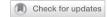
# **REVIEW ARTICLE**



# Impact of organic foods on chronic diseases and health perception: a systematic review of the evidence

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The aim of the present systematic review was to evaluate the existing data on the health impacts, of the consumption of organically grown foods versus conventionally farmed alternatives, with specific focus on the postulated health superiority of organic foods. A systematic literature research was performed in PubMed, Embase, Web of Science, and Google Scholar. Inclusion criteria were articles on adults (>18 years of age) consuming organic foods for ≥6 months, written in English language, and provision of comparative results between conventional and organic nutrition regarding health indices. From 1760 identified references, 21 primary research articles (2006–2022) met the inclusion criteria. Outcomes related to chronic disease prevalence, biomarker effects, and exposure to pesticides and other harmful substances were evaluated. A significant inverse relationship between organic food consumption and cardiometabolic risk factors, including obesity, diabetes mellitus, hypertension, and hyperlipidemia, was observed in the majority of prospective studies. The data on cancer risk and nutrient value comparison between organic and conventional foods were inconclusive. Clinical trials consistently indicated lower pesticide exposure in participants on organic diets, suggesting potential health benefits. The consumption of organic foods is associated with reduced cardiometabolic risks and pesticide exposure. However, the long-term impact on cancer risk remains undetermined. Future long-term studies are needed to establish whether an organic diet is superior to a conventional one in terms of overall health benefits.

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## INTRODUCTION

In the 20th century, during the Green Revolution, the applications of fertilizers, pesticides, and irrigation to create conditions in which modern high yielding varieties could thrive, led to a significant increase in food production and prevented widespread hunger in developing countries [1, 2]. Despite its contribution to increasing yields, it also caused serious environmental problems. More specifically, the excessive and inappropriate use of chemical fertilizers and pesticides, over time, has led to soil degradation, water pollution, undermining of biodiversity and poisoning of land workers. In addition to that irrigation practices have led to the accumulation of salts and the abandonment of some of the best agricultural land [3-6]. In addition, exposure to pesticides has been linked to various diseases, such as cancer, neurodevelopmental disorders, metabolic disorders, birth defects, among others [7-10]. All these effects on health and the environment increased the interest to new production methods, namely organic agriculture, which aim to improve the quality, to protect the environment, and to reduce the use of pesticides in farming.

In the European Union (EU), organic farming is defined by Regulation 2018/848 of the European Parliament and the Council of the EU on organic production and labeling of organic products [11]. According to the Regulation (EU) 2018/848, organic food production is defined as "an overall management system of

agricultural holdings and food production, which combines best practices for the environment and climate change, a high degree of biodiversity, the preservation of natural resources and the application of high standards of animal treatment and high standards of production that meet the demand, from a growing number of consumers, for products produced with natural substances and processes" [11]. Therefore, organic production fulfills a dual social role, on the one hand supplying a specific market that meets the consumer demand for organic products and, on the other hand, offering publicly available goods that contribute to environmental protection and animal welfare, as well as to rural development [11].

The consumer demand for organic food has grown rapidly over the past two decades. This is reflected in the increase in organic cultivated land, organic producers, and the organic market as shown in the latest research by the Research Institute of Organic Agriculture (Forschungsinstitut für biologischen Landbau, FiBL) with data from 190 countries [12]. The total area of organically cultivated land worldwide has increased significantly in the last 20 years from 11 million hectares in 1999 to 74.9 million hectares recorded in 2020 [12]. The regions with the largest organic agricultural land are Oceania, holding almost the 50% of the World's organic land, and Europe with 23% of the global organic cultivations [12]. Organic producers have also increased to 3.4

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million in 2020 from 200,000 in 1999, and it should be noted that the increase is constant, as for 2020 alone an increase of 7.6% was reported compared to 2019 [12]. Organic market as expected is also growing, reaching 120.6 billion euros in 2020 compared to 15.1 billion in 2000 [12].

This systematic review arises from the growing consumer interest in organic products, driven by environmental consciousness, animal welfare concerns, perceived superior taste, and the belief in organic food's health benefits [13–15]. The aim is to critically examine the body of evidence regarding the health effects, both direct and indirect, of consuming organically produced foods as opposed to conventionally produced counterparts, focusing solely on human health studies and excluding considerations of food composition, food safety, or sustainability metrics.

#### **MATERIALS AND METHODS**

This is a systematic review which has been conducted according to the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) guidelines (Supplementary File S1) [16]. The protocol of this study in which the research methodology of the study is described in detail was submitted to Prospero platform (CRD42022361722).

#### Search strategy

A systematic literature review was conducted in PubMed, Embase, Web of Science and Google Scholar up to December 2023, using the following search string for PubMed database: (("organic food") OR ("organic diet") OR ("organic nutrition") OR ("organics") OR ("biologic nutrition") OR ("organic products") OR ("biological products")) AND (("health") OR ("chronic disease") OR (cancer) OR (diabetes) OR (obesity) OR (hypertension) OR (non-communicable diseases), OR (neoplasms) OR (malignancies) OR (onco\*) OR (blood pressure) OR (hypotension) OR (glucose) OR (cardiovascular diseases) OR (heart diseases)), and it has been modified accordingly for the other search databases. The references selected were added to a reference manager software (Endnote X9 for Windows, Thomson Reuters) and were screened manually to obtain possible additional data. All studies obtained from the four databases were pooled together and duplicate articles were removed. Retrieved articles were screened by reading the article "title", "abstract" and "full text". The filtered articles were further screened by reading the individual manuscripts, and those not satisfying inclusion criteria (given below) were excluded. After duplicates removal, the remaining studies were screened for eligibility by two reviewers (DB and KAP). Any disagreements were resolved by the involvement of a third reviewer (MC). Reference lists of the retrieved articles were also screened for other relevant articles. Previews reviews were also investigated for relevant studies and reference searching was also included in the search strategy.

# Inclusion and exclusion criteria

Observational studies, e.g., cross sectional, and prospective studies, and controlled trials (randomized or not) were included in this systematic review. Eligibility criteria were (1) healthy adult population (>18 years old), (2) consuming organic food for ≥6 months, (3) studies focusing on the direct or indirect effect of organic food consumption on human health compared to the conventional food. Studies on individuals following a specific dietary pattern (e.g., pesco-vegeterian, vegetarian, poultry vegetarian, vegan), or who consumed organic foods for <6 months, on individuals with chronic diseases or hospitalized were excluded. There was a limitation to English language, but no limitation on the date of publication.

