

# Methods for Comparing Data across Differently Designed Agronomic Studies: Examples of Different Meta-analysis Methods Used to Compare Relative Composition of Plant Foods Grown Using Organic or Conventional Production Methods and a Protocol for a Systematic Review

Kirsten Brandt,<sup>\*,†</sup> Dominika Średnicka-Tober,<sup>‡</sup> Marcin Barański,<sup>‡</sup> Roy Sanderson,<sup>#</sup> Carlo Leifert,<sup>‡</sup> and Chris Seal<sup>†</sup>

<sup>†</sup>Human Nutrition Research Centre, School of Agriculture, Food and Rural Development, Newcastle University, Newcastle upon Tyne NE1 7RU, United Kingdom

<sup>‡</sup>Nafferton Ecological Farming Group, School of Agriculture, Food and Rural Development, Newcastle University, Stocksfield, Northumberland NE43 7XD, United Kingdom

<sup>#</sup>School of Biology, Newcastle University, Newcastle upon Tyne NE1 7RU, United Kingdom

**ABSTRACT:** Meta-analyses are methods to combine outcomes from different studies to investigate consistent effects of relatively small magnitude, which are difficult to distinguish from random variation within a single study. Several published meta-analyses addressed whether organic and conventional production methods affect the composition of plant foods differently. The meta-analyses were carried out using different options for the methodology and resulted in different conclusions. The types of designs of field trials and farm comparisons widely used in horticultural and agronomic research differ substantially from the clinical trials and epidemiological studies that most meta-analysis methodologies were developed for. Therefore, it is proposed that a systematic review and meta-analysis be carried out with the aim of developing a consolidated methodology. If successful, this methodology can then be used to determine effects of different production systems on plant food composition as well as other comparable factors with small but systematic effects across studies.

**KEYWORDS:** *vitamins, minerals, horticulture, food quality*

## INTRODUCTION

**Background and Justification.** Meta-analyses of data from multiple primary studies are used widely to improve the efficiency of the scientific process. Most often these methods are used to assess general applicability of the findings of randomized placebo-controlled clinical trials in medicinal research, but they are also increasingly used for other types of studies,<sup>1</sup> which include investigations of climate change<sup>2</sup> and trends in ecological research.<sup>3</sup> Meta-analyses are particularly useful to study consistent effects of relatively small magnitude, which are difficult to distinguish from random variation within a single study. One such topic in agricultural chemistry is whether production systems influence food composition and, if so, by how much. Numerous single-factor studies show that the composition of plant foods can be affected if the plants are exposed to substantial differences in growing conditions.<sup>4</sup> It is much less certain, however, whether organic and conventional production methods result in significant differences in composition of the plant products produced in these two systems, in particular, regarding compounds that are synthesized by the plant or naturally accumulate within it (in contrast to, e.g., pesticide residues). Until now, seven published studies<sup>5–11</sup> have included meta-analyses of the relative contents of all or some of the following groups of compounds: vitamins, minerals, macronutrients, and secondary metabolites in plant foods grown using organic or conventional production

methods. All of these studies compared data from primary publications reporting composition of comparable products produced in the two systems, and in all of these studies the aim was to determine whether the production methods result in significant differences in composition of the plant foods, primarily relating to nutritional value. The seven reviews came to very different conclusions (see Table 1), even in cases when comparable compounds were included in the analyses. Whereas to some extent differences in conclusions may reflect differences in interpretation of the outcomes (“glass half-full” versus “glass half-empty”), there are also definitive numeric differences between studies in the calculated significance levels and magnitudes of the effects of production system, which can have been caused only by the use of different methods for the meta-analysis.

