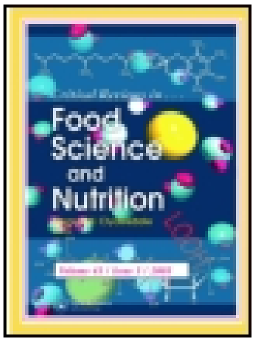

Critical Reviews in Food Science and Nutrition

ISSN: 1040-8398 (Print) 1549-7852 (Online) Journal homepage: http://www.tandfonline.com/loi/bfsn20

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To cite this article: Sara Hurtado-Barroso, Anna Tresserra-Rimbau, Anna Vallverdú-Queralt & Rosa María Lamuela-Raventós (2017): Organic food and the impact on human health, Critical Reviews in Food Science and Nutrition, DOI: 10.1080/10408398.2017.1394815

To link to this article: https://doi.org/10.1080/10408398.2017.1394815

Published online: 30 Nov 2017.

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
https://doi.org/10.1080/10408398.2017.1394815

Organic food and the impact on human health

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ABSTRACT

In the last decade, the production and consumption of organic food have increased steadily worldwide, despite the lower productivity of organic crops. Indeed, the population attributes healthier properties to organic food. Although scientific evidence is still scarce, organic agriculture seems to contribute to maintaining an optimal health status and decreases the risk of developing chronic diseases. This may be due to the higher content of bioactive compounds and lower content of unhealthy substances such as cadmium and synthetic fertilizers and pesticides in organic foods of plant origin compared to conventional agricultural products. Thus, large long-term intervention studies are needed to determine whether an organic diet is healthier than a diet including conventionally grown food products. This review provides an update of the present knowledge of the impact of an organic versus a conventional food diet on health.

KEYWORDS

Polyphenols; pesticides residues; allergies; fertility; cardiovascular; gut microbiota

Introduction

"Organic agriculture is a holistic production management system which promotes and enhances agro-ecosystem health, including biodiversity, biological cycles, and soil biological activity. It emphasizes the use of management practices in preference to the use of off-farm inputs, considering that regional conditions require locally adapted systems. This is accomplished by using, where possible, agronomic, biological, and mechanical methods, as opposed to using synthetic materials, to fulfil any specific function within the system" (FAO/WHO Codex Alimentarius Commission, 1999). Although the practice of organic agriculture has traditionally existed, the modern organic movement began in Europe around the 1920s, at the same time as industrialized agriculture. Nonetheless, this movement became highly regarded in the 1970s due to greater knowledge of the adverse effects of fertilizers and pesticides employed in conventional practices. The use of pesticides became popular during the 1960s, mainly dichloro-diphenyl-trichloroethane (DDT), which was first introduced in the 1940s (Durham, 1963). Nonetheless, since the Haughley experiment performed by Balfour in 1939 (Balfour, 1943), which aimed to compare organic and conventional food systems and to study the relationship between health and the use of organic and conventional chemical-based farming, other studies have been performed with the same objective (Brantsæter *et al.*, 2017). In addition, the growing interest in organic agriculture has promoted the foundation of several institutions such as the International Federation of Organic Agriculture Movements (IFOAM).

Since the beginning of the organic farming system, the production and markets for organic products have grown worldwide. In 2015, the global organic market reached 81.6 billion US dollars (76.8 billion euros), with the United States having the largest market for organic food (FiBL). This amount is between 4.5-fold higher than 15 years ago (FiBL). From 1999 to 2015, the number of countries using an organic agriculture system rose from 77 to 179, and more than 84% of the producers are in Asia, Africa and Latin America, being India, Ethiopia and Mexico the main producers (FiBL). However, the largest area of organic agriculture land is Australia, followed by Argentina, the USA and Spain (FiBL). Wild organic collection areas are concentrated in Europe, Africa, Asia and Latin America (FiBL). Certified organic acreage and livestock have also been expanding, mainly for fruit, vegetable, dairy, and poultry production, accounting for over 4% of the total food sales in the US (USDA ERS).

Despite the higher cost and lower productivity of organic compared to traditional agriculture, the trend to consuming these products is rising every year. Indeed, consumers are prepared to pay a higher price for organic products because they believe organic food is healthier and more sustainable with the environment. Organic foods are generally more natural products and involve less processing than conventional food. They are grown with limited synthetic pesticides or fertilizers or routine use of antibiotics or growth hormones (IFOAM). However, the limited use of pesticides and the use of animal feces may be the main cause of microbiological contamination in organic raw vegetables. Although the majority of studies have reported differences between organic compared to conventional food, there is still no common agreement on this subject. A review on the content of secondary metabolites in organic products stated that in terms of nutritional composition it is still not possible to conclude that an organic production system is better than a conventional system (Barański *et al.*, 2017). The aim of the present review was to evaluate the scientific evidence about the benefits of organic compared with conventionally produced food.

