Comparison of putative health effects of organically and conventionally produced foodstuffs: a systematic review

Report for the Food Standards Agency

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1.0 EXECUTIVE SUMMARY

There is currently no independent authoritative statement on differences in the putative health effects of organic and conventional produced foodstuffs. This systematic review of the available published literature was designed to review the evidence of differences in putative health effects of organically compared with conventionally produced foodstuffs. The focus of the review was the nutritional content of foodstuffs, and only outcomes of clear direct relevance to human health were included. This review does not address contaminant content (such as herbicide, pesticide and fungicide residues) of organically and conventionally produced foodstuffs, or the environmental impacts of organic and conventional agricultural practices.

The systematic review search process identified eleven relevant articles, published with an English abstract in peer-reviewed journals between 1st January 1958 and 15th September 2008. Articles included in the review were assessed for study quality (satisfactory quality studies provided a clear definition of organic agricultural practices, and statements on the nature of the organic component of the foodstuff or diet under investigation, the type and method of measurement of health outcomes, and the statistical methods used); one third of relevant included studies (3/11; 27%) met the pre-defined satisfactory quality criteria.

The studies included in the review contained a large degree of variability in their designs, the exposures tested and the outcomes measured, and this variability precluded any numeric meta-analysis of the reported results. In a narrative review, the following themes were highlighted:

- Study hypothesis: most studies (8/11; 73%) hypothesised that differences detected in health effects would be due to the higher levels of specific nutrients in organic foods;
- Study design: a variety of different study designs were employed; six (55%) were human studies including 4 clinical trials, one cohort study and one cross-sectional study, and five (45%) were *in vitro* or *ex vivo* studies on human cell lines or serum;
- Exposure: most studies (9/11; 82%) investigated the health effects of specific foodstuffs rather than the diet as a whole;
- Health outcomes: most studies (9/11; 82%) collected information on measures of antioxidant activity (variously defined).

The narrative review highlighted several short-comings in the design, interpretation and reporting of the studies included in the review.

In conclusion, because of the limited and highly variable data available, and concerns over the reliability of some reported findings, there is currently no evidence of a health benefit from consuming organic compared to conventionally produced foodstuffs. It should be noted that this conclusion relates to the evidence base currently available on the nutrient content of foodstuffs, which contains limitations in the design and in the comparability of studies.

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4.0 INTRODUCTION

There is uncertainty over the putative health effects of organically compared with conventionally produced foodstuffs. Organic foodstuffs are those that are produced according to specified standards which, among other things, control the use of chemicals and medicines in crop and animal production, and emphasise protection of the environment. The global demand for organically produced food is rising. In 2007 the organic food market in the UK was estimated to be worth over £2 billion – an increase of 22% since 2005.[1] The UK organic market is now the third largest in Europe after Germany and Italy. Fruit and vegetables comprise the largest sector of organic foods in the UK, closely followed by dairy products.

The shift in demand among consumers from conventionally to organically produced foodstuffs appears to have arisen at least in part from a belief that organically produced foodstuffs are healthier[2-5] and have a superior nutrient profile[6,7] than conventionally produced foodstuffs. A recent systematic review of peer-reviewed evidence published in the last 50 years,[8] concluded that organically and conventionally produced foodstuffs are broadly comparable in their nutrient content.

To date, there has been no explicitly systematic review of the available literature on the health effects of organically produced foodstuffs. In contrast to non-systematic reviews which can be biased and incomplete, the prime purpose of systematic reviews of literature is to provide a comprehensive display of all available evidence in a common format. Systematic reviews have clear principles for their conduct. First, the process of the review should be carried out according to a pre-specified method. Second, the proposed method should be open to public scrutiny and peer review. Third, the review should be comprehensive within its pre-specified criteria. A systematic approach offers clear advantages in terms of reducing bias, where for instance inclusion or exclusion of studies may be influenced by preconceived ideas of the investigators. Systematic reviews cannot improve the quality of existing published studies, but can provide details of the characteristics and quality of studies.

Given the large and increasing demand for organic foodstuffs in the UK and elsewhere, an up-to-date objective statement on the potential benefits of organic foodstuffs for human health is needed for both public policy and consumer advice. The aim of this review is to systematically review the evidence of differences in putative health effects of organically

produced compared with conventionally produced foodstuffs. The focus of the review was the nutritional content of foodstuffs, and only outcomes of clear direct relevance to human health were included. This review specifically did not set out to assess the health impact of potential food contaminants (such as herbicide, pesticide and fungicide residues) of organically and conventionally produced foodstuffs, or the environmental or environmental health impacts of organic and conventional agricultural practices.

5.0 METHODS

5.1 Review process

In line with accepted guidelines, the review process was initiated by the preparation of a protocol which pre-specified the method to be used for the conduct of the review. The protocol was reviewed by an expert independent review panel. The review panel comprised a subject expert, Dr. Julie Lovegrove (University of Reading), and an expert in public health nutrition with systematic review experience, Professor Martin Wiseman (University of Southampton and World Cancer Research Fund International). The expert independent review panel and experts at the Food Standards Agency provided feedback on the protocol which was incorporated into the version posted on-line on 18th April 2008 at http://www.lshtm.ac.uk/nphiru/research/organic/. An updated version of the protocol, modified based on the experience of conducting an earlier review[8] was finalised on 21st October 2008 and posted on-line on 30th January 2009. Relevant subject experts and external bodies were alerted to the review process and the availability of the review protocol. A draft of the final report was reviewed and approved by the expert independent review panel and by two external peer-reviewers selected by the FSA.

5.2 Search strategy

Search strategies were developed with PubMed using Medical Subject Heading [MeSH] and title abstract [tiab] terms to identify relevant exposures (organic vs. conventional production methods) and outcomes (health and health-related measures). The exposure terms searched (including all MeSH, headings, subheadings and tiab terms) were "organic", "health food", "conventional" combined with "food", "agricultural crop", "livestock", "agriculture", "production", "nutrition", "diet", "consumption". These were combined with a list of terms describing relevant health outcomes which fall under the following categories:

- Respiratory Diseases
- Inflammatory Diseases (including allergy/immune-related diseases)
- Nutrient Status and Micronutrient Deficiencies
- Reproductive Health
- Eye Diseases
- Non-communicable Chronic Diseases
- Weight gain and Obesity
- Diabetes (including Metabolic Syndrome X)

- Cardiovascular Disease (including Coronary Disease)
- Cancer
- Dental Diseases
- Osteoporosis

Multi-database searching was used to ensure comprehensive article retrieval. Searches were conducted in PubMed, ISI Web of Science, CAB Abstracts and Embase (see Appendix 1 for search terms used in each database). The search period covered 50 years, from 1st January 1958 until 15th September 2008 which was deemed an appropriate time period given that standardised regulations for production of organic foodstuffs were first introduced in the early 1990s. All languages were included in the searches but only publications with an English abstract were considered for inclusion in the review. Hand searching of the reference lists of studies included in the review was conducted to check the completeness of initial electronic searches. In-press articles were identified by direct contact with key authors. Subject experts (n=23) identified from relevant publications were contacted by email; we received 12 responses and were sent 11 publications, 10 of which were either not relevant or had previously been identified.

5.3 Study designs

We considered three main study types for inclusion in the review:

- Human studies including randomised and non-randomised controlled trials, cohort, case-control and cross-sectional study designs;
- *In vitro* and *ex* vivo studies in human or animal cell lines and serum used to investigate human-related cell mechanisms;
- Animal studies where animal models were explicitly used as a proxy for human physiological, biochemical or other hypothesised mechanisms in humans.

A conceptual framework outlining a hierarchy of study types in terms of their relevance to human health outcomes is presented in Appendix 2. Studies exclusively investigating animal health (i.e. veterinary), occupational (e.g. health of organic/conventional farmers) or environmental health outcomes were excluded.

5.4 Publication selection

The titles and abstracts of all papers identified in the search process were assessed for relevance by two reviewers (AA and AH) working together, and any disagreement resolved in discussion with the project lead (ADD). Grey literature such as dissertations,

conference proceedings (including peer-reviewed abstracts) and reports were excluded. Relevant in-press articles were reported in the review but excluded from thematic analysis. The full texts of all potentially relevant articles were retrieved and assessed for inclusion in duplicate by two independent reviewers. Articles were excluded if they:

- were not peer-reviewed
- did not have an English abstract
- did not address a relevant health outcome
- did not present a direct comparison between organic and conventional production systems
- were concerned with occupational health outcomes
- investigated animal health from a veterinary perspective, and not as a animal model for human health
- were primarily concerned with non-nutrient contaminant content (herbicides, cadmium, lead and mercury)
- were authentication studies describing techniques to identify food production methods.

5.5 Data extraction

Data extraction was performed in duplicate for all included articles by two independent reviewers. Extracted data were compared and any inconsistencies noted and corrected as necessary. Extracted data entered into summary tables included all relevant information on study characteristics, methods and results.

5.6 Study quality

Study quality was categorised based on concordance with four fundamental factors which were defined *a priori* as essential to answer the research question (i.e. comparison of putative health effects of organically and conventionally produced food). Study quality was grouped into two categories: satisfactory quality and unsatisfactory quality.

Satisfactory quality publications provided the following:

- a clear definition of the organic production methods for the foodstuff(s) under investigation in the Introduction or Methods section of the paper;
- a statement on the nature (i.e. type, amount or proportion) of the organic component of the foodstuff or diet under investigation;
- a clear definition of the health outcome and how it was measured;
- a statement of the statistical methods used for data analyses.

Unsatisfactory quality publications were those that do not specify all of the above.

5.7 Data analysis

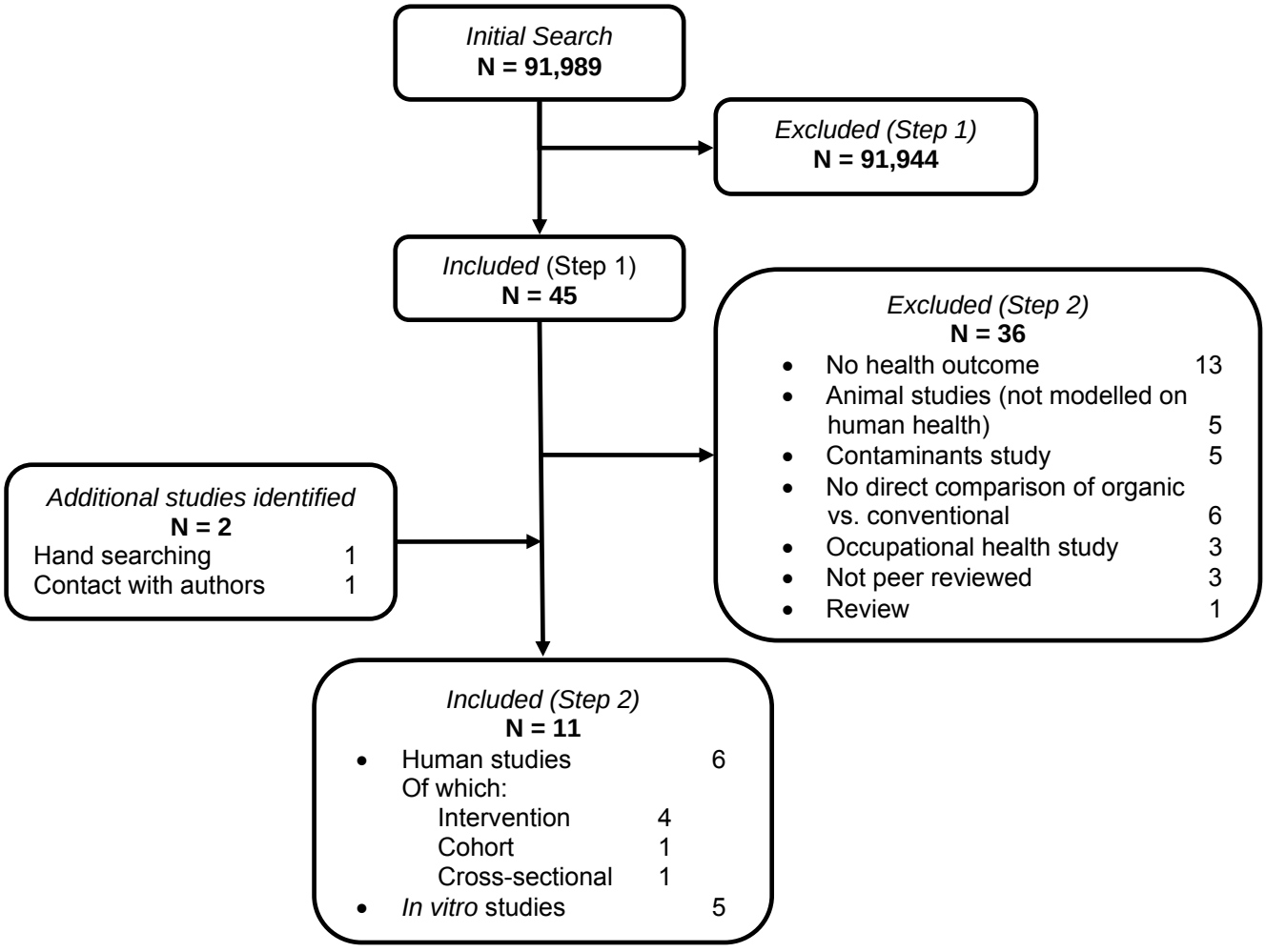
Statistical analysis was not attempted due to marked heterogeneity of study designs, exposures and outcome measures among the included studies. We followed guidance from the Cochrane handbook (http://www.cochrane-handbook.org/ section 11.7.2) supporting the use of a systematic, narrative approach when meta-analysis is inappropriate. We synthesised the results according to study hypothesis, study design, exposure and health outcomes.

6.0 RESULTS

6.1 Search results

The search strategy identified 91,989 unique citations of which 45 articles were included as potentially relevant and their full texts were retrieved. Examination of full texts resulted in the exclusion of 36 studies which did not meet inclusion criteria (see figure 2 and Appendix 3 for reasons for study exclusion). Hand searching of reference lists of the 45 potentially relevant articles identified one[9] additional relevant study. Contact with subject experts identified one[10] additional relevant study. A final total of eleven publications, six human studies[9,11-15] and five *in vitro* studies,[10,16-19] were identified and included in the review (see Figure 2). The list of publications included in this review is provided in Appendix 4, and their abstracts are provided in Appendix 5.