# Data extraction—quality assessment

Data from the studies included in the final analysis were extracted independently by two reviewers (DB and KAP) in a standardized

Microsoft Excel® form. Any disagreement was solved by consensus. Information extracted from each study were country origin, sex, age, study design, focus of the study, and the relative results. Assessment of the quality of included studies was performed by two authors (DB and KAP) using the Joanna Briggs Institute (JBI) Critical Appraisal tools for cross sectional studies [17]. Any discrepancy was solved by consensus.

#### **RESULTS**

A total of 1760 publications were identified in the databases and 1674 were initially excluded (reviews, editorials, irrelevant articles, and articles with an unavailable abstract). Of the 87 articles selected for further evaluation through abstract reading, 65 were excluded and 22 were included in the final analysis. The articles included have been divided into 3 thematic sections according to the focus of the studies. Ten studies focused on chronic diseases, seven studies on health perception, and seven on exposure to pesticides or other harmful substances. Three studies are repeated in two thematic units [18–20]. The steps followed to select articles are illustrated in the flowchart (Fig. 1).

The main reasons for excluding a study were the non-relevance to human health, studies focusing on the nutritional value of organic food, the sustainability of a diet based on organic food, soil analysis, and comparison or the profile of organic food consumers. Studies examined non-adult population were also excluded from the final analysis. The characteristics of studies included in the systematic review are presented in Tables 1–3.

#### Organic foods and non-communicable diseases

Cancer. Two studies focused on cancer [21, 22]. More specifically, Baudry et al. [20] followed for 7 years a sample of 68,946 adults with a mean age of 44.2 years, who participated in the "Nutri-Net Sante Cohort Study", a French online prospective cohort study. Collected data included information regarding the frequency of consumption for 16 certified organic food products. The results revealed a negative association of high organic food consumption with overall cancer risk [21]. Consumers in the fourth quartile had a 25% lower risk of developing cancer than those in the first (HR for Q4 vs. Q1 = 0.75, 95%CI: 0.63-0.88, p = 0.001), the absolute reduction risk was 0.6%, while for every 5-point increase in biological score (corresponding to frequent consumption of 3 different products) there was an 8% reduction in cancer risk (HR = 0.92, 95%CI: 0.88-0.96) [21]. Translating this into clinical relevance, in a population where the baseline of developing cancer is 4%, in a population of 100 individuals, this reduction would result in 1 fewer cancer case (from 4 to 3). Regarding specific cancer types, the relative HR risk was low for postmenopausal breast cancer (HR = 0.66, 95%CI:0.45-0.96, p = 0.03), non-Hodgkin lymphoma (HR = 0.14, 95%CI: 0.03–0.66, p = 0.049) and all type lymphomas (HR = 0.24 95%CI: 0.09-0.66, p = 0.02) [21]. However, it's essential to consider the multifactorial nature of cancer and how lifestyle and genetic factors may influence individual risk.

In a UK prospective cohort study Bradbury et al. [22] followed 623,080 middle-aged women for an average of 9.3 years, who completed a questionnaire on organic food consumption. The researchers analyzed the relative risks for the occurrence of 16 different types of cancer, and the overall risk of cancer, in relation to the frequency of organic food consumption [22]. The results showed no association between organic food intake and the cancer incidence except for non-Hodgkin lymphoma (RR = 0.79, 95% CI: 0.65–0.96) [22].

Overweight and obesity. The study by Kesse-Guyot et al. [23] investigated the relationship between the frequency of organic food consumption and weight change in a follow-up period of three years. With data from the prospective "Nutri-Net Sante"

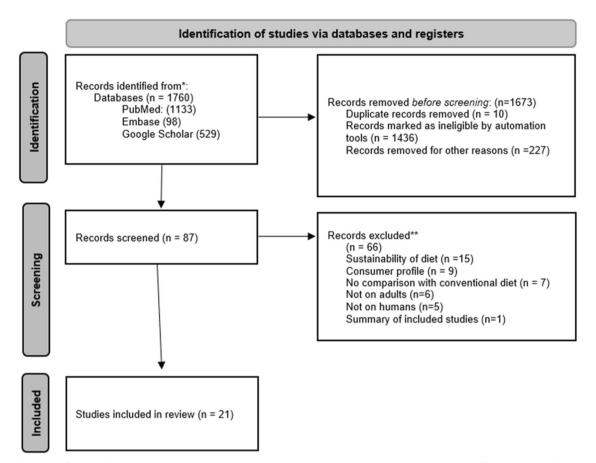


Fig. 1 Flow diagram of the study selection process (From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. https://doi.org/10.1136/bmj.n71).

study, it was reported that high consumers of the "organic diet" demonstrated a significantly lower increase in their Body Mass Index (BMI) over time (Mean difference for Q4 vs Q1 = -16%, 95% CI: -32%, -1%, p=0.05) [23]. Moreover, a significant reduction in the risk of overweight and obesity was also reported for the consumers of the organic food (mean reduction for overweight and obesity was 23 and 31% respectively) [23].

In the retrospective analysis of a sample of 3,896 French people by Gosling et al., greater organic food consumption was associated with lower BMI and lower obesity rates in adults (r = 0.964, with p = 0.013) [24]. Controlling for confounding factors such as physical activity, diet quality, and economic status did not affect statistical significance [24].

Higher consumption of organic food was also associated with lower pre-pregnancy BMI (mean BMI of organic group  $= 22.9 \pm 3.36 \, \text{kg/m}^2$  vs conventional group  $23.8 \pm 3.92$ , p < 0.001), lower incidence of obesity and gestational diabetes in the "Koala birth control study" [18].

Diabetes mellitus and cardiometabolic health. In the study by Kesse-Guyot et al. [25] the association of organic food consumption with type 2 diabetes mellitus (T2DM) was examined in a sample of 33,256 adults from the cohort of "Nutri-Net Sante" prospective study (mean age  $53\pm14$ years), in a follow-up period of 4 years [25]. The results, adjusted for confounding factors such as smoking, alcohol consumption, physical activity, showed an inverse association of high organic food consumption and the risk of developing T2DM [25]. The high consumers had a 35% lower risk than low consumers (95% CI: 0.43–0.97), while for each 5% increase in the percentage of organic food consumption there was a 3% lower risk of developing T2DM (95%CI: 0.95–0.99) [25].

In a cross-sectional study by Sun et al. 8199 adults from USA data were collected regarding organic food provision and consumption, dietary habits, health status, and medical history [26]. There was an inverse association of frequent purchase of organic food and the occurrence of DM with an odds ratio of OR = 0.80, 95%CI: 0.68–0.93 [26].

Baudry et al. [27] evaluated the effect of organic food consumption on DM and cardiometabolic risk factors, hypertension, and cardiovascular diseases (CVD) in a cross-sectional analysis with data from the prospective cohort study "Nutri-Net Sante" in 54,283 adult participants [27]. According to the study, the frequent consumption of organic food was negatively correlated with the risk of T2DM, hypertension and hypercholesterolemia (OR = 0.51, 0.57, 0.75 for women and 0.53, 0, 57, 0.67 men respectively). Regular organic food consumers also reported a lower rate of CVD (OR = 0.50, 95%CI: 0.36–0.69).

