of AD (figure 1.9). However, not all individuals with biomarker evidence of AD process will certainly progress to all the clinical phases of the illness. The stage of preclinical AD is preceded by MCI (once again demonstrating the crescent interest in MCI), with higher cognitive function impairment than the expected for age, eventually resulting in dementia (Sperling et al., 2011).

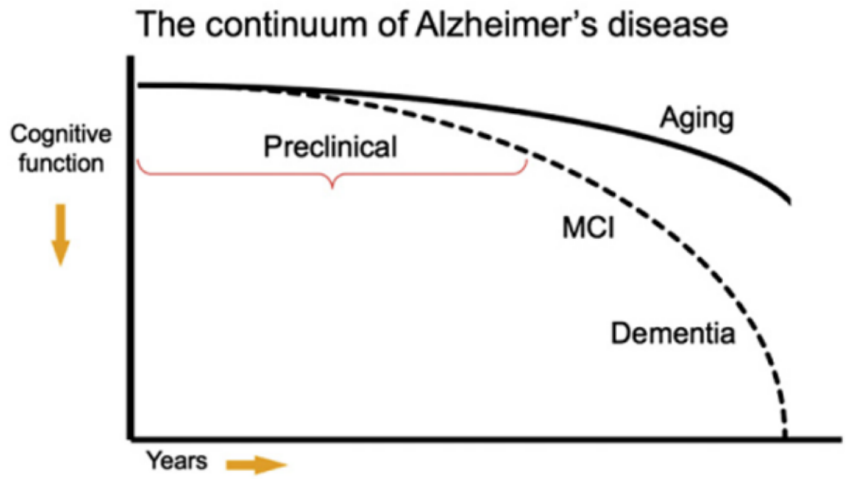


Figure 1. 9. Model of the clinical trajectory of Alzheimer's disease (AD). Adapted from Sperling et al., 2011.

Dementia manifestations differ from earlier than later-stages (Figure 1.10), with increasing impact in patient's daily life. These manifestations include cognitive, psychological, physical and behaviour changes that worsen with disease progression (Arvanitakis et al., 2019). With respect to the ability of coping with everyday life challenges there have been fixed three stages of disease: mild, moderate and severe dementia.

	Earlier-Stage Manifestations		Later-Stage Manifestations	
	Category	Examples	Category	Examples
Cognitive	Short-term memory loss (episodic memory impairment)	Forgetting appointments, to pay bills, recent events (such as family outing in last few weeks)	Memory loss in working memory (the ability to immediately process and store information)	Forgetting how to use household technology (eg, how to use the microwave, dial telephone numbers)
	Word-finding difficulties (anomia) or loss of word meaning (semantic deficits)	Frequent trouble finding exact words to express oneself, word substitutions, imprecise language ("what you eat with" for "fork")	More marked expressive difficulties and eventual loss of language (eg, global aphasia)	Paraphrasic errors while speaking, paucity of words in sentence, lack of initiation of conversations, muteness
Psychological	Apathy	Lack of initiation of thought or actions (eg, not preparing meals)	Delusions	False belief system such as a deceased relative is still alive, caregiver is stealing money
	Depressive symptoms	Hopelessness and loss of purpose in life	Anosognosia	Lack of insight into cognitive problems with attempts to continue to drive or manage money
Behavioral	Withdrawal from social engagement	Inability to participate meaningfully in casual conversations	Aggression	Verbal aggression such as screaming, physical aggression such as throwing things
	Disinhibition	Excesses in speech (eg, echolalia, palilalia) and actions (eg, hyperorality such as eating from others' plate)	Hallucinations	Visual hallucinations such as seeing small people on table; auditory hallucinations such as hearing singing
			Wandering	Walking out of home in middle of night and getting lost
Sleep	Rapid eye movement behavior disorder	Acting out dreams such as running while dreaming one is being chased	Altered sleep-wake cycle	Frequent awakening at night and getting out of bed, sleeping in late in the morning and repeated daytime napping
Physical	Gait impairment	Falls	Repetitive purposeless movements	Fidgeting with buttons on shirt for hours at a time
			Parkinsonism	Stooped posture, short stride, unsteady gait, rigidity
			Seizures	Involuntary repetitive limb jerking while unconscious

Figure 1. 10. *Manifestations of Dementia in Earlier and Later-Stages. Adapted from Arvanitakis et al., 2019*

Over time, dementia causes disability and dependency, often associated with stigmatization, hurdles to accurate diagnosis and access to formal care services. The difficulties in formal follow-up of dementia patients create high physical, psychological and economic impact on family caregivers and societies worldwide (World Health Organization, 2012). Several European studies describe the impact of dementia progression, reporting low QoL in dementia patients and caregiver's psychological and financial burden (Argimon et al., 2005; Beerens et al., 2014; Bruvik et al., 2012; E. P. C. J. Janssen et al., 2017; R. W. Jones et al., 2015; Lethin et al., 2020; Lillo-Crespo et al., 2018; Schiffczyk et al., 2010; Selwood et al., 2005; Serrano-Aguilar et al., 2006).

Additionally, AD progression is associated with increased resource utilization and costs of care that are higher in moderate/severe dementia (Jönsson & Wimo, 2009). In a special topic section on health economics and public policy of Alzheimer's & Dementia Journal, Jönsson and colleagues presented an impact-cost matrix for dementia as it progresses from preclinical to severe states. As presented in Figure 1.11, moderate and severe dementia states are related to high economic burden. Typically, the late-stage

consequences of dementia are well understood, but the impact on function and well-being in the earliest stages of the disease needs further investigation (Jönsson et al., 2017).

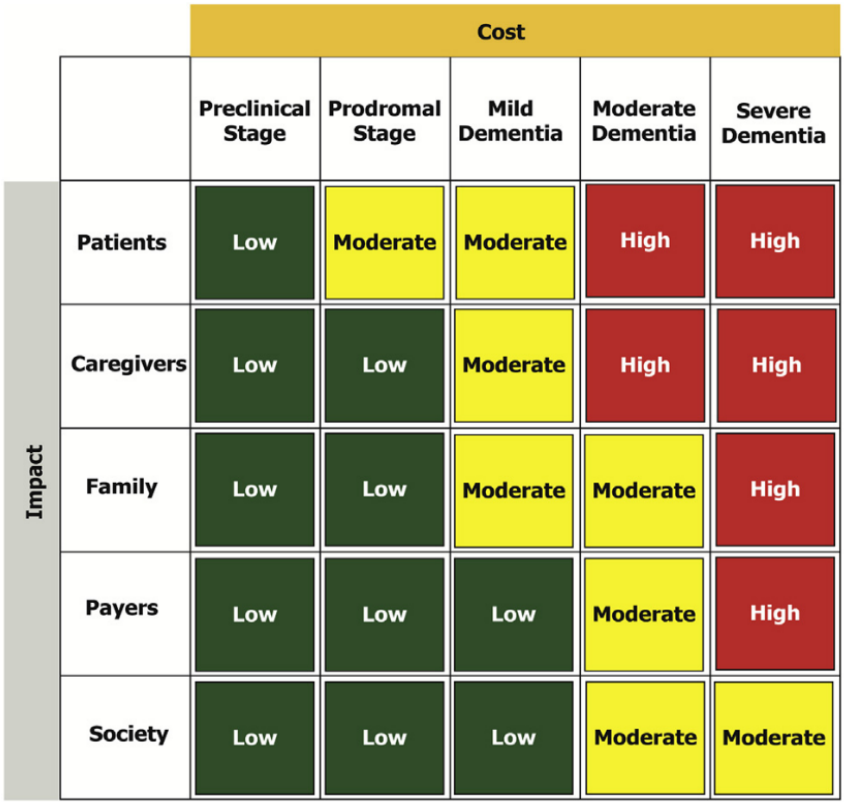


Figure 1. 11. *Impact-cost matrix along dementia progression. Adapted from Jönsson et al., 2017*

3. Caring for a person with dementia

Since dementia manifestations have great impact in patient's daily life, these patients usually need supervision and help to perform daily tasks. The provision of care for these patients can be given by the following types of caregivers: primary or secondary (through the degree of involvement in the care provided) and formal or informal (through the professional and remunerative nature of the provision of care).

A considerable proportion of dementia care is supported by informal caregivers and happens outside of formal care environments (World Health Organization, 2012). For a long time, different studies tried to find the interaction between formal and informal support, identifying roles of substitution of care (Greene, 1983) and supplementation of care (Edelman & Hughes, 1990). So, in earlier states most of caregivers would choose for formal services and in latter states, formal services were complementary to the informal care provided. Also, specialization could be a third explanation of the relationship between formal and informal care, because the provision of different types of care by formal and informal caregivers has specific domains of responsibility (Lyons & Zarit, 1999).

Studies such as EUROFAMCARE (Eurofamcare, 2006; Mestheneos & Triantafillou, 2002), offered a variety of definitions for informal and formal care that are combined in Figure 1.12 (Adapted from an European overview paper (Triantafillou. et al., 2010)).

Informal care	Formal care
• Care mainly provided by family, close relatives, friends or neighbours	• Services provided by trained, licensed and qualified professionals
• Caregivers are non-professionals and not trained to provide care; in some cases, they may benefit from special training	• Services are controlled by the state or other types of organization
• Caregivers have no contracts regarding care responsibilities	• Caregivers have contracts specifying care responsibilities
• Caregivers are not paid although they more and more commonly obtain financial contributions	• Caregivers are paid and entitled to social rights and working regulations.
• Caregivers perform a wide range of tasks (also performed by formal caregivers) including emotional support and assistance	• Care tasks are specified according to professional qualification
• No limits to time spent on care – never/rarely officially 'off duty'	• Care workers have a time schedule and go 'off duty'
• No general entitlement to social rights	

Figure 1. 12. *Informal and formal care definitions. Adapted from EUROFAMCARE studies* (Triantafillou. et al., 2010).

3.1. Informal care

Informal care refers to unpaid care provided by family, close relatives, friends, and neighbors, that must receive enough training for the tasks related to care (World Health Organization, 2012).

Older people prefer living at home in a familiar environment and older persons with dementia maintain their social network better and achieve a better QoL if they remain at home (Nikmat et al., 2011; Tucker et al., 2008). Living in their own home in a familiar environment surrounded by known objects, and maintaining their habits had proof to increase the sense of identity and integrity of persons with dementia (Moïse, P., 2004). Furthermore, the progression of disease is determinant for the resort to formal care, since in the early stages the PwD can handle daily tasks with little support provided by informal caregivers. However, severe symptoms require daily assistance and specific care, often from both informal and formal caregivers combined (Bökberg et al., 2018). So, before institutional care, family caregivers play an important role for people with dementia, helping them in their daily activities (Brodaty & Green, 2002; Dening et al., 2012; Prince et al., 2004). Taking care of a person with dementia requires several logistic tasks, including personal care, housekeeping, administration of medication, processing financial transactions and other activities (Winblad et al., 2016). The task of caregiving is complex leading to physical, mental and financial stress for caregivers (Connell et al., 2001; Gilliam & Steffen, 2006; Livingston et al., 1996). A study including 669 diary records over an 8-week period, describing daily event and experiences of primary caregivers included as positive gains the insights about dementia and acceptance of the condition; the sense of purpose and commitment to the caregiving role; feelings of gratification; mastering skills ; increased patience and tolerance; cultivating positive meanings and humor; letting go of things; developing a closer relationship; finding support, and feeling useful helping other caregivers (Cheng et al., 2016). Additionally, a sense of personal accomplishment and gratification, feelings of mutuality in a dyadic relationship, an increase of family cohesion and functionality, and a sense of personal growth and purpose in life were also identified as positive aspects of caregiving in dementia in a relevant systematic review (D. Yu et al., 2018).

An European publication (Triantafillou. et al., 2010), including national reports and European data described informal care and its caregivers showing that a high proportion (70%) of home care is provided by family caregivers and 80.9% of the informal caregivers

who also receive formal help consider it to be insufficient; and even in the most difficult conditions of dependency, only 3% of older people were in residential care, 4.9% receive integrated care at home and only 9.5% receive a dependency allowance. Additionally, the caregivers were mainly women (76%), the mean age 55 years with a distribution of 15-96 years; 22% were spouses, and 60% were children/children–in-law; 41% were employed and 56% live in same house-hold (or same building) as their relative (Triantafillou. et al., 2010).

Informal care is a substantial element of dementia related costs. According to World Alzheimer Report (2015), the global costs involving dementia were estimated to be US$ 818 billion: 40% of the costs were related to informal care, 40% to the social care sector and 20% to the medical sector. Moreover, there is a quite different scenario regarding the use of formal and informal care between countries, with informal care costs being 69% in low-income countries, comparatively to 38% in high income countries. This might be related to the fact that 60% of people with dementia live in lower and middle income countries and almost all (96%) live at home, resulting in caregiver overload (Alzheimer's Disease International, 2018). These differences demonstrate that towards the growing numbers of dependent older persons, mainly with dementia, the health and social care systems will require reformulation to better meet these population needs, being a great concern for policy-makers in all countries, but mostly in middle and low income regions (Alzheimer's Disease International, 2018).

Dementia has an immense impact on the lives of the family, and particularly women caregivers. In the 2015 World Alzheimer Report, the continued impact of dementia on women is highlighted, since they contribute to 71% of the global hours of informal care, mainly in low income countries (Alzheimer's Disease International, 2018). However, the changing population demographics and societal development (shifting family structures, generational split, migration and the increasing participation of women in the workforce) may reduce the availability of informal caregivers in the future (Alzheimer's Disease International, 2018; World Health Organization, 2012). So, shortly, dementia care will face a shift from informal care to a greater need for different kinds of formal care services (home support, day care, long term care). This scenario represents a great challenge for society that, with the growing demand for formal care support, need to reevaluate financing, staff recruitment, training and availability of this type of care (Alzheimer's Disease International, 2018). Meanwhile, support is needed to enable informal caregivers to continue to do their role for as long as possible. Supporting informal care might include

directed information to better understand dementia patients specific needs and care, training programs to assist in caring tasks, promote caregivers respite and enable their engagement in other activities besides caring and financial support (Alzheimer's Disease International, 2018; World Health Organization, 2012).

A Portuguese study founded that a large proportion of caregivers albeit informed about dementia were at risk of high burden and distress demonstrating that knowledge about dementia may not be protective of burden *per se*. Also, in comparison of primary and secondary caregivers of persons with dementia the psychological distress was high at clinically relevant levels in both caregivers, without statistically significant differences between groups, however the caregiver needs for assistance and support were identified as needing to be addressed more systematically with interventions that address the support each person provides or might provide care (Manuel Gonçalves-Pereira et al., 2010, 2020).

3.2. Formal care

Formal care for older people usually refers to paid care services provided by a healthcare institution or individual for a person in need (World Health Organization, 2012). As dementia progresses, informal care might be not enough and the caregiver might resort to formal care (such as home nursing care, day care or home support care) to ensure that the care needs of their relative are met (Bökberg et al., 2018). The resort to formal community care services can spread the caregiving overload, facilitate access to peer support and even delay institutionalization (Gaugler et al., 2003, 2005; Schulz & Martire, 2004).

However, despite the availability of formal care services, there are hurdles involving the access to this type of care including: lack of availability awareness of services, lack of understanding or stigma, previous poor experience with services, and cultural, language and financial barriers creates obstacles to service utilization (Alzheimer's Disease International, 2018). Additionally, it is widely known from the literature that primary care physicians often lack knowledge about dementia, lack confidence in recognizing and managing the symptoms (specially behavioural or psychological symptoms), are unsure on how or if to conduct cognitive screening, face constraints in providing the right support required for patients and caregivers (D. P. Harris et al., 2009; Hinton et al., 2007; Koch &

Iliffe, 2010). In a study involving people with YOD and their informal caregivers, 96.5% of the participants had high knowledge of the formal services available, however, 66.3% do not resort to any formal service since they do not meet their personal and psychological needs (Cations et al., 2017). In Portugal, a study identified relevant constraints regarding formal care utilization by patients with early to middle-stage dementia and family/caregivers. The unmet needs included psychological distress and difficulties/lack of support in ADL with significant family burden associated (Manuel Gonçalves-Pereira et al., 2019).

Altogether, there are too many factors involving formal care access and poor adaptations to dementia patient's needs, contributing to a less utilization of these services than it would be expected. With so many obstacles regarding formal care access/utilization, there is a need of implementation of specific best-practice strategies that could respond to the particular needs of this population (Manuel Gonçalves-Pereira et al., 2019). Also, there is a need on more information and education campaigns for the public, including ones directed to people with dementia and their caregivers, to improve formal care services utilization by increasing awareness, improving understanding and decreasing stigmatizing attitudes (Alzheimer's Disease International, 2018).

4. Quality of life and functional/cognitive ability assessment in dementia research

The application of questionnaires and measurement methods in dementia faces important challenges due to the cognitive impairment present in the PwD. Despite the preferable self-report methods, research including dementia patients commonly resort to proxy-report and proxy-rating methods, where the caregiver is the respondent for their relative (Beerens et al., 2014; Bruvik et al., 2012; Jönsson et al., 2006; Schiffczyk et al., 2010; Sheehan et al., 2012). Caregivers can preciously describe the behaviour and functional capacity of the care recipient, through their direct daily observation and care performance, that is related to care recipients QoL and dependency level.

To study dementia patients' health related QoL (HRQoL) there are several instruments available, with Quality of Life in Alzheimer's Disease (QoL-AD) and the EQ-5D three level (EQ-5D-3L) being typically used. To study the functional and cognitive ability, the

Blessed Dementia Rating Scale (BDRS) and the Standardized Mini-Mental State Examination (MMSE) are well known instruments widely used in research studies.

4.1. QoL-AD

The QoL-AD is a dementia-specific HRQoL instrument used in people diagnosed with dementia/AD (Logsdon et al., 1999). Consists of 13 items covering the items of physical health, energy, mood, living situation, memory, family, marriage, friends, self, ability to perform tasks at home, ability to do things for fun, money and life as a whole. It takes 10–15 minutes to administer. The complete questionnaire was validated for the Portuguese population in 2012 (H, Bárrios, 2012).

4.2. EQ-5D-3L

The EQ-5D-3L is a generic HRQoL instrument widely used, in which respondents evaluate their (or proxy) health state "at the moment" and increasingly used in patient with neurological disorders (Jönsson et al., 2006; Naglie et al., 2006). The short descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, with three levels of severity per dimension: "no problems", "some problems" or "extreme problems" (EuroQol Research Foundation, 2018). The second part of the EQ-5D consists of a visual analog scale (VAS), the EQ-5D-VAS, that records the rated health on a vertical VAS with a range of 0 (worst imaginable health state) to 100 (best imaginable health state). The EQ-5D has been developed to describe and value health in different diseases (EuroQol Research Foundation, 2018). The Portuguese version of the EQ-5D-3L was validated for the Portuguese population in 2013 (P. L. Ferreira et al., 2013). The EQ-5D-3L index is calculated using the Portuguese tariffs (L. Ferreira et al., 2014).

4.3. Blessed Dementia Rating Scale

The BDRS is a three-part scale, originally called the "Dementia Scale" (Eastwood et al., 1983; Peña-Casanova et al., 2005). It registers the patient functional behaviour change reported by informants, and the global score is the result of the sum of the three sections, A (changes in everyday activities), B (changes in daily habits) and C (changes in

personality), with a total of 22 items. It takes 15-20 minutes to complete and was translated and validated to Portuguese in 1984 (Garcia, 1984).

4.4. Mini-Mental State Examination

The MMSE is one of the most widely used measure of cognition in clinical practice worldwide (Folstein et al., 1975). This scale can be easily administered by clinicians or researchers with minimal training, takes around 10 min and assesses six cognitive domains in the areas of orientation, memory, attention and calculation, language and visual construction. Patients score between 0 and 30 points: scored 0 - when the individual does not respond or gives an incorrect answer or 1 - when the examinee provides a correct answer, so higher scores indicate better performances. Scores are usually used to classify dementia severity in stages: higher to 21 (mild), from 11 to 20 (moderate) or lower than 11 (severe) (Folstein et al., 1975).. A standardized version (Molloy et al., 1991) improved its reliability, and is probably most important for research settings. It was validated to the Portuguese population in 1994 (Guerreiro et al., 1994).

5. Physical, emotional and social burden assessment in dementia research

To study the QoL and the physical, emotional and social burden of the informal caregivers, there are some instruments available with the EQ-5D three level (EQ-5D-3L) and the Informal Caregiver Burden Assessment Questionnaire (QASCI) being typically used.

5.1. QASCI

The QASCI is an instrument built to assess the physical, emotional and social burden of the informal caregiver which consists of 32 items comprising seven dimensions: Emotional burden, implications for personal life; financial burden; reactions to demands; perception of efficacy and control mechanisms; family support; satisfaction with the role and the family member. Each item is assessed by an ordinal frequency scale ranging from one to five answer categories: “No/Never”, “Rarely”, “Sometimes”, “Almost always”,

"Always". Higher values correspond to situations with higher relevance or higher burden. This instrument is validated to the Portuguese population (Martins et al., 2003, 2004) and has already been applied to informal caregivers of older persons with dementia (Pereira, 2007).

6. Aims

6.1. General aim

This PhD thesis aims to characterize the daily impact of dementia in a Portuguese sample of persons with dementia and their informal caregivers at the individual, familiar and social level, focusing on quality of life (of the persons with dementia and their informal caregivers), dependency level of the persons with dementia, and physical, emotional, and social burden of informal caregivers, while describing their living context and the involved factors affecting the dyads quality of life.

6.2. Specific aims

The following questions were answered in the work plan:

a) What is the available knowledge on "how it is like to care day after day for a person with dementia as disease progresses", in a familiar context?
b) How are caregivers leading with their role? Which are the implications and the costs (at individual, familiar and social level) involving dementia?
c) What is the impact of dementia for the patients, in terms of quality of life and functional/cognitive ability in different living contexts?
d) Which are the factors influencing the impact on persons with dementia quality of life?
e) What is the impact of dementia for the informal caregivers, in terms of quality of life and physical, emotional, and social burden?
f) Which are the factors influencing the impact on dementia informal caregivers' quality of life and physical, emotional, and social burden?

7. Projects developed

To accomplish these objectives this project was composed by four (4) studies:

Study 1. (Chapter 2) Impact of dementia on informal care: a systematic review of family caregivers perceptions;

Study 2. (Chapter 3) Facing costs with dementia: daily life perspectives from informal caregivers;

Study 3. (Chapter 4) Quality of life and functional ability of people living with dementia: outcomes of a Portuguese sample;

Study 4. (Chapter 5) Determinants of burden and quality of life among informal caregivers of individuals with dementia.

CHAPTER 2

IMPACT OF DEMENTIA ON INFORMAL CARE: A SYSTEMATIC REVIEW OF FAMILY CAREGIVER'S PERCEPTIONS

STUDY FRAMEWORK

Considering the complexity of the task of caregiving and the fact that it can lead to physical, mental, and financial stress for caregivers, it was important to have an overview regarding the impact of dementia thought caregiver's perceptions. With the growth in ageing populations, the number of persons with dementia is increasing, with no sign of a cure for the disease (Qiu et al., 2009; Verbeek et al., 2012). Before institutional care, family caregivers play an important role for people with dementia, helping them in their daily activities, whose dependence increases with severity of the disease (Brodaty & Green, 2002; Dening et al., 2012; Prince et al., 2004). To describe the task of caregiving, it is important to approach this as a global phenomenon, understanding the caregiver's needs and perceptions that positively or negatively contribute to their quality of life and their provision of daily support as caregivers. We conclude that the holistic experience of caring for a person with dementia included positive and negative aspects and the "focus on positive aspects" is a widely known strategy of informal caregivers to overcome the overload and negative impact of caregiving tasks.

The following study was performed by **Patrícia Lindeza (PL)**, Mário Rodrigues (MR), João Costa (JC), Manuela Guerreiro (MG), Mário Miguel Rosa (MMR).

PL and MR were responsible for study conception, design and drafting of the manuscript. JC created and tested the research strategy. MG and MMR reviewed and made critical revisions to the paper. MMR supervised the study.

Lindeza P, Rodrigues M, Costa J, Guerreiro M, Rosa MM. Impact of dementia on informal care: a systematic review of family caregivers perceptions. BMJ Supportive & Palliative Care, 2020; 0:1-12. doi:10.1136/bmjspcare-2020-002242.

IMPACT OF DEMENTIA ON INFORMAL CARE: A SYSTEMATIC REVIEW OF FAMILY CAREGIVER'S PERCEPTIONS

ABSTRACT

Introduction: Caregivers play a major role in providing all the support and care in daily activities for their relatives with dementia. To fully describe the influence of dementia caregiving on family caregivers' life, we conducted a systematic review including caregivers' perceptions about the positive and negative aspects of caring and the expressed factors.

Materials and methods: We conducted a systematic review including articles from January 1998 to July 2020. Qualitative studies reporting family caregivers' perceptions about their experiences and the effects/impact of dementia caregiving were eligible. Two authors extracted the data independently, and the analysis focused on the positive and negative aspects of dementia caregiving in caregivers' life.

Results: Eighty-one studies with 3347 participants were included in this review. The positive aspects of caregiving in caregivers' life encompass personal accomplishment and strengthening relationships, which were enhanced by good medical counselling/formal care support and family/friend's support. The negative aspects included emotional and social aspects experienced by caregivers. Other factors such as inappropriate medical/formal care support, illness progression and the costs of dementia contributed to negative appraisal.

Discussion and implications: The findings provide insights into the holistic experience of caring for a person with dementia reveling the major positive and negative aspects underlying the caregiver role. The evidence emphasizes the need 'to focus on positive aspects and targeted interventions aimed at reducing the negative impact of caregiving, which has serious consequences on caregivers' quality of life. A multicomplex intervention for dementia informal caregiving should be developed, committing the society to promote mental health, address these community needs and improve the quality of life of the person with dementia and their family caregivers.

Keywords: Dementia caregiving; Family caregiving; Caregivers' quality of life; Qualitative research

1. Introduction

Dementia is a clinical syndrome characterized by a cluster of symptoms manifested by difficulties in memory, disturbances in language and cognitive functions, changes in behaviours and impairments in activities of daily living that includes a range of neurological disorders characterized by memory loss and cognitive impairment (Hung et al., 2016; Winblad et al., 2016). With the growth of ageing populations, the number of persons with dementia is increasing, with no sign of a cure for the disease. It is probably under-diagnosed, with an estimated half of primary care patients aged over 65 years not diagnosed by their primary care physicians (Qiu et al., 2009; Verbeek et al., 2012). The most common form of dementia is Alzheimer's disease (AD), accounting for 50–70% of dementia cases. Prevalence has undergone an huge increase in recent years being one of the greatest healthcare challenges of the 21st century due to the high demanding medical, social and institutional care (Brodaty & Green, 2002; Ibarria et al., 2016).

Before institutional care, family caregivers play an important role for people with dementia, helping them in their daily activities, whose dependence increases with severity of the disease (Brodaty & Green, 2002; Dening et al., 2012; Prince et al., 2004). Taking care of a person with dementia, demand for several logistics tasks, including personal care, housekeeping, administration of medication and execution of financial transactions and other activities and with the disease progression caregiving for the patient's well-being becomes more important (Emmerson et al., 2009; Winblad et al., 2016).

The task of caregiving is complex leading to physical, mental and financial stress for caregivers. Emotions such as guilt, resentment, sadness and effort expended, as well as the anticipated loss of the relative, emerge (Emmerson et al., 2009). As a result, informal caregivers suffer significantly higher levels of psychological morbidity, depression, stress and burden (Connell et al., 2001; Gilliam & Steffen, 2006; Livingston et al., 1996). The uncertainty about the future may create an ambiguous situation for family members and increase the burden on the caregiver (Givens et al., 2012). Despite these, some caregivers see their role as an opportunity to strengthen their relationship with their relatives.

Healthcare professionals have an important role in providing support to caregivers. They may refer caregivers for counselling, which has been shown to reduce caregiver distress, assist patients to stay at home longer, and inform caregivers about support organizations (Brodaty & Green, 2002). There is evidence suggesting that caregiver needs are not being met by healthcare professionals, which leads to the decline in their physical and mental health

(Pinquart & Sörensen, 2007; Sörensen & Conwell, 2011). Caregivers' perspectives are of high importance to better describe caregivers' role and identify potential ways to improve daily tasks, resulting in a more positive experience.

A large proportion of studies discuss the positive and negative influences of caregiving on particular aspects such as gender, nature of the relationship or caregivers' age (Dening et al., 2012; Garand et al., 2005; Lin et al., 2012). To describe the task of caregiving, it is important to approach this as a global phenomenon, that is, understanding the caregiver's needs and perceptions that positively or negatively contribute to their quality of life and their provision of daily support as caregivers. We conducted a systematic review of qualitative studies to understand the holistic experience of caring for a person with dementia, including not only the positive and negative aspects of caregiving through caregivers' perspectives, but also the expressed factors that affect those experiences.

2. Materials and methods

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Moher et al., 2009) and was performed to identify and summarize the impact of caring for persons with AD/dementia on family caregiver's life through their own perceptions.

2.1. Search strategy and inclusion criteria

Two authors (PL, MR) performed the electronic searches for relevant sources including OVID Medline, EMBASE, Web of Science, SCOPUS and PsycInfo. These databases were selected due to the highly relevance of their indexed articles to this study topic. The results of this search were supplemented by hand-searching the reference lists of the articles retrieved. Languages included were English, French and Spanish, with publication dates restricted to January 1998- July 2020. The start date of the review was the time when symptomatic treatment for AD was marketed and inclusion criteria for pivotal efficacy trials better discriminated AD from other dementias, namely vascular dementia (Cooper, 1970). The studies published after 1998 were more consistent with our disease and were therefore selected for this review.

The full search strategy and the inclusion/exclusion criteria are available in Box 2.1 (see Additional File 2.1 of supplementary material for more details). Studies including mixed

participants (caregivers, care recipients and/or healthcare professionals) were included in the content analysis, but the perspectives of healthcare professionals and care recipients were excluded.

After download duplicates were identified and deleted. The abstracts and full-text copies were scrutinized by two independent reviewers (PL, MR), who applied predefined inclusion/exclusion criteria (see Box 2.1) with disagreements resolved through discussion or via a third reviewer (MMR), with a presumption of inclusion in cases of doubt.

Box 2.1. Systematic review of literature: search terms, inclusion/exclusion criteria and information extraction

Search Terms

(1) Alzheimer disease OR mild cognitive impairment OR cognitive dysfunction OR dement*.
(2) Interviews OR interview* OR surveys and questionnaires OR survey* OR questionnair* OR focus groups OR geriatric assessment OR health impact assessment.
(3) Caregivers OR caregiv* OR carer OR family OR famil* OR patient care.
(4) Illness behaviour OR cost of illness OR activities of daily living OR quality of life OR self concept OR stress, psychological OR sick role OR outcome assessment health care OR health expenditures OR health care costs OR self-perception.
(5) Cohort studies OR longitudinal studies OR follow-up studies OR prospective studies OR retrospective studies OR cohort OR longitudinal OR prospective OR retrospective.
(6) 1 AND 2 AND 3 AND 4 AND 5.
(7) LIMIT 6 to year of publication: Jan 1998-July 2020.

Inclusion Criteria

1. Original qualitative empirical data.
2. Paper in English, French or Spanish.
3. Including family or informal caregivers of people with dementia and/or Alzheimer's Disease and/or mild cognitive impairment.
4. Methods including focus groups and/or survey/questionnaire and/or interviews.

Exclusion Criteria

(1) Quantitative studies, reviews of literature, opinion-based studies, protocol studies.
(2) Studies before 1998.
(3) Not addressing caregivers 'perceptions.
(4) Studies were caregivers' perceptions were related to the results of intervention programmes.
(5) Addressing other conditions than Dementia and/or Alzheimer's Disease and/or mild cognitive impairment.
(6) Addressing outcomes other than caregivers' perceptions about caregiving daily life.

Information extraction from included papers

(1) Study description, setting and population.
(2) Sampling criteria; participant numbers and response scores (when presented).
(3) Study methodologies and limitations; data analysis methods.
(4) Outcome measures.
(5) Key findings/themes/results; main conclusions.
(6) Implications for policy and practice and suggested future research.
(7) Bibliographic details.

2.2. Data extraction

For each study, two authors (PL, MR) extracted the data independently from each study: information related to authors, publication year, study aims, theoretical/conceptual frameworks, sampling/sample characteristics, analytical approach, summary and outcomes. The selected studies were analyzed in order to explore positive and negative aspects experienced by caregivers while caring for their relative and the expressed factors that contributed to these positive and negative appraisals. With regard to data extraction, divergences were solved between authors, and 100% consensus regarding data extraction was reached.

2.3. Quality appraisal

Two authors (PL, MR) independently assessed the quality of each study independently using the Critical Appraisal Skills Program (CASP), (L. Wang et al., 2015). We assigned yes/no to eight questions related to study methodology as listed in CASP: clear statement of the study aims, appropriateness of the qualitative methodology, research design, recruitment strategy, and data collection, considerations of the relationship between the researcher and participants, ethical issues, and rigor of the data analysis (see Table 2.1 of supplementary material). We did not exclude any study during the quality appraisal as they might generate new insights.

2.4. Data Analysis

A narrative review was selected as the method for data synthesis, since the included papers were qualitative studies (Dissemination, 2009). Selected papers were carefully read by the authors (PL, MR). Data findings from the primary studies were independently coded and organized (key words, short sentences and so on.) into positive or negative aspects of caregiving or expressed factors contributing to that positive or negative appraisal. Two authors independently performed the data analysis and consulted a third researcher (MMR) when required. Finally, the two authors worked together to re-examine significant statements and identify excerpts and/or the original quotations from the studies that could best illustrate the themes selected for this study.

3. Results

3.1. Type and quality of the results

The search strategy yielded 2376 publications of which 118 were selected to full-text review and finally restricted to 81 studies in this systematic review (Figure 2.1). The studies were analyzed to identify informal caregivers 'perceptions about positive and negative aspects of caregiving, and the factors that contribute to those experiences (Table 2.1). The study characteristics of the included studies are presented in supplementary material (see the supplementary material, table 2.2). With regard to methods, 52 studies used focus groups; other methods included interviews, questionnaires and mixed methods (see the supplementary material, table 2.3). A total of 3347 participants were included; 82,1% were family caregivers. Qualitative methods to identify experiences/perceptions of family caregivers were observed in all studies; a few studies also presented the views of patients with mild cognitive impairment, patients with dementia and former caregivers (these perceptions were not included in this review).

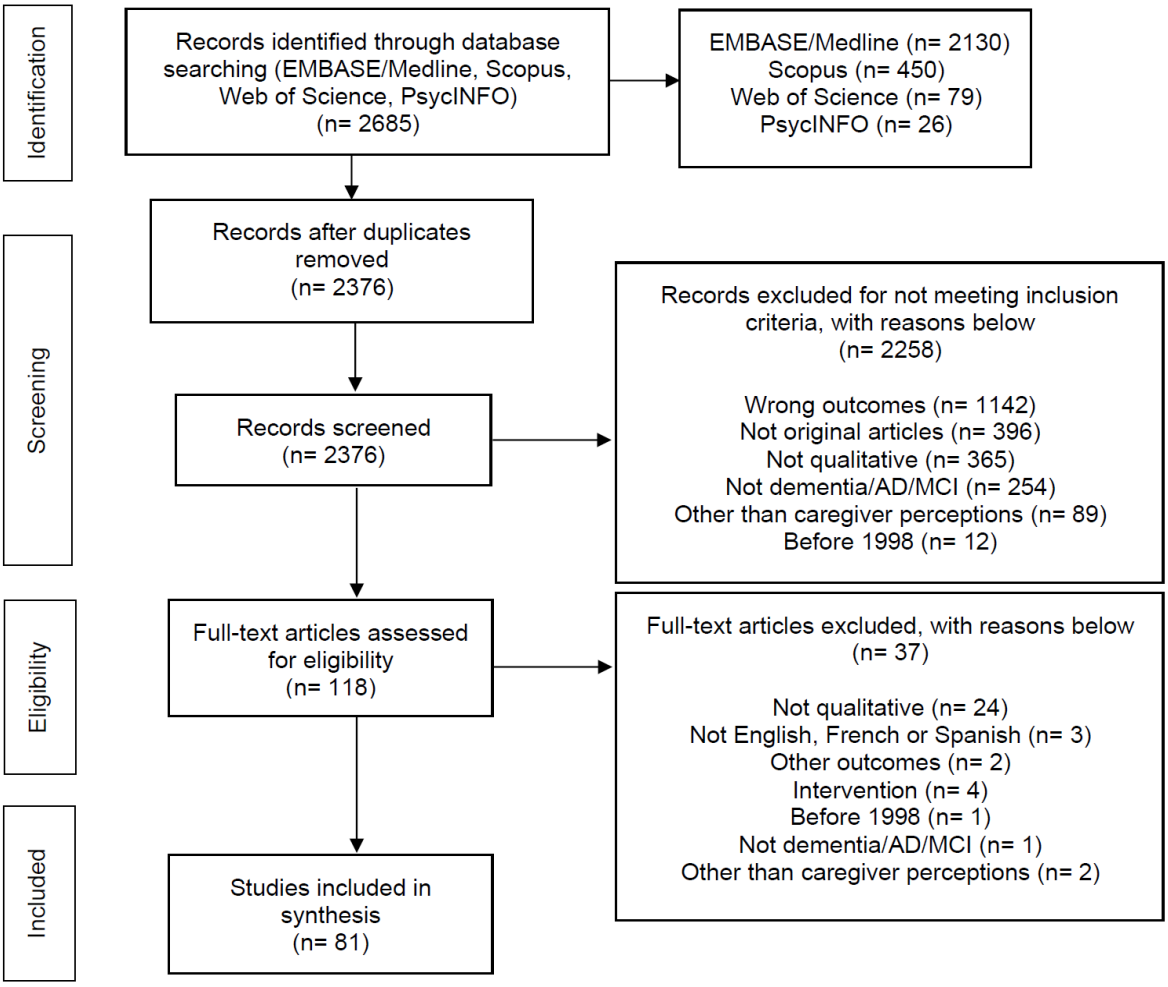


Figure 2.1. Study flowchart (AD, Alzheimer's Disease; MCI, Mild Cognitive Impairment).

3.2. Study quality

The quality of the included studies was assessed with CASP (L. Wang et al., 2015) (see the supplementary material, table 2.1). Most studies used convenience samples, while some evaluated the representativeness of participants; however, all studies clearly reported the aims, design and sampling. Data analysis was fully described in 35 studies and partly described in 46 studies, while data collection was fully described in only 9 studies. All studies either fully or partly explicitly stated the ethical issues, but only one described the relationship between the interviewer and the participants.

3.3. Caregiver's perception of the effects of caring for a person with dementia

Caregiving was described as a big life change: - "It effectively changes your life. Your priorities change. Your lifestyle changes. Your attitude to the person you are giving care to changes. Your role changes." (Butcher et al., 2001). Analysis of the included studies revealed positive remarks about the caregiving role that were present in a small number of studies (18 studies), while negative aspects were present in 76 studies, including studies that combined both aspects. Examples of each and combined aspects are presented in table 2.1 (for all studies that encompass positive and negative aspects of caregiving, see the supplementary material, table 2.2).

Table 2.1. Examples of the studies including positive, negative or combined aspects of caregiving role (n=81)

Aspects related to caregiving role	Studies (n)	Examples of studies
Positive aspects (only)	5	Habermann, et al., 2013; Gennip et al., 2014; Innes et al., 2011; Harmer and Orrel, 2008
Negative aspects (only)	63	Forbes et al., 2008; Hemingway et al., 2016; Glass, 2016; Givens et al., 2012
Positive and negative aspects (combined)	13	Banningh et al., 2008; Jennings et al., 2017; Ven LG et al.2017; Boots LM et al., 2015

The positive aspects found were presented as personal aspects experienced by caregivers that can be enhanced by good medical counselling and formal care support and family/friends support. Negative aspects were particularly related to emotional and social aspects of caregiving and factors such as inappropriate medical and care support, illness progression and costs related to dementia (eg. formal care costs, medications costs, and so on) enhanced negative appraisal (see table 2.2).

Table 2.2. Main positive and negative aspects and related factors influencing caregivers' role (n=81)

	Studies (n)	Example of studies
Positive appraisal about caregiving	**18**	
Personal aspects experienced by caregivers		
Personal accomplishment/strengthening of the relationship	10	Harris, 2013
Be able to support family and return the favor	9	Wezel, et al., 2016
Be able to do meaningful activities together	8	Harmer and Orrel, 2008
Ensure the dignity of the relative	7	Poole et al., 2018
Factors that contribute to positive appraisal		
Good medical counselling and formal care support		
Useful instructions or information about dementia	8	Boots LM et al., 2015
Good home care/day care services and homelike facilities	5	Popham and Orrell, 2012
Access to good medical support for caregiver and the person with dementia	5	Karlin et al., 2001
Early diagnosis/ relief after the diagnosis	3	Connell et al., 2004
Family/friends support		
Can count on old friends	5	Harris, 2013
Support groups	5	Ivey et al, 2012
Having family support	3	Lampley-Dallas et al., 2001
Having free time for themselves	3	Ivey et al, 2012
Negative appraisal about caregiving	**76**	
Emotional and social aspects experienced by caregivers		
Stress, loss, grieving, guilty and sad feelings	48	Peel and Harding, 2013
Feeling alone and desperate for help	23	Karlin et al., 2001
Exaggerated precautions with vigilance and safety issues	12	Phillipson and Jones, 2011
Problems with acceptance and deal with the diagnosis	9	Aminzadeh et al., 2007
Problems related to food issues	9	Taşc et al.,2012
Obligation to be a caregiver for lack of alternatives	9	Forbes et al., 2000
Uncertainty/fear about the future and loss of hope	8	Ivey et al, 2018
Social isolation	5	Lampley-Dallas et al., 2001
Not being recognized by the relative	5	Wezel, et al., 2016
Loss of old friendships	2	Lethin et al., 2016
Factors that contribute to negative appraisal		
Inappropriate medical and formal care support		
Changes in formal care teams and long process of diagnosis	9	Bunn et al., 2017
Decision-making process without medical counselling	7	Jennings et al., 2017
Bad home care service/long waiting list in formal care	7	Morgan et al., 2002
Weak support groups	4	Morgan et al., 2002
Weak explanation of disease in the moment of diagnosis	3	Connell et al., 2004
Illness progression		
Daily progression	33	Lian et al., 2017
Behaviour problems	17	Lian et al., 2017
Sleeping problems and night agitation	11	Jamieson et al., 2016
Patient co-morbidities	6	Oliveira et al., 2017
Bedridden relative	4	Elliott et at., 2009
Patient dependence on activities of daily living	50	Taşc et al.,2012
Cost of illness		
High costs of formal care/medication and assistance	28	Zabalegui et al., 2008
Have to quit job or reduce hours	9	Lampley-Dallas et al., 2001

3.3.1. Positive aspects and expressed related factors of caregiving according to caregivers' perceptions

Providing support for the relative and having *"made a difference"* to their family's life were considered to have positive effects in caregiver's life's and were a relief for caregivers, as they were able to fulfil their obligations as sons/wife's/daughters or others:

-" (...) What I am looking to do is just staying home and watch my husband. That's what I have to do. And if that's what I have to do, I don't mind doing that.", - "It gives me great joy to give back to my mom and…I tease her…uh…on a good day, and I say "Aren't you glad you took good care of me, because you set that example?" And she'll laugh and I'll laugh and…and it gives me great joy, because she…uh…was/is a great mother. And uh…and…and now, it's my turn to be a great daughter." (Banningh et al., 2008; Habermann et al., 2013; Lach & Chang, 2007; van Wezel et al., 2016).

For some family caregivers, the chance of doing meaningful activities together and be able to return the favor to their parents/family members was indicated as being grateful: - "*I enjoy the time with my mother…I love to hear her laugh…We talk all the time in the car; we pray together, watch TV."* (Habermann et al., 2013; Milte et al., 2016). Respect for the individuality of the person with dementia was reported as crucial to caregivers, who were grateful to know that the individuality of their family members was being respected in the nursing home:

- "I think their individuality and their dignity is vital.", -"They have all got their own (personal) things (in the nursing home)" (Popham & Orrell, 2012).

By having their own things, patient well-being and dignity appears to guarantee to turn institutionalization into a more personal experience. The main expressed factors that contributed to the positive aspects of caregiving were related to good medical counselling and formal care support, as well as family and friends support (table 2). Access to useful information about the disease and its evolution was considered essential for caregivers. Acquiring knowledge facilitate caregivers to better assume the caregiving role and prepare them to prevent and deal with specific situations: - *"I would like to know. I mean I am worried about the future…Because I don't know anything!"* (Groen-Van De Ven et al., 2017).

Appropriate medical counselling, formal support and healthcare professionals support for patients was found to be a good resource to overcome caregiving challenges and decision-making process that rely on caregivers: - *"Well, for me, what would improve my quality of life mostly is to have better support from healthcare professionals, (...) just keeping him clean is extremely challenging (...)"* (Oliveira et al., 2019). Caregivers considered good aspects of formal care when the staff -*"have the knowledge and techniques on how to handle the residents and their behaviours."* and - *"That it was good to see their relatives in a safe, secure and loving environment."* (Moyle et al., 2002). Caregivers also benefit from medical and psychological support, where the disease can be acknowledged and where they can be understood: - *"The regular visits to the psychologist were very helpful. It is really important you have someone to talk to during the dementia process who understands you."* (Wolfs et al., 2012).

The need for an early diagnosis of dementia was quite evident, mainly due to the bad experiences and endless diagnostic procedures previously experienced but also due to the relief felt after the diagnosis: -*"I felt very relieved when we finally got the diagnosis…I just felt validated that finally someone knew what we knew."* (Connell et al., 2004). Through caregivers perception, early diagnosis has positive effects of relief and care improvement, thus allowing to a more effective caring process of their families afterwarsds:

> - *"Well, if I had known that the man was sick, first of all, he wouldn't have been left alone as long as he was. Second of all, I wouldn't have blamed him for his actions. I would have known it was the disease. We did a lot of damage emotionally to him as well as to ourselves, and there's a lot of guilt associated with what we had done, so I think diagnosis as early on as possible is the best possible thing that can happen."* (Connell et al., 2004).

Family and friend support was another factor that positively enhanced the experience of caring. The value of old friendships that remain after diagnosis helped caregivers decreasing feelings of loneliness: -*"(...) Many of our friends, if anything, they've stepped up and they helped us."* (P. B. Harris, 2013; Mccabe et al., 2018). Family support is particularly important when it provides free time for the principal caregiver to do his own activities: - "*She would stay with my sister for approximately three months"* (Karlin et al., 2001). This aspect was regarded by caregivers as very positive to their quality of life. Unfortunately, most admitted to be single caregivers for their relative and have no spare

time for themselves or other activities besides caring (P. B. Harris, 2013; Mccabe et al., 2018).

3.3.2. Negative aspects and expressed related factors of caregiving according to caregivers' perceptions

Caregiver's perceptions about the negative aspects of caregiving comprise emotional and social aspects such as fear, worry, stress, sadness, social isolation and problems in acceptance of their relative's diagnosis. Additionally, caregivers experienced concerns about the future since they do not know what to expect and for how long they can ensure the emotional and economic support for themselves and their relatives well-being.

Mental, emotional and physical effort are seen as requirements to deal with patient sleep disorders: - "I can't handle this anymore; I'm absolutely buggered from no sleep at all night. (Jamieson et al., 2016)" and behaviour changes (that in some cases lead to physical/verbal aggressions) with some caregivers declaring their own need for therapy:

- *"In fact, I do need therapy, too. I mean if there are not two or three people to care for the patients, you are psychologically affected. I am a prisoner at home."; - "For a couple of times I cried. They say boys do not cry, but I did…". "I sometimes have nervousness, anger and crying attacks. (…) I used to be full of life; I used to like visiting and having holidays. I can say that I cannot bear this situation anymore."* (Taşci et al., 2012) .

The caregiver role demands too many hours for care, with no time for personal life, which is reflected in caregivers' difficulties in maintaining their professional and social life, and their responsibilities as parents:

- *"I can't leave him. For 24/7 I'm with John."* (Xiao et al., 2014)*; - "I would say if you're going to be a caregiver it's a full-time job. You don't have time to do anything else if you're going to do it right"* (S. Forbes et al., 2000)*; - "(...) I think that there's such isolation for the caregiver because you often don't have someone to talk to unless you have a large family. I tend to not have friends that, they don't want to hear anything that you are doing this."* (Courtney A. Polenick et al., 2018)*; - "I live a little way away and I've got four children; and that's hard in itself. I have to look after her*

as well. Some days, I might be having a crisis before I have even seen her." (Toot et al., 2013).

For caregivers, there was a permanent concern about their relative's well-being and capacity to provide safe and effective care which could prevent the possibility of serious injuries to occur, particularly fractures due to falls. The comorbidities that persons with dementia usually have, also increase the need for adaptation of care required, including special food intake:

- *" (...) He cannot swallow and coughs each time he swallows and it blocks his throat.", - "My mom was a diabetic for 40 years. If she didn't eat in the morning, hypoglycemia was inevitable. Whenever my mother would refuse eating breakfast, I would become angry and mom would also fight and insist on not eating."* (Song et al., 2018; Taşci et al., 2012).

Food was an important aspect for some caregivers, since the high level of calories needed to support their relatives has consequences on their own weight and health. Also, for many of the male caregivers, the concern with the process of feeding their relatives was new, leaving the need to learn new things, besides their relatives condition (Fjellström et al., 2010).

For some caregivers, the time of diagnosis brought great frustration due to inexistent communication with health services, constant change in formal care providers and lack of information: - *"I don't think that any of the doctors that we were involved with ever offered any help as far as what to do next."* (Bunn et al., 2017; Connell et al., 2004; Manthorpe et al., 2013). The process of dealing with health and social care services for the person with dementia was described as a "battle" or "fight" (Peel & Harding, 2014). After the diagnosis, the uncertainty about the future and the inability to accept their relatives condition lead to stress, frustration and sadness (D. A. Forbes et al., 2008; Mccabe et al., 2018; Prorok et al., 2017). For caregivers, it was difficult to deal with the fact they were not recognized by their relative with dementia: -*"And I think that the dementia would then progress rapidly to a stage where she no longer recognizes anybody."* (van Wezel et al., 2016). Some caregivers admitted started grieving the loss during the course of the disease:

-*"I have been grieving losses over the whole period of illness; there was a loss of person before a loss of body."* (Hemingway et al., 2016); - *"I started grieving years ago when mother didn't recognize us...That's when I lost my mother... When she*

physically died I felt like I lost my baby." (Juozapavicius & Weber, 2001)*, - "It may be a bad thing to say but I'm hoping before she starts really seriously deteriorating she'll pass on."* (Hemingway et al., 2016; Mccabe et al., 2018).

The social isolation due to the loss of old friendships and the lack of family support seem to have a huge negative impact on caregiver's personal and social life (Lethin, Hallberg, et al., 2016). Over time, caregivers tried to adapt to the circumstances and sought professional help, aiming to deal with their exhaustion and emotional problems:

- "I am having emotional problems from the stress and sadness of seeing such a low quality of life in my mother."; - "Dementia is an emotional process which you enter together. Eventually you reach your limit (...)" (Wolfs et al., 2012)*; - "I did not get enough emotional support."; - "I needed more emotional support from friends and community."* (Karlin et al., 2001).

For some participants, caregiving was considered an obligation that result in a higher emotional impact: - "I hardly cry, I have almost never cried. I got distressed and felt ill. I tried to manage it by myself. I was obliged to accept it when nobody gave me a hand." (Taşci et al., 2012).

The inappropriate medical and formal care support, the daily perception of disease progression and the high costs of illness were the main expressed factors that contributed to the negative aspects of caregiving (table 2).

Formal care services were largely associated with patient isolation and superficial or poor care:

- "In an ideal world one would not allow the patients to sleep all day."(Popham & Orrell, 2012)*; - "We had home care [for mother] until they [home care staff] got accused of stealing, got fired, got thrown out…"* (Morgan et al., 2002).

The lack of formal support made caregivers feel they are left alone: - "I just don't understand why they [home care staff] are so unhelpful …I think something needs to be done, because we don't seem to get any help really from anywhere. You're just a bit left on your own." (Laparidou et al., 2019). Inappropriate medical care was also reported by caregivers: - "I was kind of astonished that the doctors were unsupportive, not only unsupportive, really very negative … this is a doctor and he's telling me not to treat my

father" (Van Gennip et al., 2016). Diagnosis commonly triggered search for better medical counselling:

- *"I didn't get any help at all. He just said that my husband had depression. In the finish and because I kept going back ... and anyway it wasn't ... and I ended up having to pay for a specialist to get him referred to try and get him a diagnosis ... We didn't get any help at all. I didn't get sent anywhere…"* (Sutcliffe et al., 2015).

The decision-making process is typically the responsibility of caregivers, leading to an impact on their own feelings and well-being. For example, placing the feeding tube, resuscitating, and even choosing permanent formal care, such as a residence or nursing home, are very difficult decisions to make and bring feelings of sadness and guilt:

- *"I promised faithfully that he would never go to a residence, and I still feel guilty."* (Sarabia-Cobo et al., 2016); - *"I mean it's totally on my shoulders too. And sometimes the amount of guilt is there, I mean it just weighs me down so much. But then I have to split myself, I still have kids at home, and I have to split myself there too"* (S. Forbes et al., 2000); -*"Resuscitation was the biggest decision…I consulted with my children and my wife's sisters and they were all in agreement… she has gone through enough."* (Livingston et al., 2010).

Another negative factor that contributes to increased burden in the caregiver is the constant loss of patient competences, losing their ability to do daily activities such as walking, dressing, going to the bathroom, bathing, driving or cooking in an independent way, overloading the caregiver:

- *"I've had to do it all."*; - *"I bathe him because he is afraid. He does not finish it and leaves. He does not completely shave. For example: he cuts the right side of the moustache and leaves the other side. He eats but does it in a mess."* (Banningh et al., 2008; Fjellström et al., 2010; Habermann et al., 2013; Jennings et al., 2017; Taşci et al., 2012; C. L. Wang et al., 2018).

Witnessing the daily progressive health decline of their relatives, especially in later stages of the disease, it is a process that has significant impact on caregivers: - "*In the later stages it's so difficult for them to indicate what their needs are."* (Moreno-Cámara et al., 2016; Moyle et al., 2002; Popham & Orrell, 2012; van Wezel et al., 2016). With the patient's loss of abilities, the caregivers try to adapt to the circumstances and might

consider getting professional help at this point (Jennings et al., 2017; Karlsson et al., 2015; Laparidou et al., 2019; Mccabe et al., 2018). Another negative aspect that has a major impact is the behavioural change, which in some cases leads to physical or verbal aggressions:

- *"He's very much reliant on me (…) He's suddenly becoming aggressive, and gets angry really with no reason at all…"* (Xiao et al., 2015)*;* - *"She also gets quite aggressive when it comes to her kind of personal care really. You know she doesn't like having a shower, having her hair washed…"* (Duxbury et al., 2013)*;* - *"It is very hard for me to handle her behaviour (…) I know that you shouldn't mention it and/or joke about it. But I've noticed that I still do it. I'm still having a hard time accepting how much my mother has changed (…)."* (Huis In Het Veld et al., 2016).

On top of the above-mentioned negative aspects, the cost of the illness had a huge negative impact on caregiver's day living and well-being. Without a job in some cases, keeping up finances with the high costs of bills and home care is also a constant worry and is seen as a barrier to formal care accessing formal care:

- *"I can't afford a decent one (home care service)";* - *"Cost is a barrier for lots of people. You know, there's a limit to how much home care they use because of the cost"* (D. A. Forbes et al., 2008; Zabalegui et al., 2008).

Another concern of the caregivers is the duration of the disease:

- *"I knew we had money if mom lived for one to two years, but if she lived for 20...it was a big worry and a burden.";* - *"I don't have an unlimited amount of money for my mom. I am trying to sell her properties and get her settled. I am continually worried about resources."* (Jennings et al., 2017; Juozapavicius & Weber, 2001).

Thus, the financial guidance/support for this community is of great relevance not only to guarantee the basic daily support of food, bills and medications, but also the need for institutionalization and all other support that patients may require during their lives.

4. Discussion and implications

The current review focused on the perceptions of informal caregivers with regard to the holistic experience of caring for a person with dementia, including positive and negative aspects. The included studies reviewed the diverse feelings and emotions that caring brings to caregivers. The diagnosis of dementia seems to generate positive consequences in the relationship between the caregiver and their relatives, contributing to a stronger relationship than before (Lin et al., 2012). This strengthening of family ties has also been reported in other diseases such as cancer (Preau et al., 2011). This fact may be related to the family companionship that is needed to face the disease and is probably related to the type of disease. Chronic diseases and/or with a poor prognosis are seen to cause a very high burden to the patient but can be reduced with family being closer together. As described by Glitlin L. *et al.,* most of the caregivers found in caregiving a chance to "return the favor" to their relatives and the opportunity to do activities together, reducing both caregiver burden and behaviour symptoms of dementia, which is in agreement with our findings (Gitlin et al., 2008). Findings from Elnasseh *et al.,* are consistent with past literature showing that the quality of previous familiar relationship is relevant when a family member becomes a caregiver (Elnasseh et al., 2016). In families with healthier dynamics, caregivers are more likely to have greater personal strengths, while families with poor affinity are more likely to experience increased caregiver burden (Song et al., 2018).

Finding good medical counselling and formal care support, as well as the opportunity to enhance the family cohesion, and the presence of friendships, especially old friends who remain after the diagnosis, were factors that contributed to positive appraisal. As previous demonstrated by Vellone E., *et al.,* all kinds of help and support are welcomed by caregivers, as these give them free time for themselves (Vellone et al., 2008). Sharing caregiving tasks is a concrete way to reduce caregivers stress, with the free time being used by caregivers for activities such as going to the gym, taking a walk, going out with friends or just taking a nap. After relaxation, the caregiver would be more ready to better take care of their relatives. The availability of formal care support, in addition to positive experiences with formal care, and good home care/day care services are important to caregivers, once they have perceived the knowledge, security and dignity needed to care for a person with dementia. Furthermore, good formal care can support caregivers in their

role, reducing the burden and negative impact of their daily routine. A recent review of Yu *et al.,* describes the positive influences of caregiving related to caregivers' personal issues, highlighting feelings such as gratification and meaning in life, which is in accordance with our findings (D. S. F. Yu et al., 2018). Additionally, we identified other factors that contributed to positive and negative experiences in caregiver's daily life. This knowledge is crucial to the development of measures/programs targeted at caregivers, which should consider caregiver concerns of the caregiver, but also empower them by highlighting the positive aspects and providing support (good formal care services, family support, and so on). The result will broaden the spectrum of action of these types of programs and improve the caregiving experience on several levels.

The imbalance of negative over positive aspects of caregiving has been shown in previous studies, with implications for both mental and physical health effects in caring (Pinquart & Sörensen, 2007; Sörensen & Conwell, 2011). A study of Pinquart and Sörensen suggests that caregiving of individuals with dementia is more stressful than caring for individuals with other diseases (Pinquart & Sörensen, 2003). This phenomenon is probably related to the increased amount of time that caregiving for a person with dementia may involve, resulting in loss of spare time and consequent social isolation (Emmerson et al., 2009). Most of the caregivers sacrifice their activities and hobbies, restrict their time with friends and family, and give up employment or reduce time at work. Therefore, caregivers tend to lose their meaning in life, or set it aside, leaving an opportunity for mental health problems to emerge, which can worsen in the future as a result of the emotional burden they are exposed to (Brodaty & Hadzi-Pavlovic, 2016; Greenwood et al., 2019). Anticipated loss is common in caregivers and, as previous described in the literature, grieving over the whole period of illness increases the possibility of having a post death complicated grief (Blandin & Pepin, 2017).

