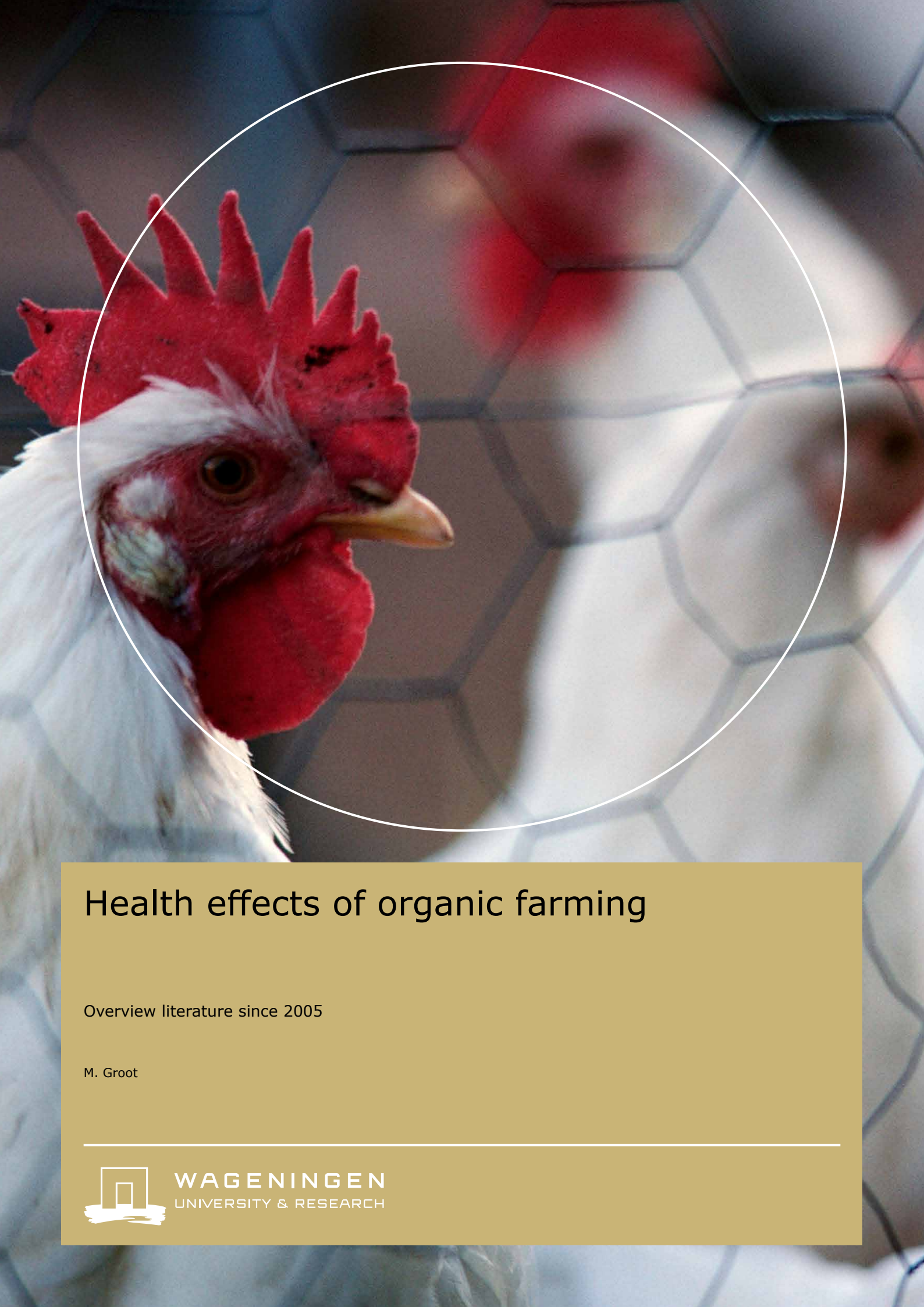

Health effects of organic farming

Overview literature since 2005

M. Groot

WAGENINGEN
UNIVERSITY & RESEARCH

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Contents

Glossary of terms

Allergic sensitization: the recognition of a specific allergen and the increasingly severe reaction to it. For an immunologically allergic reaction, the immune system must have had previous contact with the specific allergen.

Antioxidant: a substance that prevents oxidation. Antioxidants include all substances that can trap free radicals. These are harmful particles that can attack the cells of organisms.

Atopic reactions: this form of allergy is specifically directed against harmless substances found in the environment, such as dust mites or pollen from grass or trees. This condition is exclusive to an IgE-mediated reaction, in which histamine is released from mast cells and causes symptoms such as skin rashes, eczema, and an irritated upper respiratory tract.

Basal cell carcinoma: a form of skin cancer.

Biomarker: a biomarker, or biological marker, generally refers to a measurable indicator of some biological state or condition. Biomarkers are often measured and evaluated to investigate regular biological processes, pathogenic processes, or pharmacological responses to a therapeutic intervention. Biomarkers are used in many scientific fields.

BMI: body mass index: an internationally used measurement method that shows whether you have a healthy weight in relation to your height. For adults, a healthy BMI is between 18.5 and 25. From 25-29.9 is considered overweight. A BMI that is higher than 30 is considered severely overweight (obesity).

Campylobacter: is a group of gram-negative bacteria that is among the causative agents of the most common zoonoses. Infection of humans occurs through contaminated food (foodborne infection), water, and contact with animals and the feces of infected humans. It manifests as acute, watery, and sometimes bloody diarrhea with severe abdominal cramps and fever.

Cardiovascular disease: diseases that involve the heart or blood vessels.

CFU: colony-forming units: a measure of the number of living microorganisms in a sample.

Challenge: intentional intervention to see how the body responds: here an intramuscular injection of an immune-stimulating protein from the non-pathogenic, T-cell-dependent protein keyhole (protein-keyhole)(Limpet hemocyanin (KLH) in 1 ml of PBS per animal.