Simoes-Wust et al. [18] in the "Koala birth control study" in 1,339 pregnant women reported that high organic food consumption was associated with a lower prevalence of gestational diabetes mellitus and obesity. However, no correlation was found for the risk of hypertension [18]. In another prospective cohort study in 28,192 pregnant women from the "The Norwegian Mother and Child Cohort Study" (MOBA) by Torjusen et al, the consumption of organic vegetables during pregnancy was associated with a lower risk of preeclampsia (OR = 0.79, 95%Cl: 0.62-0.99, p = 0.043) [28]. No associations were found between pre-eclampsia and high consumption of other organic foods or overall organic diet [28].

In a cross sectional and longitudinal study by Aljahdali et al in 6,633 older adults, after four years of follow-up organic food consumption was inversely associated with metabolic syndrome in unadjusted models, but this association lost its significance when confounders were included in the analysis [29].

Table 1. Organic foo	od consumpti	Organic food consumption and non-communicable chronic diseases	ses.		
Researchers/Year of publication	Country	Sample	Disease	Design and duration	Results
Baudry et al. [21]	France	68,946 adults in the "Nutri-Net Sante Cohort Study" (Mean age: 44.2 years, 78% women)	Cancer	Prospective cohort study Web based FFQs for the calculation of the adherence to biological food consumption and categorization in quartiles. Q4 = higher consumption Q1 = lower consumption Duration: 7 years (5/2009-11-2016)	High organic food intake was inversely associated with overall cancer risk (HR for Q4 vs Q1 = 0.75, 95%CI: 0.63–0.88 $p$ = 0.001). Absolute HR reduction 0.6% for an increase of intake for 5 points = 0.92, 95%CI: 0.88–0.96). For specific cancer types: reduced HR (Q4 vs Q1) for postmenopausal breast cancer, non-Hodgkin lymphoma and all lymphomas.
Bradbury et al. [22]	ž	623,080 middle-aged women in the "The Million Women Study"	Cancer	Prospective Cohort study. Questionnaires for the frequency of organic food consumption. Duration: 9.3 years	No association between organic food consumption and cancer risk (RR for usually/ always vs never = 1.03, 95%CI: 0.99–1.07). Inverse association for non-Hodgkin lymphoma (RR = 0.79, 95%CI: 0.65–0.96)
Kesse-Guyot et al. [23]	France	62,224 adults from "Nutri-Net Sante Cohort Study" (mean age 45 years, 78% women)	Obesity	Prospective cohort study Web based FFQs for the calculation of the adherence to biological food consumption and categorization in quartiles. Q4 = higher consumption vs Q4 = higher consumption Weight recording once a year. Mean follow-up time: 3.12 years	Negative association between organic food consumption and BMI increase over time (mean difference Q4 vs Q1 = $-0.16$ , 95%CI: $-0.32$ , $-0.01$ , $p=0.04$ ). Higher consumption of organic foods was associated with a lower isk of overweight and obesity (QR for Q4 vs Q1 = $0.77$ , 95%CI: $0.68-0.86$ and Q4 = $0.69$ 95%CI: $0.58-0.82$ ).
Gosling et al. [24]	France	2121 adults (18–79 years) from the study INCA3 (2014–2015)	Obesity	Cross sectional study. Anthropometry and questionnaires of food habits and lifestyle	Higher consumption of organics food was associated with lower BMI and lower prevalence of obesity. (OR = $0.964$ , $p = 0.013$ )
Kesse-Guyot et al. [25]	France	33,256 adults (mean age 53 years, 76% women) from "Nutri-Net Sante Cohort Study"	T2DM	Prospective Cohort Study. Online completion of questionnaires about diet, lifestyle, health status, anthropometric data, sociodemographic characteristics. Calculation of the percentage of organic food in the diet and categorization in quintiles. Average duration of follow-up: 4 years.	Organic food consumption was associated with a lower risk of developing T2DM (Q5 vs Q1 HR = 0.65, 95%CI: 0.43–0.97. For each 5% increase in organic consumption, 3% lower risk for T2D, 95%CI: 0.95–0.99)
Sun et al. [26]	USA	8199 adults > 20 years old from "National Health and Nutrition Examination Survey"	Diabetes Mellitus	Cross sectional study. Data collection through personal interviews: Questionnaires about purchase and frequency of purchase of organic food, eating habits, health status, medical history.	Inverse association of frequent purchase of organic products with the occurrence of diabetes mellitus (OR = $0.80$ , $95\%$ CI: $0.68-0.93$ ).
Baudry et al. [27]	France	54,283 adults "Nutri-Net Sante Cohort Study"	T2DM, hypertension, cardiovascular disease, food allergies	Cross sectional study. Completion of online questionnaires on frequency of organic food consumption, lifestyle, social characteristics, medical history.	Inverse association between organic food consumption and prevalence of T2DM, hypertension and hyperlipidemia (OR = 0.51, 0.57, 0.75 respectively for women and 0.53, 0.57, 0.67 for men). Fewer regular consumers of organic foods reported having cardiovascular diseases (OR = 0.50, 95%CI: 0.36–0.69) while they were more likely to suffer from food allergies (OR = 1.69 and 1.82 for women and men respectively)

Table 1.   continued					
Researchers/Year of publication	Country	Sample	Disease	Design and duration	Results
Aljahdali AA, et al. [29]	USA	6633 adults (mean age 65.5 ± 0.3 years) for the cross-sectional analysis and a subset of 1637 (mean age 63.8 ± 0.4 years) for the longitudinal analysis from the Health and Retirement Study (HRS), and Health Care and Nutrition Study (HCNS)	Metabolic Syndrome	Cross sectional and longitudinal analysis. Organic food consumption assessed by a binary question. MetS, and its components were assessed at baseline and at the end of the study. Follow up 4 years	Unadjusted models showed inverse cross- sectional associations between organic food consumption and waist circumference, blood pressure, and HbA1C, and positive longitudinal association with HDL cholesterol. No significant associations were detected in the fully adjusted models.
Simoes-Wust et al. [18]	Holland	1339 pregnant women from the "KOALA birth cohort study"	Gestational diabetes, hypertension, overweight/ obesity	Prospective Cohort Study. Questionnaires about eating habits, health, socio-demographic characteristics. Collection of blood samples. Extraction of data on hypertension and diabetes from midwifery reports.	Association of organic food consumption with pre-pregnancy lower BMI (mean BMI of organic group = 22.9 $\pm$ 3.36 kg/m <sup>2</sup> vs conventional group 23.8 $\pm$ 3.92, $p$ < 0.001) and with lower prevalence gestational diabetes and obesity. No association with hypertension.
Torjusen et al. [28]	Norway	28,192 pregnant women from "The Norwegian Mother and Child Cohort Study" (MOBA)	Pre-eclampsia	Prospective Cohort Study, FFQs and Questionnaires on health during pregnancy week 17–22. Data on preeclampsia from the Norwegian Medical Birth Registry.	Choosing organic vegetables during pregnancy was associated with a lower risk of pre-eclampsia (OR = 0.79, 95%CI: 0.62–0.99, $p$ = 0.043). No associations were found for pre-eclampsia and high consumption of other organic foods or overall organic diet
Van de Vijver & Van Vliet [15]	Holland	566 consumers of organic products	Self-reported health perception	Web based survey. Completion by participants of a freely accessible online questionnaire about organic food consumption and perceived health effects	70% of participants reported better overall health and feeling more energetic. 30% reported a positive effect on mental wellbeing, 24% better gastrointestinal function, 19% improved condition of skin, hair, and nails.