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Results

Lifestyle of organic versus conventional consumers

To compare organic with conventional foods and their effects on health, the characteristics of the subjects who consume the two kinds of food should be taken into account. In order to achieve this goal, a research group from France designed the NutriNet-Santé study (Hercberg *et al.*, 2010), a prospective observational cohort including 500,000 participants greater than or equal to 18 years of age followed over a 10-year period. The NutriNet-Santé study (*Baudry et al.*, 2015; Eisinger-Watzl *et al.*, 2015) showed that organic food is typically more consumed by women compared to men and by people with a high level of education, who are physically active, have a lower body mass index (BMI) and who follow a vegetarian or vegan diet (Eisinger-Watzl *et al.*, 2015). Baudry *et al.* also observed that pregnant women living in rural areas consume more organic food than those living in urban areas (Baudry *et al.*, 2015), contradicting previous research (Torjusen *et al.*, 2010). The relationship between organic consumption and the use of alcohol and smoking is not clear (Baudry *et al.*, 2015; Eisinger-Watzl *et al.*, 2015; Torjusen *et al.*, 2010).

The main reasons why people choose organic food are health and environmental concerns, absence of contaminants in food and taste (Baudry *et al.*, 2017). Organic food is associated with freshness and naturalness, while conventional food is sometimes related to processed food (Baudry *et al.*, 2017). In addition, it has been reported that products of plant origin are more frequently used in this kind of diets compared to products of animal origin (eggs being an exception) (Baudry *et al.*, 2015). Therefore, in general, an organic-based dietary pattern is associated with a healthier lifestyle. However, this association between organic diet and healthier lifestyle should be considered when evaluating the health outcomes of people consuming organic food.

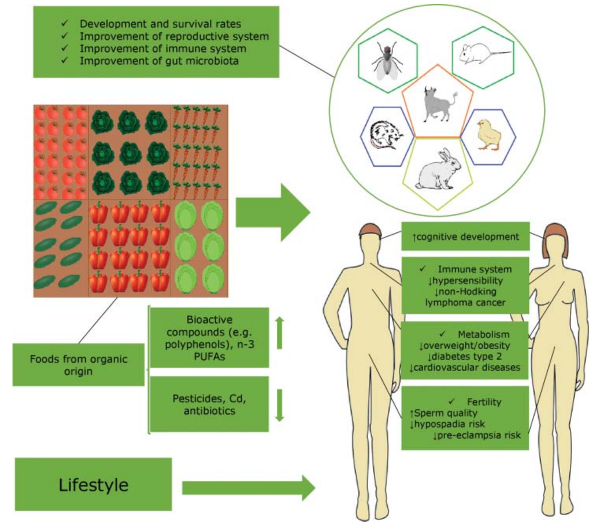

Figure 1. Effects of organic food on animal and human organisms and the possible influence of lifestyle in humans (preliminary results).

Is organic food better in bioactive compounds?

The differences between the quality of organic versus non-organic foods remain unclear, although a meta-analysis concluded that organic foods were richer in some healthy components such as polyphenols and had lower or null pesticide and cadmium (Cd) concentrations (Barański *et al.*, 2014) (see Figure 1). Polyphenols are secreted by plants in response to stress stimuli. Plants such as organically produced foods grown with fewer fertilizers are in a more stressful environment and therefore have higher concentrations of these compounds. Conversely, fertilizer may also reduce the stress of the plants. In addition, long-term use of phosphorus fertilizers can increase the level of Cd in conventional crops (Kratz *et al.*, 2016). Vallverdu-Queralt and Lamuela-Raventós reviewed the outcomes of nutrient content in organic and conventional food by foodomic technologies and concluded that organic crops had less nitrogen and higher levels of polyphenols and carotenoids (Vallverdú-Queralt and Lamuela-Raventós, 2016). However, differences in the protein content of the two crop systems is still not clear (Magkos *et al.*, 2003; Palupi *et al.*, 2012; Vallverdú-Queralt and Lamuela-Raventós, 2016) since the higher protein content in conventional food described in several studies may be, in part, due to the nitrogen content of the fertilizers used (Magkos *et al.*, 2003). However, the quality of protein in organic food is better compared to that of conventionally produced food (Magkos *et al.*, 2003).

Furthemore, differences in fatty acid profiles have been observed. Particularly, organic animal products such as meat and milk have shown a higher content of n-3 PUFA and total PUFA and higher α-linolenic acid, conjugated linoleic acid, vaccenic acid, eicosapentanoic acid and docosapentanoic acid (Palupi *et al.*, 2012; Średnicka-Tober *et al.*, 2016a; Średnicka-Tober *et al.*, 2016b). This is due to forage feeding of organically raised animals. Nonetheless, these differences in n-3 PUFA content and the level of this fatty acid in non-organic meat and milk continue to be too low to have any effect on human health. There also seems to be a trend to higher vitamin C and E and certain mineral concentrations in some organic products (Brantsæter *et al.*, 2017).

