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The Influence of the Mediterranean Diet Adherence during Pregnancy on Maternal-Fetal Outcomes: a Systematic Review

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ABSTRACT

Introduction

The Mediterranean diet has been extensively researched. Although it has been proven to prevent diseases and improve overall health, its' adherence is decreasing. With fast food becoming more available, traditions are put aside in the name of convenience.

Pregnancy has been broadly investigated and, due to the risk of complications, it must be meticulously monitored. Adjustments to the diet can have significant consequences. During pregnancy, women are motivated to adhere to healthy habits and dietary changes can be made to reduce negative outcomes.

Objective

This systematic review was conducted to analyze the impact of adherence to the Mediterranean Diet during pregnancy in maternal-fetal outcomes.

This theme has caused interest in the scientific community and it is fundamental to identify robust evidence supporting it and future challenges that can emerge from it.

Methodology

A selective literature review was carried out using PubMed after the identification of relevant studies. Only studies in English and published between 2010 and 2021 were evaluated. The following terms were selected, in addition to alternative terms: "Mediterranean Diet"; "Pregnancy"; "Obstetric Labor"; "Postnatal Care" and "Perinatal Care".

A PICO question was applied: Does adherence to the Mediterranean Diet during pregnancy affect maternal-fetal outcomes?

Results

A total of eight studies were included. All investigated the relationship between the Mediterranean Diet and maternal-fetal outcomes.

Increased Mediterranean Diet adherence during pregnancy resulted in reduced prevalence of Gestational Diabetes, excessive Gestational Weight Gain, Necrotizing Enterocolitis, and Bronchopulmonary Dysplasia. Although there was some evidence supporting its positive effect on other maternal-fetal complications, it was not as robust as for the previously referred outcomes.

Conclusion

This Systematic Review concluded that the Mediterranean Diet has a positive impact on the incidence of some maternal-fetal outcomes. However, more research needs to be made to prove its definite impact.

Keywords: Mediterranean Diet, Pregnancy, Obstetric Labor, Postnatal Care, Perinatal Care.

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RESUMO

Introdução

A Dieta Mediterrânica tem sido extensamente alvo de investigação. Embora pareça ser evidente que previne doenças e melhora a saúde, a adesão a este padrão alimentar tem vindo a diminuir. Com a oferta alimentar do tipo *fast-food* cada vez mais disponível, as tradições vão desaparecendo em detrimento da conveniência.

O período da gravidez encontra-se amplamente estudado e, devido ao risco de complicações, deve ser cuidadosamente monitorizado. Alterações favoráveis ou desfavoráveis na dieta podem ter consequências significativas ao longo deste período. A mulher grávida encontra-se motivada para aderir a hábitos saudáveis, pelo que mudanças alimentares podem ser feitas para reduzir complicações.

Objectivos

Esta revisão sistemática teve como objetivo avaliar o impacto da adesão à Dieta Mediterrânica durante a gravidez nas complicações materno-fetais.

Este tema tem causado interesse na comunidade científica e é fundamental identificar evidência robusta que o suporte.

Metodologia

A partir da questão de investigação: *Terá a adesão à Dieta Mediterrânica durante a gravidez impacto nas complicações materno-fetais?*, foi desenvolvida uma revisão seletiva da literatura usando a PubMed. Para a pesquisa foram selecionados os seguintes termos, incluindo termos alternativos: “Mediterranean Diet”; “Pregnancy”; “Obstetric Labor”; “Postnatal Care” and “Perinatal Care”. Foram selecionados estudos em inglês e publicados entre 2010 e 2021 para análise detalhada.

Resultados

Um total de oito estudos foram incluídos. Todos investigavam a relação entre a dieta Mediterrânica e complicações materno-fetais.

Maior adesão durante a gravidez resultou numa redução da prevalência de Diabetes Gestacional, ganho excessivo de peso gestacional, enterocolite necrotizante, e displasia broncopulmonar. Ainda que houvesse evidência que apoiasse os seus efeitos positivos noutras complicações, não foi tão robusta como a que apoiou as referidas anteriormente.

Conclusão

Esta revisão sistemática concluiu que a Dieta Mediterrânica terá impacto positivo na incidência de algumas complicações materno-fetais. No entanto, mais investigação é necessária para evidenciar a dimensão do seu impacto.

Palavras-chave: Dieta Mediterrânica, Gravidez, Parto Obstétrico, Cuidados Pós-natais, Cuidados Perinatais

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LIST OF ABBREVIATIONS

MedDiet – Mediterranean Diet

UNESCO – United Nations Educational, Scientific, and Cultural Organization

PREDIMED – Prevención con dieta mediterrânea

FFQ – Food Frequency Questionnaires

PE – Pre-Eclampsia

NEC – Necrotizing Enterocolitis

GD – Gestational Diabetes

BPD – Bronchopulmonary Dysplasia

mg/dL – Milligram per Deciliter

OGTT – Oral Glucose Tolerance Test

g – Grams

mmHg – Millimeters of Mercury

mm^3 – Cubit Millimeter

BMI – Body Mass Index

IOM – Institute of Medicine

GWG – Gestational Weight Gain

bpm – Beats Per Minute

GA – Gestational Age

SGA – Small for Gestational Age

LGA – Large for Gestational Age

NSAIDs – Non-Steroidal Anti-Inflammatory Drugs

GINA – Global Initiative for Asthma

DGS – Direção Geral de Saúde

RCT – Randomized Controlled Trials

UK – United Kingdom

1. INTRODUCTION

The Mediterranean Diet (MedDiet) has been around since 1960 and it is based on the eating pattern of the habitants from the countries around the Mediterranean Sea (Martínez-González & Sánchez-Villegas, 2004). This way of eating considers olive oil as an important source of dietary fats, and it encourages the consumption of plant-based foods, whole grains, seeds, and nuts. Even though it is a diet, it involves more than food. The MedDiet considers physical activity, socialization, seasonality, rest, among others (Bach-Faig et al., 2011). Its' main goal is to promote a healthy and balanced lifestyle for the people adhering to it.

The MedDiet has been linked to a lower risk of many diseases as well as a lower mortality rate (Franquesa et al., 2019; Kromhout et al., 1995; Simopoulos, 2001). Even though it has many benefits, it is becoming less and less popular in the Mediterranean countries due to the "westernization" of eating patterns (Vareiro et al., n.d.). More fast food is being consumed and consumption of fresh fruits, vegetables, olive oil, and nuts has been decreasing exponentially (Pinho et al., 2016).

Pregnancy is an important phase in a woman's life, and it has been extensively researched so far. Not only pregnancy but also the preconception and postnatal periods need to be closely monitored to prevent complications for both the mother and the child (Casanova et al., n.d.; Mendes da Graça, 2018). Such complications can have a tremendous impact on maternal-fetal morbidity and mortality. During this time, the mother's nutritional needs are increased, and diet plays a big part in making sure that the caloric and nutritional requirements are met. Nevertheless, any changes to dietary patterns during pregnancy can have a significant impact and may be a preventive factor for multiple diseases.

1.1. Objectives

The main goal of this thesis is to determine if the adoption of a MedDiet during pregnancy has any influence on maternal-fetal outcomes. Since health complications during pregnancy are very common, a diet that has proven to reduce the incidence of some diseases may have a globally positive balance in maternal-fetal complications. This

theme has caused interest in the scientific community, intending to evaluate whether there is strong evidence and identify the strengths and challenges of future research on this topic.

Since there have been a few studies in which adherence during pregnancy to this eating pattern was studied, a Systematic Review of the existing studies was conducted, to draw some conclusions regarding the potential benefits and downsides of this eating pattern in pregnancy, as well as extrapolating future recommendations for pregnant women to follow.

1.2. Main Structure

A concept review will be presented first, to understand the concepts of MedDiet and Pregnancy, as well as the relation between them. Secondly, the methods used to conduct this Systematic Review will be demonstrated, in addition to the tools used to evaluate the quality of the studies included.

Subsequently, the selected studies will be displayed with the process that went into this selection. Results from the selected studies will be presented with the respective studies' quality evaluation.

Finally, a discussion of said results will be delineated along with this Systematic Review's conclusions and future works.

2. CONCEPT REVIEW

2.1 Mediterranean Diet

The MedDiet refers to an eating pattern that incorporates the habits of the inhabitants from countries surrounding the Mediterranean Sea (Martínez-González & Sánchez-Villegas, 2004). It was first defined in the ’60s by Ancel Keys as a diet low in saturated fats and high in vegetable oils.

Although this diet has been around since 1960, it has gained popularity more recently, specifically in 1995 with the creation of the pyramid representation of it (Willett et al., 1995). In 2013, it was added to the List of Intangible Cultural Heritage of Humanity by the United Nations Educational, Scientific, and Cultural Organization (UNESCO) (*Mediterranean Diet - Intangible Heritage - Culture Sector - UNESCO*, n.d.). Having this in mind, it should be protected and encouraged in different areas such as culture, tourism, public health, agriculture, politics, and economic development. UNESCO also considers that Women are detrimental in the preservation of the MedDiet as they are responsible for passing the knowledge about it from generation to generation.

Even though the MedDiet has suffered many changes since it was first defined, its foundation consists of plant-based foods, such as vegetables, fruits, legumes, nuts, whole grains, and seeds. Extra virgin olive oil also plays an important role in this diet, as it is the prime source of unsaturated fats. It includes moderate to high consumption of dairy, white meat, eggs, fish, and seafood, whereas red meat only is eaten rarely (*What Is a Mediterranean Diet? - NHS*, n.d.). Regarding alcohol, the MedDiet includes a moderate intake of red wine during meals and respecting social beliefs. Despite this, water should be the main beverage during meals and the use of salt should be reduced, substituting it for aromatic herbs (Annexe I) (Bach-Faig et al., 2011).