The health of the caregiver has been studied by Widera *et al.,* who suggested that caregivers are less likely to engage in preventive health measures, thus leading to increased risk of mortality (Widera & Covinsky, 2011). One factor that may be contributing to this situation, is the financial burden associated with caring for a person with dementia. Moreover, the daily overload, the patients' dependence and the decision to stop working in order to care for their loved ones, lead to the postponement of medical examinations among caregivers, negatively impacting their health status (DeFeis et al., 2015; Widera & Covinsky, 2011). Usually, caring for their relatives becomes a priority; however, this process is often done alone, resulting in the tendency of caregivers to forget to take care of

themselves. Healthcare professionals have a central role in improving access and quality of health services to caregivers (which have been shown to reduce caregiver distress and assist patients to stay at home longer). However, little has been done with regard to the promotion of a healthier life for caregivers, who are known to be in need of good health support and monitoring (Brodaty & Green, 2002; Widera & Covinsky, 2011). The general health of caregivers deserves a great deal of attention as negative health outcomes contribute to the risk of future serious health problems, compromising not only caregiver's health but also the care that is being provided to the patient (Schulz & Quittner, 1998).

Previous studies have reported that the patient's dependence on activities of daily living is described by caregivers as one of the hardest things to deal with, which is due to the amount of care that needs to be provided. This is in accordance with the findings found in the studies included in this review (Gallagher et al., 2011; Gray et al., 2016). Throughout the progression of the disease, the patient's behavioural symptoms (agitation, sleep disturbance, wandering and apathy) and psychological symptoms (anxiety, depression, delusions and hallucinations) have a significant impact on caregivers, providing the negative experiences of caregivers.

Moreover, the effects of night agitation and sleep disturbances experienced during caregiving lead to poorer subjective sleep quality and higher rates of daytime sleepiness among caregivers of persons with dementia compared with non-caregivers. These factors, combined with daily routine, disease progression and patient's dependence can lead to caregiver exhaustion (Lai et al., 2009).

The costs of the illness had huge impact on caregiver's routine, with the increased cost of formal care and medication becoming a concern. Costs are probably the reason caregivers resort to formal care as the disease becomes more severe, resulting in behaviour problems and more disabilities (Bakker et al., 2013; Wiles, 2003). Supporting a person with dementia in their own home costs less than bringing them to a care home. As previous literature suggests, the transition from informal to formal care occurs mainly in the later stages of dementia and is considered as supplement to care since the caregiver remains present in all processes (Albert et al., 1998). Additionally, caregivers attribute the change from informal to formal care as a failure of their responsibilities or make them feel they are bad family members (Vossius et al., 2014; Wübker et al., 2015). The long waiting lists and the costs were further barriers that delay access to these services.

The economic environment of caregivers is never too comfortable since they are caring for their relatives and not being paid for this full-time job. As informal care is unpaid, it is

viewed as a costless substitute to formal care. However, informal caregiving is not free of costs, which makes it relevant to estimate the value of the hours that caregivers spend on caring for their relatives in order to better know the monetary costs of informal caregiving and develop better financial support to these specific cases. Timely access to dementia care services and fairer costs are crucial to reducing informal caregiver burden and increasing the quality of life of patients and caregivers (A. Wimo et al., 1999).

Although it may be thought that the caregiver's role is less important with the patient's admission to a care facility, the caregiver remains involved in terms of important legal, financial and healthcare decisions (Givens et al., 2009; Stirling et al., 2012). The decision-making process becomes tougher with the associated ethical and emotional responsibilities. Family, friends and medical support is critical as this allows caregivers to better decide and deal with the feelings associated with the decision (Bonner et al., 2014).

Due to the increasing complexity of caregiver's responsibilities, training programs are important to help caregivers understand and manage care recipients' behavioural problems and thus reduce negative experiences (Hebert et al., 2003). However, despite the several interventions developed with the goal of alleviating caregiver burden, the experience continues to be very negative for caregivers. Why are these programs/interventions not having the expected results of decreasing burden among informal caregivers? Caregivers are mostly women and elderly. Are these interventions well set to the target population? Do these programmed really fulfil the needs of families on an individual basis? It is suggested that personalized and multicomponent interventions, including a diversity of services (directed at the patient and the caregiver), will decrease burden, improve quality of life and enable home care for longer periods prior to institutionalisation (Etters et al., 2008). The transition to formal services is postponed by family caregivers who, despite all the negative aspects of caregiving, chose to care for their relatives and provide them the best care they can. Interventions should demystify institutionalisation as a failure of the caregiver and focus on facilitating a healthier transition to warrant patients and caregivers a sustained well-being for as long as possible. Also, it is important to provide interventions not only to caregivers, but also to former caregivers (who are usually neglected). There is evidence that the grieving process can be very stressful can lead to depression.

The number of people suffering from dementia is expected to increase in the coming decades, and there is a need to strengthen informal caregiving to meet not only the care recipient' needs, but also caregivers' needs. Adequate knowledge on the aspects that caregivers describe as positive and negative in caregiving experience and providing tools

to level these aspects are urgently needed. Overall, a multicomplex intervention for dementia caregiving should be developed, with the entire society being invited to promote mental health, address caregivers' needs and improve the quality of life for the person with dementia and their family caregivers.

5. Strengths and Limitations

The strength of this systematic review is it description of the phenomenon of caregiving for a person with dementia, through the views of informal caregivers, encompassing both positive and negative experiences. The use of CASP for quality appraisal by two independent researchers strengthened the results. However, some studies presented methodological limitations that may impact the level of evidence, as some of the studies did not use appropriate theoretical frameworks, which is a limitation of qualitative research. The comprehensiveness of caregiver experiences might be limited because most studies did not primarily examine caregiver's positive and negative experiences. The focus of the individuals included was on specific issues, such as caregivers' perceptions in formal care, family support, time of diagnosis, and on the like, and consequently reported limited aspects about the entire experience of caregiving.

Only qualitative studies have been included, and the results of quantitative studies were excluded. In addition, including only informal caregiver's perceptions resulted in the exclusion of views of persons with dementia and formal caregivers. It is also important to consider other aspects of caregiving. Additionally, care recipient and caregiver characteristics such as demographics, relationship, gender, and so on, which might influence the caregiver experience, where not considered.

The study findings have important implications for the development of interventions that comprehensively address caregivers' individual needs based on their experiences and demonstrate there is a need for more rigorous qualitative studies that explore the perceived positive and negative aspects of caregiving. Altogether, these studies may generate new insights into the planning and design of more robust and flexible intervention programs.

Acknowledgments

This review was funded by the "Fundação para a Ciência e Tecnologia (FCT)" Portugal and Merck Sharp & Dohme Portugal (grant number PDE/BDE/120498/2016).

Supplementary material

Table 2.1. Quality Assessment of 81 Studies Included in this systematic review

Table 2.2. Characteristics and key findings of the included studies in this systematic review (n=81)

Table 2.3. Summary of methods and participants of 81 studies included in this systematic review

Additional file 2.1 | Search strategy

Additional file 2.2 | PRISMA Checklist

CHAPTER 3

FACING COSTS WITH DEMENTIA: DAILY PERSPECTIVES FROM INFORMAL CAREGIVERS

STUDY FRAMEWORK

Following the previous study, it was important to characterize the daily lives experiences of dementia patients' informal caregivers and to uncover day-to-day sources of expenses related with dementia care, in a sample of Portuguese dyads (patient-caregiver). The negative aspects involved in informal caregiving prevail over the positive, as we have previously shown with the literature review. It is thus our belief that the high complexity of the experience of caring can only be reduced with multidirectional approach addressing these community's needs and improving the quality of life of the person with dementia and their family caregivers. Currently, there is a worldwide lack of knowledge, awareness, and in-depth understanding of dementia impact on caregiver's daily life. A qualitative study addressing the characterization of the perspectives of Portuguese informal caregivers about what it takes, in daily life, to care for a relative with dementia was lacking. Specifically, we found that the individual sociodemographic and psychosocial characteristics of each caregiver, together with a lack of adapted formal care services and low financial aid leaded to a high burden experience concerning informal care.

The following study was performed by **Patrícia Lindeza (PL)**, Ana Virgolino (AV), Osvaldo Santos (OS), Manuela Guerreiro (MG), Mário Miguel Rosa (MMR).

PL recruited and invited the participants. OS and PL moderated the focus groups. AV took written annotations in the field. **PL**, AV and OS transcribed and analysed the data. All authors were responsible for the study conception, design, drafting and reviews the manuscript. MMR and MG supervised the study.

Lindeza P, Virgolino A, Santos O, Guerreiro M, Rosa MM. Facing Costs With Dementia: Daily Lives Perspectives From Informal Caregivers. BMC Geriatrics, doi.org/10.21203/rs.3.rs-109248/v1 *(under review).*

FACING COSTS WITH DEMENTIA: DAILY LIVES PERSPECTIVES FROM INFORMAL CAREGIVERS

ABSTRACT

Background: Caregivers of people with dementia report stress, depression and economic burden compared to other caregivers. This study aimed to characterize the daily live experiences of dementia patients' informal caregivers, and to uncover day-to-day sources of expenses related with dementia care.

Research design and methods: Qualitative observational study, following a grounded theory approach. Data were collected with semi-structured focus groups with informal caregivers of persons with dementia. Discussed themes included changes in daily lives, formal care services utilization, quality of life and costs. Content analysis was conducted with Charmaz's line-by-line open coding procedure.

Results: Overall, 14 relatives of persons with dementia were included. Most of participants were female (12) and eight of them were daughters of the patient. Ages ranged from 39 to 84 years and eight had a high degree of education. Four of the caregivers were professionally active and the range of years assuming the role of main informal caregiver varied from two to 15 years.

Conclusions: Findings provide insight into the daily life experience of caring for a person with dementia, while revealing the impact on the quality of life of caregivers. The individual sociodemographic and psychosocial characteristics, together with a lack of adapted formal care services and low financial aid leaded to a high burden experience for these caregivers. A multidirectional approach addressing caregivers needs, while improving formal care services and creating social and financial support programs for families affected by dementia is required to decrease its financial and psychosocial burden.

Keywords: Dementia caregiving; Family caregiving; Caregivers' quality of life; Qualitative research

1. Introduction

As population longevity increases, so does the prevalence of dementia conditions, with no disease modifying treatment for this type of neurological diseases. In Europe, the number of people with dementia is expected to increase up to 14 million by 2029 (Anders Wimo & Prince, 2010). Dementia is a clinical syndrome characterized by impairment in language, memory and other cognitive functions, with significant changes in patient's behaviors and high dependence to perform activities of daily living (Hung et al., 2016; Winblad et al., 2016).

Dementia causes disability and dependency, often associated with stigmatization, barriers to accurate diagnosis and access to formal care services. These difficulties in formal follow-up of dementia patients create high physical, psychological and economic impact on family caregivers and societies worldwide (World Health Organization, 2012).

Over time, being cared on a daily routine by family caregivers becomes particularly important before institutionalization of people with dementia (PwD). Indeed, as patients dependency for daily life activities diminishes, the number of hours dedicated to the patient by informal caregivers increases more and more (Brodaty & Green, 2002; Dening et al., 2012; Prince et al., 2004). A recent study find out that the mean of hours per month of informal care of individuals with dementia was significantly higher when compared to formal care (Ydstebø et al., 2020). Informal care is a substitute for formal care services when a certain degree of dementia severity is reached. At some point, health support becomes harder to be provided by the family, and institutionalization is commonly considered (Bremer et al., 2017).

However, taking care of a person with dementia can entail pervasive costs. A study of Wimo et al., 2013, reveals that depending on country and AD severity group, 60% of total societal costs were supported by informal caregivers (Anders Wimo et al., 2013). There is not only a financial burden, but also a physical and emotional due to the demanding responsibilities and time expenditure that are required to supporting basic activities and supervising the patient (Connell et al., 2001; Emmerson et al., 2009; Gilliam & Steffen, 2006; Livingston et al., 1996; Olazarán et al., 2017). According to Alzheimer's Disease International, half of the dementia patients' caregivers tend to experience health problems, 49% modify their professional life and 62% have their social life seriously affected because of the caring obligations (ADI, 2019). Additionally, emotions involved in caregiving (such as guilt, resentment and loneliness) are often very difficult to cope with

by informal caregivers. On the other hand, caregivers can experience positive feelings about their caring role and find opportunities to enhance their familiar relationship after dementia diagnosis (Givens et al., 2012).

Since caregiving varies from case to case, some studies discuss how sociodemographic factors (such as gender and age of caregivers), as well the nature of relationships with the care recipient, affect the caregiving role (Dening et al., 2012; Garand et al., 2005; Lin et al., 2012). Few qualitative studies have collected the perspectives of family caregivers about the access and quality of formal care services and about informal caregivers' daily needs and difficulties related to the care of their relatives suffering from dementia (Burton et al., 2019; Risco et al., 2016; Stephan et al., 2018; Sutcliffe et al., 2015).

Published studies from Portugal or including Portuguese data focus mainly on the perspective of formal caregivers and do not allow a good and detailed characterization of the Portuguese context of dementia informal caregiving (Barbosa, A., Cruz, J., Figueiredo, D., Marques, A. & Sousa, 2011; N. Janssen et al., 2020; Kerpershoek et al., 2018, 2020). Currently, there is a worldwide lack of knowledge, awareness, and an in-depth understanding of dementia impact on caregiver's daily life. Results from a recent review have shown that the negative aspects involved in informal caregiving prevail over positive, to caregivers, and that the high complexity of the experience of caring can only be reduced with multidirectional approach addressing these community's needs and improving the quality of life of the person with dementia and their family caregivers (Lindeza et al., 2020b).

A qualitative study addressing the characterization of the perspectives of Portuguese informal caregivers about what it takes, in daily life, to care of a relative with dementia is lacking. A focus on the costs related to dementia is of particular importance to describe the perceived effects of the task of caring through caregivers' voices.

In this study, we aimed to contribute to the understanding of the informal caregiving role and its impact on caregiver's daily life's, while describing the use of financial resources and the dementia-related costs. The caregiver´s views on what is necessary to improve not only to promote better care for the affected relative, but also to promote caregivers' quality of life are of paramount importance to make informal caregiving as a positive life experience.

2. Methods

2.1. Design

This study followed a qualitative observational design. A grounded theory approach was used, with the intention of development a conceptual characterization of the phenomenon under study (informal caregivers' experiences with relatives suffering from dementia, with a special focus on costs and needs), with no *a-priori* theoretical backgrounds. Grounded theory designs constitute an adequate methodological approach for this data-driven conceptualization effort because it uses the empirical (collected) data to generate concepts and theories, through a constant data-comparison process (J. M. Corbin & Strauss, 1990; J. Corbin & Strauss, 2012; Hussein et al., 2014; Radford, 2008; Wagner et al., 1968).

Data collection was done using semi-structured face-to-face focus groups, with constitute a form of group interview that promotes interaction and encourages focused communication between the moderator (i.e., the researcher/s) and participants. This is an adequate method for promoting participants to ask questions to each other, and to spontaneously exchange personal experiences and opinions on a given subject (Kitzinger, 1995; Quible, 1998).

2.2. Focus groups composition and participants

Focus groups were performed with Portuguese informal caregivers of person with dementia. The sessions were conducted with small groups, to give participants enough time to share experiences and perspectives. Informal caregivers were considered eligible for the study if they were adults taking care of a relative with dementia (formally diagnosed as having dementia). The sample was constructed with the intention of covering a wide range of caregiving experiences. For this purpose, the focus groups composition were heterogeneous regarding the stage of the relative's disease (i.e., including, in each focus group, caregivers of relatives in early and in advanced stages), participants with different ages, different family relationships to the person with dementia (e.g. spouse, daughter) and different professional situations. We also sought to have caregivers taking care of dementia patients for different durations per day and for different moments of the day.

2.3. Sampling and recruitment process

A non-probabilistic and purposive sampling approach was followed, with caregivers selected according to the inclusion and heterogeneity criteria described above. They were invited to participate from two different settings: upon a neurology appointment at the Centro Hospitalar Universitário Lisboa Norte E.P.E (reference university hospital for dementia) and following the presentation of the project at a nursing home, located in Lisboa, Portugal. Participants received oral/written information on the details of the study (goals and procedures) at an informal meeting, followed by dedicated information and the informed consent form. Before the beginning of the focus group, informed consents form was signed by each participant. Participants were also asked to provide some written background characterization info including basic demographic information and for how long they had been caring of their relatives.

2.4. Data collection

An interview script was developed, according to four main topics: i) participants presentation, including a brief narrative about the onset process of each caregiver career (type of family relationship with the person suffering from dementia, for how long they had been caring their relatives); ii) living with dementia and main adaptations in caregivers "normal" routine; iii) experiences and concerns related to the personal and family's financial impact of dementia; iv) expectations for improving the task of caring for a person with dementia, not only to promote better care for the affected relative, but also to promote caregivers' quality of life *(see Additional file 3.1of Supplementary material* for the interview script and questionnaires applied to the caregivers).

The focus groups were conducted by two experienced and trained researchers, one as moderator who fostered an active and open discussion, and the other as a co-moderator. A third researcher was also present to ensure written annotations (field notes) for each session. Focus groups took place between November 2019 and December 2019. Most part of focus groups took place at the Institute of Environmental Health of the Lisbon School of Medicine (ISAMB-FMUL); only one was conducted in a day center facility, located in Lisboa, Portugal.

2.5. Data analysis

Focus groups were fully transcribed and the content analysis was performed MAXQDA 2020®. After a first reading of the corpus (composed by the transcriptions of all focus groups), which promoted an intuitive first set of analytical codes, the open coding evolved to a line-by-line type analysis (Radford, 2008). The chosen unit of analysis was participants' utterances (instead of each line), for each focus group, following a constant comparison process (between the whole corpus and each focus group section). This content analysis was done with two researchers, ensuring interpretation triangulation: one of the researchers who was involved in the content analysis has a background in dementia, the other has a background in psychology; both having training in qualitative research.

After completing the line-by-line content analysis, researchers examined the code system and similar concepts were collapsed into larger categories (axial coding). Finally, and taken also into account participants' sociodemographic information, a conceptual model was created linking the categories that emerged from the analysis (Radford, 2008).

Reliability was ensured by following the procedures for grounded theory studies outlined by Strauss and Corbin (J. M. Corbin & Strauss, 1990). Data were compared several times by the authors, providing a check for credibility. An executive summary was afterwards sent to the focus groups' participants, who were invited to comment and provide additional insight to the main results and conclusions of the content analysis. Their feedback was also used for the elaboration of this paper.

2.6. Independent review board approval and consent to participate

Ethical approval was obtained from the competent Ethics Committee (Centro Académico de Medicina de Lisboa - CAML) in October 2018. Participants were informed, verbally and through e-mail (or through mail, according to participants' preference), and the written consent form was signed. The participation was voluntary, and participants knew that they could withdraw at any time without any prejudice. To ensure participant's anonymity, a code number was assigned for each participant in the transcribed files and for matching between transcription contents and the short questionnaire with additional demographic data. Information having the potential to allow the identification of any participant was withdraw from the transcripts. Demographic elements were only used as a

context for interpretation the qualitative data and for describing (in an aggregated form) the involved sample.

3. Results

3.1. Description of the focus groups and participants

Fourteen caregivers attended the focus groups, in a total of four sessions. All participants were family members of PwD, the range of years since diagnosis varied between two to 15 years, 11 were woman, and the mean age was 81 years, varying from 70 to 92 years), (Table 3.1). Two of the PwD being taken care of recently moved to a nursing home, one was benefiting from formal home care for personal hygiene (due to the difficulties of the caregiver in performing those tasks), seven visited a day center and four did not benefit from any formal care services (Table 3.1).

Of the fourteen caregivers, 12 were female, the mean age at the time of the participation in the focus group was 64 years old (range: 39 to 84 years old). Eight were daughters of the PwD, one daughter-in-law, two husbands, one wife and two sisters. Eight caregivers had a university degree, three completed high school and three completed primary school. Four of the caregivers are professionally engaged (3 full-time and 1 part-time), four were unemployed and six were retired. Ten caregivers have been caring for their relatives over five years, six participants reported to spend more than 10 hours a day in tasks related to informal care (Table 3.1). Twelve were the only caregivers for their relatives, while two had additional support from other family members. One of the included caregivers did not live with the relative (who still lived alone) but maintained a very close monitoring of daily activities. Regarding caregivers' own difficulties, eight admitted to have had personal problems within last 6-12 months (Table 3.1).

Table 3. 1. Background characteristics of participants (n=14) and their relatives with dementia

Background characteristics	Number/ (%)	Background characteristics	Number/ (%)
Family caregiver (n=14)		**(Person with dementia) (n=14)**	
Age Average age (years): 63.5		Age Average age (years): 81.43	
Range: 39-84		Range: 70-92	
Gender		Gender	
Men	2 (14.3)	Men	3 (21.4)
Women	12 (85.7)	Women	11 (78.6)
Highest educational attainment		Highest educational attainment	
Did not complete any degree of study	0 (0)	Did not complete any degree of study	2 (14.3)
Primary school	3 (21.4)	Primary school	6 (42.9)
High school	3 (21.4)	High school	2 (14.3)
University	8 (57.2)	University	4 (28.6)
Relationship with Person with dementia		Years since diagnosis	
Daughter	8	Average (years): 6.14	
Husband	2	Range (years): 2-15	
Sister	2	Std. Deviation (years): 3.505	
Wife	1	Residence	
Daughter-in-law	1	Person with dementia house	8
Professional status		Caregivers' house	4
Full time employee	3 (21.4)	Nursing home	2
Part-time employee	1 (7.1)	Formal care services utilization	
Unemployed	4 (28.6)	Home care services (daily)	1
Retired	6 (42.9)	Day center (5-6h/day)	7
Time of care			
1 to 2 years	1 (7.1)		
3 to 5 years	3 (21.4)		
More than 5 years	10 (71.4)		
Daily hours of care (in the last 30 days)			
Less than 1 hour	2 (14.3)		
2 to 4 hours	1 (7.1)		
5 to 7 hours	3 (21.4)		
7 to 10 hours	2 (14.3)		
more than 10 hours	6 (42.9)		
Life problems in the last 6-12 months			
No	6 (42.9)		
Yes	8 (57.1)		
Does not specify the type of problem	1 (7.1)		
Death of a family member	2 (14.3)		
Health problems	4 (28.6)		
Several of the above	1 (7.1)		

3.2. Themes elicited from the content analysis

From the content analysis, the main themes identified (most cited/most coded) included changes in quality of life of the caregiver, costs related to dementia and the formal care services received (Table 3.2). The category "Changes in quality of life" was the most frequently referred to, accounting for 396 segments (6.43% of the total corpus' segments, all focus groups included), including: "Personal life", with 152 segments (2.47%),

"Caregivers' health", with 140 segments (2.27%) and "Emotional burden", with 104 segments (1.69%). The code "Costs related to dementia" covered 215 segments (3.49% of the total corpus) and the code "Formal care services received/lack of formal care support" covered 207 segments (3.36% of the total corpus). In this paper, only these themes are discussed in a more detailed way. For consulting the complete set of themes emerging from the content analysis, consider *Additional file 3.2 of Supplementary material.*

Table 3. 2. Content analysis: categories, themes and sub-themes

Category	Theme	Sub-theme
Quality of life Changes that affect physical, mental, and social well-being leading to disease, stress, depression, low sense of dignity, social isolation and anything different that a healthy status Changes in caregiver's personal life	Caregiver personal life	Personal activities renouncement Social isolation Life *in pause*
	Physical health	Tiredness Physical effort Sleep problems Postpone of own's health care
	Psychological health	Emotional stress Dealing with diagnosis Felling alone Decision making process
Dementia related costs Costs introduced by the disease that affect family overall financial budget – all the economic expenses that are related of the condition of dementia	Food issues	
	Hygiene issues	
	Electricity	
	Medication/medical exams	
	Formal care	Day center Nursing home Formal caregiver
	Transport	
	To cheat person with dementia	
	Lack of financial support	
Formal care services Changes daily routine related to formal care services (home care support, formal caregivers, day center, nursing home)	Home support services	Support in personal hygiene
	Day center	Positive /negative aspects
	Nursing home	Positive /negative aspects
	Barriers to access formal care	Costs Limited spaces Long process Person with dementia will/preferences Transport/road accesses
	Lack of formal support	Targeted care for person with dementia

3.2.1. Quality of life

Across all focus groups, caregivers' perceptions focused aspects related to their quality of life *(Table 1 of Additional file 3 of Supplementary material* for more examples)*:*

- *"There is no quality of life at all …"*, Caregiver, female (daughter), Focus group A, line 1374.

In fact, the changes that taking care of a person with dementia brought to the personal life of caregivers were thought of as highly relevant, leading to complex adjustments at several levels: i) professional changes:

- *"So in the beginning, let's say it was a bit difficult, because I was working, I worked at night, […], so now I work in the morning so that I can be with her* [the mother] *at night …",* Caregiver, female (daughter), Focus group D, lines 5460-5462;

- *"Yes, I suspended my activity, yes...",* Caregiver, female (daughter), Focus group C, line 4201.

ii) couple's life commitment and household changes:

- "[Problems with…] *my husband, yes... In fact, great contradictions in terms of managing the* [caring] *situations, and today I would say no, that I would not accept...* [receiving the in-laws in her house]*.",* Caregiver, female (daughter-in-law), Focus group C, lines 5155-5156.

iii) social isolation:

- *"(…) our social life disappeared completely, because our friends do not go to my house anymore, I stopped inviting people to go there…",* Caregiver, female (daughter-in-law), Focus group C, lines 4697-4699;

- *"My friends don't want to know...",* Caregiver, female (daughter), Focus group C, line 4701;

To avoid loneliness, some caregivers tried to include the patient in their social activities (which could be beneficial for both). However, the patient's behaviour can bring difficulties:

- *"(…) we went out for dinner, twice, and then he panics, he panics, I had to leave and my daughters stayed at the restaurant... Now, I never go out to have dinner with my daughters …",* Caregiver, female (wife), Focus group C, lines 5265-5267.

Over time, caregivers are entirely moved away from their personal life and, in most of the cases, the social isolation and feeling of abandonment due to the loss of old friendships can be meaningful.

The routine of caregivers can drastically change when the caregiver has to leave their house to stay in their relative's house (the most common situation, Table 1). Most of the participants admitted being single caregivers, which resulted in having no spare time for themselves, for having activities besides caring. Some caregivers even expressed their sadness for having stopped doing their usual activities, putting their life in "standby"*:*

- "*(...) I will never have a life of my own again…",* Caregiver, female (wife), Focus group C, lines 4645-4646;

-"*(...) I travelled almost every year, […] we had a group of friends and we travelled, now I don't do that anymore…* Caregiver, female (daughter), Focus group D, lines 6646-6647.

Caregiving tasks and routines had also major impact in both the physical and the psychological health of participants who affirm to be very tired:

- *"Exhausted! Completely exhausted! […] I have health problems too (...)",* Caregiver, female (daughter), Focus group B, lines 3574-3575.

Being the only caregiver also led them to postpone their health care. They are continuously worried about their relative's well-being and their own health come second and most of the participants admitted having faced health problems:

- *"A person does not have time for anything, anymore. I need to go to the doctor and I won't (...)",* Caregiver, female (daughter), Focus group A, lines 1905-1906.

Some participants referred that the moment of diagnosis brought high emotional stress with some of them expressing the necessity to receive more information and guidance. Learning more about the disease evolution was reported to could be felt as useful so they can be prepared to better deal with specific situations, while reducing the related burden. Not being recognized by the relative with dementia is something that scares and saddens the caregiver.

- "(…) *At that time, it was a shock for me...",* Caregiver, female (daughter), Focus group D, line 5428;

- *"(...) in the beginning, it was not explained to me what Alzheimer's was...",* Caregiver, female (daughter), Focus group D, line 5431;

- *"I would like to learn more about everything because a person starts from scratch!",* Caregiver, male (husband), Focus group C, line 4847.

- "(…) *I thought, "Okay, will my mom forget me?" ... It was one of the things that I was afraid of (...)",* Caregiver, female (daughter), Focus group D, line 5433-5435.

Keeping up the daily routine was a widely discussed topic as something that the person with dementia needed to be involved in, on their daily lives, so s/he may feel well:

- "*They need routines, that's what I notice, anything ...",* Caregiver, female (daughter), Focus group C, line 4548.

The night period is the moment of the day that demands more from participants. Some person with dementia can become very agitated, walking around the house and turning the lights on, which was referred to as having negative implications for the caregiver's sleep and rest:

-"(…) *I can rest a little during the day, I don't get enough sleep at night, I don't sleep more than four hours straight (...)",* Caregiver, male (husband), Focus group A, lines 853-854.

Altogether, the insufficient rest, the large amount of duties, the delay of self-health vigilance and the absence of personal/social life, were referred to highly contributed to a negative impact in caregivers' quality of life.

3.2.2. Dementia care-related costs

The topic of dementia care-related costs was raised altogether with daily challenges and experiences *(Table 2 of Additional file 3 of Supplementary material).* All participants expressed their general disappointment for the excessive lack of financial and social support, both for the person with dementia and the caregivers. However, there are

significant financial costs, as participants admitted to spend their life savings month by month, due to their caregiver function, which is seen as a potential difficulty for the future:

- "*I am putting my money, at the moment, […] it is money that I may need someday, right?... I'm putting around €400...*", Caregiver, female (daughter), Focus group D, lines 6598-6599.

Having an economic support was, therefore, highlighted as an important aid for participants. This is especially relevant because most of the participants were retired or not working (also due to their caregiver status, non-compatible with a paid professional activity), which significantly reduced their monthly income. The access to financial assistance, available from the Portuguese State from which they can benefit is referred to be very bureaucratic, hard to obtain and not covering all the expenses. Overall, participants have to pay the daily expenses such as food, hygiene products, house bills and medicines and, only in some situations receive some family support:

- "*The worst are the costs! That's right! For the costs* [formal care services]*, they ask us between €900-€1000/month… where do I get it from? I have things to pay, I have water, electricity, telephone, gas bills... Not to mention food, shoes, clothes and medicines... If I take these €900 or €1000/month, I get...nothing! And what do I do with the rest of the other things?",* Caregiver, female (daughter), Focus group D, lines 6613-6616;

- "(…) *I can't take €1000/month to pay a woman* [formal caregiver] *...",* Caregiver, male (husband), Focus group A, lines 1898-1899;

Also, hygiene products (e.g., the need for diapers and wet cleaning wipes) and medicines is described as a high burden:

-*"(...) Just for medicines, just for my husband, I spend €150 a month… apart from my own medication, which I am no longer counting!"*, Caregiver, female (wife), Focus group C, lines 4313-4315;

- *"Much* [money]*! And then more wet cleaning wipes […], her hygiene must be more, more than just diapers*!", Caregiver, male (husband), Focus group A, line 1510.

To reduce the monthly financial burden, some caregivers resort to generic medication, which is negatively perceived by caregivers:

- "(…) *It is like this...it is generic medication, if it is not generic, it is a lot of money! I had to go to a generic brand! ...Unfortunately!",* Caregiver, female (daughter), Focus group A, lines 1538-1539.

A similar problem relates to the net difference between the total amount of the monthly income from person with dementia retirement pension and the costs of needed formal care services, which is considered, by participants, as unaffordable:

- *"(...) My mom has a €400 pension, [...] If you are going to pay €1000/month by the nursing home it is a shame! It is a shame!",* Caregiver, female (daughter), Focus group C, lines 5083-5084;

-*"There is a big problem here, I think, of pensions, for the majority of the Portuguese, who are poor, and €500* [of pension] *is already a lot of money,(...)",* Caregiver, female (daughter), Focus group C, lines 4322-4323.

The lack of financial support for these patients and their caregivers was extremely evident and discussed, with caregivers sharing their multiple attempts to request financial help. The caregiver finds him/herself alone, without psychological and financial support and without adequate formal answers for their daily problems:

- *"I did not have any help, I have not received it, that's what I think I should claim that there should be. I learned that there is not, and even if the person searches and searches… There is not. I felt completely naked, in the sense of, the person looks for something and there is not!",* Caregiver, female (daughter), Focus group B, lines 3512-3514;

- *"(...), my brother* [person with dementia] *does not have any financial support…I think that he really needed…",* Caregiver, female (sister), Focus group A, lines 1970-1971.

Some caregivers exert parsimonious management of their mensal budget, avoiding some expenses (e.g. social and leisure moments, medical appointments). Other costs were reported by caregivers *(Table 2 of Additional file 3 of Supplementary material)*, such as high electricity bills related to the daily need of laundry all the linen and the patient's clothes. Earlier stages of illness revealed an extra and unexpected expenses, such as frauds or thefts, more easy to happen due to patient's state of confusion. Indeed, different events

were provided as examples of how easy it is by strangers to take advantage of person with dementia conditions. Another example of loss of money are the situations where the person with dementia is deceived and encouraged to sign service loyalties (for instance mobile and internet plans) which they could not use and that resulted in large losses of money.

Overall, considering the weak economic environment of caregivers due to a lack of adequate financial support, high costs related to dementia care and the difficulty to be employed or having a part-time job, the financial burden is an important issue that caregivers face, besides the caregiving tasks.

3.2.3. Formal care services

Many caregivers expressed their opinion regarding the problems in having access to formal care services *(Table 3 of Additional file 3 of Supplementary material)*. One of the first obstacle was participants' previous negative experiences and stigma involving nursing homes, that were often not considered as a good option in what concerns long-term care for their relatives:

> - *"They* [the person with dementia] *did not even come outside* [to the gardens]*... that was a deposit* [of people]*... […] That shocked me and I took her* [out of there]*..."*, Caregiver, female (daughter), Focus group C, lines 4139-4140.

Some caregivers admitted the possibility to only rely on a nursing home when they find the nursing home having the adequate conditions. However, in their opinion, good services at a reasonable cost do not exist, which is regarded as a main barrier for taking their relatives there:

> -*"It depends on the nursing home, if I find a good home for a reasonable cost within the budget that my mother can afford to pay […], but the problem is that there is nothing like that...",* Caregiver, female (daughter), Focus group C, lines 5114-5115;
>
> - *"It is also out of question, monetarily, you see…* [reason to not consider the nursing home]*",* Caregiver, female (daughter), Focus group C, line 5100.

Even when a nursing home is the most adequate solution, the fear and mistrust regarding this type of institution can hinder the decision towards institutionalization:

- *"(...) mine* [her mother] *will not go to a nursing home, […] She is afraid!",* Caregiver, female (daughter), Focus group A, line 2949.

So, institutionalization is considered a resource for person with dementia only at advanced stages of the disease (when not having other alternative). This solution is seen as a failure of caregivers' responsibilities (since, culturally, to care for family members is considered by participants as a family duty), with the decision-making process of opting by institutionalization described as very hard:

- "(…) *I was tired of crying because it was going to be hard for me* [the moment of her mother's institutionalization] *...It was too far from my house (...), you know?,* Caregiver, female (daughter), Focus group B, lines 2627-2630.

The long bureaucratic process, the limited number of available places (in nursing homes), the distance from home and long waiting periods to be accepted by nursing homes, all these were also seen as strong reasons for not prefer to taking their loved ones in a nursing home:

- *"(...) today I don't have this document, tomorrow I don't have another one, then another one is missing, it's just bureaucracy!...",* Caregiver, female (wife), Focus group C, lines 5103-5104;

Summing up, the patient admission to nursing homes is regarded as a difficult, time-consuming, and a painful process. Therefore, most participants tend not to consider this as an option. However, despite of the mentioned hurdles, when considered, the institutionalization brings a new opportunity for caregivers to regain their live:

- *"I now feel calmer, because I was always nervous and anxious […] and I feel that I have more time to do things that I did not have before…",* Caregiver, female (daughter), Focus Group B, lines 3527-3529.

Formal care services, such as home-based support care was welcomed by participants, that found in these a good solution for taking care of the personal hygiene of their relatives, especially when they had physical limitations. Additionally, having their relatives in a day center (5-6hours/per day), allow then to have some spare time for shopping, attend medical appointments, do physical activity, or rest:

-*"Yes, as they entered the day center that brought me back time for my yoga, for going to the gym and got my* [head] *back to work, I think, normally...",* Caregiver, female (daughter-in-law), Focus group C, lines 5140-5142.

At the same time, attending the day center was positive also for the persons with dementia, since they get to be engaged on social activities, create a routine while remaining in a safe environment, which is a relief for caregivers:

- *"[...] they have activities, they have gymnastics, they can cook, [...] they go for walk, they attend to theatre shows [...]! So, my mom has now a more busy social life than I do! (laughs*)", Caregiver, female (daughter), Focus group C, lines 4974-4977.

Another emphasized characteristic of day centers (although this happens only in a minority of them) is to have specific locations dedicated to person with dementia, with closed doors. This was very emphasized by the participants as an aspect of major importance for their relief and their relative's well-being:

- *"As in my case, my sister left one day* [run away from the day center] *... So, she is now here* [closed door floor, in the day center where the focus group was running]*, precisely because there is absolutely no danger..."*, Caregiver, female (sister), Focus group C, line 4150 and 4154.

Overall, day care centers were mostly referred as very positive for the daily lives of both patients and caregivers, and it was only regrettable, by participants, that only a minority of facilities is truly adapted and directed towards people with dementia needs.

3.3. Roadmap of factors affecting caregivers' daily life experiences and quality of life

Based on the coding system, frequency of codes and a review of the quotes sorted by category, a model was developed to better describe the burden of dementia in caregiver's daily experiences quality of life (Figure 3.1). Caregiving experiences shared by participants revealed that the process of caring of a person with dementia has an enormous impact at several levels: individual, familiar, social and professional.

The psychosocial characteristics and interpersonal skills of the person with dementia, as well as the general health and the progression of the disease define an important part of informal caring since it can mean more or less burden to the caregiver. During the process of care, the related costs of dementia and the high number of barriers to access formal care services can significantly modulate the impact of caregiving in caregiver's quality of life.

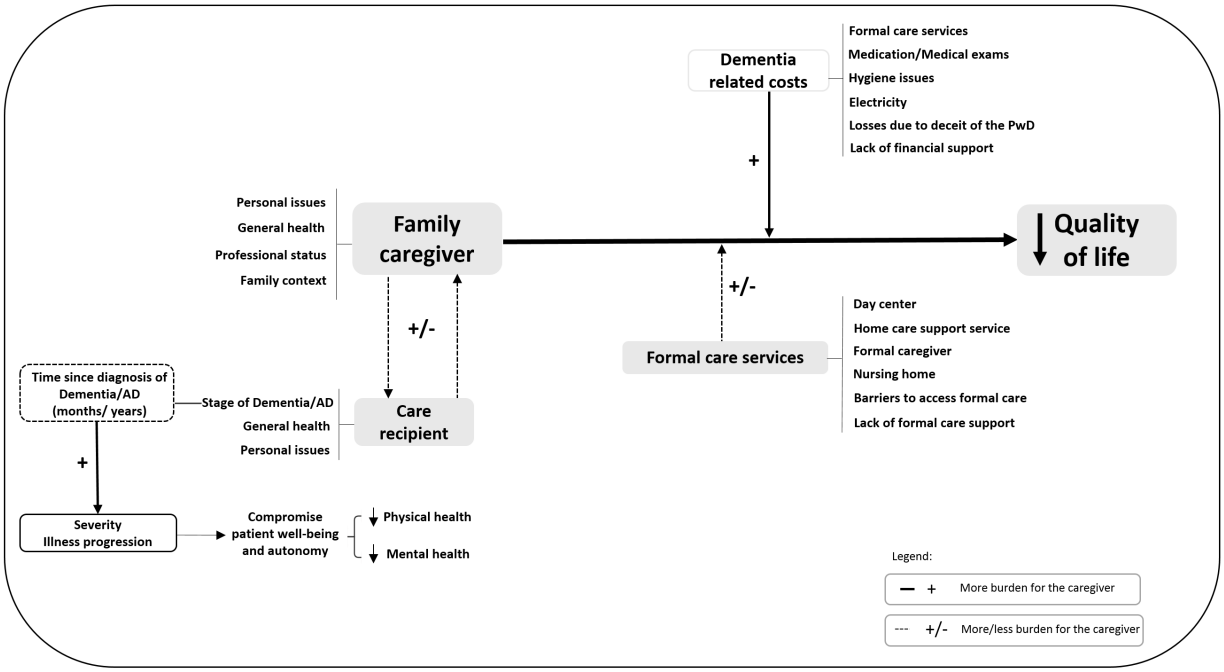


Figure 3. 1. Informal care impact to caregiver's quality of life

4. Discussion

This study aimed to explore the perceptions of informal caregivers about the experience of taking care of a person with dementia, to better understand its costs on different dimensions. Overall, the financial costs, the lack of perceived adequate support from formal care services, profoundly disrupted by the emergence and aggravation of dementia-related conditions have a tremendous impact on caregiver's quality of life.

Being a full-time caregiver for a person with dementia significantly change the caregiver's life. The moment of diagnosis comes unexpectedly, despite the slow onset of symptoms. After the diagnosis, the need of vigilance and help to perform everyday tasks

require the presence of the closest family member. As described in other studies, we also found that the daily difficulties tend to worsen as the disease progresses to its latter stages (Karlin et al., 2001). The duration of care in our study ranged from 2 to 15 years, with different difficulties related to the stages of the disease. The physical burden was present as early as the caregiver assumed his/her role, showing that caregivers physical well-being is widely affected from the beginning of care and worsen with time. The postponement of their health care monitoring due to the excessive time dedicated to taking care of the person with dementia increases the probability of caregiver's own health issues, that may later evolve into serious health problems. Physical tiredness can be explained with the effort required to perform strenuous tasks such as personal hygiene, helping to get up/out of bed and dressing/undressing the patient. Also, most of the participants had health problems, and several referred that the resulting sleep deprivation tend to affect caregivers' well-being. Indeed, sleep disturbances in caregivers of person with dementia has been a well-studied issue and findings from Peng *et al*., indicated that more that 90% of the caregivers had poor sleep quality (Peng & Chang, 2013). This is in accordance with our study that show that, even when the caregivers were younger, the severity of health conditions did not decrease when compared to the rest of the participants and sleep deprivation was always present. So, more years of care revealed a more tired and lonely caregiver, with less physical and psychological capacity to continue the role. In line with the study Greenwood et al. 2019*,* which discusses topics related to the main worries expressed by caregivers participating in our focus groups, concern about what happens to person with dementia when caregivers can no longer care (due to age or health complications), this concern was verbalized by the participants in our study, mainly when caregivers were the only family members available to care for the relatives.

According to the narratives gathered in our study, not only physical health, but also the psychological well-being of caregivers was compromised throughout the caregivers' career. This has been documented in several other studies: dementia seems to modify the quality of life of caregivers, with serious impairment on psychological health due to the daily emotional stress and burden experienced during care (Bruce et al., 2008; Etters et al., 2008; Koca et al., 2017; Vasileiou et al., 2017). In the process of care, most of the caregivers day is dedicated to the person with dementia; the caregivers' personal and social life is put off, leading to social isolation, with feelings of loneliness being typically reported (Grunfeld et al., 2004; Vasileiou et al., 2017). In our study, most of the caregivers

were single caregivers and receive few if any help from family members, constraining their time to caregiving tasks only. However, when other family members are present, caregivers can use some time to do their own activities, like going for a walk, shopping or being with friends. Supporting the caregiver on its role is crucial, since there is evidence suggesting that caregivers of persons with dementia are more exposed to suffer significantly higher levels of psychological morbidity and stress (Connell et al., 2001; Gilliam & Steffen, 2006; Livingston et al., 1996). This fact might be related to the emotional impact of dementia in caregivers, that are aware of the physical and mental decline of the patient. Moreover, due to the familiar bounds, witnessing disease progression and not being recognized by the relative with dementia seems to be one of the hardest things to manage for the caregivers included in our study.

The person with dementia is widely compared to a child, given the need to be continuously cared and attended (Karlin et al., 2001; Kramer & Lambert, 1999). This phenomenon of reversing or modifying roles (the daughter/son caregiver becomes the mother/father of the person with dementia; the wife/husband that becomes mother/father) was something considered as tough to deal with, especially when the caregivers had their own daughters or sons, due to the great effort required to this multifaceted aspect of care. Additionally, since caregivers are frequently women, there is the responsibility to take care not only of the family, but also of the home-related issues like cooking, cleaning, and so on. So, due to all chronic and emotional strains, caregivers may undergo emotional exhaustion and burnout, as previously highlighted in other studies (Alfakhri et al., 2018; Takai et al., 2009).

In our study, caregiving has a typical learning curve. After the initial shock, with time caregivers start to learn how to handle the daily struggles, while adapting his/her own personal and professional life. However, this adaptation requires that caregivers become fully dedicated to the care of the person with dementia. The fact that caregivers are unaware of the behavioral changes that the person with dementia might develop with the disease progression, seems to make it harder to handle with the aggressivity, hallucinations and constant humor change. Evidence suggests that there is a strong impact on the quality of life of caregivers with the increasing of behavioral symptoms (Arthur et al., 2018). Besides, the constant mood fluctuations of patients can thoroughly change the daily routine, since the patient can be more receptive to contribute or not with eating, bathing, walking, and so on. This permanent instability also contributes to the caregiver's physical and emotional stress.

An interesting study showed that the caregivers consider that: ensuring the safety of the person with dementia and managing their own stress are goals that can transform their task into a more positive and less impacting task (Jennings et al., 2017). This is in accordance with our results since relative's safety was of high importance for the caregivers, as well as, learning to deal with their own stress and emotions.

Another widely explored and consensual theme in the literature was the financial burden that dementia brought to the family and caregivers (Åkerborg et al., 2016; Kronborg Andersen et al., 2003; Moore et al., 2001). The high costs of dementia turns this disease into one of the most expensive for families, due to the need of a full-time caregiver. When the caregiver is the closest family member, it might involve professional changes (reduction of working hours /quit jobs), and consequently, lower financial income. Despite that, it is culturally accepted, in Portugal, that caring for the loved ones is a duty of the family, and besides the negative aspects that it brings, the caregivers of our study tend to choose caring for the person with dementia over institutionalization. Caregivers participating in our study shared the fact that they need to use their life savings to cover for the expenses related to dementia, with an obvious impact on families sustainability for the future. So, caregivers need not only to care for their relatives but also to ensure the economic income to cover all the related costs.

Interestingly, caregivers who participated in our study were practically unaware of how to obtain support from the national health and welfare system. Even when they knew how to and attempted to do it, they faced a long and bureaucratic course to unfinished paperwork and no support, being referred as a demotivating process. The expressed misinformation on financial support is in line with the results from previous studies which show the lack of professional support and guidance in this particular area (Lethin, Hallberg, et al., 2016; Stephan et al., 2018). Additionally, this lack of support and information occurs from the moment of diagnosis and initial stages of disease. After the diagnosis, caregivers expected more help from health professionals, in terms of description of the disease progression, what to expect and how to deal with the disease. Instead, caregivers reported they had to learn all about dealing with dementia by themselves, making the task harder.

The most difficult financial cost for all caregivers to bear was related with formal care services and, particularly, the cost with nursing homes, as described in other studies (Ku et al., 2016; Vossius et al., 2014; Zhu et al., 2015). This obstacle, together with the common

negative opinion about nursing home services, resulted in a huge barrier that pushes nursing homes to the last resort for caregivers (Stephan et al., 2018). Some caregivers expressed their astonishment on the possibility to apply to formal care assistance, because they were already in financial distress and could not consider the costs of these services. Interestingly, one of the cheaper formal care services available (day centers), were the best suited solution for the included caregivers, due to their better adaptations to cover dementia patient specific needs ensuring their safety.

A study from Tretteteig *et al*., highlighted the importance of day centers in meeting the person with dementia' needs, namely when allowing social integration, nutritional balance, physical activity and daily regular routines (Tretteteig et al., 2017). The fact that day centers helped to reduce the patient aggressiveness episodes and, indirectly, helped caregivers by reducing the associated burden was previously documented and also present in our study (Tretteteig et al., 2017). The positive appraisal by caregivers and great impact on patient's well-being, should prompt studies that explore the relevance of day centers adapted for person with dementia in society. The relevance of nursing homes and formal caregivers was seen, by some of the participants of our study, with disappointment and distrust due to the inadequate adaptation to patient needs and caregivers' financial budget. The opinion that nursing homes are not prepared for person with dementia and the need of some adaptation to support the course of dementia is shared in other studies (Lethin, Hallberg, et al., 2016; Stephan et al., 2018; Xiao et al., 2013).

Costs of medications and medical exams were referred as a relevant source of expense in our study and widely published in literature (Zhu et al., 2016). To overcome that, caregivers' resort to the cheaper drugs on the market: generic medicines. Still, consumption of this medication in Portugal is below EU average, which may be related to: the level of education, low health literacy and lack of information by clinicians (Efpia, 2020; Quintal & Mendes, 2012). To decrease the negative appraisal on this topic, more information and prescription should be encouraged, particularly when the caregiver itself also has health problems, resulting in a large monthly expense.

According to the present study, the task of caring for a person with dementia requires a comprehensive plan that might gather and articulate support at different levels (including social, financial, juridic and psychological), for both the caregiver and the person with dementia. So, a partnership among clinicians, healthcare workers, social workers and family members is required, endorsing a systematic and integrated experience of caring for person with dementia. Caregivers' perceptions about the related costs of dementia

caregiving are crucial to develop target interventions for this community and to reduce the negative effects on caregiver's quality of life, while maintaining a good care and promoting patient's quality of life as well.

An effective and sustainable informal healthcare approach, focused on the early promotion of caregivers' skills (i.e., with training and dementia care related literacy promotion, starting as soon as the possible when the patient is diagnosed), closer medical monitoring and optimized financial support is needed to contribute to caregiver's well-being, improve formal care response and minimize the familiar financial burden caused by dementia. A home program such as the "Going to Stay at Home" is the perfect example of a feasible and practicable model that helped both caregivers and persons with dementia, delaying the institutionalization over 12 months, while decreasing the unmet needs and behavioral symptoms in persons with dementia (Gresham et al., 2018). Additionally, also the caregiver's and patients' unique clinical and personal aspects are important, showing the need of custom interventions to meet the specific needs of each family (Holland et al., 2009). Knowing that the number of people suffering from dementia is expected to increase in the coming decades, multidirectional interventions and programs are needed to prevent a future burden and impact in informal caregivers of people with dementia.

5. Conclusion

Dementia informal care include a wide range of experiences referred by the caregivers about the disease and about the proper way of caring, as well as the drastic changes introduced in their personal lives. These experiences represent themselves important difficulties that may hinder a proper care for the person with dementia. Caregivers' perceptions about the related costs of dementia caregiving are crucial to develop targetted interventions for this community and to reduce the negative effects on caregiver's quality of life, while maintaining a good care and promoting patient's quality of life as well.

6. Strengths and limitations

The strength of this study is the description of the phenomenon of caregiving of a person with dementia through informal caregivers' views, focusing their daily life experiences.

The main limitations of this study were: a) the scarce time of caregivers conditioned by the severity of their relatives disease , leading to the inevitable exclusion of the most severe cases (caregivers of persons with dementia in advanced stages); however, caregivers of different stages of disease where included in this study; b) the focus on a single urban area of the territory; however, the sample included different living situations, familiar relationships, ages, professional status of the caregiver, different times of diagnosis and stages of severity to be as much representative of the phenomenon as possible; c) the relatively small sample size; notwithstanding, this has been an average size sample in similar studies.

7. Funding

This work was funded by the “Fundação para a Ciência e a Tecnologia (FCT)” Portugal and Merck Sharp & Dohme Portugal, under the grant number PDE/BDE/120498/2016.

8. Availability of data and materials

The dataset supporting the conclusions of this article is included within the article (and its additional files 1 and 2 of Supplementary material."

9. Ethics approval and consent to participate

All procedures performed in the study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Participants voluntarily enrolled in the study. Participants had been given time to read informed consents and were only enrolled after providing written informed consent. This study was approved by the competent Ethics Committee (Centro Académico de Medicina de Lisboa - CAML) in October 2018.

Acknowledgments

The authors acknowledge “Fundação para a Ciência e Tecnologia (FCT)” Portugal and Merck Sharp & Dohme Portugal (grant number PDE/BDE/120498/2016). We are also grateful to all the participants and National Institutions of Formal Care involved in the study.

Author’s contributions

PL recruited and invited the participants. OS and PL moderated the focus groups. AV took written annotations in the field. PL, AV and OS transcribed and analysed the data. All authors were responsible for the study conception, design, drafting and reviews the manuscript. MMR and MG supervised the study.

Author Biographies

Patrícia Lindeza has a Biomedical Sciences background and is a PhD student on Environmental Health at *Instituto de Saúde Ambiental (ISAMB), Faculdade de Medicina, Universidade de Lisboa, Portugal*. Her research interests include health and social care, dementia research, quality of life and people’s experiences of living with dementia patiens. She started her PhD trajectory with a publication on the impact of dementia on informal care, and this article is part of her PhD work.

Ana Virgolino is a Clinical and Health Psychologist and she is currently working as a research fellow at the *Instituto de Saúde Ambiental (ISAMB), Faculdade de Medicina, Universidade de Lisboa, Portugal*. Ana has been responsible for the management and supervision of several scientific nationally and internationally funded projects in the areas of environmental and public health. She has also been involved as researcher in more than twenty projects in the same fields. Throughout her career, she as received several awards for the excellence of her work.

Osvaldo Santos is a Clinical Health Psychologist and cognitive behavioural psychotherapist. He is the coordinator of the Environmental Health Behaviour (EnviHeB) Lab of the *Instituto de Saúde Ambiental da Faculdade de Medicina da Universidade de Lisboa, Portugal*. He is the coauthor of more than 60 papers, several chapters of books, and five books, mainly in the areas of health psychology and environmental health. Throughout his career, he has received several awards for the excellence of his work.

Manuela Guerreiro is a Psychologist, graduated in psychology at *Faculdade de Psicologia da Universidade do Porto, Portugal* and a doctorate in Biomedical Sciences from *Faculdade de Medicina da Universidade de Lisboa, Portugal*. She is a professor and researcher in neuropsychology of ageing and dementia and belongs to *Faculdade de Medicina da Universidade de Lisboa, Portugal*. She has participated in several clinical trials in dementia and has published articles in international journals.

Mario Miguel Rosa, MD, PhD is a neurologist and clinical pharmacologist, head of the Movement Disorders clinic at the Neurology Dept. of Centro Hospitalar Universitário de Lisboa Norte, and Professor of Neurology and Clinical Pharmacology at the Faculdade de Medicina da Universidade de Lisboa, Portugal. He is an investigator at the Instituto de Medicina Molecular (IMM), Lisboa, Portugal, with interest in clinical studies methodologies and safety. He is also a member of three Ethics Committees for Science and Health, and a Member of the Central Nervous System and of the Scientific Advice Working Parties at the European Medicines Agency.

Supplementary material

The dataset supporting the conclusions of this article is included within the article (and its additional files 3.1 and 3.2 of Supplementary material).

Additional file 3.1:

Table 3.1 - Focus group participant quotes - caregiver changes in quality of life
Table 3.2 - Focus group participant quotes - positive and negative aspects of formal care services
Table 3.3- Focus group participant quotes - dementia informal care related costs

Additional file 3.2:

-Informed consent of the participants
-Information leaflet of focus groups
-Focus groups guide
-Final report sent to participants with main results

CHAPTER 4

QUALITY OF LIFE AND FUNCTIONAL ABILITY OF OLDER ADULTS LIVING WITH DEMENTIA: OUTCOMES OF A PORTUGUESE SAMPLE

STUDY FRAMEWORK

Following previous studies, it was important to have an overview of the proxy-reported quality of life and functional/cognitive ability for a Portuguese sample of persons with dementia by their informal caregivers. This is of major importance since ageing of population is a worldwide reality and Portugal is one of the most ageing-leading countries. Several European studies describe the impact of dementia, reporting low QoL in PwD and caregiver's psychological and financial burden (e.g. Argimon et al., 2005; Beerens et al., 2014; Bruvik et al., 2012; Janssen et al., 2017; Jones et al., 2015; Lethin et al., 2020; Schiffczyk et al., 2010; Selwood et al., 2005; Serrano-Aguilar et al., 2006). In fact, this study attempts to fill the gap that involves the lack of knowledge about the impact of dementia in QoL and its relation to the functional/cognitive ability of PwD, particularly, in Portugal. For that purpose, we wrought to assess quantitatively the quality of life and functional/cognitive levels of PwD in Portugal, while describing sociodemographic data not only about patients, but also about their informal caregivers through face-to-face semi-structured interviews and questionnaires answered by the informal caregivers of PwD. We found that the included PwD presented extremely low levels of QoL and moderate to severe impairment on their functional and cognitive ability, being highly affected by dementia as it progresses.

The following study was performed by **Patrícia Lindeza (PL)**, Lara Noronha Ferreira (LNF), Manuela Guerreiro (MG) and Mário Miguel Rosa (MMR).

PL recruited and invited the participants. PL created the database. PL and LNF treated the data. All authors were responsible for the study conception, design, drafting and reviews the manuscript. MMR and MG supervised the study.

Lindeza P, Noronha F, Guerreiro M, Rosa MM. Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample. Ageing & Society *(submitted).*

QUALITY OF LIFE AND FUNCTIONAL ABILITY OF OLDER ADULTS LIVING WITH DEMENTIA: OUTCOMES OF A PORTUGUESE SAMPLE

ABSTRACT

Introduction: Dementia has become a growing health-care problem in the rapidly ageing worldwide population. This study assesses the impact of dementia and the possible factors involved in health-related quality of life (HRQoL), functional ability and cognitive impairment of persons with dementia (PwD), while describing their living situation.

Methods: Descriptive cross-sectional design with a non-probabilistic and purposive sample of 187 PwD and their caregivers. Data collection included the EQ-5D-3L, Quality of Life in Alzheimer's Disease questionnaire (QoL–AD), Blessed Dementia Rating Scale (BDRS) and Mini-Mental Examination Scale (MMSE). Descriptive analysis and correlation coefficients were used to evaluate the PwD HRQoL by proxy. Multivariate linear models were estimated to identify determinants of PwD HRQoL.

Results: The results show that the QoL of the PwD was extremely low, as well as their functional and cognitive ability. The PwD educational level, the changes in everyday life and habits were identified as potential explanatory factors of HRQoL.

Conclusions: Our findings highlight that the overall context surrounding PwD should be taken into consideration during the course of disease. The low education level and the increasing dependency of the PwD in everyday life and usual habits can decrease PwD HRQoL.

Keywords: Dementia, Health-related quality of life, EQ-5D-3L, Health status, Informal care

1. Introduction

Dementia is a major public health that remains one of the greatest challenges faced by health- care and social-care systems worldwide (Banerjee, 2013; World Health Organization, 2012). It affects not only the individuals with the condition, who gradually lose their abilities with serious impact on quality of life (QoL), as well as their relatives, that care for them as their dependency increases (Livingston et al., 2017). One of the most prevalent subtypes of dementia, Alzheimer's disease (AD), is a progressive neurodegenerative disease characterized by the impairment of cognitive and functional abilities allied with behavioural symptoms (Douma et al., 2015; Duboisa et al., 2015). Consequently, dementia has a huge impact on society due to the high demand of informal, formal, psychosocial and financial support required (Brodaty & Green, 2002; Wortmann, 2012).

The population ageing worldwide will lead to a dramatic increase in dementia prevalence in the next decades (Shah et al., 2016). Dementia is usually associated with ageing, however the uncommon young onset dementia (YOD), that is defined as first symptoms before 65 years of age, can also occur, demonstrating that age is not always associated with dementia (Rossor et al., 2010). Previous research shown that the number of people with dementia (PwD) in Europe will increase to 18,8 million by 2050 (Alzheimer Europe, 2019). In the last years, the World Health Organization (WHO) presented reports concluding that dementia should be regarded as a global public health priority due to its fast-growing worldwide (Orellana, 2003; World Health Organization, 2012). Dementia is nowadays a global research primacy and the past two decades have seen remarkable improvements in research studies that better describe the QoL in dementia (Shah et al., 2016). In PwD, QoL involves cognitive functioning, activities of daily living, social interaction and psychological well-being (Keating & Gaudet, 2012; Whitehouse et al., 1997). So, studies regarding QoL in dementia must resort to different instruments that incorporate relevant factors such as emotional, physical and social functioning and lifestyle (Bowling, 1997; Mack & Whitehouse, 2001). Several European studies describe the impact of dementia, reporting low QoL in PwD and caregiver's psychological and financial burden (e.g. Argimon et al., 2005; Beerens et al., 2014; Bruvik et al., 2012; Janssen et al., 2017; Jones et al., 2015; Lethin et al., 2020; Schiffczyk et al., 2010; Selwood et al., 2005; Serrano-Aguilar et al., 2006). A recent study including seven

European countries revealed that the psychosocial well-being, living environment and family care were important aspects that maximize patient's health and well-being (Lillo-Crespo et al., 2018). Additionally, a remarkable positive aspect of Portugal was the existence of training programs for informal caregivers, however, a negative point was its lack of dissemination in the community (Lillo-Crespo et al., 2018). In the case of caregivers of persons with YOD, a recent study described that its caregivers face particular challenges due to the lack of age-appropriate services and specific information (B. Jones et al., 2018).