The seven studies were all based on the principle of meta-analysis, where information from several independent data sets from primary studies are converted into a common metric, which allows the assessment of a treatment effect independent of the specific characteristics of each data set. Then the metric

**Received:** February 25, 2013

**Revised:** May 17, 2013

**Accepted:** May 21, 2013

**Published:** May 21, 2013

**Table 1. Summary of Outcomes from Previous Studies on Relative Nutrient Content in Organic and Conventional Plant Foods, Resulting from Analysis of Literature Data from Multiple Comparative Studies**

| Lead author<br>year published                             | Benbrook<br>2008                                    | Brandt<br>2011                                      | Dangour<br>2009                                   | Heaton<br>2001  | Hunter<br>2011  | Smith-Spangler<br>2012   | Worthington<br>2001                           |
|---|---|---|---|---|---|--|---|
| types of compds included                                  | vitamins, minerals, and secondary metabolites       | secondary metabolites and vitamin C                 | vitamins, minerals, and secondary metabolites     | vitamins, minerals, and secondary metabolites         | vitamins and minerals                                   | vitamins, minerals, and secondary metabolites                                | vitamins and minerals                         |
| no. of compd groups compared                              | 11  | 7 groups + 3 combined groups                        | 11  | 5   | 24 groups + 4 combined groups                           | 13   | 5, and 32 without test                        |
| no. of compd groups statistically significantly different | no test   | 5 groups + 3 combined groups                        | 3   | no test   | 1 group + 2 combined groups                             | 2  | 5   |
| overall conclusion  | "organic plant-based foods are ... more nutritious" | "higher than in corresponding conventional samples" | "no evidence of a difference in nutrient quality" | "organically grown crops are significantly different" | "levels of micronutrients were higher in organic foods" | "lacks strong evidence that organic foods are significantly more nutritious" | "genuine differences in the nutrient content" |
| full data set published                                   | no  | yes   | yes   | no  | no  | no   | no  |

is used to assess significance of the treatment effect across all data sets. So if, for example, a treatment is applied to plants from several different species, and most of them respond with a reduction in the content of the nutrient, then the metric will allow the analysis of this effect using the data from all the species, even if the range of nutrient content values within one species is different from that of another species. If relevant for the study designs, the analysis may include a weighting procedure to compensate for objective differences in data reliability, for example, giving more weight to studies with several independent replications than to nonreplicated ones. The primary advantage of the meta-analysis principle is that it greatly increases the statistical power and, therefore, allows statistical evaluation of effects of much smaller magnitude than what can be definitively assessed within a single experimental study. The key steps of a meta-analysis are (1) choosing the primary studies to include, (2) choosing the type of metric and calculating it, and (3) analyzing the metric and reporting the outcomes. However, a range of different options is available at each step of the procedure, and the optimal choice depends on the types of data analyzed (for example, if they are from controlled experiments or from surveys) as well as the aims of the investigation (to estimate the magnitude of an effect or only to assess its significance). A key issue is that most of the development of best practice has focused on research on humans, in either medical or social sciences,<sup>12,13,1</sup> making it relatively more difficult for researchers in the food and agriculture areas to select the most appropriate methodology for meta-analyses in their area. This is reflected in the observation that each of the seven studies carried out their meta-analysis using different specific methods (see Table 2). The differences in methodology between the reviews are so substantial that this can fully explain why the outcomes were so different, despite similar aims and substantial overlap in the primary studies included. In fact, any pair of two studies differs in more than one major element of the methodology, so it is not possible to assign the differences in outcomes to any specific elements of the methodologies. The choice of method options may substantially affect the outcome, potentially introducing a bias to the conclusions. The robustness of conclusions can, however, be objectively assessed by sensitivity analyses, comparing the outcomes resulting from different key options in the methodology. Consensus statements about best practice for meta-analyses<sup>1,12</sup> strongly emphasize the importance of clearly defined and transparently described methodology and consistent use of sensitivity analyses whenever the appropriate procedures are not self-evident. In particular, this is important for meta-analyses of observational data,<sup>1</sup> which often comprise individual studies with different designs and/or in which design and reporting have been done without consideration of the suitability of the data for subsequent meta-analyses. A particular element of best practice<sup>12</sup> is that the protocol for a planned meta-analysis should be published before the analysis is carried out, to provide a definitive documentation of the starting point for the work. This provides a means to monitor that all subsequent adaptations to the protocol are logged and explained. Publication of the protocol also serves to allow constructive criticism from the scientific community, such as suggestions for improvements to the planned procedures.