Cohort study: a research method in which researchers look at factors in a specific period in the future (prospective) or the past (retrospective). A cohort study is a kind of longitudinal study, commonly used in medicine and social sciences in which all individuals in a particular age group are followed for several months or years.

ESBL: Extended-spectrum beta-lactamase is a name for a group of enzymes made by bacteria (the ESBL-forming bacteria). These enzymes are capable of hydrolyzing the antibiotic group’s cephalosporin and penicillin (the β-lactam antibiotics), rendering them ineffective.

Phenols: a phenol is an organic connection produced by plants as a secondary plant substance (metabolite), that is, a substance that does not perform a function in the primary metabolism of the plant. Around 8,000 natural phenols are known.

Hypospadias: congenital abnormality of the urethra in boys.

Human cell lines: cultured human cells used in medical laboratory research. Many of these cells are "immortal," meaning that the cells continue to divide and multiply forever.

Longitudinal research: research that involves following the same subjects over time and examining them at fixed times, usually spread over several years.

Metabolic syndrome: a chronic metabolic disorder. Major symptoms include insulin resistance, glucose intolerance, hyperinsulinemia, high blood pressure, and dyslipidemia. The syndrome is associated with type 2 diabetes.

Neurodegenerative disorders: a collective term for several conditions that have the commonality that they primarily affect neurons in the brain. Neurons cannot normally divide nor be replaced. So when they become damaged it leads to incurable and debilitating diseases, causing problems with movement (ataxia) or mental functioning (dementia).

Non-Hodgekin lymphoma: cancer of the blood and lymphatic system. Can also be described as lymphoma.

Organophosphates: biocides based on organophosphorus compounds. These inhibit the enzyme acetyl-cholinesterase, causing an accumulation of the neurotransmitter acetylcholine.
Most organophosphate pesticides are insecticides (biocides).

PBS: Phosphate Buffered Saline. This is a buffer solution used in biological research.

Pre-eclampsia: a serious complication of pregnancy. By definition, the syndrome is characterized by high blood pressure and protein in the urine, occurring after the twentieth week of pregnancy.

Sociodemographic characteristics: includes age, gender, marital status, and family composition; the main socioeconomic characteristics of a target population are income, education, profession, religion, and social class.

SRBC: red blood cells from sheep are used in biomedical research as an antigen to evoke an immune response.

Targeted: research on a specific component, e.g. the amino acid methionine. Untargeted means looking broadly, e.g. at all nitrogen compounds

Type 2 diabetes: age-related diabetes or Diabetes Mellitus occurs when insufficient insulin is produced by the pancreas and/or when insulin stops working properly. In both cases, insulin can no longer ensure that glucose is absorbed from the blood into the tissues and that the production of glucose by the liver is inhibited. As a result the concentration of sugar in the blood increases and we can conclude that diabetes is present.

Summary

In November 2020, the TV program Zembla focused on the research "Biologically healthier" by former project leader Dr. Machteld Huber of the Louis Bolk Institute. TNO and WUR were also involved in the aforementioned research. The program was critical of the study and in particular of how the conclusions were drawn and communicated. Chickens fed organic feed showed a stronger immune response than their counterparts who did not receive the organic feed. This was in combination with a faster recovery after treatment with a foreign substance. Researchers concluded that these findings indicated a positive effect, but that the study required follow-up research to draw firm conclusions. Follow-up research did not take place, possibly because the differences found were considered too small and both groups of chickens were considered healthy. In the broadcast by Zembla this decision was deemed unjustified. In response, a study has now been carried out to determine whether, in view of current knowledge, follow-up research is warranted.

This report provides an overview of the original research data, recent literature, and public reports. After Huber's research, no comparable animal tests were carried out with organic and conventional feed. It is precisely in the case of animals that only the feed can differ, which can provide insight into the effects of using only organic nutrition. However, research has been done on the differences in composition between conventional and organic products. Human cohort studies have also been carried out on the effects of organic food on health parameters and the occurrence of various types of cancer. The problem with studies in humans is that there is often a lifestyle related to a particular diet. The various human studies differ in design, parameters investigated, and duration, making the results difficult to compare.

Conclusions
Although most researchers are very cautious about concluding the health effects of organic food, there are several relevant findings, most of which are related to the organic production method:
- Organic food contains no synthetic chemical crop protection agents and fewer biocides than conventional food.
- Organic food contains more antioxidants than conventional food.
- Organic foods contain fewer antibiotic-resistant germs than conventional foods.
- In terms of composition, organic food contains more phenols than conventional food, and milk has a more beneficial fatty acid pattern.
- There are some indications that eating organic food leads to a lower risk of developing certain conditions, such as allergies, metabolic syndrome and obesity, and certain cancers.

Whether these effects are a direct effect of the organic diet, the reduced levels of contaminants or the often different lifestyle of consumers who eat organic are not entirely clear. But the indications point to a positive health effect and call for further research.

Recommendations for further research
The following recommendations emerged from the reviewed literature and its analysis:
1. Conduct research with animal models involving both organic and regular feeding to gain insight into research directions that may be relevant to human public health (Dangour et al., 2010). For example, the pig study as recommended in the original Report Biologisch Gezonder (Organically Healthier).
2. Additional well-designed comparison studies on food composition and residues on/in food for specific crops or animal products to provide reliable comparisons of both organic and non-organic food (Baransky et al., 2017). For this purpose, a follow-up of previous research by WFSR on differences in composition and levels of residues in organic and non-organic foods could be conducted.
3. Investigate the relationship between pesticides in the diet and cancer. And the role of organic food in potentially developing cancer (Panteo, 2019) For this, a literature review of the relationship between pesticides and cancer could be conducted with an emphasis on available animal models. These could lead to future animal studies where developing cancer and eating/not eating organic food are further studied.