To address adherence to this eating pattern, the PREDIMED questionnaire can be used (Martínez-González et al., 2012):

1. Do you use olive oil as the main culinary fat? If yes, 1 point.
2. How much olive oil do you consume in each day (including the oil used for frying, salads, out-of-house meals, etc)? If ≥4 tablespoons, 1 point.

3. How many vegetable servings (1 serving: 200 g) do you consume per day? If ≥2 servings, 1 point.

4. How many fruit units (including natural fruit juices) do you consume per day? If ≥3 units, 1 point.

5. How many servings (1 serving: 100–150 g) of red meat, hamburger, or meat products (ham, sausage, etc.) do you consume per day? If <1 serving, 1 point.

6. How many servings of butter, margarine, or cream do you consume per day? (1 serving: 12 g). If <1 serving, 1 point.

7. How many sweet or carbonated beverages do you drink per day? If <1 beverage, 1 point.

8. How much wine do you drink per week? If ≥7 glasses, 1 point.

9. How many servings (1 serving: 150 g) of legumes do you consume per week? If ≥3 servings, 1 point.

10. How many servings (1 serving 100–150 g of fish or 4–5 units or 200 g of shellfish) of fish or shellfish do you consume per week? If ≥3 servings, 1 point.

11. How many times per week do you consume commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits, or custard? If <3 times, 1 point.

12. How many servings (1 serving 30 g) of nuts (including peanuts) do you consume per week? If ≥3 servings, 1 point.

13. Do you preferentially consume chicken, turkey, or rabbit meat instead of veal, pork, hamburger, or sausage? If yes, 1 point.

14. How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with sofrito (sauce made with tomato and onion, leek, or garlic and simmered with olive oil)? If ≥2 times, 1 point.

This questionnaire is rated from 0 to 14 points. Even though alcohol and juices are included in this questionnaire, usually their consumption is discouraged during pregnancy. The score is usually defined by each study, having in mind the rules used.

The higher the number of points in this questionnaire, the higher the adherence to this eating pattern. A score of 7 or fewer points represents low adherence to the MedDiet. Moreover, high adherence to this diet is defined by a score of 10 or more points. There is also an inverse correlation between the number of points and the value for fasting glucose, total/HDL cholesterol ratio, triglycerides, and risk of coronary artery disease in 10 years (Martínez-González et al., 2012).

Food Frequency Questionnaires (FFQ) can also be used to evaluate adherence to the MedDiet (Aoun et al., 2019). However, FFQ need to be specific to each country to be validated for the population in cause.

Along with the food consumption recommendations, the MedDiet gained a lot of attention with the cultural and lifestyle elements included in it. These elements consist of the following topics (Bach-Faig et al., 2011):

- Moderation - The proportions of food intake should be based on the energy requirements that are individual and reflective of habits.
- Socialization - Although the nutritional aspect of each meal is crucial, we also need to look at the cultural and social cost of it: traditions passed from generation to generation, time allocated to meals, etc. Being around family and friends while sharing a meal gives a sense of community, which gives pleasure to the people participating in it. All of this may affect eating behaviours positively, leading to a healthier relationship with food.
- Cultural activities - Cooking and eating have a place in daily life, as well as in celebrations specific to every culture. Having this in mind, not only the meal is important but also the context in which it happens.
- Physical activity - A daily target of 30 minutes of moderate activity is a necessary addition to the MedDiet, as it has plenty of health benefits. Walking, doing chores, using the stairs, etc can all be included in moderate exercise. It is, however, recommended that physical activity is practised in the presence of others, making it more pleasant and helping to fortify relationships.
- Adequate rest - Having a restful sleep during the night is crucial to be as close as possible to a healthy lifestyle. A short nap after lunch is also traditional in the

Mediterranean countries and it has been scientifically proven to be beneficial (Ficca et al., 2010).

- Seasonality - The MedDiet considers it is preferable to consume foods that are fresh and seasonal that have been minimally processed.
- Local products - In the interest of making these eating pattern as sustainable as possible, local and traditional products should be chosen. It is a way to preserve the environment and to improve the local economy.

Portugal's national MedDiet recommendations are comparable to the previously mentioned ones (Pinho et al., 2016). Seasonal local foods are preferred in addition to healthy cooking techniques. Meals are encouraged to be shared with loved ones and exercise should be promoted. Regarding which foods to eat, recommendations are equal to the ones exposed in the MedDiet Pyramid. Emphasis is given to the exclusion of alcohol during pregnancy and breastfeeding. Nonetheless, the National Health Board created a MedDiet Wheel (Annexe II). The ten MedDiet principles in Portugal are the following (Martínez-González et al., 2012):

1. Frugality and simple cooking.
2. Elevated consumption of plant-based products.
3. Consumption of vegetable products that are fresh, seasonal, and locally produced.
4. Olive oil as the main source of fat.
5. Moderate consumption of dairy products.
6. Aromatic herbs for seasoning instead of the use of salt.
7. Frequent consumption of fish and low consumption of red meat.
8. Low to moderate consumption of wine and only during the main meals.
9. Water as the main beverage throughout the day.
10. Conviviality around the table.

This way of eating has been associated with a lower risk of coronary heart disease, ischemic stroke, and cancer mortality (Franquesa et al., 2019; Kromhout et al., 1995;

Rees et al., 2019; Simopoulos, 2001). It has also been linked to a reduced likelihood of developing type 2 diabetes, metabolic syndrome, neurodegenerative diseases, such as Parkinson's Disease and Alzheimer's Disease, and inflammatory diseases (Azzini & Maiani, n.d.; Bach-Faig et al., 2011). Regarding weight, the MedDiet has been shown to improve health, prevent weight gain, and lower mortality rates in the obese and overweight population (Franquesa et al., 2019).

Another curious benefit of MedDiet involves Multiple Sclerosis. A pilot study showed that a slightly modified version of this eating pattern was beneficial in reducing fatigue and disability among patients with Multiple Sclerosis, as well as lowering the impact of its symptoms (Katz Sand et al., 2019).

Concerning allergic diseases, the MedDiet can work as a protective factor for atopy and asthma in children (Chatzi & Kogevinas, 2022).

Even though, at first sight, there are not any relevant downsides to the MedDiet, this eating pattern is becoming less frequent (Vareiro et al., n.d.). With the rise in the availability of fast food, as well as other "western diets", Mediterranean countries have been losing their eating habits: legumes, wine, olive oil, and fresh fruit consumption has been replaced by the consumption of animal fats, sweets, and processed foods. There has been an increase in obesity and cardiovascular diseases in these countries because of the loss of this way of eating. To revert this trend, changes in dietary patterns and lifestyle habits must happen before the repercussions become inevitable.

2.2. Pregnancy

Pregnancy refers to the period during which a fetus develops in a woman's uterus. It is usually 40 weeks long and it is divided into three trimesters: the first trimester happens from week 1 to week 12, the second trimester takes place from week 13 to week 28, and the third trimester takes place from week 29 to week 40. Throughout pregnancy it is crucial to evaluate the wellbeing of both the mother and the fetus, resourcing to regular blood testing and ultrasounds (Casanova et al., n.d.).

2.2.1. From Conception to the Post-natal Period

Although pregnancy usually only refers to 40 weeks (from fecundation to delivery), it is important to have in mind the preconception and postnatal periods. Pre-pregnancy care is fundamental to promoting a healthy pregnancy. Some of the actions that can take place in a pre-pregnancy appointment include (*About Pregnancy | NICHD - Eunice Kennedy Shriver National Institute of Child Health and Human Development*, n.d.):

- Increasing folic acid consumption to reduce the risk of the fetus developing neural tube defects.
- Control any medical problems that may be present.
- Offer strategies for smoking cessation, as well as alcohol and drugs consumption.
- Update all their immunizations, review all medication that is currently being used and discontinue the ones that are teratogenic.
- Provide resources to improve mental health.
- Gather a full medical history, as well as family history.
- Create a plan for the rest of their reproductive years.

Regarding postnatal care, it is important to have in mind all the changes that happen to the woman's body and mind after delivery. During the postpartum consult, six weeks after delivery, it is advised to go through all the following topics (*Department of Maternal, Newborn, Child and Adolescent Health*, 2013; *Recovering from Birth | Office on Women's Health*, n.d.):

- Contraceptive method to be used in the following months, as there should be a period of 18 to 23 months before conceiving again. It is also an opportune time to address the importance of protecting against sexually transmitted diseases.
- Evaluate breastfeeding, breast care, and nutritional status. Breastfeeding advantages are vast, and they should be given to all mothers. Some of the advantages include a stronger bond between mother and baby, a lower risk of breast cancer, a lower risk of diabetes and postpartum depression, better cognitive function, and a lower prevalence of infections in newborns.