Figure 2: Flow chart of study selection process



(Step 1) – number of articles included/excluded after viewing title and abstract
(Step 2) – number of articles included/excluded after reading full text

6.2 Study quality

The 11 studies included in the review were assessed to determine whether they met the quality criteria. All 11 studies (100%) gave a clear definition of the health outcome and how it was measured, and the methods used for statistical analysis. Ten studies (91%) clearly stated the nature of the organic component of the diet studied. One third of the studies (n=4; 36%) provided a clear definition of the organic production methods used (we required a statement of certifying body, although if no certifying body was named it was inferred when possible from the text provided). Overall, fewer than one third of studies included in the review (n=3; 27%) met the pre-defined quality criteria[10,11,18] (see Table 1). Information on the quality of each study included in the review is provided in Appendix 6.

Table 1: Number of studies included in the review meeting quality criteria

Criterion	n	%
Definition of organic	4	36
Nature of the organic component of the diet consumed	10	91
Definition of health outcome and how it was measured	11	100
Statistical methods	11	100
Overall Satisfactory Quality	3	27

6.3 Data extraction tables

A summary of the eleven studies included in the systematic review are presented in Tables 2-12.

Table 2: Paper 1

Author		**Akcay, Y.D., Yildirim, H.K., Güvenc, U. and Sözemen, E.Y.**
Title		The effects of consumption of organic and nonorganic red wine on low-density lipoprotein oxidation and antioxidant capacity in humans. (2004) Nutrition Research 24(7):541-54
Study design and type		Crossover trial Humans (plasma & in vitro)
Quality		Unsatisfactory (no organic certification body specified)
Duration of study		44 days (2 exposure days separated by 6 week washout period)
Objective		To determine the effects of polyphenols found in organic and nonorganic red wines on LDL oxidation, antioxidant activity and other antioxidant enzymes (catalase and superoxide dismutase) in vivo
Hypothesis		Ecological conditions, grape variety, degree of ripening and winemaking techniques affect the type and concentrations of polyphenols in grapes, which may be medically important due to their antioxidant and anti-inflammatory activity
Sample size		N=8
Baseline characteristics of study subject/cell		6 male, 2 female, healthy non-smokers, aged 24-45, no drug or vitamin consumption, reported minimal polyphenol consumption for 1 week preceding study; no data on differences in baseline characteristics between the two groups
Age of study subjects		24-45 years
Exposure		O&C Cabernet Sauvignon. Organic wine made from grapes of *Vitis vinifera* origin, nonmechanically crushed with active yeasts in musts, no stabilizing or fining agent. Conventional wine made from mechanically pressed grapes with commercial dry yeast, gelatin as a fining agent and plate filter for filtration.
Measurement of exposure		100mL (women) or 200mL (men) dose of wine
Duration of exposure		1 dose
Organic certification		Specified organically certified grapes; organic certification body not stated
Outcome		LDL oxidation, antioxidant activity (antioxidant capacity and levels of eSOD, eCAT and eTBARS), phenol levels
Measurement of outcome		*In vitro* LDL oxidation: TBARS level (before and after incubating LDL with 5mmol/L $CuSO_4$) *Biological* Antioxidant capacity: % radical scavenging ability (decline in absorbance in response to 0.1mmol/L DPPH) • eSOD: no unit of measurement indicated • eCAT: no unit of measurement indicated • eTBARS: no unit of measurement indicated • Phenol levels: Gallic acid equivalents (Folin-Ciocalteu method)
Statistical analysis		Multivariate exploratory techniques, Principal Component Analysis (PCA) used
Confounders adjusted for		N/A
Results	Presentation	Graphical ; no numeric data
	Significant	None
	Non-significant	Antioxidant capacity: organic higher than nonorganic 1 hr post consumption, organic lower than nonorganic 6 hrs post consumption (no significance level stated) eSOD: organic higher than nonorganic 1 and 6 hrs post consumption (no significance level stated) eCAT: organic higher than nonorganic 1 and 6 hrs post consumption (no significance level stated) eTBARS: organic lower than nonorganic 1 and 6 hrs post consumption (no significance level stated) Serum phenol levels: organic higher than nonorganic 1 hr post consumption, organic lower than nonorganic 6 hrs post consumption (no significance level stated) LDL TBARS: organic lower than nonorganic 1 hr post consumption, organic higher than nonorganic 6 hrs post consumption (no significance level stated) Cu-stimulated LDL TBARS: organic lower than nonorganic 1 hr post consumption, organic higher than nonorganic 6 hrs post consumption (no significance level stated)
	Unreported	N/A

Table 3: Paper 2

Author		**Briviba, K., Stracke, B.A., Rüfer, C.E., Watzl, B., Weibel, F.P. and Bub, A.**
Title		Effect of consumption of organically and conventionally produced apples on antioxidant activity and DNA damage in humans. (2007) J Agric Food Chem 55 (19):7716-21
Study design and type		Double-blind randomized crossover study with 1 week washout period Humans
Quality		Satisfactory
Duration of study		9 days
Objective		To compare the effects of phenolic compounds in organic and conventionally produced apples on oxidative stress and DNA damage in humans.
Hypothesis		Modulation of physiological processes in humans cannot be predicted solely by chemical composition differences; another attribute influenced by production system may differentially affect markers of carcinogenesis (which can lead to the formation of cancer)
Sample size		N=6
Baseline characteristics of study subject/cell		Healthy, non-smoking males, food high in polyphenols avoided 3 days prior to experiment, overnight fast prior to experiment
Age of study subjects		Mean: 27 years, SD: 3 years
Exposure		Organic and conventional apples (cv. Golden Delicious) from a Swiss neighbouring commercial orchard pair (1 certified organic farm, 1 conventional farm). 350 apples from each orchard were harvested at first picking passage and at optimal maturity. Fruits without wounds were transported to a cold storage room and stored at 2°C and 93% relative humidity.
Measurement of exposure		1kg apples (no seeds or core) consumed with one white roll
Duration of exposure		1 day
Organic certification		Certified (Bio Suisse, Switzerland)
Outcome		Serum glucose Serum triacylglycerol Uric acid LDL antioxidant capacity DNA damage in peripheral blood lymphocytes
Measurement of outcome		*Biological* Serum glucose: mmol/L plasma Serum triacylglycerol: mmol/L plasma Uric acid: mmol/L plasma DNA damage in peripheral blood lymphocytes: measured by single cell microgel electrophoresis before apple consumption and after 4.5 hours and 24 hours. *Ex vivo* LDL antioxidant capacity: Ex vivo oxidation of LDL (isolated from plasma sample of subjects) with myeloperoxidase-peroxynitrite
Statistical analysis		Repeated measures ANOVA to evaluate time-dependent changes in blood parameters. Where results significant ($p<0.05$), Dunnett's posthoc test used.
Confounders adjusted for		N/A
Results	Presentation	Numeric data
	Significant	None
	Non-significant	Glucose: 0.02 – 0.21mmol/L higher in organic compared to conventional up to 3 hours post consumption; 0.02 – 0.39mmol/L lower in organic compared to conventional between 4 and 24 hours post consumption Triacylglycerol: 0.04 – 0.21 mmol/L higher in organic compared to conventional up to 24 hrs post consumption Uric acid: 0 – 0.01 mmol/L higher in organic compared to conventional up to 24 hrs post consumption Ex vivo oxidation of LDL: 0.01-0.14 A_{234nm} higher in organic compared to conventional up to 24 hrs post consumption Endogenous DNA strand breaks: 0.2 – 0.29 TI% higher in conventional compared to organic post consumption Endogenous oxidative DNA damage at Endo III sites: 0.08-0.91 higher in conventional compared to organic post consumption Endogenous oxidative DNA damage at Fpg sites: 0.16 higher in conventional compared to organic 4.5 hours post consumption; 0.7 lower in conventional compared to organic 24 hrs post consumption Antioxidant capacity of lymphocytes to protect DNA (H_2O_2-induced strand breaks): 0.4 – 3.32 higher in organic compared to conventional post consumption Antioxidant capacity of lymphocytes to protect DNA ($FeCl_3$-induced strand breaks): 0.5 – 0.51 higher in conventional compared to organic post consumption
	Unreported	N/A

Table 4: Paper 3

Author		**Caris-Veyrat, C., Amiot, M., Tyssandier, V., Grasselly, D., Buret, M., Mikolajczak, M., Guilland, J., Bouteloup-Demange, C. and Borel, P.**
Title		Influence of organic versus conventional agricultural practice on the antioxidant microconstituent content of tomatoes and derived purees; consequences on antioxidant plasma status in humans. (2004) J Agric Food Chem 52(21): 6503-9.
Study design and type		RCT; subjects blinded Human (plasma)
Quality		Unsatisfactory (no organic certification)
Duration of study		3 weeks
Objective		To evaluate whether the consumption of purees made of tomatoes grown organically and conventionally affect the plasma levels of antioxidant microconstituents in humans.
Hypothesis		Growing conditions will affect the content of antioxidants in tomatoes, which in turn will affect antioxidant status in humans (i.e. lycopene, consumption of which is correlated with reduced risk of prostate cancer)
Sample size		N=20
Baseline characteristics of study subject/cells		Non-smoking females, no oral medications or supplements for 1 month prior to study; no significant differences in baseline characteristics between groups
Age of study subjects		21-39 years
Exposure		Organic and conventional tomato purees from equal amounts of 3 tomato varieties (Félicia, Izabella, Paola) grown in plastic tunnels, harvested in June/July and stored at 4°C. Purees were prepared using the "Flash-Détente" process: heating for 8 min at 95°C followed by a decrease of pressure to 70 mbar, in order to diminish micronutrient losses.
Measurement of exposure		96g tomato puree/day ingested with lunch or dinner
Duration of exposure		3 weeks
Organic certification		No organic certification specified
Outcome		Plasma levels of lycopene, beta carotene and vitamin C
Measurement of outcome		*Biological* Lycopene, beta carotene: nmol/L plasma Vitamin C: mmol/L plasma
Statistical analysis		Two-way ANOVA. Where significance found at $p<0.05$, post-hoc Newman-Keuls test for time comparisons, or Student *t* test for group comparisons at a given time used.
Confounders adjusted for		N/A
Results	Presentation	Graphical; no numeric data
	Significant	None
	Non-significant	Plasma lycopene: higher in organic compared to conventional at baseline, after 3 weeks of exposure, and after 3 week washout β-carotene: lower in organic compared to conventional at baseline, after 3 weeks of exposure, and after 3 week washout Vitamin C: lower in organic compared to conventional at baseline, higher in organic compared to conventional after 3 weeks of exposure, and no difference after 3 week washout
	Unreported	N/A

Table 5: Paper 4

Author		**Dani, C., Oliboni, L.S., Vanderlinde, D., Bonatto, D., Salvador, M. and Henriques, J.A.P.**
Title		Phenolic content and antioxidant activities of white and purple juices manufactured with organically- or conventionally-produced grapes. (2007) Food Chem Toxicol 45(12): 2574-80
Study design and type		Experimental. Ex vivo measures of antioxidant activity of organic and conventional grape juices on human serum samples.
Quality		Unsatisfactory (no organic certification)
Objective		To assess the antioxidant capacity of different types of grape juices (from organically- or conventionally-grown grapes)
Hypothesis		Organically grown grapes may have a different composition which may affect their ability to neutralize reactive species, which have a suggested relevant pathophysiological role in human diseases such as cancer and atherosclerosis
Sample size		No data
Baseline characteristics of study subjects/cells		Fresh human serum samples; no description of their origin.
Exposure		8 *Vitis labrusca* juices (white & purple, cvs *Bordo* and *Niagara*, organically and conventionally grown grapes). Organic grapes obtained from Cooperative Aecia, Brazil. Conventional grapes obtained from Vinhos Monte Reale, Brazil. Same brands used for entire study.
Measurement of exposure		Grape juices measured according to 8 groups based on combinations of 2 cultivars, commercial and pilot scale groups, organic and conventional
Duration of exposure		3 minutes to 1 hour
Other variables measured		Commercial versus pilot scale grapes
Organic certification		IFOAM, inferred in introduction
Outcome		*Ex vivo* measures of antioxidant activity Inhibition of serum lipid peroxidation assay Oxidative stress levels
Measurement of outcome		*Ex vivo:* Inhibition of serum lipid peroxidation assay. Pooled, fresh human serum of 1mL, 150µL grape juice, 15µL $CuSO_4$ incubated at 37°C for 1hour. Oxidative stress levels measured spectrophotometrically as thiobarbituric acid reactive substances concentration (TBARS).
Statistical Analysis		Assays performed in triplicate. ANOVA, means compared with Tukey's test. Groups compared with *t*-test and Mann-Whitney *U*-test.
Results	Presentation	Numeric
	Significant	N/A
	Non-significant	N/A
	Unreported *(No statistical testing for O vs. C)*	All grape juices able to suppress serum lipid peroxidation, apart from the conventional Niagara sample.