4. Well-conducted human dietary intervention studies on the effects of organic and non-organic food on health and health-related (physiological) parameters (Baranski et al., 2017)
5. Intervention studies with organic and non-organic diets in experimental animals susceptible to certain diseases (Vigar et al., 2019) Studies with animal models for various tumors and metabolic diseases.
6. Investigation of methodological differences in studies of effects in available meta-analyses of compositional data, and cohort studies (Baransky et al., 20217) This has the potential to be a student assignment.
7. More research on the specific mechanisms of action that may explain reduced cancer incidence in organic foods (Panteo, 2019). Literature review on mechanisms of cancer development and the role of organic foods and specific components (or lack thereof) (e.g., polyphenols, antioxidants).
8. New long-term studies of the effect of whole food replacement with organic interventions as a method of determining whether there are truly measurable health effects (Vigar et al., 2019) conducted through human studies.

The aforementioned literature reveals that there is primarily a lack of adequate studies with animal models and a number of specific issues that need more of a meta-analysis approach. Based on this, it is recommended that the original recommendation from the Report Biologisch Gezonder (Organically Healthier) study be implemented and a trial be started with pigs fed organic or non-organic. Pigs are considered a good model for humans. This study can cover the whole fattening period to see if the period and age at which animals are fed organic food is influential. In doing so, different (physiological/immunological) parameters will be compared. Secondly, a mild challenge can be carried out halfway to look at the direct effects on the immune system. This study can be combined with a comprehensive residue and microbiology study in animal feed to get a complete picture of the differences between organic and non-organic animal feed. Also, the composition of the tissues of the organically and non-organically fed animals could be compared. Depending on the results, further conclusions can then be drawn about the health benefits of organic food and, if necessary, a human study can be conducted.

1 Introduction

Organic food products differ from conventional food products by using organic production methods that exclude the use of artificial fertilizers, chemical-synthetic plant protection products, genetically modified seeds, synthetic additives, and radiation. In organic livestock production, the use of preventive antibiotics is not allowed and therapeutic use is limited. In addition, there are requirements for housing, pen occupancy, and nutrition, among others. Consumers seem to value organic food because of the way it is produced and processed. It is also assumed that they have less impact on the environment and there are positive effects on animal welfare (more opportunity for natural behavior, walk-outs, fewer animals per area, etc.). Whether there is a difference in 'product quality, i.e. whether there is a difference in food properties between organic food and conventional food, is a subject of debate, but most consumers of organic food believe that it is healthier (Apaolaza et al., 2018; Hoefkens et al., 2009; van de Vijver et al., 2012; van Wijk Jansen et al., 2009).

In 2005, a study was conducted to determine the difference in the health of chicks fed either organic feed or conventional feed. Animals fed organic feed showed a stronger immune response than their counterparts not fed organic feed. Researchers found that no firm conclusions could be drawn about the health status of organically fed animals. Based on the results from the study, it was decided not to commission a follow-up study because the differences would be too small.

In the meantime, science has further developed and broadened on this issue, both at the theoretical level and at the implementation level (e.g., methods and techniques). The current knowledge and insights may give the reason for and/or the possibility of still carrying out follow-up research. The aim of the question is therefore to list what research has been done since 2005 (nationally and internationally) in the field of the health effects of organic farming. What is the scientific state of affairs; what is now known, where are the blind spots, and what are the possibilities and limitations for follow-up research?

For this purpose, a summary is given of the original research and subsequent publications, as well as results from recent literature on the health effects of organic feed for animals and organic products for humans, gaps in knowledge, and possible recommendations.

2 Materials and Methods

Internet search Scopus, Research@wur (search terms: organic and health/ healthy / non-organic, conventional, animal products), conversation with Machteld Huber January 2021, broadcast of Zembla November 2020. Literature on animal testing and Report "Biologisch Gezonder" (Organically Healthier), and other public reports.

3 Results

In January 2021 a conversation was first held with Dr. Machteld Huber. She explained that the conclusion that organically fed animals were healthier was questioned by TNO and WUR in particular. At a later stage, WUR-ASG also adjusted its conclusion regarding the positive nature of the findings in subsequent publications. In addition, there was the question of whether the differences found were important enough. As a result, no further research was done and her research was discontinued.

3.1 Original Research and Summary of Results

The original research consortium consisted of the Louis Bolk Institute (Dr. Machteld Huber), TNO (Dr. Leon Coulier), Wageningen UR - Animal Sciences Group (Prof. Dr. ir. Huub Savelkoul) and RIKILT - Institute of Food Safety (now WFSR) (Dr. Ron Hoogenboom). In addition, there was a supervisory committee that included other representatives from the above institutes, the financiers (LNV, Rabobank, Triodos bank), and experts from other organizations. Trial design, progress, and interim blinded results were discussed as well as the initial conclusions before the blinding was revealed.

The report (Huber, M. (ed) 2007) describes the trial in the summary. The aim of the trial was to see whether there was a difference in health between organic and non-organic fed chickens, as a stepping stone to a study in pigs and ultimately in humans. Thus, the final goal was to see whether organic food has positive health effects on humans.

The study involved a blinded animal experiment with feed, in two generations of chickens, with identically formulated feeds composed of either organic or conventional products. Only at the end of the trial was it revealed which feed was organic and which was non-organic. That was after an initial assessment of the results. It concerned the chicken model of the so-called Wageningen Selection Lines, Leghorn hens selected over 25 generations for either high or low antibody production after injection with SRBC (sheep red blood cells), at an age of 37 days. In addition to these lines, a randomly bred control group was available of chickens of the same pedigree, representing the 'original parental wild type' of the animals. The animals were described as 'high line' (H-line or High line) for the group with a high response level to SRBC injection and a 'low line' (L-line or Low line) for the group with a low response level. The control group (C-line) was the group of animals representing the normal genetic variation pattern on SRBC injection. In parallel with the first-generation hens, a group of roosters from the same three lines was raised on the experimental feed.