- Importance should be given to sleep, and physical work should be avoided.
- Family dynamics and social support must also be addressed, for the mother not to feel overwhelmed and with her mental health at risk.
- The home environment is important as well, as a warm, well-ventilated, and clean space is better for both the mother and the baby. Hand washing is also detrimental in preventing infections.
- Substance abuse should be documented and resources for cessation of such substances should be given.
- A complete physical exam is crucial, especially taking into notice any blood losses, uterine involution, and issues with the pelvic floor.
- Sexual activity should be avoided until the healing of perineal wounds or until the scar of the cesarean delivery is fully healed.
- Discuss postpartum bleeding and lochia. Give alarm signs that mothers should be attentive to so that they can seek help urgently.
- "Baby blues" are common among women. However, it is important to differentiate between “Baby blues” and postpartum depression, as the latter can be present in 1 in 8 women (Casanova et al., n.d.). While “Baby blues” is an auto-limited condition, usually lasting around 2 weeks and consisting of sadness, anxiety, and anger, postpartum depression symptoms are more severe and extended in time, causing interference in daily activities. Risk factors for postpartum depression consist of low family support, low social-economical level, low scholarship, history of domestic violence and depression, maternal anxiety, and smoking.
- The new mother ought to be advised on a healthy and nutritious diet, as well as on the importance of drinking plenty of water, especially for women that are breastfeeding.

2.2.2. Maternal-Fetal Complications

During these 3 trimesters, it is crucial to monitor not only the mother but also the fetus, to lower the chances of a poor outcome. There are a lot of obstetrical complications that can occur such as abortion, pre-eclampsia (PE), eclampsia, preterm labour, hypertension, depression, infections, asthma, necrotizing enterocolitis (NEC), fetal growth restrictions, gestational diabetes (GD), bronchopulmonary dysplasia (BPD), urinary tract infections, excessive or insufficient weight gain, among others (Mendes da Graça, 2018). All the previous complications can occur in approximately 15% of pregnancies. However, reoccurrence of these poor outcomes is more common if a previous pregnancy was affected by them (Thiele et al., 2019). Some of these obstetric complications are now described:

1. Gestational Diabetes

Gestational Diabetes (GD) refers to glucose intolerance that develops during pregnancy. Usually, it disappears after labour, even though glucose intolerance is more common in this population in subsequent years. GD's prevalence is increasing because of an increase in obesity in the general population. Even though there are some known risk factors for it (GD in a previous pregnancy, age, ethnicity, repeated spontaneous abortions, obesity, etc), most of the patients that are diagnosed with GD do not present any risk factors. There are a few hormones during pregnancy that interfere with glucose metabolisms such as human placental lactogen, estrogen, progesterone, and insulinase. In the first trimester, fasting glucose is measured and, if is between 92 mg/dL and 126 mg/dL, the diagnosis of GD is made. If it is over 126 mg/dL, it corresponds to pre-gestational Diabetes. If the value is under 92 mg/dL, an oral glucose tolerance test (OGTT) must be performed. GD is diagnosed if the values of OGTT are: over 92 mg/dL fasting, over 180 mg/dL at 1 hour or over 153 mg/dL at 2 hours. After the diagnosis is made, this pregnancy needs closer vigilance, as it is associated with many complications, such as congenital anomalies, spontaneous abortion, macrosomia, intrauterine growth restriction, polyhydramnios, neonatal hypoglycemia, pre-eclampsia, placental abruption, and preterm labour, among others. For the management of these patients, it is crucial for the mother to self-monitor her glucose by four to six measurements per day. Adoption of a healthy diet and physical activity is also the first non-pharmacological

option of treatment. As for pharmacological treatment, insulin is the best option for pregnant women, even though metformin can also be used. Regarding delivery, labour should be performed vaginally. However, if the estimated fetal weight is over 4500 g, a caesarean section is the best option. If there are no complications, labour should happen until 40 weeks and 6 days. On the other hand, if there are complications or if metabolic control is impaired, it should happen until 39 weeks and 6 days. In both cases, if spontaneous labour does not occur, it must be induced. During postpartum, usually, insulin is not required. Nonetheless, OGTT must be repeated at 6 to 8 weeks postpartum (Casanova et al., n.d.; Mendes da Graça, 2018).

2. Pregnancy-induced Hypertension

Pregnancy-induced Hypertension stands for hypertension that develops after 20 weeks of gestation, in the absence of proteinuria. Hypertension is diagnosed if there is a systolic pressure over 140 mmHg or if the diastolic pressure is over 90 mmHg. Proteinuria is defined as urinary excretion of at least 0.3 g of protein in a 24-hour urine sample. The first line of treatment is always dietary changes and physical activity. If systolic blood pressure is higher than 160 mmHg or if diastolic blood pressure is over 110 mmHg, oral labetalol or nifedipine can be used. During the postpartum period, blood pressure, in most cases, normalizes. However, if that is not the case, chronic hypertension is diagnosed (Casanova et al., n.d.; Mendes da Graça, 2018).

3. Pre-Eclampsia

Pre-Eclampsia (PE) corresponds to the development of hypertension with proteinuria after 20 weeks of gestation. Some known risk factors for PE include nulliparity, maternal age over 40 years, PE in a previous pregnancy, chronic hypertension, obesity, antiphospholipid syndrome, pregestational diabetes, among others. PE is considered severe if systolic blood pressure is over 160 mmHg or diastolic blood pressure is over 110 mmHg on 2 occasions; Progressive renal failure; Headaches or scotomata; Hepatic dysfunction; Thrombocytopenia (platelet count under 100000/mm^3) and Pulmonary oedema. Usually, regardless of gestational age, severe PE is an indication for delivery. If PE is accompanied by convulsions, the diagnosis of Eclampsia is made, and the problem is resolved with the administration of magnesium sulfate and delivery as soon as possible. The definitive treatment for PE is labour. If there are no severity criteria, fetal

and maternal monitoring must be performed regularly until the fetus reaches term at 37 weeks, with labour being induced by then. If severity criteria are present, after 34 weeks of gestation the decision is always labour induction. Before 34 weeks, the decision is made individually but, generally, if a very severe complication is present (such as placental abruption, pulmonary oedema, eclampsia, or disseminated intravascular coagulation), labour should be induced (Casanova et al., n.d.; Mendes da Graça, 2018).

4. Gestational Weight Gain

During pregnancy, it is expected that the woman gains weight. However, weight recommendations differ for women with different preconception Body Mass Index (BMI). The gestational weight gain (GWG) recommendations are demonstrated in Table 1.

Table 1 - Institute of Medicine (IOM) Pregnancy Weight Gain Recommendations (Moore Simas et al., 2013)

Pre-pregnancy BMI	**Total weight gain**	
	Range in kg	**Range in lbs**
Underweight (BMI < 18.5 kg/m^2)	12.5 – 18	28 - 40
Normal-weight (BMI 18.5 – 24.9 kg/m^2)	11.5 – 16	25 - 35
Overweight (BMI 25.0 – 29.9 kg/m^2)	7 – 11.5	15 - 25
Obese (BMI > 30 kg/m^2)	5 - 9	11 - 20

Excessive weight gain happens when the pregnant woman gains more weight than the recommended amount for her BMI. Insufficient weight gain refers to when the pregnant woman is unable to gain the recommended weight. Even though these are general guidelines, if there is a considerable deviation from the trend, nutritional evaluation might be needed (Casanova et al., n.d.; Mendes da Graça, 2018).

5. Type of Delivery

The delivery of the baby is an important moment for the mother. There are a few different types of delivery. The delivery can occur vaginally or by cesarean delivery. The preferred mode of delivery is vaginal delivery, as it is safer due to having a lower risk of haemorrhage and infection. Cesarean delivery is only used when there is a contra-indication for vaginal delivery. Some indications for cesarean delivery include placenta previa haemorrhage, abruptio placentae, and uterine rupture. After the delivery, the

newborn is given an Apgar score. The Apgar scoring system is usually used to have an objective evaluation of the newborn condition (Table 2). The Apgar score evaluates 5 signs in the newborn: colour, heart rate, reflex activity response to stimulation, muscle tone, and respiration. All these signs are given a score of either zero, one, or two points. Scores are given at 1 minute, 5 minutes, and 10 minutes. The 5-minute score, when used on term or late preterm infants, if it is between 7 and 10, is a reassuring score. If it is between 4 and 6, it represents an infant that is mild to moderately depressed. If it is under 4, the infant is severely depressed, and more measures need to be applied (Casanova et al., n.d.; Mendes da Graça, 2018).

Table 2 - Apgar Scoring System (Casanova et al., n.d.)

Sign	0	1	2
Colour	Blue or Pale	Acrocyanotic	Completely Pink
Heart Rate	Absent	<100 bpm	>100 bpm
Reflex Activity Response to Stimulation	No Response	Grimace	Cry or Active Withdrawal
Muscle Tone	Limp	Some Flexion	Active Motion
Respiration	Absent	Weak Cry: Hypoventilation	Good, Crying

Bpm – Beats per minute

6. Gestational Age

Gestational Age (GA) refers to the number of weeks, from the first day of the mother's last menstrual cycle to the current date, and it helps define how far along the pregnancy is. The normal GA for delivery is usually between 38 and 42 weeks. Premature babies refer to infants born before week 37, whereas if the baby is born after week 42, it is postmature.

Preterm birth can be either spontaneous or induced. The main risk factors for preterm birth include multifetal gestations and a history of preterm birth in a previous gestation. Some signs and symptoms of preterm labour include cramps, backache, pelvic pressure, change in vaginal discharge, and uterine contractions. Since preterm labour is rarely preventable, it is important to recognize it as soon as possible. Transvaginal ultrasound,

laboratory tests, and amniocentesis are some of the tests that can be made to diagnose it earlier. Preterm birth has a tremendous impact on perinatal morbidity and mortality, and, for this reason, it is mandatory to do everything possible to delay delivery until term. If that is not possible, one must do the best to attain fetal maturity. Tocolytics and corticosteroids are the two drugs that must be given in the chance of preterm delivery.