nails
HR hazard ratio, OR odds ratio, CI confidence interval, p p-value, RR relative risk, BMI Body Mass Index, TZDM type 2 diabetes mellitus, HbA1c glycosylated hemoglobin.

		For each year the intake and absorption of copper and zinc were not different in the organic and conventional diets. Growing season affected copper uptake and absorption: Uptake higher $(p = 0.001)$ and absorption lower $(p < 0.005)$ in 2008 than 2009	Organic food consumption was inversely associated with blood logCRP and LogCysC concentration. (CRP: $\beta$ = $-0.096$ , 95%C1:0.159, $-0.033$ . CysC. $\beta$ = $-0.033$ , 95%C1: $-0.051$ , $\beta$ = $-0.015$ ). LogCysC not statistically significant after additional adjustments ( $\beta$ = $-0.019$ , 95%C1: $-0.039$ , $-0.000$ )	Organic food consumers had higher blood concentrations of $\alpha$ and $\beta$ carotene, lutein, zeaxanthin, magnesium, and linoleic acid. Lower concentrations in iron, palmitoleic acid, $\gamma$ -linolenic and docosapentaenoic acid. No significant differences were found between the two groups for: $\alpha$ -tocopherol, retinol, cadmium, copper, ferritin, transferrin	No significant differences were observed in plasma carotenoid concentrations between the conventional and organic diet groups	Scenario 1 and 2: Higher probability for organic food consumers to meet or exceed the dietary reference intake for β-carotene. Scenario 2: Higher intakes of lutein and calcium from
	Results	6	Organi inverse logCRF concer 95%CI: β = -0 -0.015 signific adjustr -0.035	Organi higher and $\beta$ . magne Lower palmitt docosa signiff betwee tocoph		Scenar probak consur dietary β-carot intakes
	Intervention	3 diets based on 9 plants. 1st: organic cultivation with animal manure (OA). 2nd: organic cultivation with cover crop (OB). 3rd: conventional cultivation	No intervention	No intervention	3 diets based on 9 plants. 1st: organic cultivation with animal manure (OA). 2nd: organic cultivation with cover crop (OB). 3rd: Conventional cultivation	No intervention
	Design and duration	2 double blind self-comparison trials 1st: January–April 2008 2nd: January–May 2009. For each trial 3 intervention periods of 12 days with "washout" periods of at least 2 weeks. Determination of trace element absorption from fecal excretion by ICP-MS	Cross sectional study FFQs and blood samples	Nested case-control study. FFQs. Categorization into 2 groups: High consumption (>50%) of organic food (n = 150 consumers) and low consumption (<10%) of organic food (n = 150 consumers). Blood samples at fasting stage	Double-blind self-comparison study for 2 consecutive years (from January to April). For each year 3 periods of dietary intervention of 12 days with a "washout" period of at least 2 weeks. Blood sampling on day 1 and day 13 for each intervention period	Use of 2 different databases to assess food consumption and analysis of 2 different scenarios (1st data collection effect scenario); 1st: From the "Belgian National
	Parameter studied	Intake and absorption of zinc and copper	Inflammation biomarkers (CRP and CysC)	Levels of iron, magnesium, copper, cadmium, carotenoids, vitamins A and E and fatty acids.	Plasma carotenoids	Intake of nutrients from conventionally and organically grown vegetables
Organic food consumption and biomarkers.	Sample	17 and 16 healthy adults (age 18–40 years) in two trials	3815 adults, (mean age 64.3 years, 54.4% women) from the "Health and Retirement Study"	300 adults (mean age 58 years, 30% men) from "Nutri-Net Sante Cohort Study"	Two groups of 18 adults (n = 36) (Age 18–40 years)	Representative samples of Belgians $(n = 3,245)$ and Flemish $(n = 522)$ adults (age 18–84 years
ood consump	Country	Denmark	USA	France	Denmark	Belgium
Table 2.   Organic final	Researchers/ Year of publication	Mark et al. [30]	Ludwig-Borycz et al. [31]	Baudry et al. [20]	Søltoft et al. [32]	Hoefkens et al. [19]

Table 2. continued						
Researchers/ Year of publication	Country	Sample	Parameter studied	Design and duration	Intervention	Results
				Food Consumption Survey" (2004, sample of Belgians). 2 non-consecutive 24+ recalls and FFQs. 2nd: The Flemish sample answered a questionnaire on the frequency and quantity of consumption of organic and conventional vegetables (12/2006–2/2007).		organic lettuce ( $\rho$ < 0.001). Similar nutrient intakes from spinach for organic and non-organic consumers. Generally higher intakes for organic consumers, but this is partly due to the generally high vegetable consumption of vegetables in this group
Simoes-Wust et al. [18]	Holland	1339 pregnant women from the "KOALA birth cohort study"	Blood biomarkers	Prospective Cohort Study. Questionnaires about eating habits, health, socio-demographic characteristics. Collection of blood samples.	No intervention	Organic food consumers had higher levels of pentadecanoic acid (an index of dairy intake), linoleic acid, LDL cholesterol, transfats of natural origin and lower levels of partially hydrogenated fats from industry (oleic acid). Also, they had lower plasma levels of homocysteine, 25-hydroxyvitamin D, $\alpha$ -linolenic and arachidonic acid, but the differences were statistically significant only for Statistical significance only for 25-hydroxyvitamin D, pentadecanoic acid and trans-fats of natural origin.

CI confidence interval, p p-value, ICP-MS inductively coupled plasma mass spectrometry, CRP C-reactive protein, CysC C-cystatin.

