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FMUP FACULDADE DE MEDICINA UNIVERSIDADE DO PORTO

**MESTRADO INTEGRADO EM MEDICINA**

**2020/2021**

Mónica Pinto Alberto

# Vegetarian Diets in Early Life Development: Benefits, Risks and Unanswered Questions

**Abril, 2021**

FMUP

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# Vegetarian Diets in Early Life Development: Benefits, Risks and Unanswered Questions

**Mestrado Integrado em Medicina**

**Área: Ciências da saúde**

**Tipologia: Monografia**

**Trabalho efetuado sob a Orientação de:**

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**E sob a Coorientação de:**

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**Trabalho organizado de acordo com as normas da revista:**

**Critical Reviews in Food Science and Nutrition**

**Abril, 2021**

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DESIGNAÇÃO DA ÁREA DO PROJECTO

Ciências da saúde

TÍTULO MONOGRAFIA

Vegetarian diets in early life development: benefits, risks and unanswered questions

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*À família.*

# Vegetarian Diets in Early Life Development:

# Benefits, Risks and Unanswered Questions

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Word count: 7768

Abstract

The literature suggest that vegetarian diets decrease the burden of non-communicable diseases. However, these diets may lead to deficiency of essential nutrients which raises the concern about their adequacy during pregnancy and early life, as these are periods of great vulnerability and intense transformation and growth.

The aim of this study was to revise and discuss recent literature information, about the safety and nutritional adequacy of vegetarian diets during pregnancy and childhood regarding the impact on child growth and development.

For this purpose, a search in Pubmed database was made for the terms:(Vegetarian diets AND fetal programing) OR (Vegetarian diets AND child development) OR (Vegetarian diets AND child growth) restricting the search between 2010 and 2020.

Information on the association between vegetarian diets and nutritional deficit of vitamin B12, vitamin D, iron, zinc, calcium, iodine and omega-3 fatty acids, in early live is discussed. Plus, the association of vegetarian diets during pregnancy or childhood with fetal programming and child growth and development outcomes are discussed.

Vegetarian diet seems safe for child development, if well planned. So, pregnant women and children following a vegetarian diet should seek professional advice to assess their nutritional status and avoid nutritional deficits.

*Keywords:* vegan; vegetarian; child development; child growth; fetal programing; pregnancy

## Introduction

The eating behavior is a very complex and personal process involving multiple factors with relevant impact on personal health and the environment. The choice to follow a vegetarian diet can be based on religious or cultural motivations, govern policies, social environment, health reasons and concerns regarding animal welfare, sustainability and global warming (Corrin and Papadopoulos 2017; Leitzmann 2014). There are religions, such as Hinduism and Buddhism, that recommend their disciples to adopt a vegetarian diet (Corrin and Papadopoulos 2017). Also some people do not eat meat because they believe that it is wrong to raise and slaughter animals for food, clothing and other purposes unrelated to the only purpose of their well-being (Lea and Worsley 2002).

Climate change, loss of biodiversity and water scarcity is a current reality (Rose, Heller, and Roberto 2019). The adoption of a vegetarian diet, reduces the environmental impact, since the production of food of plant origin uses less water and fossil fuels, compared to animal foods (Rose, Heller, and Roberto 2019).

Non-communicable diseases as cardiovascular diseases, cancer, type 2 diabetes (T2D) and obesity, are related to 71% of all deaths globally (World Health Organization 2018) and are associated to non-healthy lifestyles as eating disorders and low physical activity.

It has been suggested that vegetarian diets are healthier compared to omnivorous regimens, decreasing the non-communicable diseases burden (Pistollato et al. 2015). In fact, the adoption of vegetarian diets is increasing over the world and it can be estimated that in Europe, the prevalence of vegetarianism (regimens that exclude all kinds of animal flesh) ranges from 1.2%-1.5% in Portugal and Spain, to about 7% in the United Kingdom and 10% in Germany. The prevalence of veganism in Europe (more strict regimens that exclude all types of animal flesh and animal derived products) varies between 1 and 3% (Redecillas-Ferreiro, Moráis-López, and Moreno-Villares 2020).

Vegetarian adults frequently share their eating patterns with their children because they consider these diets healthier and recognize diet important factor in the management of children´s health (Baroni et al. 2018). However, concerns regarding the deficiency of some vitamins and minerals caused by vegetarian diets raised the scientific discussion about their nutritional adequacy in general but particularly about their putative risks during pregnancy and early life (Ferrara et al. 2020).

Pregnancy and childhood are periods of great vulnerability and intense transformation, in which adequate nutritional support is essential to sustain health, growth and development of the fetus and the child. Nutritional deficiencies at these stages can have severe consequences. Some of the consequences of malnutrition in pregnancy are the risk of restricted fetal growth, premature birth and maternal mortality (Ramakrishnan et al. 2012), and in childhood nutritional deficiency may impair child's growth and neurodevelopment (Lemale et al. 2018). Therefore, it is necessary to carefully evaluate food adequacy at these critical stages of life.