Regarding post-term birth, it is mostly caused by inaccurate estimation of GA, irregular ovulation, fetal adrenal hypoplasia, anencephaly, and extrauterine pregnancy, among others. It is usual for post-term pregnancy to reoccur. Other risk factors for post-term birth are maternal obesity and nulliparity. Post-term labour is associated with many conditions that can be harmful to the mother and for the baby, such as Macrosomia, shoulder dystocia, meconium aspiration syndrome, and oligohydramnios. As for management, labour can be induced, and antepartum fetal surveillance should be maintained. It is important to prevent the pregnancy from reaching 42 weeks. After 42 weeks, labour must be induced due to the exponential increase in morbidity and mortality for both parties (Casanova et al., n.d.; Mendes da Graça, 2018).

7. Birth Weight

The weight of the newborn is usually referred to in terms of percentiles: if the baby is under percentile 10, it is considered Small for Gestational Age (SGA); if it is over percentile 90, it is considered Large for Gestational Age (LGA). SGA newborns are at risk for increased morbidity and mortality. Some of the complications associated with SGA newborns include a low Apgar score, polycythemia, hypoglycemia, respiratory distress, sepsis, and neonatal death. Nevertheless, LGA newborns are also at risk of developing complications such as obesity, low Apgar score, shoulder dystocia, stillbirth, and prematurity. LGA are also linked to an increased risk of postpartum haemorrhage and lacerations in the birth canal. Any changes in fetal growth can have severe implications that last their whole lives, for example, obesity, cardiovascular diseases, and insulin resistance (Guerrero-Fdez et al., 2017).

8. Asthma

Notwithstanding asthma is a highly prevalent chronic disease and its cause is still unknown and misunderstood. It is characterized by 3 factors: airflow limitation, airway

hyper-responsiveness, and bronchial inflammation. Regarding aetiology, some of the causes and triggers of asthma include drugs (especially Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)), genetic factors, cold air, exercise, emotions, viruses, environmental exposures to allergens, pollution, among others. Diet has also been shown to play a part in asthma: an increase in the consumption of fresh fruit and vegetables has been associated with a lower risk of asthma. The symptoms of asthma are wheezing, shortness of breath, and cough. Although there is no perfect test for asthma, there are a few tests that can aid with diagnosis: peak expiratory flow rate, spirometry (showing reversibility after inhalation of a bronchodilator), exercise tests, histamine bronchial provocation test, chest X-ray, among others. Regarding treatment, it is crucial to control exposure to triggering factors and a few drugs can be used for the management of asthma, having in mind the severity of asthma.

9. Necrotizing Enterocolitis

Necrotizing Enterocolitis (NEC) is a neonatal abdominal emergency, and it is characterized by intestinal inflammation, with areas of intestinal necrosis. It is a multisystemic disease and 25% of newborns with it can develop conditions such as microcephaly and neurodevelopment delay. The symptoms are varied, going from systemic symptoms to gastrointestinal symptoms. The lower the GA of the newborn, the higher the prevalence of necrotizing enterocolitis. Regarding treatment, it should be started as soon as possible, and it must be multidisciplinary. Large spectrum antibiotics are used for 10 to 14 days. Indications for surgery include intestinal perforation, massive intestinal necrosis, and progressive clinical deterioration. This condition can be prevented with breastfeeding, small quantity feeding, and probiotics (Guerrero-Fdez et al., 2017).

10. Bronchopulmonary Dysplasia

Bronchopulmonary Dysplasia (BPD) is an important cause of preterm newborn mobility. It mainly affects low weight newborns and its incidence is inversely proportional to the GA. Even though its cause is multifactorial, it has been proven to be affected by oxygen toxicity, barotrauma, volutrauma, hyaline membrane diseases, ductus arteriosus persistency and genetic factors. BPD, despite having an array of clinical presentations, is usually characterized by respiratory distress and cardiac insufficiency. The diagnosis is

made having in mind the GA and the needs for oxygen therapy. Treatment is complex: respiratory support, nutritional support, and hemodynamic control are fundamental. As for prevention, mechanical ventilation should be shortened, and non-invasive ventilation is preferred. Treatment of infections and the treatment of ductus arteriosus persistency is important, as well as adequate nutritional support and avoidance of excessive fluids. Caffeine in the first 24 to 48 hours of life has also been proven to be beneficial (Guerrero-Fdez et al., 2017).

2.2.3. Eating Habits During Pregnancy

During pregnancy, there is an increase in energy and nutritional requirements since all the nutrition to the fetus must come from the mother's caloric intake. If the mother is undernourished, the occurrence of maternal-fetal outcomes is potentialized. There is also a nutrient reserve in the fetus that will be used up in the first few years of life, where growth is accelerated. Despite the need for a higher consumption of calories and nutrients, it is crucial that the mother has a nutritionally adequate food intake. The mother's eating habits will also help to establish her child's eating preferences (Raymond & Morrow, n.d.).

Current nutritional guidelines for pregnant women in Portugal have been given by Portugal's National Health Board (*Alimentação e Nutrição Na Gravidez*, n.d.). It is recommended that pregnant women increase their daily caloric intake, especially during the second and third trimesters of pregnancy. Regarding macronutrients, protein intake should be higher since it is essential for tissue synthesis. Animal sources of protein are considered to have a higher nutritional quality

It is then of the utmost importance to inform the mother of the early impact that her food choices during pregnancy will have on her child.

Furthermore, pregnancy is a great period for women to change their habits due to the newly acquired motivation of wanting to do what is best for the child. With that in mind, it can be used to implement better habits and to decrease harmful ones like smoking and drinking.

2.3. Main Discussion

Women throughout their whole life should adhere to a balanced and healthy diet due to the many benefits that are associated with a healthy lifestyle (Li et al., 2020). However, during pregnancy and the preconception and postpartum periods, there needs to be increased precaution with adopted lifestyle and diet because it is a critical time in the development of the child. Any changes to dietary patterns will have an impact on the fetus but also on the mother. Diet will have consequences on all the maternal-fetal outcomes that are associated with pregnancy. Moreover, it can aid in preventing complications that can be extremely detrimental to both the fetus and the mother (Casanova et al., n.d.; Mendes da Graça, 2018).

During pregnancy, women, especially primigravid, have a lot of questions since they want to know what is best for their baby. Current guidelines for pregnant women differ from country to country and they are not very specific on what constitutes the best diet for most women. It would be in the best interest if there was a general guideline for the average population (Tsakiridis et al., 2020).

Moreover, pregnancy is linked to many complications that can put not only the mother's but also the child's life at risk. Since the MedDiet has often been linked with lower risks of some diseases and with a lower mortality rate, it may be a beneficial diet to implement during pregnancy to reduce the incidence of said complications (Franquesa et al., 2019; Kromhout et al., 1995; Rees et al., 2019; Simopoulos, 2001).

3. METHODOLOGY

3.1. Selection Criteria

To define the investigation question, the inclusion criteria, and the exclusion criteria, a PICO question was defined: In pregnant women, does a high adherence to the Mediterranean Diet, compared to other eating patterns, lower the risk of maternal-fetal outcomes? The specific components of the PICO question are displayed in the Table 3.

Table 3 – PICO Question

Population	Pregnant women
Intervention	MedDiet
Comparison	Other eating pattern
Outcome	GD, PE, Pregnancy-induced Hypertension, GWG, GA, Birth Weight, Type of Delivery, Necrotizing Enterocolitis, Bronchopulmonary Dysplasia, Asthma

MedDiet – Mediterranean Diet; GD – Gestational Diabetes; PE – Pre-Eclampsia; GWG – Gestational Weight Gain; GA – Gestational Age

With this question in mind, the inclusion criteria consisted of studies that accessed adherence to the MedDiet, studies whose targeted population was limited to pregnant women, studies in Humans, Observational and Clinical studies, studies published between 2010 and 2021, studies written in English or Portuguese, and whose full version was freely available.

3.2. Research Methods

There was a time limit for the studies to restrict the results to the most up-to-date information about the topic. Studies written between 2010 and 2021 were included in the systematic review.

Regarding language, only studies written in English and Portuguese were considered. A selective literature review was carried out using PubMed as a database.

The key-word combination used were “Mediterranean Diet”, “Pregnancy”, “Obstetric Labor”, “Postnatal Care”, “Perinatal Care”, "Gestation", "Expecting", "Parturient", "Labour", "Gravidity", "Parturiency", "Maternity", "Gravid", "Pregnant", "Partum", "Delivery", “Labor”, "Postpartum", "Postnatal", "Perinatal", "Intrapartum", "Puerperium", "Childbirth", "Birth", "Giving Birth", "Parturition". MeSH terms were also used and consisted of "Diet, Mediterranean”, "Pregnancy", "Labor, Obstetric", “Gravidity", "Pregnant Women", "Delivery, Obstetric", "Postpartum Period", "Postnatal Care", "Perinatal Care", and "Parturition". Boolean operators “AND” and “OR” were used to combine and associate these different terms.

3.3. Study Selection

Both the titles and abstracts of each study were carefully analysed, having in mind the inclusion criteria previously mentioned. The full text of all studies was obtained and later they were evaluated to identify all the relevant ones.

3.4. Data Collection Procedure

The collection of the data included in the studies had in mind the title of the study, the date of publication, the sample’s characteristics, the diet followed, the outcome from the inclusion of the MedDiet, the results available, the type of results (theoretical or practical) and the conclusions of the study.

3.5. Quality Evaluation

To evaluate the quality of each study, an adapted EPHPP Quality Assessment Tool (Annexe III) was used.