Despite the increasing prevalence of dementia worldwide, published studies from Portugal or including Portuguese data are scarce; therefore, Portugal is a step behind of the most developed western countries, regarding some sociocultural indicators for dementia (Instituto Nacional de Estatística IP, 2012). Portuguese epidemiological studies indicated that the prevalence of dementia varied from 2.4% to 9.23% depending on the methods and criteria applied (C. Garcia et al., 1994; Manuel Gonçalves-Pereira et al., 2017; Gonçalves-Pereira et al., 2016; Hofman et al., 1991; Nunes et al., 2010; I. Santana et al., 2015). However, due to its publication date, most of these studies are probably outdated. A recent study of 2018 based in a population-based cohort from northern Portugal, assessed the prevalence for mild cognitive impairment (4.1%) and for dementia (1.3%), with vascular dementia being the most prevalent type of dementia (52.8%), followed by AD (36.1%) (Ruano et al., 2019). On the other hand, Portugal's absence of multicenter studies, such as EURODEM or EURODEP highlight the need for uniformized studies that allow for international comparisons (J. R. M. Copeland et al., 1991; Prince et al., 2007). Recently, in the Dementia in Europe Yearbook, the population data of Portugal is described as having a relevant decrease until 2050, however, the overall numbers of people with dementia will more than double reaching 346,905 (3.82%) by 2050 (Alzheimer Europe, 2019). The estimate of dementia prevalence in Portugal exceed the broader European trend, probably due to the number of Portuguese people aged over 70, and over 85 that doubles until 2050 (Alzheimer Europe, 2019).

Though these alarming numbers about the Portuguese population, the available studies are mostly outdated and do not describe the clinic and sociodemographic characteristics of the patients, such as health-related quality of life (HRQoL), functional ability, cognitive impairment or living situation. The absence of studies addressing QoL in dementia, with exception from a study that focused in the QoL in early stages of cognitive decline patients (Helena Bárrios, Narciso, et al., 2013). This study highlighted the need of a study that

better describe not only the PwD, but also their HRQoL and dependency level. Another study including 128 patients with mild dementia showed that being a male, good social support, and high functionality were significant predictors of better quality of life reinforcing the importance of gender, psychological morbidity, social support, and functionality in patients with mild dementia (Lima et al., 2016).

Additionally, to better describe the global phenomenon of dementia, information on the caregivers is relevant as well since they play a major role in providing all the support and care that patients need in their daily activities. Regarding formal care use, a recent Portuguese study described that company, psychological distress and daily activities were the main unmet needs of PwD and their informal caregivers (Manuel Gonçalves-Pereira et al., 2019). Some Portuguese studies found that personality of informal caregivers can indirectly influence the caregiver's distress related to behavioural and psychological symptoms of PwD, and that it determine the creation of specific strategies to deal with the referred symptoms of their relatives (Melo et al., 2011, 2017).

Given the few studies and the lack of knowledge on PwD living in Portugal, we aimed to study the HRQoL and functional/cognitive impairment in a sample of PwD and identify the factors (personal or social) that influence their QoL. Also, this study sought to describe the daily context of the PwD to better understand the impact of the surrounding environment in their life.

2. Methods

2.1. Design

This study followed a descriptive cross-sectional design using a non-probabilistic and purposive sample of PwD and their caregivers. The participants were invited to a unique semi-structured face-to-face interview of 30-40 minutes with the aim of answer questions about their relative with dementia, based on the knowledge about their relative's health condition, behaviour and performance in daily routines.

The application of questionnaires and measurement methods in dementia still faces important challenges due to the cognitive impairment present in the PwD. Despite the preferable self-report methods, in this study, we resort to proxy-report being the caregiver the respondent for their relative with dementia, as was done in previous research (Beerens

et al., 2014; Bruvik et al., 2012; Jönsson et al., 2006; Schiffczyk et al., 2010; Sheehan et al., 2012). We believe that, in this situation, the direct observation and daily care performed by the caregivers can accurately describe the behaviour and functional ability of the care recipient that is related to its HRQoL and dependency level. The sociodemographic questionnaire was the only that included questions about both the caregiver and the PwD.

2.2. Participants and recruitment process

The participants in the current study were dyads, consisting of PwD and their informal caregivers that were invited to participate from two different settings: upon a neurology appointment at the Hospital de Santa Maria of Centro Hospitalar Universitário Lisboa Norte E.P.E (reference university hospital for dementia) and after a brief presentation of the project on a recognized National Care Institution and Dementia-related Public Institutions. Informal caregivers in this study were considered the closest family member of the PwD, not being defined any minimal hours of care or the need to co-habitation with the PwD. This large spectrum of informal caregiver definition was relevant to include PwD that were in an early stage of disease and still able to live alone under caregiver's supervision.

A short presentation of the study, written information including the details of the study (goals and procedures) and the informed consent form was given to the invited participants. The caregivers that demonstrated the intention to participate in the study were interviewed by the principal investigator. Whenever possible, a cognitive impairment test was also applied to the PwD. Data collection was conducted in the previous referred facilities and took place between January and December 2019.

Informal caregivers were considered eligible if they were young adults or adults taking care of a relative with dementia (clinical diagnosis of dementia, without the need for specification of the type of dementia). Every time the patient's diagnosis was different from that intended in this study, or the person available was not the principal caregiver, participants were not eligible. The sample was constructed with the intention of covering a wide range of scenarios (i.e., including, caregivers of relatives in early and in advanced stages of dementia, participants with different ages, different time of diagnosis, different family relationships as spouse or daughter, different formal care resources utilization).

2.3. Independent review board approval and consent to participate

Ethical approval was obtained from the competent Ethics Committee (Centro Académico de Medicina de Lisboa - CAML) in October 2018. Participants were informed verbally, and the written consent form was signed. The participation was consented and voluntary. The participants knew that they could withdraw at any time without any prejudice. To ensure participant's anonymity, a code number was assigned for each participant. Information having the potential to allow the identification of any participant was withdraw from the questionnaires. Demographic elements were only used as a context for interpretation the qualitative data and for describing (in an aggregated form) the sample.

2.4. Tools

To study dementia patient HRQoL by proxy-report we have used the EQ-5D three level (EQ-5D-3L) and the Quality of Life in Alzheimer's Disease (QoL-AD) instruments; to study the functional ability of the included PwD we have used the Blessed Dementia Rating Scale (BDRS). The Mini-Mental State Examination (MMSE) was also applied whenever possible to study patient's cognitive impairment. A sociodemographic questionnaire was included to collect information on the dyads gender, age, education, familiar relationship, residence, co-habitation, professional status (of the caregiver), diagnosis and use of formal health care resources by the PwD.

2.4.1. Patient by proxy-report measures of HRQoL

EQ-5D-3L

The EQ-5D-3L is a generic HRQoL instrument widely used, in which respondents evaluate their (or proxy) health state "at the moment" and increasingly used in patient with neurological disorders (Jönsson et al., 2006; Naglie et al., 2006). The short descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, with three levels of severity per dimension: "no problems", "some problems" or "extreme problems" (EuroQol Research Foundation, 2018). The respondent is asked to indicate his/her (or proxy) health state by choosing the most appropriate response level of each of the five dimensions. This generates a five-digit number; thus 243

possible health states may be obtained. This health state is transformed through a value set into a single summary index value (index, ranging from -1 to +1) that summarizes the individual's health state and can be used in economic evaluations of healthcare interventions (EuroQol Research Foundation, 2018). The second part of the EQ-5D-3L consists of a visual analogue scale (VAS), the EQ-VAS, that records the rated health on a vertical VAS with a range of 0 (worst imaginable health state) to 100 (best imaginable health state). The EQ-5D-3L has been developed to describe and value health in different diseases (EuroQol Research Foundation, 2018). Studies such as Bryan et al., 2005, Diaz-Redondo et al., 2014 are examples of proxy versions available for populations in which self-completion is not possible (EuroQol Research Foundation, 2018); thus we have used the EQ-5D-3L patient-by-proxy assessment.

In this study, we have used the Portuguese version of the EQ-5D-3L (P. L. Ferreira et al., 2013). The EQ-5D-3L index was calculated using the Portuguese tariffs (L. Ferreira et al., 2014).

QoL-AD

The QoL-AD is a dementia-specific HRQoL instrument used in people diagnosed with dementia/AD (Logsdon et al., 1999). It consists of 13 items covering the items of physical health, energy, mood, living situation, memory, family, marriage, friends, self, ability to perform tasks at home, ability to do things for fun, money and life as a whole. Items are scored on a 4-point rating-scale ranging from 1 (poor) to 4 (excellent), ranging from 13 to 52 (lower scores mean poor QoL). There are separate versions available for patients and caregivers, but in this study, only the patient-proxy version was used. It takes 10–15 minutes to administer. The complete questionnaire was validated for the Portuguese population in 2013 (Helena Bárrios, Verdelho, et al., 2013).

2.4.2. Patient by proxy-report measure of functional ability

BDRS

The BDRS is a three-part scale, originally called the "Dementia Scale" (Blessed et al., 1968; Eastwood et al., 1983; Peña-Casanova et al., 2005). It registers the patient functional behaviour change reported by informants, and the global score is the result of the sum of the three sections, A (changes in everyday activities), B (changes in daily habits) and C

(changes in personality), with a total of 22 items. Scoring for the first eight items (section A) is on a three-point basis: 0 = none, 0.5 = some, 1 = severe, thus providing scoring gradations. The section B is scored from 0 to 3 (depending on the dependency level of the PwD). The section C is a two-point basis: 0 = absence, 1 = presence of changes in personality. The total score ranges from 0 to 28 (higher scores mean lower functional ability) (Eastwood M.R et al., 1983). Scores are generally labelled as: less than 4, no impairment; 4 to 9, slight impairment; equal to or greater than 10, presence of moderate to severe impairment (Eastwood et al., 1983; Peña-Casanova et al., 2005). It takes 15-20 minutes to complete and was translated and validated to Portuguese in 1984 (Garcia, 1984).

2.4.3. PwD cognitive impairment

MMSE

The MMSE is one of the most widely used measure of cognition in clinical practice worldwide (Folstein et al., 1975). This scale can be easily administered by clinicians or researchers with minimal training, takes around 10 min and assesses six cognitive domains in the areas of orientation, memory, attention and calculation, language and visual construction. Patients score between 0 and 30 points: scored 0 - when the individual does not respond or gives an incorrect answer or 1 - when the examinee provides a correct answer, so higher scores indicate better performances. Scores are usually used to classify dementia severity in stages: higher to 21 (mild), from 11 to 20 (moderate) or lower than 11 (severe). A standardized version (Molloy et al., 1991) improved its reliability, and is probably most important for research settings. It was validated to the Portuguese population in 1994 (Guerreiro et al., 1994), with later updates (Freitas et al., 2015; Morgado et al., 2009). The values used in the present study, despite the updates, were the values of the first validation since these continue to be the most used.

2.5. Data analysis

Data analysis was performed using IBM SPSS Statistics 26. The sociodemographic data were analyzed with descriptive statistics (i.e., mean, standard deviation (SD), frequencies and proportions (%)) to better describe the PwD and their caregivers. The EQ-5D-3L profiles, index score and VAS, as well as QoL-AD score, BDRS score and MMSE

score were presented according to three groups: PwD that used to visit day centers during the week, (n=53) (Group A); PwD were cared exclusively at home, (n=85) (Group B); PwD that were in a transition moment for formal care admission (pre-nursing-home moment), (n=49), (Group C). Descriptive analysis was also carried out using the EQ-5D-3L, QoL-AD, BDRS and MMSE instruments to describe the PwD HRQoL and functional ability and cognitive impairment. The acceptability of EQ-5D-3L was estimated through score ranges (observed *vs* possible), closeness of means to medians, floor and ceiling effects (less than 15% of responses accumulated at minimum or maximum values) and skewness (between -1 and +1) (Hays et al., 1993).

Correlations between the EQ-5D-3L and QoL-AD and BDRS scores were evaluated using Spearman's rank correlation coefficient. Correlations were classified in three categories: weak (rh0 < 0.3); moderate (0.3 < rh0 < 0.5); and strong (>0.5) (Cohen, 1977). P-value <0.05 was considered statistically significant. We hypothesized that the EQ-5D-3L would correlate at a moderate or high level with QOL-AD and BDRS proxy scales (Juniper et al., 1996). Additionally, the correlation with time, in years since diagnosis was also analyzed with the hypothesis of being moderately correlated to BDRS and EQ-5D-3L.

In addition, differences between groups of PwD were analyzed based on non-parametric tests because the EQ-5D-3L index, QoL-AD score and BDRS score do not follow a normal distribution. The Mann–Whitney *U* (i.e., two groups, such as diagnosis) and Kruskal–Wallis *H* (i.e., more than two groups) tests were the most appropriate in this context, followed by Bonferroni correction.

Based on the significant correlations identified between the EQ-5D-3L and the other variables, multivariate linear regression models were used for identifying the factors that can be potentially associated with PwD HRQoL. The explanatory variables included were years of education, time since diagnosis, BDRS domains (changes in everyday life, changes in habits, changes in personality) and the groups defined in this study (group A, group B and group C). The overall fit of the model was assessed, and the existence of multicollinearity and heteroscedasticity was tested.

3. Results

3.1. Participants

One hundred eighty-seven dyads (caregiver and PwD) were part of this study. All the sociodemographic data of included caregivers is presented in Table 4.1. The informal caregivers were family members of a PwD (32 wife's, 29 husbands, 70 daughters, 38 sons, 6 sisters and 12 were other family members) and the mean age was 61 years old. Of the caregivers, 92.5% were living with their relative with dementia and seventy-five caregivers had a professional occupation (36.4% were in working in full-time work and 3.7% in part-time). Of the 187 caregivers, 33 (17.6%) admitted to had professional changes due to their relative's diagnosis (reduced labour hours, shift changes, job changes). In most of the cases, caregivers attended school at least over four (182%) or nine years of education (12.3%), 17.6% completed 12 years of education and 40.1% completed graduation at university. In what concerns to the time of care, some caregivers were caring for their relatives with dementia for no longer than two years (20.9%), while 27.4% were caring from two to five years. In some cases, the caregiver role involved more time of care, such as at least 10 years (11.8%) and 15 years (4.8%). The daily hours of care were dependent of the professional status of the caregivers and varied from less than one hour (25.7%), two to four hours (15.5%), five to seven hours (21.9%) and more than 10 hours (25.1%) (Table 4.1). Of the 187 caregivers, 129 (68.9%) admitted being the only caregiver performing all the care tasks, while 58 (31.1%) had support from another family member.

Table 4. 1. Background characteristics of informal caregivers, (n=187)

Characteristic	***Mean (SD) or n (%)/ (minimum, maximum)***	***Characteristic***	***Mean (SD) or n (%)/ (minimum, maximum)***
Sex, (female)	115 (61.5)	**Professional status**	
Age, mean (SD)	61.0 (13.9) / (23-91)	Full-time working	68 (36.4)
Lives with the patient		Part-time working	7 (3.7)
Yes	173 (92.5)	Unemployed	27 (14.4)
No	14 (7.5)	Early retired	23 (12.3)
Relationship with PwD		Retired	48 (25.7)
Wife	32 (17.1)	Other	14 (7.5)
Husband	29 (15.5)	**Years of care**	
Daughter	70 (37.4)	Less than 2 years	39 (20.9)
Son	38 (20.3)	2 to 3 years	30 (16.0)
Sister	6 (3.2)	4 to 5 years	40 (21.4)
Grandchild	5 (2.7)	6 to 9 years	47 (25.1)
Other	7 (3.7)	10 to 15	22 (11.8)

Educational level		More than 15 years	9 (4.8)
Did not complete any degree	7 (3.7)	**Daily hours of care**	
4-year school	34 (18.2)	Less than 1 hour	48 (25.7)
6-year school	15 (8.0)	2 to 4 hours	29 (15.5)
9-year school	23 (12.3)	5 to 7 hours	41 (21.9)
12-year school	33 (17.6)	7 to 10 hours	22 (11.8)
University	75 (40.1)	More than 10 hours	47 (25.1)
Family support		**Professional changes (PwD diagnosis)**	
No	129 (68.9)	No	154 (82.4)
Yes	58 (31.3)	Yes	33 (17.6)

The sociodemographic data regarding the PwD is presented in Table 4.2. The PwD were mostly female (74.3%), the mean age was 82 years old. Seven participants presented YOD, that is defined as first symptoms before 65 years of age. The mean of time since diagnosis was 6.6 years (ranged from 0 and 20 years), and 11 of the 187 PwD had professional changes due to the diagnosis (medical discharge).

In what regards the living situation of the PwD, the preferred residence was the home of the PwD (66.8%) over the home of the caregivers (33.2%). In most of the cases, the caregiver was the person that moves into the patients' home. This fact might be related mainly to the patients' preferences to be in his own house and environment, but also because of previous establishment of nearby formal care services involving the patient and his/her address, or because caregiver is the wife or husband (live in the same house). The educational level of the patients with dementia varied from not attending to school (18.2%), 9 years of education (68.5%), 12 years of education (4.3%) and 9.1% completed university.

The utilization of formal care services covered 42.2% of the cases, including home care support services (32.9%) and day centers (29.1%). Of the PwD living with their caregivers, 49 were in the moment of transition from the informal to formal care (pre-nursing-home moment), and the information collected is concerning the exact moment of this transition.

The following results are presented by the PwD daily context: PwD that used to visit day centers during the week, (n=53) (Group A); PwD were cared exclusively at home, (n=85) (Group B); PwD that were in a transition moment for formal care admission (pre-nursing-home moment), (n=49), (Group C).

Table 4. 2. Background characteristics of PwD, (n=187)

Characteristic	***Mean (SD) or n (%) / (minimum, maximum)***
Sex (female)	139 (74.3)
Age	82.1 (7.7) / (54-97)
Years since diagnosis of dementia	6.6 (4.5) / (1-20)
Residence	
Own house	125 (66.8)
Caregiver's house	62 (33.2)
Educational level	
Did not complete any degree	34 (18.2)
4-year school	99 (52.9)
6-year school	16 (8.6)
9-year school	13 (7.0)
12-year school	8 (4.3)
University	17 (9.1)
Formal care services utilization	79 (42.2)
Home care support (1h/day)	26 (32.9)
Day center (5-6h/day)	53 (29.1)
Professional changes due to diagnosis	
No	176 (94.1)
Yes	11 (5.9)

*PwD (Person with dementia)

3.2. Quality of life (proxy-report)

The EQ-5D-3L and EQ-VAS univariate values are presented in Table 3. Regarding the EQ-5D-3L index, the mean was an extremely low value of -0.005±0.31 (-0.536-0.766), indicating that PwD had complications in multiple domains of EQ-5D-3L. According to L. Ferreira et al., 2014, the EQ-5D-3L tariffs for the Portuguese population varied between -0.536 (worst health state) and 1 (best health state). Due to the extremely low QoL of these PwD, with a negative mean for EQ-5D-3L index, there were no cases reaching a maximum of 1 (the best health status) in the EQ-5D-3L index ("no problems" in all domains). Thus, one of the main limitations of the EQ-5D-3L regarding the ceiling effect, was not seen in

this sample (Table 4.3). Regarding all the cases, the ability to perform usual activities and self-care routines were the dimensions that gathered a higher number of severe cases (revealing that PwD had extreme problems in these dimensions). Some dimensions showed ceiling effects, whereas others had floor effects (Table 4.3). The EQ-VAS mean was 36.9±1.4 (varying from 5 to 90), indicating that there were severe cases (probably bedridden PwD), and some mild cases (probably PwD in their initial phases).

Table 4. 3. EQ-5D-3L and EQ-VAS univariate values, (n=187)

	EQ-5D-3L index	EQ-VAS	Mobility	Self-care	Usual activities	Pain/ discomfort	Anxiety/ depression
Mean	-0.005	36.9	-	-	-	-	-
Median	-0.048	35.0	-	-	-	-	-
SD	0.305	1.37	-	-	-	-	-
Minimum	-0.536	5	1	1	1	1	1
Maximum	0.766	90	3	3	3	3	3
95% CI for mean	(-0.049) - (0.039)	(34.2) - (39.6)	-	-	-	-	-
Floor effect (%)	0.5	3.2	26.2	12.3	3.7	36.4	27.8
Ceiling effect (%)	0	1.1	23.5	67.9	74.3	25.1	28.9

EQ-5D-3L, EuroQol 5-dimensions 3-level; EQ-VAS, EuroQol Visual Analogue.

The proxy-responses of EQ-5D-3L and EQ-VAS are presented in Table 4.4. The EQ-5D-3L index value of group A was significantly different from group C (0.060±0.24, comparatively to -0.108±0.27), as well as group B with group C (0.014±0.35, comparatively to -0.108±0.27). Regarding the EQ-VAS results for the overall health state, there were significant differences between groups: group A (43.1±16.8), group B (34±19.0) and group C (35.4±18.9). The PwD that attended day centers were referred as the ones with higher scores, still reasonably bellow 50 (the middle between 0 and 100). The EQ-VAS of group A was significantly different from remain groups. Considering all results of the EQ-5D-3L, the QoL was better in group A.

Regarding all the 187 participants, the mobility, pain/discomfort, and depression/anxiety, PwD were mostly reported by having “some problems”, 50.3%, 38.5% and 43.3%, respectively. In the two remaining dimensions, PwD were mostly reported by having extreme problems: self-care (67.9%) and usual activities (74.3%) (Table 4.4).

In detail for the “mobility”, the group A was the one that brought together the most cases of “no problems” (26.4%) and “some problems” (71.7%), being statistically different from PwD of group C, that were reported by having mostly “some and extreme problems” (42.8% and 38.8% respectively) (Table 4.4). The group B had a higher number of “no

problems" (30.6%) compared to the other groups, however 41.2% of these PwD were having "some problems" and 28.2% "extreme problems" with mobility. Regarding the ability to do "self-care" tasks, the results were statistically different by group (group A and B were both different from group C). It was clear that most of the PwD presented "extreme problems", but with higher expression in group C (83.7%). The distribution of "no problems" and "some problems" showed that PwD of group B were more able to perform self-care tasks (17.7% had "no problems", comparatively to 4.1% in group C and 11.3% in group A). As well as in the previous dimension, the "extreme problems" was the most common answer regarding the performance of the PwD to do "usual activities" (87.7% in group C, 75.5% in group A and 65.9% in group B, with significant difference between the group and C). The percentage of "no problems" in this dimension was very small among all groups. The last two dimensions: "pain/discomfort" and "depression/anxiety" revealed a higher number of "some/extreme problems" in group B, with only 30.6% and 22.4% of "no problems" in this group. The PwD of group C were the ones that had mostly "no problems" concerning pain/discomfort (48.7%), as well as depression/anxiety (34.7%). In group A, PwD showed mostly "some problems" concerning these two dimensions (43.4% and 41.5%, respectively), however, these PwD showed a higher number of "extreme problems" facing depression/anxiety when compared to group C (Table 4.4).

Table 4. 4. Distribution of responses of the EQ-5D-3L index scores, (n=187)

	Group A 53 (28.3)	Group B 85 (45.4)	Group C 49 (26.2)	All cases, n (%) 187 (100)
Mobility, n (%)/**				
No problems	**14 (26.4)**	26 (30.6)	**9 (18.3)**	49 (26.2)
Some problems	**38 (71.7)**	35 (41.2)	**21 (42.8)**	94 (50.3)
Extreme problems	**1 (1.9)**	24 (28.2)	**19 (38.8)**	44 (23.5)
Self-care, n (%)/**				
No problems	**6 (11.3)**	**15 (17.7)**	**2 (4.1)**	23 (12.3)
Some problems	**14 (26.4)**	**17 (20)**	**6 (12.2)**	37 (19.8)
Extreme problems	**33 (62.3)**	**53 (62.4)**	**41 (83.7)**	127 (67.9)
Usual activities, n (%)/**				
No problems	1 (1.9)	**5 (5.9)**	**1 (2)**	7 (3.7)
Some problems	12 (22.6)	**24 (28.2)**	**5 (10.2)**	41 (21.9)
Extreme problems	40 (75.5)	**56 (65.9)**	**43 (87.7)**	139 (74.3)
Pain/discomfort, n (%)				
No problems	18 (33.9)	26 (30.6)	17 (48.9)	68 (36.4)
Some problems	23 (43.4)	36 (42.4)	19 (26.5)	72 (38.5)
Extreme problems	12 (22.6)	23 (27.1)	13 (24.5)	47 (25.1)
Depression/anxiety, n (%)				
No problems	16 (30.2)	19 (22.4)	17 (34.7)	52 (27.8)
Some problems	22 (41.5)	40 (47.1)	19 (38.8)	81 (43.3)
Extreme problems	15 (28.3)	26 (30.1)	13 (26.3)	54 (28.9)
EQ-5D-3L index, mean (SD)/**	**0.060 (0.24)**	**0.014 (0.35)**	**-0.108 (0.27)**	-0.005 (0.31)
EQ-VAS, mean (SD)/**	**43.1 (16.8)**	**34.0 (19.0)**	**35.4 (18.9)**	36.9 (18.7)

Group A: PwD that used to visit day centers during the week, (n=53); Group B: PwD were cared exclusively at home, (n=85); Group C: PwD that were in a transition moment for formal care admission (pre-nursing-home moment), (n=49). EQ-5D-3L, EuroQol 5-dimensions 3-level; EQ-VAS, EuroQol Visual Analogue. ***p<0.05,* ****p<0.01* for the EQ-5D-3L index/EQ-VAS. Comparisons of the EQ-5D-3L index and EQ-VAS distributions amongst groups were analyzed with the Kruskal-Wallis *H* test followed by Mann-Witney *U* test and Bonferroni correction to find the groups where the difference was significant.

To summarize the overall perception of the informal caregivers regarding their relatives' QoL, the five most frequent EQ-5D-3L scores and health states are presented in Table 4.5.

Table 4. 5. Five most common PwD EQ-5D-3L scores and health states, (n=187)

EQ-5D-3L index	Health states	Example of health states interpretation
-0.100	23322	Some problems in walking about; Extreme problems in wash or dress himself/herself; Unable to perform usual activities; Moderate pain/discomfort; Moderately anxious/depressed
0.046	23311	Some problems in walking about; Extreme problems in wash or dress himself/herself; Unable to perform usual activities; No pain/discomfort; Not anxious/depressed
-0.146	23333	Some problems in walking about; Extreme problems in wash or dress himself/herself; Unable to perform usual activities; Extreme pain/discomfort; Extremely anxious/depressed
-0.344	33322	Confined to bed; Extreme problems in wash or dress himself/herself; Unable to perform usual activities; Moderate pain/discomfort; Moderately anxious/depressed
0.332	33332	Confined to bed; Extreme problems in wash or dress himself/herself; Unable to perform usual activities; Extreme pain/discomfort; Moderately anxious/depressed

The QoL of the PwD was also analyzed using the QoL-AD questionnaire (by proxy), and the mean score considering all cases was 19.5±4.0 (15.5-23.5) (Table 4.6). The results were in accordance with EQ-5D-3L index and EQ-VAS showing that the group C had lower Qol-AD scores than the other groups, 18.6±3.7, meaning poor QoL. According to this instrument, the group A and B presented similar scores (19.8±4.4 and 19.7±3.7, respectively) (Table 4.6).

To better describe the dimensions of QoL-AD scale, an additional table was included showing the distributions of the answers by question (Table 1, supplementary material). In nearly all dimensions of the QoL-AD, the responses of the caregivers were concentrated in the lower levels (weak or reasonable) and higher levels (good or excellent) account for

very few cases or even zero. The worst-rated dimensions were physical health, memory, ability to do things at home and for fun, money and life as a whole. The statistical differences included patients' energy level in PwD of group C comparing to PwD of group B where this dimension was less affected. This fact is probably related with the different stages of disease of these PwD. Regarding the maintenance of friendships, there were statistical differences between group B and C, with 85.7 of the PwD group C with weak relations with friends.

The dimension of patient's ability to perform tasks at home showed significant differences between group C and B (100% and 85.9% “weak”, respectively) (Table 4.1, supplementary material).

Table 4. 6. Distribution of QoL-AD scores, (n=187)

	Group A 53 (28.3)	*Group B 85 (45.4)*	*Group C 49 (26.2)*	*All cases (n=187)*
QoL-AD, Mean (SD)	19.7 (3.7)	19.8 (4.4)	18.6 (3.7)	19.5 (4.0)

Group A: PwD that used to visit day centers during the week, (n=53); Group B: PwD were cared exclusively at home, (n=85); Group C: PwD that were in a transition moment for formal care admission (pre-nursing-home moment), (n=49). QoL-AD: Quality of Life in Alzheimer’s Disease (13-52, lower means poor quality of life). ***p<0.05,* ****p<0.01* for the QoL-AD score. Comparisons of the QoL-AD score distributions amongst groups were analyzed with the Kruskal-Wallis *H* test followed by Mann-Witney *U* test and Bonferroni correction to find the groups where the difference was significant.

3.3. Functional ability (proxy-report)

The functional ability of the PwD was analyzed using the BDRS questionnaire (Table 4.7). According to BDRS score, 4 PwD were consider as not having impairment (BDRS score less than 4), 16 had slight impairment (BDRS score between 5 and 10), and 167 had moderate to severe impairment (BDRS higher than 10). The mean of the BDRS score results considering all cases was 15.8±4.8 (11.0 to 20.6), and the dimension of changes related to everyday life was the one with higher scores (mean of 6.0±1.4 (4.6 to 7.4), in a range from 0-8) (Table 7). The PwD of group C were reported by their caregivers as having lower functional ability (higher scores, 16.8±4.6 (12.2 to 21.4), followed PwD of group A 16.5±4.2 (12.3 to 20.7) and group B, that were the ones with a lower score 14.8±5.1 (9.7 to 20.2), meaning a better functional performance. The differences in the BDRS score were statistically significant in Kruskal-Wallis H ($p<0.05$), however in Mann-

Witney U test with Bonferroni correction, no statistical differences were found between groups (Table 4.7).

In detail, the changes involving everyday life were significantly different between the group B and the remain groups, being the group B the less affected in this domain, meaning that PwD in this group present better performance in everyday life. No significant differences were found including the second section of BDRS, regarding daily habits such as changes in eating, dressing and autonomy. Finally, the last section "changes in personality" such as decreased flexibility, childish behaviour, flattening of affections and initiative and abandonment of hobbies was different between PwD of group A and B, with PwD of group B being the less affected in what concern behaviour problems (Table 4.7).

Table 4. 7. Distribution of BDRS scores by domain, (n=187)

	Group A 53 (28.3)	*Group B 85 (45.4)*	*Group C 49 (26.2)*	*All cases, 187 (100)*
*Changes in everyday life. range 0-8, mean (SD)/***	**6.4 (1.2)**	**5.6 (1.5)**	**6.3 (1.3)**	6.0 (1.4)
Changes in daily habits, range 0-9, mean (SD)	4.9 (2.7)	5.0 (3.2)	6.1 (2.6)	5.3 (2.9)
*Changes in personality, range 0-11, mean (SD)/***	**5.1 (1.5)**	**4.3 (1.9)**	4.5 (1.9)	4.6 (1.8)
BDRS Score, mean (SD)	16.5 (4.2)	14.8 (5.1)	16.8 (4.6)	15.8 (4.8)

Group A: PwD that used to visit day centers during the week, (n=53); Group B: PwD were cared exclusively at home, (n=85); Group C: PwD that were in a transition moment for formal care admission (pre-nursing-home moment), (n=49). BDRS: Blessed Domain Rating Scale. BDRS Score (0-28, higher scores mean lower functional ability). ***p<0.05,* ****p<0.01* for the BDRS score. Comparisons of the BDRS score distributions amongst groups were analyzed with the Kruskal-Wallis *H* test followed by Mann-Witney *U* test and Bonferroni correction to find the groups where the difference was significant.

3.4. Cognitive impairment

As the MMSE is not a patient-by proxy instrument, its application was not easy due to difficulties in accessing the PwD (bedridden; absence at the medical appointment; low ability to speak or inconsistent speech). Additionally, in some cases, the PwD did not collaborate when asked to. Thereby, the results of MMSE are presented for 43 PwD (Table 4.8). The mean of the MMSE score was 16.0±5.5 (10.5 to 21.5) and no statistical differences were found between the groups. However, the group A presented higher scores (16.6±6.6), when compared group B and C (15.8±4.9 and 15.4±4.9, respectively), meaning a higher cognitive impairment in PwD that visited day centers. As the MMSE is commonly

used to rate the disease progression, in this study twelve of the PwD had mild dementia (MMSE score of 21 to 25), twenty-seven had moderate dementia (MMSE score of 11 to 20) and four had severe dementia (MMSE score ≤10) (Table 4.8). As expected, despite the lower number of MMSE applications, a higher number of PwD were diagnosed in mild and moderate states of disease.

Table 4. 8. Distribution of MMSE scores, (n=43)

	Group A (n=16)	*Group B (n=17)*	*Group C (n=10)*	*All cases, (n=43)*
MMSE score, mean (SD)	16.6 (6.6)	15.8 (4.9)	15.4 (4.9)	16.0 (5.5)

Group A: PwD that used to visit day centers during the week, (n=53); Group B: PwD were cared exclusively at home, (n=85); Group C: PwD that were in a transition moment for formal care admission (pre-nursing-home moment), (n=49). MMSE: Mini-Mental State Examination. MMSE Score (0-30, lower means higher cognitive impairment). ***p<0.01 for the MMSE score. Comparisons of the MMSE score distributions amongst groups were analyzed with the Kruskal-Wallis *H* test followed by Mann-Witney *U* test and Bonferroni correction to find the groups where the difference was significant.

3.5. Correlations between QoL, functional ability and sociodemographic variables

The correlations for EQ-5D-3L, QoL-AD and BDRS are presented in Table 4.9. As expected, the convergent validity of the EQ-5D-3L index with QoL-AD and BDRS scales was moderately, ranging from 0.49 to 0.59 (p<0.01) in absolute values, respectively. The EQ-5D-3L correlated weakly and in a negative way with years since diagnosis, age of PwD, age of caregiver and years of care. The EQ-5D-3L correlated negatively with BDRS domains, in particular, with the domain of changes in habits (rh0 = -0.721 p<0.01), meaning that more changes in BDRS score revealed poor QoL.

The QoL-AD correlated weakly with caregivers' years of education (positively), as well as with PwD and caregiver's age (negatively). The correlation with of QoL-AD with EQ-VAS (rh0 = 0.424 p<0.01) was slightly lower than the correlation with EQ-5D-3L index (rh0 = 0.492 p<0.01). The dimension of mobility was the dimension of EQ-5D-3L that presented the best correlation with QoL-AD (rh0=-0.407 p<0.01), meaning that poor mobility was correlated to poor QoL. The QoL-AD was moderately correlated with BDRS score and with BDRS domain of changes in habits (rh0=-0.405, p<0.01 and rh0=-0.438, p<0.01). Contrary to EQ-5D-3L, the QoL-AD correlated with MMSE score (rh0=0.478, p<0.01).

Additionally, the years since diagnosis and years of care were weakly correlated to the BDRS score, demonstrating the effect of disease progression in functional impairment.

Some of EQ-5D-3L dimensions such as mobility, self-care, usual activities and anxiety/depression were found to be moderately correlated with BDRS score. A weak correlation was found between the BDRS score and MMSE score ($rh0=-0.368$, $p<0.05$).

No correlations were found regarding the familiar relationship between the PwD and the caregiver, the caregiver's professional occupation and caregivers' or PwD gender.

Table 4. 9. Correlations with EQ-5D-3L, Qol-AD and BDRS scores with each other's and sociodemographic variables, (n=187)

EQ-5D-3L	Years since diagnosis/***	-0.208
	Age (PwD)/**	-0.186
	Age (Caregiver)/**	-0.157
	Years of care/**	-0.176
	BDRS score/***	-0.592
	Changes in everyday life (BDRS domain)/***	-0.330
	Changes in habits (BDRS domain)/***	-0.721
	Changes in personality (BDRS domain)/**	-0.145
	QoL-AD/***	0.492
QoL-AD	Years of education (Caregiver)/**	0.185
	Age (PwD)/**	-0.206
	Age (Caregiver)/**	-0.157
	Mobility/***	-0.407
	Self-care/***	-0.388
	Usual activities/***	-0.375
	Anxiety/depression/***	-0.240
	EQ-VAS/***	0.424
	BDRS score/***	-0.405
	Changes in everyday life (BDRS domain)/***	-0.208
	Changes in habits (BDRS domain)/***	-0.438
	Changes in personality (BDRS domain) /**	-0.185
	MMSE Score/***	0.478
BDRS	Years since diagnosis/***	0.322
	Years of care/**	0.265
	QoL-AD/***	-0.405
	EQ-5D-3L index/***	-0.592
	EQ-VAS/***	-0.442
	Mobility/***	0.518
	Self-care/***	0.598
	Usual activities/***	0.549
	Anxiety/depression/**	0.156
	MMSE Score/**	-0.368

** *p<0.05,* ***p<0.01.* EQ-5D-3L, EuroQol 5-dimensions 3-level; EQ-VAS, EuroQol Visual Analogue. QoL-AD: Quality of life in Alzheimer's Disease. BDRS: Blessed Domain Rating Scale. MMSE: Mini-Mental State Examination Comparisons of the EQ-5D-3L index, QoL-AD and BDRS scores were analyzed using the Spearman's Coefficient.

3.6. Summary of collected data

Briefly, the results of all instruments used in this study are presented in Table 4.10, which also integrates the characteristics of informal caregivers by groups. In this table, we included the detailed situation of 14 PwD who lived alone (7 of group A and 7 of group B) to allow a more careful analysis of the context of this small group of PwD.

The 14 PwD living alone were aged 80 years old, in mean, and the educational level did not differ from the remain groups (4-years of school in 50% of the cases). In general, this small group of PwD were referred by their caregivers, mostly daughters aged 56 years old, highly educated and professional active in 71.4% of the cases, as having better QoL and lower functional and cognitive impairment, comparatively to the other groups. However, the Qol-AD score of these patients was similar to PwD of group C. The time since diagnosis of these 14 PwD was the lower, 4.2 years (ranged from 2 to 6 years). The most common amount of time of care provided by their caregivers was one to two years, and less than an hour a day. The BDRS score was the lower of all cases 13.4±6.3, demonstrating better functional ability, as well as cognitive function (MMSE score of 19.3±3.8) in this small group of PwD (Table 4.10).

The group A included PwD that attended to day centers during weekdays, the mean age was 79.7 years old, and the diagnosis time was, in mean, five years. These PwD were referred as having slightly higher scores regarding Qol, meaning better health states comparatively to other groups, but still reflecting poor Qol and significant problems in the domains of the instruments applied. This group had similar results for BDRS than group C, both higher than group B, meaning poor functional ability in these PwD. Particularly, this group was the one with higher changes in personality. The cognitive impairment was lower comparatively to other groups (16.6±6.6), but still, extremely high considering the mean time of diagnosis. These PwD were mostly cared by daughters professional active and the mean time of care was five to ten years, about five to seven daily hours (Table 4.10).

The eighty-five PwD of group B mean age was 81.4 years, diagnosed with dementia seven years ago, in mean. This group of PwD presented extremely low scores regarding QoL when compared to group A, but slightly better scores than group C (considering the EQ-5D-3L and EQ-VAS). If Qol-AD score is considered, these PwD presented similar results to group A. Regarding the functional ability, the group B presented lower scores of BDRS, meaning lower changes in everyday life and personality, compared to group A and C. The PwD of group B were mostly cared by their daughters and wife's, aged 63.5 years

old, only 30% of these caregivers were professional active and the most common time of care was five to ten years and more than ten hours daily (Table 4.10).

The group C mean age was 85.8 years old, and were diagnosed with dementia, in mean, from seven years ago. These PwD were reported by their caregivers, mostly daughters and sons, highly educated and professional active, as the ones with extremely poor QoL and health states that revealed extreme problems in multiple domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). Regarding the functional ability, these PwD had the higher BDRS score (meaning higher impairment) and were the ones with more changes affecting everyday life. The MMSE score was similar to group B (Table 4.8), but lower than PwD of group A. The years of care for these patients varied from five to seven years, but the daily hours of care were, most of the times, less than one (Table 4.10). Of the forty-nine caregivers of group C (that were in a transition moment for formal care admission), twenty-five referred that the reason to consider the institutionalization was their relative behaviour, sixteen admitted that the reason was their own psychological distress and 9 choose the “physical tiredness” as the main reason to go further with the transition to formal care.

Table 4. 10. Summary of PwD and caregiver collected data per group, (n=187)

	PwD living alone, (n=14)	All cases, (n=187)		
	Group A, (n=7) Group B, (n=7)	Group A, (n=53)	Group B, (n=85)	Group C, (n=49)
Age, mean (SD)/(range)	80.4 (4.5)/ (72-80)	79.7 (7.9)/ (54-92)	81.4 (7.7)/ (60-95)	85.8 (6.4)/ (73-97)
Sex, female, mean (SD)	8 (57.1)	45 (84.9)	52 (61.2)	42 (85.7)
Years of diagnosis, mean (SD)	4.2 (1.4)/ (2-6)	5.0 (2.6)/ (2-12)	7.0 (4.4)/ (1-20)	6.9 (4.9)/ (1-20)
Educational level, (%)	4-years school (50.0)	4-years school (56.6)	4-years school (44.7)	4-years school (63.3)
EQ-5D-3L, mean (SD)	0.134 (0.35)	0.060 (0.23)	0.014 (0.34)	-0.108 (0.27)
EQ-VAS, mean (SD)	45.1 (20.8)	43.1 (16.8)	34.0 (19.1)	35.4 (18.9)
QoL-AD, mean (SD)	18.9 (3.6)	19.8 (3.7)	19.8 (4.4)	18.6 (3.8)
BDRS, mean (SD)	13.4 (6.3)	16.5 (4.2)	14.9 (5.1)	16.9 (4.7)
Changes in everyday life, mean (SD)	5.7 (1.7)	6.4 (1.2)	5.7 (1.5)	6.9 (1.4)
Changes in habits, mean (SD)	4.1 (3.2)	4.9 (2.7)	5.0 (3.2)	4.6 (2.6)
Changes in personality, mean (SD)	4.6 (1.7)	5.1 (1.3)	4.4 (1.9)	4.6 (1.9)
MMSE, mean (SD)	19.3 (3.8)	16.6 (6.6)	15.8 (4.9)	15.4 (4.9)
Caregiver				
Most common familiar relationship	Daughters	Daughters	Daughters & Wife's	Daughters & Sons
Age, mean (SD)/(range)	56.1 (11.1)/ (42-81)	59.4 (13.9)/ (24-91)	63.5 (14.5)/ (23-86)	58.5 (12.1)/ (32-87)
Professional occupation, mean (SD)	10 (71.4)	25 (47.2)	22 (30.1)	24 (48.9)
Educational level, (%)	University (50.0)/ 12-year school (21.4)	University (39.6)/ 12-years school (26.4)	University (27.1)/ 4-year school (21.2)	University (63.3)/ 4-years school (16.3)
Years of care, (%)	1 to 2 (35.7)	5 to 10 (30.2)	5 to 10 (34.2)	5 to 7 (36.7)
Daily hours of care, (%)	< 1 hour (92.9)	5 to 7 (35.8)	> 10 hours (43.5)	< 1 hour (59.2)

*PwD: Person with dementia. Group A: PwD that used to visit day centers during the week, (n=53); Group B: PwD were cared exclusively at home, (n=85); Group C: PwD that were in a transition moment for formal care admission (pre-nursing-home moment), (n=49). QoL-AD: Quality of life in Alzheimer's Disease, BDRS: Blessed Dementia Rating Scale, MMSE: Mini-Mental State Examination.

3.7. Factors potentially associated with patients' QoL

The data analysis included a linear regression model to identify the factors related to PwD QoL. Table 4.11 show the best results of the linear regression analysis, which examined the relationship between the variables of interest and changes in EQ-5D-3L index. The model is well adjusted (F test: $p<0.001$) and explained about 57% of the observed variance in the value of the dependent variable (EQ-5D-3L score). Results showed inexistence of autocorrelation (Durbin Watson=1.930), inexistence of multicollinearity (VIF for the factors are about 1.1), but presence of heteroscedasticity (Breusch–Pagan test $p<0.05$) thus, robust standard errors were estimated.

In this model, the group were the PwD were allocated was statistically associated with changes in EQ-5D-3L score: group A (B=0.469, $p<0.001$), group B (B=0.066, p=0.110) and group C (B=0.020, p=0.592). The educational level of the PwD were statistically associated with the increase of EQ-5D-3L score (B=0.009, $p<0.01$). Also, two of the three BDRS domains (changes in everyday life, changes in habits) were statistically associated with changes in EQ-5D-3L score (B=-0.032, $p<0.01$; B=-0.066, $p<0.001$). As a higher score of BDRS mean poor functionality, was expected that high levels of this BDRS score were associated to decreased QoL. Other characteristics such as years since diagnosis (B=-0.005, p=0.180) and changes in personality (B=0.005, p=0.575), were not significant predictors of PwD QoL.

Table 4. 11. Influence of PwD and informal caregivers' characteristics in PwD QoL (EQ-5D-3L)

	B	*Std. Error*	*t*	*p*
Group A	0.469	0.075	6.224	**<0.001**
Group B	0.066	0.041	1.605	0.110
Group C	0.020	0.037	0.537	0.592
PwD characteristics				
Years of education	0.009	0.003	3.205	**<0.01**
Years since diagnosis	-0.005	0.009	-1.345	0.180
Changes in everyday life (BDRS)	-0.032	0.012	-2.640	**<0.01**
Changes in habits (BDRS)	-0.066	0.006	-11.85	**<0.001**
Changes in personality (BDRS)	0.005	0.009	0.561	0.575

*PwD, Person with dementia. SD, standard deviation. r^2=0.59, Adjusted r^2=0.57. BDRS: Blessed Dementia Rating Scale.

4. Discussion

This study sought to assess the HRQoL and functional/cognitive levels of PwD in Portugal, while describing sociodemographic data not only about patients, but also about their informal caregivers. To the best of our knowledge, this one in few Portuguese study that includes the assessment of QoL, functional ability and cognitive impairment of PwD, while including data about the living context and resort to formal care. The data provide insights into the current experience of living with dementia. It attempts to fill the gap that involves the lack of knowledge about the impact of this disease in QoL and its relation to the functional/cognitive ability of PwD, particularly, in Portugal.

With progressing severity of dementia, the patient's autonomy is reduced due to the physical and cognitive impairment leading to behavioural symptoms, less ability to do activities of daily living, increasing their dependency (Brodaty & Green, 2002; Dening et al., 2012; Prince et al., 2004). This implies the need of continuous care and supervision that is usually done by family members. As well as in other studies, Brodaty & Hadzi-Pavlovic, 2016; Moore et al., 2001, the included caregivers were mostly women and the mean age was around sixty years old. Regarding the familiar relationship, caregivers were usually wife's or daughters, reinforcing that the real scenario of informal care is mostly elderly woman's caring for their husbands or daughters caring for their mothers with dementia (Brodaty & Hadzi-Pavlovic, 2016; Moore et al., 2001). Due to the inexistence of registry of family caregivers, there is not an exact number of how many caregivers exist in Portugal, however, there is a culture of caring for family members in the best possible way, and that family caring is primarily a task for women. Additionally, the existent stigma around the use of formal services delays the moment of institutionalization to its last. In this study, the consideration of institutionalization occurred after five to seven years of caring by the caregiver, and in a group of 49 PwD that were mostly cared by daughters. That is probably related to the difficulties founded by caregivers in the moment of transition to a nursing home. For some caregivers, resort to institutionalization is still seen as a failure of the caregiver (like being a bad caregiver or not good enough to care for their relative), demonstrating that interventions should focus on facilitating a healthy transition for family caregivers (Lethin, Hallberg, et al., 2016). A study including Portugal, among other European countries, found that generally, formal care was seen as a threat to the individual independence of PwD and was avoided for as long as possible. A key role is

attributed to healthcare professionals as an essential facilitator to overcome these barriers (Stephan et al., 2018).

The PwD included were mostly elderly women and despite of the illiteracy existing at this generation, more than 80% attended school. Also, the caregivers were highly graduated in 40.1% of the cases and 75 (40%) of the caregivers had a professional occupation. The professional occupation of caregivers in forty percent of the cases is probably related with two factors: the retirement age (66.5 years old, in Portugal), and the lack of income due to low remunerations in the Portuguese work community (C. F. Rodrigues & Andrade, 2014; P. Santana, 2002). Besides these factors, the almost inexistence of financial support for informal caregivers could also lead them to work while caring their relatives. In 2019, Informal Caregiver Status was approved in Portugal to regulate support measures regarding the informal caregiver and care receiver. However, recent information published in Deco Proteste Website (www.deco.proteste.pt, published in D&D março/abril 2021), demonstrated that the benefits of this support reached only 30 Portuguese municipalities. Also, it is described as heavily bureaucratic, not fully inclusive, insufficiently disseminated in the community and as a relatively low financial support. Considering all these factors, most of the informal caregivers have no choice besides working alongside the task of caring, which might represent some loneliness for PwDs or having to resort to formal services, such as day care centers institutionalization. In our study, the caregivers of the PwD that visited day centers were professional active in 47% of the cases, a highly graduated in 40% of the cases. Similar percentages were founded in the group of PwD that still lived alone or were in a transition moment to a nursing home, demonstrating that these PwD were essentially cared mostly by highly graduated daughters/sons that were professional active. The situation of the fourteen PwD that were living alone in their homes, under the supervision of their relative trough phone calls and regular visits is probably a common situation in mild cases of dementia (MMSE mean of 19.3, dementia diagnosis from 2 to 4 years), when patients still recognize the involving environment and can perform tasks such as personal hygiene and warming food. Still, it reveals that as far as possible, there is a desire on both sides (patient and caregiver) to promote the normality and autonomy, postponing the co-habitation or formal care resort. When required due to loss of patient's autonomy, most of the included caregivers (59.4%) moved to patient home due to different factors: maintain their relative in its own environment; resort to previous formal care services near patients' home; and, sometimes, due to a financial issue related to the cheaper finance of the PwD house (in some cases,

caregiver give up of their own houses rental). All these life changes probably end with high levels of stress and concerning in caregivers, that need to adapt or even give up of their own life to care for their relatives (Andrén & Elmståhl, 2008). In 68.4% of the cases, caregivers resort to formal care services, revealing some acceptance and of the use of these type services, mainly day centers, due to its potential to give a feeling of safety and relief to caregivers (Tretteteig et al., 2016). An explanation for the high use of day centers might be related to the need of caregivers (workers, in some cases) to leave the patient somewhere during the day. Another possible explanation is that most of the patients lived in urban areas - in rural areas the neighbours usually know each other and the need for company (founded in a day center) is not so evident. Additionally, the large offer on formal care services like day centers could also explain the high use of formal services in urban areas (Manuel Gonçalves-Pereira et al., 2019; Rahman et al., 2020).

Our findings showed correlation between the different scales applied to measure QoL and functional/cognitive ability of PwD, while revealing very low scores of QoL and cognitive ability and high scores in BDRS, meaning that these patients had very poor HRQoL and high physical and cognitive impairment. The results of EQ-5D-3L demonstrate that the dimensions of self-care and usual activities were very compromised in these PwD, followed by mobility. However, the dimensions of pain/discomfort and anxiety/depression showed some unexpected results, revealing that in most of cases, PwD had “no or some problems” in these dimensions, affecting mainly the PwD of group B (exclusively cared at home). The explanation is probably the “invisible” effects of these dimensions, being harder to classify by caregivers that admitted some difficulties in understanding if their relatives were or not suffering from pain, anxiety or depression due to high levels of apathy, medications and low speech abilities. The constant supervision of the PwD of group B by their caregivers might explain this group of patients were reported as having more problems in these dimensions.

The use of the EQ-5D-3L allows the comparison of dementia health states with other diseases. Despite the care needed when comparing across different studies, since there are certainly methodological differences in their designs, a brief comparison showed that in our study the most frequent health states revealed several limitations and very low health state values. As example, a study including stroke patients using the EQ-5D-3L showed mean values of 0.584 and 54.3% for the EQ-VAS, far above from the obtained in our study

(Golicki et al., 2015). As well, Kularatna et al., 2017 conducted a study with patients with cardiovascular disease, where the mean EQ-5D-3L index was 0.802.

The application of QoL-AD in our study corroborated the previous results with dimensions of physical health, energy and ability to do tasks at home or for fun being classified mostly as "weak". Also, humour/mood, memory and the social interaction of the patients were profoundly affected. These PwD had weak or reasonable relationships with friends, being better if they were exclusively at home, probably, due to the neighbour's company. The living conditions were mostly reasonable, however life as a whole and money dimensions were mostly weak. However, the section of life conditions revealed that caregivers considered their or patients home as weak life conditions in 21.1%. This reveals that the patient houses (in most cases) did not meet the appropriate conditions for a PwD with low mobility, high dependence and behaviour problems (i.e., stairs, small areas, lack of windows and safe balconies, small bathtubs), probably due to their old age. So, this is a concerning issue that should be taken into account to improve patients QoL at home, since it could postpone their eventually need for institutionalization and promote PwD autonomy.

Regarding changes involving everyday life, daily habits and personality, PwD revealed moderate to severe impairment. The high physical damage and behaviour/personality changes resulted in mental rigidity, apathy and lack of emotional control, that together with the previous described physical impairment and progressive cognitive deterioration leaded to a profound and debilitating context for the included PwD. The PwD in a transition moment to nursing homes revealed poor QoL in all scales, with the objective dimensions (physical) being very compromised and subjective dimensions (pain/discomfort, anxiety/depression) less affected in comparison to the remaining PwD. Better QoL was reported in PwD that frequented day centers followed by PwD exclusively cared at home (in EQ-5D-3L and EQ-VAS). The routine imposed by the regularly visits to day centers is probably the explanation of better QoL in these patients, allied to a better social behaviour and communication skills acquired/maintained by the daily contact with others. Interestingly, patients that visited day centers had higher scores in MMSE scale. PwD cared exclusively at home had the best score in QoL-AD being the ones with better humour/mood, energy, family and friend's context., assessed the QoL of patients with dementia using both the EQ-5D-3L and the QoL-AD (both using patient and caregiver versions), demonstrating once again that patients rated their QoL very highly compared to their caregivers.

A brief comparison with a recent study conducted in Germany (Michalowsky et al., 2020) shows that the German PwD included presented better QoL than the PwD included in our study (mean of EQ-5D-3L in the Germany study was 0.758, EQ-VAS 60.6% and QoL-AD 33.5 comparatively to EQ-5D-3L mean of -0.005, EQ-VAS 37% and QoL-AD score 19.5, obtained in our study). A previous Germany study revealed similar results, with a mean value of 29.6 for the QoL-AD score (Römhild et al., 2018). A study conducted in Switzerland including PwD founded very similar results to Germany with EQ-5D-3L of 0.78, EQ-VAS of 64% and 32.5 for QoL-AD (Aguirre et al., 2016). This study included the MMSE, where the mean value obtained was 18.2 comparatively to 16.0 in our study. A Spanish study conducted in 2013, assessed the QoL of institutionalized adults with dementia revealing a mean EQ-5D-3L index score of 0.11, 51.5% for the EQ-VAS and 27.2 for QoL-AD, still higher values than the results obtained in our study (Diaz-Redondo et al., 2014).

A group of researchers conducted an important study to establish a neuropsychological battery as a valid measure of cognitive progression in AD by comparing several scores including MMSE, BDRS and other scales (Rossetti et al., 2010). The results obtained after five years of study were obviously worse comparatively to the first year (MMSE mean 18.4, BDRS mean 4.30, comparatively to 11.2 and 9.8, respectively at the last year of study). Together, MMSE and BDRS scores combined with other instruments, allowed the evaluation of progressive decline (Rossetti et al., 2010). Comparing our results for MMSE and BDRS scores, the included PwD present higher MMSE scores (16.0 *vs* 11.2) and higher functional impairment (15.8 *vs* 9.8 in BDRS score), meaning better cognitive function but lower functional ability. A follow-up study including timely evaluations of PwD allied to a patient-directed intervention (including physical and cognitive stimulation), is of major interest to understand the best methods to delay the impairment of PwD while increasing their QoL.

Additionally, we found association between education level of PwD, functional ability by BDRS and PwD daily context (group A) with PwD QoL. Altogether, the results obtained in this study reinforce the need for more HRQoL studies in dementia since, as showed, the health states founded were extremely bellow from other diseases and even in dementia conditions, comparatively to European studies. This highlighted the need of more studies focusing PwD QoL that resort to specific and generic instruments of HRQoL since the use of EQ-5D-3L and QoL-AD showed not to dismiss the used of the other.

This study highlights that QoL of PwD in Portugal is lower when compared to other European countries, justifying the need of more attention regarding one of the most relevant treats of ageing - the tremendous impact of dementia in QoL. Mental disorders are still undervalued in health policies; however, we cannot afford to be inactive regarding this topic any longer. It is urgent to address possible interventions intended to mitigate the impact of dementia in QoL, and due to the complexity of factors involved, an integrated community response is needed (i.e., early diagnosis, effective follow-up of the PwD/caregiver, physical and cognitive stimulation, social and economic support, formal care services aligned with PwD/caregivers needs). Additionally, this study hight the need of future research focusing informal caregivers QoL, since they play a major role supporting PwD.

5. Strengths and Limitations

The strength of this study is the description of the sociodemographic and clinical data on QoL and physical/cognitive impairment of PwD living in Portugal. Another strength is related to the diversity of the sample characteristics, including PwD at different stages of the disease, different ages and different living situations, as well as caregivers with diverse familiar relationships, professional status, and education levels. Additionally, the recruitment of participant included not only the hospital environment, but also, other health care facilities and Portuguese Alzheimer's Associations.

The main limitations of this study were: a) the non-existence of the diagnosis confirmation; b) the sample was a non-random sample, that focused mainly on single urban area of Portugal; however, as previously mentioned, the sample characteristics allowed to cover different scenarios to be as much representative of the phenomenon as possible; c) the incomplete application of MMSE, that covered just 43 of the included PwD.

Similar to the majority of other studies in this field, our data are cross-sectional rather than longitudinal, and thus, causal conclusions need to be drawn with caution. Finally, it must be noted that all data was obtained using proxy-report instruments, which constitutes a potential source of biases.

6. Conclusion

The findings of the present study show that the included PwD presented extremely low levels of QoL and moderate to severe impairment on their functional and cognitive ability. Dementia patients in Europe reveal better scores of QoL, physical and cognitive ability, and should been seen as an example to follow to achieve the goal of a healthier live for both the patient and the informal caregiver. To conquer that, the articulation and cooperation of different public services (formal care services, neurology, psychiatric, psychology, social and financial support) should be re-thought and multicomplex interventions must be created. Future research should focus on follow-up studies to evaluate patient-caregiver direct interventions impact on both QoL, while studying the application of specific and generic HRQoL instruments. Additionally, the drastic changes introduced in caregivers' personal lives should be taken into account, with future research focusing informal caregivers.

Author's contributions

PL recruited and invited the participants. PL created the database. PL and LNF treated the data. All authors were responsible for the study conception, design, drafting and reviews the manuscript. MMR and MG supervised the study.

Funding

This work was funded by the "Fundação para a Ciência e a Tecnologia (FCT)" Portugal and Merck Sharp & Dohme Portugal, under the grant number PDE/BDE/120498/2016.

Ethics approval and consent to participate

All procedures performed in the study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Participants voluntarily enrolled in the study. Written consent forms were available, and each participant provided informed consent. This study was approved by the competent Ethics Committee (Centro Académico de Medicina de Lisboa - CAML) in October 2018.