Several studies have evaluated the differences between the polyphenol content of organic and conventional grown potatoes, white cabbage, carrots, wheat, pepper, tomatoes, spinach, garlic, bell pepper, maize kernels, red grapes, lettuce, apples, and cauliflowers, as well as tomato-derived foods such as tomato juices and ketchups (Koh *et al.*, 2012; Ren *et al.*, 2001; Vallverdú-Queralt *et al.*, 2012a; Vallverdú-Queralt *et al.*, 2014; Vallverdú-Queralt *et al.*, 2011; Vallverdú-Queralt *et al.*, 2012b; Mitchell *et al., 2007*;Borguini, 2006; Györe-Kis et al., 2012; Stracke *et al.*, 2009a; Roussos and Gasparatos, 2009; Wang *et al.*, 2008; Rosati *et al.*, 2014; Lo Scalzo *et al.*, 2013; Raigón *et al.*, 2010; Rossetto *et al.*, 2009; Carbonaro *et al.*, 2002; Asami *et al.*, 2003 and Lima *et al.*, 2008). Koh *et al.* compared the levels of flavonoids in 27 spinach varieties grown in organic and conventional cropping systems (Koh *et al.*, 2012). The levels of flavonoids were significantly higher in organically grown spinach (40.48 $\pm$ 6.16 and 2.83 $\pm$ 0.03 mg/kg) compared to the conventionally grown product (25.75 $\pm$ 6.12 and 2.27 $\pm$ 0.02 mg/kg). Ren *et al.* determined the polyphenol content of five vegetables grown in organic and conventional cultivation systems commonly consumed in Japan (collard greens, Chinese cabbage, spinach, garlic and green bell pepper) and found the quercetin and caffeic acid content in organically grown plants to be 1.3–10.4 times higher than in conventional plants, suggesting the influence of the different cultivation practices (Ren *et al.*, 2001). Other studies carried out in tomatoes, tomato juices, and ketchups have also reported differences between organic and conventional products (Vallverdú-Queralt *et al.*, 2012a; Vallverdú-Queralt *et al.*, 2014; Vallverdú-Queralt *et al.*, 2011; Vallverdú-Queralt *et al.*, 2012b). One study using a metabolomic approach to identify metabolites with the greatest impact on the overall metabolomic profile of organic versus conventional ketchups (Vallverdú-Queralt *et al.*, 2011) showed that the tomato production system may increase the content of phenols and other metabolites in ketchups. Moreover, the same authors also compared the carotenoid content of organic and conventional tomato-based products (tomato juices and ketchups) (Vallverdú-Queralt *et al.*, 2014) and found statistically higher levels of carotenoid compounds in the organic products. Similarly, Mitchell *et al.* carried out a targeted approach to analyze quercetin and kaempferol levels in tomatoes (Mitchell *et al.*, 2007). The levels of quercetin and kaempferol in organic tomatoes were 79 and 97% higher, respectively, than in conventional tomatoes. Another targeted approach found higher levels of phenolic compounds and ascorbic acid in organic tomatoes (Borguini, 2006). Similarly, Györe-Kis *et al.* recorded a higher content of phenolic compounds in nine cultivars of organic tomatoes in three consecutive years (2008, 2009 and 2010) (Györe-Kis et al., 2012).

Stracke *et al.* evaluated the polyphenol profile of apples (Golden Delicious) grown under defined organic and conventional conditions and described that organically produced apples showed significantly higher concentrations of chlorogenic acid, flavonols, flavanols and dihydrochalcones (Stracke *et al.*, 2009a). However, Roussos and Gasparatos assessed the total phenol, total *o*-diphenol, total flavanol and total flavonoid content in apples cultivated according to organic and conventional procedures and found higher contents in the conventional products (Roussos and Gasparatos, 2009).

In another study, Wang *et al.* evaluated the effects of organic or conventional culture systems on sugar, organic acid, anthocyanin, and phenolic content, as well as antioxidant activity in blueberries and concluded that organically produced fruit had a higher content of phytochemicals (Wang *et al.*, 2008).

Another approach was applied to determine whether organic versus conventional practices affect olive fruit and oil composition in two cultivars (Rosati *et al.*, 2014). The characteristics of the fruit (i.e. fresh and dry weight of pulp and pit, and oil content) did not differ and neither did the oil chemical traits except for an increased content of polyphenols in the organic products. A targeted approach was applied to green Italian cauliflowers (HF1 Emeraude and a local variety, Velox) grown in organic and conventional management systems (Lo Scalzo *et al.*, 2013). Compared to the conventional cauliflowers, organic Velox showed a 21 and 13% higher content of polyphenols and carotenoids, respectively.

Other studies have also reported higher concentrations of total phenolic compounds in organic eggplants (Raigón *et al.*, 2010), beets (Rossetto *et al.*, 2009), peaches and pears (Carbonaro *et al.*, 2002), marionberries (Asami *et al.*, 2003) and miscellaneous plants (Lima *et al.*, 2008).

Organic food and human health

Some studies comparing organic with conventional food have described lower pesticide levels and a higher nutritional value in organic crops, but few clinical and epidemiological studies have been carried out so far. However, dietary intervention and epidemiological studies have observed higher amounts of some bioactive compounds in organic crops, which could be linked to a decrease of the risk of chronic diseases, including cardiovascular and neurodegenerative diseases and certain cancers. This suggests that the consumption of organic food may be beneficial (Johansson *et al.*, 2014).