4. RESULTS

4.1. Selected Works

The first sample consisted of 26 studies. After reading the titles and abstracts of these studies, some were excluded for not checking the inclusion criteria. Three were excluded from the sample due to not addressing pregnant women. Two other were excluded due to not addressing the MedDiet. Four studies were excluded due to not having published results at the date of writing this systematic review. Therefore, 17 studies were selected as potential candidates for meeting the requirements previously mentioned. Of these 17 studies, 9 were excluded from the sample selection after their full analysis. One was excluded due to only addressing the recruitment process for the study. Five were excluded since the implementation of the MedDiet did not occur during pregnancy. Three other studies were excluded from the selection because they consisted of a sub-analysis of other studies that were already included in the sample (Figure 1).

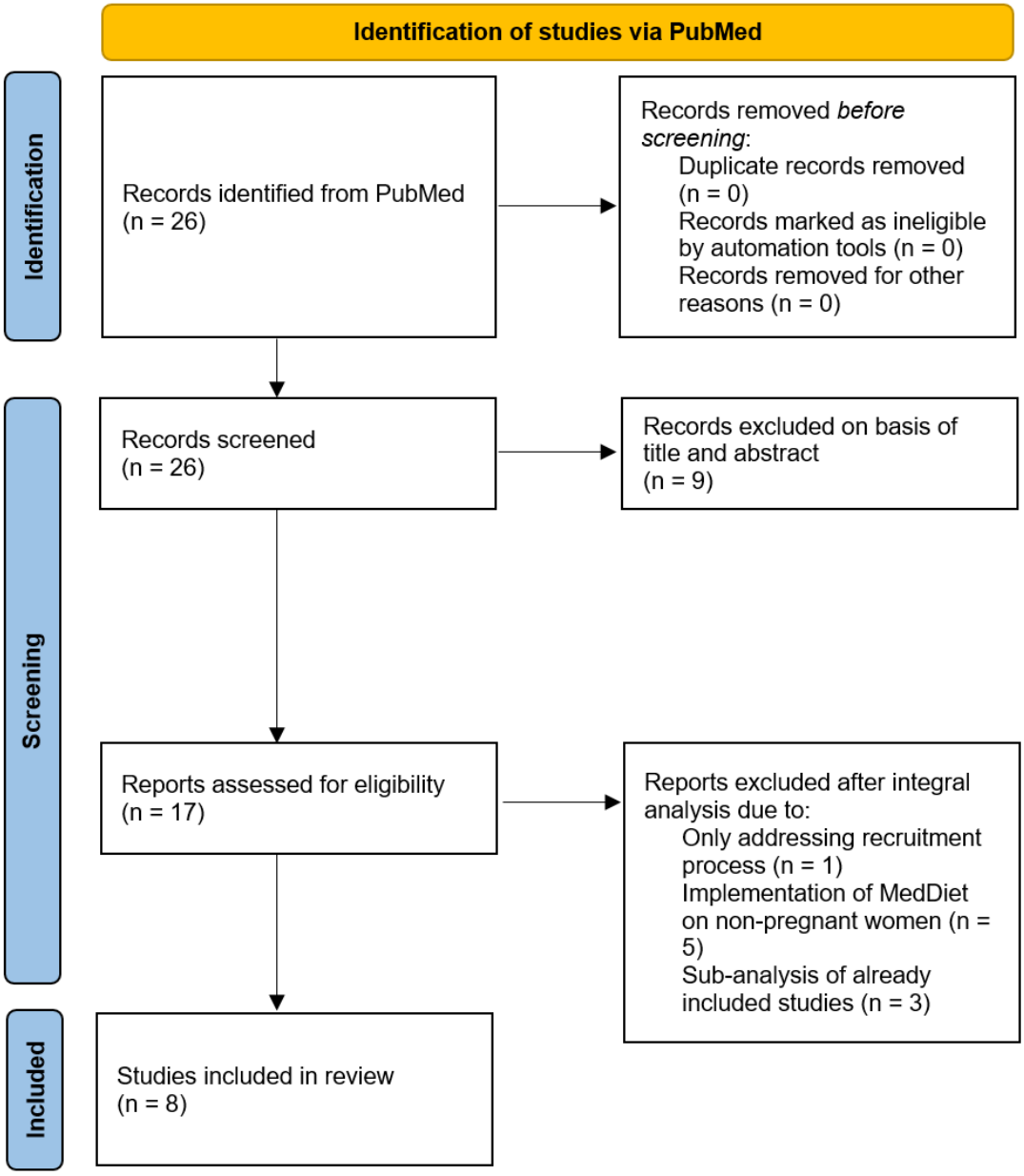

Figure 1 - PRISMA diagram

The final sample of studies, after the selection process, consisted of eight studies. All the selected studies are included in Table 4.

Table 4 – Description of selected studies

Author	Date	Study Type	Sample Dimension	Age (average)	Method of Dietary Assessment	Control Group	Intervention	Maternal-Fetal Outcomes Assessed
Bassel H. Al Wattar et al.	2019	RCT	1138	31,4	FFQ and Modified Short Questionnaire	Dietary Advice (UK National Recommendations for antenatal care and weight management during pregnancy)	Individualized dietary advice was given at 18, 20 and 28 weeks of gestation	PE; GD; GWG; Type of delivery; Birth Weight
Nuria García de la Torre et al.	2019	RCT	932	32,4	FFQ	Normoglycaemic	MedDiet recommendations were given, as well as meal ideas	GD
Elisavet Parlapani et al.	2019	Longitudinal	82	Not Addressed	MedDiet score	Low MedDiet Adherence	Observational study	GD; Pregnancy-induced Hypertension; PE; GWG; Birth Weight; NEC; BPD
Carla Assaf-Balut et al.	2017	RCT	874	33,2	FFQ	Standard-care (Fat consumption limited to 30% of caloric intake)	Both groups received MedDiet recommendations. The intervention group was given extra virgin olive oil and nuts	Pregnancy-induced Hypertension; PE; Type of Delivery; GA; Birth Weight
D. A. Sewell et al.	2017	RCT	28	32,2	FFQ	Standard-care (no structured dietary advice session and follow up supportive telephone calls)	MedDiet recommendations were given to the intervention group, as well as 2 supermarket vouchers	GWG; Birth Weight
B Karamanos et al.	2014	Longitudinal	1003	31,9	FFQ	Low MedDiet Adherence	Observational study	GD
Kristina M Renault et al.	2014	RCT	389	31,2	FFQ	No recommendations for Physical Activity and Diet	One group received exercise recommendations, another group received exercise and MedDiet recommendations and the control group received no recommendations	GWG; GD; Pregnancy-induced Hypertension; PE; Type of Delivery; GA; Birth Weight
Nancy E. Lange et al.	2010	Longitudinal	1376	32,4	FFQ	No control group	Observational study	Asthma

RCT – Randomized Controlled Trials; FFQ – Food Frequency Questionnaires; MedDiet – Mediterranean Diet; UK – United Kingdom; PE – Pre-Eclampsia; GD – Gestational Diabetes; GWG – Gestational Weight Gain; NEC – Necrotizing Enterocolitis; BPD – Bronchopulmonary Dysplasia; GA – Gestational Age

All the studies selected were written in English. Out of the eight studies, five were Randomized Controlled Trials and three were Observational Studies. All eight studies referred to MedDiet adherence during pregnancy.

H. Al Wattar et al. (2019) accessed the effect of MedDiet on pregnant women with metabolic risk factors, such as obesity, chronic hypertension and hypertriglyceridaemia, in comparison to standard advice based on United Kingdom Recommendations. It consisted of an RCT with a sample size of over a thousand pregnant women with an average age of 31,4 years. Participants received dietary advice on three different occasions and no exercise recommendations were given. The outcomes assessed were PE, GD, GWG, type of delivery, and birth weight.

De La Torre et al. (2019) investigated MedDiet recommendations' influence on GD, while also addressing the differences between women with glucose tolerance and normoglycaemic women. On this RCT, dietary advice was given only on one occasion to almost a thousand women and no exercise recommendations were given. The only maternal-fetal outcome assessed was GD.

Parlapani et al. (2019) studied the influence of MedDiet on women delivering prematurely, as well as its' impact on birth size and prematurity complications. This was an observational study with a sample of 82 women that did not receive any dietary recommendations. A MedDiet score was used and women with a higher score were compared to women with a lower score. The outcomes assessed were GD, pregnancy-induced hypertension, PE, GWG, Birth Weight, NEC, and BPD.

Assaf-Balut et al. (2017) researched the impact of MedDiet with additional olive oil and pistachios on maternal-fetal complications, as opposed to a diet consisting of limited fat consumption. This RCT had a sample size of over eight hundred women with an average age of 33,2 years. Dietary recommendations were given on 4 different occasions and exercise advice consisted of over 30 minutes of walking per day. The following outcomes were assessed: Pregnancy-induced Hypertension, PE, Type of Delivery, GA and Birth Weight.

Sewell et al. (2017) investigated if the MedDiet had any repercussions on the prevalence of allergic diseases in infants, analysing maternal urinary inflammatory markers. GWG

and birth weight were the maternal-fetal outcomes that were also assessed. Dietary advice was given on 4 occasions to 28 women.

Karamanos et al. (2014) only accessed the impact of MedDiet on GD, consisting of an observational study with a sample size of over a thousand pregnant women. No exercise or dietary recommendations were given throughout the duration of the study.