It is well known that environmental exposure during perigestational period may impact offspring and child development and may also program for metabolic disorders later in life (Hanley et al. 2010). Vegetarianism is a dietary regimen based mainly on foods of plant origin, and free of meat and fish (Potter-Dunlop and Alice 2012). Although a strict classification of vegetarian diets is difficult, there are three main types of vegetarian diets, which exclude all types of animal flesh and may be divided in the ovolactovegetarian diet (OLV), which includes eggs, milk and dairy products, the lactovegetarian diet (LV), which excludes eggs and additionally. A more restrict vegetarianism, also called veganism (VEG), which excludes all animal flesh and animal derived products, which means that this diet is free from eggs, milk and dairy products, including only plant-based foods (Bettinelli et al. 2019). In addition to these regimens, there is a less strict regimen, the called fish-

vegetarianism, which is similar to OLV, but includes the consumption of fish (Yisahak et al. 2021). Finally, the egg-vegetarian diet is similar to the vegan diet, with the difference that it eats eggs (Yen et al. 2008).

The aim of this study is to revise and discuss recent literature information, about the risks and benefits of vegetarian diets during pregnancy and childhood and their impact on early life and child health and development.

## Material and Methods

To conduct this review articles were searched in the Pubmed database with the terms (Vegetarian diets AND fetal programing) OR (Vegetarian diets AND child development) OR (Vegetarian diets AND child growth) between 2010 and 2020, written in English, Portuguese and Spanish. 79 articles were found and 25 were excluded, because they did not address the theme of the study or because were replicates. During the analysis of these 54 papers, other papers 17 were included due to their relevance to the theme. Norms from the General Directorate of Health (DGS) and the World Health Organization (WHO) were also included.

## Vegetarian Diets During Early Periods of Development: Major Nutrition Concerns

Although vegetarian diets may represent a healthier dietary pattern protecting from several non-communicable diseases, when compared to omnivorous diets, concerns have been raised regarding its association with nutritional deficiency of some essential nutrients such as vitamin B12, vitamin D, iron, zinc, calcium, iodine and some essential fatty acids (Agnoli et al. 2017; Amit 2010; Craig and Mangels 2009; Lemale et al. 2019). This concerns are particularly serious during in pregnancy and childhood, due to the critical importance of those nutrients during these periods of great vulnerability.

### *Vitamin B12*

Vitamin B12, also called cobalamin, is an essential micronutrient for metabolism, being a cofactor of enzymes involved in folate metabolism and in DNA synthesis (Dror and Allen 2008). Its deficiency can be caused by a deficient absorption and metabolism or by nutritional deficits (Guez et al. 2012).

Vitamin B12 is fundamental, particularly in pregnancy, for normal fetal neuro cognitive development and it may be deficient in pregnant women who follow vegetarian diets (Visentin et al. 2016), as these types of diets are low in vitamin B12 (Craig and Mangels 2009). In fact, this vitamin is present only in animal products as this vitamin is present only in animal products. In addition, the need of this vitamin increases during pregnancy due to greater absorption and placental transport to the fetus (Murphy et al. 2007).

The low concentration of vitamin B12 can impair the development of the fetal nervous system, and increases the risk of pre-eclampsia (Penney and Miller 2008).
Guez et al. (2012) describe a case of an Italian boy hospitalized at 5 months of age with iron and B12 deficiency due to nutritional deficiency, as he was exclusively breastfed and his mother was vegan for several years although she was supplemented with multivitamins during the second and third trimester of pregnancy, but not during lactation.

### *Vitamin D*

Vitamin D can be obtained through exposure to UVB radiation or by ingestion, it is necessary for calcium absorption and bone formation as for other functions that have been recently attributed to vitamin D as cellular growth regulation, immune system activation, anti-inflammatory properties and metabolism modulation (Chun et al. 2019; Kolp et al. 2017). Its deficiency during pregnancy has serious consequences for both pregnant woman and fetus (Kazemi et al. 2009), increasing the risk of premature birth, pre-eclampsia, gestational diabetes and low gestational age (Dror and Allen 2010).

### *Calcium*

Vegetarians may also have calcium deficiency due to the inhibition of calcium absorption caused by phytates and oxalates present in dietary vegetables (Baroni et al. 2018). This can be a problem, as calcium is essential for bone growth and fracture prevention (Black et al. 2002).

It is described in the literature that calcium supplementation of pregnant women with low calcium levels does not reduce the incidence of pre-eclampsia, although it decreased its severity and neonatal mortality (Villar et al. 2006).

### *Iron and Zinc*

Iron is a micronutrient necessary for the development of the fetal nervous system (Crozier et al. 2019). It participates in the myelinization of neurons (Connor and Menzies 1996) and the synthesis of neurotransmitters (Youdim and Yehuda 2000). A deficiency of this ion impairs these processes with a negative impact in child's cognitive function (Lukowski et al. 2010; McCann and Ames 2007). Iron is also an element of heme which is present in hemoglobin, important in the transport of oxygen (Wang and Pantopoulos 2011). In addition, it is a cofactor of several enzymes, being required for the synthesis of DNA and for reactions of the citric acid cycle (Wang and Pantopoulos 2011).

Vegetarian diets are associated with decreased bioavailability of iron and zinc, caused by the greater amount of phytates and polyphenols present in these diets which inhibit the absorption of iron and zinc. Impaired bioavailability of iron and zinc are also caused by the absence of meat in the diet, as iron from flesh is more easily absorbed (Gibson, Heath, and Szymlek-Gay 2014) This causes vegetarians to have a lower serum ferritin concentration when compared to omnivores (Gibson, Heath, and Szymlek-Gay 2014). Nevertheless, these deficiencies can be mitigated by enriching the vegetarian diet cereals or whole grains, which increase the amount of iron and zinc in the diet that reaches the systemic circulation.

Increasing the ingestion of vitamin C - rich foods, also improves iron absorption (Gibson, Heath, and Szymlek-Gay 2014).