	TBARS (nmol/mL)
Conventional Bordo Commercial	4.41±0.00
Conventional Bordo Pilot	2.94±0.03
Organic Bordo Commercial	4.58±0.00
Organic Bordo Pilot	3.51±0.03
Conventional Niagara Commercial	3.77±0.03
Conventional Niagara Pilot	4.90±0.00
Organic Niagara Commercial	4.33±0.06
Organic Niagara Pilot	4.01±0.00

Table 6: Paper 5

Author		**Grinder-Pedersen, L., Rasmussn, S.E., Bügel, S., Jørgensen, L.V., Dragsted, L.O., Gundersen, V. and Sandström, B.**
Title		Effect of diets based on foods from conventional versus organic production on intake and excretion of flavonoids and markers of antioxidative defence in humans. (2003) J Agric Food Chem 51 (19):5671-6
Study design and type		Double-blinded randomized crossover intervention study Humans
Quality		Unsatisfactory (no organic certification)
Duration of study		65 days (two 22 day intervention periods with strict control of dietary intake, separated by a three week washout period)
Objective		To investigate the effect of conventionally and organically produced diets on markers of antioxidative defence in humans.
Hypothesis		Cultivation techniques may affect the absorption and availability of polyphenolic substances, which have suggested health benefits
Sample size		N=16
Baseline characteristics of study subject/cell		6 males, 10 females, healthy, non-pregnant, non-lactating, nonsmokers, no regular medication
Age of study subjects		21-35 years
Exposure		Controlled intervention diets (organic and conventional) consisting of same food types and same 4 menus. Organic pork originated from conventionally bred Danish parents; pigs were raised organically after weaning. Organic and conventional pork was processed in the same factory; and recipes omitting additives were used for both. Organic dairy products were from a Danish organic dairy; conventional dairy products were from a Danish dairy where conventional farming methods were employed. Eggs were collected directly from organic or conventional farmers. Organic and conventional vegetables were sown and harvested in the same week, and collected from fields within a similar geographic location in Denmark (>3km from cities with >1000 inhabitants, >3km from major roads, >10km from industries with extensive omission, >15km from highways). Organic apples were purchased from a small Danish organic specialty shop. Conventionally and organically produced wheat and rye seeds were purchased directly from farmers by a Danish bakery specializing in organic bread; seeds were ground into flour and identical recipes were used for organic and conventional breads. The remaining fruits and groceries were purchased in a Danish supermarket.
Measurement of exposure		Menus and quantities were identical in organic and conventional diets, with some variance in cultivars. Individual portions of meals were weighed according to estimated energy requirement, and no food or drink other than those provided by the study were permitted.
Duration of exposure		22 days
Organic certification		No organic certification
Outcome		Excretion of flavonoids (quercetin, kaempferol, isorhamnetin, naringenin & hesperetin) Plasma antioxidant capacity (superoxidase dismutase, glutathione peroxidase glutathione reductase, catalase in erythrocytes, Trolox equivalent capacity, ferric reducing ability of plasma)
Measurement of outcome		*Biological* Excretion of flavonoids: urinary quercetin, kaempferol, isorhamnetin, naringenin and hesperetin in µg and as a percentage of intake. Twenty-four hour urine samples collected on days 0 and 22 of intervention period; individuals were given 80mg p-aminobenzoic acid with each meal on both collection days to validate the completeness of urine collection. Plasma antioxidant capacity: fasting blood samples collected on days -1, 0, 22 and 23 of intervention period. Superoxidase dismutase (SOD): automated assay using commercially available kit SD125; units/g of Hb Glutathione peroxidase (GSH-Px): automated assay using commercially available kit RS506; units/g of Hb Glutathione reductase (GR): automated assay using Wheeler et al. method; units/g of Hb Catalase in erythrocytes (CAT): automated assay using Wheeler et al. method; units/g of Hb Trolox equivalent capacity (TEAC): automated assay using commercially available kit NX2332; mmol/L Ferric reducing ability of plasma (FRAP): automated assay using Benzie and Strain method; nmol/L Malondialdehyde (MDA): using TBARS HPLC method as per Young et al.; pmol/mg of protein 2-aminoadipic semialdehyde (2-AAS): using Daneshvar et al. method; pmol/mg of protein
Statistical analysis		Means of duplicates used for analysis. Unpaired *t* test used in first period only for effect of intervention.
Confounders adjusted for		N/A
Results	Presentation	Numeric data
	Significant	Quercetin: 6µg higher in organic compared to conventional ($p<0.05$) Kaempferol: 3µg higher in organic compared to conventional ($p<0.05$) TEAC: 0.078mmol/L lower in organic compared to conventional ($p<0.05$)
	Non-significant	Hesperetin: 6µg higher in organic compared to conventional Naringenin: 3µg higher in organic compared to conventional Isorhamnetin: No difference between conventional and organic SOD: 3 units/g Hb lower in organic compared to conventional

	CAT: 0.26units/g Hb lower in organic compared to conventional GSH-Px: 0.16units/g Hb higher in organic compared to conventional GR: 0.19units/g Hb lower in organic compared to conventional FRAP: 6nmol/L higher in organic compared to conventional 2-AAS: 0.34pmol/mg protein higher in organic compared to conventional MDA: 0.38pmol/mg protein higher in organic compared to conventional
Unreported	N/A

Table 7: Paper 6

Author		**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. and Dagnelie, P.C.**
Title		Consumption of organic foods and risk of atopic disease during the first 2 years of life in the Netherlands. (2007) British Journal of Nutrition 99(3):598-605
Study design and type		Cohort Humans (infants)
Quality		Unsatisfactory (no definition or certification of organic production methods)
Duration of study		2 year follow up period
Objective		To determine whether organic food consumption by infants is associated with developing atopic manifestations in the first two years of life.
Hypothesis		Higher levels of antioxidants and CLA in organic products have been suggested to be preventative against wheezing and atopic reactions respectively
Sample size		N=2764
Baseline characteristics of study subject/cell		Healthy, term infants
Age of study subjects		0-2 years
Exposure		Organic diets: strictly organic (>90%), moderately organic (50-90%), conventional (no organic food)
Measurement of exposure		Parental reported diet of infant in second year of life (percentage of organic food consumed in various diet categories: meat, eggs, vegetables, fruit, dairy products, bread/pasta/rice/beans/wheat). The mean of all diet categories was used in analysis. Maternal dietary information was used as a proxy for missing infant data given strong correlation between these variables (Pearson's *R* 0.85; p<0.001)
Duration of exposure		1 year (reported)
Organic certification		Not certified
Outcome		Eczema Wheeze IgE antibodies
Measurement of outcome		*Self-reported* Eczema and Wheeze: Assessed by questionnaires from the International Study of Asthma and Allergies in Childhood, at age 7, 12 and 24 months. Eczema was defined as an itchy rash that came and went (unless it was reported as nappy rash, rash around the eyes and/or scalp scaling). Recurrent wheeze was defined as presence of wheezing with at least four attacks in the first two years; prolonged wheeze was classified as ever having been awake due to wheezing in both the first and second year. *Biological* IgE antibodies: IU/ml serum; measured using RIA
Statistical analysis		Unadjusted associations examined with logistic regression. Multivariate logistic regression models fitted to control for potential confounders.
Confounders adjusted for		Sex, maternal education, BMI in infant at 1 year, parental history of allergy, sibling history of allergy, number of older siblings, breastfeeding, day-care attendance, pets, exposure to environmental tobacco smoke, vaccinations, antibiotic intake through breastfeeding or through oral medication, vegetarian diet
Results	Presentation	Numeric data
	Significant	Eczema: Adjusted OR of 0.64 for consumption of strictly organic dairy products compared to conventional dairy products (p=0.02) OR of 0.63 (95% CI 0.43-0.93) for consumption of strictly organic dairy products compared to conventional dairy products, excluding infants who had never consumed raw or farm milk. OR of 0.67 (95% CI 0.46-0.98) for maternal consumption of strictly organic dairy products compared to conventional dairy products during pregnancy. OR of 0.67 (95% CI 0.46-0.99) for maternal consumption of strictly organic dairy products compared to conventional dairy products during pregnancy, excluding mothers who did not consume dairy products.
	Non-significant	Eczema, recurrent wheeze, prolonged wheeze, allergen-specific IgEs: adjusted OR range of 0.51 – 0.95 for moderately organic compared to conventional; adjusted OR range of 0.51 – 1.64 for strictly organic compared to conventional Eczema: adjusted OR range of 0.89 – 1.40 for moderately organic compared to conventional in analysis of dairy, meat, fruit, vegetables, eggs consumption; adjusted OR range of 0.71 – 1.03 for strictly organic compared to conventional in analysis of meat, fruit, vegetables, eggs consumption OR of 0.69 (95% CI 0.48-1.01) for consumption of strictly organic dairy products compared to conventional, excluding infants who had never consumed dairy products.
	Unreported	N/A

Table 8: Paper 7

Author		**Olsson, M.E., Anderson, C.S., Oredsson, S., Berglund, R.H. and Gustavson, K.E.**
Title		Antioxidant levels and inhibition of cancer cell proliferation in vitro by extracts from organically and conventionally cultivated strawberries. (2006) J Agric Food Chem 54 (4):1248-55
Study Design and type		Experimental. In vitro
Quality		Unsatisfactory (no organic certification)
Objective		To study the effects of extracts from different cultivars of strawberries on the proliferation of colon cancer cells and breast cancer cells, and analyse possible correlations with the different levels of several antioxidants in the cultivars.
Hypothesis		Growing conditions will affect the antioxidant content of strawberries, and thus impact their proliferative capacity for colon cancer and breast cancer cells
Sample size		2×10^4 cells
Baseline characteristics of study subjects/cells		Human colon carcinoma cells (HT29) and oestrogen-receptor-positive breast carcinoma cells (MCF-7) obtained from American Tissue Culture Collection
Exposure		Extracts of organic and conventional strawberry cultivars (cvs *Honeyoe* and *Cavendish*) grown at Rånna research station, Sweden, harvested at commercial ripeness. All samples treated consistently regardless of cultivar or cultivation method.
Measurement of exposure		4 different concentrations of extract used (0.025%, 0.05%, 0.25%, 0.5% plant dry matter of total weight in wells); equal amount of solvent (50% ethanol) added. After 24hrs, 20µl reagent added, samples incubated 1hr (HT29 cells) and 3hrs (MCF-7 cells). 3 replicates used for each extract.
Duration of exposure		Extracts added to medium and incubated 24hrs.
Organic certification		Not certified, but fertilization, planting, harvesting, etc. described
Outcome		Proliferation of breast and colon cancer cells
Measurement of outcome		Ability of cells to cleave the tetrazolium salt WST-1 to formazan, a measure of mitochondrial activity. Formation of formazan determined photometrically, by microplate reader. All measures conducted with 3 independent samples for each concentration of extract and for each cell line. All repeated on 3 occasions. Results reported as cell proliferation as % of control
Statistical Analysis		One-way ANOVA. Significance measured at $p<0.05$ Correlations between contents of different antioxidants and cancer cell proliferation calculated.
Results	Presentation	Numeric and graphical
	Significant	0.5% & 0.25%: significantly higher cell proliferation in organically grown strawberries for HT29 and MCF-7 cells. 0.5% & 0.25%: significant growth inhibitory effect when all organic compared to all conventional cultivars (no values presented). HT29 cells (0.5%): *All cultivars:* C 50.3, O 40.0 ($p\leq0.005$); *Cavendish:* C 51.3, O 41.7 ($p\leq0.01$); *Honeyoe:* C 48.1, O 41.4 ($p\leq0.05$) MCF-7 cells (0.5%): *All cultivars:* C 62.1, O 46.9 ($p\leq0.005$); *Cavendish:* C 74.4, O 51.8 ($p\leq0.01$); *Honeyoe:* C 57.1, O 44.8 ($p\leq0.05$) HT29 cells (0.25%): *All cultivars:* C 70.2, O 57.2 ($p\leq0.005$); *Honeyoe:* C 73.6, O 57.5 ($p\leq0.01$) MCF-7 cells (0.25%): *All cultivars:* C 81.8 O 70.2 ($p\leq0.005$); *Honeyoe:* C 82.0, O 66.0 ($p\leq0.05$)
	Non-significant	0.25% *cv. Cavendish,* growth inhibitory effect ($p=0.07$) 0.05% & 0.025%: inhibitory effect on cancer cell proliferation (no values presented). 0.05% & 0.025%: no significant difference between O & C for cancer cell proliferation for MCF-7 cells or HT29 cells, with the exception of *cv. Pavana* (no values presented). HT29 cells (0.25%): *Cavendish:* C 70.0, O 60.9, NS MCF-7 cells (0.25%): *Cavendish:* C 90.4, O 79.0, NS
	Unreported	N/A

Table 9: Paper 8

Author		**Rist, L., Mueller, A., Barthel, C., Snijders, B., Jansen, M., Simões-Wüst, A.P., Huber, M., Kummeling, I., von Mandach, U., Steinhart, H. and Thijs, C.**
Title		Influence of organic diet on the amount of conjugated linoleic acids in breast milk of lactating women in the Netherlands. (2007) British Journal of Nutrition 97(4):735-743
Study design and type		Cross-sectional Human
Quality		Unsatisfactory (No definition or certification of organic production methods)
Duration of study		N/A
Objective		To determine whether the incorporation of organic dairy and meat products in the maternal diet affects the contents of the conjugated linoleic acid isomers and trans-vaccenic acid in human breast milk.
Hypothesis		Organic meat and dairy contains higher levels of CLA and TVA, leading to higher levels of these fatty acids in human breastmilk
Sample size		N=312
Baseline characteristics of study subject/cell		Lactating women; 146 conventional lifestyle, 166 alternative lifestyle
Age of study subjects		No data
Exposure		Organic meat and dairy intake categorized into four groups: • >90% organic (>90% meat and dairy is organic, or >90% dairy is organic and no meat is consumed, or >90% meat is organic and no dairy is consumed) • moderately organic diet (>50% meat and dairy is organic and <90% meat or dairy is organic, 50-90% meat is organic and no dairy is consumed, or 50-90% dairy is organic and no meat is consumed) • conventional diet (<50% meat and dairy is organic, or <50% dairy is organic and no meat is consumed, or <50% meat is organic and no dairy is consumed) • other (other combinations of < 50% organic meat and >50% organic dairy, or vice versa, and missing or inconsistent data)
Measurement of exposure		Self-administered food frequency questionnaire in week 34 of pregnancy and at time of breast milk sampling, with questions on frequency of consumption, portion size, and food source (organic, conventional or biodynamic). Organic and biodynamic consumers were asked to estimate if their intake of each food group was <50% organic, 50-90% organic, or greater than 90% organic.
Duration of exposure		No data
Organic certification		No data
Outcome		*Biological* Fatty acid composition of breast milk: Rumenic acid; Other conjugated linoleic acids; Trans-Vaccenic acid; LA (C18:2n-6); Sum of LA derivatives; LA + LA derivatives α-Linolenic acid; Sum of ALA derivatives; ALA + ALA derivatives; Total PUFA; Total MUFA; Total SFA; C16:0; C18:2; C18:0; C14:0; C12:0; Trans9-C18:1; C20:4; C18:3n-6 (di homo); C22:6; C17:0; C15:0; C14:1
Measurement of outcome		GC-free induction decay and Ag^{+}-HPLC All outcomes measured as weight percentage of total milk fat
Statistical analysis		Duplicate values averaged. Student's *t* test assessed differences between groups. Significance measured at $P \leq 0.05$. Linear regression analysis and interactions between origin and fat intake tested by adding interaction terms to linear regression models.
Confounders adjusted for		In regression analysis: recruitment group, maternal age, maternal education, use of supplements, season and fat intake from dairy and ruminant meat
Results	Presentation	Numeric data
	Significant	Rumenic acid: 0.04% higher in >50% O (p<0.05), 0.09% higher in >90%0 (p<0.001) compared to conventional; 0.06% higher in >90% O (p<0.001) in regression analysis after adjusting for recruitment group, maternal age, maternal education, use of supplements and season; 0.04% higher in >90% O (p<0.01) in regression analysis after adjusting for recruitment group, maternal age, maternal education, use of supplements, season and fat intake from dairy and ruminant meat Other conjugated linoleic acids: 0.01% lower in >50% O (p<0.05) compared to conventional Trans-Vaccenic acid: 0.11% higher in >90% O (p<0.001), 0.05% higher in other (p<0.05) α-Linolenic acid: 0.16% lower in >50% O (p<0.05), 0.23% lower in >90% O (p<0.001), 0.12% lower in other compared to conventional ALA + ALA derivatives: 0.19% lower in >50% O (p<0.05), 0.23% lower in >90% O (p<0.05) compared to conventional Total MUFA: 2.27% lower in >90% O (p<0.001) compared to conventional C14:0: 1.02% higher in >50% O (p<0.01), 1.09% higher in >90% O (p<0.05), 0.57% higher in other (p<0.05) Trans9-C18:1: 0.14% lower in >50% O (p<0.001), 0.41% lower in >90% O (p<0.05), 0.37% lower in other (p<0.01) compared to conventional C20:4: 0.05% lower in >50% O and >90% O (p<0.01), 0.03% lower in other compared to conventional C18:3n-6 (di homo): 0.07% higher in >90% O (p<0.01) compared to conventional C17:0: 0.05% higher in >50% O (p<0.001) compared to conventional C15:0: 0.08% higher in >50% O (p<0.001), 0.1% higher in >90% O (p<0.001), 0.07% higher in other (p<0.001) compared to conventional C14:1: 0.06% higher in >50% O (p<0.01), >90% O (p<0.05), and other (p<0.001) compared to conventional
	Non-significant	Rumenic acid: 0.02% higher in other compared to conventional