Renault et al. (2014) studied the effect of exercise, with and without MedDiet recommendations, in obese pregnant women. It consisted of an RCT with a sample size of 400 women that received between 11 and 13 sessions of dietary recommendations. The outcomes assessed were GWG, GD, Pregnancy-induced Hypertension, PE, Type of Delivery, GA and Birth Weight.

Finally, Lange et al. (2010) researched the influence between following the MedDiet and recurrent wheeze in children, as well as of asthma and other atopic diseases. This observational study had a sample size of almost a thousand and 400 women, with an average age of 32,4 years. There was no control group, and no dietary advice was given.

To evaluate the diet followed by each woman, FFQ were used in all the studies, except in one. The answers to the FFQ were analysed according to the PREDIMED questionnaire. MedDiet adherence was indirectly inferred from the FFQ. The one study that did not use FFQ, resorted directly to a MedDiet score. Regarding exercise, only two studies gave specific recommendations to be followed. Dietary recommendations were not given at any time in 3 different studies. Only one out of the eight selected studies did not have a control group.

4.2. Main Results

In the eight studies that referred to the implementation of the MedDiet during pregnancy, various maternal-fetal outcomes were assessed:

1. Gestational Diabetes

A total of five studies investigated the effects of the MedDiet on GD. Three studies concluded that higher adherence to this eating pattern was associated with a lower risk of developing GD. H. Al Wattar et al. (2019) showed that the MedDiet had the potential to lower the risk of GD in women with metabolic risk factors. De La Torre et al. (2019)

showed that it reduces the incidence of GD universally when applied early. Karamanos et al. (2014) also concluded that the risk of developing GD is inversely related to the degree of adherence to the MedDiet.

However, two studies from this selection showed no association between adherence to the MedDiet and GD. Parlapani et al. (2019) showed no correlation between adherence to MedDiet and the incidence of GD in women that delivered prematurely. Renault et al. (2014) showed no link between adherence to MedDiet and the incidence of GD in obese pregnant women.

2. Pregnancy-induced Hypertension

Three studies addressed Pregnancy-induced hypertension. Parlapani et al. (2019) showed that MedDiet reduced the risk of this outcome in women delivering prematurely. Both Assaf-Balut et al. (2017) and Renault et al. (2014) did not find any correlation between MedDiet adherence and Pregnancy-induced hypertension.

3. Pre-Eclampsia

From the eight studies, four assessed the impact of the MedDiet on the incidence of PE. Only Parlapani et al. (2019) showed that in women delivering prematurely, adhering to the MedDiet lowered the risk of developing PE. All the other studies showed no correlation between adherence to this dietary pattern and PE. H. Al Wattar et al. (2019) referred to women with metabolic risk factors and found that there was no significant effect on PE between women adhering to MedDiet and women following UK's National Recommendations. Assaf-Balut et al. (2017) showed that this eating pattern had no impact on PE rates. Lastly, Renault et al. (2014) concluded that there were no significant differences in the prevalence of PE in obese women that adhered to the MedDiet, in comparison to the ones that did not adhere to it.

4. Gestational Weight Gain

Five studies investigated the impact of adhering to MedDiet during pregnancy in GWG. H. Al Wattar et al. (2019) concluded that women following this dietary pattern gained less weight during pregnancy, in comparison to the control group. Parlapani et al. (2019)'s results showed a higher weight gain in women with low MedDiet adherence. Assaf-Balut et al. (2017) found that the MedDiet lowered GWG. Sewell et al. (2017)

showed no difference in weight gain between the intervention and the control groups. Renault et al. (2014) concluded that adhering to the MedDiet while increasing physical activity, reduced GWG. However, the same results were achieved by women not following the MedDiet and just increasing physical activity.

5. Type of Delivery

Three studies investigated the types of delivery in women adhering to MedDiet during pregnancy. Assaf-Balut et al. (2017) and Renault et al. (2014) both demonstrated that emergency caesarean sections were less likely to occur if the mother had high MedDiet adherence. H. Al Wattar et al. (2019) found no significant impact of this eating pattern on performed caesarean sections.

6. Gestational Age

GA was evaluated in four different studies. Assaf-Balut et al. (2017) concluded that MedDiet adherence was associated with a lower risk for prematurity. Moreover, H. Al Wattar et al. (2019), Parlapani et al. (2019), and Renault et al. (2014) all showed that this eating pattern did not lower the chances of having a premature baby.

7. Birth Weight

Five studies assessed the impact of MedDiet on birth weight. Only Assaf-Balut et al. (2017) demonstrated that adhering to the MedDiet lowered the prevalence of SGA and LGA babies. H. Al Wattar et al. (2019) did not observe any reduction in the prevalence of SGA and LGA in pregnant women with metabolic risk factors adhering to this eating pattern. In women delivering prematurely, Parlapani et al. (2019) found no contrast between low and high adherence to the MedDiet and birth weight. As for Sewell et al. (2017) and Renault et al. (2014), birth weight was practically the same in both the control and the intervention groups.

8. Asthma

Throughout this selection of studies, only Lange et al. (2010) addressed the impact of maternal adherence to the MedDiet on childhood asthma prevalence. It concluded that there was no association between adhering to the MedDiet during pregnancy and the incidence of asthma or recurrent wheezing in children.

9. Necrotizing Enterocolitis

Even though only Parlapani et al. (2019) investigated this outcome, it concluded that high maternal adherence to the MedDiet correlated with a decreased risk of necrotizing enterocolitis in premature infants.

10. Bronchopulmonary Dysplasia

According to Parlapani et al. (2019), Bronchopulmonary Dysplasia was less likely to occur in premature newborns from mothers with higher adherence to the MedDiet.

4.3. Quality Assessment

The promenorized application of the adapted EPHPP Quality Assessment Tool are described in Annexe IV. The main results from the application of this tool are presented in Table 5.

From the eight studies, two were considered of strong quality, two were considered of moderate quality and four were considered of weak quality.

Table 5 – Rating of Quality Assessment

Rating	**Studies**							
	H. Al Wattar et al. (2019)	De La Torre et al. (2019)	Parlapani et al. (2017)	Assaf-Balut et al. (2017)	Sewell et al. (2017)	Karamanos et al. (2014)	Renault et al. (2014)	Lange et al. (2010)
Study Design	Strong	Strong	Moderate	Strong	Strong	Moderate	Strong	Moderate
Blinding	Moderate	Moderate	-	Moderate	Moderate	-	Moderate	-
Representativeness (Selection Bias)	Strong	Strong	Strong	Moderate	Moderate	Moderate	Moderate	Weak
Representativeness (Withdrawals and Drop-Outs)	Moderate	Weak	Weak	Strong	Moderate	Weak	Moderate	Weak
Confounders	Strong	Weak	Strong	Strong	Weak	Strong	Weak	Strong
Data Collection	No rating	Weak	No rating	No rating	Weak	Moderate	Weak	Strong
Data Analysis	Strong	Moderate	Strong	Strong	Weak	Strong	Strong	Strong
Reporting	Strong	Strong	Strong	Strong	Strong	Strong	Strong	Moderate
Overall	**Strong**	**Weak**	**Moderate**	**Strong**	**Weak**	**Moderate**	**Weak**	**Weak**

5. DISCUSSION

In this systematic review, eight studies were included, after the selection process and careful review of the body of each study. Even though many outcomes were assessed in these studies, this review focused on the maternal-fetal outcomes that were assessed in a higher number of studies or that were of higher clinical significance due to being not only more prevalent among pregnant women and their offspring, but also impactful on morbidity and mortality.

Regarding GD, 60% of the studies (De La Torre et al., 2019; H. Al Wattar et al., 2019; Karamanos et al., 2014) that addressed this outcome concluded that MedDiet was beneficial in reducing the incidence of GD, while the other studies (Parlapani et al., 2019; Renault et al., 2014) did not find any significant correlation between these two variables. The studies that proved that there is a potential benefit from the MedDiet in GD were studies of Strong and Moderate quality. Contrarily, Parpalani et al (2019) was a moderate quality study, while Renault et al. (2014)'s study quality was low. With this information in mind, it is possible to conclude that adhering to the MedDiet can reduce the likelihood of developing GD during pregnancy.

Other systematic reviews investigated the impact of adherence to the MedDiet during pregnancy and the incidence of GD. Amati et al. (2019) concluded that this eating pattern could be beneficial in reducing the rates of GD among pregnant women. Zaragoza-Marti et al. (2021) also supported these findings regarding GD.

Parlapani et al. (2019) was the only study that found favourable evidence between this eating pattern and pregnancy-induced hypertension. Both Assaf-Balut et al. (2017) and Renault et al. (2014) concluded that there did not exist any relationship among them. It is hard to extrapolate a strong conclusion having in mind the number and quality of said studies.

Concerning PE, the MedDiet was only considered favourable for reducing its risk by Parlapani et al. (2019), a study of moderate quality. H. Wattar et al. (2019), Assaf-Balut et al. (2017) and Renault et al. (2014) did not find any concordance between the two variables. Only Renault et al. (2014) was determined to be of low quality, whereas the other two were qualitatively strong studies. Even though Parlapani et al. (2019) supports

this positive correlation between MedDiet and PE, no definite conclusions can be taken due to the low number of studies supporting this matter, as well as the existence of qualitatively strong studies showing no connection.