***Iodine***

Iodine is a micronutrient obtained through diet. It is essential to produce thyroid hormones, which are fundamental for child's physical and mental development (Aakre et al. 2021). Vegetarian diets, especially vegan ones, are poor in iodine (Craig and Mangels 2009). Aakre et al. (2021) assessed women iodine levels during pregnancy and 18 months postpartum (Aakre et al. 2021). They used a cohort of pregnant women of the four health regions in Norway and measured maternal urinary iodine concentrations during pregnancy and at 6 weeks postpartum, 6 months postpartum and 18 months postpartum. They found that the amount of iodine was below the limit recommended both in pregnancy and in the postpartum. Pregnant women that drank milk and were supplemented with iodine presented higher urinary iodine levels to those that did not (Aakre et al. 2021).

***Omega-3 fatty acids***

The ingestion of omega-3 fatty acids is important as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) deficiencies are associated with disorders of the central nervous system, such as hyperactivity and attention deficit disorder, dyslexia, dyspraxia and autism (Lauritzen et al. 2016). In the view of this it is important to maintain adequate levels of these fatty acids during pregnancy, particularly for the development of the fetal central nervous system (Schuchardt et al. 2010).

Many studies demonstrated that EPA and DHA levels are lower in vegetarians and vegans than in omnivores (Burdge, Tan, and Henry 2017). Accordingly, another study revealed that omega-6 and DHA plasmatic levels were lower in vegetarian women comparing to omnivores ones, in pregnancy (Crozier et al. 2019).

## Vegetarian Diets During Pregnancy

Pregnancy is a period of intense transformation, when there is a global increased demand of nutrients essential to support the growth and development of the fetus (Ferrara et al. 2020). Although data on the prevalence of vegetarianism during pregnancy are scarce, it is known that in the UK, between 2012 and 2018, the number of young vegetarian adults aged 16 and over increased from 2 to 5% (Rashid, Meier, and Patrick 2021). These data suggest that women of reproductive age seem prone to adopt this type of dietary regimens. Importantly, it has been claimed that women generally keep their dietary habits during pregnancy (Sebastiani et al. 2019).

There are controversies about the adequacy of vegetarian diet during the period of pregnancy and the need for micronutrient supplementation at this stage. The Academy of Nutrition and Dietetics considers that a well-planned vegetarian diet provides all the nutrients required in this period (Melina, Craig, and Levin 2016) and it is not necessary any type of supplementation beyond the Association's recommendations to all pregnant women (Procter and Campbell 2014). However, this Association warns to the fact that vegans, due to the increased risk of B12 deficit, may need supplementation (Melina, Craig, and Levin 2016). In contrast, the Portuguese Directorate General of Health (DGS), does not recommend vegetarian diets during pregnancy because these diets are considered nutritionally insufficient during this particularly susceptible period requiring micronutrient supplementation (Directorate General of Health 2019).

Bellows et al. (2020), carried out a study on 627 LV and non-vegetarian pregnant women from India, with the objective of evaluating the intake of energy, macronutrients and micronutrients between the two groups. The study population included 46.4% LV and 53.6% non-vegetarian pregnant women. The average age in both groups was 25 years. The results of this study revealed that energy and micronutrient intake was inadequate in both groups, with

no statistical differences between dietary groups, when analyses were adjusted for potential confounders. This study evidences pregnancy as a particular susceptible period for nutritional unbalances, disregard of the type of dietary regimen. In fact, WHO data for 2008 also refer that 30% of women of childbearing potential and 40% of vegetarian and non-vegetarian pregnant women worldwide have anemia (De Benoist et al. 2008), which corroborates pregnancy as a particularly susceptible period regarding nutrient demand.

## Vegetarian Diets During Childhood

Childhood may be divided in several stages according to developmental milestones. The period ranging from birth until 3 years old corresponds to a period of intensive growth and neurodevelopment which is particularly vulnerable to appropriate nutritional support. Similarly to pregnancy, this stage of the life cycle is particularly vulnerable to dietary unbalances which may prevent the achievement of a full health status during adulthood. The succeeding periods of development that run through pre-school, school-age and adolescence are also very important, but vulnerability to nutritional unbalances is likely to decrease with increasing age.

Data regarding prevalence of vegetarianism and veganism during childhood is scant. Nevertheless, it is believed that the increasing trend in these kind of dietary regimens that is globally observed in adult population is accompanied by children (Farella, Panza, and Baldassarre 2020). In fact, it is known that the reason for following this type of diet in this age group is related to sharing parents' diet (Bettinelli et al. 2019). A German study (Patelakis et al. 2019) has shown that the prevalence of vegetarians between the years 2003 and 2006 was 1.4% and 5% in the age groups of 6-11 and 12-17 years old, respectively, with girls representing the majority of these groups.

There is little knowledge about health effects of vegetarian diets during childhood (Ferrara et al. 2017). The lack of this kind of studies and information lead several researchers to consider that this diet may be unsuitable in childhood, defending the necessity of supplementation of children practicing vegetarian diets, particularly vegan diet, due to its high restrictive nature (Grieger, Grzeskowiak, and Clifton 2014; Lemale et al. 2019). Authors argue that vegan diets are a cause of nutritional deficits that are especially severe in children, so children undergoing these diets must be referred to health professionals (Potter-Dunlop and Alice 2012) as they may need supplements (Gibson, Heath, and Szymlek-Gay 2014; Grieger, Grzeskowiak, and Clifton 2014; Lemale et al. 2019).