	Results	Lower urinary concentrations of biomarkers of exposure to pyrethroid pesticides in the organic group compared to the conventional group. Detection frequencies: 3-PBA 81% vs 68%, $p = 0.14$ . Trans-DCCA 16% vs 14%, $p = 0.05$ . 4F-3PBA = 5% vs 4%, $p = 1.0$ . No significant differences were observed for organophosphate pesticides	Lower levels of urinary organophosphates after one week of an organic-based diet. The mean total DAP results for the biological phase were 89% [Mean = 0.032 $\pm$ 0.038 and 0.294 $\pm$ 0.435 for biological and conventional respectively, p = 0.013). For total dimethyl-DAP 96% reduction (Mean=0.011 and 0.252 respectively, $p = 0.013$ ).	Pesticide exposure levels vary across food groups depending on the pesticide being studied. A 100% organic diet appears to reduce overall exposure significantly. Vegetarians appear to be the least exposed of the other groups, due to their tendency to choose organic products more offen.	Among conventional diet consumers, the tertile of highest estimated organophosphate exposure was associated with higher DAP concentrations $(p < 0.05)$ . DAP concentrations were significantly lower in organic food consumers $(p < 0.002)$ . The estimates were verified by the measurements.	Significant reduction in the levels of organophosphate and pyrethroid pesticides after the intervention of organic food
	Intervention	Two groups of 10 women each (organics vs conventional team Participants were asked to include in their diet fresh fruit and vegetables provided by the study weekly (organic in the organic and conventional in the conventional group)	Participants were asked to eat as much as possible (>80%) organic or conventional food for 7 days and then crossed over to the alternative diet for each group for another 7 days	No intervention	No intervention	11 days of conventional diet and 18 days of exclusively organic diet
	Design and duration	Double blind randomized trial. Dietary intervention for 24 weeks during during the 2nd and 3rd trimester of pregnancy. Weekly collection of urine samples	Randomized self-comparison study. 2 phases of dietary intervention (7 days each). Collection of urine samples on day 8 of each phase and completion of questionnaires on factors that may influence chemical exposure.	Cross sectional study Online completion of food consumption frequency questionnaires and for anthropometric data, sociodemographic characteristics, lifestyle, data on pesticide residues in organically grown food extracted from the CVU Stuttgart database.	Cross sectional study, FFQs. Calculation of individual dietary exposure to pesticides by combining data from questionnaires and average organophosphate pesticide residue levels in each food (USDA PDP). Urine samples collection to verify estimates	Self-Comparison Pilot Study. 2-phase dietary intervention and urine sampling in both phases. Dietary diaries for the entire duration of the intervention. Sample analysis. Duration of intervention: 29 days
	Parameter studied	Pyrethroid and organophosphate pesticides in urine	Organophosphate pesticides in urine	Pesticides	Organophosphate pesticides in urine	Pesticides in urine
Organic food consumption and pesticides residuals.	Sample	20 women (18–35 years old) in the first trimester of pregnancy	13 adults (18–65 years)	33,018 adult omnivores, 555 pesco-vegetarians, 501 vegetarians and 368 vegans from the "Nutri- Net Sante Cohort Study"	4,466 adults (Age 45–84 years, 53% women) from the study "Multi-Ethnic Study of atherosclerosis".	2 adults (1 woman & 1 man)
ood consumpti	Country	USA	Australia	France	USA	Switzerland
Table 3. Organic f	Researchers/ Year of publication	Curl et al. [33]	Oates et al. [34]	Baudry et al. [35]	Curl et al. [36]	Göen et al. [37]

97

Table 3. continued	p					
Researchers/ Year of publication	Country	Sample	Parameter studied	Design and duration	Intervention	Results
Rempelos et al. [38]	Greece/ England	27 healthy adults (mean age 27.5 years)	Pesticides in urine	Randomized controlled trial. Dietary intervention lasting 2 weeks. Urine and blood samples. Dietary diaries by the participants before, during and after the intervention	Two groups following a typical Mediterranean type menu. Conventional group: exclusive consumption of conventional food items. Organic group: Exclusive consumption of organic products  Before and after the intervention both groups followed a typical western conventional diet	Mean daily urinary excretion of total pesticides was 91% lower for the Organic group (17 μg/d, 95% CI: 15–19 vs 180 μg/d, 95% CI: 153–208) during the intervention (ρ < 0.0001). The relative reduction in urinary pesticide residue excretion differed significantly depending on the pesticide measured
Hoefkens et al. [19]	Belgium	Representative samples of Belgians ( $n = 3245$ ) and Flemish ( $n = 522$ ) adults (age 18–84 years	Pesticides from vegetables	Use of 2 different databases to assess food consumption and analysis of 2 different scenarios (1st data collection effect scenario, 2nd consumption effect scenario): 1st: From the "Belgian National Food Consumption Survey" (2004, sample of Belgians). 2 non-consecutive 24-h recalls and FFQs. 2nd: The Flemish sample answered a questionnaire on the frequency and quantity of consumption of organic and conventional vegetables (12/2006-2/2007).	No intervention	Higher intakes of pesticides from consumption of non-organic vegetables ( $p < 0.001$ ). But higher nitrate intakes in organic consumers from lettuce due to high consumption, despite the lower nitrate contamination of organic lettuce ( $p < 0.001$ ). Significantly higher intake of lead for organic consumers from carrots due to higher lead contamination of organic carrots

OR odds ratio, CI confidence interval, p p-value, HI hazard index, 3-PBA 3-phenoxy benzoic acid, Trans-DCCA trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid, 4-F-3PBA 4-fluoro-3-phenoxy benzoic acid, DAPs dialkyl phosphate metabolites.

Overall health perception. Van de Vijver and Van Vliet investigated the health perception of a diet based on organic products, based on the self-reported experiences of 566 organic food consumers [15]. Thirty per cent of participants reported experiencing no health effect, while the remaining 70% reported improved general health, resistance to illness and feeling more energetic [15]. Additionally, 30% of the participants reported observing a positive effect on mental well-health, 24% better gastrointestinal function, and 19% improved skin, hair, and nail condition [15].

Biomarkers. Mark et al. examined the effect of organic food on the intake and absorption of zinc and copper [30]. Two doubleblind self-comparison trials were performed in two consecutive years, with three periods of dietary intervention lasting 12 days each and with "washout" periods of at least two weeks [30]. Seventeen and 16, for the first and second trial respectively, healthy men aged 18-40 years followed three different diets based on nine plants either organically grown using animal manure, organically grown using a cover crop, or conventionally grown [30]. The intervention diet was strictly controlled with designated meals delivered at home or eaten under supervision and no other food not provided by the study allowed [30]. No difference was observed between conventional and organic diets in the intake and absorption of copper and zinc [30]. The growing season appeared to affect the absorption and uptake of copper with uptake being higher (p = 0.001) and absorption lower (p < 0.005) in the first than the second year [30].