	Other conjugated linoleic acids: no difference in >90% O and other compared to conventional Trans-Vaccenic acid: 0.06% higher in >50% O compared to conventional LA (C18:2n-6): 0.08% higher in >50% O, 1.17% higher in >90% O, 0.67% lower in other compared to conventional Sum of LA derivatives: 0.04% lower in >50% O, 0.03% higher in >90% O, 0.03% lower in other compared to conventional LA + LA derivatives: 0.04% higher in >50% O, 1.2% higher in >90% O, 0.69% lower in other compared to conventional Sum of ALA derivatives: 0.02% lower in >50% O, no difference in >90% O, 0.02% higher in other compared to conventional ALA + ALA derivatives: 0.1% lower in other compared to conventional Total PUFA: 0.18% lower in >50% O, 1.06% higher in >90% O, 0.79% lower in other compared to conventional Total MUFA: 1.36% lower in >50% O, 0.56% lower in other compared to conventional Total SFA: 1.54% higher in >50% O, 1.2% higher in >90% O, 0.36% higher in other compared to conventional C16:0: 0.17% higher in >50% O, 0.01% higher in >90% O, 0.59% higher in other compared to conventional C18:2: 0.08% higher in >50% O, 1.17% higher in >90% O, 0.67% lower in other compared to conventional C18:0: 0.42% lower in >50% O, 0.15% lower in >90% O, 0.07% lower in other compared to conventional C12:0: 0.39% higher in >50% O, 0.13% higher in >90% O, 0.05% higher in other compared to conventional C18:3n-6 (di homo): 0.02% higher in >50% O, 0.01% higher in other compared to conventional C22:6: 0.01% lower in >50% O, no difference in >90% O, 0.2% higher in other compared to conventional C17:0: 0.03% higher in >90% O, 0.02% higher in other compared to conventional
Unreported	N/A

Table 10: Paper 9

Author		**Tarozzi, A., Hrelia, S., Angeloni, C., Morroni, F., Biagi, P., Guardigli, M., Cantelli-Forti, G. and Hrelia, P.**
Title		Antioxidant effectiveness of organically and non-organically grown red oranges in cell culture systems. (2006) European Journal of Nutrition 45(3):152-8
Study design and type		Experimental. In vitro
Quality		Satisfactory
Objective		To determine if organic red oranges have higher total antioxidant activity and in vitro bioactivity, in terms of protective effect against oxidative damage at cellular level, than non-organic oranges.
Hypothesis		Factors such as cultivation, industrial processing and storage may affect the final concentration of phenolics in food, and their eventual bioactivity (antioxidant, cytoprotective and antiproliferative activity human colon carcinoma)
Sample size		Number of human samples not given
Baseline characteristics of study subjects/cells		Human colon carcinoma cells (Caco-2) routinely grown at 37°C, seeded at density of $8x10^4$ cells/m^2. Completely differentiated cells used at 12-14days post seeding.
Exposure		Organic and integrated red orange extracts (cv. *Tarocco*) from organic and integrated production, produced in eastern Sicily, Italy and purchased from a single retail outlet. Fruits with no physical defects or pathogen contamination, processed within 48-72hrs of purchase.
Measurement of exposure		Different concentrations of extracts, corresponding to 6.25-50mg fruit/ml
Duration of exposure		Cells incubated for 24hrs with orange extracts.
Organic certification		All organic and integrated fruits produced in line with EC regulations.
Outcome		Antioxidant activity (formation of intracellular reactive oxygen species [ROS]) Cytoprotective activity (cytotoxicity)
Measurement of outcome		After treatment with a compound used to induce oxidative stress (*t*-BuOOH): ROS formulation measured spectrofluorometrically, using fluorescent probe. Expressed as % inhibition of intracellular ROS after treatment with *t*-BuOOH. Cytotoxicity monitored by trypan blue uptake. Both measures: 3 independent experiments for each sample
Statistical Analysis		Student's *t* test for comparison of means and Pearson's correlation coefficient for relations among variables. Significance measured at $p<0.05$.
Results	Presentation	Graphical; no numeric data
	Significant	Marked dose-dependent increase of intracellular antioxidant activity. 25-50mg/ml: significantly higher in organic than integrated ($p<0.05$)
	Non-significant	No significant differences in cytoprotective activity between integrated and organic.
	Unreported	No numeric values reported

Table 11: Paper 10

Author		**Tarozzi, A., Marchesi, A., Cantelli-Forti, G. and Hrelia, P.**
Title		Cold-storage affects antioxidant properties of apples in Caco-2 cells. (2004) Journal of Nutrition 134(5):1105-9
Study design and type		Experimental. In vitro
Quality		Satisfactory
Objective		To investigate the influence of commercial cold-storage periods on the antioxidant content and health-related properties of apples grown either by organic or integrated systems.
Hypothesis		Growing conditions affect anthyocyanin levels which may play a role in the prevention of human pathologies related to oxidative damage
Sample size		Number of human samples not given
Baseline characteristics of study subjects/cells		Human colon carcinoma cells (Caco-2) routinely grown at 37°C, seeded at density of $8x10^4$ cells/m^2. No description given of humans from which cells originated. Differentiated and un-differentiated cells used.
Exposure		Organic and integrated apple extracts (cv. *Golden Delicious*) from organic and integrated production, harvested in Peregrine Valley, Italy. Analysed immediately or stored for up to 6months.
Measurement of exposure		50mg/L apple extracts
Duration of exposure		For intracellular antioxidant and cytoprotective activity studies, cells incubated with 50mg/L integrated and organic apple extracts for 24hrs. For cell proliferation studies, cells incubated for 96hrs.
Other variables measured		Apples with and without skin, at 3 and 6months post-harvest.
Organic Certification		Described as 'strictly' organic but not certified
Outcome		Antioxidant activity (formation of intracellular reactive oxygen species [ROS]) Cytoprotective activity (cytotoxicity) Cell proliferation
Measurement of outcome		After treatment with *t*-BuOOH (a compound used to induce oxidative stress): • ROS formulation: spectrofluorometrically, using fluorescent probe. Expressed as % inhibition of intracellular ROS after treatment with *t*-BuOOH. • Cytotoxicity: monitored by trypan blue uptake. Cell proliferation: colorimetric MTT assay, using a tetrazolium reagent. Expressed as % inhibition of proliferation of Caco-2 cells. All measures: 3 independent experiments performed for each sample
Statistical Analysis		Student's *t* test for comparison of means and Pearson's correlation coefficient for relations among variables. Significance measured at $p<0.05$
Results	Presentation	Graphical
	Significant	None
	Non-significant	Cultivation did not affect intracellular antioxidant, cytoprotective, antiproliferative activity ($p<0.1$). All markers higher in integrated apples (with and without skin) with exception of cytoprotective activity in apples without skin.
	Unreported	N/A

Table 12: Paper 11

Author		**Yildirim, H.K., Akçay, Y.D., Güvenç, U. and Sözmen, E.Y.**
Title		Protection capacity against low-density lipoprotein oxidation and antioxidant potential of some organic and non-organic wines. (2004) Int J Food Sci Nutr 55(5):351-62
Study design and type		Experimental. In vitro
Quality		Unsatisfactory (no statement on the nature of organic produce)
Objective		To determine the antioxidant capacity and inhibition of LDL oxidation of some organic and non-organic wines
Hypothesis		Organic and nonorganic wines may differ in their phenol content and thus antioxidant capacity, which has been shown to inhibit atherogenesis
Sample size		*n*=66
Baseline characteristics of study subjects/cells		Healthy donors (22 females, 40 males). Exclusion criteria: presence of acute or chronic diseases, alcohol intake, smoking, any medication or antioxidant supplementation in 8 weeks before study entry
Exposure		Organic and non-organic Cabernet Sauvignon wines
Measurement of exposure		No statement describing the addition of wine to the LDL samples
Duration of exposure		No data
Organic certification		Certified organic grapes (INAC, Turkey)
Outcome		LDL oxidation
Measurement of outcome		LDL oxidation: % of inhibition of LDL oxidation, calculated from different in MDA-diene levels between pre-copper & post-copper induction, vs. blank stimulation.
Statistical Analysis		One-way ANOVA. Significance measured at $p<0.05$. Multivariate techniques: principal components analysis.
Results	Presentation	Graphical; no numeric data. Results presented according to wine variety rather than organic vs. non-organic.
	Significant	N/A
	Non-significant	N/A
	Unreported	N/A

7.0 DISCUSSION

7.1 Review process

To our knowledge, this is the only systematic review ever conducted on the putative health effects of organic compared with conventionally produced foodstuffs. Despite an extensive search strategy, the review only identified eleven relevant articles meeting our inclusion criteria and published, with an English abstract, in peer-reviewed journals since January 1958 (50 years). All of the publications in the review were written in English.

The current report focuses only on direct comparisons of health effects of organically and conventionally produced foodstuffs. This review specifically did not set out to assess the health impact of potential food contaminants (such as herbicide, pesticide and fungicide residues) of organically and conventionally produced foodstuffs, or the environmental or environmental health impacts of organic and conventional agricultural practices.

The 11 papers were extremely heterogeneous in terms of study design, study population or cell line, exposure, outcomes and quality. The findings are synthesised and discussed in Section 7.3 using a systematic narrative approach according to the following themes: study hypotheses, study designs, study exposures and health outcomes.

7.2 Study quality

The pre-specified quality criteria used in the review process identified a recurrent weakness in the publications studying the putative health effects of organically compared with conventionally produced foodstuffs. Nearly two thirds of the included studies failed to provide a clear description of the organic regimen under which the crops or livestock products (the study exposures) were produced. While some papers made no mention at all of specific certification schemes, or other descriptors of organic production methods, several papers merely stated that the produce was obtained from “certified” organic farms without giving further details. In order to be able systematically to compare organically with conventionally produced foodstuffs it is essential to have a clear definition of the exposure, which requires details of the production methods used to produce the foodstuffs. We propose that the study quality criteria applied during this review are a minimum standard required to improve the quality of research published in this field.

7.3 Study hypotheses

Eight of the eleven studies were predicated on the understanding that organic production methods result in higher nutrient levels in foodstuffs (Table 13), and hypothesised that these compositional differences would result in different health responses.[9,12,14-19] All studies included in this review preceded a recent systematic review of nutrient content of organic foods[8] which concluded that organically and conventionally produced foodstuffs are broadly comparable in their nutrient content. Three studies hypothesized that any health effects of organic foodstuffs in humans are not likely to be due solely to differences in chemical/ nutrient composition of food.[10,11,13] The hypotheses varied but proposed a range of mechanisms of action including that production methods differentially affect markers of carcinogenesis[11], availability of polyphenolic substances[13] or bioactivity of phenolics.[10] Of these latter studies, Briviba et al. tested 9 outcomes and found no statistically significant differences between production methods,[11] Grinder-Pedersen et al. detected statistically significant differences (at the 5% level) for 3 of 13 outcomes,[13] and Tarozzi et al. detected a statistically significant difference (at the 5% level) for 1 of 2 outcomes.[10] No numeric data are available from the Tarozzi et al. study to permit estimation of the size of the difference detected,[10] while the differences detected by Grinder-Pedersen were small (3-6µg for urinary flavonoids; 0.078mmol/L plasma for trolox equivalent capacity).[13]

Table 13: Hypotheses tested in papers included in systematic review

Hypothesis type	Author	Hypothesis
Nutrient composition is the mechanism for health effects	Ackay (2004)	Ecological conditions, grape variety, degree of ripening and winemaking techniques affect the type and concentrations of polyphenols in grapes, which may be medically important due to their antioxidant and anti-inflammatory activity
	Caris-Veyrat (2004)	Growing conditions will affect the content of antioxidants in tomatoes, which in turn will affect antioxidant status in humans (i.e. lycopene, consumption of which is correlated with reduced risk of prostate cancer)
	Dani (2007)	Organically grown grapes may have a different composition which may affect their ability to neutralize reactive species, which have a suggested relevant pathophysiological role in human diseases such as cancer and atherosclerosis
	Kummeling (2007)	Higher levels of antioxidants and CLA in organic products have been suggested to be preventative against wheezing and atopic reactions respectively
	Olsson (2006)	Growing conditions will affect the antioxidant content of strawberries, and thus impact their proliferative capacity for colon cancer and breast cancer cells
	Rist (2007)	Organic meat and dairy contains higher levels of CLA and TVA, leading to higher levels of these fatty acids in human breastmilk
	Tarozzi (2004)	Growing conditions affect anthyocyanin levels which may play a role in the prevention of human pathologies related to oxidative damage
	Yildirim (2004)	Organic and nonorganic wines may differ in their phenol content and thus antioxidant capacity, which has been shown to inhibit atherogenesis
Non-compositional mechanism for health effects	Briviba (2007)	Modulation of physiological processes in humans cannot be predicted solely by chemical composition differences; another attribute influenced by production system may differentially affect markers of carcinogenesis (which can lead to the formation of cancer)
	Grinder-Pedersen (2003)	Cultivation techniques may affect the absorption and availability of polyphenolic substances, which have suggested health benefits
	Tarozzi (2006)	Factors such as cultivation, industrial processing and storage may affect the final concentration of phenolics in food, and their eventual bioactivity (antioxidant, cytoprotective and antiproliferative activity human colon carcinoma)

7.4 Study designs

Of the included studies, six were human studies (four clinical trials,[9,11-13] one cohort[14] and one cross-sectional[15]), and five were conducted using *in vitro* or *ex vivo* techniques on human cell lines[10,17-19] or serum[16] (Table 14). All four of the clinical trials had limitations in their study designs; a major concern being the small number of participants recruited (ranging from 6 to 20 in total), as small sample sizes severely limit the ability of clinical trials to detect real effects. One of the four clinical trials[13] reported statistically significant results: two of five urinary flavonoids tested were higher in individuals consuming the organic rather than the conventional diet, while plasma antioxidant activity was found to be lower in individuals consuming the organic rather than the conventional diet.