A total of 80% of the studies (Assaf-Balut et al., 2017; H. Al Wattar et al., 2019; Parlapani et al., 2019; Renault et al., 2014) that investigated GWG showed that MedDiet was advantageous for reducing GWG. H. Al Wattar et al. (2019) and Assaf-Balut et al. (2017) were qualitatively strong studies, while Parlapani et al. (2019) and Renault et al. (2014) were moderate and weak, respectively. Sewell et al. (2017) showed no link between excessive or insufficient GWG and adhering to the MedDiet. Nonetheless, this study was qualitatively weak. In conclusion, there is potential in this eating pattern for preventing excessive GWG.

As for the impact of the MedDiet on the type of delivery, two studies concluded that adhering to this diet lowered the risk of having to perform an emergency cesarian section (Assaf-Balut et al. (2017); Renault et al., 2014). Assaf-Balut et al. (2017) and Renault et al. (2014) were regarded as strong and weak studies regarding quality, respectively. H. Al Wattar et al. (2019) showed no correlation between the rates of emergency cesarian sections and the adherence to the MedDiet. Despite only having one study demonstrating no connection between the two topics, this was conceived to be a qualitatively strong study. Taking this into consideration, it is difficult to conclude whether this eating pattern has any influence on the type of delivery.

Assaf-Balut et al. (2017), a qualitatively strong study, analysed the association between GA and MedDiet and concluded that this diet was associated with lower rates of premature infants. On the other hand, no association was found on Renault et al. (2014) and Parlapani et al. (2019), qualitatively weak and moderate studies respectively. H. Al Wattar et al. (2019), also considered to be a qualitatively strong study, found no impact on gestational age. Notwithstanding the fact that only one study proved a positive relationship between this eating pattern and GA, more research needs to be done to discover if the MedDiet may be detrimental in reducing the incidence of prematurity in infants of mothers adhering to it.

Biagi et al. (2019) found some evidence of the MedDiet's benefits on preterm delivery. However, these findings were not definite, and more research should be done to

successfully categorize this eating pattern as a way to significantly reduce the risk of prematurity. On another hand, both Amati et al. (2019) and Zaragoza-Marti et al. (2021) were able to successfully conclude that adherence to the MedDiet is positively correlated with a lower rate of prematurity among newborns.

Only Assaf-Balut et al. (2017) concluded that MedDiet adherence had an impact on birth weight, even though this was a strong study in terms of quality. H. Al Wattar et al. (2019), Parlapani et al. (2019), Sewell et al. (2017), and Renault et al. (2014) all concluded that birth weight was similar in both the control and the intervention groups. It is unlikely that the Mediterranean diet interferes directly with birth weight. Nonetheless, research regarding this topic must continue for the scientific community to arrive at a valid conclusion.

Zaragoza-Marti et al. (2021) concluded that this eating pattern was associated with a lower risk of low birth weight. Since low birth weight is caused in part by placental insufficiency, the authors extrapolated that this diet could improve placental flow. Evidence for this association between low birth weight and the MedDiet was also supported by Amati et al. (2019) and Biagi et al. (2019).

According to Lange et al. (2010), a qualitatively weak study, the MedDiet showed no impact on asthma's prevalence. Nonetheless, Sewell et al. (2017) investigated maternal MedDiet adherence and its relationship with urinary biomarkers of antioxidant capacity and of oxidative stress. Adoption of this eating pattern showed a reduction in biomarkers of antioxidant capacity and an increase in biomarkers of oxidative stress. Since in asthma there might be an increase in oxidative stress, MedDiet can be linked to lower rates of asthma and atopy in children. However, this study was contemplated as qualitatively weak and only assessed urinary biomarkers, not the prevalence of asthma and atopy. At this time it is not possible to extrapolate a valid association between the MedDiet and asthma.

Regarding asthma, Biagi et al. (2019) evaluated 7 different studies and concluded that there is still not enough evidence to support the positive impact of MedDiet adherence during pregnancy on asthma and recurrent wheezing. Nonetheless, Amati et al. (2019) concluded that the risk of asthma could be reduced with a high adherence to this eating pattern.

The incidence of NEC and BPD, while only being assessed in Parlapani et al. (2019), proved to be significantly lower in pregnant women adhering to the MedDiet. This was a moderate quality study. There is potential in this eating pattern to reduce the incidence of both these outcomes.

In conclusion, adherence during pregnancy to the MedDiet has proved to be significantly effective in reducing the risk of GD, excessive GWG, NEC, and BPD. This eating pattern also showed some potential in lowering the incidence of other maternal-fetal outcomes such as PE, pregnancy-induced hypertension, prematurity, and emergency caesarean section rates. Nonetheless, the number of studies that were included in this Systematic Review was not enough to withdraw any definite conclusions and more need to be conducted to obtain more evidence on this matter.

6. CONCLUSIONS AND FUTURE WORK

6.1. Conclusions

The MedDiet has been proven to reduce the prevalence of many diseases, being beneficial for most of the population to adhere to it. With pregnancy being an important period for both the mother and the fetus, it is crucial to adopt strategies that reduce the incidence of maternal-fetal adverse outcomes. This Systematic Review investigated the impact of adherence to the MedDiet during pregnancy regarding these outcomes. A total of 8 studies were included in this systematic review and the main conclusions include a reduction in the prevalence of some maternal-fetal outcomes, such as GD, GWG, NEC, and BPD. There is also some evidence showing that MedDiet has the potential to reduce rates of PE, pregnancy-induced hypertension, prematurity, and emergency cesarian sections.

One of the limitations of this Systematic Review is the reduced number of studies that address this theme. Even though most of the studies had a big sample of pregnant women, there needs to be more research so that conclusions can be extrapolated for most of the population. Nonetheless, this is a great starting point for this research to be built on. Another limitation was the low quality of the individual studies included. Four studies out of the eight included ones were of weak quality, which can create some doubt about the validity of their results. Finally, only one database was used while doing this selective literature review which can limit the number of studies that were first analysed.

In conclusion, there is some evidence that MedDiet can be beneficial in preventing some maternal-fetal outcomes. However, more studies should be conducted to prove the validity of these results.

6.2. Future work

Future research could include the impact of MedDiet adherence during the pre-pregnancy period and the postpartum period on maternal-fetal outcomes. The pre-pregnancy period should investigate the impact on fertility, specifically in Fertilization in

vitro success rates. Regarding the postpartum period, it would be important to analyse this eating pattern's impact while breastfeeding.

More studies need to be done to confirm the results demonstrated by the studies included in this systematic review. These studies should be focused on prevalent maternal-fetal outcomes, and they should include a more heterogeneous population to be more applicable to most pregnant women. MedDiet recommendations should be more specific and with practical guidelines for pregnant women to follow. There needs to be a bigger number of studies on this topic to enhance maternal and fetal health. In these studies, exercise ought to be more consistent throughout all the participants to reduce the impact of it on the results of the studies.

6.3. Practical Applications

Increasing adherence to MedDiet during pregnancy can be important to reduce all-around morbidity and mortality. This can be achieved through the implementation of mandatory nutrition consults during pregnancy that focus on improving compliance with this eating pattern. Some steps to better implement the MedDiet during pregnancy include (Pinho et al., 2016):

1. Make at least 3 main meals each day.
2. Include vegetables and fruits daily.
3. Drink enough water throughout the day.
4. Consume dairy products twice a day.
5. Give preference to olive oil.
6. Avoid excess consumption of salt.
7. Eat small amounts of olives, nuts, and seeds.
8. Include fish, white meat and eggs, in addition to beans.
9. Lower the consumption of red and processed meats.
10. Use spices and aromatic herbs.

On a more practical level, MedDiet-inspired culinary workshops can be advertised on obstetric consults to facilitate adherence to this diet, with more recipes available for pregnant women to follow.

Regarding education, nutrition should be included in all medical students' education, not only regarding the general population but also regarding the most optimal nutrition during pregnancy. Educational courses and lectures should also be provided to Medical Students and Doctors with the aim of educating them on the MedDiet, with the final aim of best advising pregnant women.

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ANNEXE I – MEDITERRANEAN DIET PYRAMID

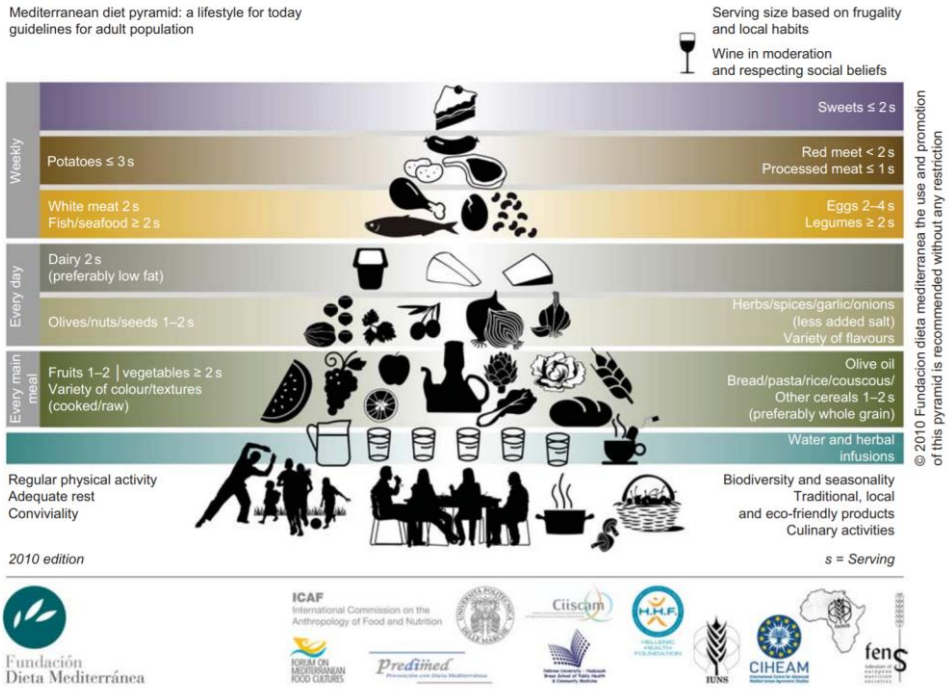

Figure 2 - Mediterranean Diet Pyramid (Bach-Faig et al., 2011)

ANNEXE II – MEDITERRANEAN DIET WEEL

Figure 3 - Mediterranean Diet Food Wheel (Portuguese version) *(A RODA DA ALIMENTAÇÃO MEDITERRÂNICA • Nutrimento, n.d.)*

ANNEXE III - EPHPP QUALITY ASSESSMENT TOOL (adapted)

STUDY DESIGN

(**Q1**) The study design is:

1. Experimental
    i. Individual-randomised
    ii. Group-randomised
    iii. Non-randomised
2. Observational
    i. Cross-sectional
    ii. Longitudinal (also natural experiment or pre-post tests)
    iii. Case-control
3. Any other method (i.e. pre-post test without control group) or did not state method

(**Q2**) Was this an intervention study?