Acknowledgments

The authors acknowledge “Fundação para a Ciência e Tecnologia (FCT)” Portugal and Merck Sharp & Dohme Portugal (grant number PDE/BDE/120498/2016). We are also grateful to all the participants and National Institutions of Formal Care involved in the study. A special acknowledgment to Professor Daisy de Abreu for her statistical accompaniment.

Supplementary material

Table 4.1. Distribution of QoL-AD score by domain, (n=187)

Additional file 4.1:

-Informed consent of the participant – Informal caregiver
- Informed consent of the participant (for MMSE application to the person with dementia)
-Applied instruments (Sociodemographic questionnaire, EQ-5D-3L, QoL-AD, BDRS and MMSE)

CHAPTER 5

DETERMINANTS OF BURDEN AND QUALITY OF LIFE AMONG INFORMAL CAREGIVERS OF INDIVIDUALS WITH DEMENTIA

STUDY FRAMEWORK

Following the last two studies and the available literature we had suggestion that the Portuguese population of informal caregivers for persons with dementia could present low levels of quality of life and high physical, emotional and social burden due to the high dependency levels of their relatives with dementia. It is well known that dementia has a considerable negative impact on patients' family members, placing physical, emotional, and financial strains on these non-professional caregivers (World Health Organization, 2012). As a result, informal caregivers of adults with dementia experience high distress and burden leading to prolonged consequences of poor physical, emotional health and burnout (Gérain & Zech, 2019; Srivastava et al., 2016). In this study it was possible to assess the quality of life and physical, emotional and social burden in a sample of informal caregivers caring for persons with dementia. Specifically, we found that they reported low quality of life, problems in performing usual activities, suffered from pain and were quite depressed and anxious. We found that the major dimensions of burden included financial and emotional burden and implications for their personal life. In sum, the results obtained suggests that dementia has tremendous impact in the informal caregiver's life and that multiple factors are involved in quality of live and burden.

The following study was performed by **Patrícia Lindeza (PL)**, Lara Noronha Ferreira (LNF), Manuela Guerreiro (MG) and Mário Miguel Rosa (MMR).

PL recruited and invited the participants. PL created the database. PL and LNF treated the data. All authors were responsible for the study conception, design, drafting and reviews the manuscript. MMR and MG supervised the study.

Lindeza P, Noronha F, Guerreiro M, Rosa MM. Determinants of burden and quality of life among informal caregivers of individuals with dementia. Ageing & Society *(submitted)*.

DETERMINANTS OF BURDEN AND QUALITY OF LIFE OF INFORMAL CAREGIVERS OF INDIVIDUALS WITH DEMENTIA

ABSTRACT

Introduction: The ageing of the population is expected to lead to an increase in the prevalence of dementia. The aim of the study is to access the QoL and burden of informal caregivers of PwD and identify its associated factors.

Methods: Descriptive cross-sectional design with a non-probabilistic and purposive sample of 187 caregivers of PwD. Data collection included the EQ-5D-3L and the Informal Caregiver Burden Assessment Questionnaire (QASCI). Descriptive analysis and correlation coefficients were used to evaluate the QoL and burden. Multivariate linear models were estimated to identify determinants of informal caregivers QoL and burden.

Results: The results show that the QoL of the informal caregivers was low, and overall burden was found to be moderate. Different explanatory factors were identified for QoL and burden, however, in both cases the familiar relationship with the PwD and PwD pain/discomfort were identified as potential explanatory factors.

Conclusions: Our findings highlight that multiple factors of the informal caregiver and the PwD were correlated with QoL and burden suggesting that the informal care occurs in a complex environment determined by dyads characteristics that together can result in high or low impact for caregiver's personal life. It is crucial to include informal caregivers as a priority topic regarding dementia health policies, being essential to promote their wellbeing and prevent serious burden, which might also lead to better care and improved QoL for the PwD as well.

Keywords: Emotional burden, Quality of life, EQ-5D-3L, Informal caregivers, Caregiver health

1. Introduction

Worldwide, more than 35 million people live with dementia (PwD) and this is predicted to increase to 115 million by 2050, representing 18,8 million of dementia cases in Europe (Alzheimer Europe, 2019; Prince et al., 2013b). In the last years, according to World Health Organization (WHO) reports, dementia should be regarded as a global public health priority due to its fast-growing worldwide that will lead to a dramatic increase in its prevalence in the next decades, remaining a major public health faced by health-care and social-care systems worldwide (Banerjee, 2013; Orellana, 2003; Shah et al., 2016; World Health Organization, 2012). Dementia affects not only the individuals with the condition, who gradually lose their abilities and autonomy with serious impact on quality of life (QoL), as well as their relatives, that care for them as their dependency increases, as informal caregivers (Brodaty & Green, 2002; Livingston et al., 2017; Wortmann, 2012).

Informal care is commonly known as unpaid care or family care and constitute a significant share of the total long-term care provision in European countries, predicted as over than 80%, depending on the countries (Hoffmann & Rodrigues, 2010). A large amount of the informal caregivers are often women at retirement age, either providing care to a partner, parents or parents-in-law (Colombo et al., 2011). Typically, caregivers provide assistance to patients in their own home, helping patients in activities of daily living (ADLs) such as walking, toileting, bathing; in instrumental activities of daily living (IADLs) like managing finance, transportation, shopping, meal preparation, communication and managing medications, but also providing emotional support (OECD, 2017).

Dementia has a considerable negative impact on patients' family members, placing physical, emotional, and financial strains on these non-professional caregivers (World Health Organization, 2012). As a result, informal caregivers of adults with dementia experience high distress and burden leading to prolonged consequences of poor physical, emotional health and burnout (Gérain & Zech, 2019; Srivastava et al., 2016). Helping their relative's dementia with daily activities systematically along time is wearing and overwhelming (Gérain & Zech, 2019). According to the World Alzheimer Report (A. International., 2019), half of the dementia patients' caregivers tend to experience health problems, 49% modify their professional life and 62% have their social life affected because of the caring obligations. Additionally, emotions involved in caregiving (such as guilt, resentment, anticipated loss, sadness and loneliness) are often very difficult to cope

with. On the other hand, previous studies demonstrated that despite the negative aspects of informal caregiving, it is emotionally rewarding, bringing up self-esteem and sense of worthiness and life mission (ADI, 2019; Gérain & Zech, 2019; Givens et al., 2012; Lindeza et al., 2020a). Despite the positive aspects, being an informal caregivers mean, in many cases, combining the care with labor responsibilities. As a result, some caregivers quit their jobs to be able to respond the patient needs, and this decision may be detrimental in their life as it compromises future employability (OECD, 2011).

The relevance of informal care is likely to become even higher in the future due to demographic change leading to the favoring community care options over institutionalization where possible, with informal care being a substitute for formal care services until once a certain degree of dementia severity is reached. (Riedel, 2012). At some point, health support becomes harder to be provided by the family and institutionalization is commonly considered (Bremer et al., 2017). Informal care is a cost-effective alternative and a well-being alternative for patients who may remain at their homes. So in several countries across Europe, different public supports have been offered to informal care as a form of incentive and support to these families (OECD, 2011).

Since caregiving varies from case to case, some studies discuss how sociodemographic factors, such as gender, the nature of relationships with the care recipient or the age of caregiver affect the caregiving role (Dening et al., 2012; Garand et al., 2005; Lin et al., 2012). Available studies from Portugal or including Portuguese data focus mainly on the perspective of formal caregivers and do not allow a good and fully characterization of the Portuguese context of dementia informal caregiving (Barbosa, A., Cruz, J., Figueiredo, D., Marques, A. & Sousa, 2011; Kerpershoek et al., 2018). A study with Portuguese informal caregivers for relatives with Alzheimer's disease (AD) concluded that they the caregivers suffer important repercussions in their lives, especially physical overload and emotional changes that compromise their well-being as well as that of the patient (Pereira, 2007).

Despite the increasing development in the research of degenerative dementias, there is still a current worldwide mismatch between current knowledge, the lack of awareness and in-depth understanding of dementia, as well as the impact of informal care in caregiver's life.

Due to the lack of studies and knowledge on informal caregivers of PwD in Portugal, the main objective of this study was to access the QoL and physical, emotional and social burden of informal caregivers of PwD, in a Portuguese sample of informal caregivers. Moreover, we also aimed to explore the relationship between informal caregivers QoL and

their relatives' demographics, disease characteristics, functional and cognitive status and daily context (data collected in our previous study: Chapter 4*, "Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample"*). According to our knowledge, this is one in few studies focusing informal caregivers of PwD QoL associated factors (including PwD characteristics) in Portugal. Results will be extremely useful, as community service for dementia in Portugal to describe the unknown scenario of the impact of dementia in informal caregivers and its associated factors.

2. Methods

2.1. Design

This study followed a descriptive cross-sectional design using a non-probabilistic and purposive sample of informal caregivers. The participants were invited to a unique semi-structured face-to-face interview of 30-40 minutes with the aim of answer questions about themselves and their relative with dementia (results for PwD are described in Chapter 4*, "Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample"*). The questionnaire applied to informal caregivers of PwD included data about caregivers Qol and physical, emotional and social burden.

2.2. Participants and recruitment process

The recruitment process applied in the present study is the same of Chapter 4*, "Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample"*.

Briefly, a short presentation of the study, written information including the details of the study (goals and procedures) and the informed consent form was given to the invited participants. Informal caregivers were invited to participate from two different settings: upon a neurology appointment at the Hospital de Santa Maria of Centro Hospitalar Universitário Lisboa Norte E.P.E (reference university hospital for dementia) and after a brief presentation of the project on a recognized National Care Institution and Dementia-related Public Institutions and data collection occurred between January and December 2019.

Informal caregivers were considered the closest family member of the PwD (clinical diagnosis of dementia, without the need for specification of the type of dementia), not being defined any minimal hours of care or the need to co-habitation with the PwD. The sample was constructed with the intention of covering a wide range of scenarios (i.e., including, caregivers of relatives in early and in advanced stages of dementia, participants with different ages, different time of diagnosis, different family relationships as spouse or daughter, different formal care resources utilization).

2.3. Independent review board approval and consent to participate

Ethical approval was obtained from the competent Ethics Committee (Centro Académico de Medicina de Lisboa - CAML) in October 2018. Participants were informed verbally, and the written consent form was signed. The participation was consented and voluntary. The participants knew that they could withdraw at any time without any prejudice. To ensure participant's anonymity, a code number was assigned for each participant. Information having the potential to allow the identification of any participant was withdraw from the questionnaires. Demographic elements were only used as a context for interpretation the qualitative data and for describing (in an aggregated form) the sample.

2.4. Tools

To study informal caregivers HRQoL and burden we used the EQ-5D three level (EQ-5D-3L) and the Informal Caregiver Burden Assessment Questionnaire (QASCI). The other questionnaires applied to informal caregivers were already described and presented in Chapter 4*, "Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample",* namely: sociodemographic data about the dyad, PwD EQ-5D-3L, the Quality of Life in Alzheimer's Disease (QoL-AD), Blessed Dementia Rating Scale (BDRS) and the Mini-Mental State Examination (MMSE) of PwD.

2.4.1. Informal Caregivers QoL

EQ-5D-3L

The EQ-5D-3L is a generic HRQoL instrument widely used, in which respondents evaluate their (or proxy) health state "at the moment" and increasingly used in patient with neurological disorders (Jönsson et al., 2006; Naglie et al., 2006). The short descriptive system comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression, with three levels of severity per dimension: "no problems", "some problems" or "extreme problems" (EuroQol Research Foundation, 2018). The respondent is asked to indicate his/her (or proxy) health state by choosing the most appropriate response level of each of the five dimensions. This generates a five-digit number; thus 243 possible health states may be obtained. This health state is transformed through a value set into a single summary index value (index, ranging from -1 to +1) that summarizes the individual's health state and can be used in economic evaluations of healthcare interventions (EuroQol Research Foundation, 2018). The second part of the EQ-5D-3L consists of a visual analogue scale (VAS), the EQ-VAS, that records the rated health on a vertical VAS with a range of 0 (worst imaginable health state) to 100 (best imaginable health state). The EQ-5D-3L has been developed to describe and value health in different diseases (EuroQol Research Foundation, 2018). Studies such as Bryan et al., 2005, Diaz-Redondo et al., 2014 are examples of proxy versions available for populations in which self-completion is not possible (EuroQol Research Foundation, 2018); thus we have used the EQ-5D-3L patient-by-proxy assessment.

In this study, we have used the Portuguese version of the EQ-5D-3L (P. L. Ferreira et al., 2013). The EQ-5D-3L index was calculated using the Portuguese tariffs (L. Ferreira et al., 2014).

2.4.2. Informal Caregiver Burden Assessment Questionnaire (QASCI)

The QASCI is an instrument built to assess the physical, emotional and social burden of the informal caregiver which consists of 32 items comprising seven dimensions: Emotional burden (4 items- 4 to 20 points), Implications for personal life (11 items- 11 to 55 points); Financial burden (two items- 2 items- 2 to 10 points); Reactions to demands (five items-5 to 25 points); Perception of efficacy and control mechanisms (three items- 3 to 15 points); Family support (two items- 2 to 10 points); Satisfaction with the role and the

family member (five items- 5 to 25 points). Each item is assessed by an ordinal frequency scale ranging from one to five answer categories: "No/Never", "Rarely", "Sometimes", "Almost always", "Always". The final score results from the sum of the answers obtained for the 32 items (possible range from 32 to 160) related to each field, divided by the total number of domains or by the mean of items (range from one to five) after reversal of scores in the items of the three positive dimensions. Higher values correspond to situations with higher relevance or higher burden. In order for the final scores of each dimension to present homogeneous and comparable values, all items were added together, and a formula was applied to them to promote a uniform and comparable reading of what each factor (values between 0 and 100). Although there are no established cut-off points (since they are under study), the author of this instrument, Professor Teresa Martins, suggests that the value of 0 indicates no overload; 10 to 25 suggests a slight overload; from 25 to 50 corresponds to a moderate overload; 50 to 75 indicates a severe overload and a value greater than 75 indicates an extremely severe overload). This instrument is validated to the Portuguese population (Martins et al., 2003, 2004) and has already been applied to informal caregivers of older persons with dementia (Pereira, 2007).

2.5. Data analysis

Data analysis was performed using IBM SPSS Statistics 26. The EQ-5D-3L index score and visual analog scale (VAS), were presented according to age groups and caregiver genders to allow a comparison with the Portuguese population norms (L. N. Ferreira et al., 2014). The QASCI score were presented according to its seven dimensions. Descriptive analysis was also carried out using the EQ-5D-3L and QASCI instruments to describe the informal caregivers HRQoL by its personal life and characteristics and PwD related factors. The acceptability of EQ-5D-3L was estimated through score ranges (observed *vs* possible), closeness of means to medians, floor and ceiling effects (less than 15% of responses accumulated at minimum or maximum values) and skewness (between -1 and +1) (Hays et al., 1993).

Correlations between the EQ-5D-3L, QASCI scores, caregivers' personal characteristics and PwD scores obtained in Chapter 4*, "Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample"* were evaluated using Spearman's rank correlation coefficient (for EQ-5D-3L) and Pearson Coefficient (for

QASCI). Correlations were classified in three categories: weak (*p/*rh0 < 0.3); moderate (0.3 < *p/*rh0 < 0.5); and strong (*p/*rh0>0.5) (Cohen, 1977). P-value <0.05 was considered statistically significant. We hypothesized that the EQ-5D-3L and QASCI score would correlate at a moderate or high level with and PwD BDRS, EQ-5D-3L, Qol-AD and MMSE (Juniper et al., 1996). Additionally, the correlation with time of care was also analyzed with the hypothesis of being moderately correlated to EQ-5D-3L and QASCI scores and that both instruments correlated with BDRS score or domains.

In addition, differences between age groups were analyzed based on non-parametric tests because the EQ-5D-3L index do not follow a normal distribution. The Mann–Whitney *U* (i.e., two groups, such as diagnosis) and Kruskal–Wallis *H* (i.e., more than two groups) tests were the most appropriate in this context, followed by Bonferroni correction.

Based on the significant correlations identified between the EQ-5D-3L and QASCI with the sociodemographic variables and the instruments applied to PwD (in Chapter 4*, "Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample"*), multivariate linear regression models were used for identifying the factors that can be potentially associated with informal caregivers HRQoL (model 1) and burden (model 2). The overall fit of the models was assessed, and the existence of multicollinearity and heteroscedasticity was tested.

3. Results

3.1. Participants

One hundred eighty-seven dyads informal caregivers were part of this study, together with their relative with dementia in included in Chapter 4 *"Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample".* All the sociodemographic data of included caregivers and PwD is presented in Table 4.1 and Table 4.2, respectively, of Chapter 4 *"Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample".*

Briefly, the informal caregivers were family members of a PwD (32 wife's, 29 husbands, 70 daughters, 38 sons, 6 sisters and 12 were other family members) and the mean age was 61 years old. Of the caregivers, 92.5% were living with their relative with dementia and seventy-five caregivers had a professional occupation (36.4% were in working in full-time work and 3.7% in part-time). The PwD were mostly female (74.3%),

the mean age was 82 years old, with dementia diagnosis from 6.6 years (ranged from 1 and 20 years). The PwD scores obtained in Chapter 4 *"Quality of life and functional ability of older adults living with dementia: outcomes of a Portuguese sample",* were in mean -0.005±0.31 (-0.536-0.766), indicating that PwD had complications in multiple domains of EQ-5D-3L, 36.9±1.4 (varying from 5 to 90) for EQ-VAS, 19.5±4.0 (15.5-23.5) for QoL-AD score, 15.8±4.8 (11.0 to 20.6) to BDRS score and 16.0±5.5 (10.5 to 21.5) for MMSE.

3.2. Quality of life

The frequency distributions for the EQ-5D-3L dimensions, as well as the means of EQ-5D-3L/EQ-VAS for the overall sample and by age group are presented in Table 5.1. Regarding the EQ-5D-3L index, the mean was 0.375±0.28 (-1.11-1.00), indicating that the informal caregivers had complications usually in two or three domains of EQ-5D-3L. According to L. Ferreira et al., 2014, the EQ-5D-3L tariffs for the Portuguese population varied between -0.536 (worst health state) and 1 (best health state). In our study, the minimum obtained for EQ-5D-3L index was the value of -1.112, revealing a lower minimal value (revealing worst states of health) and a lower mean value, in comparison to the Portuguese population norms (0.375±0.28 *vs* 0.758 (SD not shown), respectively) (L. N. Ferreira et al., 2014). Despites the low QoL of these caregivers, there were some cases (six cases, corresponding to 3.2%) reaching a maximum of 1 (the best health status) in the EQ-5D-3L index ("no problems" in all domains). Thus, one of the main limitations of the EQ-5D-3L regarding the ceiling effect, seen in this sample, in 3.2% of the cases and 2.7% in the EQ-VAS (value of 100). These six caregivers were a wife (85 years old), two daughters (23 and 43 years old), two sons (52 and 55 years old) and a grandchild (42 years old), the EQ-VAS varied from 55 to 90 and the time since PwD diagnosis was mostly less than 4 years, with exception to two cases where it reached 7 and 16 years. The EQ-VAS mean considering all cases was 60.7±19.7 (varying from 10 to 100), indicating that there were cases of very bad QoL related to extreme problems in multiple domains (probably informal caregivers with multiple health conditions, or caring for PwD in advanced stages), and some mild cases (caregivers of PwD in their initial phases, younger caregivers, or caregivers that dedicated less hours in caring tasks). As well as in the EQ-5D-3L, the mean value found for EQ-VAS was lower when comparing to Portuguese population norms (60.7±19.7 *vs* 74.9 (SD not shown), respectively) (L. N. Ferreira et al., 2014).

In our study, there were statistical differences regarding both EQ-5D-3L and EQ-VAS between age groups. In detail, for the EQ-5D-3L index, there were differences between the group of caregivers aged 70 or more years and the group aged 30-49 years old (p=0.002), and between 50-59 years old and 30-49 years old (p=0.01), with the EQ-5D-3L mean value being higher caregivers aged 30-49 years old, so, younger caregivers. Additionally, the older group (aged 70 or more years old), differed from 30-49 (p=0.001) and 50-59 years old groups (p=0.02) for the EQ-VAS score, presenting the lowest value. Also, there were differences by caregivers' gender, with EQ-5D-3L being most of the times better in men's comparatively to woman's (with exception to 18-29 years old group), with this difference being statistically significant for the caregivers aged 50-59 years old (p<0.01).

Regarding all the cases (Table 5.1), the dimensions such as mobility and ability to do self-care tasks reveal mostly "no problems" (96.8% and 93.6%, respectively). In the dimension of usual activities, informal caregivers had mostly "some problems" (41.7%) and "no problems" in 35.3%. The dimensions that gathered a higher number of cases with "extreme problems" were pain/discomfort and anxiety/depression, (42.8% and 59.4% respectively), while 34.8% and 29.4% had "some problems" and 22.5% and 11.2% had "no problems" regarding these dimensions. In detail, it is possible to see in Table 1 that despites the group age, caregiver's mobility was almost not compromised. Some of the caregivers aged 70 or more years presented some or extreme problems regarding self-care tasks, while the difficulties in usual activities (i.e., work, housework, family activities) started sooner, in the group aged 30-49 and aggravated in older ages. Finally, in the last two domains of EQ-5D-3L (pain/discomfort and anxiety/depression), the younger caregivers (18-29 years old), present almost "no problems", while the remain groups revealed mostly "extreme problems", mainly in the groups of 50-69 and more than 70 years old, and in anxiety/depression dimension (Table 5.1).

The comparisons between the results obtained for QoL in our study and the overall Portuguese population (L. N. Ferreira et al., 2014), showed that, despites the age group and the gender, the informal caregivers had lower QoL than the non-caregivers, at same age: 18-29 years old (0.59±0.36 *vs* 0.86 (SD not shown)), 30-49 years old (0.51±0.23 *vs* 0.82 (SD not shown)), 50-69 years old (0.35±0.27 *vs* 0.69 (SD not shown)), 70 or more years old (0.29±0.29 *vs* 0.60 (SD not shown)). The same occurred for the EQ-VAS score: 18-29 years old (70±19 *vs* 84.3 (SD not shown)), 30-49 years old (68±20 *vs* 79.8 (SD not shown)), 50-69 years old (62±19 *vs* 68.5 (SD not shown)), 70 or more years old (53±19 *vs* 62.1 (SD not shown)).

Table 5. 1.Frequency distributions by EQ-5D-3L dimensions and means of EQ-5D-3L/EQ-VAS for the overall sample and by age group

	18-28 (n=3)	**30-49 (n=37)**	**50-69 (n=90)**	**70+ (n=57)**	**All cases (n=187)**
Mobility					
No problems	3	37	89	52	181 (96.8)
Some problems	0	0	0	5	5 (2.7)
Extreme problems	0	0	1	0	1 (0.5)
Self-care					
No problems	3	36	87	49	175 (93.6)
Some problems	0	1	3	8	12 (6.4)
Extreme problems	0	0	0	9	0 (0)
Usual activities					
No problems	3	20	33	10	66 (35.3)
Some problems	0	14	37	27	78 (41.7)
Extreme problems	0	3	20	20	43 (23)
Pain/discomfort					
No problems	1	11	18	12	42 (22.5)
Some problems	0	18	27	20	65 (34.8)
Extreme problems	2	8	45	25	80 (42.8)
Anxiety/depression					
No problems	2	7	9	3	21 (11.2)
Some problems	1	13	27	14	55 (29.4)
Extreme problems	0	17	54	40	111 (59.4)
EQ-5D-3L, mean (SD)/**	0.59 (0.36)	**0.51 (0.23)**	**0.35 (0.27)**	**0.29 (0.29)**	0.375 (0.28)
EQ-5D-3L, mean (SD) by gender/***					
Male	0.50	0.54 (0.19)	**0.47 (0.27)**	0.34 (0.32)	
Female	0.64 (0.49)	0.50 (0.25)	**0.29 (0.25)**	0.25 (0.26)	
EQ-5D-3L, (min)-(máx)	(0.29)-(1.00)	(0.01)-(1.00)	(-0.08)-(1.00)	(-0.11)-(1.00)	(-1.11)-(1.00)
EQ-VAS, mean (SD)/**	70 (19)	**68 (20)**	**62 (19)**	**53 (19)**	60.7 (19.7)
EQ-VAS, (min)-(máx)	(49)-(85)	(10)-(100)	(20)-(100)	(20)-(90)	(10)-(100)

EQ-5D-3L, EuroQol 5-dimensions 3-level; EQ-VAS, EuroQol Visual Analogue. ***p<0.05,* ****p<0.01* for the EQ-5D-3L index/EQ-VAS. Comparisons of the EQ-5D-3L index and EQ-VAS distributions amongst groups were analyzed with the Kruskal-Wallis *H* test followed by Mann-Witney *U* test and Bonferroni correction to find the groups where the difference was significant. EQ-5D-3L index by gender was analyzed by Mann-Witney *U* test and Bonferroni correction comparing by age groups.

3.3. Informal caregiver physical, emotional and social burden

The QASCI univariate values are presented in Table 5.2. The overall score in our study ranged between 48 to 155. The mean value was 99.6±17.8, corresponding to 53 (when the values are normalized to 0-100) meaning moderate burden. Regarding the seven dimensions of QASCI, the domain of financial burden was the one that reached high levels

(73±26), revealing an extremely severe overload situation. The followed dimensions with higher scores were the emotional burden (66±21) and implications in personal life (62±21), meaning moderate burden. The remain four dimensions of QASCI presented lower values meaning slight burden regarding the reactions to demands, perception of efficacy and control mechanism, family support and satisfaction with caregiver role and their relative with dementia. In sum, the included caregivers presented high levels of burden regarding financial, emotional and personal life issues.

Table 5. 2. Distribution of responses of the QASCI score by domain, (n=187)

	Min-Max	Mean (SD)	Normalized values (0-1), mean (SD)
Emotional burden, (4 to 20)	5-20	14.6 (3.3)	66 (21)
Implications in personal life, (11 to 55)	14-55	38.3 (9.1)	62 (21)
Financial burden, (2 to 10)	2-10	7.9 (2.1)	73 (26)
Reactions to demands, (5 to 25)	5-23	11.9 (3.6)	35 (30)
Perception of efficacy and control mechanisms, (3 to 15)	4-15	8.5 (1.9)	37 (13)
Family support, (2 to 10)	2-10	5.4 (2.3)	42 (29)
Satisfaction with role and family member, (5 to 25)	5-25	13.1 (3.7)	40 (18)
Caregiver QASCI Score, (32 to 160)	48-155	99.6 (17.8)	53 (14)

QASCI: Informal Caregiver Burden Assessment Questionnaire. Higher values correspond to situations with higher relevance or higher burden (Martins et al., 2003, 2004). QASCI score range: 32 to 160, converted to 0 to 100 in the normalized values column for easy comparation. The value of 0 correspond to the absence of burden; 1 to 25: slight burden; 25 to 50: moderate burden; 50-75: severe burden and over 75 correspond to extremely severe burden.

3.4. Impact of dementia according to informal caregivers and PwD related factors

Briefly, the results of the instruments used in this study are presented in Table 5.3 according to the caregiver's characteristics (familiar relationship with the PwD, professional situation, educational level, parenthood, years of care, hours of care). This table also integrates the characteristics of the PwD (daily occupation and educational level). Regarding the familiar relationship, the wife's were the ones with lower QoL and higher burden (0.232±0.24 EQ-5D-3L, 50.9±18.5 EQ-VAS, 57±15 QASCI), followed by the daughters (0.359±0.27 EQ-5D-3L, 62.2±19.4 EQ-VAS, 53±12 QASCI). The husbands presented slightly high scores regarding QoL than wife's but experienced lower levels of burden. The sons were the ones with high QoL and less burden. Other familiar relationships (grandchild, daughter-in-low…) presented the highest scores of QoL,

however, the QASCI score was as high as the wife's, being higher than daughters, husbands, and sons.

Regarding the professional occupation of the caregivers, the ones that were professional active presented better QoL and less overall burden (slight overload) than the ones that were professionally inactive (moderate overload).

The educational level revealed that for the caregivers that attend school for less or during six years there was no big differences regarding the QoL (by EQ-5D-3L) and burden experienced, however, more years of education revealed more QoL (by EQ-VAS). The caregivers that attended school over 9 years revealed highest levels of EQ-5D-3L than the previous ones, but the lower EQ-VAS score (53.7±19.7). Finally, caregivers that had 12 or more years of education revealed high scores of EQ-5D-3L and EQ-VAS, meaning higher QoL than caregivers with lower education. Moreover, the caregivers with more years of education presented lower scores in QASCI score, which means lower burden, still, moderate burden, despite the level of education.

The fact that caregivers had or not children did not affect QoL since the obtained values regarding the EQ-5D-3L index, EQ-VAS and QASCI score were very similar in both situations.

The years of care for the PwD indicated that more years of care corresponded to poor QoL and higher overload to the caregiver. When the duration of care was less than 2 years comparing to 3 years of care, the QoL of life increased (0.365±0.31 EQ-5D-3L, 66.2±19.7 EQ-VAS comparing to 0.531±0.24, 72.6±16.2, respectively). However, the QASCI score was very similar in the two situations, revealing slight overload. The period including four to fifteen years showed similar EQ-5D-3L index values and QASCI scores (moderate burden), but the EQ-VAS was high in when caregivers were caring for ten to fifteen years. Finally, when caring included more than fifteen years, only in nine cases, the EQ-5D-3L index decrease a lot comparatively to the remain situations and the QASCI score was the highest level when considering only the years of care (59±10). The same occurred with hours of care, where more hours corresponded to less QoL and higher overload. The impact of hours of care in decreasing QoL and increasing caregiver's burden was noticed when caregivers spend more than five hours in caring tasks, being more evident when the hours of care increased to 7 or ten hours a day. So, the caregivers that were caring for their relatives for more than fifteen years and during more than ten hours a day (n=5) were extremely affected in both QoL and overall burden (0.05±0.21 EQ-5D-3L, 50±12.3 EQ-VAS and 67±5 QASCI score).

Considering the PwD characteristics, the resort to day centers during the week resulted in a slight increased QoL for the caregiver, particularly, in the EQ-VAS, however in both situations caregivers revealed moderate burden (56±15 if PwD visited the day center and 52±13 if PwD did not attended to day centers). If the PwD educational level is considered, more years of education resulted in better QoL for the caregivers (0.350±0.27 EQ-5D-3L, 59.4±20.8 EQ-VAS in caregivers of PwD that attended less than 6 years of school, comparing to 0.411±0.27 EQ-5D-3L, 64.0±17.7 EQ-VAS when PwD that attended to school for more than 12 years). The burden of the caregiver was nearly the same in all educational levels, being moderate.

Table 5.3. Distribution of responses of the EQ-5D-3L index score, EQ-VAS and QASCI score according to informal caregivers and PwD related factors, (n=187)

Caregivers' characteristics	EQ-5D-3L index, *mean (SD)*	EQ-5D-VAS, *mean (SD)*	QASCI, *mean (SD)*
Familiar relationship			
Daughter (n=70)	0.359 (0.27)	62.2 (19.4)	53 (12)
Sons (n=38)	0.510 (0.24)	70.0 (16.8)	47 (15)
Wife (n=32)	0.232 (0.24)	50.9 (18.5)	57 (15)
Husband (n=29)	0.359 (0.31)	55.5 (20.1)	52 (10)
Other (n=18)	0.425 (0.31)	61.1 (19.2)	57 (18)
Professional situation			
Professional active (n=75)	0.468 (0.25)	67.8 (19.1)	49 (14)
Professional inactive (n=112)	0.313 (0.28)	55.9 (18.6)	55 (13)
Educational level			
Less than 6-years school (n=41)	0.261 (0.30)	47.5 (18.6)	56 (14)
6-years school (n=15)	0.271 (0.23)	61.4 (15.4)	56 (12)
9-years school (n=23)	0.285 (0.26)	53.7 (19.7)	58 (16)
12-years school (n=33)	0.378 (0.23)	60.0 (14.2)	52 (13)
More than 12 years school (n=75)	0.483 (0.27)	70.3 (18.3)	49 (13)
Parenthood			
Do not have kids (n=35)	0.400 (0.29)	60.2 (17.0)	54 (14)
Have kids (n=151)	0.366 (0.28)	60.8 (20.2)	52 (14)
Years of care			
Less than 2 years (n=39)	0.365 (0.31)	66.2 (19.7)	49 (15)
2 to 3 years (n=30)	0.531 (0.24)	71.6 (16.2)	47 (10)
4 to 5 years (n=40)	0.369 (0.27)	57.3 (21.2)	53 (15)
6 to 9 years (n=47)	0.323 (0.26)	52.1 (17.8)	57 (14)
10 to 15 (n=22)	0.370 (0.27)	63.4 (18.0)	55 (10)
More than 15 years (n=9)	0.182 (0.28)	52.7 (10.6)	59 (10)
Hours of care			
Less than 1 hour (n=48)	0.466 (0.27)	69.2 (18.5)	47 (15)
2 to 4 hours (n=29)	0.463 (0.34)	65.0 (24.6)	50 (13)
5 to 7 hours (n=41)	0.382 (0.23)	61.6 (18.1)	52 (13)
7 to 10 hours (n=22)	0.312 (0.28)	54.0 (17.5)	56 (8)
More than 10 hours (n=47)	0.247 (0.23)	51.6 (14.9)	60 (12)
PwD' characteristics			
Daily occupation			
Visit day center (n=53)	0.395 (0.27)	63.4 (18.7)	56 (15)
Do not visit day center (n=134)	0.366 (0.29)	59.6 (19.9)	52 (13)
Educational level			
Less than 6-years school (n=133)	0.350 (0.27)	59.4 (20.8)	53 (14)
6-years school (n=16)	0.439 (0.32)	63.8 (14.6)	54 (13)
9-years school (n=13)	0.467 (0.35)	63.9 (16.0)	53 (16)
More than 12 years school (n=25)	0.411 (0.27)	64.0 (17.7)	51 (1)
All cases (n=187)	0.375 (0.28)	60.7 (19.7)	53 (14)

EQ-5D-3L, EuroQol 5-dimensions 3-level; EQ-VAS, EuroQol Visual Analogue. QASCI: Informal Caregiver Burden Assessment Questionnaire. Higher values correspond to situations with higher relevance or higher burden (Martins et al., 2003, 2004). QASCI score range: 32 to 160, converted to 0 to 100 in the normalized values column for easy comparison. The value of 0 correspond to the absence of burden; 1 to 25: slight burden; 25 to 50: moderate burden; 50-75: severe burden and over 75 correspond to extremely severe burden.

3.5. Correlations between QoL, overall burden and sociodemographic variables of informal caregiver and their relatives with dementia

The correlations for EQ-5D-3L and QASCI with each other and with sociodemographic variables of the informal caregivers and their relatives with dementia are presented in Table 5.1 of supplementary material. As expected, the convergent validity of the EQ-5D-3L index with QASCI score was moderate and negative, (rh0=-0.476, $p<0.01$), meaning that the increase of the burden leaded to low QoL. Regarding the QASCI seven dimensions, only two (emotional burden and implications in personal life) correlated in a moderate negative way with EQ-5D-3L, while the financial burden, and perception of efficacy and control mechanisms showed a weak negative correlation, meaning that burden decreased caregivers QoL. The EQ-VAS showed a strong correlation with EQ-5D-3L (rh0=0.610, $p<0.01$).

In what concerns to informal caregivers' characteristics, the majority of the correlations founded were weak, however age (rh0=-0.314, $p<0.05$), educational level (rh0=0.334, $p<0.01$) and hours of care (rh0=-0.306, $p<0.05$) showed moderated correlations with QoL. The EQ-5D-3L correlated weakly with the majority of sociodemographic variables of the PwD (gender, age, educational level, EQ-5D-3L, mobility, anxiety/depression, EQ-VAS, QoL-AD, BDRS score and one of the BDRS domains) (see Table 5.1 of supplementary material).

The QASCI score correlated mainly weakly with the informal caregivers' characteristics, but moderated correlations were founded for hours of care (p=0.351, $p<0.01$) and some PwD characteristics such as EQ-5D-3L (p=-0.363, $p<0.01$), and some of its dimensions (mobility, self-care, pain/discomfort and anxiety/depression (weak correlation) and usual activities (moderate correlation). Contrary to EQ-5D-3L, the QASCI score correlated moderately to QoL-AD score (p=-0.471, $p<0.01$), BDRS score (p=0.401, $p<0.01$) and with the three dimensions of BDRS score (changes in everyday life, changes in habits and changes in personality).

No statistically significant correlations were found for both instruments (EQ-5D-3L and QASCI) with the familiar relationship of daughter and husband, years of PwD diagnosis, PwD attend to day centers and MMSE scores.

3.6. Factors potentially associated with caregivers' QoL and overall burden

The data analysis included linear regression models to identify the factors related to informal caregivers QoL and burden (Table 5.2 (model 1) and Table 5.3 (model 2) of supplementary material, respectively).

The model for QoL is well adjusted (F test: $p<0.001$) and explained about 39% of the observed variance in the value of the dependent variable (EQ-5D-3L score). Results showed inexistence of autocorrelation (Durbin Watson= 1.831), and inexistence of heteroscedasticity (Breusch–Pagan test, $p>0.05$). The model for overall burden is well adjusted (F test: $p<0.001$) and explained about 57% of the observed variance in the value of the dependent variable (QASCI score). Results showed inexistence of autocorrelation (Durbin Watson= 2.208), and inexistence of heteroscedasticity (Breusch–Pagan test, $p>0.05$).

In the first model, regarding informal caregivers QoL, the age of caregiver was statistically associated with changes in EQ-5D-3L index, despites its small effect, (B=-0.005, $p<0.05$). The familiar relationship of the caregiver with the PwD presented statistical differences when comparing husbands/wife's, sons/daughters, brothers/sisters with other family members. Being brother or sister of the PwD resulted in better QoL, followed by being nephew, grandchild or son/daughter-in-law. The husband and wives were the ones where the increase on EQ-5D-3L index was smaller, as well as sons/daughters. Regarding the effect of burden in QoL, two of the QASCI domains were included in this model, with only one being statically associated with EQ-5D-3L index: implication in caregivers' personal life (B=-0.49, $p<0.05$), meaning that the impact of dementia in caregivers life decreased its QoL. The characteristics of the PwD that were statically associated with caregivers EQ-5D-3L index included the age (B=-0.005, $p<0.05$) and the pain/discomfort where the increase of PwD problems and age resulted in decreased caregiver QoL. The caregiver gender and PwD mobility were not statistically associated with changes in EQ-5D-3L score, but the presence of these variables increased the model quality.

In what concerns to the informal caregiver overall burden (model 2, Table 5.3 of supplementary material), the pain/discomfort felt by caregivers, their familiar relationship with the PwD and professional situation were the caregivers-related factors statistically associated to its burden. In detail, the familiar relationship where the burden was more inflected (by increasing the QASCI score) was the nephew, followed by sons/daughters-in-

law, grandchild, husband/wife's, brothers/sisters and finally, the sons/daughters. This demonstrates that there were differences regarding the familiar relationship in caregivers perceived burden. For caregivers, being professional occupied in full or part-time resulted in less increased QASCI score, meaning lower overall burden comparatively to domestic or unemployed caregivers. The PwD characteristics statically associated with informal caregivers' burden were the ability to perform self-care tasks ($B=0.084$, $p<0.001$), were more difficulties of the PwD resulted in higher burden, and changes in PwD personality (BDRS domain) ($B=0.015$, $p<0.05$). The QoL of the PwD (QoL-AD score), was also statically associated with informal caregivers' burden, despites its low effect ($B=-0.01$, $p<0.001$).

The caregiver ability to perform daily activities, anxiety/depression, hours of care, educational level and the PwD mobility, pain/discomfort were not statistically associated with changes in QASCI score, but the presence of these variables increased the model quality. A briefly analysis of the effect of these variables showed that more hours of care and higher educational levels of the caregivers were associated to higher burden (Table 5.3 of supplementary material).

4. Discussion

The current study sought to assess the HRQoL and physical, emotional and social burden of informal caregivers of PwD in Portugal, while identifying the dyads characteristics that might be influencing the impact of dementia in caregivers HRQoL. The data provide insights involving informal caregivers and PwD characteristics to better describe the current experience of caring for a PwD. It attempts to fill the gap that involves the lack of knowledge about the impact of this disease in informal caregivers and its relation their own and PwD characteristics, particularly in Portugal.

Informal caregiving can have negative impacts on the physical and psychological health of caregivers, especially due to stress that comes with this responsibility, especially when taking care of people affected by any form of dementia. Informal caregivers are of major importance as the severity of dementia increases due to the compromise of patient's autonomy and requirement of continuous care and supervision that is usually done by family members, mostly wife's or daughters, strengthening that informal care is mostly performed by adult woman's, in accordance with our study (Brodaty & Green, 2002;

Brodaty & Hadzi-Pavlovic, 2016; Dening et al., 2012; Moore et al., 2001; Prince et al., 2004). In fact, women face higher risks of serving as informal caregivers for AD patients (6.8% vs. 4.0%) comparing to men's, as well as having AD itself (15.5% vs. 13.1%) (Yang & Levey, 2015).

Regarding the QoL of the informal caregivers included in our study, the results of EQ-5D-3L and EQ-VAS were illustrative of a very compromised QoL, where two or three domains of the EQ-5D-3L were affected (mainly the ability to perform usual activities, pain/discomfort, and anxiety/depression). In fact, previous studies reported depression symptoms among dementia informal caregivers (D'Aoust et al., 2015; Karg et al., 2018; Wulff et al., 2020). The domains of ability to perform usual activities and pain/discomfort were also the mostly affected in a recent Spanish study involving informal caregivers of PwD, however the values obtained for the means of EQ-5D-3L and EQ-VAS were extremely higher than the values obtained in our study (0.76±0.22 mean for the EQ-5D-3L index score and 66±13 mean EQ-VAS, comparing to 0.37±0.28 and 60.7±19.7, respectively, in our study) (Madruga et al., 2020). In comparison to the Portuguese population norms (L. N. Ferreira et al., 2014), in all age groups and even after the adjustment for caregivers gender, informal caregivers of PwD reported lower QoL than Portuguese non-caregivers. A study performed in Spain including two hundred thirty-seven informal caregivers reported the score of 0.67 (SD not shown) for EQ-5D-3L, far above from the score found in our study (Lopez-Bastida et al., 2006). In the Geras study, that included France, Germany and the UK, the overall mean and standard deviation (SD) of EQ-5D-3L index score of the included AD caregivers was 0.84±0.20 and 75.1±17.5 for the EQ-VAS (Reed et al., 2017), once again greater than the scores obtained in our study. When comparing our results with caregivers of patients with other health problems than dementia, for example, caregivers of autistic children, the results that we obtained for QoL were also extremely lower (0.82±0.16 mean for the EQ-5D-3L index score and 76±16 mean EQ-VAS in caregivers of autistic children, comparing to 0.37±0.28 for the EQ-5D-3L index score and 60.7±19.7 for the EQ-VAS, in our study) (Khanna et al., 2013).

About physical, emotional and social burden of the informal caregivers, our results indicated severe burden and the most affected dimensions were the financial burden, implications for personal life and emotional burden. In a study performed also in Portugal, that included a rehabilitation program for informal caregivers of people with musculoskeletal injuries (L. M. P. Rodrigues, 2018), the same QASCI dimensions were founded as the most affected, however, contrary to our study, the domain of perception of

efficacy and control mechanisms was the key contributor to the overall burden in these caregivers. Considering the global QASCI score, the informal caregivers of people with musculoskeletal injuries experienced lower burden (moderate overload) than the informal caregivers of PwD included in our study (severe overload), both before and after the intervention program (before the intervention: 44.1±5.6 and after the intervention 37.7±4.0, compared to 53±14 in our study) (L. M. P. Rodrigues, 2018). Another Portuguese study accessed the physical, emotional and social burden of informal caregivers for their elderly relatives that was found to be moderate (31.8±15.4), with implications for personal life and the perception of efficacy and control mechanisms being the domains with higher impact, while the financial burden was the domain with lower impact for this caregivers (Félix, 2008). In a Portuguese including informal caregivers for AD patients, the implications for personal life was the domain with higher punctuation, followed by emotional burden, while the QASCI score was 43.7±18.6, suggestive of sight burden (Pereira, 2007). Also, in the referred study, the male caregivers also presented lower burden than female caregivers, and older caregivers experienced higher burden that is in accordance with our study, unfortunately this study did not access informal caregivers QoL for comparison (Pereira, 2007).

Considering the global context, our results indicated that informal caregivers and PwD characteristics influence differently the caregivers QoL and experienced burden. In general, caregivers with lower burden reported significantly better perceived health and higher EQ-5D-3L and EQ-VAS mean score than caregivers with higher burden. However, since caregiving varies from case to case, some studies discuss how sociodemographic factors (such as gender and age of caregivers), as well the nature of relationships with the care recipient, affect the caregiving role (Kwak et al., 2012; Lin et al., 2012). In accordance with previous studies, in our study the included female caregivers reported having lower QoL and elevated burden than male caregivers, in detail, wife's and daughters in comparison to husbands and sons (Lin et al., 2012). Contrarily to Kwak et al., 2012, in our study the sons and daughters did not experience the stress and burden process similarly, since sons were the ones among all the familiar relationships with lower QASCI scores and higher EQ-5D-3L, meaning less physical, emotional and social burden and better QoL. In fact, other familiar relationships such as nephew, grandchild, or sons/daughters-in-law, presented lower QoL scores and higher levels of burden than informal caregivers that were sons of the PwD. This fact is possible related to a more distant familiar relationship in these situations that resulted in a lesser understanding of the

obligation to care for that PwD particularly, since it was not their parent or companion, leading to a higher impact in these cases. With that being said, studies including other familiar relationships besides the parents, sons/daughters and brothers/sisters, must be considered as important as the most directed family members.

Another widely explored theme in the literature was also illustrated in our study: the financial burden that dementia brought to the family and caregivers (Åkerborg et al., 2016; Kronborg Andersen et al., 2003; Moore et al., 2001). The high costs of dementia make this one of the most expensive diseases for families, due to the need of a full-time caregiver that might involve professional changes (reduction of working hours/quit jobs), and consequently, lower financial income. However, despite the severe financial burden present in our study, that is in accordance with previous studies, the professional occupation of the informal caregivers revealed better QoL and lower overall burden suggesting that it worked as a relief, a free time from the care tasks and obviously a higher familiar income (Åkerborg et al., 2016; Kronborg Andersen et al., 2003; Moore et al., 2001). Contrarily to what was found by Karg et al., 2018, where higher levels of QoL occurred in unemployed caregivers suggesting that work played an important role in the development of stress, in our study, having a job seemed to have the exactly opposite effect. Of the included caregivers in our study, 40% were professional active and this is probably related with the retirement age (66.5 years old, in Portugal), the lack of income due to low remunerations in the Portuguese work community and the almost inexistence of financial support for informal caregivers (C. F. Rodrigues & Andrade, 2014; P. Santana, 2002). Despites the approval of the Informal Caregiver Status in Portugal from almost two years, this support measure was described as a relatively low financial support and not fully inclusive or sufficiently disseminated in the community (www.deco.proteste.pt, published in D&D março/abril 2021). It is estimated that within the EU, between 50 and 100 million people provide care to people with functional limitation (usually unpaid). As a result, these caregivers usually face a higher chance of poverty, an increased risk of unhealthy behaviours and a 20% higher prevalence of mental health problems (Eurocarers, 2017).

The educational levels of caregivers demonstrated that more years of education lead to better QoL and less overall burden, especially when caregivers attend school for more than 12 years. Interestingly, caregivers that attended school for 9 years were the ones with high QASCI scores. The educational levels of the PwD revealed that caregivers for PwD that

attended less than 6 years of school reported poor QoL in comparison to the remain caregivers, however, in all cases, the burden experienced was moderate.

Regarding the years of care, caring for PwD less than 2 until 15 years did not change EQ-5D-3L index score, with the differences being more evident in the EQ-VAS, that decreased as years of care increased. About the burden, the increase of years of care resulted in higher burden for the informal caregivers. However, in the group of caregivers that were caring for 2 to 3 years, a different comportment was found, since they were the ones with higher EQ-5D-3L, EQ-VAS and lower QASCI scores. This fact must could possibly be related to some transitional relief of the PwD symptoms or some external factors of the caregiver life, deserving further investigation. The increase of hours of care resulted, as expected, in higher burden and less QoL for the informal caregivers, due to the all the physical and emotional environment involved. The daily occupation of the PwD, by attending day centers during the week did not changed the QoL and burden of informal caregiving.

As well as in previous studies (Karg et al., 2018; Madruga et al., 2020), the QoL and burden of the informal caregiver were founded to be correlated also in our results. In addition, the dimensions of QASCI that were strongly correlated with EQ-5D-3L were emotional burden and implications in personal life, indicating a deeply involvement of personal and emotional issues related to caregiving. Concerning the PwD characteristics, weak/moderate correlations with the caregiver QoL (PwD EQ-5D-3L, PwD EQ-VAS, age, educational level, mobility, anxiety/depression, BDRS score, changes in PwD habits), however a higher number of correlations were founded between PwD characteristics and the informal caregiver burden (QASCI score). Particularly, QASCI score correlated moderately with hours of care, caregivers QoL, caregiver's ability to perform usual activities, pain/discomfort, anxiety/depression, PwD Qol, and, most important, PwD functional ability (BDRS score), indicating that the functional ability of the patient had higher effect on burden than QoL of the caregivers.

In addition, the results of the multiple analysis showed that different explanatory variables were related to informal caregivers QoL and physical, emotional and social burden. The only explanatory variables that were common in the two models were the familiar relationship with the PwD and PwD pain/discomfort. The model for EQ-5D-3L included besides the previous variables, the caregiver age and gender, as well as the emotional burden and implications for personal life (from QASCI). While the model for overall burden included from the caregiver (the ability to perform activities of daily living,

pain/discomfort, educational level and professional situation), and from the PwD (the ability to perform self-care tasks, changes in daily habits, changes in personality and QoL). In sum, there was a strong association between higher levels of caregivers QoL in younger caregivers, daughters or sons, with lower implications in personal life, caring for younger PwD with less pain and discomfort; and lower overall burden in daughter/sons with less pain/discomfort problems, professional active, caring for PwD with less problems in performing self-care tasks, less changes in personality (behaviour problems) and with better QoL.

In Portugal, one remarkable positive aspect regarding informal caregiving is the existence of training programs, however, its lack of dissemination in the community is probably compromising their results (Lillo-Crespo et al., 2018). So, to better reach the target these programs should probably address specifically the informal caregiver of PwD in a more easily and direct way.

A follow-up study including an intervention focusing informal caregivers needs (increasing free time to personal life issues, controlling emotional burden and pain/discomfort) and PwD needs (by promoting mobility and decreasing pain/discomfort and control the changes in personality), with timely evaluations of both informal caregivers and PwD QoL, is of major interest to understand the best methods to reduce the physical, emotional and social burden associated to informal care for PwD, while increasing the dyad QoL.

This study highlights that QoL of informal caregivers of PwD in Portugal is lower when compared to other European countries and higher if compared to other diseases. This is an important topic, deserving more attention due its tremendous impact in family members and in PwD himself. The informal caregivers of PwD are still forgotten in research studies and health policies, which result in a deeply unknowledge of the holistic experience and impact of caring for a relative with dementia; however, we cannot afford to be inactive regarding this topic any longer, especially with the results obtained in our study. It is urgent to address possible interventions intended to mitigate the impact of dementia in informal caregivers QoL and overload, and due to the complexity of factors involved, an integrated community response is necessary involving both PwD/caregivers needs. Additionally, this study high the need of future research focusing informal caregivers QoL and burden, since the choice of being an informal caregiver for a relative with dementia must not be synonym of physical, emotional, and social burden and decreased QoL.

5. Strengths and Limitations

The strength of this study is the description of the sociodemographic and clinical data on QoL and physical, emotional and social burden of informal caregivers living in Portugal that was deeply unknown. As far as we are aware, this is the first Portuguese study to collect such information together, while describing data on PwD as well. Another strength is related to the diversity of the sample characteristics, including informal caregivers of PwD at different stages of the disease, different ages and different living situations, as well as diverse familiar relationships, professional status, and education levels. Additionally, the recruitment of participant included not only the hospital environment, but also, other health care facilities and Portuguese Alzheimer's Associations.

The main limitations of this study were: a) the sample was a non-random sample, that focused mainly on single urban area of Portugal; however, as previously mentioned, the sample characteristics allowed to cover different scenarios to be as much representative of the phenomenon as possible. b) lack of dementia differential diagnosis clinical confirmation.

Similar to the majority of other studies in this field, our data are cross-sectional rather than longitudinal, and thus, causal conclusions need to be drawn with caution. Results from longitudinal data would be necessary to establish a more comprehensive picture of the impact of caregiving on informal caregivers QoL and burden. Finally, it must be noted that all data was obtained using self-report instruments, which constitutes a potential source of biases.

6. Conclusion

The findings of the present study show that the informal caregivers of PwD had low quality of life, their ability to perform usual activities was compromised, and they suffered from pain/discomfort and anxiety/depression and moderate physical, emotional and social burden (due to financial and emotional burden, allied to the implications of caregiving for their personal life's).

In line with previous literature, the results of the current study showed that caregiving for a PwD is associated with greater objective (i.e., gender, age, educational level, professional situation, PwD QoL and physical impairment) and subjective strain (i.e., familiar relationship, implications for personal life, emotional issues), combined with

greater burden scores and poor QoL. The present study provides valuable insight into the differences between the associated factors with QoL and burden of the informal caregiver, while identifying the source of these factors (informal caregivers, PwD related factors, or both).

Author's contributions

PL recruited and invited the participants. PL created the database. PL and LNF treated the data. All authors were responsible for the study conception, design, drafting and reviews the manuscript. MMR and MG supervised the study.

Funding

This work was funded by the "Fundação para a Ciência e a Tecnologia (FCT)" Portugal and Merck Sharp & Dohme Portugal, under the grant number PDE/BDE/120498/2016.

Ethics approval and consent to participate

All procedures performed in the study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Participants voluntarily enrolled in the study. Written consent forms were available and each participant provided informed consent. This study was approved by the competent Ethics Committee (Centro Académico de Medicina de Lisboa - CAML) in October 2018.

Acknowledgments

The authors acknowledge "Fundação para a Ciência e Tecnologia (FCT)" Portugal and Merck Sharp & Dohme Portugal (grant number PDE/BDE/120498/2016). We are also grateful to all the participants and National Institutions of Formal Care involved in the study. A special acknowledgment to Professor Daisy de Abreu for her statistical accompaniment.

Supplementary material

Table 5.1. Correlations with EQ-5D-3L and QASCI score with each other's and sociodemographic variables of informal caregivers and their relatives with dementia, (n=187)

Table 5.2. Influence of informal caregivers' and PwD characteristics in caregivers' QoL (EQ-5D-3L)

Table 5.3. Influence of informal caregivers' and PwD characteristics in caregivers' overall burden (QASCI score)

Additional file 5.1

-Informed consent of the participant and EQ-5D-3L (the same of additional file 4.1)
- Informal Caregiver Burden Assessment Questionnaire (QASCI)

CHAPTER 6

DISCUSSION AND CONCLUSIONS

1. General discussion

In this work we describe the daily impact of dementia in a Portuguese sample of PwD and their informal caregivers at the individual, familiar and social levels.

A systematic review envisaging the perceptions of informal caregivers based on holistic experience of caring for a PwD was conducted to better understand informal care. The task of caregiving was described in literature as complex, heavily time-consuming and laborious resulting in physical, mental and financial stress for caregivers, which are usually the closest family members.

Positive aspects have been raised and the strength of these are the major motivation to dementia informal care. It is the personal gratification: as wife, husband, daughter or son - the family boundaries were a key to informal care (Harris 2013) . The family has probably the greatest personal importance for many individuals (Krys et al., 2019). Independently of the situation, the familial support plays a central role in individual's well-being trough life (Merz et al., 2009; Thomas et al., 2017). Facing life adversities, the pre-stablished familiar relationship worked as a keystone to face and overcome the difficulties related with the dependency introduced by dementia (Merz et al., 2009; Thomas et al., 2017). According to our systematic review, being able to return the favor for their parents or life companions was one of the main reasons for caregivers to deal with all the physical and mental efforts required. The opportunity to strengthen the previous unbalanced relationships was also pointed as a positive factor, with dementia diagnosis functioning as a reason for familiar re-gathering. In fact, the relationship quality between a person with dementia and a family carer may influence their health and quality of life. Recent findings of Marques et al., emphasized the importance of carer-perceived social support and sense of coherence, and of reducing neuropsychiatric symptoms, in maintaining a good relationship quality (Marques et al., 2019, 2021). Also, as suggested in previous studies such as Van Gennip et al. 2016 and Van Wijngaarden et al. 2018, it is important for caregivers to maintain PwD dignity. As dementia progresses the physical and cognitive impairment become more evident and caregivers ensure that the dependency of the PwD do not result in low dignity and depersonalization (Poole et al., 2018). The factors that were referred by these caregivers that contributed to the positive side of informal care were, for instance, the

access to good medical counselling, information and instructions about dementia, good formal care support and the possibility of an earlier diagnosis.

Despite the reasoned positive aspects, dementia informal care was more likely and deeply associated with negative aspects in the studies included in our systematic review. Initially, caregivers faced problems dealing with relatives' diagnosis, which come with uncertainty feelings, fear and loss of hope about the future (Connell et al., 2004) . This might be related to the chronic nature of dementia and the absence of a cure. Additionally, mental health still faces stigmatization and weak recognition in society, becoming the diagnosis the most dramatic moment for the family members (Aminzadeh et al., 2007; Robinson et al., 2008). Disease progression and patient dependency increased the caregiver's responsibility and consequently, more hours of caring, leading to social isolation. Altogether, caregivers experienced a wide range of feelings including stress, loss, guilt, anticipated grieving, sadness and fear of not being recognized by their relatives. Besides all these emotions, caregivers also had to deal with tough decisions involving the management of their relatives' belongings and interdiction; lack of medical advice; lack of access to formal care services; PwD behavior problems and dependency and high costs related to medication, food and hygiene products (Lampley-Dallas et al., 2001; Taşci et al., 2012). Several studies are in agreement about the emotional and physical burden experienced by dementia caregivers (Aminzadeh et al., 2007; L. J. Garcia et al., 2012; Ivey et al., 2013; Karlin et al., 2001; Peel & Harding, 2014). A study of Pinquart and Sörensen, suggests that caregiving of a PwD is more stressful than caring for individuals with other diseases. This phenomenon is probably related to the increased amount of time that caregiving for a PwD demand. Thus, caregivers sacrifice their activities and hobbies, restrict their time with friends and family, and give up of their employment or reduce time at work. Therefore, caregivers tend to lose their meaning in life, or set it aside, paving the way to mental health problems, which may get worse in the future (Brodaty & Hadzi-Pavlovic, 2016; Greenwood et al., 2019).

The imbalance of the negative over the positive aspects of caregiving, have been shown in previous studies, with implications in both mental and physical health in the caregivers directly, but also in PwD well-being as well (Gray et al., 2016). Factors such as finding good medical support and family/friends help were favorably to reduce caregiver's burden and its negative appraisal about informal care. As previously demonstrated by Vellone et al. 2008, all support is welcomed by caregivers, allowing free time for

themselves to do activities such as going to the gym, taking a walk, going out with friends or just taking a nap. Reduction or elimination of the referred negative issues related to dementia care would improve and facilitate the role of caregivers and the overall dyad well-being. There are several interventions aimed at the caregiver burden alleviation. Still, its effectiveness should be debatable; otherwise, it would be intriguing why caring for a PwD continues to be so harmful for caregivers. Why are these programs/interventions not having the expected results of decreasing burden among informal caregivers? Are these interventions well set to the target population (women's/daughters/wife's)? Do these programs really fulfil the needs of families? A recent meta-analysis reviewed the effect of 282 studies with different interventions to help caregivers dealing with the dementia care. There was a significant small-to-moderate effect on the improvement of ability/knowledge, well-being, burden and depression, however, due the small effects produced, there is still space for improvement (Walter & Pinquart, 2020). A careful observation of all the aspects referred by the informal caregivers suggest that a more personalized and multi-directed intervention is needed, due to the personal features involved in dementia informal care.