Barnard and Leroy (2020), defend the need to supplement children's vegetarian diet with vitamin B12 and that, with this supplementation, the vegetarian diet is healthy for children and nutritionally superior to the non-vegetarian diet (Barnard and Leroy 2020). Accordingly, many scientific associations, such as the Canadian Pediatric Society (2010) (Amit 2010), the Academy of Nutrition and Dietetics (2016) (Melina, Craig, and Levin 2016), the Italian Society of Human Nutrition (2017) (Agnoli et al. 2017) and DGS (2016) (Pinho et al., 2016), as well as several researchers (Amit 2010; Craig 2010; Weder et al. 2019) consider these types of diets safe during childhood, as long as they are well planned to provide all the necessary nutrients in this age group for child normal growth and development.

## Vegetarian Diets in Pregnancy: Outcomes for Children Health

Fetal development is a complex process and the environment in which it occurs is decisive for the future of the baby. A hostile intrauterine environment causes epigenetic changes responsible for appearance of health problems later in life (fetal programming) (Saffery and Novakovic 2014). A diet that does not provide the necessary nutrients for fetal development is an example of an unfavourable environment that can cause changes in the

epigenome that may manifest in the future (Barker 2017). The existence of nutritional deficits during pregnancy is associated with an increased risk of obesity, T2D, metabolic syndrome and cardiovascular diseases in adulthood (Hanley et al. 2010). It was also described in the literature that children of vegetarian and vegan mothers who had B12 deficits during pregnancy have an increased risk of depression in adulthood (Pepper and Black 2011). The first trimester of pregnancy is particularly sensitive to nutrition, as it is a period of rapid cell division and differentiation and, therefore, nutritional deficiencies at this time induce, through fetal programming, the appearance of chronic diseases in adulthood (Fowles 2006). Today, it is also known that a diet deficient in essential nutrients in the early half of pregnancy increases the risk of developing hypertension in later life (Gardner, Bell, and Symonds 2007).

Importantly, fetal growth restriction during pregnancy increases the risk of growth retardation and reduced cognitive development in children (Christian et al. 2013). Birth weight, in addition to being an indicator of newborn health, is a predictor of health outcomes in adulthood (Zulyniak et al. 2017).

Grieger, Grzeskowiak, and Clifton (2014) investigated the relationship between the type of food in the 12 months prior to conception of 309 women and fetal growth and premature birth. Three dietary patterns were identified: high protein/fruit type; high fat/sugar/take away type and vegetarian type. The research revealed that a diet rich in protein, fruits and few grains reduces the possibility of premature birth, while the pattern of high fat/sugar/take away is associated with premature birth and shorter length.

This study shows the impact of nutrition during pregnancy on neonatal parameters. Healthy foods typical of the vegetarian diet, such as fruit and grains, were positively associated with reduces the possibility of premature birth, unlike the other types of food, less healthy and high in fat, more typical of omnivores (Grieger, Grzeskowiak, and Clifton 2014).

Ferrara et al. (2020) compared the diets followed during pregnancy and the anthropometric parameters of the newborn at birth (sample mother and child pairs). According to the diet followed during pregnancy, mothers were classified into three groups: VEG, OLV/LV and omnivores. The results show no significant differences in length, body mass index (BMI) and head circumference at birth among the three studied groups.

Yisahak et al. (2021) studied 1948 pregnant women from the USA, 99 vegetarians and 1534 non-vegetarians. Of the vegetarians, only 22 were “complete vegetarians” (they did not eat meat or fish), the remaining were fish-vegetarians (7) or semi-vegetarians (301).

The results revealed that newborns from complete vegetarians were smaller for gestational age [adjusted odds ratio (ORadj) = 2.51, 95% confidence interval: 1.01, 6.21]. The study also showed that complete vegetarian mothers had a lower gestational weight gain [ORadj = 2.24, 95% confidence interval: 0.95, 5.27]. Nevertheless, these results were not associated with postnatal morbidity (Yisahak et al. 2021). The considerable difference between the number of complete vegetarians and non-vegetarians in the study may be skew the result of the study.

The fact that complete vegetarian mothers have a lower energy consumption (1,678 kcal/day) when compared to non-vegetarians (2,304 kcal/day), may justify the lower weight gain of vegetarian mothers and the reason why their newborns are smaller for gestational age when compared to non-vegetarians (Yisahak et al. 2021).

Crozier et al. (2019) conducted a prospective cohort study with the aim of assessing whether the ingestion of vegetarian diet during pregnancy was related to maternal nutritional changes and cognitive functions of children aged six to seven years. It involved 3,158 women aged between 20 and 24 years. Of these, 2,222 (78 vegetarians and 2,144 omnivores) provided data on diet and blood samples at 11 weeks of gestation and 2,643 (91 vegetarians and 2,552 omnivores) provided data relevant to diet and blood samples at 34 weeks of

gestation. To assess children's cognitive functions, the authors used the Wechsler Abbreviated Intelligence Scale to test IQ (Crozier et al. 2019) and the Cambridge Neuropsychological Battery to assess executive function (Crozier et al. 2019). The authors concluded that maternal vegetarianism at the beginning or end of pregnancy was not associated with reductions in IQ or cognitive functions at ages of 6 to 7 years. However, the study found that hemoglobin levels of vegetarian mothers were 3 g/L lower than those of omnivores, in both periods of pregnancy (Crozier et al. 2019).

### Vegetarian Diet in Childhood: Outcomes for Child Growth and Development

As already mentioned, pregnancy and childhood are periods of intense changes, in which the adequate nutritional supply is crucial for normal growth and development. Vegetarian diet, if not properly planned, can cause severe deficiencies in rearing and jeopardize their growth (Farella, Panza, and Baldassarre 2020; Lemale et al. 2018).