In a cross-sectional study by Ludwig-Borycz et al., the relationship of organic food consumption and the concentration of inflammatory biomarkers in the blood was evaluated in a sample of 3,815 adults with mean age of 64.3  $\pm$  0.3 years [31]. Based on the results of the study, there was an inverse association of organic food consumption with the logarithm of the concentration of C-reactive protein (CRP) ( $\beta$  = -0.096, 95% Cl:0.159, -0.033) and cystatin C (CysC) ( $\beta$  = -0.033, 95%Cl: -0.051, -0.015) in blood, although after additional adjustments for potential confounders, the statistical significance maintained only for CysC ( $\beta$  = -0.019, 95%Cl: -0.039, -0.000) [31].

In a nested case-control study within the "Nutri-Net Sante" prospective cohort study, Baudry et al. investigated the potential differences in nutritional biomarkers in relation to the frequency of organic food consumption [20]. The 300 participants in the "Nutri-Net Sante Cohort Study" were adults with an average age of 58 years [20]. The volunteers were either high organic food consumers (more than 50% of the total diet) or low organic food consumers (less than 10% of the total diet) [20]. The analysis showed that the high consumers group had higher levels of carotene  $\alpha$  and  $\beta$ , lutein, zeaxanthin, magnesium, and linoleic acid but lower concentrations of iron, palmitoleic acid,  $\gamma$ -linolenic and docosapentaenoic acid [20]. No significant differences were found between the two groups in the concentrations of  $\alpha$ -tocopherol, retinol, cadmium, copper, ferritin, and transferrin [20].

In two double-blind self-comparison studies by Søltoft et al., the intake and plasma concentration of carotenoids in relation to the consumption of organic food was evaluated [32]. The studies were conducted in two consecutive years with a sample of 18 adult men for each year [32]. During the intervention, three different diets were followed, one conventional and two organic, with the latter having differences in the way the plans were grown (farming using animal manure or cover cropping) [32]. According to the results, no significant differences were observed in plasma carotenoid concentrations between the conventional and organic diet groups [32].

Hoefkens et al. calculated and compared nutrient intake from organically and conventionally grown vegetables [19]. Data regarding the frequency and amount of consumption of organic and conventional vegetables were analyzed from a representative sample of 3,245 Belgian and a sample of 522 Flemish adults aged

18 to 84 [19]. The results of the study revealed a higher probability for consumers of organic vegetables to meet or exceed the dietary reference intake for  $\beta$ -carotene [19]. Moreover, higher lutein, and calcium intakes from organic lettuce (p < 0.001) but similar nutrient intakes from spinach were calculated for organic and conventional consumers [19].

In the study by Simoes-Wust et al. which has already been mentioned [18], the researchers examined the relationship between the consumption of organic food and the concentration of biomarkers in the blood. Higher levels of pentadecanoic acid, an indicator of dairy intake, and higher trans fatty acids from natural origin was reported for organic food consumers [18]. Lower plasma levels 25-hydroxyvitamin D, were also observed [18]. These differences were attributed mainly to the different dietary patterns between organic and conventional food consumers [18].

Pesticides residues. Curl et al., in a randomized controlled blind trial examined the exposure of 20 pregnant women aged 18 to 35 years, in their first trimester of pregnancy, to pyrethroid and organophosphate pesticides after a 24-week dietary intervention [33]. Urine analysis showed lower concentrations of biomarkers of exposure to pyrethroid pesticides for the women in the organic group compared to the conventional group [33]. Regarding organophosphate pesticides, no significant differences were observed between the two groups [33].

In another randomized self-comparison study by Oates et al. [34], the organophosphate pesticide exposure of thirteen adults aged 18 to 65 years was studied. The participants were divided into two groups and asked, without changing their eating habits, to consume as much as possible (more than 80% of the total diet) organically or conventionally grown food, depending on the group, for 7 days, and then there was crossover in the alternative for each diet group for another 7 days [34]. According to the analysis of the results, lower levels of organophosphates in urine was reported after one week of an organic-based diet [34]. More specifically, the results of the average total dialkyl phosphate metabolites (DAP) for the biological phase were 89% lower than the conventional (mean Biological = 0.032  $\pm$  0.038 vs mean conventional 0.294  $\pm$  0.435, p = 0.013) [34].

In the study by Baudry et al. the pesticide exposure of people from four different dietary groups, considering the cultivation system of the plant foods consumed was evaluated [35]. A total of 33,018 omnivorous, 555 pesco-vegetarians, 501 vegetarians, and 368 vegans adults from the "Nutri-Net Sante" prospective cohort study were recruited [35]. The results showed that the estimated levels of exposure to pesticide residues varied in the different dietary groups depending on the pesticide studied [35]. An allorganic diet appeared to reduce overall exposure significantly, while vegetarians appeared to be the least exposed of the other groups, due to their tendency to choose organic products more often [35].

In a cross-sectional study by Curl et al. [36], estimated individual exposure to organophosphate pesticides by combining data on the consumption of specific foods and their average levels of pesticide residues in those foods. Data were drawn from the *Multi-Ethnic Study of Atherosclerosis* where 4,466 participants aged 45 to 84 years were recruited [36]. For consumers of conventional diets, the tertile of highest estimated exposure to organophosphates was associated with higher concentrations of DAP metabolites (p < 0.05), while for consumers of organic food the estimated concentrations of DAP metabolites were significantly lower (p < 0.002) [36].

Goen et al. conducted a pilot self-comparison study involving two subjects, one male and one female [37]. The dietary intervention consisted of two phases and lasted 29 days. At the beginning, for 11 days the participants followed a common conventional diet while for the next 18 days they followed a diet based exclusively on organic food [37]. Samples were analyzed to measure pesticides excreted in urine, including DAP and pyrethroid metabolites, chlorinated phenoxycarboxylic acids and glyphosate [37]. The measurements showed a remarkable decrease in the levels of almost all organophosphate and pyrethroid pesticide metabolites after the intervention of the organic diet [37].

Levels of excreted pesticide residues in urine and their association with organic food consumption were also investigated in the randomized controlled blind trial of Rempelos et al [38]. Twenty-seven healthy adults aged from 21–36 years participated in a two-week dietary intervention, where they were randomly divided into two groups, one conventional and one organics [38]. It was observed that the average daily urinary excretion of total pesticides was 91% lower for the organics group (17  $\mu$ g/d, 95%Cl: 15–19) compared to the conventional group (180  $\mu$ g/d, 95% Cl: 153–208) during the intervention (p < 0.0001) [38]. However, depending on the pesticide measured, the relative reduction in urinary pesticide residue excretion varied significantly [38].