Regarding the feeds, it could be concluded that the analytical differences in the ingredients and feeds were most evident in the content of proteins and amino acids, and some micronutrients. Although differences were observed, the feeds were sufficiently nutritious for the growing chickens, and except as a result of the proteins, no major differences in effect on the chosen health parameters were expected. Although all chickens were healthy, obvious differences in the measured parameters were observed.

The conventionally fed animals from the control line showed a stronger weight gain, while the organically fed animals showed a stronger immune response, a stronger response to the challenge (test to measure the immune response), and a slightly stronger recovery from the challenge in terms of catch-up growth. As a challenge, second-generation animals of 9 weeks old received an intramuscular injection into the pectoral muscle with an immune-stimulating protein. The results are based on the findings in the animals of the control line, as they represented the natural genetic variation. But the results from the special high and low-line chickens in this research model supported the conclusion regarding an enhanced immune reactive capacity in the animals that received organically grown feed.

As for the nutritional factors that could explain these differences, the higher protein content of the conventional feed should be considered as a factor which could have caused the stronger weight gain in this

group. The factor(s) in the feed that could cause the physiological differences in response to the challenge are not yet clear. There are indications in the literature that enhanced immune reactivity could be related to the lower body weight of the animals involved. The meaning of the different physiological responses with respect to the short and long-term health of these animals is still unclear according to the research consortium.

This should be further clarified in a follow-up study. In summary, it was concluded that the study generated an enormous amount of information and also yielded unforeseen results. An important outcome of this study is that feed ingredients of different origins can have a small but significant effect on the immune system and on the metabolism of healthy animals. Furthermore, it became clear that the concept of health and the physiology and immunology of health is an as yet relatively unexplored area in the research landscape. With respect to a potential 'greater' beneficial effect on the health of either feed, no definitive conclusions could be drawn. Both feeds were healthy as such. The concept of 'health' and the related physiology and immunology needs further elaboration before definitive conclusions can be drawn.

With regard to the first research question: "Can differences be found between the ingredients of the chicken feed obtained from organic and conventional cultivation systems?", it could be concluded that the ingredients obtained from organic and conventional cultivation differed the most in protein and amino acid content. But at the same time it was clear that many, but not all, ingredients were analyzed. Later RIKILT conducted research in which untargeted as well as targeted were measured. In this study, the substance N, N0-di-feruloyl putrescine (DFP) was found in corn, which was different in organic and conventional corn (Ruiz-Aracama et al., 2012). Unfortunately not much was known about that substance, but it could be a research topic for follow-up research. There was also a difference in isoflavones.

The second research question, "Can biomarkers for health effects be identified related to the consumption of organic feed in comparison with the conventional feed?" could be answered in the affirmative, even though the implications of the observed differences in relation to health were not yet entirely clear and further research is necessary. It should be noted that in this project only one selection of products from one harvest was studied.

In the recommendations, the following is stated: The study showed that small differences in feed, resulting from different cropping systems, can have effects on immune reactivity, metabolism, and gene expression in healthy animals. Before these results can be used for humans (the final goal), the results need to be confirmed. This would first have to be done again in chickens, which should be followed for an extended period of time (perhaps until natural death), and examined after a stronger challenge with an infection model or other disease model.

Feed ingredients for such follow-up studies should be obtained from "best practice" farms in the same region. The feeds given to animals should be extensively researched in order to relate the effects found in the animals to the contents in the feed. In addition, the ingredients should be thoroughly investigated, also in relation to the products purchased by the consumer, to gain more insight into the representativeness of the products. In the future, a study with mammals is recommended, preferably with pigs, because these animals are most comparable to humans. Research on humans is the final objective. This concludes the report.

In the various publications resulting from the study, aspects are presented differently than in the original report (Huber, M. (ed) 2007). The publication by Adriaansen (Adriaansen- Tennekes[a] et al., 2011) talks about a hyperreactive immune system, which would imply a negative effect on health. The other publication (Adriaansen-Tennekes[b] et al., 2011) mentions feed contamination as a possible cause for the difference in an immune response. This is not found in the original report (Huber, M. (ed.) 2007). In both publications, Huber is listed as a co-author, by her own admission against her will. In her own article (Huber et al., 2010), following the report, it did report a stronger immune response and a faster recovery after the challenge of the organically fed animals. This would indicate a positive effect on the health and resilience of the animals. WUR and TNO were co-authors.

3.2 Recent Literature on Health Effects on Animals

Not much has been published on the health effects of organically raised animals. Kijlstra and Eijck (2006) point out the higher risk of organically raised animals for infectious diseases because they are kept outside. Organic turkeys (hens) are twice as likely to have their carcasses rejected as conventional turkeys (Dressel et al., 2019). This study relied on slaughter data from organic and conventional turkeys. It is indicated that the requirements of organic husbandries, such as outdoor runs and smaller animal density, are not necessarily positive for health status. In contrast, Karreman and Fulwider (2015) state that in organic dairy farming, better management, more robust animals and more opportunity for species-specific behavior actually result in much less disease. And that other means than antibiotics are available in case of illness. However, they do indicate that some high-yielding breeds are not suitable for organic farming. Legal requirements for organic farming, such as mandatory outdoor grazing, would reduce lameness, but parasitic infections require extra attention. Sutherland et al. (2013) evaluate animal welfare in organic livestock and see animal health as the most important factor determining welfare. Although management and natural means are well able to keep animals healthy, there is often a lack of scientific support for this.