Nieczuja-Dwojacka et al. (2020) conducted a study on 218 children from Warsaw aged between 3 and 15 years old, of whom 47 were vegetarians and 171 were non-vegetarians. The objective of the study was to verify if there were differences between these dietary groups in relation to body composition and reaction time. For this, the authors used a questionnaire to parents, that included questions such as date of birth, anthropometric measurements at birth, child's diet, mother's diet, mother's diet during pregnancy, whether the child was breastfed and if so, mother's diet during that period, parent literacy and socioeconomic status. Parameters such as height, weight and skin fat folds were measured in children and BMI was calculated by the research team. Children’s reaction time was assessed by the “QuickStick Ruler” (Nieczuja-Dwojacka et al. 2020).

The results revealed that vegetarian children aged between 3 and 15 years old, were shorter, had a lower BMI, a lower sum of the measured skinfolds and a longer reaction time when compared to non-vegetarians.

On contrary, a cross-sectional study by Weder et al. (2019) regarding the ingestion of vegetarian and vegan diets during childhood revealed that these types of diets can provide the same amount of energy and nutrients as an omnivorous diet, allowing normal growth of the child. Although there were no significant differences between the groups, omnivorous children were those who ingested more protein and fat and vegetarian were those who ingested more fiber and carbohydrates. The study involved collecting data by relatives of children on diet, lifestyle, weight and height of the population in studies according to the inclusion criteria (1 to 3 years old vegetarian, VEG and omnivorous).

In a study including 49 Taiwan children (aged between 2 and 6 years old), 28 children were omnivorous and 21 were vegetarian (of these 18 were OLV and 3 were egg-vegetarians) (Yen et al. 2008). The sample size was a limitation of this study, and the lack of significant difference found may have been due to the small sample size.

Ambroszkiewicz et al. (2011) conducted a study with 90 children from Warsaw (4 - 10 years) 30 vegetarians, 30 normal weight omnivorous and 30 obese omnivorous. They found no significant differences between the vegetarians and omnivorous from normal weight groups with regard to weight, height, BMI and lean mass. However, vegetarians' children had less fat mass than the matched weight omnivorous group.

Despite those observations, the energy and macronutrient content of the different diets were all within the advised daily consumption (Ambroszkiewicz et al. 2011). However, vegetarian children had lower fat intake, lower total cholesterol levels (151.5 ± 18.0 mg / dL), lower low density lipoprotein (81.0 ± 13.6 mg / dL), triacylglyceride (61.6 ± 20.5 mg / dL); ($p < 0.05$) comparing to normal weight omnivores (Ambroszkiewicz et al. 2011). The results

of this study show that the adoption of vegetarian diets during childhood seems healthier than omnivorous diet, not only regarding prevention of obesity, but also dyslipidemia as differences in lipid profile values between groups, were clearly better in vegetarian's children. The vegetarian diet also provided energy and macronutrients within the recommended limits and did not interfere with the child's normal growth (weight, height and BMI without differences between vegetarian and omnivorous children).

## Vegetarian Diets During Early Periods of Development: Health Benefits?

The previous sections describe health outcomes, not always beneficial, that have been found to be associated with plant-based regimens during early periods of development. Despite that, well planned vegetarian diets, including the stricter vegan diets, are considered to be nutritionally adequate and beneficial to health (Melina, Craig, and Levin 2016) and potentially suitable for all stages of the life cycle: pregnancy, lactation, childhood, adolescence and adulthood (Melina, Craig, and Levin 2016).

Vegetable-based diets in childhood can prevent the incidence of cardiometabolic diseases later in adulthood, increasing the average life expectancy (Desmond et al. 2018).

The low amount of saturated fat and the high amount of fiber and phytochemicals found in vegetarian and vegan diets are considered to be responsible for low total cholesterol and low density lipoprotein levels, as well as for a better control of plasma glucose levels (Melina, Craig, and Levin 2016). Transforming growth factor beta 1 (TGF-β1), an anti-inflammatory growth factor that regulates the growth and development of babies, is present in breast milk and in higher concentrations in vegetarian mothers (Alsharnoubi et al. 2019).

Preeclampsia is a disease responsible for maternal and fetal morbidity and mortality (Kuklina, Ayala, and Callaghan 2009). When present, it causes a high risk of fetus prematurity and the onset of cardiovascular disease in the mother in later life (Kuklina, Ayala,

and Callaghan 2009). It is known that overweight during pregnancy is related to higher risk of pre-eclampsia (Pilis et al. 2014) and that vegetarian diet is associated with a low BMI (Pilis et al. 2014). So, a well-planned vegetarian diet during pregnancy could eventually reduce the risk of pre-eclampsia. This should be a matter of further investigation.

Folic acid is a water-soluble vitamin of the B complex that participates in DNA synthesis. Deficient levels of this vitamin during pregnancy is responsible for neural tube defects, an important cause of neonatal mortality and morbidity (Blencowe et al. 2010). LV diet was positively associated with the concentration of folate in the blood (Kehoe et al. 2014). One possible explanation for this, is the fact that vegetarian diets are based on vegetables, which are rich in folic acid.

In addition to folate, vitamin B12 is particularly important for women in reproductive age due to their involvement in fetal growth and development (Chandyo et al. 2016). Chandyo et. al. (2016) assessed vitamin B12 and folate levels in 500 women of childbearing age in Nepal, where diets are mostly vegetarian. The researchers concluded that there was a high prevalence of vitamin B12 deficiency (42%), however folate deficiency was rare (5%).