The available studies including Portuguese data do not allow a good and detailed characterization of the Portuguese context of dementia informal care. We conducted focus groups with informal caregivers of PwD to characterize the impact of disease in their daily lives and its related costs. The reported daily impact was found to be in accordance with literature, exposing the complex environment that dementia care demands. Dementia informal care brought drastic changes into caregivers' personal life leading to physical and mostly, emotional burden: tiredness, sleep problems, physical pain, emotional stress, depression, low sense of dignity, social isolation, activities renouncement. Taking care of a PwD required adjustments at personal, familiar, professional and social levels resulting in postponement of caregiver's life in multiple dimensions. As reported in other studies, the caregivers included in our focus groups also described that the daily difficulties tend to get worse as the disease progresses to its later stages, changing in the course of disease (Karlin et al., 2001). There is evidence suggesting that there is a strong impact on the QoL of caregivers with the increasing of PwD behavioural symptoms (Arthur et al., 2018). Besides, the constant mood fluctuations of patients can thoroughly change the daily routine, since the patient can be more less receptive to contribute with eating, bathing, walking, and other daily activities. This was also a complicated issue for caregivers due to the lack of support and information about dementia. In the moment of diagnosis, caregivers

expected more help from health professionals, in terms of description of disease progression, what to expect and how to deal with the patient behavior. Instead, caregivers reported that they had to learn all about dealing with dementia by themselves, making the task harder, in accordance with previous studies (Connell et al., 2004; Jennings et al., 2017).

The caregivers included in the focus groups were manly women, the mean age was 63.5 years old and more than 70% were caring for their relatives for at least 5 years. In accordance with literature, caregivers are often women, since they have an increased responsibility to take care not only of the family, but also of the home related issues (i.e., cooking and cleaning) (Brodaty & Hadzi-Pavlovic, 2016; Moore et al., 2001). There is a tendency for the caregiver to be the daughter or son, as described in a European study of Triantafillou. et al. 2010. In this sample the main caregivers were the daughters caring for one of their parents. Likewise, other familiar relationships included spouses, husbands, sisters and daughters-in-law. The different familiar relationships certainly influenced the perceptions reported in our study, but the inclusion of different points of view was a strength of these focus groups.

Caregivers also reported changes in the financial budget of the family by the introduction of costs related to dementia, in agreement with several studies (Åkerborg et al., 2016; Kronborg Andersen et al., 2003; Moore et al., 2001). Caregivers mentioned some examples of expenses: food, hygiene products, electricity, medication, formal care services and losses of money by the PwD. Despite the free time, four caregivers that had a professional occupation agreed to participate, which contributed to better understanding the financial burden introduced by dementia in the familiar budget. The amount of financial costs was, mostly, covered by patient and caregiver's life savings, especially because most of caregivers were retired or unemployed. Even when employed with a reasonable monthly income, caregivers admitted resorting to life savings to support all the costs related to dementia. To overcome the high amount of money with medications (sometimes, caregivers were also medicated), they resort to cheaper medicines such as generics. There is an underuse of this medication in Portugal probably related to the low health literacy of population and lack of information (Efpia, 2020; Quintal & Mendes, 2012). However, Portugal has been increasing its trend in terms of consumption of generics, from 18% (2014) to 22.6% (2020), almost in the European average (Efpia, 2014, 2020).

Finally, caregivers' perceptions included the changes in daily routine related to PwD formal care services utilization or admission. Many caregivers expressed several barriers to access formal care: bad experiences, stigma, high costs, lack of targeted care for PwD, mistrust, long and bureaucratic process of admission, limited spaces and long waiting lists. Despite the time-consuming process involved, formal care services such as home-based support care and day centers were welcomed by the caregivers. This type of support were important to ensure PwD personal hygiene, especially when caregivers had physical limitations, providing simultaneously free time for caregivers. Moreover, in caregiver's opinion, the PwD attending to the day center was a relief not only for them, but also for the patients, by allowing them to be engaged by social activities, participation in physical and cognitive classrooms and create a routine (like a school, as described by caregivers and PwD itself). The benefits of day centers in supporting family caregivers and PwD were recently reviewed (Maffioletti et al., 2019). In fact, attending day care was significantly associated with higher self-reported scores of QoL by PwD (Tretteteig et al., 2017).

The resort to nursing home was just considered in advanced stages of the disease (or when not having other alternative), and if facilities had good conditions - however, in caregivers' opinion, good services at a reasonable cost do not exist. Also, the nursing homes are not prepared for PwD, requiring some adaptation to support the course of dementia, as described in other studies (Lethin, Hallberg, et al., 2016; Stephan et al., 2018; Xiao et al., 2013). The need for a more adapted care regarding dementia features was an agreement issue between the caregivers. Thus, the stigma around the use of nursing homes delays the moment of institutionalization to its last, with caregivers avoiding it as longer as possible. However, considering the caregivers availability to care for their relatives, when they also have professional occupations, probably increased the use of formal care services to avoid PwD loneliness. Institutionalization is never an easy choice for the caregiver because nursing homes are often associated with fair or poor QoL by public perceptions and several published studies reported its negative consequences in the institutionalized residents: depression, loneliness, alienation and a decrease in functional ability (Aneshensel et al., 2000; Ball et al., 2000; Hogan & Mickus, 2002). As a result, a study including former caregivers of PwD revealed greater burden in the moment of their relative's institutionalization (Andrén & Elmståhl, 2002). The transition to a nursing home was seen as a failure of the caregiver (like being a bad caregiver or not good enough to care for their relative). There are also cultural traditions supporting home care, with care

for older adults being viewed as responsibility of their children's (Nikmat et al., 2011). Our findings, in line with previous studies demonstrate that interventions should be focused on a healthier transition for family caregivers in the moment of admission of their relatives in a nursing home (Lethin, Leino-Kilpi, et al., 2016; Verbeek et al., 2012).

Our study also assessed the HRQoL and functional/cognitive levels of 187 PwD in different daily contexts. All the caregivers were family members of a PwD, mostly daughters or wife's aged around sixty years old. In our study, when the caregiver had other familiar relationship than wife or husband (that already lived with the patient), the caregiver was the person that moved into the patients' home. This fact might be mainly related to the patients' preferences to be in his own house and environment, but also because of previous establishment of nearby formal care services involving the patient and his/her address.

Caregivers' education level varied but the majority attended university and had a professional occupation or were retired. Importantly, we found that 40% of caregivers were working while caring, showing that many caregivers maintained a professional occupation. This fact can be explained by their mean age of 60 years old, that was below the retirement age of 66.5 years old in Portugal (67.4% of the caregivers were younger than 67 years old). However, 3.9% of the caregivers were professional active despite their age (above 66.5 years old). The age is a factor for retirement, but there are other conditions that can result in early retirement. As a result, some caregivers below 66.5 years old were also retired (43% of the caregivers). Consequently, the percentage of retired caregivers professionally active can be higher than the reported. Other reasons to be professional active, even when retired, are the financial struggle introduced by dementia; the low income achieved in a regular monthly job during lifetime and the scarse financial support by social security among the Portuguese informal caregivers' community (C. F. Rodrigues & Andrade, 2014; P. Santana, 2002). In 2019, Informal Caregiver Status was approved in Portugal to establishing support measures. However, recent information published in Deco Proteste Website (www.deco.proteste.pt, published in D&D março/abril 2021), demonstrated that the application of this support suffered constraints due to the Covid-19 pandemic. Still, it is mentioned that this support is heavily involved in bureaucracies, it is not fully inclusive, it is insufficiently disseminated in the community and the financial support offered is relatively low (a mean of €315). As a result, most of caregivers admitted to carefully manage their monthly budget, avoiding extra expenses (i.e., social and leisure

moments, medical appointments), resort to their life savings and have a professional occupation, whenever possible, to support the dementia related costs.

The caregiver profile in our sample – living with the PwD, mostly women (wife/daughter), mean age of 60 years old, with high education and professional occupation - was in agreement with the features of informal caregivers of PwD included in other studies (Grunfeld et al., 2004; Kawaharada et al., 2019; Mossello et al., 2008; H. Yu et al., 2015). However, in some cases, the mean age of caregivers and their years of education were lower than the demonstrated in our study.

The PwD were mostly female, the mean age was 82 years old (ranged from 54 to 97 years old; 3.7% below 65 years old). The daily context of PwD included PwD that used to visit day centers during the week, PwD were cared exclusively at home, and PwD that were in a transition moment for formal care admission (pre-nursing-home moment). Our findings show that more than 80% of the dementia patients included attended school, despite the illiteracy levels observed in Portugal in that moment. This is an important aspect regarding dementia, since years of education of PwD are often pointed in research studies as a possible contributor to dementia prevalence. In our study, the educational level of PwD was significantly associated to QoL and functional ability, however its effects were quite low. A study of Brayne et al. 2010, founded that longer years in education were associated with decreased dementia risk and greater brain weight but had no relationship to neurodegenerative or vascular pathologies. The relationship of education and dementia was already reviewed by Sharp & Gatz, where of the 88 studies included, 58% reported significant effects of lower education on risk for dementia and the relationships founded were more consistent in developed compared to developing regions (Sharp & Gatz, 2011). To better describe the association of education on risk for dementia, further studies should be developed.

In our study, the resort to formal care services was high (68.4%), revealing some acceptance the use of these type services, mainly the day centers, due to its potential to give a feeling of safety and relief to caregivers (Tretteteig et al., 2016). So, despite the previous reported difficulties in accessing formal care, the high demand for day centers is possible related to the need of caregivers to leave the patient somewhere during the day. Another possible explanation is that most of the patients lived in urban areas, whereas in rural areas the neighbors usually know each other and the need for company (like day center role) is not so evident. The large offer on formal care services like day centers could

also explain the high use of formal services in urban areas (Manuel Gonçalves-Pereira et al., 2019; Rahman et al., 2020). Additionally, as previously mentioned by caregivers in our study, day centers had positive effects in PwD routine, social, mental and physical activity.

Regarding HRQoL, we describe that the most frequent health conditions among Portuguese PwD were associated with very poor states of health. The results of EQ-5D-3L demonstrate that the dimensions of self-care and usual activities were very compromised, followed by mobility issues. However, the dimensions of pain/discomfort and anxiety/depression showed that patients had "no or some problems" in these dimensions, in particular patients cared at home exclusively. The explanation is probably related to the "invisible" effects of these dimensions. For the caregiver it was harder to identify if their relatives were or not suffering from pain, anxiety or depression due to high levels of apathy, medications and low speech abilities. Thef EQ-5D-3L results allow the comparison of health states with other diseases, an advantage to realize the impact of different diseases in patients. As an example, a study including patients with stroke using EQ-5D-3L showed mean values of 0.584 and 54.3 for the EQ-VAS, far above from the obtained in our study (Golicki et al., 2015). As well, Kularatna et al. 2017, conducted a study with patients with cardiovascular disease, which mean of EQ-5D-3L was 0.802.

The QoL was also analyzed by the QoL-AD that also reported poor quality of life. In almost all dimensions of the QoL-AD, the responses were in the lower levels (weak or reasonable). The worst-rated dimensions were physical health, memory, ability to do things at home and for fun, money and life as a whole. A brief comparison of our data with other studies including PwD revealed that the QoL of these PwD in Portugal was extremely low, with mean values of EQ-5D-3L of -0.005±0.31, EQ-VAS 37±18.7 and QoL-AD score 19.5±4.0, comparatively to 0.758, 60.6 and 33.5, respectively, in Germany (Michalowsky et al., 2020). A previous Germany study revealed similar results (29.6) for the QoL-AD score (Römhild et al., 2018). A study conducted in Switzerland including PwD found very similar results to Germany with EQ-5D-3L of 0.78, EQ-VAS of 64 and 32.5 for QoL-AD (Aguirre et al., 2016). A Spanish study conducted in 2013 assessed the QoL of institutionalized adults with dementia revealing a mean EQ-5D index score of 0.11, 51.5 for the EQ-VAS and 27.2 for QoL-AD, still higher values than the results obtained to this Portuguese sample (Diaz-Redondo et al., 2014).

We also found that the functional and cognitive ability of these PwD were especially affected, revealing moderate to severe states of impairment. The dimension of "changes

related to everyday life" was highest score (more impairment), particularly in physical dimensions. The mean of the MMSE score indicated moderate to severe cognitive impairment. Comparing the results obtained with the Rossetti et al. 2010 study, the Portuguese sample of PwD had slightly higher MMSE scores (16.0 *vs* 11.2), but higher functional impairment (15.8 *vs* 9.8 in BDRS score), than US AD patients. Our data revealed very low scores of QoL (both EQ-5D-3L and QoL-AD), and high scores of BDRS and MMSE, meaning that these patients had very poor QoL and high physical and cognitive impairment. As expect, the convergent validity of the EQ-5D index and EQ-VAS with the QoL-AD and BDRS scales was moderately, demonstrating a correlation between QoL and functional ability of PwD (better Qol when BDRS score was lower). Additionally, the QoL-AD and BDRS scores moderately correlated with some of EQ-5D dimensions such as mobility, self-care, usual activities and anxiety/depression. The tools used in the assessment related in different ways with the studied variables. The health state "at the moment", measured by EQ-5D-3L for the PwD by proxy correlated weakly and in a negative way with years since diagnosis, age of PwD, age of caregiver and years of care which means that these factors presented low influence in decreasing PwD QoL and, EQ-5D-3L correlated strongly with the BDRS domain of changes in habits, meaning that more changes in PwD habits revealed poor QoL. The QoL-AD correlated weakly and positively with caregivers' years of education, but in a negative way with PwD and caregiver's age. Also, the QoL-AD correlated moderately and negatively with BDRS score and with BDRS domain of changes in habits, meaning that more changes in functional ability revealed poor QoL. Additionally, the years since diagnosis and years of care were weakly correlated to the BDRS score, meaning that more years of diagnosis resulted in higher scores of BDRS so, less functional ability. Additionally, in a multivariate linear regression model for EQ-5D-3L score, we found association between education level of PwD (more years of education, better EQ-5D-3L), its functional ability by BDRS (more changes in functional ability decreased the EQ-5D-3L), and the PwD daily context. Attending to day center were significantly associated to PwD QoL increased, with these patients being reported with high scores of EQ-5D-3L. Of note, attending their centers were also associated to a decrease in BDRS score, meaning better functional capacity. The differences indicated that EQ-5D-3L and BDRS were related to different aspects in these patients, in detail, physical and personal domains, respectively, that are affected differently if they are attending in the day center. The day center is an opportunity for the PwD to communicate with other

persons beside their caregivers and attend to physical and cognitive games and classes. The daily routine introduced by attending the day center and the social context involved might positively contributed to PwD well-being.

Altogether, the results obtained for the Portuguese sample of PwD regarding QoL and functional/cognitive ability were low and far below, when compared to European countries and even with other incapacitating diseases as stroke or cardiovascular diseases. The analysis between the daily context of PwD was important to better understand the environment surrounding the PwD and how the different situations changed the PwD QoL and functional/cognitive ability.

Finally, we assess the QoL and burden of informal caregivers of PwD, identifying its associated factors. Regarding the EQ-5D-3L index (health status index), the indicated that the informal caregivers had complications usually in two or three domains of EQ-5D-3L. As well as in the EQ-5D-3L, the mean value found for EQ-VAS was lower when comparing to Portuguese population norms (60.7±19.7 *vs* 74.9 (SD not shown), respectively) (L. N. Ferreira et al., 2014), and with other informal caregivers of PwD (Lopez-Bastida et al., 2006; Madruga et al., 2020; Reed et al., 2017). Even when comparing our results with caregivers of patients with other health problems than dementia, for example, caregivers of autistic children, the results that we obtained for QoL were also extremely below (Khanna et al., 2013). Regarding the physical, emotional and social burden of the informal caregivers, our results indicated severe burden and the most affected dimensions were the financial burden, implications for personal life and emotional burden. In comparison with other Portuguese studies using QASCI, the results obtained to physical, emotional and social burden in our sample of informal caregivers of PwD were always higher (Félix, 2008; Pereira, 2007; L. M. P. Rodrigues, 2018). In general, caregivers with lower burden reported significantly better perceived health and higher EQ-5D-3L and EQ-VAS mean score than caregivers with higher burden. However, since caregiving varies from case to case, some studies discuss how sociodemographic factors (such as gender and age of caregivers), as well the nature of relationships with the care recipient, affect the caregiving role (Kwak et al., 2012; Lin et al., 2012). In accordance with previous studies (Lin et al., 2012), in our study the included female caregivers reported having lower QoL and elevated burden than male caregivers, in detail, wife's and daughters in comparison to husbands and sons, however in our study the sons and daughters did not experience the stress and burden process similarly, since sons were the

ones among all the familiar relationships with lower QASCI scores and higher EQ-5D-3L, meaning less physical, emotional and social burden and better QoL, in disagreement with Kwak et al., 2012.

The dimension of financial burden was the dimension more affected in our study, and that is another widely explored theme in the literature (Åkerborg et al., 2016; Kronborg Andersen et al., 2003; Moore et al., 2001). However, contrarily to what was found by Karg et al., 2018, where higher levels of QoL occurred in unemployed caregivers suggesting that work played an important role in the development of stress, in our study having a job seemed to have the exactly opposite effect suggesting that it worked as a relief, a free time from the care tasks and obviously a higher familiar income (Åkerborg et al., 2016; Kronborg Andersen et al., 2003; Moore et al., 2001). Also, the educational level of caregivers demonstrated that more years of education lead to better QoL and less overall burden, especially when caregivers attend school for more than 12 years, while the educational level of the PwD revealed that caregivers for PwD that attended less than 6 years of school reported poor QoL in comparison to the remain caregivers, however, in all cases, the burden experienced was moderate. This might be related with better incomes of highly educated caregivers, that probably can afford for formal care services like a formal caregiver, decreasing the impact on their QoL.

Caring for PwD less than 2 until 15 years did not changed EQ-5D-3L index score, with the differences being more evident in the EQ-VAS, that decreased as years of care increased. About the burden, the increase of years of care resulted in higher burden for the informal caregivers. However, in the group of caregivers that were caring for 2 to 3 years, a different comportment was found, since they were the ones with higher EQ-5D-3L, EQ-VAS and lower QASCI scores. This fact could possibly be related to some transitional relief of the PwD symptoms or some external factors of the caregiver life, deserving further investigation. The increase of hours of care resulted, as expected, in higher burden and less QoL for the informal caregivers, due to the all the physical and emotional environment involved.

In sum, the results of the multiple analysis showed that different explanatory variables were related to informal caregivers QoL and physical, emotional and social burden. The only explanatory variables that were common in the two models were the familiar relationship with the PwD and PwD pain/discomfort. There was a strong association between higher levels of caregivers QoL in younger caregivers, daughters or sons, with

lower implications in personal life, caring for younger PwD with less pain and discomfort; and lower overall burden in daughter/sons with less pain/discomfort problems, professional active, caring for PwD with less problems in performing self-care tasks, less changes in personality (behaviour problems) and with better QoL. Overall, this study highlights that QoL of informal caregivers of PwD in Portugal is lower when compared to other European countries and higher if compared to other diseases. This is an important topic, deserving more attention due its tremendous impact in family members and in PwD himself.

Generally, is it understood that dementia care is impacted by multiple factors including features of both PwD and the caregiver, their relationship, their living context and the daily context surrounding the dyads which are unique in each case. These multicomplex atmosphere involving dementia, the available support programs and measures do not meet caregivers and PwD personal needs. These results can be used to inform Portuguese policy makers, health care professionals and researchers in issues related with PwD HRQoL and dependency level to improve health care policy and community interventions to better embrace these patients and caregivers' personal needs and mainly promote their QoL and decrease dementia burden. It is highlighted that dementia informal care included a wide range of experiences signaled by the caregivers about the disease, as well as the drastic changes introduced in their personal lives. Therefore, a dedicated intervention including multiple domains regarding dementia informal care should be developed, committing the society to promote mental health, address these community needs and improve the QoL of the PwD and their family caregivers.

This project has not finished: the resource utilization in dementia (RUD) was also applied to describe the resort to health services and formal care support of both patients and caregivers. Importantly, these results will strongly contribute to better describe the holistic phenomenon of dementia care in a sample of Portuguese dyads, increasing the knowledge regarding dementia related costs and formal services utilization.

In conclusion, the data of our studies allow a more detailed comparison of the Portuguese scenario with European countries. Our study highlights that QoL of PwD and their informal caregivers in Portugal (regarding our sample) is lower when compared to other European countries. This justifies the need for extra attention when discussing policies facing one of the most relevant threats of ageing - the immense impact of dementia in QoL. Mental disorders are still undervalued in health policies, but ageing countries cannot afford to remain inactive regarding this topic any longer. It is urgent to address

possible interventions intended to mitigate the negative impact of dementia in QoL. The complexity of factors requires an integrated community response. This means early diagnosis, effective follow-up of the patient and the caregiver, physical and cognitive stimulation, social and economic support, formal care services aligned with dementia patients and caregivers needs and closer support groups. A holistic intervention (directed to the patient and the caregiver needs), will likely decrease burden and improve QoL in dementia. Additionally, this study reveals the need of studies focusing the QoL of dementia informal caregivers, as well as on their burden due to informal care.

2. Study limitations

The studies described in this thesis present limitations. Among the most relevant are a) the inclusion of only qualitative studies in our systematic review; b) limited sample and scarce time with caregivers at focus groups; and c) lack of dementia differential diagnosis clinical confirmation in the quantitative assessment group, d) the incomplete application of MMSE, that covered just 43 of the included PwD.

Qualitative studies presented methodological limitations or did not use appropriate theoretical frameworks to the systematic review. This is a common limitation of qualitative research. The comprehensiveness of caregiver experiences might be limited because several studies did not primarily examine caregivers' positive and negative experiences. However, the data of the systematic review have important implications for the development of interventions that comprehensively address caregivers' individual needs based on their experiences and demonstrate there is a need for more rigorous qualitative studies focusing the perceived positive and negative aspects of caregiving.

In focus groups sessions, the main limitations were the scarce time of caregivers imposed by the severity of their relative's disease, leading to the inevitable exclusion of the most severe cases (caregivers of persons with dementia in advanced stages) and the focus on a single urban area of the Portuguese territory. However, the sample focused different living situations, familiar relationships, ages, professional status of the caregiver, different times of diagnosis and stages of severity envisaging a better representation of dementia informal care as possible.

Finally, the main limitations of the quantitative study involving PwD were the non-existence of a diagnosis confirmation, the non-random sample from a single urban area of Portugal. This study allowed the description of the sociodemographic and clinical data on QoL and physical/cognitive impairment of the PwD in Portugal that is a bottleneck of studies reported in literature. So far, this was the first study that collected impact of dementia qualitatively and data on QoL and functional/cognitive impairment, while describing data on informal caregivers as well. Additionally, the source of recruitment of participants was diverse, including the Neurology outpatients' clinic at the Centro Hospitalar Universitário Lisboa Norte E.P.E, health care facilities of a recognized National Care Institution, and Portuguese Alzheimer's Associations.

3. Conclusions

Dementia informal care included a wide range of experiences referred by the caregivers about the disease and the proper way of caring, as well as the drastic changes introduced in their personal lives. Caregivers' perceptions about the related costs of dementia caregiving, and its positive and negative aspects are crucial to develop targeted interventions for this community. These would likely reduce the impact on caregiver's well-being, promoting quality of life to both caregiver and PwD.

In Portugal, PwD demonstrated to have very low levels of QoL and a severe impairment on their functional and cognitive ability (patient-by proxy). Factors such as PwD age, years of diagnosis PwD, educational level, and caregivers age are correlated to QoL and functional capacity of PwD. Regarding the caregivers QoL and burden, different factors were found, however, in both cases the familiar relationship with the PwD and PwD pain/discomfort were identified as potential explanatory factors.

Dementia patients, in other European Member States, should be regarded as an example to be followed based on their intervention approaches in order to enhance the QoL in Portuguese dementia patients. The articulation and cooperation of different public services (formal care services, neurology, psychiatric, psychology, social and financial support) should be re-thought and multicomplex interventions must be developed envisaging the need of each case. More Portuguese studies are needed to better describe the hurdles, the needs of dementia care and HRQoL in these patients to further develop programs, reducing the negative effects of dementia on patient's QoL, while promoting caregiver's QoL as well. Future research should focus on follow-up studies to evaluate patient-caregiver direct interventions impact on both QoL, while studying the application of specific and generic HRQoL instruments. Additionally, the dramatic changes introduced in caregivers' personal lives should be taken into account, and future research should also include caregivers as a central aim of study.

4. Future perspectives

With these studies, we were able to gather information suggesting the Portuguese PwD presented very low QoL and high functional and cognitive impairment. The informal caregivers were exposed to high psychical, emotional, social and financial burden and reported their QoL as low.

As next steps, we intend to analyze the formal resource utilization (RUD – resource utilization in dementia) of the dyads and determinate the economic costs related to dementia, that are widely unknown in Portugal. The determination of dementia-related costs is crucial to better understand its financial burden, already described in our qualitative study.

Finally, we aim to compare the HRQoL instruments used in our study to measure QoL, that are commonly applied in medical research and assess the differences between them as disease-specific measures (QoL-AD) and generic instruments (EQ-5D-3L) and determine which is most adapted to use in different research contexts.

CHAPTER 7

REFERENCES

Aalami, O. O., Fang, T. D., Song, H. M., & Nacamuli, R. P. (2003). Physiological features of aging persons. *Archives of Surgery*, *138*(10), 1068–1076. https://doi.org/10.1001/archsurg.138.10.1068

ADI. (2019). World Alzheimer Report 2019, Attitudes to dementia. *Alzheimer's Disease International: London*, 1–15. www.daviddesigns.co.uk

Aguirre, E., Kang, S., Hoare, Z., Edwards, R. T., & Orrell, M. (2016). How does the EQ-5D perform when measuring quality of life in dementia against two other dementia-specific outcome measures? *Quality of Life Research*, *25*(1), 45–49. https://doi.org/10.1007/s11136-015-1065-9

Åkerborg, Ö., Lang, A., Wimo, A., Sköldunger, A., Fratiglioni, L., Gaudig, M., & Rosenlund, M. (2016). Cost of Dementia and Its Correlation with Dependence. *Journal of Aging and Health*, *28*(8), 1448–1464. https://doi.org/10.1177/0898264315624899

Alberdi, A., Aztiria, A., & Basarab, A. (2016). On the early diagnosis of Alzheimer's Disease from multimodal signals: A survey. *Artificial Intelligence in Medicine*, *71*, 1–29. https://doi.org/10.1016/j.artmed.2016.06.003

Albert, S. M., Sano, M., Bell, K., Merchant, C., Small, S., & Stern, Y. (1998). Hourly care received by people with Alzheimer's disease: Results from an urban, community survey. *Gerontologist*, *38*(6), 704–714. https://doi.org/10.1093/geront/38.6.704

Alfakhri, A. S., Alshudukhi, A. W., Alqahtani, A. A., Alhumaid, A. M., Alhathlol, O. A., Almojali, A. I., Alotaibi, M. A., & Alaqeel, M. K. (2018). Depression among caregivers of patients with dementia. *Inquiry (United States)*, *55*, 4–9. https://doi.org/10.1177/0046958017750432

Alzheimer's Disease International. (2013). *Alzheimer's Disease International. Policy Brief for G8 Heads of Government. The Global Impact of Dementia 2013-2050. London*.

Alzheimer's Disease International (ADI). (2018). Global estimates of informal care. *Alzheimer's Disease International*. https://www.alz.co.uk/adi/pdf/global-estimates-of-informal-care.pdf

Alzheimer Europe. (2019). Dementia in Europe Yearbook. Estimating the prevalence of dementia in Europe. *European Union's Health Programme (2014–2020)*, 108.

Alzheimers Association. (2013). In Brief for Healthcare Professionals: Differentiating Dementias. *Alzheimer's Association*, *13*(7), 1–2. https://doi.org/10.4088/PCC.11r01190.Table

American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders, 3rd edn, revised*.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders 4th ed.*

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders. (IV-TR).*

American Psychiatric Association. (2013a). *Diagnostic and statistical manual of mental disorders (5th ed.).*

American Psychiatric Association. (2013b). *Major Neurocognitive Disorder. Diagnostic*

and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). 602–603.

Aminzadeh, F., Byszewski, A., Molnar, F. J., & Eisner, M. (2007). Emotional impact of dementia diagnosis: Exploring persons with dementia and caregivers' perspectives. *Aging and Mental Health*, *11*(3), 281–290. https://doi.org/10.1080/13607860600963695

Andrén, S., & Elmståhl, S. (2002). Former Family Carers' Subjective Experiences of Burden:A comparison between group living and nursing home environments in one municipality in Sweden. *Dementia*, *1*(2), 241–254. https://doi.org/10.1177/147130120200100209

Andrén, S., & Elmståhl, S. (2008). The relationship between caregiver burden, caregivers' perceived health and their sense of coherence in caring for elders with dementia. *Journal of Clinical Nursing*, *17*(6), 790–799. https://doi.org/10.1111/j.1365-2702.2007.02066.x

Aneshensel, C. S., Pearlin, L. I., & Schuler, R. H. (2000). Mortality Among People With Dementia. *Journal of Gerontology: Social Sciences*, *55*(3), 152–162.

Arai, A., Matsumoto, T., Ikeda, M., & Arai, Y. (2007). Do family caregivers perceive more difficulty when they look after patients with early onset dementia compared to those with late onset dementia? *International Journal of Geriatric Psychiatry*, *22*(12), 1255–1261. https://doi.org/10.1002/gps.1935

Argimon, J. M., Limon, E., Vila, J., & Cabezas, C. (2005). Health-related quality-of-life of care-givers as a predictor of nursing-home placement of patients with dementia. *Alzheimer Disease and Associated Disorders*, *19*(1), 41–44. https://doi.org/10.1097/01.wad.0000160343.96562.8e

Arnerić, S. P., Batrla-Utermann, R., Beckett, L., Bittner, T., Blennow, K., Carter, L., Dean, R., Engelborghs, S., Genius, J., Gordon, M. F., Hitchcock, J., Kaplow, J., Luthman, J., Meibach, R., Raunig, D., Romero, K., Samtani, M. N., Savage, M., Shaw, L., … Yule, S. (2016). Cerebrospinal fluid biomarkers for Alzheimer's disease: A view of the regulatory science qualification landscape from the coalition against major diseases CSF biomarker team. *Journal of Alzheimer's Disease*, *55*(1), 19–35. https://doi.org/10.3233/JAD-160573

Arthur, P. B., Gitlin, L. N., Kairalla, J. A., & Mann, W. C. (2018). Relationship between the number of behavioral symptoms in dementia and caregiver distress: What is the tipping point? *International Psychogeriatrics*, *30*(8), 1099–1107. https://doi.org/10.1017/S104161021700237X

Arvanitakis, Z., Shah, R. C., & Bennett, D. A. (2019). Diagnosis and Management of Dementia: Review. *JAMA - Journal of the American Medical Association*, *322*(16), 1589–1599. https://doi.org/10.1001/jama.2019.4782

Bakker, C., De Vugt, M. E., Van Vliet, D., Verhey, F. R. J., Pijnenburg, Y. A., Vernooij-Dassen, M. J. F. J., & Koopmans, R. T. C. M. (2013). The use of formal and informal care in early onset dementia: Results from the NeedYD study. *American Journal of Geriatric Psychiatry*, *21*(1), 37–45. https://doi.org/10.1016/j.jagp.2012.10.004

Ball, M. M., Whittington, F. J., Perkins, M. M., Patterson, V. L., Hollingsworth, C., King, S. V., & Combs, B. L. (2000). Quality of life in assisted living facilities: Viewpoints of residents. *Journal of Applied Gerontology*, *19*(3), 304–325.

https://doi.org/10.1177/073346480001900304

Banerjee, S. (2013). Good news on dementia prevalence - We can make a difference. *The Lancet*, *382*(9902), 1384–1386. https://doi.org/10.1016/S0140-6736(13)61579-2

Banningh, L. J. W., Vernooij-Dassen, M., Rikkert, M. O., & Teunisse, J. P. (2008). Mild cognitive impairment: Coping with an uncertain label. *International Journal of Geriatric Psychiatry*, *23*(2), 148–154. https://doi.org/10.1002/gps.1855

Barbosa, A., Cruz, J., Figueiredo, D., Marques, A. & Sousa, L. (2011). Cuidar de idosos com demência, dificuldades e necessidades percepcionadas pelos cuidadores formais. *Revista Psicologia, Saúde & Doenças*, *12 (1)*(1), 119–129.

Bárrios, H; (2012). *Adaptação Cultural e Linguística e Validação do Instrumento QOL-AD para Portugal*. 1–106.

Bárrios, Helena, Narciso, S., Guerreiro, M., Maroco, J., Logsdon, R., & De Mendonça, A. (2013). Quality of life in patients with mild cognitive impairment. *Aging and Mental Health*, *17*(3), 287–292. https://doi.org/10.1080/13607863.2012.747083

Bárrios, Helena, Verdelho, A., Narciso, S., Gonçalves-Pereira, M., Logsdon, R., & De Mendonça, A. (2013). Quality of life in patients with cognitive impairment: Validation of the Quality of Life-Alzheimer's Disease scale in Portugal. *International Psychogeriatrics*, *25*(7), 1085–1096. https://doi.org/10.1017/S1041610213000379

Beerens, H. C., Sutcliffe, C., Renom-Guiteras, A., Soto, M. E., Suhonen, R., Zabalegui, A., Bökberg, C., Saks, K., & Hamers, J. P. H. (2014). Quality of life and quality of care for people with dementia receiving long term institutional care or professional home care: The European righttimeplacecare study. *Journal of the American Medical Directors Association*, *15*(1), 54–61. https://doi.org/10.1016/j.jamda.2013.09.010

Berger L, M.-P. D. (1995). *Pessoas idosas: uma abordagem global* (Lusodidacta (ed.)).

Bird, M. L., Pittaway, J. K., Cuisick, I., Rattray, M., & Ahuja, K. D. K. (2013). Age-related changes in physical fall risk factors: Results from a 3 year follow-up of community dwelling older adults in Tasmania, Australia. *International Journal of Environmental Research and Public Health*, *10*(11), 5989–5997. https://doi.org/10.3390/ijerph10115989

Blanchet S, McCormick L, Belleville S, Gély-Nargeot M- C, J. Y. (2002). Les troubles cognitifs légers de la personne âgée: revue critique. *Revue Neurologique*, *158*, 29–40.

Blandin, K., & Pepin, R. (2017). Dementia grief: A theoretical model of a unique grief experience. *Dementia*, *16*(1), 67–78. https://doi.org/10.1177/1471301215581081

Blessed, G., Tomlinson, B. E., & Roth, M. (1968). The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *The British Journal of Psychiatry : The Journal of Mental Science*, *114*(512), 797–811. https://doi.org/10.1192/bjp.114.512.797

Bökberg, C., Ahlström, G., & Karlsson, S. (2018). Utilisation of formal and informal care and services at home among persons with dementia: a cross-sectional study. *Scandinavian Journal of Caring Sciences*, *32*(2), 843–851. https://doi.org/10.1111/scs.12515

Bonner, G. J., Wang, E., Wilkie, D. J., Ferrans, C. E., Dancy, B., & Watkins, Y. (2014).

Advance care treatment plan (ACT-Plan) for African American family caregivers: A pilot study. *Dementia*, *13*(1), 79–95. https://doi.org/10.1177/1471301212449408

Bouchard, R. W. (2007). Diagnostic criteria of dementia. *Canadian Journal of Neurological Sciences*, *34*(SUPPL. 1), 11–18. https://doi.org/10.1017/s0317167100005497

Bowling, A. (1997). *Research Methods in Health: Investigating Health and Health Services* (Trowbridge Oxford University (ed.)). Trowbridge Oxford University.

Brayne, C., Ince, P. G., Keage, H. A. D., McKeith, I. G., Matthews, F. E., Polvikoski, T., & Sulkava, R. (2010). Education, the brain and dementia: Neuroprotection or compensation? *Brain*, *133*(8), 2210–2216. https://doi.org/10.1093/brain/awq185

Bremer, P., Challis, D., Hallberg, I. R., Leino-Kilpi, H., Saks, K., Vellas, B., Zwakhalen, S. M. G., & Sauerland, D. (2017). Informal and formal care: Substitutes or complements in care for people with dementia? Empirical evidence for 8 European countries. *Health Policy*, *121*(6), 613–622. https://doi.org/10.1016/j.healthpol.2017.03.013

Brodaty, H., & Green, A. (2002). Who cares for the carer? The often forgotten patient. *Australian Family Physician*, *31*(9), 7–10.

Brodaty, H., & Hadzi-Pavlovic, D. (2016). Psychosocial effects on carers of living with persons with dementia. *Australasian Psychiatry*, *24*(3), 351–361. https://doi.org/10.3109/00048679009077702

Bronikowski, A., & Flatt, T. (2010). Aging and its demographic measurement. *Nature Education Knowedge*, *3*(January 2010), 3–9.

Bruce, J. M., McQuiggan, M., Williams, V., Westervelt, H., & Tremont, G. (2008). Burden among spousal and child caregivers of patients with mild cognitive impairment. *Dementia and Geriatric Cognitive Disorders*, *25*(4), 385–390. https://doi.org/10.1159/000122587

Bruvik, F. K., Ulstein, I. D., Ranhoff, A. H., & Engedal, K. (2012). The quality of life of people with dementia and their family carers. *Dementia and Geriatric Cognitive Disorders*, *34*(1), 7–14. https://doi.org/10.1159/000341584

Bryan, S., Hardyman, W., Bentham, P., Buckley, A., & Laight, A. (2005). Proxy completion of EQ-5D in patients with dementia. *Quality of Life Research*, *14*(1), 107–118. https://doi.org/10.1007/s11136-004-1920-6

Budson, A. E., & Solomon, P. R. (2011). *Memory Loss: A Practical Guide for Clinicians*. Elsevier Saunders. https://books.google.pt/books?id=0eZUYgEACAAJ

Bukov, A., Maas, I., & Lampert, T. (2002). Social participation in very old age: Cross-sectional and longitudinal findings from BASE. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *57*(6), 510–517. https://doi.org/10.1093/geronb/57.6.P510

Bunn, F., Burn, A. M., Robinson, L., Poole, M., Rait, G., Brayne, C., Schoeman, J., Norton, S., & Goodman, C. (2017). Healthcare organisation and delivery for people with dementia and comorbidity: A qualitative study exploring the views of patients, carers and professionals. *BMJ Open*, *7*(1), 1–9. https://doi.org/10.1136/bmjopen-2016-013067

Burton, E., Slatyer, S., Bronson, M., Nichols, P., Quested, E., Hill, A., Maher, S., Aoun, S., Hill, K. D., Kuno, Y., & Toye, C. (2019). Development and pilot testing of the "focus on the person" form: Supporting care transitions for people with dementia. *Dementia*, *18*(6), 2018–2035. https://doi.org/10.1177/1471301217736594

Butcher, H. K., Holkup, P. A., & Buckwalter, K. C. (2001). The experience of caring for a family member with Alzheimer's disease. *Western Journal of Nursing Research*, *23*(1), 33–55. https://doi.org/10.1177/01939450122044943

Cabeza, R., & Moscovitch, M. (2013). Memory Systems, Processing Modes, and Components: Functional Neuroimaging Evidence. *Perspectives on Psychological Science*, *8*(1), 49–55. https://doi.org/10.1177/1745691612469033

Calderon-Garcidueñas, A. L., & Duyckaerts, C. (2018). Alzheimer disease. *Handbook of Clinical Neurology*, *145*, 325–337. https://doi.org/10.1016/B978-0-12-802395-2.00023-7

Cations, M., Withall, A., Horsfall, R., Denham, N., White, F., Trollor, J., Loy, C., Brodaty, H., Sachdev, P., Gonski, P., Demirkol, A., Cumming, R. G., & Draper, B. (2017). Why aren't people with young onset dementia and their supporters using formal services? Results from the INSPIRED study. *PLoS ONE*, *12*(7), e0180935. https://doi.org/10.1371/journal.pone.0180935

Charles, S., & Carstensen, L. (2010). Social and Emotional Aging. *Annual Review of Psychology*, *61*, 383–409. https://doi.org/10.1146/annurev.psych.093008.100448

Charles, S. T., Piazza, J. R., Luong, G., & Almeida, D. M. (2009). Now You See It, Now You Don't: Age Differences in Affective Reactivity to Social Tensions. *Psychology and Aging*, *24*(3), 645–653. https://doi.org/10.1037/a0016673

Cheng, S. T., Mak, E. P. M., Lau, R. W. L., Ng, N. S. S., & Lam, L. C. W. (2016). Voices of Alzheimer caregivers on positive aspects of caregiving. *Gerontologist*, *56*(3), 451–460. https://doi.org/10.1093/geront/gnu118

Chételat, G., La Joie, R., Villain, N., Perrotin, A., De La Sayette, V., Eustache, F., & Vandenberghe, R. (2013). Amyloid imaging in cognitively normal individuals, at-risk populations and preclinical Alzheimer's disease. *NeuroImage: Clinical*, *2*(1), 356–365. https://doi.org/10.1016/j.nicl.2013.02.006

Cohen, J. (1977). The Significance of a Product Moment rs. In Hillsdale (Ed.), *Statistical Power Analysis for the Behavioral Sciences* (Statistica). Lawrence Erlbaum Associates. https://doi.org/10.1016/b978-0-12-179060-8.50008-6

Colombo, F., Llena-Nozal, A., Mercier, J., & Tjadens, F. (2011). Help Wanted? Providing and Paying for Long-Term Care. *Health Policy Studies, OECD Publishing, Paris*. https://doi.org/10.1787/9789264097759-en.

Comfort, A. (1979). *The Biology of Senescence, 3rd Edn.* Edinburgh and London: Churchill Livingstone.

Comission, E. (2020). *Ageing Europe. Looking at the lives of older people in the EU*. Publications Office of the European Union.

Connell, C. M., Boise, L., Stuckey, J. C., Holmes, S. B., & Hudson, M. L. (2004). Connell_2004_Attitudes Toward the Diagnosis and Disclosure of Dementia Among Family Caregivers and Primary Care Physicians.pdf. *The Gerontologist*, *44*(4), 500–

507.

Connell, C. M., Janevic, M. R., & Gallant, M. P. (2001). The costs of caring: Impact of dementia on family caregivers. *Journal of Geriatric Psychiatry and Neurology*, *14*(4), 179–187. https://doi.org/10.1177/089198870101400403

Cooper, P. (1970). Advances in the treatment of depression. *Midwife and Health Visitor*, *6*(8), 308.

Copeland, J. R. M., Dewey, M. E., & Saunders, P. (1991). The epidemiology of dementia: GMS-AGECAT studies of prevalence and incidence, including studies in progress. *European Archives of Psychiatry and Clinical Neuroscience*, *240*(4–5), 212–217. https://doi.org/10.1007/BF02189529

Copeland, M. P., Daly, E., Hines, V., Mastromauro, C., Zaitchik, D., Gunther, J., & Albert, M. (2003). Psychiatric symptomatology and prodromal Alzheimer's disease. *Alzheimer Disease and Associated Disorders*, *17*(1), 1–8. https://doi.org/10.1097/00002093-200301000-00001

Corbin, J. M., & Strauss, A. (1990). Grounded theory research: Procedures, canons, and evaluative criteria. *Qualitative Sociology*, *13*(1), 3–21. https://doi.org/10.1007/BF00988593

Corbin, J., & Strauss, A. (2012). Basics of Qualitative Research (3rd ed.): Techniques and Procedures for Developing Grounded Theory. In *Basics of Qualitative Research (3rd ed.): Techniques and Procedures for Developing Grounded Theory* (3rd editio, Vol. 3, Issue 2). https://doi.org/10.4135/9781452230153

D'Aoust, R. F., Brewster, G., & Rowe, M. A. (2015). Depression in informal caregivers of persons with dementia. *International Journal of Older People Nursing*, *10*(1), 14–26. https://doi.org/10.1111/opn.12043

de Moraes, F. M., & Bertolucci, P. H. F. (2017). Clinical variables related to the diagnostic stability of demential syndromes. *International Psychogeriatrics*, *29*(10), 1735–1741. https://doi.org/DOI: 10.1017/S1041610217001053

Deckers, K., Van Boxtel, M. P. J., Schiepers, O. J. G., De Vugt, M., Sánchez, J. L. M., Anstey, K. J., Brayne, C., Dartigues, J. F., Engedal, K., Kivipelto, M., Ritchie, K., Starr, J. M., Yaffe, K., Irving, K., Verhey, F. R. J., & Köhler, S. (2015). Target risk factors for dementia prevention: A systematic review and Delphi consensus study on the evidence from observational studies. *International Journal of Geriatric Psychiatry*, *30*(3), 234–246. https://doi.org/10.1002/gps.4245

DeFeis, B. L., Zhu, C. W., Azar, M., Gu, Y., Stern, Y., & Cosentino, S. (2015). P2-276: The cost of disordered awareness: An examination of medicare use in dementia. *Alzheimer's & Dementia*, *11*(7S_Part_13), P597–P597. https://doi.org/10.1016/j.jalz.2015.06.817

Dening, K. H., Greenish, W., Jones, L., Mandal, U., & Sampson, E. L. (2012). Barriers to providing end-of-life care for people with dementia: A whole-system qualitative study. *BMJ Supportive and Palliative Care*, *2*(2), 103–107. https://doi.org/10.1136/bmjspcare-2011-000178

Diaz-Redondo, A., Rodríguez-Blázquez, C., Ayala, A., Martinez-Martin, P., Forjaz, M. J., MJoão Forjaz, Fernández-Mayoralas, G., Rojo-Pérez, F., Martínez-Martín, P., Frades-

Payo, B., León-Salas, B., ávila, M., & Prieto-Flores, M. E. (2014). EQ-5D rated by proxy in institutionalized older adults with dementia: Psychometric pros and cons. *Geriatrics and Gerontology International*, *14*(2), 346–353. https://doi.org/10.1111/ggi.12108

Dissemination, C. for R. and. (2009). *Systematic Reviews - CRD's guidande for undertakin reviews in health care*. University of York.

Dobriansky, P. J., Suzman, R. M., & Hodes, R. J. (2007). Why Population Aging Matters - A Global Perspective. *US Department of State*, 1–32. papers2://publication/uuid/4B8865DB-5866-4285-A74D-168F45ED1109

Douma, J. G., Volkers, K. M., Vuijk, J. P., Sonneveld, M. H., Goossens, R. H. M., & Scherder, E. J. A. (2015). The effects of observation of walking in a living room environment, on physical, cognitive, and quality of life related outcomes in older adults with dementia: A study protocol of a randomized controlled trial. *BMC Geriatrics*, *15*(1), 26. https://doi.org/10.1186/s12877-015-0024-1

Driscoll, I., Hamilton, D. A., Petropoulos, H., Yeo, R. A., Brooks, W. M., Baumgartner, R. N., & Sutherland, R. J. (2003). The Aging Hippocampus: Cognitive, Biochemical and Structural Findings. *Cerebral Cortex*, *13*(12), 1344–1351. https://doi.org/10.1093/cercor/bhg081

Duboisa, B., Padovanib, A., Scheltensc, P., Rossid, A., & Agnello, G. D. (2015). Timely diagnosis for alzheimer's disease: A literature review on benefits and challenges. *Journal of Alzheimer's Disease*, *49*(3), 617–631. https://doi.org/10.3233/JAD-150692

Duxbury, J., Pulsford, D., Hadi, M., & Sykes, S. (2013). Staff and relatives' perspectives on the aggressive behaviour of older people with dementia in residential care: A qualitative study. *Journal of Psychiatric and Mental Health Nursing*, *20*(9), 792–800. https://doi.org/10.1111/jpm.12018

Eastwood, M. R., Lautenschlaeger, E., & Corbin, S. (1983). A Comparison of Clinical Methods for Assessing Dementia. *Journal of the American Geriatrics Society*, *31*(6), 342–347. https://doi.org/10.1111/j.1532-5415.1983.tb05744.x

Edelman, P., & Hughes, S. (1990). The impact of community care on provision of informal care to homebound elderly persons. *Journals of Gerontology*, *45*(2), 74–84. https://doi.org/10.1093/geronj/45.2.S74

Efpia. (2014). *Annual Report 2014*. 1–51.

Efpia. (2020). *The Pharmaceutical Industry : a Key Asset To Scientific and Medical Progress the Pharmaceutical Industry*. 28.

Elnasseh, A. G., Trujillo, M. A., Peralta, S. V., Stolfi, M. E., Morelli, E., Perrin, P. B., & Arango-Lasprilla, J. C. (2016). Family dynamics and personal strengths among dementia caregivers in Argentina. *International Journal of Alzheimer's Disease*, *2016*. https://doi.org/10.1155/2016/2386728

Emmerson, L. C., Ben-Zeev, D., Granholm, E., Tiffany, M., Golshan, S., & Jeste, D. V. (2009). Prevalence and longitudinal stability of negative symptoms in healthy participants. *International Journal of Geriatric Psychiatry*, *24*(12), 1438–1444. https://doi.org/10.1002/gps.2284

Emre, M. (2009). Classification and diagnosis of dementia: A mechanism-based approach.

European Journal of Neurology, *16*(2), 168–173. https://doi.org/10.1111/j.1468-1331.2008.02379.x

Ercoli, L., Siddarth, P., Huang, S. C., Miller, K., Bookheimer, S. Y., Wright, B. C., Phelps, M. E., & Small, G. (2006). Perceived loss of memory ability and cerebral metabolic decline in persons with the apolipoprotein E-IV genetic risk for Alzheimer disease. *Archives of General Psychiatry*, *63*(4), 442–448. https://doi.org/10.1001/archpsyc.63.4.442

Etters, L., Goodall, D., & Harrison, B. E. (2008). Caregiver burden among dementia patient caregivers: A review of the literature. *Journal of the American Academy of Nurse Practitioners*, *20*(8), 423–428. https://doi.org/10.1111/j.1745-7599.2008.00342.x

Eurocarers. (2017). Non-Communicable Diseases. *Mental Health and Informal Care.*

Eurofamcare. (2006). *"Services for Supporting Family Carers of Older Dependent People in Europe: Characteristics, Coverage and Usage", The Trans-European Survey Report*. *February*, 260. http://www.uke.de/extern/eurofamcare/documents/deliverables/teusure_web_080215.pdf

Félix, L. (2008). Sobrecarga e dificuldades dos cuidadores informais dos mais velhos. Tese para a obtençao de Mestrado em Psicogerontologia. Faculdade de Medicina de Lisboa. Universidade de Lisboa. 2008 (Tese não publicada). *Universidade de Lisboa*.

Ferencz, B., & Gerritsen, L. (2015). Genetics and Underlying Pathology of Dementia. *Neuropsychology Review*, *25*(1), 113–124. https://doi.org/10.1007/s11065-014-9276-3

Ferreira, L. N., Ferreira, P. L., Pereira, L. N., & Oppe, M. (2014). EQ-5D Portuguese population norms. *Quality of Life Research*, *23*(2), 425–430. https://doi.org/10.1007/s11136-013-0488-4

Ferreira, P. L., Ferreira, L. N., & Pereira, L. N. (2013). Contributos para a validação da versão Portuguesa do EQ-5D. *Acta Medica Portuguesa*, *26*(6), 664–675.

Ferrucci, L., Giallauria, F., & Guralnik, J. M. (2008). Epidemiology of Aging. *Radiologic Clinics of North America*, *46*(4), 643–652. https://doi.org/10.1016/j.rcl.2008.07.005

Fjellström, C., Starkenberg, Å., Wesslén, A., Licentiate, M. S., Tysén Bäckström, A. C., & Faxén-Irving, G. (2010). To be a good food provider: An exploratory study among spouses of persons with alzheimers disease. *American Journal of Alzheimer's Disease and Other Dementias*, *25*(6), 521–526. https://doi.org/10.1177/1533317510377171

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*(3), 189–198. https://doi.org/10.1016/0022-3956(75)90026-6

Forbes, D. A., Markle-Reid, M., Hawranik, P., Peacock, S., Kingston, D., Morgan, D., Henderson, S., Leipert, B., & Jansen, S. L. (2008). Availability and acceptability of Canadian home and community-based services: Perspectives of family caregivers of persons with dementia. *Home Health Care Services Quarterly*, *27*(2), 75–99. https://doi.org/10.1080/01621420802022548

Forbes, S., Bern-Klug, M., & Gessert, C. (2000). End-of-life decision making for nursing

home residents with dementia. *Journal of Nursing Scholarship*, *32*(3), 251–258. https://doi.org/10.1111/j.1547-5069.2000.00251.x

Foundation, E. R. (2018). *EQ-5D-3L User Guide*. *Available*.

Freitas, S., Simões, M. R., Alves, L., & Santana, I. (2015). The Relevance of Sociodemographic and Health Variables on MMSE Normative Data. *Applied Neuropsychology: Adult*, *22*(4), 311–319. https://doi.org/10.1080/23279095.2014.926455

Gallagher, D., Mhaolain, A. N., Crosby, L., Ryan, D., Lacey, L., Coen, R. F., Walsh, C., Coakley, D., Walsh, J. B., Cunningham, C., & Lawlor, B. A. (2011). Dependence and caregiver burden in Alzheimer's disease and mild cognitive impairment. *American Journal of Alzheimer's Disease and Other Dementias*, *26*(2), 110–114. https://doi.org/10.1177/1533317510394649

Garand, L., Dew, M. A., Eazor, L. R., DeKosky, S. T., & Reynolds, C. F. (2005). Caregiving burden and psychiatric morbidity in spouses of persons with mild cognitive impairment. *International Journal of Geriatric Psychiatry*, *20*(6), 512–522. https://doi.org/10.1002/gps.1318

Garcia, C. (1984). A doença de Alzheimer: problemas do diagnóstico clínico. Tese Doutoramento (não publicada). *Repositório Da Universidade de Lisboa*, *http://hdl.handle.net/10451/4451*. http://hdl.handle.net/10451/4451

Garcia, C., Costa, C., Guerreiro, M., Leitão, O., Mendonça, A. D. E., & Umbelino, J. (1994). Estimativa da prevalencia da demencia e da doença de alzheimer em Portugal. *Acta Médica Portuguesa*, *7*, 487–491.

Garcia, L. J., Hébert, M., Kozak, J., Sénécal, I., Slaughter, S. E., Aminzadeh, F., Dalziel, W., Charles, J., & Eliasziw, M. (2012). Perceptions of family and staff on the role of the environment in long-term care homes for people with dementia. *International Psychogeriatrics*, *24*(5), 753–765. https://doi.org/10.1017/S1041610211002675

Garret, C., Santos, F., Tracana, I., Barrreto, J., Sobral, M., & Fonseca, R. (2003). *Avaliação Clínica da Demência. In a Mendonça, M. Guerriro e Grupo de Estudos de Envelhecimento Cerebral e Demências (Eds). Escalas e Testes na demência*. 11–26.

Gaugler, J. E., Jarrott, S. E., Zarit, S. H., Stephens, M. A. P., Townsend, A., & Greene, R. (2003). Respite for dementia caregivers: The effects of adult day service use on caregiving hours and care demands. *International Psychogeriatrics*, *15*(1), 37–58. https://doi.org/10.1017/S1041610203008743

Gaugler, J. E., Kane, R. L., Kane, R. A., & Newcomer, R. (2005). Early community-based service utilization and its effects on institutionalization in dementia caregiving. *Gerontologist*, *45*(2), 177–185. https://doi.org/10.1093/geront/45.2.177

Gérain, P., & Zech, E. (2019). Informal Caregiver burnout? Development of a theoretical framework to understand the impact of caregiving. *Frontiers in Psychology*, *10*(JULY). https://doi.org/10.3389/fpsyg.2019.01748

Getsios, D., Blume, S., Ishak, K. J., MacLaine, G., & Hernández, L. (2012). An economic evaluation of early assessment for Alzheimer's disease in the United Kingdom. *Alzheimer's and Dementia*, *8*(1), 22–30. https://doi.org/10.1016/j.jalz.2010.07.001

Gilliam, C. M., & Steffen, A. M. (2006). The relationship between caregiving self-efficacy

and depressive symptoms in dementia family caregivers. *Aging and Mental Health*, *10*(2), 79–86. https://doi.org/10.1080/13607860500310658

Ginó, S., Mendes, T., Maroco, J., Ribeiro, F., Schmand, B. A., De Mendonça, A., & Guerreiro, M. (2010). Memory complaints are frequent but qualitatively different in young and elderly healthy people. *Gerontology*, *56*(3), 272–277. https://doi.org/10.1159/000240048

Gitlin, L. N., Winter, L., Burke, J., Chemett, N., Dennis, M. P., & Hauck, W. W. (2008). Tailored activities to manage neuropsychiatric behaviors in persons with dementia and reduce caregiver burden: A randomized pilot study. *American Journal of Geriatric Psychiatry*, *16*(3), 229–239. https://doi.org/10.1097/01.JGP.0000300629.35408.94

Givens, J. L., Kiely, D. K., Carey, K., & Mitchell, S. L. (2009). Healthcare proxies of nursing home residents with advanced dementia: Decisions they confront and their satisfaction with decision-making: Clinical investigations. *Journal of the American Geriatrics Society*, *57*(7), 1149–1155. https://doi.org/10.1111/j.1532-5415.2009.02304.x

Givens, J. L., Lopez, R. P., Mazor, K. M., & Mitchell, S. L. (2012). Sources of stress for family members of nursing home residents with advanced dementia. *Alzheimer Disease and Associated Disorders*, *26*(3), 254–259. https://doi.org/10.1097/WAD.0b013e31823899e4

Golicki, D., Niewada, M., Karlińska, A., Buczek, J., Kobayashi, A., Janssen, M. F., & Pickard, A. S. (2015). Comparing responsiveness of the EQ-5D-5L, EQ-5D-3L and EQ VAS in stroke patients. *Quality of Life Research*, *24*(6), 1555–1563. https://doi.org/10.1007/s11136-014-0873-7

Gonçalves-Pereira, M, Verdelho, A., Prina, M., Marques, M. J., & Xavier, M. (2021). How Many People Live with Dementia in Portugal? A Discussion Paper of National Estimates. *Portuguese Journal of Public Health*, *39*(1), 58–68. https://doi.org/10.1159/000516503

Gonçalves-Pereira, Manuel, Cardoso, A., Verdelho, A., Alves da Silva, J., Caldas De Almeida, M., Fernandes, A., Raminhos, C., Ferri, C. P., Prina, A. M., Prince, M., & Xavier, M. (2017). The prevalence of dementia in a Portuguese community sample: A 10/66 Dementia Research Group study. *BMC Geriatrics*, *17*(1). https://doi.org/10.1186/s12877-017-0647-5

Gonçalves-Pereira, Manuel, Carmo, I., da Silva, J. A., Papoila, A. L., Mateos, R., & Zarit, S. H. (2010). Caregiving experiences and knowledge about dementia in Portuguese clinical outpatient settings. *International Psychogeriatrics*, *22*(2), 270–280. https://doi.org/DOI: 10.1017/S1041610209991050

Gonçalves-Pereira, Manuel, Marques, M. J., Balsinha, C., Fernandes, A., Machado, A. S., Verdelho, A., Barahona-Corrêa, B., Bárrios, H., Guimarães, J., Grave, J., Alves, L., de ALMEIDA, M. C., Reis, T. A., Orrell, M., Woods, B., de VUGT, M., & Verhey, F. (2019). Needs for care and service use in dementia: Baseline assessment of portuguese participants in the actifcare cohort study. *Acta Medica Portuguesa*, *32*(5), 355–367. https://doi.org/10.20344/amp.11136

Gonçalves-Pereira, Manuel, Zarit, S. H., Cardoso, A. M., Alves da Silva, J., Papoila, A. L.,

& Mateos, R. (2020). A comparison of primary and secondary caregivers of persons with dementia. *Psychology and Aging*, *35*(1), 20–27. https://doi.org/10.1037/pag0000380

Gonçalves-Pereira, M., Cardoso, A., Verdelho, A., Alves da Silva, J., Caldas de Almeida, M., Fernandes, A., Raminhos, C., Ferri, C. P., Prince, M., & Xavier, M. (2016). Implementação em Portugal de um estudo de prevalência da demência e da depressão geriátrica: a metodologia do 10/66 Dementia Research Group. *Revista Portuguesa de Saude Publica*, *34*(2), 134–143. https://doi.org/10.1016/j.rpsp.2016.03.002

Gray, R. S., Hahn, L., Thapsuwan, S., & Thongcharoenchupong, N. (2016). Strength and stress: Positive and negative impacts on caregivers for older adults in Thailand. *Australasian Journal on Ageing*, *35*(2), E7–E12. https://doi.org/10.1111/ajag.12266

Greene, V. L. (1983). Substitution between formally and informally provided care for the impaired elderly in the community. *Medical Care*, *21*(6), 609–619. https://doi.org/10.1097/00005650-198306000-00003

Greenwood, N., Pound, C., Smith, R., & Brearley, S. (2019). Experiences and support needs of older carers: A focus group study of perceptions from the voluntary and statutory sectors. *Maturitas*, *123*(February), 40–44. https://doi.org/10.1016/j.maturitas.2019.02.003

Gresham, M., Heffernan, M., & Brodaty, H. (2018). The Going to Stay at Home program: Combining dementia caregiver training and residential respite care. *International Psychogeriatrics*, *30*(11), 1697–1706. https://doi.org/10.1017/S1041610218000686

Groen-Van De Ven, L., Smits, C., De Graaff, F., Span, M., Eefsting, J., Jukema, J., & Vernooij-Dassen, M. (2017). Involvement of people with dementia in making decisions about their lives: A qualitative study that appraises shared decision-making concerning daycare. *BMJ Open*, *7*(11), 1–13. https://doi.org/10.1136/bmjopen-2017-018337

Grunfeld, E., Coyle, D., Whelan, T., Clinch, J., Reyno, L., Earle, C. C., Willan, A., Viola, R., Coristine, M., Janz, T., & Glossop, R. (2004). Family caregiver burden: Results of a longitudinal study of breast cancer patients and their principal caregivers. *Cmaj*, *170*(12), 1795–1801. https://doi.org/10.1503/cmaj.1031205

Guerreiro, M., Silva, A. P., Botelho, M. A., Leito, O., Castro-Caldas, A., & Garcia, C. (1994). Adaptação à população portuguesa da tradução do Mini Mental State Examination (MMSE). *Revista Portuguesa de Neurologia*, *1*, 9–10.