In the study by Hoefkens et al, which was also mentioned above [19], the intake of harmful elements from conventional and organic vegetables was assessed. Results associated non-organic vegetable consumption with higher pesticide intakes (p < 0.001) [19]. However, consumers of organic vegetables appeared to take in higher amounts of nitrates from lettuce, due to high consumption, despite the lower contamination of organic lettuce with nitrates (p < 0.001) [19] Also, significantly higher lead intakes were estimated for consumers of organic carrots due their higher lead contamination [19].

According to the assessment of the potential bias, the results showed that all studies were characterized as "good" or "moderate", with a low or moderate estimated risk of bias and there were no studies with a "poor" rating. Summary tables detailing the results of the assessments are presented in Tables 4 and 5.

## DISCUSSION

According to the results of our review on non-communicable diseases, the consumption of organic foods seems to induce positive effects. More specifically, lower risk of cancer, T2DM, overweight and obesity was reported among the organic food consumers, compared to the conventional ones. These results should be interpreted with caution, as studies followed different designs and methodologies. In a previously published review by Magos et al, the same considerations were raised [39].

Moreover, despite the evidence for positive effects of organic food consumption on human health, the potential impact on the validity of the results from lifestyle differences between organic and conventional consumers should not be ignored. Data from the observational studies included in our review ("Nutri-Net Sante Cohort Study", "The Million Women Study", "French Individual and National Food Consumption 3", "National Health and Nutrition Examination Survey", "The Norwegian Mother and Child Cohort Study" (MOBA), "KOALA birth cohort study"), show that regular consumers of organic food generally tend to lead a healthier and more active lifestyle, they usually do not smoke and follow a healthy dietary pattern that includes lower meat consumption and higher consumption of plant products such as vegetables, fruits, whole grains [18, 21-28]. As plant-based diets, namely the Mediterranean diet, the Okinawa diet the DASH diet, vegetarian and vegan diets have been associated with better cardiometabolic health, beter glycemic control and lower incidence of cancer, it is difficult to attribute the positive effect solely to the type of plant products and not on the overall dietary pattern [40-42]. Moreover, it has been reported that organic consumers are mostly vegetarians or vegans [18, 27]. Therefore, it could be assumed that consumers of organic foods are not a representative sample of the population and therefore, it is possible that the observed beneficial results of the studies are due to the healthier lifestyle and not to the direct effect of the organic diet.

In organic farming, the use of chemical fertilizers and pesticides is not allowed. The lower concentration of pesticide residues and heavy metals is one of the most important advantages of organic food. Several dietary intervention studies and some crosssectional studies included in the review studied the exposure of organic and conventional consumers to pesticides by measuring excreted pesticide metabolites in human urine which are considered as exposure indicators. All studies observed a significant reduction in urinary pesticide residue excretion following an organic diet intervention, while cross-sectional studies also estimated lower concentrations of these compounds for organic food consumers compared to conventional ones. Given the complete agreement in results and the experimental design in most studies, which allows establishing the causality of the observed associations, the reduced exposure to a range of pesticides with an organic-based diet is indisputable. This finding is important for human health because of the growing scientific evidence of the negative effects of long-term dietary or occupational exposure to pesticides. Exposure to pesticides has been linked to an increased risk of certain cancers especially non-Hodgkin lymphoma lung cancer and soft tissue sarcoma [7, 8, 43], results which is supported by the results of 2 studies that linked organic food consumption with a reduced risk of cancer [21, 22].

Many organophosphate insecticides and herbicides widely used in agriculture, such as malathion and glyphosate, were classified in 2015 by the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) as potentially carcinogenic [44]. Moreover, many pesticides used in Europe, such as pyrethroids and organophosphates, have been linked to the development of neurodevelopmental disorders [45, 46], while some chemical compounds are acting as endocrine disruptors, causing adverse effects on metabolism, neurological, reproductive cardiovascular, and immune system [9, 47, 48]. In addition to that, pesticide exposure has been linked to Alzheimer's, Parkinson's, amyotrophic lateral sclerosis, asthma, bronchitis, infertility, attention deficit hyperactivity disorder, autism, diabetes, obesity, and birth defects [9, 10].

It should be noted that all food items intended for human or animal consumption in the European Union are subject to a maximum pesticide residue limit (MRL) and values below the MRL are considered safe [49]. In most cases the concentrations do not exceed the MRLs, but a significant percentage of crop samples contain pesticide residues above the legally defined limits [50]. In addition, chemical substances used as pesticides that have been shown to cause hormonal disruptions act in very small doses [43, 51] and even when no effects are observed from the dose of each chemical substance individually, their combination has the ability to produces significant effects [52]. Therefore, the actual health risk from low exposure to pesticides may be underestimated by established safe limits as their additive or synergistic effects are not taken into account.

It is worth noting that the products in which the MRL limits are most often exceeded are fruits and vegetables [50]. Moreover, higher concentrations of pesticides are contained in whole grain products than in processed grains as the outer husk of the grain seeds, which is removed during processing, contains higher levels of pesticides [50, 53]. Therefore, by adhering to the current dietary guidelines that recommend an increase in the intake of whole grains, fruits, and vegetables, consumers are simultaneously being led to an increased exposure to pesticide residues. Data from a recent study suggested that the cardiovascular benefits of fruit and vegetable consumption may be modified by exposure to pesticide residues as a reduced risk of coronary heart disease was associated with high intake of fruits and vegetables with reduced pesticide load [54].

Table 4. Joanna Briggs Institute Risk of Bias Assessment Tool for Prospective and Cross-sectional Studies.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	% Yes	Risk of bias
Baudry et al. (2019)	<b>√</b>	<b>√</b>	х	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	87.,5	Low
Bradbury et al. (2015)	<b>√</b>	<b>√</b>	х	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	87.5	Low
Kesse-Guyot et al. (2017)	<b>√</b>	<b>√</b>	х	<b>√</b>	<b>√</b>	<b>√</b>	х	<b>√</b>	75	Low
Gosling et al. (2021)	✓	<b>√</b>	Х	✓	<b>√</b>	<b>√</b>	✓	✓	87.5	Low
Kesse-Guyot et al. (2020)	<b>√</b>	<b>√</b>	х	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	87.5	Low
Sun et al. (2018)	✓	<b>√</b>	Х	✓	✓	<b>√</b>	✓	✓	87.5	Low
Baudry et al. (2015)	<b>√</b>	<b>√</b>	Х	Х	✓	<b>√</b>	Х	<b>√</b>	62.5	Moderate
Simoes-Wust et al. (2017)	<b>√</b>	<b>√</b>	х	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	87. 5	Low
Torjusen et al. (2014)	✓	<b>√</b>	Х	✓	✓	✓	✓	✓	87.5	Low
Ludwig-Borycz et al. (2021)	<b>√</b>	<b>√</b>	х	<b>✓</b>	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	87.5	Low
van de Vijver et al. (2012)	<b>√</b>	<b>√</b>	х	x	N/A	N/A	х	<b>√</b>	50	Moderate
Hoefkens et al. (2010)	✓	✓	Х	<b>√</b>	N/A	N/A	✓	✓	83.3	Low
Baudry et al. (2021)	<b>√</b>	<b>√</b>	х	<b>√</b>	N/A	N/A	✓	✓	83.3	Low
Curl et al. (2015)	✓	✓	х	<b>√</b>	✓	<b>√</b>	<b>√</b>	✓	87.5	Low
Ali Aljahdali A, et al, 2022	<b>√</b>	<b>√</b>	х	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	87.5	Low