As vegetarian diets are rich in folic acid, they may have an important role against pathologies associated with its deficiency. This study also reinforces once again the idea that the vegetarian diets are positively associated with the concentration of folic acid, but that it might be necessary to supplement these diets with other essential nutrients, like vitamin B12, in order to achieve healthy diets with the necessary proportions of all nutrients.

According to the World Health Organization (2017), in 2016, 41 million of children in the world were overweight. Childhood obesity is a global epidemic, and an important risk factor for cardiovascular disease, T2D and premature death in adults (World Health Organization 2017). The World Health Organization also reveals that vegetarian diet is

associated with a lower BMI and a better lipid profile (Pilis et al. 2014) and, therefore, the adoption of a vegetarian diet in childhood may be a way of preventing childhood obesity.

## Conclusions

Well planned vegetarianism seems to be safe in all stages of life, however it is known that the absence of meat in the diet makes it difficult to acquire some nutrients and vitamins. The more restricted the vegetarian diet is, the greater the difficulty of obtaining all the necessary nutrients. Therefore, vegetarian diets must be well planned, with the right foods in the right amounts, to avoid nutritional deficits.

Women of childbearing age, pregnant women and children, who follow a vegetarian diet, should seek a professional to assess their nutritional status and control for potential nutritional deficits with have very serious consequences on health, growth and development.

## Unanswered questions

There is globally a lack of knowledge on the practice of vegetarianism, particularly in vulnerable periods of the life cycle, such as pregnancy and childhood.

This review evidences that research endeavors should focus important still unanswered questions:

1) What are the proportion of pregnant women and of children in the different stages of development following any kind of plant-based diets?
2) How can the observed plant-based regimens among those vulnerable population groups be classified in terms of nutritional quality?
3) What are the health outcomes of such dietary regimens according to their nutritional quality?

The answer to these questions should be sought by promoting more observational studies throughout different countries with different cultures and religions, that have the power to describe the population in terms of prevalence of each dietary regimens.

In addition, the creation of dietary quality indexes focused on plant-based diets will find answers to those questions. This indexes will also be a powerful tool that can be used in favor of population literacy to guide their nutritional choices, when adopting specific plant-based dietary regimens.

**Funding**

This work was supported by National Funds through FCT- Fundação para a Ciência e a Tecnologia/MCTES within CINTESIS, R&D Unit (reference UID/IC/4255/2019).

**Declaration of interest statement**

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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*Updated 31-08-2020*

# Adenda ao Projeto/Dissertação MIMED

# Scale for the Assessment of Narrative Review Articles – SANRA

Please rate the quality of the narrative review article in question, using categories 0–2 on the following scale. For each aspect of quality, please choose the option which best fits your evaluation, using categories 0 and 2 freely to imply general low and high quality. These are not intended to imply the worst or best imaginable quality.

Nota: Para a UC de Dissertação/Projecto, todos os seis items devem ser cumpridos em nível 2.

**1) Justification of the article's importance for the readership**

| | | |
|---|---|---|
| The importance is not justified. | 0 | |
| The importance is alluded to, but not explicitly justified. | 1 | 2 |
| The importance is explicitly justified. | 2 | |

**2) Statement of concrete aims or formulation of questions**

| | | |
|---|---|---|
| No aims or questions are formulated. | 0 | |
| Aims are formulated generally but not concretely or in terms of clear questions. | 1 | 2 |
| One or more concrete aims or questions are formulated. | 2 | |

**3) Description of the literature search**

| | | |
|---|---|---|
| The search strategy is not presented. | 0 | |
| The literature search is described briefly. | 1 | 2 |
| The literature search is described in detail, including search terms and inclusion criteria. | 2 | |

**4) Referencing**

| | | |
|---|---|---|
| Key statements are not supported by references. | 0 | |
| The referencing of key statements is inconsistent. | 1 | 2 |
| Key statements are supported by references. | 2 | |

**5) Scientific reasoning**

*(e.g., incorporation of appropriate evidence, such as RCTs in clinical medicine)*

| | | |
|---|---|---|
| The article's point is not based on appropriate arguments. | 0 | |
| Appropriate evidence is introduced selectively. | 1 | 2 |
| Appropriate evidence is generally present. | 2 | |

**6) Appropriate presentation of data**

*(e.g., absolute vs relative risk; effect sizes without confidence intervals)*

| | | |
|---|---|---|
| Data are presented inadequately. | 0 | |
| Data are often not presented in the most appropriate way. | 1 | 2 |
| Relevant outcome data are generally presented appropriately. | 2 | |

**Sumscore** 12

**Fig. 1** SANRA - Scale

Nota 1: O ponto 5 diz respeito à contextualização da evidência científica em relação ao tipo de estudo(s) que a produziu (e, idealmente, à qualidade do(s) mesmo(s)). O ponto 6 diz respeito a sustentar as afirmações com os dados quantitativos mais apropriado. A título de exemplo, para cumprir o ponto 5 e o ponto 6, ao invés de afirmar "já foi evidenciado que os testes de alergia às penicilinas apresentam alta especificidade e moderada sensibilidade", dever-se-á indicar "uma revisão sistemática com meta-análise de acuidade diagnóstica evidenciou que os testes de alergia às penicilinas apresentam alta especificidade (valor meta-analítico: 97%; IC95%=94-98%) e moderada sensibilidade (valor meta-analítico: 31%; IC95%=19-46%).