Table 14: Study designs employed in papers included in systematic review

Study design type	Author	Study Design
Human	Ackay (2004)	Crossover trial
	Briviba (2007)	Double-blind randomised crossover trial
	Caris-Veyrat (2004)	Blinded randomised controlled trial
	Grinder-Pedersen (2003)	Double-blind randomised crossover trial
	Kummeling (2007)	Cohort
	Rist (2007)	Cross-sectional
Human cell lines	Dani (2007)	Ex vivo (serum)
	Olsson (2006)	In vitro (HT29 and MCF-7 cells)
	Tarozzi (2004)	In vitro (Caco-2 cells)
	Tarozzi (2006)	In vitro (Caco-2 cells)
	Yildirim (2004)	In vitro (LDL)

The cohort[14] and cross-sectional[15] studies included in the review, while conducted with substantially larger samples (2764 and 312 respectively), had a number of weaknesses in their approaches to collecting and analysing the data. The two reports were based on a study population recruited as part of the KOALA Birth Cohort Study investigating influences of lifestyle and genetic constitution on child and parent health.[20] Both studies used a self-reported measure of exposure.[14,15] Rist et al. gave no information on the duration of exposure.[15] Kummeling et al. also used self-reported measures for the primary outcome (atopic manifestations).[14] Both reports conducted multiple statistical testing; Rist et al. conducted statistical testing on 24 fatty acid outcome variables,[15] and Kummeling et al. conducted 28 statistical tests on the association of dietary exposures and risk of atopic manifestations.[14]

The five *in vitro* studies[10,16-19] used different approaches to test different biological materials. Two of the *in vitro* studies reported statistically significant differences in responses to samples from different production methods.[10,17] It is not possible directly to extrapolate results from the *in vitro* studies to human health as the proposed mechanism of action is unclear.

7.5 Exposures

The majority of the eleven papers included in the review were concerned with studying the effects of specific foodstuffs (Table 15): six studied fruit,[10-12,16-18] two studies wine[9,19] and one studied livestock products.[15] Eight studies specifically investigated foodstuffs known to be rich in antioxidants (for example tomatoes, apples and oranges),[9-12,16-19] and six of these did not detect any statistically significant differences of organic and conventional foodstuffs on antioxidant activity.[9,11,12,16,18,19] Tarozzi et al. reported that organic red orange extracts increased antioxidant activity,[10] Olson et al. reported that organic strawberry extracts had higher antiproliferative activity,[17] while Grinder-Pedersen et al. reported that the organic intervention diet decreased plasma antioxidant activity.[13] The two studies on wine from different production methods did not report any statistical significant differences in outcomes.[9,19] A recent systematic review found that biologically plausible differences in content of certain phytochemicals exist between organic and conventionally produced crops, but concluded that the health benefits of increased dietary intake of these phytochemicals is currently unknown.[8]

Table 15: Exposures used in studies included in the systematic review

Exposure type	Author	Exposure
Fruit	Briviba (2007)	Organic and conventional apples
	Caris-Veyrat (2004)	Organic and conventional tomato purees
	Dani (2007)	Organic and conventional grape juice
	Olsson (2006)	Organic and conventional strawberry extracts
	Tarozzi (2004)	Organic and integrated apple extracts
	Tarozzi (2006)	Organic and integrated red orange extracts
Wine	Ackay (2004)	Organic and nonorganic Cabernet Sauvignon wines
	Yildirim (2004)	Organic and nonorganic wines
Meat and dairy	Rist (2007)	>90% organic diet, moderately organic diet (50-90%), conventional diet (<50% organic) and other diet (combinations of <50% organic meat and >50% organic dairy and vice versa)
Diet	Grinder-Pedersen (2003)	Organic and conventional controlled intervention diet
	Kummeling (2007)	Strictly organic diet (>90%), moderately organic diet (50-90%) and conventional diet (0% organic)

Only two studies investigated organic food as part of the whole diet. Kummeling et al. reported no statistically significant findings for the association of the organic diet as a whole on atopic manifestations in children.[14] Separate statistical analyses for the associations of selected organic foodstuffs on parent-reported asthma, wheeze and on a biological measure of atopic sensitisation found an association between organic dairy product consumption and eczema risk, but no association for any of the other dietary groups or health outcomes.[14] It was not clear from the published report whether these separate food analyses were part of the pre-specified hypotheses of the study.

The methods used for the measurement of exposure also varied. The majority of studies compared a specified ‘exposure’ or ‘dose’ of a foodstuff as part of a controlled exposure

study (see section on study design). The two longitudinal population studies[14,15] used measures of self-reported exposure and there is therefore a chance that the results presented in these papers may have been affected by misclassification and recall bias. Kummeling et al. also used maternal dietary information as a proxy for missing infant data for 16% of study participants.[14]

Two studies which reporting statistically significant differences between foodstuffs from organic and conventional production methods did not clearly specify the specific certification of the organic exposure,[13,17] while another compared organically produced oranges with oranges produced by integrated agricultural methods.[10] It is important to note that integrated agricultural methods are specifically not "conventional" and the results of the two papers by Tarozzi et al.[10,18] therefore need to be interpreted with caution.

7.6 Health outcomes

Most of the included papers did not study direct human health outcomes (Table 16); in nine of the eleven papers, the outcome was a change in antioxidant activity in response to exposure to organic or conventional foodstuffs.[9-13,16-19] Antioxidant status is a biomarker, and not equivalent to a health outcome. Of these nine papers, three reported significant differences in outcomes between organic and conventional foodstuffs.[10,13,17]

Table 16: Outcomes measured in studies included in the systematic review

Outcome type	Author	Health Outcome
Antioxidant activity	Ackay (2004)	LDL oxidation, antioxidant activity (antioxidant capacity and levels of eSOD, eCAT and eTBARS), phenol levels
	Briviba (2007)	Serum glucose, serum triacylglycerol, uric acid, LDL antioxidant capacity, DNA damage in peripheral blood lymphocytes
	Caris-Veyrat (2004)	Plasma levels of lycopene, beta carotene and vitamin C
	Dani (2007)	Inhibition of serum lipid peroxidation; oxidative stress levels
	Grinder-Pedersen (2003)	Excretion of flavonoids (quercetin, kaempferol, isorhamnetin, naringenin & hesperetin)
		Plasma antioxidant capacity (superoxidase dismutase, glutathione peroxidase glutathione reductase, catalase in erythrocytes, Trolox equivalent capacity, ferric reducing ability of plasma)
	Olsson (2006)	Proliferation of HT29 and MCF-7 cells
	Tarozzi (2004)	Antioxidant activity (formation of intracellular reactive oxygen species [ROS]), cytoprotective activity (cytotoxicity), cell proliferation
	Tarozzi (2006)	Antioxidant activity (formation of intracellular reactive oxygen species [ROS]), cytoprotective activity (cytotoxicity)
	Yildirim (2004)	LDL oxidation
Atopic manifestations	Kummeling (2007)	Eczema, wheeze, IgE antibodies
Breastmilk fatty acid composition	Rist (2007)	Fatty acid composition of breast milk: Rumenic acid, other conjugated linoleic acids, trans-Vaccenic acid, LA (C18:2n-6), sum of LA derivatives, LA + LA derivatives, α-Linolenic acid, sum of ALA derivatives, ALA + ALA derivatives, total PUFA, total MUFA, total SFA, C16:0, C18:2, C18:0, C14:0, C12:0, Trans9, C18:1, C20:4, C18:3n-6 (di homo), C22:6, C17:0, C15:0, C14:1

Weaknesses in exposure specification in two of these latter papers have previously been discussed: Olsson et al. did not provide information on certification of the organic

strawberry extracts produced used;[17] Tarozzi et al. compared oranges produced by organic and integrated (as opposed to conventional) agricultural methods.[10] Grinder-Pedersen et al. reported that for those consuming organic diets, antioxidant capacity was lower, while urinary excretion of some flavonoids was higher.[13] Inter-individual variation in rates of flavonoid excretion must be considered when interpreting these latter results. Furthermore, the intervention diets were not organically certified, and contain some varietal differences which may explain some of the reported effects.[13]

Numerous health benefits have been ascribed to antioxidants, but evidence of action is mixed. The recent World Cancer Research Fund (WCRF) report graded the evidence as "probable" that foods containing vitamin C and beta-carotene decreased the risk of oesophageal cancer, while they graded the evidence as "limited – suggestive" that foods containing vitamin E reduced the risk of oesophageal and prostate cancers.[21] The WCRF explicitly did not ascribe benefits specifically to these nutrients (hence "foods containing…"), or to antioxidant activity. A recent large Cochrane review of randomised controlled trials which used antioxidant supplements for primary or secondary prevention of disease[22] found no evidence of benefit from supplementation and found possible evidence of harm associated with vitamin A, beta-carotene and vitamin E supplementation. It is important to recognise that nutrients consumed in the form of dietary supplements may behave differently from those consumed in the food matrix.

The remaining two papers not investigating antioxidant activity were both drawn from the same cohort.[14,15] Kummeling et al. used self-reported measures for the primary outcome (atopic manifestations): a source of potential reporting bias in the study findings.[14] Rist et al. examined fatty acid composition of breast milk and implied possible health benefits for infants of higher levels of conjugated linoleic acids in breast milk of mothers consuming diets high in organic products.[15] No actual measure of health of infants (or mothers) was reported, and the results may also be confounded by non-dietary factors which affect breast milk composition.[15] Trans fats comprise a small percentage of milk fat and any compositional difference is unlikely to have significant health effects.[23]

7.7 Review limitations

It is important to recognise the potential limitations of the review process.

7.7.1 Review methods

It is possible that this review did not identify all relevant publications. Some studies may have been missed although we attempted to minimise this possibility by repeating our search in the four most relevant scientific publication databases. We also hand searched reference lists of relevant articles for potential papers, and contacted relevant subject experts.

We are aware of one relevant paper, published after our cut-off date, which reports on a 6-week clinical trial of the effects of conventionally or organically produced carrots, or no carrots, on various health-related outcomes including plasma antioxidant capacity, endogenous DNA strand breaks and immune parameters.[24] The study sample was small (n=12 per study arm) and included only non-smoking men aged 19-54 years. The study reported no effect of agricultural production system on any of the health-related outcomes measured.[24]

Significant efforts were made to ensure that data were accurately extracted from all the included studies. All data were extracted by two review team members and compared to ensure consistency. It is possible that small errors occurred in data extraction and that these errors have been incorporated in the analysis. However, as we did not use quantitative approaches to summarise the data, such as meta-analysis, this will have little impact on the findings reported.

Study quality was assessed using criteria, based on key components of study design developed for this review, which we considered to be a minimum standard required. These criteria are subjective and could be criticised for not being sufficiently rigorous as they do not include assessment of factors such as sample size, quality of laboratory methods used or suitability of statistical analysis. In addition, it is important to note that although the EC organic farming regulations[25] are most applicable to organic farming and foodstuffs in the UK, studies met quality criteria if they mentioned other organic certification bodies. No judgement was made on the quality of these organic definitions, which may be wide-ranging and thereby reduce comparability between organic studies.

There are a number of factors that could have introduced publication bias in our findings. Foreign language publications which did not have an English language abstract, and grey

literature, were excluded from the review. Additionally, it is possible that peer-reviewed journals were less likely to publish papers reporting non-significant differences.[26] It is possible that authors did not report all laboratory analyses conducted in their research (reporting bias). Non-significant findings are more likely to be omitted from research papers.[26]

7.7.2 Data quality

The findings of our review are restricted by important shortcomings present in the studies included in the review, such as problems with study design, sample size, and measurement of exposure and health outcomes. For example, four of the six human studies were conducted with samples of 20 or fewer participants.[9,11-13] Small studies have less statistical power to demonstrate a real effect. None of the intervention studies presented the power calculations they used to determine the number of study subjects required to detect a difference in their outcome of interest. There are also concerns over the rationale for the quantity and duration of exposure in the clinical trials. For example, one cross-over trial used an exposure of 100-200mL doses of wine from different production methods consumed over 15 minutes and separated by a six week wash-out period,[9] while another used an exposure of 1kg doses of apples from different production methods consumed after an overnight fast and separated by seven days.[11]

Four of the six human studies did not take into account possible confounding effects of the habitual diets of the participants.[9,11,12,15] This is a particular concern given that many of the foodstuffs were given in small amounts and often for only a short time. In addition, seven of the eleven studies included in the review did not specify organic certification of the food exposure,[9,12-17] thus complicating direct comparisons across studies.

The majority of studies in this review include some sort of measure of antioxidant activity. The methods used to assess antioxidant activity differed between studies and may not be directly comparable. It should also be remembered that antioxidant activity is primarily a biomarker which, although relevant to human health, is not a direct health outcome in itself. It has been suggested that biomarkers may play an important role in measuring disease, particularly those with long latency periods, such as cancer. However, care should be taken when extrapolating these results to human populations.

The papers included in our review employed a wide range of study designs. While randomised controlled trials (RCTs) are the optimal design for determining the effect of an

exposure on a specific outcome, studies of all designs must be conducted and reported in line with recognised guidelines to eliminate bias and confounding. None of the clinical trials in the review were reported according to CONSORT guidelines (http://www.consort-statement.org/) which are an evidence-based, minimum set of recommendations for reporting RCTs. In some papers included in the review, it was difficult to interpret the design or methods used as important details were often not reported. For example, both papers by Tarozzi et al. do not fully describe the integrated production methods used;[10,18] Yildirim et al. does not describe any characteristics of the LDL samples used, other than that they were from 'healthy' donors, and does not describe the procedures for the addition of wine extracts to LDL samples;[19] Dani et al. does not describe the samples used for the *in vitro* techniques.[16]

8.0 CONCLUSION

This systematic review of the available published literature was designed to determine the strength of the evidence that human health effects could be attributed to eating organic compared with conventionally produced food. Despite an extensive search, the systematic review process identified only eleven articles relating to nutrient content that met our inclusion criteria. The studies included in the review were very heterogeneous in terms of study design, exposure and health outcome. Taken together, the eleven articles do not currently provide any evidence of health benefits from consuming organic compared to conventionally produced foods. This review does not address contaminant content (such as herbicide, pesticide and fungicide residues) of organically and conventionally produced foodstuffs, or the environmental impacts of organic and conventional agricultural practices.