Nutritional markers in humans

Despite the differences in bioactive compounds described in organic compared to conventional food, the nutritional intervention studies performed so far have not shown a clear association between antioxidant levels in humans and the organic or conventional cropping system (Table 1). Three non-cross-over (Caris-Veyrat *et al.*, 2004; Stracke *et al.*, 2010; Stracke *et al.*, 2009b) and three cross-over trials (Akçay *et al.*, 2004; Briviba *et al.*, 2007; Søltoft *et al.*, 2011) did not observe significant differences in the antioxidant capacity or bioavailability of bioactive compounds such as carotenoids, vitamin C, and polyphenols, while two nutritional cross-over intervention studies observed several significant differences (Grinder-Pedersen *et al.*, 2003; Di Renzo *et al.*, 2007). Grinder-Pedersen *et al.* evaluated the intake and excretion of five selected flavonoids in 16 healthy individuals and the effects on biomarkers of oxidative defense (Grinder-Pedersen *et al.*, 2003). They found the urinary excretion of quercetin and kaempferol to be higher after 22 days of organic food intake. It seems that the conditions of food growth may affect the content of the major flavonoids, quercetin and kaempferol, not only in foods, but also in the excretion of urinary flavonoids and biomarkers of oxidation in humans. In the cross-over study carried out by Di Rienzo *et al.* comparing the consumption of organically and conventionally produced apples in 10 healthy men antioxidant levels in plasma were higher after the intake of organic apples (Di Renzo *et al.*, 2007).

Differences between the two cultivation systems in terms of minerals are not clear. A cross-over intervention trial reported no differences in the intake and bioavailability of copper and zinc in men after consuming organic versus conventional products (Mark *et al.*, 2013). Factors such as the kind of soil could be more significant in mineral concentrations than the cultivation system.

Finally, the cross-sectional KOALA study showed higher levels of vaccenic acid and conjugated linoleic acid in breast milk of lactating women who consumed an organic diet (Rist *et al.*, 2007).

Cropping system and diseases

The first studies to evaluate the effects of organic and conventional practices on health were carried out in animals in the 1930s. Improvement in the growth and survival rates, higher fertility/reproductive function, immune stimulation, lower weight gain and more stress resistance have been the main outcomes described to date in rats, mice, rabbits, chicken and bulls fed by organic systems (Velimirov *et al.*, 2010) (see Figure 1), with these results having been corroborated in more recent studies. Roselli *et al.* showed an enhancement in the immune systems of mice fed with organic carrots compared to those fed with conventional carrots (Roselli *et al.*, 2012). A nutrigenomic approach found differences in the jejunal gene expression involved in cholesterol biosynthesis and immunological process in chickens fed an organic diet (De Greeff *et al.*, 2010). Longer

Table 1. Nutritional markers associated with the organic diet intake in humans: Scientific evidences.

End point	Type of Study	Subjects	Intervention	Outcomes	Reference
Antioxidant status	Non-crossover study	36 healthy men, aged 19–54 years	Consumption of 200 g /day blanched carrots from organic or conventional agricultural systems for 2 weeks with a main meal and with a minimum of 10 g fat.	No effect on the biodisponibility of carotenoids.	Stracke et al., 2009b
	Cross-over study	6 healthy men, aged 23–32 years	Consumption of 1000 g of either organically and conventionally produced apples.	No differences between organic and conventional apples on antioxidant capacity of LDL and DNA damage.	Briviba et al., 2007
	Cross-over study	16 healthy volunteer subjects, aged 21–35 years	Consumption for 22 days of the organic and conventional diet.	Higher urinary excretion of flavonoids, particularly quercetin and kaempferol.	Grinder-Pedersen et al., 2003
	Cross-over study	18 adult and healthy men	Conventional or organic using animal manure or organic using cover crops diet for 12 days.	No differences between the agricultural in plasma status of carotenoids.	Søltoft et al., 2011
	Non-crossover study	20 healthy women, aged 21–39 years	Consumption of 96 g/day of organic or conventional tomato puree for 3 weeks.	No significant difference on plasma levels of vitamin C and carotenoids.	Caris-Veyrat et al., 2004
	Cross-over study	10 healthy men, aged 30–65 years	Consumption of a conventional diet first for first 14 days and then an organic diet for other 14 days.	Higher antioxidant capacity (ORAC) after intake of an organic diet.	Di Renzo et al., 2007
	Non-crossover study	43 healthy men, aged 22–40 years	Consumption of organically or conventionally produced apples (500 g/day; 4 weeks) or no apples.	No difference in the bioavailability of apple polyphenols.	Stracke et al., 2010
	Cross-over	8 healthy volunteer subjects, aged 24–45 years	Consumption of organic red wine (200 mL with alcohol content 24 g in men and 100 mL with alcohol content 12 g in women) and then consumption of non-organic red wine (200 mL with alcohol content 22.4 g in men and 100 mL with alcohol content 11.2 g in women).	No significant differences between two types of wines with respect to LDL-TBARS blood levels.	Akçay et al., 2004
Intake and absorption of minerals	Two cross-over studies	17 and 16 healthy men, aged 18–40 years	Conventional and organic diet and administration of stable enriched isotopes (12 days).	No difference in the intake and absorption of copper and zinc.	Mark et al., 2013
Conjugated linoleic acids in breast milk	Cross-sectional within the study KOALA Birth Cohort Study	312 breastfeeding mothers, 1 month after partum.	Does not apply	Higher rumenic acid and trans-vaccenic acid in human breast milk in the mothers following a diet that contained organic dairy and meat products, in comparison with mothers consuming a conventional diet.	Rist et al., 2007