# SANRA – explanations and instructions

This scale is intended to help editors assess the quality of a narrative review article based on formal criteria accessible to the reader. It cannot cover other elements of editorial decision making such as degree of originality, topicality, conflicts of interest or the plausibility, correctness or completeness of the content itself. SANRA is an instrument for editors, authors, and reviewers evaluating individual manuscripts. It may also help editors to document average manuscript quality within their journal and researchers to document the manuscript quality, for example in peer review research. Using only three scoring options, 0, 1 and 2, SANRA is intended to provide a swift and pragmatic sum score for quality, for everyday use with real manuscripts, in a field where established quality standards have previously been lacking. It is not designed as an exact measurement of the quality of all theoretically possible manuscripts. For this reason, the extreme values (0 and 2) should be used relatively freely and not reserved only for perfect or hopeless articles.

We recommend that users test-rate a few manuscripts to familiarize themselves with the scale, before using it on the intended group of manuscripts. Ratings should assess the totality of a manuscript, including the abstract. The following comments clarify how each question is designed to be used.

### Item 1 – Justification of the article's importance for the readership

Justification of importance for the readership must be seen in the context of each journal's readership.
Consider how well the manuscript outlines the clinical problem and highlights unanswered questions or evidence gaps – thoroughly (2), superficially (1), or not at all (0).

### Item 2 – Statement of concrete/specific aims or formulation of questions

A good paper will propose one or more specific aims or questions which will be dealt with or topics which will be reviewed.
Please rate whether this has been done thoroughly and clearly (2), vaguely or unclearly (1), or not at all (0).

### Item 3 – Description of the literature search

A convincing narrative review will be transparent about the sources of information on which the text is based. Please rate the degree to which you think this has been achieved. To achieve a rating of 2, it is not necessary to describe the literature search in as much detail as for a systematic review (searching multiple databases, including exact descriptions of search history, flowcharts, etc.), but it is necessary to specify search terms, and the types of literature included. A manuscript which only refers briefly to its literature search would score 1, while one not mentioning its methods would score 0.

### Item 4 – Referencing

No manuscript references all statements. However, those that are essential for the arguments of the manuscript – "key statements" – should be backed by references in all or almost all cases. Exceptions could reasonably be made for rating purposes where a key statement has uncontroversial face-validity, such as "Diabetes is among the commonest causes of chronic morbidity worldwide."
Please rate the completeness of referencing: for most or all relevant key statements (2), inconsistently (1), sporadically (0).

### Item 5 – Scientific reasoning

The item describes the quality of the scientific point made. A convincing narrative review presents evidence for key arguments. It should mention study design (randomized controlled trial, qualitative study, etc), and where available, levels of evidence.
Please rate whether you feel this has been done thoroughly (2), superficially (1), or hardly at all (0). Unlike item 6, which is concerned with the selection and presentation of concrete outcome data, this item relates to the use of evidence and of types of evidence in the manuscript's arguments.

### Item 6 – Appropriate presentation of data:

This item describes the correct presentation of data central to the article's argument. Which data are considered relevant varies from field to field. In some areas relevant data would be absolute rather than relative risks or clinical versus surrogate or intermediate endpoints. These outcomes must be presented correctly. For example, it is appropriate that effect sizes are accompanied by confidence intervals. Please rate how far the paper achieves this – thoroughgoingly (2), partially (1), or hardly at all (0). Unlike item 5, which relates to the use of evidence and of types of evidence in the manuscript's arguments, this item is concerned with the selection and presentation of concrete outcome data.

**Fig. 2** SANRA—explanations and instructions document

**SANRA- Justification**

**Item 1**

Page 3: “It has been suggested that vegetarian diets are healthier compared to omnivorous regimens, decreasing the non-communicable diseases burden (Pistollato et al. 2015). In fact, the adoption of vegetarian diets is increasing over the world and it can be estimated that in Europe, the prevalence of vegetarianism (regimens that exclude all kinds of animal flesh) ranges from 1.2%-1.5% in Portugal and Spain, to about 7% in the United Kingdom and 10% in Germany. The prevalence of veganism in Europe (more strict regimens that exclude all types of animal flesh and animal derived products) varies between 1 and 3% (Redecillas-Ferreiro, Moráis-López, and Moreno-Villares 2020).”

Page 3: “Vegetarian adults frequently share their eating patterns with their children because they consider these diets healthier and recognize diet important factor in the management of children´s health (Baroni et al. 2018). However, concerns regarding the deficiency of some vitamins and minerals caused by vegetarian diets raised the scientific discussion about their nutritional adequacy in general but particularly about their putative risks during pregnancy and early life (Ferrara et al. 2020).”

Page 3: “Pregnancy and childhood are periods of great vulnerability and intense transformation, in which adequate nutritional support is essential to sustain health, growth and development of the fetus and the child. Nutritional deficiencies at these stages can have severe consequences. Some of the consequences of malnutrition in pregnancy are the risk of restricted fetal growth, premature birth and maternal mortality (Ramakrishnan et al. 2012), and in childhood nutritional deficiency may impair child's growth and neurodevelopment (Lemale et al. 2018). Therefore, it is necessary to carefully evaluate food adequacy at these critical stages of life.”

Page 18: “**Unanswered questions**

There is globally a lack of knowledge on the practice of vegetarianism, particularly in vulnerable periods of the life cycle, such as pregnancy and childhood.