Habermann, B., Hines, D., & Davis, L. (2013). Caring for parents with neurodegenerative disease: A qualitative description. *Clinical Nurse Specialist*, *27*(4), 182–187. https://doi.org/10.1097/NUR.0b013e318295576b

Harada, C. N., Natelson Love, M. C., & Triebel, K. L. (2013). Normal cognitive aging. *Clinics in Geriatric Medicine*, *29*(4), 737–752. https://doi.org/10.1016/j.cger.2013.07.002

Harris, D. P., Chodosh, J., Vassar, S. D., Vickrey, B. G., & Shapiro, M. F. (2009). Primary care providers' views of challenges and rewards of dementia care relative to other conditions. *Journal of the American Geriatrics Society*, *57*(12), 2209–2216. https://doi.org/10.1111/j.1532-5415.2009.02572.x

Harris, P. B. (2013). Dementia and friendship: the quality and nature of the relationships that remain. *International Journal of Aging & Human Development*, *76*(2), 141–164. https://doi.org/10.2190/AG.76.2.c

Hays, R. D., Anderson, R., & Revicki, D. (1993). Psychometric considerations in evaluating health-related quality of life measures. *Quality of Life Research*, *2*(6), 441–449. https://doi.org/10.1007/BF00422218

Hebert, L. E., Scherr, P. A., Bienias, J. L., Bennett, D. A., & Evans, D. A. (2003). Alzheimer disease in the US population: Prevalence estimates using the 2000 census. *Archives of Neurology*, *60*(8), 1119–1122. https://doi.org/10.1001/archneur.60.8.1119

Hemingway, D., MacCourt, P., Pierce, J., & Strudsholm, T. (2016). Together but apart: Caring for a spouse with dementia resident in a care facility. *Dementia*, *15*(4), 872–890. https://doi.org/10.1177/1471301214542837

Hinton, L., Franz, C. E., Reddy, G., Flores, Y., Kravitz, R. L., & Barker, J. C. (2007). Practice constraints, behavioral problems, and dementia care: Primary care physicians' perspectives. *Journal of General Internal Medicine*, *22*(11), 1487–1492. https://doi.org/10.1007/s11606-007-0317-y

Hoffmann, F., & Rodrigues, R. (2010). *Informal Carers: Who Takes Care of Them?*

Hofman, A., Rocca, W. A., Brayne, C., Breteler, M. M. B., Clarke, M., Cooper, B., Copeland, J. R. M., Dartigues, J. F., Droux, A. D. S., Hagnell, O., Heeren, T. J., Engedal, K., Jonker, C., Lindesay, J., Lobo, A., Mann, A. H., Mölsä, P. K., Morgan, K., O'connor, D. W., … Amaducci, L. (1991). The prevalence of dementia in Europe: A collaborative study of 1980-1990 findings. *International Journal of Epidemiology*, *20*(3), 736–748. https://doi.org/10.1093/ije/20.3.736

Hogan, A. J., & Mickus, M. A. (2002). *Through Rose Colored Glasses: Public Perceptions of Nursing Home Quality*.

Holland, J. M., Currier, J. M., & Gallagher-Thompson, D. (2009). Outcomes From the Resources for Enhancing Alzheimer's Caregiver Health (REACH) Program for Bereaved Caregivers. *Psychology and Aging*, *24*(1), 190–202. https://doi.org/10.1037/a0014303

Huis In Het Veld, J., Verkaik, R., Van Meijel, B., Verkade, P. J., Werkman, W., Hertogh, C., & Francke, A. (2016). Self-management by family caregivers to manage changes in the behavior and mood of their relative with dementia: An online focus group study. *BMC Geriatrics*, *16*(1), 1–8. https://doi.org/10.1186/s12877-016-0268-4

Hung, Y. N., Kadziola, Z., Brnabic, A. J. M., Yeh, J. F., Fuh, J. L., Hwang, J. P., & Montgomery, W. (2016). The epidemiology and burden of Alzheimer's disease in Taiwan utilizing data from the National Health Insurance Research Database. *ClinicoEconomics and Outcomes Research*, *8*, 387–395. https://doi.org/10.2147/CEOR.S93323

Hussein, M. El, Hirst, S., Salyers, V., & Osuji, J. (2014). The Qualitative Report Using Grounded Theory as a Method of Inquiry: Advantages and Disadvantages Using Grounded Theory as a Method of Inquiry: Advantages and Disadvantages. *The Qualitative Report*, *19*(27), 1–15. https://nsuworks.nova.edu/tqr/vol19/iss27/3%0Ahttp://nsuworks.nova.edu/tqr%5Cnhttp://nsuworks.nova.edu/tqr/vol19/iss27/3

Hvidsten, L. (2019). *Quality of life in young-onset dementia*.

Ibarria, M., Alegret, M., Valero, S., Morera, A., Guitart, M., Cañabate, P., Moreno, M., Lara, S., Diego, S., Hernández, J., Tantinyá, N., Vera, M., Hernández, I., Becker, J. T., Ruíz, A., Boada, M., & Tárraga, L. (2016). Beneficial effects of an integrated psychostimulation program in patients with Alzheimer's disease. *Journal of Alzheimer's Disease*, *50*(2), 559–566. https://doi.org/10.3233/JAD-150455

Ihle-Hansen, H., & Ihle-Hansen, H. (2018). Aging Brain and Neurological Changes. *Rehabilitation Medicine for Elderly Patients*, 15–20. https://doi.org/10.1007/978-3-319-57406-6_2

INE. (2019a). As pessoas, 2019. *Instituto Nacional de Estatística, I.P*.

INE. (2019b). INE, Tabuas de Mortalidade, 2016-2018. *Instituto Nacional de Estatística, I.P*.

Instituto Nacional de Estatística IP. (2012). INE - Instituto Nacional de Estatística. Censos 2011: Resultados definitivos - Portugal. *Editors*, *Av. António José de Almeida*, *1000-043 Lisboa*, *Portugal*.

Ivey, S. L., Laditka, S. B., Price, A. E., Tseng, W., Beard, R. L., Liu, R., Fetterman, D., Wu, B., & Logsdon, R. G. (2013). Experiences and concerns of family caregivers providing support to people with dementia: A cross-cultural perspective. *Dementia*, *12*(6), 806–820. https://doi.org/10.1177/1471301212446872

Jamieson, M., Grealish, L., Brown, J. A., & Draper, B. (2016). Carers: The navigators of the maze of care for people with dementia—A qualitative study. *Dementia*, *15*(5), 1112–1123. https://doi.org/10.1177/1471301214554930

Janssen, E. P. C. J., de Vugt, M., Köhler, S., Wolfs, C., Kerpershoek, L., Handels, R. L. H., Orrell, M., Woods, B., Jelley, H., Stephan, A., Bieber, A., Meyer, G., Engedal, K., Selbaek, G., Wimo, A., Irving, K., Hopper, L., Maria Marques, M. M., Gonçalves-Pereira, M., … Verhey, F. R. (2017). Caregiver profiles in dementia related to quality of life, depression and perseverance time in the European Actifcare study: the importance of social health. *Aging and Mental Health*, *21*(1), 49–57. https://doi.org/10.1080/13607863.2016.1255716

Janssen, N., Handels, R. L., Köhler, S., Gonçalves-Pereira, M., Marques, M. J., Irving, K., Hopper, L., Bieber, A., Orrell, M., Selbæk, G., Michelet, M., Wimo, A., Zanetti, O., Portolani, D. M., Woods, B., Jelley, H., Evers, S. M. A. A., & Verhey, F. R. J. (2020). Profiles of Met and Unmet Needs in People with Dementia According to Caregivers' Perspective: Results from a European Multicenter Study. *Journal of the American Medical Directors Association*, *21*(11), 1609-1616.e1. https://doi.org/10.1016/j.jamda.2020.05.009

Jennings, L. A., Palimaru, A., Corona, M. G., Cagigas, X. E., Ramirez, K. D., Zhao, T., Hays, R. D., Wenger, N. S., & Reuben, D. B. (2017). Patient and caregiver goals for dementia care. *Quality of Life Research*, *26*(3), 685–693. https://doi.org/10.1007/s11136-016-1471-7

Jones, B., Gage, H., Bakker, C., Barrios, H., Boucault, S., Mayer, J., Metcalfe, A., Millenaar, J., Parker, W., & Orrung Wallin, A. (2018). Availability of information on young onset dementia for patients and carers in six European countries. *Patient Education and Counseling*, *101*(1), 159–165.

https://doi.org/10.1016/j.pec.2017.07.013

Jones, R. W., Romeo, R., Trigg, R., Knapp, M., Sato, A., King, D., Niecko, T., & Lacey, L. (2015). Dependence in Alzheimer's disease and service use costs, quality of life, and caregiver burden: The DADE study. *Alzheimer's and Dementia*, *11*(3), 280–290. https://doi.org/10.1016/j.jalz.2014.03.001

Jonker, C., Geerlings, M. I., & Schmand, B. (2000). Are Memory Complaints Predictive for Dementia? *International Journal of Geriatric Psychiatry*, *15*(11), 983–991. http://www.ncbi.nlm.nih.gov/pubmed/11113976

Jönsson, L., Andreasen, N., Kilander, L., Soininen, H., Waldemar, G., Nygaard, H., Winblad, B., Jönhagen, M. E., Hallikainen, M., & Wimo, A. (2006). Patient- and proxy-reported utility in Alzheimer disease using the EuroQoL. *Alzheimer Disease and Associated Disorders*, *20*(1), 49–55. https://doi.org/10.1097/01.wad.0000201851.52707.c9

Jönsson, L., Lin, P. J., & Khachaturian, A. S. (2017). Special topic section on health economics and public policy of Alzheimer's disease. *Alzheimer's and Dementia*, *13*(3), 201–204. https://doi.org/10.1016/j.jalz.2017.02.004

Jönsson, L., & Wimo, A. (2009). The cost of dementia in europe: A review of the evidence, and methodological considerations. *PharmacoEconomics*, *27*(5), 391–403. https://doi.org/10.2165/00019053-200927050-00004

Juniper, E. F., Guyatt, G. H., & Jaeschke, R. (1996). How to develop and validate a new health-related quality of life instrument. *Quality of Life and Pharmacoeconomics in Clinical Trials*, *2*, 49–56. https://www.scirp.org/(S(i43dyn45teexjx455qlt3d2q))/reference/ReferencesPapers.aspx?ReferenceID=801083

Juozapavicius, K. P., & Weber, J. A. (2001). A reflective study of Alzheimer's caregivers. *American Journal of Alzheimer's Disease and Other Dementias*, *16*(1), 11–20. https://doi.org/10.1177/153331750101600108

Karg, N., Graessel, E., Randzio, O., & Pendergrass, A. (2018). Dementia as a predictor of care-related quality of life in informal caregivers: A cross-sectional study to investigate differences in health-related outcomes between dementia and non-dementia caregivers. *BMC Geriatrics*, *18*(1), 1–9. https://doi.org/10.1186/s12877-018-0885-1

Karlin, N. J., Bell, P. A., & Noah, J. L. (2001). Long-term consequences of the Alzheimer's caregiver role: A qualitative analysis. *American Journal of Alzheimer's Disease and Other Dementias*, *16*(3), 177–182. https://doi.org/10.1177/153331750101600306

Karlsson, S., Bleijlevens, M., Roe, B., Saks, K., Martin, M. S., Stephan, A., Suhonen, R., Zabalegui, A., Hallberg, I. R., Jan, P. H. H., Afram, B., Beerens, H. C., Bleijlevens, M. H. C., Verbeek, H., Zwakhalen, S. M. G., Ruwaard, D., Emilsson, U. M., Bokberg, C., Lethin, C., … Vellas, B. (2015). Dementia care in European countries, from the perspective of people with dementia and their caregivers. *Journal of Advanced Nursing*, *71*(6), 1405–1416. https://doi.org/10.1111/jan.12581

Kawaharada, R., Sugimoto, T., Matsuda, N., Tsuboi, Y., Sakurai, T., & Ono, R. (2019). Impact of loss of independence in basic activities of daily living on caregiver burden

in patients with Alzheimer's disease: A retrospective cohort study. *Geriatrics and Gerontology International*, *19*(12), 1243–1247. https://doi.org/10.1111/ggi.13803

Keating, N., & Gaudet, N. (2012). Quality of life of persons with dementia. *Journal of Nutrition, Health and Aging*, *16*(5), 454–456. https://doi.org/10.1007/s12603-011-0346-4

Kerpershoek, L., de Vugt, M., Wolfs, C., Woods, B., Jelley, H., Orrell, M., Stephan, A., Bieber, A., Meyer, G., Selbaek, G., Handels, R., Wimo, A., Hopper, L., Irving, K., Marques, M., Gonçalves-Pereira, M., Portolani, E., Zanetti, O., & Verhey, F. (2018). Needs and quality of life of people with middle-stage dementia and their family carers from the European Actifcare study. When informal care alone may not suffice. *Aging and Mental Health*, *22*(7), 897–902. https://doi.org/10.1080/13607863.2017.1390732

Kerpershoek, L., Woods, B., Wolfs, C., Verhey, F., Jelley, H., Bieber, A., Stephan, A., Michelet, M., Selbaek, G., Handels, R., Wimo, A., Hopper, L., Irving, K., Marques, M. J., Gonçalves-Pereira, M., Portolani, E., Zanetti, O., & de Vugt, M. (2020). Do caregiver profiles predict the use of dementia care services? Findings from the Actifcare study. *Aging & Mental Health*, *24*(2), 272–279. https://doi.org/10.1080/13607863.2018.1544215

Khanna, R., Jariwala, K., & Bentley, J. P. (2013). Psychometric properties of the EuroQol Five Dimensional Questionnaire (EQ-5D-3L) in caregivers of autistic children. *Quality of Life Research*, *22*(10), 2909–2920. https://doi.org/10.1007/s11136-013-0423-8

Kitzinger, J. (1995). Qualitative Research: Introducing focus groups. *Bmj*, *311*(7000), 299. https://doi.org/10.1136/bmj.311.7000.299

Koca, E., Taşkapilioğlu, Ö., & Bakar, M. (2017). Caregiver burden in different stages of Alzheimer's disease. *Noropsikiyatri Arsivi*, *54*(1), 82–86. https://doi.org/10.5152/npa.2017.11304

Koch, T., & Iliffe, S. (2010). Editorial: The role of primary care in the recognition of and response to dementia. *Journal of Nutrition, Health and Aging*, *14*(2), 107–109. https://doi.org/10.1007/s12603-010-0021-1

Kramer, B. J., & Lambert, J. D. (1999). Caregiving as a life course transition among older husbands: A prospective study. *Gerontologist*, *39*(6), 658–667. https://doi.org/10.1093/geront/39.6.658

Kronborg Andersen, C., Lauridsen, J., Andersen, K., & Kragh-Sørensen, P. (2003). Cost of dementia: Impact of disease progression estimated in longitudinal data. *Scandinavian Journal of Public Health*, *31*(2), 119–125. https://doi.org/10.1080/14034940210134059

Krys, K., Zelenski, J. M., Capaldi, C. A., Park, J., van Tilburg, W., van Osch, Y., Haas, B. W., Bond, M. H., Dominguez-Espinoza, A., Xing, C., Igbokwe, D. O., Kwiatkowska, A., Luzniak-Piecha, M., Nader, M., Rizwan, M., Zhu, Z., & Uchida, Y. (2019). Putting the "We" Into Well-being: Using Collectivism-Themed Measures of Well-Being Attenuates Well-being's Association With Individualism. *Asian Journal of Social Psychology*, *22*(3), 256–267. https://doi.org/10.1111/ajsp.12364

Ku, L. J. E., Pai, M. C., & Shih, P. Y. (2016). Economic impact of dementia by disease severity: exploring the relationship between stage of dementia and cost of care in

Taiwan. *PLoS ONE*, *11*(2), 1–12. https://doi.org/10.1371/journal.pone.0148779

Kularatna, S., Byrnes, J., Chan, Y. K., Ski, C. F., Carrington, M., Thompson, D., Stewart, S., & Scuffham, P. A. (2017). Comparison of the EQ-5D-3L and the SF-6D (SF-12) contemporaneous utility scores in patients with cardiovascular disease. *Quality of Life Research*, *26*(12), 3399–3408. https://doi.org/10.1007/s11136-017-1666-6

Kusne, Y., Wolf, A. B., Townley, K., Conway, M., & Peyman, G. A. (2017). Visual system manifestations of Alzheimer's disease. *Acta Ophthalmologica*, *95*(8), e668–e676. https://doi.org/10.1111/aos.13319

Kwak, M., Ingersoll-Dayton, B., & Kim, J. (2012). Family conflict from the perspective of adult child caregivers: The influence of gender. *Journal of Social and Personal Relationships*, *29*(4), 470–487. https://doi.org/10.1177/0265407511431188

Lach, H. W., & Chang, Y. P. (2007). Caregiver perspectives on safety in home dementia care. *Western Journal of Nursing Research*, *29*(8), 993–1014. https://doi.org/10.1177/0193945907303098

Lai, C. K. Y., Yeung, J. H. M., Mok, V., & Chi, I. (2009). Special care units for dementia individuals with behavioural problems. *Cochrane Database of Systematic Reviews*, *4*. https://doi.org/10.1002/14651858.CD006470.pub2

Lampley-Dallas, V. T., Mold, J. W., & Flori, D. E. (2001). Perceived needs of African-American caregivers of elders with dementia. *Journal of the National Medical Association*, *93*(2), 47–57.

Laparidou, D., Middlemass, J., Karran, T., & Siriwardena, A. N. (2019). Caregivers' interactions with health care services – Mediator of stress or added strain? Experiences and perceptions of informal caregivers of people with dementia – A qualitative study. *Dementia*, *18*(7–8), 2526–2542. https://doi.org/10.1177/1471301217751226

Lethin, C., Hallberg, I. R., Karlsson, S., & Janlöv, A. C. (2016). Family caregivers experiences of formal care when caring for persons with dementia through the process of the disease. *Scandinavian Journal of Caring Sciences*, *30*(3), 526–534. https://doi.org/10.1111/scs.12275

Lethin, C., Leino-Kilpi, H., Bleijlevens, M. H. C., Stephan, A., Martin, M. S., Nilsson, K., Nilsson, C., Zabalegui, A., & Karlsson, S. (2020). Predicting caregiver burden in informal caregivers caring for persons with dementia living at home – A follow-up cohort study. *Dementia*, *19*(3), 640–660. https://doi.org/10.1177/1471301218782502

Lethin, C., Leino-Kilpi, H., Roe, B., Soto, M. M., Saks, K., Stephan, A., Zwakhalen, S., Zabalegui, A., & Karlsson, S. (2016). Formal support for informal caregivers to older persons with dementia through the course of the disease: An exploratory, cross-sectional study. *BMC Geriatrics*, *16*(1), 32. https://doi.org/10.1186/s12877-016-0210-9

Lillo-Crespo, M., Riquelme, J., Macrae, R., De Abreu, W., Hanson, E., Holmerova, I., Cabañero, M. J., Ferrer, R., & Tolson, D. (2018). Experiences of advanced dementia care in seven European countries: implications for educating the workforce. *Global Health Action*, *11*(1). https://doi.org/10.1080/16549716.2018.1478686

Lima, S., Gago, M., Garrett, C., & Pereira, M. G. (2016). Predictors and Moderators of

Quality of Life in Alzheimer's Disease Patients. *Journal of Alzheimer's Disease : JAD*, *54*(3), 1113–1121. https://doi.org/10.3233/JAD-160256

Lin, I. F., Fee, H. R., & Wu, H. S. (2012). Negative and Positive Caregiving Experiences: A Closer Look at the Intersection of Gender and Relationship. *Family Relations*, *61*(2), 343–358. https://doi.org/10.1111/j.1741-3729.2011.00692.x

Lindeza, P., Rodrigues, M., Costa, J., Guerreiro, M., & Rosa, M. M. (2020a). Impact of dementia on informal care: A systematic review of family caregivers' perceptions. *BMJ Supportive and Palliative Care*, bmjspcare-2020-002242. https://doi.org/10.1136/bmjspcare-2020-002242

Lindeza, P., Rodrigues, M., Costa, J., Guerreiro, M., & Rosa, M. M. (2020b). Impact of dementia on informal care: A systematic review of family caregivers' perceptions. *BMJ Supportive and Palliative Care*, bmjspcare-2020-002242. https://doi.org/10.1136/bmjspcare-2020-002242

Livingston, G., Leavey, G., Manela, M., Livingston, D., Rait, G., Sampson, E., Bavishi, S., Shahriyarmolki, K., & Cooper, C. (2010). Making decisions for people with dementia who lack capacity: Qualitative study of family carers in UK. *BMJ (Online)*, *341*(7771), 494. https://doi.org/10.1136/bmj.c4184

Livingston, G., Manela, M., & Katona, C. (1996). Depression and other psychiatric morbidity in carers of elderly people living at home. *British Medical Journal*, *312*(7024), 153–156. https://doi.org/10.1136/bmj.312.7024.153

Livingston, G., Sommerlad, A., Orgeta, V., Costafreda, S. G., Huntley, J., Ames, D., Ballard, C., Banerjee, S., Burns, A., Cohen-Mansfield, J., Cooper, C., Fox, N., Gitlin, L. N., Howard, R., Kales, H. C., Larson, E. B., Ritchie, K., Rockwood, K., Sampson, E. L., … Mukadam, N. (2017). Dementia prevention, intervention, and care. *The Lancet*, *390*(10113), 2673–2734. https://doi.org/10.1016/S0140-6736(17)31363-6

Lobo, A., Launer, L. J., Fratiglioni, L., Andersen, K., Di Carlo, A., Breteler, M. M. B., Copeland, J. R. M., Dartigues, J. F., Jagger, C., Martinez-Lage, J., Soininen, H., & Hofman, A. (2000). Prevalence of dementia and major subtypes in Europe: A collaborative study of population-based cohorts. *Neurology*, *54*(11 SUPPL. 5).

Logsdon, R. G., Gibbons, L. E., McCurry, S. M., & Teri, L. (1999). Quality of life in Alzheimer's Disease: Patient and caregiver reports. *Journal of Mental Health and Aging*, *5*(1), 21–32.

Lopez-Bastida, J., Serrano-Aguilar, P., Lilisbeth, ;, Mpsych, P.-P., & Oliva-Moreno, J. (2006). From the Planning and Evaluation Unit. *Neurology*, *67*, 2186–2191. www.neurology.org

Lyons, K. S., & Zarit, S. H. (1999). Formal and informal support: the great divide. *International Journal of Geriatric Psychiatry*, *14*(3), 183–192. https://doi.org/10.1002/(sici)1099-1166(199903)14:3<183::aid-gps969>3.3.co;2-a

M Prince, R Bryce, E Albanese, A Wimo, W Ribeiro, C. F. (2019). The global prevalence of latent tuberculosis: A systematic review and meta-analysis. *European Respiratory Journal*, *54*(3), 63–75. https://doi.org/10.1183/13993003.00655-2019

Mack, J. L., & Whitehouse, P. J. (2001). Quality of life in dementia: State of the art-report of the international working group for harmonization of dementia drug guidelines and

the Alzheimer's society satellite meeting. *Alzheimer Disease and Associated Disorders*, *15*(2), 69–71. https://doi.org/10.1097/00002093-200104000-00005

Madruga, M., Gozalo, M., Prieto, J., Adsuar, J. C., & Gusi, N. (2020). Psychological symptomatology in informal caregivers of persons with dementia: Influences on health-related quality of life. *International Journal of Environmental Research and Public Health*, *17*(3). https://doi.org/10.3390/ijerph17031078

Maffioletti, V. L. R., Baptista, M. A. T., Santos, R. L., Rodrigues, V. M., & Dourado, M. C. N. (2019). Effectiveness of day care in supporting family caregivers of people with dementia: A systematic review. *Dementia e Neuropsychologia*, *13*(3), 268–283. https://doi.org/10.1590/1980-57642018dn13-030003

Mangialasche, F., Solomon, A., Winblad, B., Mecocci, P., & Kivipelto, M. (2010). Alzheimer's disease: clinical trials and drug development. *The Lancet Neurology*, *9*(7), 702–716. https://doi.org/10.1016/S1474-4422(10)70119-8

Manthorpe, J., Samsi, K., Campbell, S., Abley, C., Keady, J., Bond, J., Watts, S., Robinson, L., Warner, J., & Iliffe, S. (2013). From forgetfulness to dementia: Clinical and commissioning implications of diagnostic experiences. *British Journal of General Practice*, *63*(606), 69–75. https://doi.org/10.3399/bjgp13X660805

Marchand, H. (2005). *Psicologia do adulto e do idoso* (Quarteto (ed.)).

Marques, M. J., Tan, E. Y. L., Woods, B., Jelley, H., Kerpershoek, L., Hopper, L., Irving, K., Bieber, A., Stephan, A., Sköldunger, A., Sjölund, B.-M., Selbaek, G., Røsvik, J., Zanetti, O., Portolani, D. M., Marôco, J., de Vugt, M., Verhey, F., & Gonçalves-Pereira, M. (2021). Trajectories of relationship quality in dementia: a longitudinal study in eight European countries. *Aging & Mental Health*, 1–9. https://doi.org/10.1080/13607863.2021.1969641

Marques, M. J., Woods, B., Hopper, L., Jelley, H., Irving, K., Kerpershoek, L., Meyer, G., Bieber, A., Stephan, A., Sköldunger, A., Sjölund, B.-M., Selbaek, G., Rosvik, J., Zanetti, O., Portolani, E., de Vugt, M., Verhey, F., & Gonçalves-Pereira, M. (2019). Relationship quality and sense of coherence in dementia: Results of a European cohort study. *International Journal of Geriatric Psychiatry*, *34*(5), 745–755. https://doi.org/10.1002/gps.5082

Martins, T., Ribeiro, J., & Garrett, C. (2003). Estudo de validação do questionário de avaliação da sobrecarga para cuidadores informais. *Psicologia, Saúde & Doenças*, *4*(1), 131–148.

Martins, T., Ribeiro, J. L. P., & Garrett, C. (2004). Questionário de Avaliação da Sobrecarga do Cuidador Informal (QASCI)- Reavaliação das propriedades psicométricas. *Referência*, *11*, 17–31.

Mccabe, L., Robertson, J., & Kelly, F. (2018). Scaffolding and working together: A qualitative exploration of strategies for everyday life with dementia. *Age and Ageing*, *47*(2), 303–310. https://doi.org/10.1093/ageing/afx186

McKhann G, Drachman D, Folstein M, Katzman R, Price D, S. E. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology. 1984; 34: 939-44. *Neurology*, *34*, 939–944.

Melo, G., Maroco, J., & De Mendonça, A. (2011). Influence of personality on caregiver's burden, depression and distress related to the BPSD. *International Journal of Geriatric Psychiatry*, *26*(12), 1275–1282. https://doi.org/10.1002/gps.2677

Melo, G., Maroco, J., Lima-Basto, M., & de Mendonça, A. (2017). Personality of the caregiver influences the use of strategies to deal with the behavior of persons with dementia. *Geriatric Nursing*, *38*(1), 63–69. https://doi.org/10.1016/j.gerinurse.2016.08.001

Mendonça, A., Guerreiro, M., Ribeiro, F., Mendes, T., & Garcia, C. (2004). Mild Cognitive Impairment. Focus on Diagnosis. Review article. *Journal of Molecular Neuroscience*, *23*.

Merz, E. M., Consedine, N. S., Schulze, H. J., & Schuengel, C. (2009). Wellbeing of adult children and ageing parents: Associations with intergenerational support and relationship quality. *Ageing and Society*, *29*(5), 783–802. https://doi.org/10.1017/S0144686X09008514

Mestheneos, E., & Triantafillou, J. (2002). *The project EUROFAMCARE is supported by the European Union - Contract: QLK6-CT-2002-02647 The project EUROFAMCARE is supported by the European Union - Contract: QLK6-CT-2002-02647*.

Michalowsky, B., Xie, F., Kohlmann, T., Gräske, J., Wübbeler, M., Thyrian, J. R., & Hoffmann, W. (2020). Acceptability and Validity of the EQ-5D in Patients Living With Dementia. *Value in Health*, *23*(6), 760–767. https://doi.org/10.1016/j.jval.2020.01.022

Milte, R., Shulver, W., Killington, M., Bradley, C., Ratcliffe, J., & Crotty, M. (2016). Quality in residential care from the perspective of people living with dementia: The importance of personhood. *Archives of Gerontology and Geriatrics*, *63*, 9–17. https://doi.org/10.1016/j.archger.2015.11.007

Mitchell, A. J. (2008). The Clinical Significance of SMC in the Diagnosis of MCI and dementia. *International Journal of Geriatric Psychiatry*, *December 2007*, 1191–1202. https://doi.org/10.1002/gps

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., Altman, D., Antes, G., Atkins, D., Barbour, V., Barrowman, N., Berlin, J. A., Clark, J., Clarke, M., Cook, D., D'Amico, R., Deeks, J. J., Devereaux, P. J., Dickersin, K., Egger, M., Ernst, E., … Tugwell, P. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement (Chinese edition). *Journal of Chinese Integrative Medicine*, *7*(9), 889–896. https://doi.org/10.3736/jcim20090918

Moïse, P., M. S. and M. U. (2004). Dementia Care in 9 OECD Countries: A Comparative Analysis. In *OECD Health Working Papers: Vol. No. 13*. OECD Publishing.

Molloy, D. W., Alemayehu, E., & Roberts, R. (1991). Reliability of a standardized mini-mental state examination compared with the traditional mini-mental state examination. *American Journal of Psychiatry*, *148*(1), 102–105. https://doi.org/10.1176/ajp.148.1.102

Moore, M. J., Zhu, C. W., & Clipp, E. C. (2001). Informal costs of dementia care: Estimates from the National Longitudinal Caregiver Study. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *56*(4), S219–S228.

https://doi.org/10.1093/geronb/56.4.S219

Moreno-Cámara, S., Palomino-Moral, P. Á., Moral-Fernández, L., Frías-Osuna, A., & del-Pino-Casado, R. (2016). Problemas en el proceso de adaptación a los cambios en personas cuidadoras familiares de mayores con demencia. *Gaceta Sanitaria*, *30*(3), 201–207. https://doi.org/10.1016/j.gaceta.2016.02.004

Morgado, J., CS, R., Maruta, C., Guerreiro, M., & Pavão Martins, I. (2009). Novos valores Normativos do mini-mental state examination. *Sinapse*, *9*(2), 10–16.

Morgan, D. G., Semchuk, K. M., Stewart, N. J., & D'Arcy, C. (2002). Rural families caring for a relative with dementia: Barriers to use of formal services. *Social Science and Medicine*, *55*(7), 1129–1142. https://doi.org/10.1016/S0277-9536(01)00255-6

Morgeson, F. P., Aguinis, H., Waldman, David, A., & Sengiel, Donald, S. (2013). Tau PET imaging in aging and early Alzheimer's disease. *Personnel Psychology*, *79*(1), 1–29. https://doi.org/10.1002/ana.24546.Tau

Mossello, E., Caleri, V., Razzi, E., Di Bari, M., Cantini, C., Tonon, E., Lopilato, E., Marini, M., Simoni, D., Cavallini, M. C., Marchionni, N., Biagini, C. A., & Masotti, G. (2008). Day Care for older dementia patients: Favorable effects on behavioral and psychological symptoms and caregiver stress. *International Journal of Geriatric Psychiatry*, *23*(10), 1066–1072. https://doi.org/10.1002/gps.2034

Moyle, W., Edwards, H., & Clinton, M. (2002). Living with loss: dementia and the family caregiver. *The Australian Journal of Advanced Nursing : A Quarterly Publication of the Royal Australian Nursing Federation*, *19*(3), 25–31.

Murman, D. L. (2015). The Impact of Age on Cognition Cognition and the Aging Auditory System. *Seminars in Hearing*, *36*(1), 111–121. http://dx.doi.org/10.1055/s-0035-1555115.

Naglie, G., Tomlinson, G., Tansey, C., Irvine, J., Ritvo, P., Black, S. E., Freedman, M., Silberfeld, M., & Krahn, M. (2006). Utility-based quality of life measures in Alzheimer's disease. *Quality of Life Research*, *15*(4), 631–643. https://doi.org/10.1007/s11136-005-4364-8

Nations, U. (2019). World Population Ageing 2019. In *World Population Ageing 2019*. http://link.springer.com/chapter/10.1007/978-94-007-5204-7_6

Netto MP, P. J. (2000). *Envelhecimento: desafio na transição do século.* (Atheneu (ed.); Gerontolog).

Nikmat, A. W., Hawthorne, G., & Al-Mashoor, S. H. (2011). Quality of life in dementia patients: Nursing home versus home care. *International Psychogeriatrics*, *23*(10), 1692–1700. https://doi.org/10.1017/S1041610211001050

Nunes, B., Silva, R. D., Cruz, V. T., Roriz, J. M., Pais, J., & Silva, M. C. (2010). Prevalence and pattern of cognitive impairment in rural and urban populations from Northern Portugal. *BMC Neurology*, *10*(42), 42. https://doi.org/10.1186/1471-2377-10-42

OECD. (2011). Help Wanted? Providing and Paying for Long-Term Care. *Health Policy Studies.*, *Paris: OEC*.

OECD. (2017). Informal carers. *Health at a Glance. OECD Indicators.*, *Paris*.

OECD. (2020). *OECD Labour Force Statistics 2020*. OECD. https://doi.org/10.1787/5842cc7f-en

Olazarán, J., Agüera-Ortiz, L., Argimón, J. M., Reed, C., Ciudad, A., Andrade, P., & Dilla, T. (2017). Costs and quality of life in community-dwelling patients with Alzheimer's disease in Spain: Results from the GERAS II observational study. *International Psychogeriatrics*, *29*(12), 2081–2093. https://doi.org/10.1017/S1041610217001211

Oliveira, D., Vass, C., & Aubeeluck, A. (2019). Quality of Life on the Views of Older Family Carers of People with Dementia. *Dementia*, *18*(3), 990–1009. https://doi.org/10.1177/1471301217700741

Orellana, C. (2003). Global action against cancer. *Lancet Oncology*, *4*(7), 389. https://doi.org/10.1016/S1470-2045(03)01154-9

Ossenkoppele, R., Schonhaut, D. R., Schöll, M., Lockhart, S. N., Ayakta, N., Baker, S. L., O'Neil, J. P., Janabi, M., Lazaris, A., Cantwell, A., Vogel, J., Santos, M., Miller, Z. A., Bettcher, B. M., Vossel, K. A., Kramer, J. H., Gorno-Tempini, M. L., Miller, B. L., Jagust, W. J., & Rabinovici, G. D. (2016). Tau PET patterns mirror clinical and neuroanatomical variability in Alzheimer's disease. *Brain*, *139*(5), 1551–1567. https://doi.org/10.1093/brain/aww027

Peel, E., & Harding, R. (2014). "It's a huge maze, the system, it's a terrible maze": Dementia carers' constructions of navigating health and social care services. *Dementia*, *13*(5), 642–661. https://doi.org/10.1177/1471301213480514

Peña-Casanova, J., Monllau, A., Böhm, P., Aguilar, M., Sol, J. M., Hernández, G., Blesa, R., Manero, R. M., Espel, G., Marti, A. M., Meza, M., Soler, T., Zabay, C., Riera, M., Castellvi, M., Rivero, A. I., Santiago, M. J., Toiran, E., & Crespo, M. C. (2005). Valor diagnóstico y fiabilidad test-retest de la Escala de Demencia de Blessed (BDRS) para la enfermedad de Alzheimer: Datos del proyecto NORMACODEM. *Neurologia*, *20*(7), 349–355.

Peng, H. L., & Chang, Y. P. (2013). Sleep disturbance in family caregivers of individuals with dementia: A review of the literature. *Perspectives in Psychiatric Care*, *49*(2), 135–146. https://doi.org/10.1111/ppc.12005

Pereira, M. (2007). *Cuidadores informais de doentes de Alzheimer: sobrecarga física, emocional e social e psicopatologia. Dissertação de Mestrado não publicada. Instituto de Ciências Biomédicas de Abel de Salazar, Universidade do Porto, Portugal.*

Petersen, R. C. (2006). Mild cognitive impairment. *Lancet*, *367*(9527), 1979. https://doi.org/10.1016/S0140-6736(06)68881-8

Pinquart, M., & Sörensen, S. (2003). Differences between caregivers and noncaregivers in psychological health and physical health: A meta-analysis. *Psychology and Aging*, *18*(2), 250–267. https://doi.org/10.1037/0882-7974.18.2.250

Pinquart, M., & Sörensen, S. (2007). Correlates of physical health of informal caregivers: A meta-analysis. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *62*(2), 126–137. https://doi.org/10.1093/geronb/62.2.P126

Pires, C., Silva, D., Maroco, J., Ginó, S., Mendes, T., Schmand, B. A., Guerreiro, M., & De Mendonça, A. (2012). Memory complaints associated with seeking clinical care.

International Journal of Alzheimer's Disease, *2012*. https://doi.org/10.1155/2012/725329

Polenick, Courtney A., Struble, L. M., Stanislawski, B., Turnwald, M., Broderick, B., Gitlin, L. N., & Kales, H. C. (2018). "The Filter is Kind of Broken": Family Caregivers' Attributions About Behavioral and Psychological Symptoms of Dementia. *American Journal of Geriatric Psychiatry*, *26*(5), 548–556. https://doi.org/10.1016/j.jagp.2017.12.004

Polenick, Courtney Allyn, & Martire, L. M. (2013). Caregiver Attributions for Late-Life Depression and Their Associations with Caregiver Burden. *Family Process*, *52*(4), 709–722. https://doi.org/10.1111/famp.12032

Poole, M., Bamford, C., McLellan, E., Lee, R. P., Exley, C., Hughes, J. C., Harrison-Dening, K., & Robinson, L. (2018). End-of-life care: A qualitative study comparing the views of people with dementia and family carers. *Palliative Medicine*, *32*(3), 631–642. https://doi.org/10.1177/0269216317736033

Popham, C., & Orrell, M. (2012). What matters for people with dementia in care homes? *Aging and Mental Health*, *16*(2), 181–188. https://doi.org/10.1080/13607863.2011.628972

Preau, M., Bouhnik, A. D., Rey, D., & Mancini, J. (2011). Two years after cancer diagnosis, which couples become closer? *European Journal of Cancer Care*, *20*(3), 380–388. https://doi.org/10.1111/j.1365-2354.2010.01191.x

Prince, M., Bryce, R., Albanese, E., Wimo, A., Ribeiro, W., & Ferri, C. P. (2013a). The global prevalence of dementia: A systematic review and metaanalysis. *Alzheimer's and Dementia*, *9*(1), 63-75.e2. https://doi.org/10.1016/j.jalz.2012.11.007

Prince, M., Bryce, R., Albanese, E., Wimo, A., Ribeiro, W., & Ferri, C. P. (2013b). The global prevalence of dementia: A systematic review and metaanalysis. *Alzheimer's and Dementia*, *9*(1), 63-75.e2. https://doi.org/10.1016/j.jalz.2012.11.007

Prince, M., Ferri, C. P., Acosta, D., Albanese, E., Arizaga, R., Dewey, M., Gavrilova, S. I., Guerra, M., Huang, Y., Jacob, K. S., Krishnamoorthy, E. S., McKeigue, P., Rodriguez, J. L., Salas, A., Sosa, A. L., Sousa, R. M. M., Stewart, R., & Uwakwe, R. (2007). The protocols for the 10/66 dementia research group population-based research programme. *BMC Public Health*, *7*(generally 2000), 1–18. https://doi.org/10.1186/1471-2458-7-165

Prince, M., Quraishi, S., Copeland, J., Varghese, M., Murali, T., Srinivasan, L., Thara, R., Samuel, R., Krishnamoorthy, E. S., Patel, V., Sangath, Dias, A., Verma, M. A., Anand, B., Shaji, K. S., Lal, K. P., Shuran, L., Liu, J., Chiu, H., … Olebuezie, F. (2004). Care arrangements for people with dementia in developing countries. *International Journal of Geriatric Psychiatry*, *19*(2), 170–177. https://doi.org/10.1002/gps.1046

Promislow, D. E. L., Bronikowski, A. M. (2006). *"The evolutionary genetics of senescence," in: Evolutionary Genetics: Concepts and Case Studies* (C. F. J. B. Wolf (ed.)). New York: Oxford University Press.

Prorok, J. C., Hussain, M., Horgan, S., & Seitz, D. P. (2017). 'I shouldn't have had to push and fight': health care experiences of persons with dementia and their caregivers in primary care. *Aging and Mental Health*, *21*(8), 797–804.

https://doi.org/10.1080/13607863.2016.1159280

Qiu, C., Kivipelto, M., & Von Strauss, E. (2009). Epidemiology of Alzheimer's disease: Occurrence, determinants, and strategies toward intervention. *Dialogues in Clinical Neuroscience*, *11*(2), 111–128. https://doi.org/10.31887/dcns.2009.11.2/cqiu

Quible, Z. K. (1998). A Focus on Focus Groups. *Business Communication Quarterly*, *61*(2), 28–38. https://doi.org/10.1177/108056999806100205

Quintal, C., & Mendes, P. (2012). Underuse of generic medicines in Portugal: An empirical study on the perceptions and attitudes of patients and pharmacists. *Health Policy*, *104*(1), 61–68. https://doi.org/10.1016/j.healthpol.2011.10.001

Radford, M. (2008). Reviews. In *Library and Information Science Research* (Vol. 30, Issue 2). https://doi.org/10.1016/j.lisr.2007.11.003

Rahman, M., White, E. M., Thomas, K. S., & Jutkowitz, E. (2020). Assessment of Rural-Urban Differences in Health Care Use and Survival Among Medicare Beneficiaries With Alzheimer Disease and Related Dementia. *JAMA Network Open*, *3*(10), e2022111. https://doi.org/10.1001/jamanetworkopen.2020.22111

Reed, C., Barrett, A., Lebrec, J., Dodel, R., Jones, R. W., Vellas, B., Wimo, A., Argimon, J. M., Bruno, G., & Haro, J. M. (2017). How useful is the EQ-5D in assessing the impact of caring for people with Alzheimer's disease? *Health and Quality of Life Outcomes*, *15*(1). https://doi.org/10.1186/s12955-017-0591-2

Reid, L. M., & MacLullich, A. M. J. (2006). Subjective memory complaints and cognitive impairment in older people. *Dementia and Geriatric Cognitive Disorders*, *22*(5–6), 471–485. https://doi.org/10.1159/000096295

Riedel, M. (2012). Financial Support for Informal Care Provision in European Countries : A Short Overview. *Health and Ageing Newsletter*, *27*. https://www.genevaassociation.org/media/77165/ga2012-health27-riedel.pdf

Risco, E., Cabrera, E., Farré, M., Alvira, C., Miguel, S., & Zabalegui, A. (2016). Perspectives about Health Care Provision in Dementia Care in Spain: A Qualitative Study Using Focus-Group Methodology. *American Journal of Alzheimer's Disease and Other Dementias*, *31*(3), 223–230. https://doi.org/10.1177/1533317515603818

Robinson, A. L., Emden, C. G., Elder, J. A., Lea, E. J., Vickers, J. C., & Turner, P. A. (2008). Multiple views reveal the complexity of dementia diagnosis. *Australasian Journal on Ageing*, *27*(4), 183–188. https://doi.org/10.1111/j.1741-6612.2008.00316.x

Rodrigues, C. F., & Andrade, I. (2014). Ageing and poverty: how older Portuguese adults became less poor in the noughties. *European Journal of Ageing*, *11*(4), 285–292. https://doi.org/10.1007/s10433-014-0319-7

Rodrigues, L. M. P. (2018). Influência de um programa de intervenção de Enfermagem de Reabilitação no cuidador informal-minimização da Sobrecarga e prevenção de lesões músculo-esqueléticas associadas ao cuidar. Relatório de Estágio de Mestrado em Enfermagem de Reabilitação. *Instituto Politécnico de Braçança (Tese Não Publicada).*

Römhild, J., Fleischer, S., Meyer, G., Stephan, A., Zwakhalen, S., Leino-Kilpi, H., Zabalegui, A., Saks, K., Soto-Martin, M., Sutcliffe, C., Rahm Hallberg, I., & Berg, A.

(2018). Inter-rater agreement of the Quality of Life-Alzheimer's Disease (QoL-AD) self-rating and proxy rating scale: Secondary analysis of RightTimePlaceCare data. *Health and Quality of Life Outcomes*, *16*(1), 1–13. https://doi.org/10.1186/s12955-018-0959-y

Rose, M. R. (1991). *Evolutionary Biology of Aging.* New York: Oxford University Press.

Rossetti, H. C., Cullum, C. M., Hynan, L. S., & Lacritz, L. H. (2010). The CERAD neuropsychologic battery total score and the progression of Alzheimer disease. *Alzheimer Disease and Associated Disorders*, *24*(2), 138–142. https://doi.org/10.1097/WAD.0b013e3181b76415

Rossor, M. N., Fox, N. C., Mummery, C. J., Schott, J. M., & Warren, J. D. (2010). *The diagnosis of young-onset dementia*. *9*(8), 793–806. https://doi.org/10.1016/S1474-4422(10)70159-9.The

Ruano, L., Araújo, N., Branco, M., Barreto, R., Moreira, S., Pais, R., Cruz, V. T., Lunet, N., & Barros, H. (2019). Prevalence and Causes of Cognitive Impairment and Dementia in a Population-Based Cohort From Northern Portugal. *American Journal of Alzheimer's Disease and Other Dementias*, *34*(1), 49–56. https://doi.org/10.1177/1533317518813550

Salthouse, T. A. (2004). What and when of cognitive aging. *Current Directions in Psychological Science*, *13*(4), 140–144. https://doi.org/10.1111/j.0963-7214.2004.00293.x

Santana, I., Farinha, F., Freitas, S., Rodrigues, V., & Carvalho, Á. (2015). The epidemiology of dementia and Alzheimer disease in Portugal: Estimations of prevalence and treatment-costs. *Acta Medica Portuguesa*, *28*(2), 182–188. https://doi.org/10.20344/amp.6025

Santana, P. (2002). Poverty, social exclusion and health in Portugal. *Social Science and Medicine*, *55*(1), 33–45. https://doi.org/10.1016/S0277-9536(01)00218-0

Sarabia-Cobo, C. M., Pérez, V., de Lorena, P., Nuñez, M. J., & Domínguez, E. (2016). Decisions at the end of life made by relatives of institutionalized patients with dementia. *Applied Nursing Research*, *31*, e6–e10. https://doi.org/10.1016/j.apnr.2016.02.003

Sataloff, R. T., Johns, M. M., & Kost, K. M. (1994). Self-reported memory complaints and memory performance in elderly french community residents: results of the PAQUID research program. *Neuroepidemiology*, *13*, 145–154.

Schiffczyk, C., Romero, B., Jonas, C., Lahmeyer, C., Müller, F., & Riepe, M. W. (2010). Generic quality of life assessment in dementia patients: A prospective cohort study. *BMC Neurology*, *10*. https://doi.org/10.1186/1471-2377-10-48

Schneider, J. A., Arvanitakis, Z., Bang, W., & Bennett, D. A. (2007). Mixed brain pathologies account for most dementia cases in community-dwelling older persons. *Neurology*, *69*(24), 2197–2204. https://doi.org/10.1212/01.wnl.0000271090.28148.24

Schulz, R., & Martire, L. M. (2004). Family Caregiving of Persons with Dementia: Prevalence, Health Effects, and Support Strategies. *American Journal of Geriatric Psychiatry*, *12*(3), 240–249. https://doi.org/10.1097/00019442-200405000-00002

Schulz, R., & Quittner, A. L. (1998). Caregiving for children and adults with chronic

conditions: Introduction to the special issue. *Health Psychology*, *17*(2), 107–111. https://doi.org/10.1037/h0092707

Selwood, A., Thorgrimsen, L., & Orrell, M. (2005). Quality of life in dementia - A one-year follow-up study. *International Journal of Geriatric Psychiatry*, *20*(3), 232–237. https://doi.org/10.1002/gps.1271

Sequeira, C. (2007). *Cuidar de idosos dependentes* (Q. Editora (ed.)).

Serrano-Aguilar, P. G., Lopez-Bastida, J., & Yanes-Lopez, V. (2006). Impact on health-related quality of life and perceived burden of informal caregivers of individuals with Alzheimer's disease. *Neuroepidemiology*, *27*(3), 136–142. https://doi.org/10.1159/000095760

Shah, H., Albanese, E., Duggan, C., Rudan, I., Langa, K. M., Carrillo, M. C., Chan, K. Y., Joanette, Y., Prince, M., Rossor, M., Saxena, S., Snyder, H. M., Sperling, R., Varghese, M., Wang, H., Wortmann, M., & Dua, T. (2016). Research priorities to reduce the global burden of dementia by 2025. *The Lancet Neurology*, *15*(12), 1285–1294. https://doi.org/10.1016/S1474-4422(16)30235-6

Sharp, E. S., & Gatz, M. (2011). Relationship between education and dementia: An updated systematic review. *Alzheimer Disease and Associated Disorders*, *25*(4), 289–304. https://doi.org/10.1097/WAD.0b013e318211c83c

Sheehan, B. D., Lall, R., Stinton, C., Mitchell, K., Gage, H., Holland, C., & Katz, J. (2012). Patient and proxy measurement of quality of life among general hospital in-patients with dementia. *Aging and Mental Health*, *16*(5), 603–607. https://doi.org/10.1080/13607863.2011.653955

Shilpa Amarya, Kalyani Singh, M. S. (2018). *Ageing Process and Physiological changes: Vol. Chapter 1*. IntechOpen. https://doi.org/10.5772/intechopen.76249

Simoes, M. R. (2015). Escalas e testes na demencia. *Grupo e Estudos de Envelhecimento Cerebral e Demências – Colaboração Da UCB Pharma (Novartis Farma) – Produtos Farmacêuticos*.

Song, J. A., Park, M., Park, J., Cheon, H. J., & Lee, M. (2018). Patient and Caregiver Interplay in Behavioral and Psychological Symptoms of Dementia: Family Caregiver's Experience. *Clinical Nursing Research*, *27*(1), 12–34. https://doi.org/10.1177/1054773816678979

Sörensen, S., & Conwell, Y. (2011). Issues in dementia caregiving: Effects on mental and physical health, intervention strategies, and research needs. *American Journal of Geriatric Psychiatry*, *19*(6), 491–496. https://doi.org/10.1097/JGP.0b013e31821c0e6e

Spenceley, S. M., Sedgwick, N., & Keenan, J. (2015). Dementia care in the context of primary care reform: An integrative review. *Aging and Mental Health*, *19*(2), 107–120. https://doi.org/10.1080/13607863.2014.920301

Sperling, R. A., Aisen, P. S., Beckett, L. A., Bennett, D. A., Craft, S., Fagan, A. M., Iwatsubo, T., Jack, C. R., Kaye, J., Montine, T. J., Park, D. C., Reiman, E. M., Rowe, C. C., Siemers, E., Stern, Y., Yaffe, K., Carrillo, M. C., Thies, B., Morrison-Bogorad, M., … Phelps, C. H. (2011). Toward defining the preclinical stages of Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.

Alzheimer's and Dementia, *7*(3), 280–292. https://doi.org/10.1016/j.jalz.2011.03.003

Srivastava, G., Tripathi, R. K., Tiwari, S. C., Singh, B., & Tripathi, S. M. (2016). Caregiver burden and quality of life of key caregivers of patients with dementia. *Indian Journal of Psychological Medicine*, *38*(2), 133–136. https://doi.org/10.4103/0253-7176.178779

Stefanacci, R. G. (2011). The costs of Alzheimer's disease and the value of effective therapies. *The American Journal of Managed Care*, *17 Suppl 1*(november), S356-62. https://doi.org/53094 [pii]

Stephan, A., Bieber, A., Hopper, L., Joyce, R., Irving, K., Zanetti, O., Portolani, E., Kerpershoek, L., Verhey, F., De Vugt, M., Wolfs, C., Eriksen, S., Røsvik, J., Marques, M. J., Gonçalves-Pereira, M., Sjölund, B. M., Jelley, H., Woods, B., Meyer, G., … Machado, A. (2018). Barriers and facilitators to the access to and use of formal dementia care: Findings of a focus group study with people with dementia, informal carers and health and social care professionals in eight European countries. *BMC Geriatrics*, *18*(1), 1–16. https://doi.org/10.1186/s12877-018-0816-1

Stirling, C., Leggett, S., Lloyd, B., Scott, J., Blizzard, L., Quinn, S., & Robinson, A. (2012). Decision aids for respite service choices by carers of people with dementia: Development and pilot RCT. *BMC Medical Informatics and Decision Making*, *12*(1), 21. https://doi.org/10.1186/1472-6947-12-21

Strollo, F., Gentile, S., Strollo, G., Mambro, A., & Vernikos, J. (2018). Recent progress in space physiology and aging. *Frontiers in Physiology*, *9*(NOV), 1–9. https://doi.org/10.3389/fphys.2018.01551

Sutcliffe, C. L., Roe, B., Jasper, R., Jolley, D., & Challis, D. J. (2015). People with dementia and carers' experiences of dementia care and services: Outcomes of a focus group study. *Dementia*, *14*(6), 769–787. https://doi.org/10.1177/1471301213511957

Takai, M., Takahashi, M., Iwamitsu, Y., Ando, N., Okazaki, S., Nakajima, K., Oishi, S., & Miyaoka, H. (2009). The experience of burnout among home caregivers of patients with dementia: Relations to depression and quality of life. *Archives of Gerontology and Geriatrics*, *49*(1), e1. https://doi.org/10.1016/j.archger.2008.07.002

Taşci, S., Kartin, P. T., Ceyhan, Ö., Sungur, G., & Göriş, S. (2012). Living with an alzheimer patient in Turkey. *Journal of Neuroscience Nursing*, *44*(4), 228–234. https://doi.org/10.1097/JNN.0b013e3182527627

Tatar, M. (2001). *"Senescence," in: Evolutionary Ecology – Concepts and Case Studies, C. W. Fox, D. A. Roff, and D. J. Fairbairn (New York: Oxford University Press), 128–141.* (D. J. F. C. W. Fox, D. A. Roff (ed.)). New York: Oxford University Press.

Thomas, P. A., Liu, H., & Umberson, D. (2017). Family Relationships and Well-Being. *Innovation in Aging*, *1*(3), 1–11. https://doi.org/10.1093/geroni/igx025

Toot, S., Hoe, J., Ledgerd, R., Burnell, K., Devine, M., & Orrell, M. (2013). Causes of crises and appropriate interventions: The views of people with dementia, carers and healthcare professionals. *Aging and Mental Health*, *17*(3), 328–335. https://doi.org/10.1080/13607863.2012.732037

Tretteteig, S., Vatne, S., & Rokstad, A. M. M. (2016). The influence of day care centres for people with dementia on family caregivers: An integrative review of the literature.

Aging and Mental Health, *20*(5), 450–462. https://doi.org/10.1080/13607863.2015.1023765

Tretteteig, S., Vatne, S., & Rokstad, A. M. M. (2017). The influence of day care centres designed for people with dementia on family caregivers - A qualitative study. *BMC Geriatrics*, *17*(1), 1–11. https://doi.org/10.1186/s12877-016-0403-2

Triantafillou., J., Naiditch., M., Repkova., K., Stiehr., K., Carretero., S., Emilsson., T., Santo., P. Di, Bednarik, R., Brichtova., L., Ceruzzi., F., Cordero., L., Mastroyiannakis., T., Ferrando., M., Mingot., K., J.Ritter, & Vlantoni., D. (2010). *INTERLINKS - Informal care in the long-term care system. European Overview Paper WP5 - European Centre for Social Welfare Policy and Research*. *223037*, 11. https://www.euro.centre.org/downloads/detail/768

Tucker, S., Hughes, J., Burns, A., & Challis, D. (2008). The balance of care: Reconfiguring services for older people with mental health problems. *Aging and Mental Health*, *12*(1), 81–91. https://doi.org/10.1080/13607860701366038

Tynan, H., & Allen, D. (2002). The impact of service user cognitive level on carer attributions for aggressive behaviour. *Journal of Applied Research in Intellectual Disabilities*, *15*(3), 213–223. https://doi.org/10.1046/j.1468-3148.2002.00120.x

Van Der Flier, W. M., & Scheltens, P. (2005). Epidemiology and risk factors of dementia. *Neurology in Practice*, *76*(SUPPL. 5), 2–7. https://doi.org/10.1136/jnnp.2005.082867

Van Gennip, I. E., Pasman, H. R. W., Oosterveld-Vlug, M. G., Willems, D. L., & Onwuteaka-Philipsen, B. D. (2016). How Dementia Affects Personal Dignity: A Qualitative Study on the Perspective of Individuals with Mild to Moderate Dementia. *Journals of Gerontology - Series B Psychological Sciences and Social Sciences*, *71*(3), 491–501. https://doi.org/10.1093/geronb/gbu137

van Wezel, N., Francke, A. L., Kayan-Acun, E., LJM Devillé, W., van Grondelle, N. J., & Blom, M. M. (2016). Family care for immigrants with dementia: The perspectives of female family carers living in the Netherlands. *Dementia*, *15*(1), 69–84. https://doi.org/10.1177/1471301213517703

Van Wijngaarden, E., Van Der Wedden, H., Henning, Z., Komen, R., & The, A. M. (2018). Entangled in uncertainty: The experience of living with dementia from the perspective of family caregivers. *PLoS ONE*, *13*(6), 1–21. https://doi.org/10.1371/journal.pone.0198034

Vasileiou, K., Barnett, J., Barreto, M., Vines, J., Atkinson, M., Lawson, S., & Wilson, M. (2017). Experiences of loneliness associated with being an informal caregiver: A qualitative investigation. *Frontiers in Psychology*, *8*(APR), 1–11. https://doi.org/10.3389/fpsyg.2017.00585

Vellone, E., Piras, G., Talucci, C., & Cohen, M. Z. (2008). Quality of life for caregivers of people with Alzheimer's disease. *Journal of Advanced Nursing*, *61*(2), 222–231. https://doi.org/10.1111/j.1365-2648.2007.04494.x

Verbeek, H., Meyer, G., Leino-Kilpi, H., Zabalegui, A., Hallberg, I. R., Saks, K., Soto, M. E., Challis, D., Sauerland, D., & Hamers, J. P. H. (2012). A European study investigating patterns of transition from home care towards institutional dementia care: The protocol of a RightTimePlaceCare study. *BMC Public Health*, *12*(1), 68. https://doi.org/10.1186/1471-2458-12-68

Vossius, C., Rongve, A., Testad, I., Wimo, A., & Aarsland, D. (2014). The use and costs of formal care in newly diagnosed dementia: A three-year prospective follow-up study. *American Journal of Geriatric Psychiatry*, *22*(4), 381–388. https://doi.org/10.1016/j.jagp.2012.08.014

Wagner, H. R., Glaser, B. G., & Strauss, A. L. (1968). The Discovery of Grounded Theory: Strategies for Qualitative Research. In *Social Forces* (Vol. 46, Issue 4). https://doi.org/10.2307/2575405

Walter, E., & Pinquart, M. (2020). How Effective Are Dementia Caregiver Interventions? An Updated Comprehensive Meta-Analysis. *Gerontologist*, *60*(8), E609–E619. https://doi.org/10.1093/geront/gnz118

Wang, C. L., Kuo, L. M., Chiu, Y. C., Huang, H. L., Huang, H. L., Hsu, W. C., Lu, C. H., Huang, T. H., Huang, S., & Shyu, Y. I. L. (2018). Protective preparation: A process central to family caregivers of persons with mild cognitive impairment. *International Psychogeriatrics*, *30*(3), 375–384. https://doi.org/10.1017/S1041610217001764

Wang, L., Chopp, M., Szalad, A., Jia, L., Lu, X., Lu, M., Zhang, L., Zhang, Y., Zhang, R., & Zhang, Z. G. (2015). Sildenafil ameliorates long term peripheral neuropathy in type II diabetic mice. *PLoS ONE*, *10*(2), 6. https://doi.org/10.1371/journal.pone.0118134

Weichbold, B. (2015). Careways of dementia care. *Psychiatria Danubina*, *27*(4), 439–445.