longevity and fertility were observed in a *Drosophyla melanogaster* fly model incubated in controlled conditions of humidity, temperature and light cycle and fed with homogenized organic food (bananas, potatoes, raisins, soy beans) compared with a conventional diet (Chhabra *et al.*, 2013). Recently, Parelho *et al.* associated higher hepatic lead loads and testicular damage in mice with conventional farming (Parelho *et al.*, 2016). However, Jensen *et al.* observed lower prostaglandin E2 concentrations in rat offspring of mothers fed with the organic plant-based diet compared to those fed with a conventional plant-based diet (Jensen *et al.*, 2013).

In humans, several observational studies have described beneficial effects of organic food on allergic, atopic, eczema and asthma symptoms, as well as other hypersensitivity diseases with the use of immunoglobulin E (Ig E) measurements and questionnaires in children (Alfvén *et al.*, 2006; Alm *et al.*, 1999; Kummeling *et al.*, 2008; Stenius *et al.*, 2011) and adults (Smit *et al.*, 2007) (Table 2). The effects of an organic diet on allergies and atopic diseases were observed mainly in childhood in the PARSIFAL, KOALA and ALADDIN studies. The PARSIFAL (Alfvén *et al.*, 2006) (cross-sectional study) and ALADDIN (Stenius *et al.*, 2011) (prospective study) studies were carried out in children belonging to European families following an anthroposophic or non-anthroposophic lifestyle.

In relation to other diseases, a cross-over study showed a lower risk of developing cardiovascular diseases in both healthy men and patients with chronic kidney diseases after an organic diet (De Lorenzo *et al.*, 2010), while a prospective study did not observe any significant differences in the presentation of cancer in women who ate organic food compared with those who consumed conventional food (Bradbury *et al.*, 2014) (Table 2).

Organic diet on fertility and pregnancy

Table 3 shows the studies related to the effects of organic food intake on fertility and pregnancy in humans. Three cross-sectional studies reported better sperm quality (Abell *et al.*, 1994; Jensen *et al.*, 1996; Juhler *et al.*, 1999) and one described a lower prevalence of previous genital disorders (Jensen *et al.*, 1996) in organic farmers compared to traditional farmers or other workers consuming conventional food. *Larsen et al.* found no significant differences in sperm quality, although organic farmers showed slightly higher inhibin B concentrations and a higher testosterone/sex hormone binding globulin ratio compared to conventional farmers (Larsen *et al.*, 1999). In the two prospective studies within the MoBa study which included a cohort of children and mothers and was aimed at comparing the effects of organic versus conventional food consumption, the risk of pre-eclampsia in pregnant women was found to be lower (Torjusen *et al.*, 2014) as was the risk of presenting

Table 2. Overview of scientifics evidences about the organic food intake on the risk of diseases in humans.

End point	Type of Study	Subjects	Intervention	Outcomes	Reference
Hypersensitivity diseases	Cross-sectional study	675 children, aged 5–13 years, at anthroposophic and neighbouring schools	Does not apply	Lower prevalence of atopy in children from anthroposophic families than in children from other families	Alm et al., 1999
	Cross-sectional study within the PARSIFAL study (Prevention of Allergy Risk factors for Sensitization In children related to Farming and Anthroposophic Lifestyle)	14893 children, aged 5–13 years, from families with an anthroposophic lifestyle compared with children from appropriate reference groups	Does not apply	Lower prevalence of allergic symptoms and sensitization in children with anthroposophic lifestyle	Alfvén et al., 2006
	Cross-sectional study	1798 male adults, conventional and organic farmers	Does not apply	Lower wheezing with shortness of breath in organic farmers than in conventional farmers, suggesting a lower risk of asthma-like symptoms in organic farmers	Smit et al., 2007
	Prospective study within the ALADDIN study (Assessment of Lifestyle and Allergic Disease During Infancy)	330 children from families with an anthroposophic, partly anthroposophic, or nonanthroposophic lifestyle	Does not apply	Reduced risk of IgE sensitization already in infancy is associated with anthroposophic lifestyle	Stenius et al., 2011
	Cross-sectional study within the KOALA Birth Cohort Study in the Netherlands	2764 children, aged 2 years	Does not apply	Lower eczema risk was associated with consumption of organic dairy products	Kummeling et al., 2008
Cancer	Prospective study	623 080 middle-aged women	Does not apply	Slight or no decrease in the incidence of cancer associated with consumption of organic food, except possibly for non-Hodgkin lymphoma	Bradbury et al., 2014
Cardiovascular diseases	Cross-over study	100 healthy male individuals, aged 30–65 years and 50 male patients with Chronic Kidney Disease but stable renal function, aged 42–54 years	Consumption of mediterranean diet with conventional and organic products for 14 days each intervention	The Italian Mediterranean Organic Diet reduces total homocysteine, phosphorus, microalbuminuria levels and CVD risk in healthy individuals and in CDK patients	De Lorenzo et al., 2010

Table 3. Overview of scientifics evidences about the organic food intake on fertility and pregnancy in humans.