3.3 Literature on Health Effects on Humans

To do this, we looked at reviews after the study was published in 2007. Dangour et al. (2010) conducted a literature review on the health effects of organic farming. For this, a systematic review was done between January 1958 and March 2010. In addition, experts were consulted and the effects of eating organic food compared to non-organic food were examined. After extensive selection, a total of 12 publications were reviewed in detail. These included eight reports of human studies, including six clinical studies, one cohort study, and four reports of studies with animals or human cell lines. Most studies looked at the effects of specific foods (10 of 12), seven articles examined the effects of fruits and vegetables, two articles examined wine, and only one examined animal products. Most studies did not look at direct effects on human health, but rather at e.g. flavonoids or antioxidant activity as biomarkers. This means that certain markers for effects on health have been looked at. Furthermore, the occurrence of atopic (allergic) reactions as a primary outcome has been looked at (Kummeling et al., 2008) and the composition of breast milk in terms of conjugated linoleic acids has been examined (Rist et al., 2007). The largest study (Kummeling et al., 2008) showed that consumption of only organic dairy gave a significantly reduced risk of eczema in children, but the other studies did not indicate any nutrition-related effects. Dangour's group (2010) cited the research with animal models (Huber et al., 2010) as extremely useful for gaining insight into research directions that may be relevant to human health. Regarding the occurrence of ESBL-producing microorganisms in chicken fillets from stores in the Netherlands, they were found to be present on 100% of the meat from conventional chickens and 84% of the organic chickens. However, the degree of contamination was much less in organic chickens than in conventional chickens (median content of ESBL-producing bacteria was 80 (range <.20-1360) in conventional and <.20 (range 0-260) CFU/25 g in organic samples ($p = 0.001$) (Cohen Stuart et al., 2012). Furthermore, a subsequent systematic review of differences between organic and conventional husbandry methods showed a lower occurrence of antibiotic resistance (van Wagenberg et al., 2017).

Smith-Spangler et al. (2012) state in their review that there is no strong evidence in the literature available up to that point that organic food is more nutritious than conventional food, but there is evidence that exposure to pesticides and antibiotic-resistant germs is lower when consuming organic food. Children who consumed more than 90% organic milk products had a 50% lower risk of developing eczema compared to children who received less than 50% organic milk products (Kummeling et al., 2008), as mentioned earlier. Three other studies looked at exposure to plant protection products and biocides, finding significantly fewer organophosphates in the urine of children who received an organic diet. On the other hand, eating organic meat (only in the winter) was found to give a higher risk of campylobacter. In the Dutch KOALA study on the composition of breast milk of women who ate organic or not, the milk of organic-eating women was shown to contain more beneficial fatty acids (conjugated linoleic acid and trans-vaccenic acid). No consistent differences were found in vitamin levels. Other research, described in the review (Smith-Spangler et al., 2012), showed that organic produce was higher only in phosphorus and total phenols. Organic chicken contained more omega-3 fatty acids than conventional chickens (Jahan et al., 2004). Research by RIKILT,

Louis Bolk Institute, CDI, and Biologica looked at differences in microorganisms and contamination between organic and conventional products (Hoogenboom et al., 2006). Although it was a momentary study (one moment of sampling spread over one/two production years) some differences were found. Such as lower nitrate levels in organic lettuce, higher nitrate levels in organic carrots, less antibiotic resistance in chickens meant for meat production, and less Salmonella but more Campylobacter in chickens meant for meat production. They also found a lower incidence of antibiotic-resistant bacteria in organic pigs and lower Salmonella incidence in organic farms with more experience.

A more recent review (Baranski et al., 2017) described significant and nutritionally relevant compositional differences between organic and conventional foods. These included higher levels of antioxidants and lower levels of cadmium and pesticides in organic crops, and higher levels of omega-3 fatty acids in organic meat and dairy products. They also found, based on a number of human cohort studies, positive correlations between eating organic food and the occurrence of a number of acute conditions such as pre-eclampsia, hypospadias, and obesity. A possible negative health effect could be lower iodine content in organic milk, but this is not supported by human cohort studies. There is virtually no information from long-term cohort studies on chronic diseases, and controlled human dietary interventions comparing organic and non-organic diets. Therefore, according to the authors, it is difficult to say what the effect of organic food is on human health. However, there is some data on organic products. For example, organic crops have between 18 and 69% higher levels of antioxidants. Increased intakes of polyphenols and antioxidants are associated with reduced risk of certain chronic diseases, such as cardiovascular disease, neurodegenerative disease, and certain cancers (Baranski et al., 2014). Common crops have higher levels of the toxic metal cadmium and are four times more likely to contain measurable levels of chemical pesticides than organic crops. Organic meat, milk, and dairy products contain higher levels of desirable omega-3 fatty acids. Organic milk contains higher levels of conjugated linoleic acid, iron, and α-tocopherol, all three of which are nutritionally desirable components. Conventional milk, on the other hand, contains more selenium and iodine. Although milk is not the primary source of selenium, in countries where salt is not iodized, it is the primary source of iodine. Lack of iodine during pregnancy is associated with the health effects on the baby. Conventional meat has higher levels of certain saturated fatty acids (myristin and palmitic acid), which are linked to an increased risk of cardiovascular disease. Previous research (Dangour et al., 2009), in a systematic review of differences in nutritional quality between organic and conventional foods, found that conventional products contained more nitrogen and organic products contained more phosphorus and more titratable acid (this is related to maturity at harvest).

A later review (Vigar et al., 2019) examined 35 papers on clinical trials and observational data on the difference in the health of people who ate organic or conventional food. Most studies did not look at direct health effects but limited themselves to differences in exposure to e.g. chemical plant protection products and biocides and other indirect parameters. Significant positive effects were mainly seen in longitudinal studies where an increase in eating organic food was associated with reduced incidence of infertility, birth defects, allergic sensitization, middle ear infection, pre-eclampsia, metabolic syndrome, higher BMI, and non-Hodgkin lymphomas. According to the authors, the results are not sufficient for establishing firm conclusions but add to the growing number of positive findings on the health effects of organic products.