Whitehouse, P. J., Orgogozo, J. M., Becker, R. E., Gauthier, S., Pontecorvo, M., Erzigkeit, H., Rogers, S., Mohs, R. C., Bodick, N., Bruno, G., & Dal-Bianco, P. (1997). Quality-of-life assessment in dementia drug development. Position paper from the International Working Group on Harmonization of Dementia Drug Guidelines. *Alzheimer Disease and Associated Disorders*, *11 Suppl 3*, 56–60.

Widera, E., & Covinsky, K. E. (2011). Fulfilling our obligation to the caregiver it's time for action. *Archives of Internal Medicine*, *171*(4), 359–360. https://doi.org/10.1001/archinternmed.2011.17

Wiles, J. (2003). Informal caregivers' experiences of formal support in a changing context. *Health and Social Care in the Community*, *11*(3), 189–207. https://doi.org/10.1046/j.1365-2524.2003.00419.x

Wimo, A., Rönnbäck, E., Larsson, B., Eriksson, T., Eriksson, I. B., & Thorslund, M. (1999). "Misplacement" of elderly people in the caring organisation: Reasons and alternatives. *Archives of Gerontology and Geriatrics*, *28*(3), 227–237. https://doi.org/10.1016/S0167-4943(99)00006-0

Wimo, Anders, & Prince, M. (2010). World Alzheimer Report 2010. *Dementia*, 96. http://www.alz.co.uk/research/files/WorldAlzheimerReport.pdf

Wimo, Anders, Religa, D., Edlund, A. K., Winblad, B., Eriksdotter, M., & Spångberg, K. (2013). Costs of diagnosing dementia: Results from SveDem, the Swedish Dementia registry. *International Journal of Geriatric Psychiatry*, *28*(10), 1039–1044. https://doi.org/10.1002/gps.3925

Winblad, B., Amouyel, P., Andrieu, S., Ballard, C., Brayne, C., Brodaty, H., Cedazo-Minguez, A., Dubois, B., Edvardsson, D., Feldman, H., Fratiglioni, L., Frisoni, G. B., Gauthier, S., Georges, J., Graff, C., Iqbal, K., Jessen, F., Johansson, G., Jönsson, L., … Zetterberg, H. (2016). Defeating Alzheimer's disease and other dementias: A

priority for European science and society. *The Lancet Neurology*, *15*(5), 455–532. https://doi.org/10.1016/S1474-4422(16)00062-4

Wolfs, C. A. G., de Vugt, M. E., Verkaaik, M., Haufe, M., Verkade, P. J., Verhey, F. R. J., & Stevens, F. (2012). Rational decision-making about treatment and care in dementia: A contradiction in terms? *Patient Education and Counseling*, *87*(1), 43–48. https://doi.org/10.1016/j.pec.2011.07.023

World Health Organization. (2012). Dementia as a Public Health Priority. *Journal of Psychiatrists' Association of Nepal*, 1.

World Health Organization. (2018). The epidemiology and impact of dementia. Current state and future trends. *World Health Organization*, 3–6.

Wortmann, M. (2012). Dementia: A global health priority - Highlights from an ADI and World Health Organization report. *Alzheimer's Research and Therapy*, *4*(5), 4–6. https://doi.org/10.1186/alzrt143

Wübker, A., Zwakhalen, S. M. G., Challis, D., Suhonen, R., Karlsson, S., Zabalegui, A., Soto, M., Saks, K., & Sauerland, D. (2015). Costs of care for people with dementia just before and after nursing home placement: primary data from eight European countries. *European Journal of Health Economics*, *16*(7), 689–707. https://doi.org/10.1007/s10198-014-0620-6

Wulff, J., Fänge, A. M., Lethin, C., & Chiatti, C. (2020). Self-reported symptoms of depression and anxiety among informal caregivers of persons with dementia: a cross-sectional comparative study between Sweden and Italy. *BMC Health Services Research*, *20*(1), 1–15. https://doi.org/10.1186/s12913-020-05964-2

Xiao, L. D., De Bellis, A., Habel, L., & Kyriazopoulos, H. (2013). The experiences of culturally and linguistically diverse family caregivers in utilising dementia services in Australia. *BMC Health Services Research*, *13*(1), 1. https://doi.org/10.1186/1472-6963-13-427

Xiao, L. D., Habel, L., & De Bellis, A. (2015). Perceived Challenges in Dementia Care by Vietnamese Family Caregivers and Care Workers in South Australia. *Journal of Cross-Cultural Gerontology*, *30*(3), 333–352. https://doi.org/10.1007/s10823-015-9264-y

Xiao, L. D., Wang, J., He, G. P., De Bellis, A., Verbeeck, J., & Kyriazopoulos, H. (2014). Family caregiver challenges in dementia care in Australia and China: A critical perspective. *BMC Geriatrics*, *14*(1), 1–13. https://doi.org/10.1186/1471-2318-14-6

Yang, Z., & Levey, A. (2015). Gender Differences: A Lifetime Analysis of the Economic Burden of Alzheimer's Disease. *Women's Health Issues*, *25*(5), 436–440. https://doi.org/10.1016/j.whi.2015.06.001

Ydstebø, A. E., Benth, J. Š., Bergh, S., Selbæk, G., & Vossius, C. (2020). Informal and formal care among persons with dementia immediately before nursing home admission. *BMC Geriatrics*, *20*(1), 1–9. https://doi.org/10.1186/s12877-020-01703-8

Yu, D., Cheng, S.-T., & Wang, J. (2018). Unravelling positive aspects of caregiving in dementia: An integrative review of research literature. *International Journal of Nursing Studies*, *79*, 1–26. https://doi.org/10.1016/j.ijnurstu.2017.10.008

Yu, D. S. F., Cheng, S. T., & Wang, J. (2018). Unravelling positive aspects of caregiving

in dementia: An integrative review of research literature. *International Journal of Nursing Studies*, *79*(October 2017), 1–26. https://doi.org/10.1016/j.ijnurstu.2017.10.008

Yu, H., Wang, X., He, R., Liang, R., & Zhou, L. (2015). Measuring the caregiver burden of caring for community-residing people with Alzheimer's disease. *PLoS ONE*, *10*(7), 1–13. https://doi.org/10.1371/journal.pone.0132168

Zabalegui, A., Bover, A., Rodriquez, E., Cabrera, E., Diaz, M., Gallart, A., González, A., Gual, P., Izquierdo, M. D., López, L., Pulpón, A. M., & Ramírez, A. (2008). Informal caregiving: Perceived needs. *Nursing Science Quarterly*, *21*(2), 166–172. https://doi.org/10.1177/0894318408314978

Zanni, G. R., & Wick, J. Y. (2007). Differentiating dementias in long-term care patients. *Consultant Pharmacist*, *22*(1), 14–28. https://doi.org/10.4140/TCP.n.2007.14

Zhu, C. W., Cosentino, S., Ornstein, K., Gu, Y., Andrews, H., & Stern, Y. (2016). P2-434: Cost Implications of Dementia Severity and Comorbidities. *Alzheimer's & Dementia*, *12*(7), P812–P812. https://doi.org/10.1016/j.jalz.2016.06.1646

Zhu, C. W., Scarmeas, N., Ornstein, K., Albert, M., Brandt, J., Blacker, D., Sano, M., & Stern, Y. (2015). Health-care use and cost in dementia caregivers: Longitudinal results from the Predictors Caregiver Study. *Alzheimer's and Dementia*, *11*(4), 444–454. https://doi.org/10.1016/j.jalz.2013.12.018

SUPPLEMENTARY MATERIAL

Supplementary material of Chapter 2

Table 2.1 Quality Assessment of 81 Studies Included in this Systematic Review

Table 2.2. Characteristics and key findings of the included studies in this systematic review (n=81)

Table 2.3. Summary of methods and participants of 81 studies included in this systematic review

Additional file 2.1: Search strategy

Additional file 2.2: PRISMA Checklist

Supplementary material of Chapter 3

Additional file 3.1:

Table 3.1 - Focus group participant quotes - caregiver changes in quality of life
Table 3.2 - Focus group participant quotes - positive and negative aspects of formal care services
Table 3.3- Focus group participant quotes - dementia informal care related costs

Additional file 3.2:

-Informed consent of the participants
-Information leaflet of focus groups
-Focus groups guide
-Final report sent to participants with main results

Supplementary material of Chapter 4

Table 4.1. Distribution of QoL-AD scores by domain, (n=187)

Additional file 4.1:

-Informed consent of the participant – Informal caregiver
- Informed consent of the participant (for MMSE application to the person with dementia)
-Applied instruments (Sociodemographic questionnaire, EQ-5D-3L, QoL-AD, BDRS and MMSE)

Supplementary material of Chapter 5

Table 5.1. Correlations with EQ-5D-3L and QASCI score with each other's and sociodemographic variables of informal caregivers and their relatives with dementia, (n=187)

Table 5.2. Influence of informal caregivers' and PwD characteristics in caregivers' QoL (EQ-5D-3L)

Table 5.3. Influence of informal caregivers' and PwD characteristics in caregivers' overall burden (QASCI score)

Additional file 5.1:

-Informed consent of the participant – Informal caregiver (the same of additional file 4.1)
- Applied instruments: EQ-5D-3L (the same of additional file 4.1) and QASCI

Table 2.1. Quality Assessment of 81 Studies Included in this Systematic Review

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
(Aminzadeh *et al.*, 2007)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	1.No discussion on contraditory data 2.No discussion on researcher bias
Berry *et al.,* 2015)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	No information on ethical issues	1.No discussion on contraditory data 2.No in-depth description of the data analysis process
(Boots LM *et al.,* 2015)	Yes	Yes	No discussion about why selecting the Grounded Theory Approach Modified	Yes	1. No discussion on why selecting the interview approach	No details	Yes, but no details about how researchers explained issues to participants	Yes
(Boughtwood *et al.,* 2011)	Yes	Yes	No discussion about the study design	Yes	1. No discussion on why selecting the focus group approach	No details	Yes	1.No discussion on contraditory data 2.No in-depth description about how themes were identified
(Bunn *et al.,* 2017)	Yes	Yes	No discussion about the study design	Yes	1. No in-depht information on interview schedule 2. No discussion about saturation data 3. No details about family caregiver's relation to the patient	No details	Yes	1.No discussion on contraditory data 2.No in-depth description about how themes were identified

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
(Butcher *et al.,* 2001)	Yes	Yes	Yes	Yes	1. No in-depht information on interview schedule 2. No discussion about saturation data	No details	Yes, but no details about how researchers explained issues to participants	1.No discussion on contraditory data 2.No discussion on researcher bias
(Byszewski *et al.*, 2007)	Yes	Yes	Yes	Yes	1. No discussion about saturation data 2. No details about family caregivers gender, relation to the patient or age	No details	Yes	Yes
(Chang *et al.,* 2010)	Yes	Yes	No discussion about why selecting the Phenomenology Approach *(described by Colaizzi)*	Yes	1. No in-depht information on interview schedule 2. No discussion about saturation data	No details	Yes	1.No in-depth description about how themes were identified
(Connell *et al.,* 2004)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data 2. No details about care recipient gender or age	No details	Yes, but no details about how researchers explained issues to participants	Yes
(Duxury *et al.,* 2013)	Yes	Yes	No discussion about the study design	1. No discussion on why these participants were the most appropriate 2. No discussion on what participant selection criteria were used	1. No discussion about saturation data 2. No details about caregiver gender, age or relation to patient 3. No details about care recipient gender or age	No details	Yes	1. No discussion on contraditory data 2.No discussion on researcher bias 3. No in-depth description about how themes were identified
(Elliott *el at.*, 2009)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	Yes

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
					2. No details about family caregivers and care recipients age			
(Fjellstrom *et al.,* 2010)	Yes	Yes	Yes	Yes	1. No in-depht information on interview schedule 2. No details about family caregivers relation to the care recipient 3. No details about care recipients age	No details	Yes	1.No discussion on contraditory data 2. No in-depth description about how themes were identified
(Fleming *et al.,* 2015)	Yes	Yes	Yes	Yes	1. No discussion about saturation data 2. No details about family caregivers relation to the care recipient 3. No details about family caregivers and care recipients age	No details	Yes	1.No discussion on contraditory data 2. No in-depth description about how themes were identified
(Forbes *et al.*, 2000)	Yes	Yes	Yes	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data	No details	Information on how researchers explained issues to participants No information about the signature of the informed consent	Yes
(Forbes *et al.*, 2008)	Yes	Yes	No discussion about the study design	Yes	Yes	No details	Yes	1.No discussion on contraditory data 2. No in-depth description about how themes were identified

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
(Frank *et al.*, 2006)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data	No details	Yes	1.No discussion on contraditory data 2. No in-depth description about how themes were identified
(Garcia *et al.,* 2012), Canada	Yes	Yes	No discussion about the study design	Yes	1. No details about family caregivers relation to the care recipient 2. No details about family caregivers age	No details	Yes	1. No discussion on the use of quotations to support the findings
(Gennip *et al.,* 2014)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data 2. No details about family caregivers relation to the care recipient 3. No details about family caregivers age	No details	Yes	1 No in-depth description about how themes were identified
(Gessert *et al.*, 2001)	Yes	Yes	Yes	1. No discussion on what participant selection criteria were used	1. No discussion about saturation data 2. No details about family caregivers relation to the care recipient 3. No details about family caregivers and care recipient age	No details	No information on ethical issues	1. No in-depth description about how themes were identified
(Gessert *et al.*, 2006)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data	No details	No information on ethical issues	1. No in-depth description about how themes were identified
(Givens *et al.*, 2012)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data 2. No details about family caregivers	No details	Yes, but no details about how researchers explained issues to	Yes

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
					relation to the care recipient 3. No details about care recipient age		participants	
(Glass, 2016)	Yes	Yes	Yes	1. No discussion on why these participants were the most appropriate 2. No discussion on what participant selection criteria were used	Yes	No details	Yes, but no details about how researchers explained issues to participants	Yes
(Habermann, *et al.,* 2013)	Yes	Yes	Yes	Yes	1. No in-depht information on interview schedule 2. No discussion about saturation data	No details	Yes, but no details about how researchers explained issues to participants	1. No in-depth description about how themes were identified 2.No discussion on contraditory data 3.No discussion on researcher bias
(Harmer and Orrel, 2008)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	1. No in-depth description about how themes were identified 2.No discussion on contraditory data 3.No discussion on researcher bias
(Harris, 2013)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	1. No in-depth description about how themes were identified 2.No discussion on

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
								contradictory data 3.No discussion on researcher bias
(Hemingway *et al.,* 2016)	Yes	Yes	Yes	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data	No details	Yes	1. No in-depth description about how themes were identified 2.No discussion on contradictory data
(Huis in het Veld *et al.,* 2016)	Yes	Yes	No discussion about the study design	Yes	1. No details about care recipient age	No details	Yes	1.No discussion on contradictory data
(Innes *et al.*, 2005)	Yes	Yes	No discussion about the study design	Yes	Yes	No details	Yes	1. No in-depth description about how themes were identified 2.No discussion on contradictory data 3.No discussion on researcher bias
(Innes *et al.,* 2011)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data 2. No details about family caregivers relation to the care recipient 3. No details about care recipient age	No details	Yes	Yes
(Ivey *et al.*, 2012)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data No details about care recipient age	No details	Yes, but no details about how researchers explained issues to participants	Yes

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
(Jamieson *et al.*, 2016)	Yes	Yes	No discussion about the study design	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data 2. No details about family caregivers and care recipient age	No details	Yes	1. No in-depth description about how themes were identified 2.No discussion on contraditory data 3.No discussion on researcher bias
(Jennings *et al.*, 2017)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data	No details	Yes	Yes
(Juozapavicius and Weber, 2001)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data	No details	No information on ethical issues	1. No in-depth description about how themes were identified 2.No discussion on contraditory data 3.No discussion on researcher bias
(Karlin *et al.*, 2001)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data 2. No details about care recipient age	No details	No information on ethical issues	1. No in-depth description about how themes were identified 2.No discussion on contraditory data 3.No discussion on researcher bias
(Karlsson *et al.,* 2014)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data	No details	Yes, but no details about how researchers explained issues to participants	Yes

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
(Kunneman *et al.*, 2017)	Yes	Yes	No discussion about the study design	Yes	1. No details about family caregivers relation to the care recipient	No details	Yes	1. No in-depth description about how themes were identified 2.No discussion on contraditory data
(Lach and Chang, 2007)	Yes	Yes	Yes	Yes	1. No details about family caregivers age	No details	Yes	Yes
(Lamahewa *et al.*, 2017)	Yes	Yes	Yes	Yes	1. No discussion about saturation data 2. No details about family caregivers relation to the care recipient 3. No details about family caregivers and care recipient age	No details	Yes	1. No in-depth description about how themes were identified 2.No discussion on contraditory data
(Lamech *et al.*, 2017)	Yes	Yes	Yes	Yes	1. No details about family caregivers relation to the care recipient 2. No details about care recipient age	No details	Yes	Yes
(Lamech *et al.*, 2017)	Yes	Yes	Yes	Yes	1. No details about family caregivers relation to the care recipient 2. No details about care recipient age	No details	Yes	Yes
(Lampley-Dallas *et al.*, 2001)	Yes	Yes	Yes	Yes	1. No details about care recipient age	No details	Yes, but no details about how researchers explained issues to participants	1. No in-depth description about how themes were identified
(Lethin *et al.*, 2016)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes, but no details about how researchers explained issues to participants	Yes

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
(Levkoff and Hinton, 1999)	Yes	Yes	Yes	1. No discussion on what participant selection criteria were used	1. No discussion about saturation data	No details	No information on ethical issues	1. No in-depth description about how themes were identified
(Lian *et al.*, 2017)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	Yes
(Livingston *et al.*, 2010)	Yes	Yes	Yes	Yes	Yes	No details	Yes	1. No in-depth description about how themes were identified
(Madsen and Birkelund, 2013)	Yes	Yes	Yes	1. No discussion on why these participants were the most appropriate 2. No discussion on what participant selection criteria were used	1. No in-depht information on interview schedule	No details	Yes	Yes
(Manthorpe *et al.*, 2013)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	Yes
(McCabe *et al.*, 2017)	Yes	Yes	Yes	Yes	1. No discussion about saturation data 2. No details about family caregivers relation to the care recipient 3. No details about family caregivers and care recipient age	No details	Yes	1. No in-depth description about how themes were identified
(Meyer, 2015)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data 2. No in-depht information on	No details	Yes	1. No in-depth description about how themes were identified

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
					interview schedule			
(Milte *et al.,* 2016)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	Yes
(Moreno-Cámara *et al.,* 2016)	Yes	Yes	Yes	Yes	1. No details about care recipient age	No details	Yes	Yes
(Morgan *et al.*, 2002)	Yes	Yes	Yes	Yes	1. No discussion about saturation data 2. No in-depht information on interview schedule 3. No details about family caregivers and care recipient age	No details	Yes	1. No in-depth description about how themes were identified
(Moyle *et al.*, 2002)	Yes	Yes	Yes	Yes	1. No discussion about saturation data 2. No details about family caregivers and care recipient age or relation	No details	Yes	1.No discussion on contraditory data 2.No discussion on researcher bias
(Oliveira *et al.*, 2017)	Yes	Yes	Yes	Yes	1. No discussion about saturation data 2. No details about care recipient age	No details	Yes	Yes
(Paton *et al.*, 2004)	Yes	Yes	No discussion about the study design	Yes	1. No discussion about saturation data 2. No details about care recipient age	None were family caregivers (all female)	Yes	1.No discussion on contraditory data 2.No discussion on researcher bias
(Peel and Harding, 2013)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	1. No in-depth description about how themes were

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
								identified
(Phillipson and Jones, 2011)	Yes	Yes	Yes	1. No discussion on why these participants were the most appropriate 2. No discussion on what participant selection criteria were used	1. No discussion about saturation data	No details	Yes	1. No in-depth description about how themes were identified 2.No discussion on contraditory data 3.No discussion on researcher bias
(Polenick *et al.*, 2018)	Yes	Yes	No discussion about the study design	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data	No details	Yes	Yes
(Polenick *et al.*, 2018)	Yes	Yes	No discussion about the study design	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data	No details	Yes	Yes
(Poole *et al.*, 2018)	Yes	Yes	No discussion about the study design	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data 2. No details about familiar caregivers and care recipient age	No details	Yes	Yes
(Polenick *et al.*, 2018)	Yes	Yes	No discussion about the study design	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data	No details	Yes	Yes

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
(Polenick *et al.*, 2018)	Yes	Yes	No discussion about the study design	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data	No details	Yes	Yes
(Poole *et al.*, 2018)	Yes	Yes	No discussion about the study design	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data 2. No details about familiar caregivers and care recipient age	No details	Yes	Yes
(Popham and Orrell, 2012)	Yes	Yes	Yes	1. No discussion on why these participants were the most appropriate	1. No discussion about saturation data 2. No details about familiar caregivers age	No details	Yes	Yes
(Prorok *et al.*, 2016)	Yes	Yes	Yes	Yes	Yes	No details	Yes	Yes
(Qazi *et al.,* 2010)	Yes	Yes	Yes	1. No discussion on what participant selection criteria were used	1. No discussion about saturation data	No details	Yes	1.No discussion on researcher bias
(Quinn *et al.,* 2014)	Yes	Yes	Yes	1. No discussion on why these participants were the most appropriate 2. No discussion on what participant selection criteria were used	1. No discussion about saturation data	No details	Yes	Yes

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
(Robinson *et al.,* 2008)	Yes	Yes	Yes	1. No discussion on why these participants were the most appropriate 2. No discussion on what participant selection criteria were used	1. No discussion about saturation data 2. No details about familiar caregivers age or relation to the patient	No details	Yes	1. No discussion on the use of quotations to support the findings
(Sarabia-Cobo *et al.*, 2016)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes, but no details about how researchers explained issues to participants	Yes
(Scott *et al.*, 2016)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	Yes
(Skaalvik *et al.,* 2016)	Yes	Yes	Yes	Yes	1. No discussion about saturation data 2. No details about familiar caregivers age or relation to the patient	No details	Yes	Yes
(Skaalvik *et al.,* 2016)	Yes	Yes	Yes	Yes	1. No discussion about saturation data 2. No details about familiar caregivers age or relation to the patient	No details	Yes	Yes
(Song *et al.*, 2018)	Yes	Yes	Yes	Yes	1. No discussion about saturation data	No details	Yes	Yes

Studies	Clear statement of study aims	Qualitative methodology appropriate	Study design appropriate to address the study aim	Recruitment appropriate	Data collection	Relationship between research and participants	Ethical issues considered	Data analysis
(Sutcliffe *et al.*2015)	Yes	Yes	No discussion about the study design	Yes	1. No details about familiar caregivers relation to the patient	No details	Yes	1. No in-depth description about how themes were identified
(Taşc *et al.*,2012)	Yes	Yes	No discussion about the study design	Yes	1. No in-depht information on interview schedule 2. No discussion about saturation data 3. No details about care recipient age	No details	Yes	1. No in-depth description about how themes were identified 2. No discussion on contraditory data 3.No discussion on researcher bias
(Toot *et al.,* 2013)	Yes	Yes	No discussion about the study design	Yes	Yes	No details	Yes	Yes
(Ven LG *et al.*2017)	Yes	Yes	No discussion about the study design	Yes	1. No details about family caregivers age	No details	Yes	Yes
(Wang *et al.*, 2018)	Yes	Yes	Yes	Yes	Yes	No details	Yes	1. No in-depth description about how themes were identified
(Wezel, *et al.,* 2016)	Yes	Yes	Yes	Yes	1. No details about care recipient age	No details	Yes	1. No in-depth description about how themes were identified

Table 2.2. Characteristics and key findings of the included studies in this systematic review (n=81)

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
(Aminzadeh *et al.*, 2007), Canada	To examine the emotional impact of disclosure of a dementia diagnosis on people with dementia both from their perspectives and those of their caregivers	Interviews following focus groups Thematic analysis	Quality of life Negative aspects
(Berry *et al.*, 2015), United States	To fill an important gap in research about how family members manage the risks of functional decline at home	Interviews Grounded theory analysis	Quality of life Illness progression Activities of daily living Negative aspects
(Boots LM *et al.*, 2015), Netherlands	To gain insight into the problems, needs and wishes that caregivers of persons with dementia during the early stages of the disease; To explore if an early stage intervention for dementia caregivers would be helpful and to explore which factors influence caregivers' perspectives	Focus Group Thematic analysis	Quality of life Positive and negative aspects
(Boughtwood *et al.*, 2011), Australia	To explore Arabic-speaking, Chinese-speaking, Italian-speaking and, Spanish-speaking communities caregivers' experiences and perceptions regarding caregiving and being a carer for a person with dementia	Focus Group Thematic analysis	Quality of life Illness progression Activities of daily living Costs Negative aspects
(Bunn *et al.*, 2017), United Kingdom	To explore the impact of dementia on access to non-dementia services and identify ways of improving service delivery for these persons with dementia	Interviews and focus groups Thematic analysis	Illness progression Costs Negative aspects
(Butcher *et al.*, 2001), United States	To describe the essential structure of the lived experience of caring for a family member with AD and related dementia among a large and diverse sample of informal family caregivers	Interviews Phenomenological analysis	Quality of life Illness progression Activities of daily living Negative aspects
(Byszewski *et al.*, 2007), Canada	To report the findings of a descriptive, exploratory, qualitative study of patient and caregiver perspectives of the disclosure of a dementia diagnosis	Interviews following focus groups Thematic analysis	Quality of life Activities of daily living Negative aspects
(Chang *et al.*, 2010), United Kingdom	To report the lived experience and perceived service needs of caregivers of persons with dementia in Hong Kong	Focus Group Thematic analysis	Quality of life Negative aspects

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
(Connell *et al.*, 2004), United States	To examine the attitudes of caregivers and physicians toward assessing and diagnosing dementia with an emphasis on how a diagnosis is disclosed	Interviews following focus groups Thematic analysis	Quality of life Negative aspects
(Duxury *et al.*, 2013), United Kingdom	To explore the views of nursing staff and relatives and identify the reasons for and ways of responding to aggressive behaviour	Focus groups Thematic analysis	Quality of life Illness progression Activities of daily living Positive and negative aspects
(Elliott *el at.*, 2009), United States	To describe and understand the ethical thinking used in end-of-life decision-making by family surrogates on behalf of their cognitively impaired elders	Focus group Thematic analysis	Quality of life Negative aspects
(Fjellstrom *et al.*, 2010), Sweden	To examine how people living with persons with Alzheimer's disease perceived everyday life aspects of food choices, cooking and food-related work	Focus Group Thematic analysis	Quality of life Activities of daily living Negative aspects
(Fleming *et al.*, 2015), Australia	To identify the environmental features that are desirable in buildings used and identify ways to improve provided care for people with dementia nearing the end of their lives	Focus Group Thematic analysis	Quality of life Illness progression Negative aspects
(Forbes *et al.*, 2000), United States	To describe families' decision-making processes, both cognitive and affective, regarding end-of-life treatments for nursing home residents with severe dementia	Focus group Thematic analysis	Quality of life Illness progression Negative aspects
(Forbes *et al.*, 2008), Canada	To describe experiences of family caregivers who received Canadian home and community-based services that aim to assist them in caring for their family member with dementia	Focus Group and interview Thematic analysis	Quality of life Costs Negative aspects
(Frank *et al.*, 2006), United Kingdom and United States	To identify key aspects of the impact of cognitive impairment on patients with MCI and mild probable AD and their informants, and identify overlap and differences between the groups	Focus group Thematic analysis	Quality of life Illness progression Activities of daily living Negative aspects
(Garcia *et al.*, 2012), Canada	To explore the perceptions of family and staff members on the potential contribution of environmental factors that influence disruptive behaviours and quality of life of residents with	Focus Group Thematic analysis	Quality of life Negative aspects

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
	dementia living in long-term care homes		
(Gennip *et al.*, 2014), Netherlands	To examine how dementia affects personal dignity in individuals with mild to moderate dementia from their perspective	Interview Thematic analysis	Quality of life Activities of daily living Positive aspects
(Gessert *et al.*, 2001), United States	To identify areas where better communication between health professionals and patients/families might be expected to be most beneficial to families facing end-of-life decisions	Focus group Phenomenological analysis	Quality of life Illness progression Negative aspects
(Gessert *et al.*, 2006), United States	To describe and understand rural and urban differences in attitudes toward death and in end-of-life decision making	Focus group Thematic analysis	Quality of life Negative aspects
(Givens *et al.*, 2012), United States	To describe the sources of stress for families of nursing home residents with advanced dementia	Interview Thematic analysis	Quality of life Illness progression Negative aspects
(Glass, 2016), United States	To document and examine the context of the environment and the role of hospice in the experience of caring for persons with dementia	Interview Phenomenological analysis	Quality of life Negative aspects
(Habermann, *et al.*, 2013), United States	To explore the positive aspects experienced by adult children in providing care to their parent who either has Parkinson's or Alzheimer's disease	Interview Content analysis	Quality of life Activities of daily living Positive and negative aspects
(Harmer and Orrel, 2008), United Kingdom	To explore the concept of meaningful activity for older people with dementia in care homes, from the perspectives of the care staff, family caregivers and residents themselves	Focus Group Thematic analysis	Activities of daily living Positive aspects
(Harris, 2013), United States	To examine the quality of the friendships that remain and continue, despite a diagnosis of some type of dementia	Interviews and focus groups Thematic analysis	Quality of life Positive and negative aspects
(Hemingway *et al.*, 2016), Canada	To better understand the lived experience of spousal caregivers providing care to partners with AD and related dementias resident in a care facility	Interview and Focus Group Thematic analysis	Quality of life Illness progression Costs Negative aspects

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
(Huis in het Veld *et al.*, 2016), Netherlands	To give insight into why changes in behaviour and mood are stressful for family caregivers and what self-management strategies family caregivers use when managing these changes and the stress they experience	Focus Group Thematic analysis	Quality of life Negative aspects
(Innes *et al.*, 2005), United Kingdom	To develop a qualitative understanding of service use from the point of view of people with dementia and their caregivers in rural Scotland	Interview and Focus Group Thematic analysis	Quality of life Costs Negative aspects
(Innes *et al.*, 2011), United Kingdom	To report on the views of people with dementia who live in care homes and their family caregivers on aspects of design that are important to them, discussing the relation to developing physical care environments as a respond to the wishes of people with dementia and their family	Focus Group Thematic analysis	Quality of life Positive aspects
(Ivey *et al.*, 2012), United States	To examine participants' daily life experiences as informal caregivers to individuals with dementia and explore how experiences and concerns may differ by ethnicity	Focus Group Thematic analysis	Quality of life Illness progression Activities of daily living Costs Negative aspects
(Jamieson *et al.*, 2016), Australia	To investigate the experiences of people with dementia and their caregivers when transitioning home from hospital	Interview and Focus Group Thematic analysis	Quality of life Negative aspects
(Jennings *et al.*, 2017), United States	To explore the goals of people with dementia, both from the perspective of people living with early-stage disease and from the perspective of caregivers of people with all stages of dementia	Focus group Thematic analysis	Quality of life Illness progression Activities of daily living Costs Positive and negative aspects
(Juozapavicius and Weber, 2001), United States	To explore the issues faced by former Alzheimer's caregivers identifying the factors which precipitated the beginning of the caregiver role and use the reflective information to identify the stages which comprise the transition out of the caregiver role	Interview Thematic analysis	Quality of life Costs Negative aspects
(Karlin *et al.*, 2001), United States	To investigate the experience of caregiving for family members with Alzheimer's disease	Interview Thematic analysis	Quality of life Positive aspects

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
(Karlsson *et al.*, 2014), England, Estonia, Finland, France, Germany, Netherlands, Spain and Sweden	To investigate persons with dementia and their informal caregivers' views of inter-sectoral information, communication and collaboration throughout the trajectory of dementia care in eight European countries	Focus Group Thematic analysis	Illness progression Negative aspects
(Kunneman *et al.*, 2017), Netherlands	To assess patients' and caregivers' views on and experiences with decisions about diagnostic testing for Alzheimer's disease and receiving test results	Focus group Content analysis	Quality of life Costs Negative aspects
(Lach and Chang, 2007), United States	To explore caregivers' perceptions of safety problems and identify how they manage safety concerns and explore the application of health behaviour change models to the caregiver situation	Focus group Thematic analysis	Quality of life Activities of daily living Negative aspects
(Lamahewa *et al.*, 2017), United Kingdom	To explore difficulties in decision making for practitioners and family caregivers at the end of life for people with dementia	Focus Group and interview Thematic analysis	Quality of life Negative aspects
(Lamech *et al.*, 2017), India	To explore the needs of family caregivers of persons with dementia in India	Focus Group and interview Thematic analysis	Quality of life Activities of daily living Costs Negative aspects
(Lampley-Dallas *et al.*, 2001), United States	To assess the perceived needs of African-American caregivers and their expectations of the health care system, perceived level of success and satisfaction in meeting their needs and their level of distress	Focus group Thematic analysis	Quality of life Costs Positive and negative aspects
(Lethin *et al.*, 2016), Sweden	To investigate caregivers' experiences of formal care when caring for a person with dementia through the process of the disease	Focus Group Content analysis	Quality of life Illness progression Activities of daily living Negative aspects
(Levkoff and Hinton, 1999), United States	To show how family caregivers draw on their cultural/personal resources to create stories about the nature and meaning of illness and to ask how ethnic identity may influence the kinds of stories family caregivers tell	Interview Thematic analysis	Quality of life Illness progression Negative aspects

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
(Lian *et al.*, 2017), China	To understand the experiences of people with dementia and their caregivers in engaging in dementia diagnosis	Focus Group and interview Thematic analysis	Quality of life Activities of daily living Costs Negative aspects
(Livingston *et al.*, 2010), United Kingdom	To identify common difficult decisions made by family caregivers on behalf of people with dementia and facilitators of and barriers to such decisions in order to produce information about overcoming barriers	Focus Group and interview Thematic analysis	Quality of life Illness progression Activities of daily living Negative aspects
(Madsen and Birkelund, 2013), Denmark	To examine the experiences family caregivers of persons with dementia highlighting these similarities or differences	Focus group Phenomenological analysis	Quality of life Negative aspects
(Manthorpe *et al.*, 2013), United Kingdom	To increase understanding of the experiences of people developing dementia and of their caregivers and to inform practice and decision making	Interview Thematic analysis	Quality of life Negative aspects
(McCabe *et al.*, 2017), United Kingdom	To understand the strategies for everyday life with dementia by scaffolding and working together in community and formal support	Focus group and interviews Thematic analysis	Quality of life Illness progression Activities of daily living Costs Negative aspects
(Meyer, 2015), United States	To describe the beliefs and experiences of Vietnamese caregivers caring for a family member with dementia and to elicit their ideas about promising interventions	Interview Thematic analysis	Quality of life Negative aspects
(Middlemass *et al.* 2018), United Kingdom	To explore the experiences/perceptions of informal caregivers of people with dementia when interacting with the health care system and to investigate healthcare professionals' views and current practice regarding people with dementia and their interactions with informal caregivers	Focus Group and interview Thematic analysis	Quality of life Illness progression Costs Negative aspects
(Milte *et al.*, 2016), Australia	To describe the meaning of quality residential care from the perspective of people with cognitive impairment and their family members	Focus Group and interview Thematic analysis	Costs Positive and negative aspects

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
(Moreno-Cámara *et al.*, 2016), Spain	Identify and analyse the problems that arise in the adaptation process of the caregiver to changes during family care to a person affected by dementia	Focus group Grounded Theory	Quality of life Illness progression Costs Negative aspects
(Morgan *et al.*, 2002), Canada	To obtain input from decision-makers and others to develop the objectives and design for a study of rural dementia care to fight the low use of formal supportive services such as home care and support groups by family caregivers	Focus Group Thematic analysis	Quality of life Costs Negative aspects
(Moyle *et al.*, 2002), Australia	To investigate family caregivers' perceptions of having a relative in a dementia care unit	Focus group Content analysis	Quality of life Illness progression Positive and negative aspects
(Oliveira *et al.*, 2017), United Kingdom	To explore how persons with dementia make sense of their own quality of life and to identify the factors that enhance or compromise their quality of life	Focus group Phenomenological analysis	Quality of life Activities of daily living Costs Positive and negative aspects
(Paton *et al.*, 2004), United Kingdom	To gain insight into caregivers' understanding of the causes of behaviours they find problematic in people with Alzheimer's disease in order to inform the development of educational strategies	Interview Thematic analysis	Illness progression Negative aspects
(Peel and Harding, 2013), United Kingdom	To explore the issue of accessing health and social care support services from caregivers' own perspectives	Focus group, interview and questionnaires (online and paper) Thematic analysis	Quality of life Costs Negative aspects
(Phillipson and Jones, 2011), Australia	To explore the utility of behavioural theories to identify the beliefs that contribute to service non-use and to determine whether the beliefs of service users and non-users differ	Focus Group and interview Content analysis	Quality of life Negative aspects
(Polenick *et al.*, 2018), United States	To examine causal attributions about BPSD among individuals caring for a family member with dementia	Focus Group Thematic analysis	Quality of life Activities of daily living Costs Negative aspects
(Polenick *et al.*, 2018), United States	To examine family caregivers' strategies for managing behaviour and psychological symptoms of dementia	Focus Group Thematic analysis	Quality of life Positive and negative aspects

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
(Poole *et al.*, 2018), United Kingdom	To investigate the views of people with dementia and the views of their family caregivers on important factors regarding care at end of life	Focus Group and interview Thematic analysis	Quality of life Illness progression Positive aspects
(Popham and Orrell, 2012), United Kingdom	To determine to what extent the care home environment met the requirements of residents with dementia in the context of the views of managers, family caregivers and staff	Focus Group and interview Thematic analysis	Quality of life Illness progression Positive and negative aspects
(Prorok *et al.*, 2016), Canada	To examine the perceived primary care health care experiences of both persons with dementia and their caregivers	Focus Group Thematic analysis	Quality of life Costs Negative aspects
(Qazi *et al.*, 2010), United Kingdom	To identify symptoms, risk factors and intervention strategies for anxiety of people with dementia, family caregivers and care staff	Focus Group Mind-map technique	Quality of life Illness progression Activities of daily living Negative aspects
(Quinn *et al.*, 2014), United Kingdom	To explore how family members and care staff understand awareness in people with severe dementia and what this awareness means to them	Focus Group Thematic analysis	Quality of life Negative aspects
(Robinson *et al.*, 2008), Australia	To reveal views about dementia diagnosis derived from a larger study of information needs of caregivers of people with dementia in Australia	Focus Group Thematic analysis	Quality of life Negative aspects
(Sarabia-Cobo *et al.*, 2016), Spain	To describe the processes of decision-making used by families regarding treatments at the end of life of institutionalized patients with advanced stages of dementia	Focus Group Thematic analysis	Quality of life Negative aspects
(Scott *et al.*, 2016), United Kingdom	To develop an understanding of challenging behaviour and how it impacted on the lives of family caregivers	Focus group Content analysis	Quality of life Negative aspects
(Skaalvik *et al.*, 2016), Norway	To describe how people with AD express their sense of self in accordance with the theory of selfhood described by Harré (1998)	Interview Phenomenological and thematic analysis	Quality of life Activities of daily living Negative aspects
(Song *et al.*, 2018), Korea	To identify family caregivers' experiences in managing the BPSD with particular focus on their interpersonal interactions with patient with dementia	Focus group Content analysis	Quality of life Activities of daily living Negative aspects

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
(Sutcliffe *et al.*2015), United Kingdom	To present the views of people with dementia and caregivers on a range of topics including their positive and negative experiences of dementia care; access to information and its communication; and suggestions to improve dementia care	Focus Group Thematic analysis	Quality of life Illness progression Costs Negative aspects
(Taşc *et al.*,2012), Turkey	To examine the physical and psychological demands experienced by caregivers of patients with AD in light of the lack of home care support in Turkey	Focus Group Thematic analysis	Quality of life Activities of daily living Negative aspects
(Toot *et al.*, 2013), United Kingdom	To identify which factors may lead to crisis for people with dementia and their caregivers and identify interventions these individuals believe could help in crisis	Focus Group Thematic analysis	Quality of life Negative aspects
(Ven LG *et al.*2017), Netherlands	To explore how people with dementia, their informal caregivers and their professionals participate in decision making about day-care and to develop a typology of participation trajectories	Interview Content analysis	Quality of life Illness progressionActivities of daily living Positive and negative aspects
(Wang *et al.*, 2018), China	To develop a theoretical model explaining the longitudinal changes in the caregiving process for family caregivers of persons with mild cognitive impairment in Taiwan	Interview Content analysis	Quality of life Illness progression Activities of daily living Costs Negative aspects
(Wezel, *et al.*, 2016), Netherlands	To describe the perspectives of female Turkish, Moroccan and Surinamese Creole family caregivers in the Netherlands about providing family care to a close relative with dementia	Focus Group and interview Content analysis	Quality of life Illness progression Positive and negative aspects
(Wijngaarden *et al., 2018*), Netherlands	To develop an in-depth understanding of what it means to live with dementia and to gain insight into what constitutes the art of living with dementia, both from the perspective of family caregivers	Focus Group and interview Thematic analysis	Quality of life Illness progression Activities of daily living Negative aspects
(Wolfs *et al.*, 2012), Netherlands	To gain caregivers' insights into the decision-making process in dementia patients with regard to treatment and care	Focus groups and Interviews Grounded Theory Analysis	Quality of life Illness progression Negative aspects

Authors, publication years & countries	Study aims	Data collection & analysis	Aspects focused
(Xiao *et al.*, 2013), Australia	To explore the experiences of family caregivers from Chinese, Greek, Italian and Vietnamese groups in utilising dementia service	Interview and focus groups Thematic analysis	Quality of life Illness progression Activities of daily living Negative aspects
(Xiao *et al.*, 2014), Australia and China	To compare socially and culturally constructed enablers and barriers pertinent to dementia caregivers in one capital city in Australia and one capital city in China through critical reflection on the caregivers' subjective and objective experiences for the improvement of dementia care services in both countries	Focus Group and interview Giddens' Structuration Theory	Quality of life Activities of daily living Negative aspects
(Xiao *et al.*, 2015), Australia	To explore the perceived challenges of dementia care from Vietnamese family caregivers and Vietnamese care workers in South Australia	Focus Group and interview Thematic analysis	Quality of life Illness progression Activities of daily living Costs Negative aspects
(Zabalegui *et al.*, 2008), Spain	To better understand informal caregivers' views about the resources that are available to them or should be available to them	Focus group Content analysis	Quality of life Costs Negative aspects

MCI: Mild Cognitive Impairment; AD: Alzheimer's Disease; BPSD: Behaviour and psychological symptoms of dementia

Table 2.3. Summary of methods and participants of 81 studies included in this systematic review

	People with AD/Dementia	**Family Caregivers**	**Former Caregivers**	**Dyads**	**Number of studies**
Focus group	10	41	1	0	52
Qualitative interview	4	15	1	0	20
Questionnaire	0	1	0	0	1
Mixed methods	9	24	2	2	37
Number of studies	23	81	4	2	108

Additional file 1 | Search strategy

Proposed Medline Search Terms*

Controlled vocabulary and text/key words

"Alzheimer Disease" [MeSH Major Topic] OR "Mild cognitive impairment" OR "Cognitive Dysfunction" [MeSH Major Topic]Dementia [Title/Abstract]

Method

"Interviews as Topic" [MeSH] OR Interview* [Title/Abstract]
"Surveys and Questionnaires" [MeSH] OR Survey* OR Questionnair* [Title/Abstract]
"Focus Groups" [MeSH]
"Geriatric Assessment" [MeSH] OR "Health Impact Assessment" [MeSH]

Population Terms

"Caregivers" [MeSH]
Caregiv* OR Carer [Title/Abstract]
"Family" [MeSH]
Famil* [Title/Abstract]
"Patient Care" [MeSH]

Outcome

"Illness Behavior" [MeSH]
"Cost of Illness" [MeSH]
"Activities of Daily Living" [MeSH]
"Quality of Life" [MeSH]
"Self Concept" [MeSH]
"Stress, Psychological" [MeSH]
"Sick Role" [MeSH]
"Outcome Assessment Health Care" [MeSH]
"Health Expenditures" [MeSH]
"Health Care Costs" [MeSH]
Self-Perception [Title/Abstract]

Studies Terms

"cohort studies" [MeSH]
"longitudinal studies" [MeSH]
"follow-up studies" [MeSH]
"prospective studies" [MeSH]
"retrospective studies" [MeSH]
Cohort OR Longitudinal OR Prospective OR Retrospective [all fields]

Filters activated

Publication date from 01.01.1998 to 15.07.20

*Search terms and strategy will be adapted to database: Embase, PsycInfo, Web of Science and Scopus

Additional file 2.2: PRISMA Checklist

Topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4-6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Available from author
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Figure 1 Additional file I
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Figure 1 Additional file I
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4-6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4-6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

Additional file 3.1

Table 3.1- Focus group participant quotes - caregiver changes in quality of life

Theme	Sub-theme	Quote
Caregiver personal life	Activities renouncement	*"I used to go to the cinema every week, it was something I stopped doing…. Going to the cinema with her is unthinkable, I stopped doing it…", Caregiver, female (daughter), Focus group C, lines 4708-4709.*
		"I already went to water aerobics and took my husband, at the beginning, (...) until I started, I gave up on him and I started to go and take him, he stayed in the coffee, it had a big glass, until he I started to disappear and I no longer had to give up ...", Caregiver, female (wife), Focus group C, lines 5207-5211.
		"Yes, and I had to give up many things, I was like going out with friends, right? Either I would drink coffee or go to the disco and still go to the gym and even that I had to abdicate, because every time we say I have it later I dedicate it to her ...", Caregiver, female (daughter), Focus group D, lines 5832-5834.
	Social isolation	*"No, I haven't been with my friends in a while ... A long time ago ... I isolated myself, yes, they really say that I isolated myself… Practically ...", Caregiver, female (daughter), Focus group D, lines 5819-5820.*
		"Nor is it, I mean, I don't have the patience to be ...", Caregiver, male (husband), Focus group A, line 1346.
		"Friendships I have lost, I have not lost, I move away a little… there is no time… because…", Caregiver, female (sister), Focus group A, line 1202.
	Life *in pause*	*"I don't know, sometimes it was, but it was very complicated, it was a lot of wear, it was a lot of wear… Because it's like that, I almost stopped having life, right?", Caregiver, female (daughter), Focus group B, line 2886-2887.*
		"Because we no longer have a life of our own ... Even with money, we no longer have a life of our own, so whether or not we really have the money to hire someone and be comfortable, or we stay the same!", Caregiver, female (daughter), Focus group C, lines 4308-4311.
Physical health	Tiredness	*"(…) Because I think, ok, she's at home all week, while I'm at work, on the days when I'm off, sometimes… Ok, I'm at home because sometimes I don't feel like being leave, or I'm so tired ... ", Caregiver, female (daughter), Focus group D, lines 5839-5841.*
	Physical effort	*"I have to carry with her that my mother is heavier than me… [laughs]… I have to carry with her into the bathtub and then she shakes, and then "there it's hot", "there it's cold" and put my white hair [laughs]… more essentially for that…", Caregiver, female (daughter), Focus Group A, lines 463-465.*
	Sleep problems	*"Right now, being with her night and day, permanently ... Even when I am, I am more tired, I don't sleep at all, do I?", Caregiver, male (husband), Focus Group A, lines 659-660.*
	Postpone health care	*"A person does not have time for anything, I need to go to the doctor and I will not go, because I am already saturated, in the hospital and at the doctor… I need to go and deal with this, I need to see a problem in my throat, and I will not, because I already know, if I go, it's exams exams exams ... I stay!! ... Just thinking that I have to do all that with my mother, I mean, it's the time that there is no time for us too, nor patience ...", Caregiver, female (sister), Focus group A, 1903-1906.*
Psychological health		(next page)
(next page)		

		"This is life? Life is if I was fine, we would go for a walk and that's it, even if it was just going for a walk, drinking a cup of coffee …", Caregiver, male (husband), Focus Group A, lines 1295-1296.
		"... That is, my life is to live one day at a time, one day ... because I have no taste in living, I already told my daughter, the youngest, that she is a teacher, I said look at me, talking, I am a person who tells everything, they are asking questions or you want something ... I throw everything out, nothing is hidden, what comes out will have to come out ...", Caregiver, male (husband), Focus group A, lines 1278-1281.
	Emotional stress	*"...Even horrible! And it's costing me a lot, but it's like this, it's impossible, it's like this, it's impossible to have her at home, even if I wanted to find people…", Caregiver, female (daughter), Focus group B, lines 2636-2637.*
Psychological health	Dealing with diagnosis	*"And then, I, at the beginning, didn't really explain what Alzheimer was ... I went to the internet out of curiosity and everything I read, I just wanted to send the cell phone, because I was watching through the cell phone, by the air ... Because it was each story and each testimony that a person was left: "Okay, will my mother forget me?" ... Yeah ... It was just one of the things that I was afraid of, is that my mother would look at me and not know who I was ...", Caregiver, female (daughter), Focus group D, lines 5437-5441.* *"It is a bit difficult [laughs]…. It is a bit difficult to manage the things that at this moment ... (...) My mother and that, in the first exam, did not accuse well, well what was it ... Only later, (…) yes, it was that he was accused of dementia ... At that time it was a shock for me ...", Caregiver, female (daughter), Focus group D, lines 5425-5433.*
	Felling alone	*"And then, there is also loneliness, because this implies the person giving up going out with friends, in my case, because she lives alone with me!", Caregiver, female (daughter), Focus group B, lines 3578-3580.*
	Decision making	*" (…) I already lived alone, so when I brought her it was an option, my son was against it, my daughter-in-law was against it, but it was what I chose, was what I decided…", Caregiver, female (daughter), Focus group B, lines 2928-2930.*

Table 3.2- Focus group participant quotes - positive and negative aspects of formal care services

Theme	Sub-theme	Quote
Home support services	Support in personal hygiene	*"(…)He gets up and I see that he is all wet, the lady has been going twice a week to bathe him because he can't do it and I'm not here either, I can't do this job …", Caregiver, female (sister), Focus group A, lines 1048-1050.*
Day center	Positive aspects	*"(...) And as for the day care center, I must say that in problems with dementia I had a fantastic welcome!", Caregiver, female (daughter), Focus group B, lines 2497-2498.* *"(...) The day center was good, I had assistance, there were some, cognitive stimulation, they had a gym, ready, and I started taking it 3 days a week ..", Caregiver, female (daughter), Focus group D, lines 5581-5583.*
	Negative aspects	*"But by chance it is a pity, that there are no more day centers like this one, because this one, gives me an idea that it must be the only one that is a closed day center!", Caregiver, female (daughter), Focus group C, lines 4145-4146.*
Nursing home	Positive aspects	*(After putting the mother at the nursing home) "I recovered (my life) a little, but ... I enrolled in a senior university, to force myself to leave the house, because I am not much to stay at home…", Caregiver, female (daughter), Focus group D, lines 6169-6170.*
	Negative aspects	*"Sometimes we get a little angry, but that is sometimes good because I think, when I go, I've already gone to nursing homes and I think: This is better for us to be angry with him, than for him to be here… Okay, this is true, frankly that's what I think", Caregiver, female (sister), Focus group A, lines 1068-1071.* *"It is the problem of homes I think, it is the big problem, because a person is not enough to feed him and give him a roof! It is not enough! And that is the problem!", Caregiver, female (daughter), Focus group C, lines 4142-4143.*
Barriers to access formal care	Cost	*"The answer is either the person puts it in a residence, like I put it this year to go on vacation, put it in a residence, or else contact those companies like I hired that are expensive, right? One week I paid 900€!", Caregiver, female (daughter), Focus group B, lines 3592-3594.* *"How can I have a caregiver at home, if the caregivers are around 750€ and up ... Where do I get this money if I don't have it?", Caregiver, female (daughter), Focus group D, lines 5890-5891.* *"And we also have no possibility to pay for a nursing home…. Monetarily…", Caregiver, female (wife), Focus group C, line 4691.*
	Limited spaces	*"And it was very complicated and so, they chose, both he and my sister-in-law, to arrange a day center, because the nursing home was impossible to find like that from one moment to the next…", Caregiver, female (daughter-in-low), Focus group C, lines 4688-4689.*
	Long process	*"There I am, for my husband there, I prefer to be paid a person to have at home, the (name of the institution), where we go, today I lack this paper, tomorrow I lack that, then another , it's just bureaucracy! …", Caregiver, female (wife), Focus group C, lines 5104-5106.*
	PwD will	*My (mother), I tried, but she didn't want (to go to the day center)…", Caregiver, female (daughter), Focus group B, line 2410.*
	Transport/road accesses	*"No, but I don't drive, if my husband gets sick, I can't bring him …", Caregiver, female (daughter-in-low), Focus group C, line 5360.* *"And then no and that, the bus is on the road to (location) and she has to go up the whole street to get home (...) everything is going up, I mean, she has arthrosis in her hips, there are many I mean, it's a situation, they ask for a lot of money for the van …", Caregiver, female (daughter), Focus group C, lines 5397-5399.*
Lack of formal support	Targeted care	*"Now this is how it is going to be? Is it a long shot? Yes! Portugal is in the third world, it is, in terms of that, these patients need very special care!", Caregiver, female (daughter), Focus group B, lines 3660-3661.*

**PwD: Person with dementia*

Table 3.3- Focus group participant quotes - dementia informal care related costs

Theme	Sub-theme	Quote
Food issues		*"If I didn't have it, and I'm very aware of it, to write it down, I have a son-in-law as I said he has a factory related to food, he has twenty-one employees and he gives me the food because if I had to buy the food with a reform it's €450, (…) If he didn't give me the meals, I couldn't eat or there wasn't that woman I pay €500 a month, 3 hours a day, that's €7.50 an hour, gives €120 a week, something like that ... I couldn't pay!", Caregiver, male (husband), Focus group A, lines 1459-1464.*
		"I, for example, think that hygiene (…), I don't know more or less how much I spend, I don't know, but I do know that my brother eats very well, really well and I never cut it, so it is not enough for all the…And ready, what can be done is done.", Caregiver, female (sister), Focus group A, lines 1563-1565.
Hygiene issues		*"Yes! ... Especially to have someone who would take care of her, for the bath… mainly for the bath, which is what costs me the most because she runs away from the water and screams that she doesn't want a bath… So much so that she now has medication reinforced to calm her down in the morning, when I want her… get her ready and give her a bath… -"let's go to the bath", "I don't want to, I already washed, I already took, why so much bath, why so much bath?", Caregiver, female (daughter), Focus group A, lines 458-462.*
		"It is when she urinate all over and it is crazy in this big country that diapers…, there are no diapers that can withstand the urine she makes…", Caregiver, male (husband), Focus group A, lines 821-822.
Electricity		*"Yes, there are two clothes machines every day ...", Caregiver, female (sister), Focus group A, lines 1567-1568.*
Medication/medical exams		*"No, no, it is like this ... it is generic medication, if it is not generic it is a lot of money! I had to go to generics! ... Unfortunately! ...", Caregiver, female (daughter), Focus group A, lines 1537-1538.*
		"(...) So what do we caregivers (…), who work, have expenses, have things to pay, how do we do for our expenses and not only for the expenses of the patient, because unfortunately the drugs are expensive ... How do we do it, or how do we manage it?", Caregiver, female (daughter), Focus group D, lines 5478-5481.
		"Oh, for example, when we are going to do some exams, there are her exams ... Just yesterday, I went to do the multipurpose exam with her, I paid her €12 …", Caregiver, female (sister), Focus group D, lines 6009-6010.
Formal care	Day center	*"It is the social day center, which is not free, unfortunately there are still people who find it expensive, you know?… There are people who think it is very expensive, €7 a month… you know that there are people with a lot of difficulties…", Caregiver, male (husband), Focus group A, lines 1550-1552.*
	Nursing home	*"€1700, €, 2000it's a shame what I was asked for!", Caregiver, female (wife), Focus group C, line 5088.*
		"(...), so I pay €850, before I paid €1000, and in the meantime, I asked for it at nursing home (...), Then I presented my income there, my monthly fee went down, at this point I pay €850 (...) ", Caregiver, female (daughter), Focus group D, lines 6088-6089.
	Formal caregiver	*"(...) So this lady helped me with daily hygiene, but she went two hours a day in the morning, on weekends she didn't go and I paid her €600 a month… Until she was a year and then I had to give up because I couldn´t take more!", Caregiver, female (daughter-in-low), Focus group C, lines 4293-4295.*
		"Having someone at home is, I ordered a lot, I have been these months, I have not stopped looking and they ask me, at least €1000, more everything ... And they asked me for more …", Caregiver, female (daughter), Focus group C, lines 4270-4271.
Transport		*"So, I already must pay almost €200 if I want my mother's transport (to day center), (...) I mean, €200, so I pay an instalment for a car, right? With 200€ ...", Caregiver, female (daughter), Focus group C, lines 5316-5318.*
Deceit the PwD		*"The man says: -"Ah, now I need the money", so this, go down to the ATM… (...) In conclusion, she takes €100 from the account, gives the man €100, but, and it was enough, it was… it was my fault at that time, he takes the card from her without her realizing it, right?", Caregiver, female*

	(daughter), Focus group A, lines 971-975.
Lack of financial support	*"And… and then he has a reform, despite being a doctor, very small…", Caregiver, female (sister), Focus group A, line 291.* *"She (PwD) has a subsidy, a fortune, of 105€ a month ...", Caregiver, male (husband), Focus group A, line 362.*

**PwD: Person with dementia*

Additional file 3.2

INFORMAÇÃO AO PARTICIPANTE

(para participação em Grupos de Foco)

Grupos de Foco sobre o impacto da Demência nas vidas dos doentes e cuidadores Portugueses a nível familiar, económico e social

Objetivo do Estudo

O presente estudo de investigação, tem como objetivo descrever em narrativas/perceções o ponto de vista dos cuidadores informais sobre os custos percebidos individualmente e na família, impacto na qualidade de vida e expectativas sobre a evolução da doença e de "Como é viver com Demência?"; "Qual é o impacto da doença na vida dos doentes e seus cuidadores a nível familiar, económico e social?"