This review evidences that research endeavors should focus important still unanswered questions:

1)What are the proportion of pregnant women and of children in the different stages of development following any kind of plant-based diets?

2)How can the observed plant-based regimens among those vulnerable population groups be classified in terms of nutritional quality?
3)What are the health outcomes of such dietary regimens according to their nutritional quality?"
The answer to these questions should be sought by promoting more observational studies throughout different countries with different cultures and religions, that have the power to describe the population in terms of prevalence of each dietary regimens.
In addition, the creation of dietary quality indexes focused on plant-based diets will find answers to those questions. This indexes will also be a powerful tool that can be used in favor of population literacy to guide their nutritional choices, when adopting specific plant-based dietary regimens."

**Item 2**

Page 5: "The aim of this study is to revise and discuss recent literature information, about the risks and benefits of vegetarian diets during pregnancy and childhood and their impact on early life and child health and development."
Page 5: "Vegetarian Diets During Early Periods of Development: Major Nutrition Concerns"
Page 9: "Vegetarian Diets During Pregnancy"
Page 10: "Vegetarian Diets During Childhood"
Page 11: "Vegetarian Diets in Pregnancy: Outcomes for Children Health"
Page 14: "Vegetarian Diet in Childhood: Outcomes for Child Growth and Development"

**Item 3**

Page 5: "To conduct this review articles were searched in the Pubmed database with the terms (Vegetarian diets AND fetal programing) OR (Vegetarian diets AND child development) OR (Vegetarian diets AND child growth) between 2010 and 2020, written in English, Portuguese and Spanish. 79 articles were found and 25 were excluded, because they did not address the theme of the study or because were replicates. During the analysis of these 54 papers, other papers 17 were included due to their relevance to the theme. Norms from the General Directorate of Health (DGS) and the World Health Organization (WHO) were also included."

**Item 4**

Page 4: “Pregnancy and childhood are periods of great vulnerability and intense transformation, in which adequate nutritional support is essential to sustain health, growth and development of the fetus and the child. Nutritional deficiencies at these stages can have severe consequences. Some of the consequences of malnutrition in pregnancy are the risk of restricted fetal growth, premature birth and maternal mortality (Ramakrishnan et al. 2012), and in childhood nutritional deficiency may impair child's growth and neurodevelopment (Lemale et al. 2018).”

Page 5: “Although vegetarian diets may represent a healthier dietary pattern protecting from several non-communicable diseases, when compared to omnivorous diets, concerns have been raised regarding its association with nutritional deficiency of some essential nutrients such as vitamin B12, vitamin D, iron, zinc, calcium, iodine and some essential fatty acids (Agnoli et al. 2017; Amit 2010; Craig and Mangels 2009; Lemale et al. 2019).”

Page 9: “Pregnancy is a period of intense transformation, when there is a global increased demand of nutrients essential to support the growth and development of the fetus (Ferrara et al. 2020).”

Page 12: “The existence of nutritional deficits during pregnancy is associated with an increased risk of obesity, T2D, metabolic syndrome and cardiovascular diseases in adulthood (Hanley et al. 2010).”

Page 12: “It was also described in the literature that children of vegetarian and vegan mothers who had B12 deficits during pregnancy have an increased risk of depression in adulthood (Pepper and Black 2011).”

Page 14: “Vegetarian diet, if not properly planned, can cause severe deficiencies in rearing and jeopardize their growth (Farella, Panza, and Baldassarre 2020; Lemale et al. 2018).”

Page 16: “Despite that, well planned vegetarian diets, including the stricter vegan diets, are considered to be nutritionally adequate and beneficial to health (Melina, Craig, and Levin 2016) and potentially suitable for all stages of the life cycle: pregnancy, lactation, childhood, adolescence and adulthood (Melina, Craig, and Levin 2016).

Page 16: “Vegetable-based diets in childhood can prevent the incidence of cardiometabolic diseases later in adulthood, increasing the average life expectancy (Desmond et al. 2018).”

**Item 5**

Page 13: “Crozier et al. (2019) conducted **a prospective cohort study** with the aim of assessing whether the ingestion of vegetarian diet during pregnancy was related to maternal nutritional changes and cognitive functions of children aged six to seven years.
Page 15: “On contrary, **a cross-sectional study** by Weder et al. (2019) regarding the ingestion of vegetarian and vegan diets during childhood revealed that these types of diets can provide the same amount of energy and nutrients as an omnivorous diet, allowing normal growth of the child.

**Item 6**

Page 13: “The results revealed that newborns from complete vegetarians were smaller for gestational age [adjusted odds ratio (ORadj) = 2.51, 95% confidence interval: 1.01, 6.21]. The study also showed that complete vegetarian mothers had a lower gestational weight gain [ORadj = 2.24, 95% confidence interval: 0.95, 5.27].”
Page 14: However, the study found that hemoglobin levels of vegetarian mothers were 3 g/L lower than those of omnivores, in both periods of pregnancy (Crozier et al. 2019).
Page 15: “Despite those observations, the energy and macronutrient content of the different diets were all within the advised daily consumption (Ambroszkiewicz et al. 2011). However, vegetarian children had lower fat intake, lower total cholesterol levels (151.5 ± 18.0 mg / dL), lower low density lipoprotein (81.0 ± 13.6 mg / dL), triacylglyceride (61.6 ± 20.5 mg / dL); ($p < 0.05$) comparing to normal weight omnivores (Ambroszkiewicz et al. 2011).”
Page 17: “The researchers concluded that there was a high prevalence of vitamin B12 deficiency (42%), however folate deficiency was rare (5%). “