Yes – proceed

No – go to question 7

(**Q3**) Is the intervention of interest clearly described?

1. Yes
2. No
3. Not applicable (if using an existing database and referring to design article*)

(**Q4**) Were (groups of) subjects randomized into intervention groups?

1. Yes
2. No
3. Can't tell
4. Not applicable (if using an existing database and referring to design article*)

(**Q5**) Was the intervention assignment concealed from participants and care givers until recruitment was completed?

1. Yes
2. No
3. Can't tell
4. Not applicable (if using an existing database and referring to design article*)

(**Q6**) Was (were) the intervention or exposure status of participants concealed from the outcome assessors?

1. Yes
2. No
3. Can't tell
4. Not applicable (if using an existing database and referring to design article*)

(**Q7**) Were power/sample size calculations conducted?

1. Yes, details of calculation provided
2. Yes, no details provided
3. Not reported or post hoc computation
4. Not applicable (if using an existing database and referring to design article*)

Rating study design: **Strong:** Q1 is 1

Moderate: Q1 is 2

Weak: Q1 is 3

Rating blinding: **Strong:** Q5 and Q6 are 1

Moderate: Q5 or Q6 is 1**; or** Q5 or Q6 are 3

Weak: Q5 and Q6 are 2; **or** Q5 and Q6 are 3

No rating: Q5 and Q6 are 4

(No rate is given when study is not an intervention study)

** If the study is using data from a large existing database such as HSE, NHANES, BRFSS, etc., often the authors refer to the design paper of the original study and no information*

in the present article is being described about power calculations, validity of tools, intervention description, etc.

REPRESENTATIVENESS (selection bias)

(**Q8**) Is the spectrum of individuals selected to participate likely to be representative of the wider population who experience the intervention/exposure/situation?

1. Very likely
2. Somewhat likely
3. Not likely (selected group of users e.g., volunteers)
4. Can´t tell*
5. Not applicable*

(**Q9**) What percentage of the selected participants agreed to participate?

1. ……..%
2. Can't tell
3. Not applicable

(**Q10**) Were inclusion/exclusion criteria specified and number of exclusions reported?

1. Criteria and number of exclusions reported
2. Criteria or number of exclusions not reported
3. Criteria and number not reported
4. Not applicable (if using an existing database and authors refer to design article)

Rating: **Strong:** Q8 is 1

Moderate: Q8 is 2

Weak: Q8 is 3 or 4

No rating: Q8 is 5

***** *Rate the representativeness of each study uniquely, according to each study specific context (community, specific group of the population, particular place, etc.). If a paper is using a large national dataset and refers to a design paper in their methods section, we answer Q8 with 5 (not applicable). However, if the authors used an existing database and do not refer to a design article, the rating should be 4 (can't tell). As a result, if you*

have rated Q8 with 5 (not applicable), than it is not possible to give a rating for representativeness.

REPRESENTATIVENESS (withdrawals and drop-outs)

(**Q11**) Were withdrawals and drop-outs reported in terms of numbers and reasons per group?

1. Numbers and reasons provided
2. Numbers but no reasons provided
3. Can't tell (if longitudinal data)
4. Not applicable (if cross-sectional data or if using an existing database and authors refer to design article)

If Q11 is 1 or 2, proceed to Q12. Otherwise, proceed to Q13.

(**Q12**) What was the loss to follow-up (report the percentage completing the study and if it differs by groups, record the lowest)?

1. ……..%
2. Not provided
3. Not applicable

Rating: **Strong:** Q11 is 1

Moderate: Q11 is 2

Weak: Q11 is 3

No rating: Q11 is 4

CONFOUNDERS

(**Q13#**) What confounders were the analyses adjusted for?

……..

……..

(**Q13**) Were analyses appropriately adjusted for confounders?

1. For most confounders
2. For some confounders
3. No or can't tell

The following are examples of confounders: race, sex, marital status/family, age, SES (income or class), education, health status, pre-intervention score on outcome measure. Rate the confounding as good if the authors took into account several factors (independent of whether they treated them as confounders, covariables, moderators or mediators). Consider as minimum for 'most confounders' controlling for age, gender, SES.

Considering the study design, were appropriate methods for controlling confounding variables and limiting potential biases used? Confounding can be addressed by appropriate use of randomization, restriction, matching, stratification, or multivariable methods. Sometimes use of a single method may be inadequate. Some biases can be limited by institution of data collection or study procedures that support validity of the study (e.g. training and/or blinding of interviewers or observers, interviewers and observers are different from interventions' implementers etc). Example: if between-group differences persist after randomization or matching, statistical control should also have been used.

Rating: Strong: Q13 is 1

Moderate: Q13 is 2

Weak: Q13 is 3

DATA COLLECTION

(**Q14**) Were validity and reliability of the data collection tools discussed?

1. Both validity and reliability were discussed
2. Validity or reliability were discussed
3. None of them were discussed
4. A larger dataset was used and authors provided adequate information to find information on validity and reliability

Rating: Strong: Q14 is 1

Moderate: Q14 is 2

Weak: Q14 is 3

No rating: Q14 is 4

DATA ANALYSIS

(**Q15**) Were appropriate statistical analyses conducted (including correction for multiple tests where applicable*)?

1. a. Statistical methods were described, appropriate and comprehensive, and used a sophisticated approach

   b. Statistical methods were described, appropriate and comprehensive, and used a simple approach
2. Statistical methods were described and less appropriate
3. No description of statistical methods or inappropriate methods

Rating: **Strong:** Q15 is 1

Moderate: Q15 is 2

Weak: Q15 is 3

** Consider statistical analyses to be appropriate if they account for confounding factors (so correlation analysis only is not enough). Do not punish papers for not correcting for multiple tests, if the rest of the analyses are appropriate.*

REPORTING

(**Q16**) Are the hypotheses/aims/objectives of the study clearly described?

1. Yes
2. No

(**Q17**) Are the main outcomes to be measured clearly described?

1. Yes
2. No

(**Q18**) Are the main findings clearly described?

1. Yes
2. No

(**Q19**) Have actual probability values been reported (i.e., p = .345 instead of p > .050; same goes for t-values, 95% CIs, etc.)?

1. Yes
2. No

Rating: **Strong:** Q16 and Q19 are 1

Moderate: Q16 or Q19 are 1

Weak: Q16 and Q19 are 2

Studies can have between six and eight component ratings. The overall rating for each study is determined by assessing the component ratings. **Strong** will be attributed to those with no WEAK ratings and at least four STRONG ratings; **Moderate** will be given to those with one WEAK rating or fewer than four STRONG ratings; **Weak** will be attributed to those with two or more WEAK ratings. (If only six ratings have been given, Strong will be attributed to those with no WEAK ratings and at least three STRONG ratings.) The final decision of both reviewers will be: strong, moderate, or weak.

ANNEXE IV – QUESTIONS FOR QUALITY ASSESSMENT RATING

Table 6 - Questions for Quality Assessment Rating

	H. Al Wattar et al. (2019)	De La Torre et al. (2019)	Parlapani et al. (2019)	Assaf-Balut et al. (2017)	Sewell et al. (2017)	Karamanos et al. (2014)	Renault et al. (2014)	Lange et al (2010)
Q1	1	1	2	1	1	2	1	2
Q2	Yes	Yes	No	Yes	Yes	No	Yes	No
Q3	1	1	-	1	1	-	1	-
Q4	1	2	-	1	1	-	1	-
Q5	2	2	-	2	2	-	2	-
Q6	1	3	-	1	3	-	3	-
Q7	1	1	3	1	3	3	1	3
Q8	1	1	1	2	2	2	2	3
Q9	1 (69.5%)	1 (97.7%)	2	1 (62%)	1 (3.5%)	2	1 (67.8%)	2
Q10	1	2	2	1	2	1	1	2
Q11	2	3	3	1	2	3	2	3
Q12	1 (93.3%)	-	-	1 (86.8%)	1 (85.2%)	-	1 (88%)	-
Q13	1	3	1	1	3	1	3	1
Q14	4	3	4	4	3	2	3	1
Q15	1	2	1	1	3	1	1	1
Q16	1	1	1	1	1	1	1	1
Q17	1	1	1	1	1	2	1	1
Q18	1	1	1	1	1	1	1	1
Q19	1	1	1	1	1	1	1	2