Q1. Were the criteria for inclusion in the sample clearly defined? Q2. Were the study subjects and setting described in detail? Q3. Was the exposure measured in a standardized, valid, and reliable way? Q4. Were objective, standardized criteria used to measure the condition? Q5. Were confounders identified? Q6. Were strategies for dealing with confounding factors mentioned? Q7. Were the outcomes assessed in a standardized, valid, and reliable way? Q8. Were the outcomes assessed in a standardized, valid, and reliable way?

Before advocating the consumption of organic food on a large scale, the high price and low yield of production using organic farming practices, e.g without the use of pesticides and chemical fertilizers, should be considered. The significantly higher cost of organic food compared to conventional food is the main obstacle to the further increase in their demand [55]. According to the International Food and Agriculture Organization (Food and Agriculture Organization of the United Nations, FAO), certified organic products are generally more expensive than their conventional counterparts for the following reasons: (a) limited supply in relation to demand, (b) higher production and labor costs, (c) more difficult post-harvest handling due to the mandatory separation of organic and conventional products, especially for processing and transport, (d) inefficient marketing and distribution chain. However, the cost of production, processing, distribution, and marketing of organic products and therefore their price is expected to decrease in the years to come as the increasing demand is expected to cause an increased production [56]. Another important question that arises is whether organic agriculture has the capacity to provide food for a significant part of the population and whether it would increase or decrease global food security. Overall, yields in organic farming systems are lower than yields in intensive conventional production systems and range from 5 to 34% yields, depending on system and region characteristics [57, 58]. However, data from meta-analyses shows that under certain conditions biological systems can reach near conventional yields [57, 58].

Apart from that, it should also be noted that organic farming increases the risk of microbial contamination. Based on available research, organic vegetables have been found to be higher in *Escherichia coli*, mesophilic bacteria, yeasts, and mold compared to the conventional ones, resulting in higher risk of food borne illnesses [59, 60]. This on its turn can pose significant health risks for vulnerable groups of the population, especially pregnant women, older adults and immunocompromised patients [61]. Therefore guidance relating to safety should be provided to minimize the risks.

# Limitations

The current systematic review attempted to summarize the effects of organic foods in health in adults. Nonetheless, the articles chosen were only in English language, something that could have led to the exclusion of studies in other languages than English. Finally, it should be noted that the studies were characterized of great heterogeneity (e.g., variations in organic farming practices, population demographics,), and different methodologies for the dietary assessment, that did not allow us to perform a meta-analysis in specific areas of interest.

Table 5. Joanna Briggs Institute Risk of Bias Assessment Tool for Patient-Control and Intervention Studies.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	% Yes	Risk of bias
Mark et al. (2013)	<b>/</b>	<b>/</b>	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	Х	<b>√</b>	<b>√</b>	<b>√</b>	90	Low
Soltoft et al. (2011)	<b>√</b>	<b>√</b>	✓	<b>√</b>	<b>√</b>	х	х	✓	<b>√</b>	<b>√</b>	80	Low
Curl et al. (2019)	<b>✓</b>	<b>√</b>	<b>√</b>	✓	<b>√</b>	<b>√</b>	Х	<b>√</b>	<b>√</b>	<b>√</b>	90	Low
Oates et al. (2014)	✓	<b>√</b>	<b>√</b>	х	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	<b>√</b>	90	Low
Goen et al. (2017)	<b>√</b>	<b>√</b>	<b>√</b>	х	<b>√</b>	х	х	<b>√</b>	<b>√</b>	<b>√</b>	70	Low
Rempelos et al. (2022)	<b>√</b>	100	Low									

Q1. Were the groups comparable except for the presence of disease in the patients or the absence of disease in the controls? Q2. Were patients and controls appropriately matched? Q3. Were the same criteria used to identify patients and controls? Q4. Was the exposure measured in a standardized, valid, and reliable way? Q5. Was exposure measured the same way for patients and controls? Q6. Were confounders identified? Q7. Were strategies for dealing with confounding factors mentioned? Q8. Were outcomes assessed in a standardized, valid, and reliable manner for patients and controls? Q9. Was the exposure period of interest long enough to be meaningful? Q10. Was the appropriate statistical analysis used?

Y = Yes, X = No, ? = Unclear, N/A = Not Applicable.

#### CONCLUSIONS

The consumption of organically grown and raised foods is linked to a growing number of important findings about human health. The studies included in the review that measured direct health effects, e.g., those that focused on chronic diseases, were observational and therefore not suitable for inferring a causal relationship between exposure and outcomes. Well-designed controlled clinical trials are necessary to confirm the effects of organic nutrition on health and to determine the causality of the observed associations. In conclusion, although there is some evidence from observational and experimental studies for the superiority of an organic-based diet, the limited number of studies, the design and the inconsistencies between studies make difficult to draw definitive conclusions. Further research and specifically well controlled, long-term dietary intervention studies in humans are needed to answer the question of whether organic foods are superior compared to conventional ones. In addition, before proposing the implementation of organic farming on a large scale, other factors besides health aspects such as food security, food safety, environmental, economic, and social factors should be considered.

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# **AUTHOR CONTRIBUTIONS**

KAP: Conception and design of the systematic review, literature review, study selection, data extraction, quality assessment, manuscript writing. DRB contribution in the study protocol, performed protocol registration, literature review, study selection, data extraction. MA took part in the literature review, study selection, data extraction, quality assessment. EP: Drafted the initial manuscript based on the synthesis of findings. AZ: Drafted the initial manuscript based on the synthesis of findings. MC: Drafted the initial manuscript based on the synthesis of findings literature review, study selection, data extraction. All authors critically reviewed the manuscript for intellectual content, accuracy, and coherence.

# **COMPETING INTERESTS**

The authors declare no competing interests.

#### ADDITIONAL INFORMATION

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