End point	Type of Study	Subjects	Intervention	Outcomes	Reference
Sperm quality and reproductive hormones	Cross-sectional study	30 male organic farmers (aged 28–44 years) and 73 blue-collar workers (aged 20–50 years)	Does not apply	Higher sperm quality in organic farmers	Abell et al., 1994
	Cross-sectional study	55 male organic farmers (aged 20–45 years) and 141 healthy men and working in an airline company (aged 23–43 years)	Does not apply	Higher sperm concentration and lower prevalence of previous genital disorders in men eating organically produced food.	Jensen et al., 1996
	Cross-sectional study	256 male farmers (171 traditional farmers and 85 organic farmers), aged ≤50 years	Does not apply	Lower proportion of morphologically normal spermatozoa in the group of men without organic food intake	Juhler et al., 1999
	Cross-sectional study	256 male farmers (171 traditional farmers and 85 organic farmers), aged ≤50 years	Does not apply	Slight differences in concentrations of reproductive hormones, but no significant differences in semen quality between organic and traditional farmers.	Larsen et al., 1999
Pre-eclampsia	Prospective cohort study within the Norwegian Mother and Child Cohort Study (MoBa)	28 192 pregnant women (nulliparous)	Does not apply	Lower risk of pre-eclampsia who reported frequent consumption of organically produced vegetables in pregnant women.	Torjusen et al., 2014
	Case-control study	306 mothers of boys operated for hypospadias and 306 mothers of healthy boys	Does not apply	Higher prevalence of hypospadias was associated with the consumption of high fat products and nonorganic milk and eggs diary	Christensen et al., 2013
Hypospadias and cryptorchidism	Prospective cohort study within the Norwegian Mother and Child Cohort Study (MoBa)	35107 mothers of singleton maleinfants	Does not apply	Lower prevalence of hypospadias was associated with the organic consumption, particularly organic vegetables and milk and dairy products, but it was not associated with the prevalence of cryptorchidism.	Brantsæter et al., 2016

hypospadias in male infants of mothers eating organically produced food (Brantsæter *et al.*, 2016). Likewise, another case-control study associated non-organic animal products such as milk and eggs with a higher prevalence of hypospadias (Christensen *et al.*, 2013) (Table 3).

Furthermore, it has been demonstrated that pesticides induce adverse health outcomes, such as neurotoxic effects and lower intellectual development (Ross *et al.*, 2013). Thus, in order to decrease the risk of developing certain diseases, dietary exposure to pesticide residues should be reduced, especially among pregnant women and children.

Pesticides: Are they really dangerous?

It is known that the widespread distribution of pesticides in food production could have possible long-term effects, triggering the development of diseases. A controlled study carried out by 85 traditional farmers using pesticides and 36 organic farmers not using pesticides living in the same geographical area showed that the use of pesticides induces genotoxic effects, immunological alterations and genetic damage (Costa *et al.*, 2014). In the Children's Pesticide Exposure Study (CPES), Lu *et al.* studied in 23 children aged 3–11 years who consumed only a conventional diet (Lu *et al.*, 2006; Lu *et al.*, 2008; Lu *et al.*, 2010). The children were fed an organic diet for 5 consecutive days after which several urinary metabolites of organophosphorus pesticides commonly used throughout the world were measured. The children were found to have lower pesticide levels in urine following the organic diet intervention. Likewise, an organic diet was associated with lower urinary pesticides in 4,466 participants aged 45–84 years included in the Multi-Ethnic Study of Atherosclerosis (MESA) (Curl *et al.*, 2015). Additionally, in a prospective, randomized, cross-over study in 30 healthy adults following a diet including at least 80% organic or conventional food during a period of one week, a reduction in organophosphorus metabolite concentrations was observed in the urine of the subjects consuming the mainly organic diet (Oates *et al.*, 2014). A recent report to the European Parliament declared that the risk to human health due to pesticide exposure is far lower for organic than for conventional food (EPRS, European Parliamentary Research Servive and STOA, Scientific Foresight Unit).

Use of antibiotics in food-producing animals from organic and conventional farming

At present, the use of antibiotics in farming is controlled and a withdrawal time has been defined for each drug used in food-producing animals. Nevertheless, several studies have reported a lower efficiency of antibiotic treatment in human medical care because of the use of antibiotics in livestock (Martinez, 2009; Laxminarayan *et al.*, 2013; STAG-AMR, WHO), while other studies found no association between the use of antibiotics in farm animals and drug resistance in humans (Mather *et al.*, 2012; Mather *et al.*, 2013). According to European Legislation, both organic and conventional farming can use antibiotic treatments in animals with diseases (EC, The Council Of the European Union, 2007). However, unlike conventional practices, the use of antibiotics as subtherapeutic prophylactic treatment is forbidden in organic farming (EC, The Council Of the European Union, 2007).