A surprising and important finding of this review is the extremely limited nature of the evidence base on this subject, both in terms of the number of studies and the quality of studies found. It is essential that future research (both human and *in vitro* studies) is better designed and, at the very least, meets the minimum quality criteria applied in this review, including an accurate description of the organic certification process. It is recommend that in future, high quality randomised controlled trials should be conducted which have samples of sufficient size to reliably detect the presence of effects, longer and more realistic dietary exposures, and more accurate and objective approaches to measuring dietary intake and health outcomes. It is further recommended that the results of all studies, and all analyses, be published to ensure that reporting and publication bias of null findings is minimized. Finally, the reporting of future studies should follow internationally agreed approaches as outlined by the Equator Network (http://www.equator-network.org) to assist critical appraisal and interpretation. Evidence in this field may be improved if more inter-disciplinary approaches to, and funding for, agricultural-health research were supported.

9.0 REFERENCES

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Appendix 1: Search Terms

Pubmed search terms:

EXPOSURE SEARCH TERM

((ORGANIC*[TIAB] OR ORGANIC* OR ECO OR ECO[TIAB] OR REGENERATIVE OR REGENERATIVE[TIAB] OR ECOLOGICAL* OR ECOLOGICAL*[TIAB] OR BIODYNAMIC* OR BIODYNAMIC*[TIAB] OR HEALTH FOOD[MESH] OR HEALTH FOOD[TIAB] OR HEALTH FOOD OR CONVENTIONAL*[TIAB] OR CONVENTIONAL*)) AND ((FOOD*[MESH] OR FOOD[TIAB] OR FOOD OR AGRICULTURAL CROP[MESH] OR AGRICULTURAL CROP[TIAB] OR AGRICULTURAL CROP OR LIVESTOCK[MESH] OR LIVESTOCK[TIAB] OR LIVESTOCK OR AGRICULTUR*[MESH] OR AGRICULTUR*[TIAB] OR AGRICULTUR*))

OUTCOME SEARCH TERM

respiratory tract diseases[MeSH] OR respiratory tract diseases[tiab] OR respiratory tract diseases OR arthritis[MeSH] OR arthritis[tiab] OR arthritis OR irritable bowel syndrome[MeSH] OR irritable bowel syndrome[tiab] OR irritable bowel syndrome OR celiac disease[MeSH] OR celiac disease[tiab] OR celiac disease OR asthma[MeSH] asthma[tiab] OR asthma OR eczema[MeSH] OR eczema[tiab] OR eczema OR inflammatory disease*[tiab] OR inflammatory disease* OR avitaminosis[MeSH] OR avitaminosis[tiab] OR avitaminosis OR nutritional status[MeSH] OR nutritional status[tiab] OR nutritional status OR ((vitamin[MeSH] OR vitamin[tiab] OR vitamin) AND (deficienc*[tiab] OR deficienc*)) OR ((micronutrient[MeSH] OR micronutrient[tiab] OR micronutrient) AND (deficienc*[tiab] OR deficienc*)) OR reproductive health[MeSH] OR reproductive health[tiab] OR reproductive health OR lactation[MeSH] OR lactation[tiab] OR lactation OR breast feeding[MeSH] OR breast feeding[tiab] OR breast feeding OR semen[MeSH] OR semen[tiab] OR semen OR eye diseases[MeSH] OR eye diseases[tiab] OR eye diseases OR obesity[MeSH] OR obesity[tiab] OR obesity OR weight gain[MeSH] OR weight gain[tiab] OR weight gain OR weight loss[MeSH] OR weight loss[tiab] OR weight loss OR adiposity[MeSH] OR adiposity[tiab] OR adiposity OR overweight[MeSH] OR overweight[tiab] OR overweight OR body weight changes [MeSH] OR body weight changes[tiab] OR body weight changes OR body mass index[MeSH] OR body mass index[tiab] OR body mass index OR overeat*[tiab] OR overeat* OR over eat*[tiab] OR over eat* OR over feed*[tiab] OR over feed* OR anthropometry[MeSH] OR anthropometry[tiab] OR anthropometry OR body composition[MeSH] OR body composition[tiab] OR body composition OR body constitution[MeSH] OR body constitution[tiab] OR body constitution OR body mass[tiab] OR body mass OR waist circumference[tiab] OR waist circumference OR hip circumference[tiab] OR hip circumference OR waist hip ratio*[tiab] OR waist hip ratio* OR diabetes mellitus type 2[MeSH] OR diabetes mellitus type 2[tiab] OR diabetes mellitus type 2 OR insulin resistance[MeSH] OR insulin resistance[tiab] OR insulin resistance OR hyperglycemia[MeSH] OR hyperglycemia[tiab] OR hyperglycemia OR cardiovascular disease[MeSH] OR cardiovascular disease[tiab] OR cardiovascular disease OR coronary disease[MeSH] OR coronary disease[tiab] OR coronary disease OR osteoporosis[MeSH] OR osteoporosis[tiab] OR osteoporosis OR bone density[MeSH] OR bone density[tiab] OR bone density OR neoplasms[MeSH] OR neoplasm[tiab] OR neoplasm OR tooth diseases[MeSH] OR tooth diseases[tiab] OR tooth diseases OR chronic disease[MeSH] OR chronic disease[tiab] OR chronic disease OR health[MeSH] OR health[tiab] OR health OR disease[MeSH] OR disease[tiab] OR disease

Web of Science search terms:

EXPOSURE SEARCH TERM

((TI=ORGANIC* OR TS=ORGANIC* OR TI=ECO OR TS=ECO OR TI=REGENERATIVE OR TS=REGENERATIVE OR TI=ECOLOGICAL* OR TS=ECOLOGICAL* OR TI=BIODYNAMIC* OR TS=BIODYNAMIC* OR TI=HEALTH FOOD OR TS=HEALTH FOOD OR TI=CONVENTIONAL* OR TS=CONVENTIONAL*)) AND ((TI=FOOD* OR TS=FOOD OR TI=AGRICULTURAL CROP OR TS=AGRICULTURAL CROP OR TI=LIVESTOCK OR TS=LIVESTOCK OR TI=AGRICULTUR* OR TS=AGRICULTUR*))

OUTCOME SEARCH TERM

TI=respiratory tract disease* OR TS=respiratory tract disease* OR TI=arthritis OR TS=arthritis OR TI=irritable bowel syndrome OR TS=irritable bowel syndrome OR TI=celiac disease OR TS=celiac disease OR TI=asthma OR TS=asthma OR TI=eczema OR TS=eczema OR TI=inflammatory disease* OR TS=inflammatory disease* OR TI=avitaminosis OR TS=avitaminosis OR TI=nutritional status OR

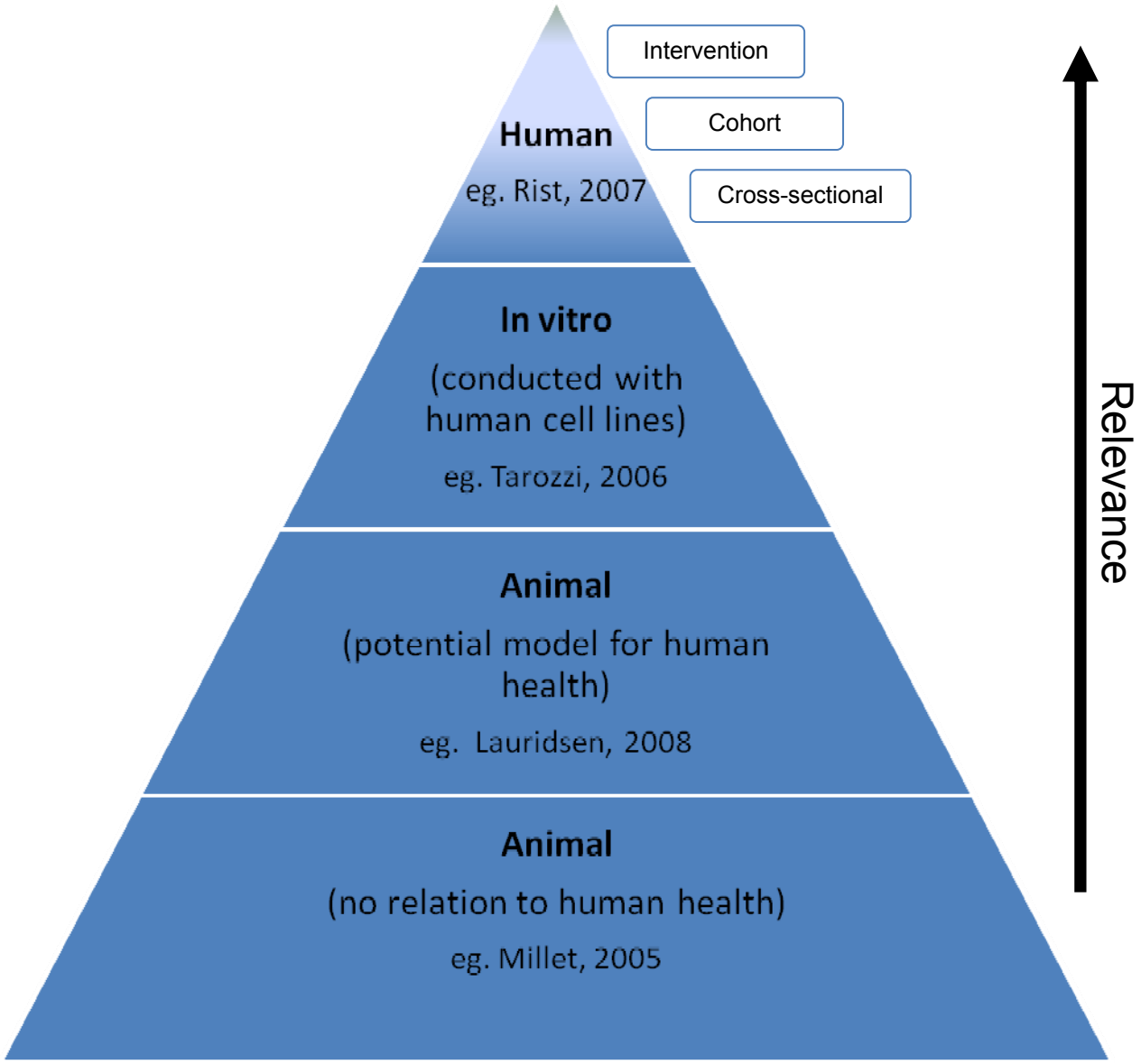
TS=nutritional status OR ((TI=vitamin OR TS=vitamin) AND (TI=deficienc* OR TS=deficienc*)) OR ((TI=micronutrient OR TS=micronutrient) AND (TI=deficienc* OR TS=deficienc*)) OR TI=reproductive health OR TS=reproductive health OR TI=lactation OR TS=lactation OR TI=breast feeding OR TS=breast feeding OR TI=semen OR TS=semen OR TI=eye diseases OR TS=eye diseases OR TI=obesity OR TS=obesity OR TI=weight gain OR TS=weight gain OR TI=weight loss OR TS=weight loss OR TI=adiposity OR TS=adiposity OR TI=overweight OR TS=overweight OR TI=body weight changes OR TS=body weight changes OR TI=body mass index OR TS=body mass index OR TI=overeat* OR TS=overeat* OR TI=over eat* OR TS=over eat* OR TI=over feed* OR TS=over feed* OR TI=anthropometry OR TS=anthropometry OR TI=body composition OR TS=body composition OR TI=body constitution OR TS=body constitution OR TI=body mass OR TS=body mass OR TI=waist circumference OR TS=waist circumference OR TI=hip circumference OR TS=hip circumference OR TI=waist hip ratio* OR TS=waist hip ratio* OR TI=diabetes mellitus type 2 OR TS=diabetes mellitus type 2 OR TI=insulin resistance OR TS=insulin resistance OR TI=hyperglycemia OR TS=hyperglycemia OR TI=cardiovascular disease OR TS=cardiovascular disease OR TI=coronary disease OR TS=coronary disease OR TI=osteoporosis OR TS=osteoporosis OR TI=bone density OR TS=bone density OR TI=neoplasm OR TS=neoplasm OR TI=tooth diseases OR TS=tooth diseases OR TI=chronic disease OR TS=chronic disease OR TI=health OR TS=health OR TI=disease OR TS=disease

CAB Abstracts and Embase search terms:

EXPOSURE SEARCH TERM
((ORGANIC$.sh OR ORGANIC$.ab,ti OR ORGANIC$ OR ECO.sh OR ECO OR ECO.ab,ti OR REGENERATIVE.sh OR REGENERATIVE OR REGENERATIVE.ab,ti OR ECOLOGICAL$ OR ECOLOGICAL$.SH OR ECOLOGICAL$.ab,ti OR BIODYNAMIC$ OR BIODYNAMIC$.SH OR BIODYNAMIC$.ab,ti OR HEALTH FOOD.sh OR HEALTH FOOD.ab,ti OR HEALTH FOOD OR CONVENTIONAL$.ab,ti OR CONVENTIONAL$ OR CONVENTIONAL$.SH) AND (FOOD$.sh OR FOOD$.ab,ti OR FOOD$ OR AGRICULTURAL CROP.sh OR AGRICULTURAL CROP.ab,ti OR AGRICULTURAL CROP OR LIVESTOCK.sh OR LIVESTOCK.ab,ti OR LIVESTOCK OR AGRICULTUR$.sh OR AGRICULTUR$.ab,ti OR AGRICULTUR$))