The effects of organic food on the incidence of various types of cancer have been described in a prospective cohort study (Pantuso, T., 2019). A cohort study with more than 68,000 adult French showed that a greater frequency of eating organic foods was negatively associated with cancer risk, compared to a high-quality diet with a low frequency of organic foods. This study was part of a larger research project, the NutriNet- Santé study, which examined the relationship between diet and health and other determinants of dietary behavior and nutritional status in France. This study involved people aged 18 years and older, 78% of whom were women and with a mean age of 44.2 years at the start of the study. After enrolment, participants were tracked through a website specifically designed for this purpose. Upon participation, a questionnaire was completed on socio-demographic parameters, such as health status, lifestyle, physical activity, and diet. After two months, participants were asked about information on 16 groups of organic products including vegetables, fruits, soy products, dairy products, meat, fish, eggs, cereals, bread, cookies, etc. The frequency of intake was determined semi-quantitatively through a system in which people could choose between usually, sometimes, never and the reason for the choice. A point system was attached to the choices leading to a biological score from 0 to 32 points. Daily food intake was also tracked over a number of days and food quality was determined using a validated method from the Programme National Nutrition Santé Guideline

Score (PNNS-GS). In this study, participants kept annual records of their health. When a case of cancer was reported, medical records were requested by the physician involved in this study. An independent medical committee reviewed all major health cases. This study included all new cases of cancer except basal cell carcinoma between the study's start and November 2016. The researchers used the COX proportional hazards regression model to calculate the risks.

A 95% confidence interval and $P < 0.05$ were considered statistically significant. Participants were followed for 4.5 years and 1340 primary cancers were found during this period, including 459 cases of breast cancer, 180 prostate cancer, 135 skin cancer, 99 colon cancer, 47 non-Hodgkin lymphomas, and 15 other lymphomas. A high intake of organic foods was linearly related to a reduced overall risk of cancer. A reduced risk of postmenopausal breast cancer ($P = 0.03$), Non-Hodgkin lymphomas ($P = 0.049$), and other lymphomas ($P = 0.02$) was found in patients with a high frequency of organic food intake.

A study in the United Kingdom, the Million Women Study (9 years of follow-up), found in 623,080 women that eating organic food did not give the reduced risk of cancer (Bradbury et al., 2014). In fact, it was found of women who frequently ate organic had a slightly increased risk of breast cancer. Although, a 21% reduced risk of non-Hodgkin lymphoma was found. The more recent Sister study (USA, 9 years follow-up) did find a reduced risk of breast cancer with a high intake of organic food (Park et al., 2019).

Differences in the studies lie in the different countries, follow-up period, and composition of the participants. An additional point is that people who regularly eat organic food often also have a healthier diet, eating less meat and more fruits and vegetables (Panteo 2019). In addition, they often have a healthier lifestyle in terms of exercise, smoking, and alcohol consumption. The NutriNet Santé study previously showed that individuals with an increased intake of organic produce had a reduced risk of obesity, hypertension, type-2 diabetes, and elevated cholesterol compared to those who ate less organic produce. They also found a reduced risk of cardiovascular disease in this group. Organic food contains more antioxidants in fruits and vegetables and more omega-3 fatty acids in meat and milk than conventional products.

Organic production has positive impacts on the health of the environment associated with reduced pesticide and antibiotic loads, which is more sustainable for the environment, the health of the growers, and the local residents. In addition, organic production leads to reduced occupational exposure to synthetic pesticides and biocides and reduction of residues in food (Panteo, 2019). One of the risk factors for the development of cancer is exposure to pesticides (Moustafolou et al., 2017).

A problem in assessing the effects on human and animal health is that health is not well defined. The old WHO definition (1948) was, "Health is a state of complete physical, mental and social well-being and not of mere absence of disease." This is a wishful idea of health, which hardly anyone meets. Usually, the absence of disease is considered healthy. Huber, in her doctoral dissertation (Huber, 2014), has created a new definition of health that reads, "Health as the ability to adapt and take charge of oneself, in the face of life's social, mental and physical challenges. This concept is divided into six main dimensions: physical functions, mental functions and perception, the spiritual/existential dimension, quality of life, social participation, and daily functioning. This is based more on resilience and adaptability (Huber et al., 2011; Huber et al., 2012).

3.4 Knowledge Gaps

As of now, there is sufficient consensus on the nutritionally relevant differences in the composition of organic and non-organic food (Baranski et al., 2017). The question remains to what extent these differences have an effect on human health and what mechanism of action underlies them.

No similar trials have been conducted with animals after Huber's study with chickens. Especially in animals, you can only vary the nutrition, which can give insight into the effects of only organic food. The problem with studies on humans is that there is often a lifestyle related to a certain diet.

The various human studies differ in design, parameters investigated, and duration, making the results difficult to compare.

3.5 Recommendations for Further Research

The following recommendations emerged from the literature reviewed and analyzed:

1. To conduct research with animal models involving both organic and regular feeding to gain insight into research directions that may be relevant to human health (Dangour et al., 2010). For example, the study with pigs as recommended in the original Biological Healthier report.
2. Additional well-designed comparison studies on food composition and residues on/in food for specific crops or animal products to provide reliable comparisons of both organic and non-organic foods (Baransky et al., 2017). For this purpose, a follow-up to previous research by WFSR on differences in composition and levels of residues in organic and non-organic foods could be conducted.
3. Investigate the relationship between pesticides in diet and cancer. And the role of organic food in potentially developing cancer (Panteo, 2019) For this, a literature review of the relationship between pesticides and cancer could be conducted with an emphasis on available animal models. These could lead to future animal studies where developing cancer and eating/not eating organic food are further studied.
4. Well-designed human dietary intervention studies on the effects of organic and non-organic food on health and health-related (physiological) parameters (Baranski et al., 2017).
5. Intervention studies with organic and non-organic diets in experimental animals susceptible to certain diseases (Vigar et al., 2019) Studies with animal models for various tumors and metabolic diseases.
6. Investigation of methodological differences in studies of effects in available meta-analyses of compositional data, and cohort studies (Baransky et al., 20217) This could be an assignment for students.
7. More research on the specific mechanisms of action that may explain reduced cancer incidence in organic foods (Panteo, 2019). Literature review on mechanisms of cancer development and the role of organic foods and specific components (or lack thereof) (e.g., polyphenols, antioxidants).
8. New long-term studies of the effect of whole food replacement with organic interventions as a method of determining whether there are truly measurable health effects (Vigar et al., 2019) through human studies.