The use of antibiotics is strongly associated with housing in intensive livestock production such as in conventional farming practices. In order to increase production levels, resources such as space and feed are restricted, leading to animal stress and a higher risk of developing diseases requiring antibiotic treatment (Colson *et al.*, 2006; EFSA, 2007).

Risk of microbiological contaminations: Are there differences between organic and conventional food?

This issue is controversial especially taking into account what happened in Europe in 2011 when 3,950 people were affected by *Escherichia coli O104:H4* bacteria and 53 died. This outbreak of foodborne disease was caused by an enteroaggregative *E. coli* (EAEC) strain that had acquired genes producing Shiga toxins present in organic fenugreek sprouts (King *et al.*, 2012).

Contamination by microorganisms such as *E. coli O157:H7* and mycotoxins is more frequent in organic food (Ceuppens *et al.*, 2014; Gomes *et al.*, 2012; Maffei *et al.*, 2013; Oliveira *et al.*, 2010; Kuzdraliński *et al.*, 2013; Piqué *et al.*, 2013). Studies from different areas of the world have shown a greater prevalence of *E. coli* in organic lettuce samples compared to lettuce from conventional agriculture (Ceuppens *et al.*, 2014; Gomes *et al.*, 2012; Maffei *et al.*, 2013; Oliveira *et al.*, 2010). However, a study performed in Canada comparing the levels of *E.coli* in organic and conventional fresh produce samples found no differences between the two groups (Bohaychuck *et al.*, 2009). Khalil and Gomaa detected a higher amount of *E. coli* in leafy greens from Egypt when they were produced by a conventional versus an organic system (Khalil and Gomaa, 2014). Other authors have reported that the microbiological quality and safety of fresh vegetables are not affected by organic or conventional farming practices (Tango *et al.*, 2014; Marine *et al.*, 2015; Kuan *et al.*, 2017). Ürkek *et al.* described significantly lower total aerobic mesophilic bacteria, coliform and yeast and mold counts in raw milk of organic origin in Turkey; however, somatic cell and *Staphylococcus aureus* counts were higher in organic milk (Ürkek *et al.*, 2017).

Mycotoxin levels in organic and conventional food differ. Kuzdraliński *et al.* studied the mycotoxin content of organic and conventional oats from Poland and observed that the number of mycotoxin-positive samples was higher in organic compared to conventional farming (Kuzdraliński *et al.*, 2013). However, the concentration of diacetoxyscirpenol, a mycotoxin from Fusarium, was four times lower in organic oats (Kuzdraliński *et al.*, 2013). A study carried out by Piqué *et al.* showed a higher incidence and concentration of another type of mycotoxin called patulin in organic apple purees compared to conventional purees (Piqué *et al.*, 2013).

Despite evidence indicating the higher risk of microbiological contamination in organic products, the wide use of antibiotics in conventional practices has been associated with the presence of antibiotic-resistant microorganisms in animal products (Saptoka *et al.*, 2014).

Does organic food benefit the gut microbiota?

Several ongoing studies are currently investigating the relationship between diet and the gut microbiota. There is strong evidence regarding the role of gut microbiota in health and its implication in immune-related disorders such as type 2 diabetes and obesity, as well as the risk of developing cardiovascular disease (Tai *et al.*, 2015; Miele *et al.*, 2015). Although the direct effects of an organic diet on the gut microbiota are not yet known, some studies have described a beneficial influence (Figure 2).

The diversity of microbials in soil varies in organic compared to conventional farming (Ottesen *et al.*, 2009; Hartmann *et al.*, 2014). Torjusen *et al.* hypothesized that an organic diet may be associated with a more diverse microbiota due to the intake of probiotic substances from fresh produce such as vegetables (Torjusen *et al.*, 2014). Pesticides and cooking practices have also been associated with the gut microbiota. When food is fermented, pesticide concentrations may be decreased, but may, at the same time, slow the fermentation process by yeast (Regueiro *et al.*, 2013). Polyphenols have been positively related to gut microbiota by the reciprocal relationship that they may contribute to host health benefits (Ozdal *et al.*, 2016; Conlon and Topping, 2016; Xue *et al.*, 2016). The higher polyphenol content of organic compared with conventional food could be an advantage to the development of healthy microbiota.