OUTCOME SEARCH TERM
respiratory tract diseases.sh OR respiratory tract diseases.ab,ti OR respiratory tract diseases OR arthritis.sh OR arthritis.ab,ti OR arthritis OR irritable bowel syndrome.sh OR irritable bowel syndrome.ab,ti OR irritable bowel syndrome OR celiac disease.sh OR celiac disease.ab,ti OR celiac disease OR asthma.sh OR asthma.ab,ti OR asthma OR eczema.sh OR eczema.ab,ti OR eczema OR inflammatory disease$.ab,ti OR inflammatory disease$ OR avitaminosis.sh OR avitaminosis.ab,ti OR avitaminosis OR nutritional status.sh OR nutritional status.ab,ti OR nutritional status OR ((vitamin.sh OR vitamin.ab,ti OR vitamin) AND (deficienc$.ab,ti OR deficienc$)) OR ((micronutrient.sh OR micronutrient.ab,ti OR micronutrient) AND (deficienc$.ab,ti OR deficienc$)) OR reproductive health.sh OR reproductive health.ab,ti OR reproductive health OR lactation.sh OR lactation.ab,ti OR lactation OR breast feeding.sh OR breast feeding.ab,ti OR breast feeding OR semen.sh OR semen.ab,ti OR semen OR eye diseases.sh OR eye diseases.ab,ti OR eye diseases OR obesity.sh OR obesity.ab,ti OR obesity OR weight gain.sh OR weight gain.ab,ti OR weight gain OR weight loss.sh OR weight loss.ab,ti OR weight loss OR adiposity.sh OR adiposity.ab,ti OR adiposity OR overweight.sh OR overweight.ab,ti OR overweight OR body weight changes.sh OR body weight changes.ab,ti OR body weight changes OR body mass index.sh OR body mass index.ab,ti OR body mass index OR overeat$.ab,ti OR overeat OR over eat$.ab,ti OR over eat OR over feed$.ab,ti OR over feed OR anthropometry.sh OR anthropometry.ab,ti OR anthropometry OR body composition.sh OR body composition.ab,ti OR body composition OR body constitution.sh OR body constitution.ab,ti OR body constitution OR body mass.ab,ti OR body mass OR waist circumference.ab,ti OR waist circumference OR hip circumference.ab,ti OR hip circumference OR waist hip ratio$.ab,ti OR waist hip ratio$ OR diabetes mellitus type 2.sh OR diabetes mellitus type 2.ab,ti OR diabetes mellitus type 2 OR insulin resistance.sh OR insulin resistance.ab,ti OR insulin resistance OR hyperglycemia.sh OR hyperglycemia.ab,ti OR hyperglycemia OR cardiovascular disease.sh OR cardiovascular disease.ab,ti OR cardiovascular disease OR coronary disease.sh OR coronary disease.ab,ti OR coronary disease OR osteoporosis.sh OR osteoporosis.ab,ti OR osteoporosis OR bone density.sh OR bone density.ab,ti OR bone density OR neoplasms.sh OR neoplasm.ab,ti OR neoplasm OR tooth diseases.sh OR tooth diseases.ab,ti OR tooth diseases OR chronic disease.sh OR chronic disease.ab,ti OR chronic disease OR health.sh OR health.ab,ti OR health OR disease.sh OR disease.ab,ti OR disease

Appendix 2: Conceptual framework of hierarchy of study types



Studies selected after Step 1 of the search were categorized according to the above four study types. Study types were then ranked based on their relevance to human health outcomes.

Appendix 3: Studies excluded from the review and reasons for exclusion

No health outcome n=13

1. Asami DK, Hong YJ, Barrett DM, Mitchell AE. Comparison of the total phenolic and ascorbic acid content of freeze-dried and air-dried marionberry, strawberry, and corn grown using conventional, organic, and sustainable agricultural practices. *Journal of Agricultural and Food Chemistry*, 2003;**51**:1237-41.
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Animal study (not modelled on human health) n=5

1. Acamovic T, Sandilands V, Kyriazakis I, Sparks N. The effect of organic diets on the performance of pullets maintained under semi-organic conditions. *Animal*, 2008;**2**: 117-24.
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Contaminants study n=5

1. Curl CL, Fenske RA, Elgethun K. Organophosphorus pesticide exposure of urban and suburban preschool children with organic and conventional diets. *Environ Health Perspect,* 2003;**111**(3)**:**377-82.
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No direct comparison of organic vs. conventional n=6

1. Galli C, Rise P, Marangoni F. Omega 3 fatty acids. From food to man: bioavailability, metabolic conversion and blood levels in the population. *Progress in Nutrition,* 2007;**9**:88-93.
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3. Kajiya T, Kuroda A, Hokonohara D, Tei C. Heart failure caused by hookworm infection possibly associated with organic food consumption. *Intern Med*, 2006;**45**:827-9.
4. Lauridsen C, Yong C, Halekoh U, Bugel SH, Brandt K, Christensen LP, Jorgensen H. Rats show differences in some biomarkers of health when eating diets based on ingredients produced with three different cultivation strategies. *Journal of the Science of Food and Agriculture* 2008;**88**(4)**:**720-32.
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6. Weller RF, Cooper A. Health status of dairy herds converting from conventional to organic dairy farming. *Veterinary Record* 1996;**139:**141-2.

Occupational health study n=3

1. Cross P, Edwards RT, Hounsome B, Edwards-Jones G. Comparative assessment of migrant farm worker health in conventional and organic horticultural systems in the United Kingdom. *Sci Total Environ,* 2008;**391**:55-65.
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3. Smit LAM, Zuurbier M, Doekes G, Wouters IM, Heederik D, Douwes J. Hay fever and asthma symptoms in conventional and organic farmers in The Netherlands. *Occupational and Environmental Medicine,* 2007;**64**:101-7.

Not peer reviewed n=3

1. Baranska A, Skwaro-Sonta K, Rembiakowska E, Brandt K, Lueck L, Leifert C. The effect of short term feeding with organic and conventional diets on selected immune parameters in rat. Improving sustainability in organic and low input food production systems. Frick Switzerland: Research Institute of Organic Agriculture (FiBL), 2007: 108-111.
2. Rembiakowska E, Hallmann E, Rusaczonek A, Bennett RN, Brandt K, Lueck L, Leifert C. The content of bioactive compounds in rat experimental diets based on organic, low-input and conventional plant materials. Improving sustainability in organic and low input food production systems. Frick Switzerland: Research Institute of Organic Agriculture (FiBL), 2007: 112-117.

3. Rios A, Sanchez-Perez HJ, Hellin J. Child nutrition in Mexico under conventional and organic agriculture. LEISA Magazine. Amersfoort, Netherlands: Centre for Information on Low External Input and Sustainable Agriculture, 2007;**23**:16-7.

Review n=1

1. Kuchler F, Ralston K, Tomerlin JR. Do health benefits explain the price premiums for organic foods? *American Journal of Alternative Agriculture*, 2000;**15**:9-18.

Appendix 4: Studies included in the review

1. Akcay YD, Yildirim HK, Guvenc U, Sozmen EY. The effects of consumption of organic and nonorganic red wine on low-density lipoprotein oxidation and antioxidant capacity in humans. *Nutrition Research* 2004;**24**(7)**:**541-554.
2. Briviba K, Stracke BA, Rüfer CE, Watzl B, Weibel FP, Bub A. Effect of consumption of organically and conventionally produced apples on antioxidant activity and DNA damage in humans. *Journal of Agricultural and Food Chemistry* 2007;**55**(19)**:**7716-7721.
3. Caris-Veyrat C, Amiot MJ, Tyssandier V, Grasselly D, Buret M, Mikolajczak M, Guilland JC, Bouteloup-Demange C, Borel P. Influence of organic versus conventional agricultural practice on the antioxidant microconstituent content of tomatoes and derived purees; Consequences on antioxidant plasma status in humans. *Journal of Agricultural and Food Chemistry* 2004;**52**(21)**:**6503-6509.
4. Dani C, Oliboni LS, Vanderlinde R, Bonatto D, Salvador M, Henriques JA. Phenolic content and antioxidant activities of white and purple juices manufactured with organically- or conventionally-produced grapes. *Food Chem Toxicol* 2007;**45**(12)**:**2574-80.
5. Grinder-Pedersen L, Rasmussen SE, Bugel S, Jorgensen LV, Dragsted LO, Gundersen V, Sandstrom B. Effect of diets based on foods from conventional versus organic production on intake and excretion of flavonoids and markers of antioxidative defense in humans. *J Agric Food Chem* 2003;**51**(19)**:**5671-6.
6. Kummeling I, Thijs C, Huber M, van de Vijver LPL, Snijders BEP, Penders J, Stelma F, van Ree R, van den Brandt PA, Dagnelie PC. Consumption of organic foods and risk of atopic disease during the first 2 years of life in the Netherlands. *British Journal of Nutrition* 2008;**99**(3)**:**598-605.
7. Olsson ME, Andersson CS, Oredsson S, Berglund RH, Gustavsson KE. Antioxidant levels and inhibition of cancer cell proliferation in vitro by extracts from organically and conventionally cultivated strawberries. *Journal of Agricultural and Food Chemistry* 2006;**54**(4)**:**1248-1255.
8. Rist L, Mueller A, Barthel C, Snijders B, Jansen M, Simoes-Wust AP, Huber M, Kummeling I, von Mandach U, Steinhart H, Thijs C. Influence of organic diet on the amount of conjugated linoleic acids in breast milk of lactating women in the Netherlands. *Br J Nutr* 2007;**97**(4)**:**735-43.
9. Tarozzi A, Hrelia S, Angeloni C, Morroni F, Biagi P, Guardigli M, Cantelli-Forti G, Hrelia P. Antioxidant effectiveness of organically and non-organically grown red oranges in cell culture systems. *Eur J Nutr* 2006;**45**(3)**:**152-8.
10. Tarozzi A, Marchesi A, Cantelli-Forti G, Hrelia P. Cold-storage affects antioxidant properties of apples in caco-2 cells. *Journal of Nutrition* 2004;**134**(5)**:**1105-1109.
11. Yildirim HK, Akcay YD, Guvenc U, Sozmen EY. Protection capacity against low-density lipoprotein oxidation and antioxidant potential of some organic and non-organic wines. *International Journal of Food Sciences and Nutrition* 2004;**55**(5)**:**351-362.

Appendix 5: Abstracts of included studies

Akcay YD, Yildirim HK, Guvenc U, Sozmen EY. The effects of consumption of organic and nonorganic red wine on low-density lipoprotein oxidation and antioxidant capacity in humans. *Nutrition Research* 2004;**24**(7)**:**541-554.

It is known that moderate red wine consumption can reduce the risk of cardiovascular disease. The protective effects of wine have been attributed to phenolic compounds that are efficient scavengers of free radicals and breakers of lipid peroxidative chain reactions. Besides antioxidant activity, phenols also have anti-inflammatory effects and may protect low-density lipoproteins (LDL) against oxidative modification . The aim of this study was to determine the effects of the so-called "organic" wines (i.e. those that are produced from genetically nonmodified grapes and without fertilization) and "nonorganic" red wines (i.e. those that are produced in a conventional manner) on LDL oxidation, antioxidant activity, and other antioxidant enzymes such as catalase and superoxide dismutase. Male subjects *(n*=6) drank 200mL and female subjects drank *(n*=2) 100mL of red wine (the so-called organic wine) wine, and after 6 weeks the experiment was repeated with the nonorganic red wine. Blood samples were obtained at baseline and after 60 and 360 minutes. Total phenol, erythrocyte superoxide dismutase (eSOD), erythrocyte catalase (eCAT), erythrocyte thiobarbituric acid reactive substances (eTBARS), serum total antioxidant activity (AOA), LDL-TBARS, and Cu-stimulated LDL-TBARS levels were determined. Although the Cabernet Sauvignon wine caused a significant increase in eSOD activity during hour I *(P*=0.046) and hour 6 *(P*=0.028) of the experiment compared to the baseline levels, it led to an insignificant increase in eCAT activity in hour I *(P*=0.08) and hour 6 *(P*=0.069). There was no significant difference between two types of wines with respect to LDL-TBARS blood levels, and only the nonorganic wine led to a decrease in Cu-stimulated LDL-TBARS. There were noteworthy differences in the alcohol and phenol content of the organic and nonorganic wines.

- *Study type*: Human clinical trial
- *Study quality*: Unsatisfactory

Briviba K, Stracke BA, Rüfer CE, Watzl B, Weibel FP, Bub A. Effect of consumption of organically and conventionally produced apples on antioxidant activity and DNA damage in humans. *Journal of Agricultural and Food Chemistry* 2007;**55**(19)**:**7716-7721.

The present study was performed to compare the effects on antioxidant activity and on DNA damage of organic and conventionally produced apples grown under controlled conditions in human peripheral blood lymphocytes. Six healthy volunteers consumed either organically or conventionally grown apples (Golden Delicious, 1000 g) from two neighbouring commercial farms in a double-blinded, randomized, cross-over study. The average content of total identified and quantified polyphenols in the organically and conventionally produced apples was 308 and 321µg/g fresh weight, respectively. No statistically significant differences in the sum of phenolic compounds or in either of the polyphenol classes were found between the agricultural methods. Consumption of neither organically nor conventionally grown apples caused any changes in antioxidant capacity of low-density lipoproteins (lag time test), endogenous DNA strand breaks, Fpg protein-sensitive sites, or capacity to protect DNA against damage caused by hydrogen peroxide. However, a statistically significant decrease in the levels of endonuclease III sensitive sites and an increased capacity to protect DNA against damage induced by iron chloride were determined 24h after consumption in both groups of either organic or conventionally grown apples, indicating the similar antigenotoxic potential of both organically and conventionally grown apples.

- *Study type*: Human clinical trial
- *Study quality*: Satisfactory

Caris-Veyrat C, Amiot MJ, Tyssandier V, Grasselly D, Buret M, Mikolajczak M, Guilland JC, Bouteloup-Demange C, Borel P. Influence of organic versus conventional agricultural practice on the antioxidant microconstituent content of tomatoes and derived purees; Consequences on antioxidant plasma status in humans. *Journal of Agricultural and Food Chemistry* 2004;**52**(21)**:**6503-6509.

The present study aims first to compare the antioxidant microconstituent contents between organically and conventionally grown tomatoes and, second, to evaluate whether the consumption at purees made of these tomatoes can differently affect the plasma levels of antioxidant microconstituents in humans, When results were expressed as fresh matter, organic tomatoes had higher vitamin C, carotenoids, and polyphenol contents (except for chlorogenic acid) than conventional tomatoes. When results were expressed as dry matter, no significant difference was found for lycopene and naringenin. In tomato purees, no difference in carotenoid content was found between the two modes of culture, whereas the concentrations of vitamin C and polyphenols remained higher in purees made out of organic tomatoes. For the nutritional intervention, no significant difference (after 3 weeks of consumption of 96 g/day of tomato puree) was found between the two purees with regard to their ability to affect the plasma levels of the two major antioxidants, vitamin C and lycopene.

- *Study type*: Human clinical trial
- *Study quality*: Unsatisfactory

Dani C, Oliboni LS, Vanderlinde R, Bonatto D, Salvador M, Henriques JA. Phenolic content and antioxidant activities of white and purple juices manufactured with organically- or conventionally-produced grapes. *Food Chem Toxicol* 2007;**45**(12)**:**2574-80.