Descrição e Métodos do Estudo:

Serão realizadas quatro sessões de Grupos de Foco com cuidadores informais. As informações recolhidas centram-se na perceção dos participantes sobre custos relacionados com a doença, impacto na qualidade de vida, perspetivas de evolução e de futuro com a doença.
Será obtido um consentimento informado conforme as boas práticas em investigação.

Riscos previsíveis

Não existem quaisquer riscos previsíveis na participação deste estudo.

Possíveis Benefícios para os Participantes

Para além do aspeto benemérito de participação num estudo científico que visa perceber a vivencia com a demência e o seu impacto na qualidade de vida e na saúde dos doentes, não existem quaisquer benefícios diretos para o participante.

Participação Voluntária e Direitos de Recusa da Participação ou de Abandono

Terá toda a liberdade para recusar-se a participar no estudo ou retirar o seu consentimento, suspendendo a participação em qualquer momento. A participação é voluntária e a sua recusa em participar não envolverá qualquer penalização ou perda de benefícios.

Confidencialidade

Compreendo que a informação sobre mim será recolhida e analisada como parte deste estudo. Esta informação poderá ser recolhida e combinada com informação de outros participantes. Toda a informação que me identifica será guardada pela equipa de investigação e será mantida confidencial.
A minha identificação no estudo será efetuada com um número. Esta informação poderá ser analisada por pessoas ou entidades autorizadas pelo investigador e, nalgumas instâncias, pela Comissão de Ética da Faculdade de Medicina da Universidade de Lisboa, com o objetivo de confirmar a veracidade dos dados do estudo. Compreendo também que informação que não me identifica será recolhida durante o estudo e guardada numa base de dados, podendo vir a fazer parte dos resultados publicados. O meu nome não será identificado em nenhum relatório ou publicação decorrente deste estudo. Estes dados poderão também fazer parte de projetos de investigação futuros e poderão ser comunicados a Autoridades Regulamentares.

A Quem Deve Colocar Questões Relacionadas com Este Estudo

Se tiver qualquer dúvida sobre este estudo poderá contactar: Prof. Drº. Mário Miguel Rosa, e-mail: mrosa@medicina.ulisboa.pt; Profª. Drª. Manuela Guerreiro, email: mgil@medicina.ulisboa.pt; Patrícia Lindeza, e-mail: patricialindeza@campus.ul.pt

DECLARAÇÃO DE CONSENTIMENTO INFORMADO
(para participação em Grupos de Foco)

Grupos de Foco sobre o impacto da Demência nas vidas dos doentes e cuidadores Portugueses a nível familiar, económico e social

INVESTIGADOR: _____
NOME DO PARTICIPANTE: _____
NÚMERO DE ESTUDO DO PARTICIPANTE:

Eu,_____
declaro ter tomado conhecimento e aceitar participar num estudo que tem por objetivo descrever em narrativas/perceções o ponto de vista dos cuidadores informais sobre os custos percebidos individualmente e na família, impacto na qualidade de vida e expectativas sobre a evolução da doença e de "Como é viver com Demência?".
Para esse efeito participar em quatro sessões de Grupos Focus e ter a possibilidade de ser selecionado para uma Entrevista compostas por perguntas relacionadas com a perceção dos custos associados à doença, perspetivas de evolução e futuro com a doença. Poderei, no entanto, revogar a autorização para utilização das informações presentes no questionário em qualquer altura. O estudo proposto foi-me claramente explicado. Foi-me dada a oportunidade de colocar questões. Declaro que aceito participar, voluntariamente, neste estudo.

Recebi uma cópia desta declaração de consentimento informado, devidamente assinada e datada.

Data_____
Assinatura do Participante_____

Discuti este estudo de investigação com o participante, utilizando uma linguagem compreensível e apropriada. Informei adequadamente o participante sobre a natureza deste estudo e sobre os seus possíveis benefícios e riscos, considerando que o participante compreendeu a minha explicação.

Data	Nome do Investigador	Assinatura do Investigador
__/__/__		_____

_____

IMPACTO DA DEMÊNCIA NA QUALIDADE DE VIDA DE FAMILIARES CUIDADORES
(GUIÃO DE *FOCUS GROUPS*)

GRUPO DE FOCO Nº_____ Data:___/___/___

Local:_____

Número de participantes:_____

Tópicos de Discussão:

1. **INTRODUÇÃO**

- Breve apresentação do estudo
- Objetivos e regras da discussão em grupo
- Apresentação dos participantes (*warm up*): Nome, relação ao doente, vive ou não com o doente, profissão que tiveram ou têm

2. **VIVÊNCIA DA DOENÇA, PELO FAMILIAR CUIDADOR**

- Vivência com a doença ao longo da sua progressão
- Alterações do dia-a-dia determinadas pelo cuidar do doente
- Tempo dedicado aos cuidados da pessoa com demência
- Sobrecarga física, psicológica, emocional e social
- Implicações na qualidade de vida do cuidador

3. **CUSTOS ASSOCIADOS A DOENÇA**

- Principais encargos
- Custos diretos, em termos pessoais, familiares, financeiros, ...

4. Custos indiretos diretos, em termos pessoais, familiares, financeiros, ...**ASPETOS A MELHORAR PARA AUMENTO DE QdV DOS CUIDADORES INFORMAIS**

- Acesso a cuidados de saúde (para doentes e cuidadores)
- Informação / Formação / Treino
- Fontes de apoio financeiro

Faculdade de Medicina
Universidade de Lisboa
Lisboa, Portugal
Setembro de 2020

Assunto: Conclusões dos *focus groups* de cuidadores informais de pessoas com demência

Caro participante, serve a presente carta para, mais uma vez, lhe agradecer o profundo contributo para este projeto que procura descrever o impacto da demência no dia-a-dia dos cuidadores informais de pessoas com demência. Graças à sua participação, conseguimos um retrato fiel do assunto, que é da máxima importância.

Neste breve relatório são apresentadas as principais conclusões dos *focus groups* com cuidadores informais de pessoas com demência (em que colaborou). São indicadas as opiniões dos participantes, de forma agrupada e mantendo o anonimato das afirmações, que dizem respeito aos temas com mais impacto na vida diária do cuidador informal.

1. *Caracterização dos participantes*

Entre 21 de Novembro e 12 de Dezembro de 2019, foram realizados quatro *focus groups* envolvendo um total de 14 participantes. Entre eles, 12 eram mulheres (85,7%), 8 das quais eram filhas, 2 irmãs, 1 esposa e 1 nora da pessoa com demência. Os 2 participantes homens eram maridos da pessoa com demência. A média de idades dos participantes foi de 64 anos e 57,1% tinham até 12 anos de escolaridade. A maioria dos participantes era cuidador há mais de 5 anos (71,4%). A média de idades dos familiares cuidados foi de 82 anos e eram, na sua maioria, mulheres.

2. *Principais categorias abordadas nos focus groups com cuidadores informais de pessoas com demência*

- Verificou-se um consenso acerca dos temas com mais impacto na vida pessoal dos cuidadores informais, sendo eles os 3 seguintes: 1) Mudanças na qualidade de vida do

cuidador, 2) Aspetos relacionados com cuidados formais, 3) Custos da demência para o agregado familiar.

- Dentro dos temas referidos, os participantes expressaram as suas opiniões que foram discutidas e organizadas em subtemas como se apresenta na tabela 1.

Tabela 1- Principais categorias, temas e subtemas dos focus groups com cuidadores informais de pessoas com demência

Categorias	Temas	Subtemas
Qualidade de vida Mudanças que afetam o bem-estar físico, mental e social do cuidador Podem levar a doenças, stress, depressão, baixa autoestima e isolamento social	Vida pessoal do cuidador	Abandono de atividades Isolamento social Vida adiada
	Saúde física	Cansaço Esforço físico Problemas de sono Adiar cuidados de saúde
	Saúde psicológica	Stress Lidar com o diagnóstico do familiar Solidão Tomada de decisão (pelo familiar com demência)
Cuidados formais Mudanças na rotina diária do cuidador relacionadas com os serviços formais (apoio domiciliários, cuidadores formais, centros de dia e lares de idosos)	Serviços de apoio domiciliários	Ajuda na higiene pessoal do familiar com demência
	Centro de dia	Aspetos positivos
	Lar de idosos	Aspetos negativos
	Barreiras no acesso a cuidados formais	Custos elevados Vagas limitadas Processo longo e burocrático Vontade do familiar com demência Transporte/acessos pedonais
	Falta de apoio formal	Falta de apoio especializado para a demência
Custos relacionados com a doença Custos introduzidos pela doença que afetam o orçamento financeiro familiar – todas as despesas económicas que estão relacionadas com a condição de demência	Alimentação	
	Produtos de higiene	
	Eletricidade	
	Medicamentos e exames médicos	
	Cuidados formais	Centro de dia Lar Cuidador formal/empresas
	Transporte	
	Burlas ao familiar com demência	
	Falta de apoio financeiro (ao cuidador e pessoa com demência)	

3. *Principais perspetivas relativas às mudanças na qualidade de vida*

- Verificou-se uma concordância entre os participantes relativamente às mudanças que afetaram negativamente a sua qualidade de vida.
- A qualidade de vida do cuidador é extremamente afetada com a introdução de grandes alterações na vida pessoal, como por exemplo: mudança de casa, mudanças no agregado familiar e dinâmicas familiares, abandono de atividades/tempos-livres, isolamento social que conduz a solidão, adiamento de objetivos pessoais/profissionais e familiares, alteração de horários de trabalho e abandono da atividade profissional.
- As tarefas e rotinas do ato de cuidar resultaram também em modificações na saúde física e psicológica dos participantes que afirmam estar exaustos e sozinhos. A saúde física é prejudicada pelo cansaço, privação de sono e também pelo adiamento da vigilância do seu estado de saúde (devido à falta de tempo, disposição ou pelo impedimento de ir ao médico com regularidade).
- Verificou-se consenso entre os participantes relativamente ao impacto de cuidar na saúde psicológica, tendo estes admitido que têm dificuldades em lidar com o diagnostico do familiar, estão expostos a elevado stress diário e se vêm forçados a tomar decisões no lugar do seu familiar com demência, por vezes, com sentimentos de culpa, arrependimento e tristeza associados.

4. *Principais perspetivas relativas aos cuidados formais*

- Verificou-se uma concordância entre os participantes relativamente ao impacto dos cuidados formais no dia-a-dia dos cuidadores, sendo que alguns serviços reuniram maioritariamente opiniões positivas (serviços de apoio domiciliários, centros de dia) e outros reuniram maioritariamente opiniões negativas (cuidadores formais, empresas contratadas e lares de idosos).
- Relativamente aos serviços de apoio domiciliários, as impressões foram positivas tendo sido referidos como uma boa ajuda ao cuidador, nomeadamente no auxílio à higiene pessoal da pessoa com demência. Os centros de dia, foram os serviços formais que mais contribuíram para melhorar o dia-a-dia dos participantes. Entre os aspetos positivos dos centros de dia estão: a criação de uma rotina para a pessoa com demência, a estimulação cognitiva disponibilizada, a existência de momentos de treino

físico, a disponibilidade em facultar o almoço e alguns cuidados de higiene e, por fim, a garantia de que o familiar está seguro e vigiado (centro de dia com "porta fechada"). Para além dos aspetos positivos relacionados com o bem-estar da pessoa com demência (que contribuem indiretamente para o bem-estar do cuidador), está também a existência de tempo livre para o cuidador, que aproveita para tratar de assuntos da sua vida pessoal, descansar, realizar compras, trabalhar, etc.

- A contração de cuidadores formais ou empresas para essa finalidade foi relatada como uma experiência muito negativa, com custos demasiado elevados e prejudicial devido à grande rotatividade de cuidadores semanal/mensal que não favorecem a relação prolongada com a pessoa cuidada.
- Os lares de idosos foram considerados pelos cuidadores como uma solução de último recurso devido às elevadas barreiras de acesso a este serviço: custos muito elevados (e muitas vezes impossíveis de suportar), falta de cuidados direcionados para pessoas com demência, processo longo e burocrático, vontade/medo da pessoa com demência de ir ou não para o lar, estigma existente face a este serviço (sentimentos de culpa/tristeza envolvidos). Contudo, a existência de cuidados de enfermagem permanentes em algumas destas instituições foi considerada um aspeto positivo. A maioria dos cuidadores referiu que apesar dos pontos negativos descritos relativamente aos lares, este poderia ser um serviço a adotar no futuro caso a resposta destes serviços fosse adaptada às necessidades das pessoas com demência e os preços praticados fossem acessíveis.

5. *Principais perspetivas relativas aos custos relacionados com a doença*

- Relativamente aos custos relacionados com a demência, as opiniões dos participantes foram concordantes e os exemplos de despesas descritos foram transversais à maioria dos casos.
- Os principais custos introduzidos pela demência no agregado familiar foram: medicamentos/exames médicos, produtos de higiene (toalhetes, cremes de corpo, fraldas, etc.), custos dos cuidados formais (mensalidade do centro de dia, salário elevado de cuidadores formais e mensalidade dos lares de idosos).

- Foram ainda relatados custos extra relacionados com a alimentação, transporte (para centro de dia/consultas), despesas de eletricidade (relacionadas com o número elevado de máquinas de roupa realizadas) e perdas de dinheiro por parte da pessoa com demência (por burla ou desorientação).
- A falta de apoio financeiro, quer para o cuidador, quer para a pessoa com demência, foi um assunto amplamente discutido. Na opinião dos participantes, existem muito poucos apoios financeiros para esta população e os que existem são difíceis de obter (devido à elevada burocracia envolvida) e de baixo/insuficiente valor monetário.

Caro participante, uma vez apresentadas as conclusões dos *focus groups* vimos por este meio convidá-lo a, se desejar, informar-nos acerca da sua opinião sobre os resultados obtidos, podendo enviar-nos sugestões (sobre temas pertinentes que não tenham sido incluídos ou para completar algum ponto em particular) para: *patricialindeza@campus.ul.pt* ou para a morada:

EnviHeB Lab – Instituto de Saúde Ambiental, Faculdade de Medicina da Universidade de Lisboa, Av. Prof. Egas Moniz, Ed. Egas Moniz, Piso 0, Ala C, 1649-028 Lisboa, Portugal

Gratos pela sua participação!

Melhores cumprimentos,

Patrícia Lindeza,

Estudante de Doutoramento

Faculdade de Medicina da Universidade de Lisboa

Table 4.1. Distribution of QoL-AD scores by domain (n=187)

	Group A n=53	Group B n=85	Group C n=49	All cases, n=187
Physical health				
Weak	24 (45.3)	56 (65.9)	31 (63.3)	111 (58.4)
Reasonable	25 (47.2)	21 (24.7)	18 (36.7)	64 (33.7)
Good	4 (7.5)	8 (9.4)	0 (0.0)	12 (6.3)
Excellent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Energy/**				
Weak	40 (75.5)	**55 (64.7)**	**42 (85.7)**	137 (72.1)
Reasonable	11 (20.8)	**21 (24.7)**	**3 (6.1)**	35 (18.4)
Good	2 (3.8)	**8 (9.4)**	**4 (8.2)**	14 (7.4)
Excellent	0 (0.0)	**1 (1.2)**	**0 (0.0)**	1 (0.5)
Humour/mood				
Weak	29 (54.7)	44 (51.8)	23 (46.9)	96 (50.5)
Reasonable	20 (37.7)	29 (34.1)	17 (34.7)	66 (34.7)
Good	4 (7.5)	12 (14.1)	9 (18.4)	25 (13.2)
Excellent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Life conditions				
Weak	8 (15.1)	18 (21.2)	7 (14.3)	33 (17.4)
Reasonable	30 (56.6)	44 (51.8)	29 (59.2)	103 (54.2)
Good	15 (28.3)	22 (25.9)	12 (24.5)	49 (25.8)
Excellent	0 (0.0)	1 (1.2)	1 (2.0)	2 (1.1)
Memory				
Weak	50 (94.3)	82 (96.5)	47 (95.9)	179 (94.2)
Reasonable	2 (3.8)	2 (2.4)	2 (4.1)	4 (2.1)
Good	1 (1.9)	1 (1.2)	0 (0.0)	3 (1.6)
Excellent	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Family/***				
Weak	17 (32.1)	20 (23.5)	7 (14.3)	44 (23.5)
Reasonable	22 (41.5)	43 (50.6)	24 (49.0)	89 (47.6)
Good	10 (18.9)	16 (18.8)	16 (32.7)	42 (22.5)
Excellent	3 (5.7)	6 (7.1)	2 (4.1)	11 (5.9)
Missing	1 (1.9)	0 (0.0)	0 (0.0)	1 (0.5)
Marriage				
Weak	10 (18.9)	11 (12.9)	9 (18.4)	30 (16.0)
Reasonable	16 (30.2)	28 (32.9)	15 (30.6)	59 (31.6)
Good	17 (32.1)	34 (40.0)	11 (22.4)	62 (33.2)
Excellent	3 (5.7)	2 (2.4)	1 (2.0)	6 (3.2)
Missing	7 (13.2)	10 (11.8)	13 (26.5)	30 (16.0)
Friends/**				
Weak	37 (69.8)	**54 (63.4)**	**42 (85.7)**	133 (70.0)
Reasonable	15 (28.3)	**21 (24.7)**	**5 (10.2)**	41 (21.9)
Good	1 (1.9)	**10 (11.8)**	**2 (4.1)**	13 (7.0)
Excellent	0 (0.0)	**0 (0.0)**	**0 (0.0)**	0 (0.0)
In general, how do patient feel				
Weak	32 (60.4)	53 (62.4)	38 (77.6)	123 (64.7)

	Group A n=53	Group B n=85	Group C n=49	All cases, n=187
Reasonable	16 (30.2)	29 (34.1)	7 (14.3)	52 (27.4)
Good	5 (9.4)	3 (3.5)	3 (6.1)	11 (5.8)
Excellent	0 (0.0)	0 (0.0)	1 (2.0)	1 (0.5)
Ability to perform tasks at home/**				
Weak	46 (86.8)	**73 (85.9)**	**49 (100)**	168 (88.4)
Reasonable	7 (13.2)	**12 (14.1)**	**0 (0.0)**	19 (10.0)
Good	0 (0.0)	**0 (0.0)**	**0 (0.0)**	0 (0.0)
Excellent	0 (0.0)	**0 (0.0)**	**0 (0.0)**	0 (0.0)
Ability to do things for fun				
Weak	43 (81.1)	69 (81.2)	43 (87.8)	155 (81.6)
Reasonable	9 (17.0)	15 (17.6)	6 (12.2)	30 (15.8)
Good	1 (1.9)	1 (1.2)	0 (0.0)	2 (1.1)
Excellent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Money				
Weak	36 (67.9)	60 (70.6)	36 (73.5)	132 (69.5)
Reasonable	16 (30.2)	18 (21.2)	9 (18.4)	43 (22.6)
Good	1 (1.9)	7 (8.2)	3 (6.1)	11 (5.8)
Excellent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Life as a whole				
Weak	25 (47.2)	53 (62.4)	35 (71.4)	113 (59.5)
Reasonable	23 (43.4)	29 (34.1)	10 (20.4)	62 (32.6)
Good	5 (9.4)	3 (3.5)	3 (6.1)	11 (5.8)
Excellent	0 (0.0)	0 (0.0)	1 (2.0)	1 (0.5)

Group A: PwD that used to visit day centers during the week, (n=53); Group B: PwD that are cared exclusively at home, (n=85); Group C: PwD that were in a transition moment for formal care admission (pre-nursing-home moment), (n=49). Qol-AD: Quality of life in Alzheimer's Disease. QoL-AD (13 questions. scale from weak to excellent). **p<0.05. ***p<0.01. for the QoL-AD distributions. Comparisons of the QoL-AD frequencies by groups were analyzed with the Kruskal-Wallis *H* test followed by Mann-Witney *U*, followed by Bonferroni correction to find the groups where the difference was significant.

Additional file 4.1

INFORMAÇÃO AO PARTICIPANTE

(para preenchimento de questionários para determinação de custos associados à demência, capacidade funcional, impacto na qualidade de vida e sobrecarga física, emocional e social)

Questionário de levantamento de dados sobre custos, capacidade funcional, qualidade de vida, e sobrecarga em Pessoas com Demência e seus Cuidadores Informais

Objetivo do Estudo

O presente estudo de investigação, tem como objetivo determinar os custos associados (tendo como base a frequência de consultas, internamentos, medicamentos associados, custos de deslocação, custos relacionamentos com cuidados informais etc, e custos indiretos relacionados com a perda de produtividade quer dos doentes quer dos seus cuidadores informais) à Demência em Portugal bem como a qualidade de vida tanto no doente como no cuidador e a sobrecarga física, emocional e social nos cuidadores informais de pessoas com demência.

Descrição e Métodos do Estudo:

Tendo como base a prevalência da demência descrita na literatura, serão determinados os custos da Demência após recolha de informações especificas por questionário. Será determinada a qualidade de vida na pessoa com demência e no cuidador, e ainda a sobrecarga física, emocional e social no cuidador. Os questionários serão preenchidos por Cuidadores Informais associados à Demência em Portugal e as informações recolhidas centram-se nos cuidadores informais e no doente. Será obtido um consentimento informado conforme as boas práticas em investigação.

Riscos previsíveis

Não existem quaisquer riscos previsíveis na participação deste estudo.

Possíveis Benefícios para os Participantes

Para além do aspeto benemérito de participação num estudo científico que visa determinar a qualidade de vida e impacto da Demência em Portugal, não existem quaisquer benefícios diretos para o participante.

Participação Voluntária e Direitos de Recusa da Participação ou de Abandono

Terá toda a liberdade para recusar-se a participar no estudo ou retirar o seu consentimento, suspendendo a participação em qualquer momento. A participação é voluntária e a sua recusa em participar não envolverá qualquer penalização ou perda de benefícios.

Confidencialidade

Compreendo que a informação sobre mim será recolhida e analisada como parte deste estudo. Esta informação poderá ser recolhida e combinada com informação de outros participantes. Toda a informação que me identifica será guardada pela equipa de investigação e será mantida confidencial.
A minha identificação no estudo será efetuada com um número. Esta informação poderá ser analisada por pessoas ou entidades autorizadas pelo investigador e, nalgumas instâncias, pela Comissão de Ética da Faculdade de Medicina da Universidade de Lisboa, com o objetivo de confirmar a veracidade dos dados do estudo. Compreendo também que informação que não me identifica será recolhida durante o estudo e guardada numa base de dados, podendo vir a fazer parte dos resultados publicados. O meu nome não será identificado em nenhum relatório ou publicação decorrente deste estudo. Estes dados poderão também fazer parte de projetos de investigação futuros e poderão ser comunicados a Autoridades Regulamentares.

A Quem Deve Colocar Questões Relacionadas com Este Estudo

Se tiver qualquer dúvida sobre este estudo poderá contactar: Prof. Drº. Mário Miguel Rosa, e-mail: mrosa@medicina.ulisboa.pt; Profª. Drª. Manuela Guerreiro, email: mgil@medicina.ulisboa.pt; Patrícia Lindeza, e-mail: patricialindeza@campus.ul.pt

DECLARAÇÃO DE CONSENTIMENTO INFORMADO

(para preenchimento de questionários para determinação de custos associados à demência, capacidade funcional, impacto na qualidade de vida e sobrecarga física, emocional e social)

Questionário de levantamento de dados sobre custos, qualidade de vida, e sobrecarga em Pessoas com Demência e seus Cuidadores Informais

INVESTIGADOR: _____
NOME DO PARTICIPANTE: _____
NÚMERO DE ESTUDO DO PARTICIPANTE:

Eu,_____de claro ter tomado conhecimento e aceitar participar num estudo que tem por objetivo determinar os custos associados (tendo como base a frequência de consultas, internamentos, medicamentos associados, custos de deslocação, custos relacionamentos com cuidados informais etc, e custos indiretos relacionados com a perda de produtividade quer dos doentes quer dos seus cuidadores informais) à Demência em Portugal bem como a qualidade de vida tanto no doente como no cuidador e a sobrecarga física, emocional e social nos cuidadores informais de pessoas com demência.
Para esse efeito responder a vários questionários para determinação da qualidade de vida, capacidade funcional da pessoa com demência, custos associados à demência e sobrecarga física, emocional e social. Poderei, no entanto, revogar a autorização para utilização das informações presentes no questionário em qualquer altura. O estudo proposto foi-me claramente explicado. Foi-me dada a oportunidade de colocar questões. Declaro que aceito participar, voluntariamente, neste estudo.

Recebi uma cópia desta declaração de consentimento informado, devidamente assinada e datada.

Data_____

Assinatura do Participante_____

Discuti este estudo de investigação com o participante, utilizando uma linguagem compreensível e apropriada. Informei adequadamente o participante sobre a natureza deste estudo e sobre os seus possíveis benefícios e riscos, considerando que o participante compreendeu a minha explicação.

Data Nome do Investigador Assinatura do Investigador

Questionário CARACTERIZAÇÃO SOCIODEMOGRÁFICA DE FAMILIARES
(Responsáveis pelo doente e/ou Cuidador Informal)

Nº de caso_____

Por favor marque com um X a sua opção

1.Género: (1) Masculino ☐ (2) Feminino ☐

2. Data de Nascimento ____/____/____

3.Localidade: _____

4.Estado Civil:

(1) Solteiro (a) ☐
(2) Casado (a) ou união de facto ☐
(3) Separado (a) ☐
(4) Divorciado (a) ☐
(5) Viúvo (a) ☐

5. Filhos:

(1) Não ☐
(2) Sim. Quantos_____ ☐

6. Escolaridade em anos aprovados: _____anos

7. Escolaridade (último ano com aprovação):

(1) Não estudei (0 anos) ☐
(2) Escola primária/1ºCiclo (4 anos) ☐
(3) 2ºCiclo (5 a 6 anos) ☐
(4) 3º Ciclo (7 a 9 anos) ☐
(5) Ensino Secundário (10 a12 anos) ☐
(6) Ensino Superior (mais de 12 anos) ☐

8.Estatuto Profissional:

(1) Empregado/a tempo inteiro ☐
(2) Empregado/a tempo parcial ☐
(3) Trabalhador/a-estudante ☐
(4) Estudante ☐
(5) Doméstico/a ☐
(6) Desempregado/a ☐
(7) De baixa médica ☐
(8) Reforma antecipada ☐
(9) Reforma não antecipada ☐
(10) Pensão de invalidez ☐

9. Existiu alguma mudança no seu estatuto profissional devido à situação do seu familiar:

(1) Não ☐
(2) Sim ☐
Se sim, qual?_____

10.Grau de parentesco com a pessoa cuidada:

(1) Marido/ Esposa ☐
(2) Companheiro/ Companheira ☐
(3) Filho/ Filha ☐
(4) Irmão/ Irmã ☐
(5) Neto/ Neta ☐
(6) Primo/ Prima ☐
(7) Sobrinho/ Sobrinha ☐
(8) Genro/ Nora ☐
(9) Amigo/ Amiga ☐
(10) Vizinho/Vizinha ☐
(11) Outro ☐
Qual?_____

11. Selecione a situação que o identifica:

(1) Sou o cuidador informal e responsável pelo doente ☐
(2) Sou o responsável pelo doente e o seu cuidador é informal (outro familiar) ☐
(3) Sou o responsável pelo doente e o seu cuidador é formal ☐
(4) Outra situação. Qual?_____ ☐

12. No caso de ser o cuidador informal do doente, há quanto tempo já cuida do doente?

(1) Não aplicável (não sou o cuidador) ☐
(2) Menos de 1 ano ☐
(3) Entre 1 a 2 anos ☐
(4) Entre 2 a 3 anos ☐
(5) Entre 3 a 5 anos ☐
(6) Mais de 5 anos ☐

13. No caso de existir um cuidador formal do doente, qual é a situação:

(1) Não existe um cuidador formal ☐
(2) Um(a) empregado(a) a tempo parcial (meio dia) ☐
(3) Um(a) empregado(a) a tempo inteiro (todo o dia) ☐
(4) Um(a) empregado(a) a tempo integral (dia/noite) ☐
(5) Outro cuidador, qual?_____ ☐

14. No caso de existir um cuidador formal do doente, tem formação profissional (formação para a prestação de cuidados de saúde)?

(1) Não existe um cuidador formal ☐
(2) Não tem formação ☐
(3) Tem formação ☐
(4) Não sei essa informação ☐

15.Situação da pessoa doente cuidada:

(1) Na sua própria casa (casa do doente) ☐
(2) Em minha casa ☐
(3) Em casa de outro familiar ☐
(4) Numa instituição ☐

Se escolher (4)
15.1. Qual?
(1) Centro de dia ☐
(2) Lar ☐
(3) Outra, qual?_____ ☐

Se escolher (4)
15.2 Motivo da institucionalização?
(5.1) Não aplicável (doente não institucionalizado) ☐
(5.2) Desgaste ou incapacidade física ☐
(5.3) Desgaste ou incapacidade emocional/psicológica ☐
(5.4) Razões relacionadas com o comportamento ☐
(5.4) Mais do que uma opção ☐

16.Neste momento, vive na mesma casa que o doente?

(1) Não ☐
(2) Sim ☐

17.Relativamente aos últimos 30 dias, quanto tempo dedicou à pessoa doente:

(1) Menos de 1 hora por dia ☐
(2) Entre 2 a 4 horas por dia ☐
(3) Entre 5 a 7 horas por dia ☐
(4) Entre 7 a 10 horas por dia ☐
(5) Mais de 10 horas por dia ☐

18. Já recorri/recorro a grupos ou instituições de apoio a familiares de pessoas com demência:

(1) Não ☐
(2) Sim ☐

19. Qual é o diagnóstico da pessoa que cuida?_____

20. Em que data (ano civil) foi dado o referido diagnóstico?_____

21. Teve alguma situação grave de saúde nos últimos 6-12 meses?_____

(1) Não ☐
(2) Sim ☐

21.1. Se sim, qual?_____

Questionário CARACTERIZAÇÃO SOCIODEMOGRÁFICA DE PESSOAS COM DEMÊNCIA

(Questionário a ser preenchido com a ajuda do entrevistador ou Profissional de Saúde)

Nº de caso_____

Por favor marque com um X a sua opção

1.Género da pessoa idosa:

(1) Masculino ☐ (2) Feminino ☐

2. Data de Nascimento____/____/___

3.Localidade: _____

4. Escolaridade em anos aprovados: _____anos

5. Escolaridade (último ano com aprovação):

(1) Não estudei (0 anos) ☐
(2) Escola primária/1ºCiclo (4 anos) ☐
(3) 2ºCiclo (5 a 6 anos) ☐
(4) 3º Ciclo (7 a 9 anos) ☐
(5) Ensino Secundário (10 a12 anos) ☐
(6) Ensino Superior (mais de 12 anos) ☐

6.Estatuto Profissional:

(1)	Empregado/a tempo inteiro ☐	(6) Desempregado/a	☐
(2)	Empregado/a tempo parcial ☐	(7) De baixa médica	☐
(3)	Trabalhador/a-estudante ☐	(8) Reforma antecipada	☐
(4)	Estudante ☐	(9) Reforma não antecipada	☐
(5)	Doméstico/a ☐	(10) Pensão de invalidez	☐

7. Existiu alguma mudança no seu estatuto profissional devido ao seu diagnóstico?

(1) Não ☐ (2) Sim ☐

Se sim, qual?_____
_____
_____

Muito obrigada pela sua colaboração!

AVALIAÇÃO DE GANHOS EM SAÚDE - E Q - 5 D

Assinale com uma cruz (assim [X]), um quadrado de cada um dos seguintes grupos, indicando qual das afirmações descreve melhor o seu estado de saúde hoje.

▶ Mobilidade

Não tenho problemas em andar ..... ❑1
Tenho alguns problemas em andar ..... ❑2
Tenho de estar na cama ..... ❑3

▶ Cuidados Pessoais

Não tenho problemas em cuidar de mim ..... ❑1
Tenho alguns problemas a lavar-me ou vestir-me ..... ❑2
Sou incapaz de me lavar ou vestir sozinho/a ..... ❑3

▶ Actividades Habituais *(ex. trabalho, estudos, actividades domésticas, actividades em família ou de lazer)*

Não tenho problemas em desempenhar as minhas actividades habituais ..... ❑1
Tenho alguns problemas em desempenhar as minhas actividades habituais ..... ❑2
Sou incapaz de desempenhar as minhas actividades habituais ..... ❑3

▶ Dor / Mal Estar

Não tenho dores ou mal estar ..... ❑1
Tenho dores ou mal estar moderados ..... ❑2
Tenho dores ou mal estar extremos ..... ❑3

▶ Ansiedade / Depressão

Não estou ansioso/a ou deprimido/a ..... ❑1
Estou moderadamente ansioso/a ou deprimido/a ..... ❑2
Estou extremamente ansioso/a ou deprimido/a ..... ❑3

▶ Comparado com o meu nível geral de saúde durante os últimos 12 meses, o meu estado de saúde hoje é:

Melhor ..... ❑1
O mesmo ..... ❑2
Pior ..... ❑3

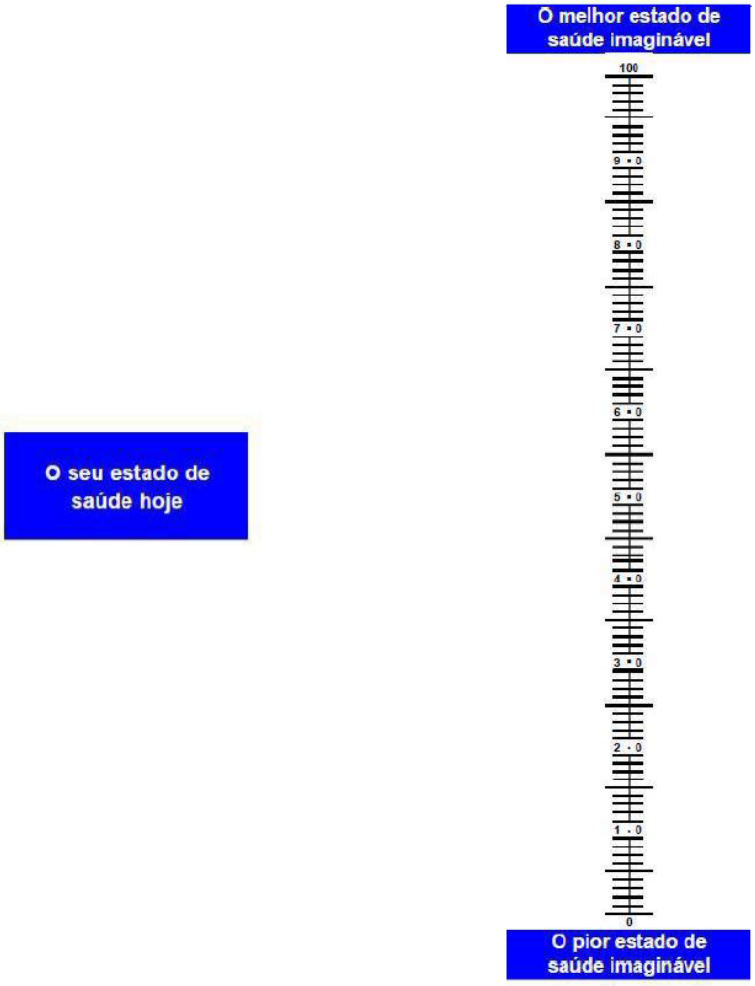
ASSINALE O QUADRADO APROPRIADO

Copyright © EuroQol Group
Copyright © Versão Portuguesa, 1997, 1998. Centro de Estudos e Investigação em Saúde da Universidade de Coimbra

Referência: Ferreira, L.N. et al. 2014. The valuation of the EQ-5D in Portugal. Quality of life Research, 23(2), pp.413-423.

- Para ajudar as pessoas a classificarem o seu estado de saúde, desenhámos uma escala (semelhante a um termómetro) na qual o melhor estado de saúde que possa imaginar é marcado por 100 e o pior estado de saúde que possa imaginar é marcado por 0.

  Gostaríamos que indicasse nesta escala qual é hoje, na sua opinião, o seu estado de saúde. Por favor, desenhe uma linha a partir do rectângulo que se encontra à esquerda, até ao ponto da escala que melhor classifica o seu estado de saúde hoje.



Muito obrigado por ter preenchido este questionário.

Copyright © EuroQol Group
Copyright © Versão Portuguesa, 1997, 1998. Centro de Estudos e Investigação em Saúde da Universidade de Coimbra

Referência: Ferreira, L.N. et al. 2014. The valuation of the EQ-5D in Portugal. Quality of life Research, 23(2), pp.413-423.

QOL – AD *versão portuguesa*

(Versão de questionário para familiar ou prestador de cuidados)

As questões seguintes dizem respeito à Qualidade de Vida do doente:

Quando pensa sobre a vida do doente, podemos considerar vários aspectos, alguns dos quais estão abaixo mencionados. Por favor, pense em cada um dos itens e classifique a qualidade de vida actual do doente, como ele a consideraria, em cada área usando uma de quatro palavras: **fraco, razoável, bom, excelente**. Classifique estes itens com base na vida do doente no momento presente (ou seja, nas últimas semanas). Se tiver questões acerca de qualquer item, por favor peça ajuda à pessoa que lhe forneceu este questionário.

Faça um círculo à volta das respostas:

1- Saúde Física	Fraco	Razoável	Bom	Excelente
2- Energia	Fraco	Razoável	Bom	Excelente
3- Humor/ Disposição	Fraco	Razoável	Bom	Excelente
4- Condições de vida	Fraco	Razoável	Bom	Excelente
5- Memória	Fraco	Razoável	Bom	Excelente
6- Família	Fraco	Razoável	Bom	Excelente
7- Casamento	Fraco	Razoável	Bom	Excelente
8- Amigos	Fraco	Razoável	Bom	Excelente
9- Em geral, como se sente	Fraco	Razoável	Bom	Excelente
10- Capacidade de realizar as tarefas em casa	Fraco	Razoável	Bom	Excelente
11- Capacidade de fazer coisas para se divertir	Fraco	Razoável	Bom	Excelente
12- Dinheiro	Fraco	Razoável	Bom	Excelente
13- Vida como um todo	Fraco	Razoável	Bom	Excelente

Comentários:

_____

_____

_____

Referência: Bárrios, H., 2012. Adaptação Cultural e Linguística e Validação do Instrumento QOL-AD para portugal., pp.1–106.

ESCALA DE DEMÊNCIA DE BLESSED

Blessed G, Tomlinson BE, Roth M, 1968. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. British Journal of Psychiatry 114: 797-811

A PREENCHER COM UM ACOMPANHANTE
(Pontuação máxima = 28)

A. Vida quotidiana

Classificação: Ausência de defeito = 0; Presença de defeito = 1; Presença inconsistente = 0.5)

1. Incapacidade de realizar tarefas caseiras
   (cozinhar, tratar da roupa, fazer limpezas, jardinar, fazer arranjos em casa, cuidar do carro..) _____
2. Incapacidade para lidar com pequenas importâncias de dinheiro
   (no café, pequenas compras, conferir trocos.....) _____
3. Incapacidade para recordar pequenas listas
   (compras, números de telefones.....) _____
4. Tendência a desorientar-se na sua própria casa
   (quer ir para a sala e entra na cozinha, fica parado a procurar a divisão da casa para onde quer ir.....) _____
5. Tendência a desorientar-se em ruas familiares
   (quer ir a uma loja e dirige-se para o lado oposto, tem dificuldade em retomar o percurso correcto para casa...) _____
6. Incapacidade para interpretar correctamente o ambiente
   (reconhecer se está num hospital, se está numa agência bancária.....) _____
7. Incapacidade para recordar acontecimentos recentes
   (passeios, saídas, visitas....) _____
8. Tendência a rememorar o passado
   (fala mais de acontecimentos passados do que do presente, recorda factos da sua infância de uma maneira que não era habitual .....) _____

B. Mudança de hábitos

Classificação: a indicada em cada item (0, 1, 2, 3)

9. Comer
   - Asseadamente, com os talheres adequados
     (sem alterações) (0) _____
   - Come sem asseio e só com a colher
     (come com a mão, usa talheres ao acaso....) (2) _____
   - Come só sólidos
     (biscoitos, pão....) (2) _____
   - Tem que ser alimentado (3) _____

Referência: Garcia, C., 2003. Escalas e testes na demência. Grupo e estudos de Envelhecimento Cerebral e Demências – Colaboração da UCB Pharma (Novartis Farma) – Produtos Farmacêuticos.

10. Vestir
- – Sem ajuda (sem alterações) (0) _____
- – Apresenta alguma dificuldade (Abotoa botões fora do sítio; esquece ocasionalmente peças de vestuário.....). (1) _____
- – Peças de vestuário na sequência errada (esquece com frequência peças de vestuário...) (2) _____
- – Incapaz de se vestir (3) _____

11. Esfíncteres
- – Controlo completo (sem alterações) (0) _____
- – Urina na cama (ocasionalmente) (1) _____
- – Urina na cama (com frequência) (2) _____
- – Incontinência de fezes e urina (3) _____

C. Alterações na Personalidade, nos interesses, no entusiasmo;

Classificação: Ausência de defeito = 0; Presença = 1)

12. Flexibilidade diminuída (rigidez mental - comportamento infantil - quando lhe dizem, por exemplo, que hoje tem de ir ao médico, não descansa enquanto não sai de casa e pergunta consecutivamente "então não vamos?"...) (1) _____

13. Egocentrismo aumentado (comportamento infantil - tem comportamentos de chamada de atenção sobre si; amealha tudo, não quer dar nada.....) (1) _____

14. Diminuição da atenção pelos sentimentos dos outros (Diz coisas ofensivas,ou que magoam os outros sem se preocupar nada com isso, ...) (1) _____

15. Aplanamento dos afectos (durante o dia está sempre com o mesmo humor, não mostra reacção diferente perante acontecimentos tristes ou alegres,.....) (1) _____

16. Diminuição do controlo emocional (irritabilidade exacerbada) (1) _____

17. Hilariedade em situações inapropriadas (ri, sem motivo que o justifique) (1) _____

18. Embotamento das respostas emocionais (não mostra alegria se vê alguém de quem gostava, ...) (1) _____

19. Comportamento sexual bizarro (comportamentos sexuais diferentes do seu habitual) (1) _____

20. Abondono dos interesses ("hobbies") (deixou de fazer renda, costura, ler, jogos,...) (1) _____

21. Diminuição da iniciativa (apatia) (1) _____

22. Hiperactividade (sem finalidade) (levanta-se e senta-se frequentemente, mexe e remexe gavetas, sem justificação, ...) (1) _____

TOTAL: _____

Referência: Garcia, C., 2003. Escalas e testes na demência. Grupo e estudos de Envelhecimento Cerebral e Demências – Colaboração da UCB Pharma (Novartis Farma) – Produtos Farmacêuticos.

DECLARAÇÃO DE CONSENTIMENTO INFORMADO

(para realização da escala de avaliação cognitiva Mini Mental State Examination - MMSE)

Aplicação da escala de avaliação cognitiva Mini-Mental State Examination -MMSE

INVESTIGADOR: _____
NOME DO PARTICIPANTE: _____
NÚMERO DE ESTUDO DO PARTICIPANTE:

Caro participante,

No âmbito do Projeto *"Demência e Doença de Alzheimer em Portugal: da progressão aos custos económicos"* venho por este meio pedir a sua participação por ser conveniente fazer algumas questões acerca da sua memória.
Se concordar em participar, agradeço que assine este documento a confirmar a sua participação de forma voluntária e devidamente esclarecida.
Receberá uma cópia desta declaração de consentimento informado, devidamente assinada e datada.

Eu, _____ declaro ter tomado conhecimento e aceitar participar num estudo que tem por objetivo determinar a qualidade de vida, a sobrecarga e os custos associados à Demência em Portugal e para esse efeito aceitar que seja realizada a aplicação de uma escala de avaliação cognitiva (MMSE).
Poderei, no entanto, revogar a autorização para utilização das informações presentes no questionário em qualquer altura. O estudo proposto foi-me claramente explicado. Foi-me dada a oportunidade de colocar questões. Declaro que aceito participar, voluntariamente, neste estudo.
Recebi uma cópia desta declaração de consentimento informado, devidamente assinada e datada.

Data_____ ____/____/____

Assinatura do Participante_____

Assinatura da Testemunha_____

Discuti este estudo de investigação com o participante, utilizando uma linguagem compreensível e apropriada. Informei adequadamente o participante sobre a natureza deste estudo e sobre os seus possíveis benefícios e riscos, considerando que o participante compreendeu a minha explicação.

Data Nome do Investigador Assinatura do Investigador

_____/__/__ _____ _____

MINI MENTAL STATE EXAMINATION (Folstein, Folstein & McHugh,1975, com adaptação de Guerreiro e colaboradores, 1994)

I. ORIENTAÇÃO

Vou fazer-lhe algumas perguntas. A maior parte delas são fáceis. Tente responder o melhor que for capaz." (Dar 1 ponto por cada resposta correta)

1. Em que ano estamos? _____
2. Em que mês estamos? _____
3. Em que dia do mês estamos? _____
4. Em que estação do ano estamos? _____
5. Em que dia da semana estamos? _____
6. Em que País estamos? _____
7. Em que Distrito vive? _____
8. Em que Terra vive? _____
9. Em que casa estamos? _____
10. Em que andar estamos? _____

Nota: _____

II. RETENÇÃO

"Vou dizer-lhe três palavras. Queria que as repetisse e que procurasse decorá-las porque dentro de alguns minutos vou pedir-lhe que me diga essas três palavras." As palavras são:

PERA **GATO** **BOLA**

"Repita as três palavras". (Dar 1 ponto por cada palavra correta)

PERA _____ GATO _____ BOLA _____ Nota: _____

II. ATENÇÃO E CÁLCULO

"Agora peço-lhe que me diga quantos são 30 menos 3 e que ao número encontrado volte a subtrair 3 até eu lhe dizer para parar."

(Dar 1 ponto por cada resposta correta. Parar ao fim de 5 respostas. Se fizer um erro de subtração, mas continuando a subtrair corretamente partir do erro, conta-se como um único erro)

(30) (27) (24) (21) (18) (15) Nota: _____

IV. EVOCAÇÃO

(Só se efetua no caso do sujeito ter aprendido as três palavras referidas na prova de retenção) "Agora veja se me consegue dizer quais foram as três palavras que lhe pedi há pouco para repetir." (Dar 1 ponto por cada resposta correta)

PERA _____

GATO _____

BOLA _____ Nota: _____

V. LINGUAGEM

(Dar 1 ponto por cada resposta correta)

a) Mostrar o relógio de pulso.

"Como se chama isto?" Nota: _____

b) Mostrar um lápis.

"Como se chama isto?" Nota: _____

c) Repetir a frase:

"O rato rói a rolha" Nota: _____

d) "Vou dar-lhe uma folha de papel. Quando eu lhe entregar o papel, pegue nele com a sua mão direita, dobre-o ao meio e coloque-o no chão".

(Dar 1 ponto por cada etapa bem executada. A pontuação máxima é de 3 pontos.)

Pega no papel com a mão direita _____

Dobra o papel ao meio _____

Coloca o papel no chão _____ Nota: _____

e) "Leia e cumpra o que diz neste cartão."

Mostrar o cartão com a frase: "FECHE OS OLHOS". (Dar 1 ponto por cada realização correta).

Nota: _____

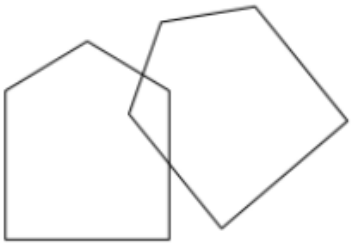
f) "Escreva uma frase."

(A frase deve ter sujeito, verbo e ter sentido para ser pontuada com 1 ponto. Erros gramaticais ou com erros de trocas de letras não contam como erros.)

Nota: _____

g) “Copie o desenho que lhe vou mostrar.” Mostrar o desenho num cartão.

(os 10 ângulos devem estar presentes e 2 deles devem estar intersectados para pontuar 1 ponto. Tremor e erros de rotação não são valorizados)



Nota: _____

NOTA TOTAL: _____

Table 5.1. Correlations with EQ-5D-3L and QASCI score with each other's and sociodemographic variables of informal caregivers and PwD, (n=187)

	EQ-5D-3L	QASCI
Caregiver characteristics		
Gender	-0.216/***	0.149/**
Age	-0.314/**	0.150/**
Educational level	0.334/***	-0.210/**
Professional active	0.262/***	-0.206/**
Familiar relationship (wife)	-0.224/***	-0.229/**
Familiar relationship (daughter)	-0.61	-0.043
Familiar relationship (husband)	-0.004	-0.022
Familiar relationship (son)	0.245/***	0.234/**
Years of care	-0.160/**	0.233/***
Hours of care	-0.306/***	0.351/***
EQ-VAS	0.610/***	-0.449/***
EQ-5D-3L	-	-0.444/***
Mobility, (EQ-5D-3L)	-	-0.030
Self-care, (EQ-5D-3L)	-	-0.019
Usual activities, (EQ-5D-3L)	-	0.313/***
Pain/discomfort, (EQ-5D-3L)	-	0.519/***
Anxiety/depression, (EQ-5D-3L)	-	0.519/***
QASCI score	-0.476/***	-
Emotional burden, (QASCI)	-0.452/***	-
Implications in personal life, (QASCI)	-0.514/***	-
Financial burden, (QASCI)	-0.286/***	-
Reactions to demands, (QASCI)	-0.187/**	-
Perception of efficacy and control mechanisms, (QASCI)	-0.241/***	-
Family support, (QASCI)	-0.136	-
Satisfaction with role and family member, (QASCI)	-0.075	-
PwD characteristics		
Gender	0.166/**	-0.034
Age	-0.206/***	0.063
Educational level	0.200/***	-0.086
Years since diagnosis	-0.097	0.050
Attend to day center	0.064	0.047
EQ-5D-3L	0.233/***	-0.363/***
Mobility	-0.167/**	0.253/***
Self-care	0.062	0.270/***
Usual activities	-0.109	0.317/***
Pain/discomfort	-0.117	0.183/**
Anxiety/depression	-0.267/***	0.248/***
EQ-VAS	0.319/***	-0.367/***
QoL-AD	0.278/***	-0.471/***
BDRS score	-0.170/**	0.401/***
Changes in everyday life (BDRS)	-0.118	0.302/***
Changes in habits (BDRS)	-0.149/**	0.321/***
Changes in personality (BDRS)	-0.137	0.324/***
MMSE (n=43)	0.233	0.240

** *p<0.05,* ***p<0.01.* EQ-5D-3L, EuroQol 5-dimensions 3-level; EQ-VAS, EuroQol Visual Analogue. QASCI: Informal Caregiver Burden Assessment Questionnaire. QoL-AD: Quality of life in Alzheimer's Disease. BDRS: Blessed Domain Rating Scale. Comparisons of the EQ-5D-3L index were analyzed using the Spearman's Coefficient. Comparisons of the QASCI score were analyzed using the Pearson's Coefficient.

Table 5.2. Influence of informal caregivers' and PwD characteristics in caregivers' QoL (EQ-5D-3L), model 1

	B	***Std. Error***	***t***	***p***
Caregiver characteristics				
Age	-0.005	0.002	-2.417	**<0.05**
Gender (compared to female)	0.058	0.038	1.526	0.129
Familiar relationship (compared with other family members)				
Husband/wife	0.378	0.102	3.722	**<0.001**
Son/daughter	0.383	0.079	4.818	**<0.001**
Brother/sister	0.553	0.125	4.435	**<0.001**
Grandchild	0.413	0.225	1.834	0.068
Nephew	0.5	0.332	1.506	0.134
Son/daughter-in-law	0.391	0.198	1.976	0.05
Emotional burden (QASCI)	-0.201	0.13	-1.544	0.124
Implications in personal life (QASCI)	-0.49	0.143	-3.419	**<0.05**
PwD characteristics				
Age	-0.006	0.003	-2.129	**<0.05**
Mobility (comparing with extreme problems)				
No problems	-0.065	0.05	-1.309	0.192
Some problems	0.051	0.043	1.181	0.239
Pain/discomfort (comparing with extreme problems)				
No problems	0.125	0.047	2.681	**<0.05**
Some problems	0.071	0.039	1.809	**<0.05**

PwD, Person with dementia. SD, standard deviation. QASCI: Informal Caregiver Burden Assessment Questionnaire.

r2=0.44, Adjusted r2=0.39

Table 5.3. Influence of informal caregivers' and PwD characteristics in caregivers' overall burden (QASCI score), model 2

	B	***Std. Error***	***t***	***p***
Caregiver characteristics				
Activities of daily living (compared with extreme problems)				
No problems	0.002	0.026	0.087	0.931
Some problems	0.002	0.023	0.078	0.938
Pain/discomfort (compared with extreme problems)				
No problems	-0.095	0.028	-3.362	**<0.001**
Some problems	-0.09	0.02	-4.439	**<0.001**
Anxiety/depression (compared with extreme problems)				
No problems	-0.04	0.028	-1.441	0.152
Some problems	-0.029	0.023	-1.263	0.209
Hours of care (compared with more than 10 hours)				
Less than 1 hour	-0.05	0.032	-1.581	0.116
2 to 4 hours	-0.027	0.028	-0.978	0.33
5 to 7 hours	-0.018	0.025	-0.74	0.46
7 to 10 hours	0.006	0.022	0.263	0.793
Familiar relationship (compared with other family members)				

Husband/wife	0.186	0.087	2.142	**<0.05**
Son/daughter	0.168	0.077	2.17	**<0.05**
Brother/sister	0.184	0.102	1.803	**<0.05**
Grandchild	0.2	0.084	2.388	**<0.05**
Nephew	0.401	0.16	2.5	**<0.05**
Son/daughter-in-law	0.288	0.096	2.993	**<0.05**
Education level (compared to university)				
Did not study	-0.045	0.045	-1	0.319
4-years of school	0.009	0.024	0.371	0.711
6-years of school	0.034	0.032	1.053	0.294
9-years of school	-0.039	0.035	-1.106	0.27
12-years of school	-0.036	0.021	-1.725	0.087
Professional situation (compared to disability pension)				
Full-time	0.106	0.043	2.463	**<0.05**
Part-time	0.157	0.049	3.204	**<0.05**
Student	0.048	1.168	0.041	0.967
Domestic	0.175	0.064	2.758	**<0.05**
Unemployed	0.151	0.047	3.182	**<0.05**
Medical leave	0.077	0.056	1.386	0.168
Early retirement	0.132	0.043	3.091	**<0.05**
Unanticipated retirement	0.077	0.041	1.895	0.06
PwD characteristics				
Mobility (comparing with extreme problems)				
No problems	-0.022	0.031	-0.719	0.474
Some problems	0.015	0.023	0.62	0.536
Pain/discomfort (comparing with extreme problems)				
No problems	-0.032	0.022	-1.416	0.159
Some problems	-0.022	0.021	-1.038	0.301
Self-care (comparing with extreme problems)				
No problems	0.034	0.037	0.919	0.36
Some problems	0.084	0.022	3.743	**<0.001**
Changes in daily habits (BDRS)	0.007	0.004	1.647	0.102
Changes in personality (BDRS)	0.015	0.005	3.176	**<0.05**
QoL-AD score	-0.01	0.003	-3.923	**<0.001**

PwD, Person with dementia. SD, standard deviation. QoL-AD: Quality of life in Alzheimer's Disease. BDRS: Blessed Domain Rating Scale. r2=0.65, Adjusted r2=0.57.

Additional file 5.1

-Informed consent of the participant and EQ-5D-3L (the same of additional file 4.1)
- Informal Caregiver Burden Assessment Questionnaire (QASCI)

Avaliação do impacto físico, emocional e social do papel de cuidador informal (QASCI)*

No quadro seguinte apresentamos uma lista de situações que outras pessoas, que prestam assistência a familiares doentes, consideraram importantes ou mais frequentes. Por favor indique referindo-se às últimas 4 semanas, a frequência com que as seguintes situações ocorreram consigo.

Nas últimas 4 semanas	Não/ Nunca	Rara-mente	Às vezes	Quase sempre	Sempre
Sobrecarga emocional					
1. Sente vontade de fugir da situação em que se encontra?	**1**	**2**	**3**	4	**5**
2. Considera que, tomar conta do seu familiar, é psicologicamente difícil?	**1**	**2**	**3**	4	**5**
3. Sente-se cansada(o) e esgotada(o) por estar a cuidar do seu familiar?	**1**	**2**	**3**	4	**5**
4. Entra em conflito consigo própria por estar a tomar conta do seu familiar?	**1**	**2**	**3**	4	**5**
Implicações na vida pessoal					
5. Pensa que o seu estado de saúde tem piorado por estar a cuidar do seu familiar?	**1**	**2**	**3**	4	**5**
6. Cuidar do seu familiar tem exigido um grande esforço físico?	**1**	**2**	**3**	4	**5**
7. Sente que perdeu o controlo da sua vida desde que o seu familiar adoeceu?	**1**	**2**	**3**	4	**5**
8. Os planos que tinha feito para esta fase da vida têm sido alterados em virtude de estar a tomar conta do seu familiar?	**1**	**2**	**3**	4	**5**
9. Acha que dedica demasiado tempo a cuidar do seu familiar e que o tempo é insuficiente para si?	**1**	**2**	**3**	4	**5**
10. Sente que a vida lhe pregou uma partida?	**1**	**2**	**3**	4	**5**
11. É difícil planear o futuro, dado que as necessidades do seu familiar não se podem prever (são imprevisíveis)?	**1**	**2**	**3**	4	**5**
12. Tomar conta do seu familiar dá-lhe a sensação de estar presa(o)?	**1**	**2**	**3**	4	**5**
13. Evita convidar amigos para sua casa, por causa dos problemas do seu familiar?	**1**	**2**	**3**	4	**5**
14. A sua vida social, (p. ex., férias, conviver com familiares e amigos) tem sido prejudicada por estar a cuidar do seu familiar ?	**1**	**2**	**3**	4	**5**
15. Sente-se só e isolada(o) por estar a cuidar do seu familiar?	**1**	**2**	**3**	4	**5**

Sobrecarga financeira					
16. Tem sentido dificuldades económicas por estar a tomar conta do seu familiar?	1	2	3	4	5
17. Sente que o seu futuro económico é incerto, por estar a cuidar do seu familiar?	1	2	3	4	5
Reacções a exigências					
18. Já se sentiu ofendida(o) e zangada(o) com o comportamento do seu familiar?	1	2	3	4	5
19. Já se sentiu embaraçada(o) com o comportamento do seu familiar?	1	2	3	4	5
20. Sente que o seu familiar a(o) solicita demasiado para situações desnecessárias?	1	2	3	4	5
21. Sente-se manipulada(o) pelo seu familiar?	1	2	3	4	5
22. Sente que não tem tanta privacidade como gostaria, por estar a cuidar do seu familiar?	1	2	3	4	5
Mecanismo de eficácia e de controlo					
23. Consegue fazer a maioria das coisas de que necessita, apesar do tempo que gasta a tomar conta do seu familiar?	1	2	3	4	5
24. Sente-se com capacidade para continuar a tomar conta do seu familiar por muito mais tempo?	1	2	3	4	5
25. Considera que tem conhecimentos e experiência para cuidar do seu familiar?	1	2	3	4	5
Suporte familiar					
26. A família (que não vive consigo) reconhece o trabalho que tem, em cuidar do seu familiar?	1	2	3	4	5
27. Sente-se apoiada(o) pelos seus familiares?	1	2	3	4	5
Satisfação com o papel e com o familiar					
28. Sente-se bem por estar a tomar conta do seu familiar?	1	2	3	4	5
29. O seu familiar mostra gratidão pelo que está a fazer por ele?	1	2	3	4	5
30. Fica satisfeita(o), quando o seu familiar mostra agrado por pequenas coisas (como mimos)?	1	2	3	4	5
31. Sente-se mais próxima(o) do seu familiar por estar a cuidar dele?	1	2	3	4	5
32. Cuidar do seu familiar tem vindo a aumentar a sua auto-estima, fazendo-a(o) sentir-se uma pessoa especial, com mais valor?	1	2	3	4	5

* Martins, T; Ribeiro, JLP; Garrett, C (2003)