Hartmann *et al.* (Hartmann *et al.*, 2014) demonstrated that the use of fertilizers and particularly the application and quality of organic fertilizers, is the major determinant of the microbial diversity of soil. A review by Jin *et al.* reported that exposure to environmental pollutants can alter the composition of the gut microbiome, leading to disorders of energy metabolism, nutrient absorption and immune system function or other toxic symptoms (Jin *et al.*, 2017). Conventional cropping practices

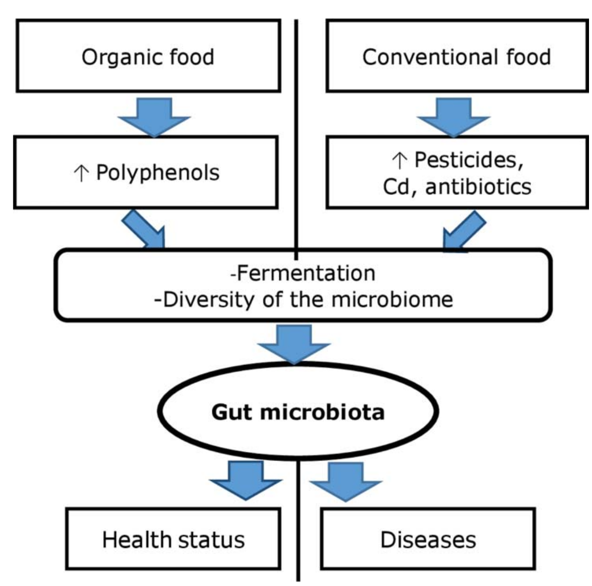

Figure 2. Mechanisms through which organic and conventional food could have effects on the gut microbiota contributing to health and unhealth status respectively (preliminary results).

are related to the use of environmental pollutants such as pesticides (mainly in vegetables and fruits), antibiotics (in meat and milk after administration to animals) and probably a larger amount of some heavy metals (e.g. Cd). Moreover, conventional food is often more processed and is more likely to contain food additives. Several studies in animals showed the potential of pesticides to change the gut microbiota and induce symptoms such as neurotoxicity, hepatotoxicity, immunotoxicity, reproductive toxicity and endocrine disruption because of the antimicrobial activity of some of these pesticides (Jin *et al.*, 2017). In the early 1950s, antibiotics were used by farmers to promote livestock growth. Nowadays, it is known that antibiotics can influence energy metabolism by affecting the gut microbiome (Jin *et al.*, 2017). In addition, the effects of antibiotics on human gut microbiota can persist over longer periods of time (Jakobsson *et al.*, 2010; Fouhy *et al.*, 2012). Exposure to heavy metals and food additives (e.g. non caloric artificial sweeteners and emulsifiers) can also lead to gut microbiota dysbiosis and induce immune-related disorders (Jin *et al.*, 2017).

Thus, it seems that conventional food has indirect negative effects on the gut microbiota because of the toxic components used in cropping. In addition, more diverse microflora has been observed in children from anthroposophic families, as well as a lower incidence of hypersensitivity diseases (Penders *et al.*, 2007). Furthemore, Torjusen *et al.* hypothesized that the incidence of pre-eclampsia could also be related to an altered microbiota (Torjusen et al., 2014). All these aspects should be explored in specific studies aimed at elucidating the role of organic food on human gut microbiota.

Conclusion: Is organic food really healthier?

Organic food seems to be healthier compared to conventional food due to its higher content of bioactive compounds (e.g. polyphenols, vitamin C and carotenoids) and n-3 PUFA, which could be implicated in the incidence of metabolic diseases. Moreover, organic food has a lower Cd content and other unhealthy substances such as pesticides that are related to gut microbiota dysbiosis and immune-related disorders and toxicity in humans.

However, the health outcomes reported by some studies could also be closely linked to the lifestyle of organic food consumers. A lower incidence of metabolic diseases such as cardiovascular diseases, diabetes mellitus type 2 and overweight or obesity can be the result of following a healthy dietary pattern. The diet of consumers of organic foods is richer in fruits, vegetables, legumes and wholegrains and lower in meat intake. Moreover, the greater content of dietetic fiber in organic food may have a positive effect on the gut microbiota and health, reducing the risk of diseases.

Although several studies have attempted to associate health-related biomarkers (such as antioxidant activity and status, LDL oxidation, semen quality, homocysteine, among others) with organic diet intake, the results remain unclear. Thus, at present, pesticide concentrations are the most commonly used biomarkers of conventional food intake.

Few studies have analyzed the effects of organic cropping on health and most of these studies have some limitations such as the short study duration or that they did not take into account crop variety, soil type, weather, climatic conditions and other factors which might affect crop composition. Therefore, long-term, randomized, controlled dietary intervention trials comparing organic and conventional food of the same variety and similar growing conditions are needed to determine the possible beneficial effects of organic diet on human health.

Funding

This work was supported in part by Ministerio de Economia y Competitividad (MCOC) under grant AGL2016-75329-R, Generalitat de Catalunya – Departament d'Agricultura, Ramaderia, Pesca i Alimentació – Direcció General d'Agricultura i Ramaderia under grant 53 05012 2016 and Centro de Investigación Biomédica en Red Fisiopatología de la Obesidad y Nutrición (CIBEROBN) from the Ministerio de Economía, Industria y Competitividad (MINECO) and Fondo Europeo de desarrolo regional/ Fondo social europeo, Unión Europea (FEDER/FSE, UE). The CIBEROBN is an initiative from the Instituto de Salud Carlos III (ISCIII).

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