Although the beneficial effects of moderate wine intake are well-known, data on antioxidant capacity of grape juices are scarce and controversial. The purpose of this study was to quantify total polyphenols, anthocyanins, resveratrol, catechin, epicatechin, procyanidins, and ascorbic acid contents in grape juices, and to assess their possible antioxidant activity. Eight *Vitis labrusca* juices – white or purple, from organically- or conventionally-grown grapes, and obtained in pilot or commercial scale – were used. Organic grape juices showed statistically different ($p < 0.05$) higher values of total polyphenols and resveratrol as compared conventional grape juices. Purple juices presented higher total polyphenol content and *in vitro* antioxidant activity as compared to white juices, and this activity was positively correlated ($r=0.680$; $p<0.01$) with total polyphenol content. These results indicate that white and purple grape juices can be used as antioxidants and nutritional sources.

- *Study type*: *Ex vivo* experiment
- *Study quality*: Unsatisfactory

Grinder-Pedersen L, Rasmussen SE, Bugel S, Jorgensen LV, Dragsted LO, Gundersen V, Sandstrom B. Effect of diets based on foods from conventional versus organic production on intake and excretion of flavonoids and markers of antioxidative defense in humans. *J Agric Food Chem* 2003;**51**(19)**:**5671-6.

Different food production methods may result in differences in the content of secondary metabolites such as polyphenolic compounds. The present study compared conventionally (CPD) and organically produced (OPD) diets in a human crossover intervention study (n=16) with respect to the intake and excretion of five selected flavonoids and effect on markers of oxidative defense. The urinary excretion of quercetin and kaempferol was higher after 22 days of intake of the OPD when compared to the CPD (P<0.05). The excretions of flavonoids in urine as a percentage of intake (0.6-4%) were similar after both interventions. Most markers of antioxidative defense did not differ between the diets, but intake of OPD resulted in an increased protein oxidation and a decreased total plasma antioxidant capacity compared to baseline (P<0.05). Some varietal difference was seen in the study, and because selection of more resistant varieties is of central importance to organic farming, it cannot be excluded that the observed effects originate from these differences. The food production method affected the content of the major flavonoid, quercetin, in foods and also affected urinary flavonoids and markers of oxidation in humans.

- *Study type*: Human clinical trial
- *Study quality*: Unsatisfactory

Kummeling I, Thijs C, Huber M, van de Vijver LPL, Snijders BEP, Penders J, Stelma F, van Ree R, van den Brandt PA, Dagnelie PC. Consumption of organic foods and risk of atopic disease during the first 2 years of life in the Netherlands. *British Journal of Nutrition* 2008;**99**(3)**:**598-605.

We prospectively investigated whether organic food consumption by infants was associated with developing atopic manifestations in the first 2 years of life. The KOALA Birth Cohort Study in the Netherlands (n 2764) measured organic food consumption, eczema and wheeze in infants until age 2 years using repeated questionnaires. Diet was defined as conventional (<50% organic), moderately organic (50–90% organic) and strictly organic (>90% organic). Venous blood samples taken from 815 infants at 2 years of age were analysed for total and specific IgE. Multivariate logistic regression models were fitted to control for potential confounding factors. Eczema was present in 32% of infants, recurrent wheeze in 11% and prolonged wheezing in 5%. At 2 years of age, 27% of children were sensitised against at least one allergen. Of all the children, 10% had consumed a moderately organic diet and 6% a strictly organic diet. Consumption of organic dairy products was associated with lower eczema risk (OR 0·64 (95% CI 0·44, 0·93)), but there was no association of organic meat, fruit, vegetables or eggs, or the proportion of organic products within the total diet with the development of eczema, wheeze or atopic sensitisation. Further studies to substantiate these results are warranted.

- *Study type*: Human cohort study
- *Study quality*: Unsatisfactory

Olsson ME, Andersson CS, Oredsson S, Berglund RH, Gustavsson KE. Antioxidant levels and inhibition of cancer cell proliferation in vitro by extracts from organically and conventionally cultivated strawberries. *Journal of Agricultural and Food Chemistry* 2006;**54**(4)**:**1248-1255.

The effects of extracts from five cultivars of strawberries on the proliferation of colon cancer cells HT29 and breast cancer cells MCF·7 were investigated, and possible correlations with the levels of several antioxidants were analyzed. In addition, the effects of organic cultivation compared to conventional cultivation on the content of antioxidants in the strawberries and strawberry extracts on the cancer cell proliferation were investigated. The ratio of ascorbate to dehydroascorbate was significantly higher in the organically cultivated strawberries. The strawberry extracts decreased the proliferation of both HT29 cells and MCF-7 cells in a dose-dependent way. The inhibitory effect for the highest concentration of the extracts was in the range of 41-63% (average 53%) inhibition compared to controls for the HT29 cells and 26-56% (average 43%) for MCF-7 cells. The extracts from organically grown strawberries had a higher antiproliferative activity for both cell types at the highest concentration than the conventionally grown, and this might indicate a higher content of secondary metabolites with anticarcinogenic properties in the organically grown strawberries. For HT29 cells, there was a negative correlation at the highest extract concentration between the content of ascorbate or vitamin C and cancer cell proliferation, whereas for MCF-7 cells, a high ratio of ascorbate to dehydroascorbate correlated with a higher inhibition of cell proliferation at the second highest concentration. The significance of the effect of ascorbate on cancer cell proliferation might lie in a synergistic action with other compounds.

- *Study type*: *In vitro* experiment
- *Study quality*: Unsatisfactory

Rist L, Mueller A, Barthel C, Snijders B, Jansen M, Simoes-Wust AP, Huber M, Kummeling I, von Mandach U, Steinhart H, Thijs C. Influence of organic diet on the amount of conjugated linoleic acids in breast milk of lactating women in the Netherlands. *Br J Nutr* 2007;**97**(4)**:**735-43.

The aim of the present study was to find out whether the incorporation of organic dairy and meat products in the maternal diet affects the contents of the conjugated linoleic acid isomers (CLA) and trans-vaccenic acid (TVA) in human breast milk. To this purpose, milk samples from 312 breastfeeding mothers participating in the KOALA Birth Cohort Study have been analysed. The participants had documented varying lifestyles in relation to the use of conventional or organic products. Breast milk samples were collected 1 month postpartum and analysed for fatty acid composition. The content of rumenic acid (the main CLA) increased in a statistically significant way while going from a conventional diet (no organic dairy/meat products, 0·25 weight % (wt%), n 186) to a moderately organic diet (50–90% organic dairy/meat, 0·29 wt%, n 33, P=0·02) and to a strict organic diet (>90% organic dairy/meat, 0·34 wt%, n 37, $P \leq 0{\cdot}001$). The levels of TVA were augmented among the participants with a moderately organic diet (0·54 wt%) and those with a strict organic diet (0·59 wt%, $P \leq 0{\cdot}001$), in comparison with the conventional group (0·48 wt%). After adjusting for covariables (recruitment group, maternal age, maternal education, use of supplements and season), statistical significance was retained in the group of the strict organic dairy users ($P<0{\cdot}001$ for rumenic acid). Hence, the levels of CLA and TVA in human milk can be modulated if breastfeeding mothers replace conventional dairy and/or meat products by organic ones. A potential contribution of CLA and TVA to health improvement is briefly discussed.

- *Study type*: Human cross-sectional study
- *Study quality*: Unsatisfactory

Tarozzi A, Hrelia S, Angeloni C, Morroni F, Biagi P, Guardigli M, Cantelli-Forti G, Hrelia P. Antioxidant effectiveness of organically and non-organically grown red oranges in cell culture systems. *Eur J Nutr* 2006;**45**(3)**:**152-8.

Background: Consumers consider plant food products from organic origin healthier than the corresponding conventional plant foods. Clear experimental evidence supporting this assumption is still lacking. *Aim of study:* To determine if the organic red oranges have a higher phytochemical content (i.e. phenolics, anthocyanins and ascorbic acid), total antioxidant activity and *in vitro* bioactivity, in terms of protective effect against oxidative damage at cellular level, than nonorganic red oranges. *Methods:* Total phenolics were measured using the Folin Ciocalteau assay, while total anthocyanins and ascorbic acid levels were determined by spectrophotometric and HPLC analysis, respectively. In addition, the total antioxidant activity of red orange extracts was measured by the ABTS test. The ability of red orange extracts to counteract conjugated diene containing lipids and free radical production in cultured rat cardiomyocytes and differentiated Caco-2 cells, respectively, was assessed. *Results:* Organic oranges had significantly higher total phenolics, total anthocyanins and ascorbic acid levels than the corresponding non-organic oranges (all $p<0.05$). Moreover, the organic orange extracts had a higher total antioxidant activity than non-organic orange extracts ($p<0.05$). In addition, our results indicate that red oranges have a strong capacity of inhibiting the production of conjugated diene containing lipids and free radicals in rat cardiomyocytes and differentiated Caco-2 cells, respectively. Statistically higher levels of antioxidant activity in both cell models were found in organically grown oranges as compared to those produced by integrated agriculture practice. *Conclusions:* Our results clearly show that organic red oranges have a higher phytochemical content (i.e. phenolics, anthocyanins and ascorbic acid), total antioxidant activity and bioactivity than integrated red oranges. Further studies are needed to confirm whether the organic agriculture practice is likely to increase the antioxidant activity of other varieties of fruits and vegetables.

- *Study type*: *In vitro* experiment
- *Study quality*: Satisfactory

Tarozzi A, Marchesi A, Cantelli-Forti G, Hrelia P. Cold-storage affects antioxidant properties of apples in caco-2 cells. *Journal of Nutrition* 2004;**134**(5)**:**1105-1109.

Data on the composition of phenolic antioxidant compounds present in food plants and assessment of their activity are essential for epidemiological explanation of the health benefits of fruit and vegetables. Various factors such as cultivation methods, industrial processing, and storage may affect the final concentrations of phytochemicals in food plants and their eventual bioactivity. This study investigated the influence of commercial cold-storage periods on the antioxidant properties of apples grown either by organic or integrated systems. In both cases, total phenolics and total antioxidant activity decreased only in the first 3 mo and only in apples with skin ($P<0.05$), suggesting that cold storage rapidly impoverishes these properties in skin but not in pulp. Assessment of antioxidant bioactivity in vitro, measured in terms of intracellular antioxidant, cytoprotective, and antiproliferative activity in human colon carcinoma (Caco-2) cells (differentiated to normal intestinal epithelia for intracellular antioxidant and cytoprotective effects), showed strong, time-related decreases over 6 mo of cold storage for all 3 parameters ($P<0.01$), irrespective of the cultivation system. These findings with integrated and organic apples further support the concept that organic systems of cultivation do not generally provide real health benefits. Moreover, the data from the present study clearly show that factors such as cold storage may affect the antioxidant properties of apples. Epidemiological studies on the cancer-preventive benefits of fruits and vegetables should take into account the cold-storage bias for apples, and possibly for other products.

- *Study type*: *In vitro* experiment
- *Study quality*: Satisfactory

Yildirim HK, Akcay YD, Guvenc U, Sozmen EY. Protection capacity against low-density lipoprotein oxidation and antioxidant potential of some organic and non-organic wines. *International Journal of Food Sciences and Nutrition* 2004;**55**(5)**:**351-362.

Current research suggests that phenolics from wine may play a positive role against oxidation of low-density lipoprotein (LDL), which is a key step in the development of atherosclerosis. Considering the effects of different winemaking techniques on phenols and the wine consumption preference influencing the beneficial effects of the product, organically and non-organically produced wines were obtained from the grapes of *Vitis vinifera* origin var: Carignan, Cabernet Sauvignon, Merlot, Grenache, Columbard and Semillon. Levels of total phenols [mg/l gallic acid equivalents (GAE)], antioxidant activity (%) and inhibition of LDL oxidation [%, inhibition of diene and malondialdehyde (MDA) formation] were determined. Some phenolic acids (gallic acid, *p*-hydroxybenzoic acid, syringic acid, 2,3-dihydroxybenzoic acid, ferulic acid, *p*-coumaric acid and vanillic acid) were quantified by high-performance liquid chromatography equipped with an electrochemical detection carried at + 0.65 V (versus Ag/AgCl, 0.5 µA full scale). The highest concentrations of gallic, syringic and ferulic acids were found in organic Cabernet Sauvignon; 2,3-dihydroxybenzoic acid in organic Carignan and *p*-coumaric and vanillic acids in non-organic Merlot wine. High levels of antioxidant activity (AOA), inhibition of LDL oxidation and total phenol levels were found in non-organic Merlot (101.950% AOA; 88.570% LDL-diene; 41.000% LDL-MDA; 4700.000 mg/l GAE total phenol) and non-organic Cabemet Sauvignon (92.420% AOA; 91.430% LDL-diene; 67.000% LDL-MDA; 3500.000 mg/l GAE total phenol) grape varieties. Concentrations of some individual phenolic constituents (ferulic, *p*-coumaric, vanillic) are correlated with high antioxidant activity and inhibition of LDL oxidation. The best *r* value for all examined characteristics was determined for gallic acid, followed by 2,3-dihydroxybenzoic, syringic, ferulic and *p*-coumaric acids..Negative correlation of vanillic with MDA and *p*-hydroxybenzoic acid with LDL were confirmed by principal components analysis (PCA) analyses. Red wines display a higher antioxidant activity (81.110% AOA) than white ones (19.512% AOA). The average level of LDL inhibition capacity in red wine was determined as 87.072% and for the white as 54.867%.

- *Study type*: *In vitro* experiment
- *Study quality*: Unsatisfactory

Appendix 6: Quality criteria of included studies

Author	Clear definition of organic production methods	Statement on the nature of the organic component of the dietary exposure	Clear definition of the health outcome and how it was measured	Statement of the statistical methods used for data analyses	Quality
Akcay 2004	Described (not certified)	Yes	Yes	Yes	Unsatisfactory
Briviba 2007	Yes	Yes	Yes	Yes	**Satisfactory**
Caris-Veyrat 2004	Described (not certified)	Yes	Yes	Yes	Unsatisfactory
Dani 2007	No	Yes	Yes	Yes	Unsatisfactory
Grinder-Pederson 2003	No	Yes	Yes	Yes	Unsatisfactory
Kummeling 2007	No	Yes	Yes	Yes	Unsatisfactory
Olsson 2006	Described (not certified)	Yes	Yes	Yes	Unsatisfactory
Rist 2007	No	Yes	Yes	Yes	Unsatisfactory
Tarozzi 2004	Certified (not specified)	Yes	Yes	Yes	**Satisfactory**
Tarozzi 2006	Yes	Yes	Yes	Yes	**Satisfactory**
Yildirim 2004	Certified (not described)	No	Yes	Yes	Unsatisfactory
Total (n)	4	10	11	11	3
Total (%)	36%	91%	100%	100%	27%