4 Conclusions

Although most researchers are very cautious about drawing conclusions about the health effects of organic food, there are a number of relevant findings, most of which are related to the organic production method:

- Organic food contains no synthetic chemical plant protection products and fewer biocides than conventional food
- Organic food contains more antioxidants than conventional food
- Organic food contains fewer antibiotic-resistant germs than conventional food
- In terms of composition, organic food contains more phenols than conventional food, and milk has a more beneficial fatty acid pattern
- There are indications that eating organic food leads to a lower risk of developing certaindisorders, such as allergies, metabolic syndrome and obesity, and certain cancers.

Whether these effects are a direct effect of the organic diet, the reduced levels of contaminants or the often different lifestyle of consumers who eat organic are not entirely clear. But the overall picture points to a positive health effect and calls for further research.

5 Recommendations for Further Research

Based on the aforementioned literature, it appears that there is mainly a lack of good studies with animal models and specific issues that need more of a meta-analysis approach. Based on this, it is recommended that the original recommendation from the Biological Healthier study be implemented and that a trial be started with pigs fed organic or non-organic. Pigs are considered a good model for humans. This study can cover the whole fattening period to see if the period and age at which animals are fed organic food has an influence. In doing so, different (physiological/immunological) parameters will be compared. Secondly, a mild challenge can be carried out halfway to look at the direct effects on the immune system. This study can be combined with a comprehensive residue and microbiology study in animal feed to get a complete picture of the differences between organic and non-organic animal feed. Also, the composition of the tissues of the organically and non-organically fed animals could be compared. Depending on the results, further conclusions can then be drawn about the health of organic food and, if necessary, a human study can be set up.

References

Adriaansen-Tennekes[a], R., de Vries Reilingh, G., Pieters, R.H.H., van Loveren, H., Huber, M., Hoogenboom, R., Parmentier, H.K., Savelkoul, H.F.J., 2011. "Sensitivity of innate and adaptive cellular immune parameters of poultry to minor macro- and micronutrient differences in two nutritionally complete layer feeds". Biological Agriculture and Horticulture 27(3-4): 261-277.

Adriaansen-Tennekes[b], G. de Vries Reilingh, M. G.B. Nieuwland, R. H.H. Pieters, H. van Loveren, M. Huber, R. Hoogenboom, H. K. Parmentier & H. F.J. Savelkoul, 2011. "Sensitivity of humoral immune parameters of poultry to minor macro- and micronutrient differences in two nutritionally complete layer feeds". Biological Agriculture & Horticulture, 27(3-4): 241-260.

Apaolaza, V., Hartmann, P., D'Souza, C., López, C.M. 2018. "Eat organic–Feel good? The relationship between organic food consumption, health concern and subjective wellbeing". Food Qual. Prefer. 63, 51–62.

Barański M., Średnicka-Tober D., Volakakis, N., Seal, C., Sanderson, R., Stewart, G.B., Benbrook, C., Biavati, B., Markellou, E., Giotis, C., Gromadzka-Ostrowska, J., Rembiałkowska, E. 2014. "Higher antioxidant and lower cadmium concentrations and lower incidence of pesticide residues in organically grown crops: a systematic literature review and meta-analyses". Br J Nutr. 112: 794–811.

Barański, M., Rempelos, L., Iversen, P.O., Leifert, C. 2017. "Effects of organic food consumption on human health; the jury is still out!" Food and Nutrition Research 61(1), 1287333.

Baudry, J., Méjean, C., Péneau, S., Galan, P., Hercberg, S., Lairon, D., Kesse-Guyot, E., 2015. "Health and dietary traits of organic food consumers: Results from the NutriNet-Santé Study". Br J Nutr 114: 2064-2073.

Bradbury, K.E., Balkwill, A., Spencer, E.A., Roddam, A.W., Reeves G.K., Green J., Key T.J., Pirie, K., Banks, E., Beral, V., English, R., Patnick, J. 2014. Organic food consumption and the incidence of cancer in a large prospective study of women in the United Kingdom". Br J Cancer 110: 2321-2326.

Cohen Stuart, J., T. van den Munckhof, G. Voets, J. Scharringa, A. Fluit, and M.L. Hall. 2012. "Comparison of ESBL contamination in organic and conventional retail chicken meat". Int. J. Food Microbiol., 154(3): 212-4.

Dangour, A.D., Sakhi K Dodhia, Arabella Hayter, Elizabeth Allen, Karen Lock, and Ricardo Uauy. 2009. "Nutritional quality of organic foods: a systematic review1–4". American Journal Clinical Nutrition 90: 680–5.

Dangour, A.D., Lock, K., Hayter, A., Aikenhead, A., Allen, E., Uauy, R., 2010. "Nutrition-related health effects of organic foods: A systematic review." American Journal of Clinical Nutrition 92(1): 203-210.

Di Renzo, L., De Lorenzo, A., Merra, G., Gualtieri, P., 2020. Comment on: "a systematic review of organic versus conventional food consumption: Is there a measurable benefit on human health? Nutrients 2020, 12, 7" Nutrients 12(3), 69.

Hoefkens, C.; Verbeke, W.; Aertsens, J.; Mondelaers, K.; Van Camp, J. 2009. "The nutritional and toxicological value of organic vegetables". Br. Food. J. 111: 1062–1077.

Hoogenboom, L.A.P., J. G. Bokhorst, M.D. Northolt, N.J.G. Broex, D. Mevius, J.A.C. Meijs, J. van der Roest. 2006. "Contaminanten en micro-organismen in biologische producten. Vergelijking met gangbare producten". RIKILT Rapport 2006.002

Huber, M. 2014. "Towards a new, dynamic concept of Health Its operationalisation and use in public health and healthcare, and in evaluating health effects of food". Thesis Maastricht.

Huber, M. (ed.), 2007. "Organic, More Healthy? A search for biomarkers of potential health effects induced by organic products, investigated in a chicken model." Louis Bolk Instituut, publication number M22.

Huber, M., Bakker, M.H., Dijk, W., Prins, H.A.B., Wiegant, F.A.C., 2012. "The challenge of evaluating health effects of organic food; Operationalisation of a dynamic concept of health." Journal of the Science of Food and Agriculture 92(14): 2766-2773.

Huber, M., Knottnerus. J.A., Green, L., van der Horst, H., Jadad, A.R., Kromhout, D., Leonard, B., Lorig, K., Loureiro, M.I., Van Der Meer, J.W.M., Schnabel, P., Smith, R. 2011. "How should we define health?" Br Med J 343(4163): 235–237.

Huber, M., Rembiałkowska, E., Średnicka, D., Bügel, S., Van De Vijver, L.P.L., 2011. "Organic food and impact on human health: Assessing the status quo and prospects of research." NJAS - Wageningen Journal of Life Sciences 58(3-4): 103-109.

Huber, M., Van De Vijver, L.P.L., Parmentier, H., Savelkoul, H., Coulier, L., Wopereis, S., Verheij, E., Van Der Greef, J., Nierop, D., Hoogenboom, L.A.P., 2010. "Effects of organically and conventionally produced feed on biomarkers of health in a chicken model." British Journal of Nutrition 103(5): 663-676.

Jahan, K., Paterson, A., Spickett, C.M. 2004. "Fatty acid composition, antioxidants and lipid oxidation in chicken breasts from different production regimes". International Journal of Food Science and Technology 39(4: 443-453.

Karreman, H.J., Fulwider, W. 2015. "Animal well-being on organic farms (Book Chapter) in Improving Animal Welfare: A Practical Approach": 2nd Edition, 267-277.

Kummeling I., Thijs C., Huber M., van de Vijver, L.P.L., Snijders, B.E.P., Penders, J., Stelma, F., van Ree, R., van den Brandt, P.A., Dagnelie, P.C. 2008. "Consumption of organic foods and risk of atopic disease during the first 2 years of life in the Netherlands". Br J Nutr 99: 598–605.

Moustafalou, S., Abdollahi, M., 2017. "Pesticides: An update of human exposure and toxicity". Arc Toxicol 91: 549-599.

Pantuso, T., 2019. "Organic food consumption and cancer risk." Integrative Medicine Alert 22(9): 100-102.

Park, Y.M.M., White, A., Niehoff, N., O'Brien, K., Sandler, D. 2019. "Association between organic food consumption and breast cancer risk: Findings from the Sister Study (P18-038-19)". Curr Dev Nutr 3 (Suppl 1): nzz039.P18-038-19.

Rist, L., Mueller, A., Barthel, C., Snijders, B., Jansen, M., Simões-Wüst, A.P., Huber, M., Kummeling, I., von Mandach, U., Steinhart, H., Thijs, C. 2007. "Influence of organic diet on the amount of conjugated linoleic acids in breast milk of lactating women in the Netherlands". Br J Nutr 97: 735–43.

Ruiz-Aracama, A., A. Lommen, M. Huber, L. Van De Vijver and R. Hoogenboom, 2012. "Application of an untargeted metabolomics approach for the identification of compounds that may be responsible for observed differential effects in chickens fed an organic and a conventional diet". Food Additives and Contaminants - Part A Chemistry, Analysis, Control, Exposure and Risk Assessment 29: 323-332. http://dx.doi.org/10.1080/19440049.2011.641163

Smith-Spangler, C., Brandeau, M.L., Hunter, G.E., Clay Bavinger, J., Pearson, M., Eschbach, P.J., Sundaram, V., Liu, H., Schirmer, P., Stave, C., Olkin, I., Bravata, D.M., 2012. "Are organic foods safer or healthier than conventional alternatives?: A systematic review." Annals of Internal Medicine 157(5): 348-366.

Sutherland, M.A., Webster, J., Sutherland, I., 2013. "Animal health and welfare issues facing organic production systems". Animals 3(4): 1021-1035

van de Vijver, L.P.L.; van Vliet, M.E.T. 2012."Health effects of an organic diet-Consumer experiences in the Netherlands". J. Sci. Food Agric. 92, 2923–2927.

Vigar, V., Myers, S., Oliver, C., Arellano, J., Robinson, S., Leifert, C., 2020. "A systematic review of organic versus conventional food consumption: Is there a measurable benefit on human health?" Nutrients 12(1): 7.

Vigar, V., Oliver, C., Leifert, C., Myers, S.P. 2020. "Reply to "comment on: A systematic review of organic versus conventional food consumption: Is there a measurable benefit on human health? nutrients 2020, 12, 7" Nutrients 12(3): 695.

van Wagenberg, C.P.A., Y. de Haas, H. Hogeveen, M.M. van Krimpen, M.P.M. Meuwissen, C.E. van Middelaar, T.B. Rodenburg 2017. "Animal Board Invited Review: Comparing conventional and organic livestock production systems on different aspects of sustainability." Animal 11(10): 1839-1851.

Wijk-Jansen, E.E.C. van, A. Ronteltap en L. Jager. 2009. "Het gezonde van biologisch voedsel: de beleving van consumenten". Rapport 2009-080 LEI Wageningen UR.

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