However, in each of the seven above-mentioned reviews<sup>5–11</sup> only one method was used to select the data to include in the meta-analysis, only one of the studies published a protocol in

Table 2. Summary of Methods Used in Previous Studies

| lead author<br>year published<br>publication<br>year for data  | Benbrook<br>2008<br>1980–2007  | Brandt<br>2011<br>1992–2009   | Dangour<br>2009<br>1993 (1958 in protocol)–2007   | Heaton<br>2001<br>1974–2000   | Hunter<br>2011<br>1980–2007  | Smith-Spangler<br>2012<br>1978–2012   | Worthington<br>2001<br>1951–1997  |
|--|--|---|---|---|--|---|---|
| selection criteria for organic treatment                       | a combination of the following using points: produced under qualified organic management; stated appropriate conversion period; stated adherence to appropriate regulation or certification body; input list provided that conforms with what is allowed by appropriate regulation or certification body                 | at least one of the following: stated adherence to appropriate regulation or certification body; input list provided that conforms with what is allowed by appropriate regulation or certification body; the word "organic" used in a "legally defined context": a time and place where it is illegal to use it for production methods that do not conform with what is allowed by appropriate regulation | stated adherence to appropriate regulation or certification body; nonstandard organic certified systems such as "biodynamic" were excluded in principle, but included if organic certification was stated | produced under qualified organic management including explicitly stated appropriate conversion period   | described as "organic" or "biodynamic" or utilized "organic manure" without the use of synthetic inputs; plant protection methods not specifically mentioned, but presumably excluded synthetic pesticides | included biodynamic and defined by investigators' stated adherence, "farming practice" (probably plant protection)    | stated use of organic fertilizer or organic system; plant protection methods not specifically mentioned           |
| selection criteria for conventional treatment                  | as defined by author where more than one nonorganic system is included in a study; commonly used certified nonorganic systems ("integrated", "good agricultural practice", etc.) considered ("integrated", "good agricultural practice", etc.) considered conventional, unless explicitly contrasted with other practice | as defined by author where more than one nonorganic system is included in a study; commonly used certified nonorganic systems ("integrated", "good agricultural practice", etc.) considered conventional, unless explicitly contrasted with other practice  | only explicitly "conventional" practice considered conventional; nonorganic certified systems such as "integrated" were excluded in principle, but included if certification was not mentioned            | required to reflect typical conventional practice, but also accepted inclusion of otherwise acceptable studies that compared only fertilization but not crop protection methods | described as "conventional", "integrated", "low input", or "minimal fertilizers"; plant protection methods not specifically mentioned  | stated use of conventional fertilizer or conventional system; plant protection methods not specifically mentioned     | stated use of conventional fertilizer or conventional system; plant protection methods not specifically mentioned |
| selection criteria for general quality of publications         | included if method descriptions sufficiently detailed to allow assessment of the other criteria and the data are not duplicated in another publication   | included if method descriptions sufficiently detailed to allow assessment of the other criteria and the data are not duplicated in another publication  | only peer-reviewed publications included; identification and removal of duplicate data not mentioned  | included if method descriptions sufficiently detailed to allow assessment of the other criteria and the data are not duplicated in another publication                          | included if method descriptions sufficiently detailed to allow assessment of the other criteria; also "mixed foods" and studies where harvest date was not specified were excluded                         | only peer-reviewed English-language publications included; identification and removal of duplicate data not mentioned | no specific criteria mentioned  |
| selection criteria for publications regarding analysis methods | studies excluded if using analytical methods considered imprecise or not defined   | no specific criteria, other than exclusion of studies that explicitly stated the use of inappropriate methods   | studies excluded if methods or statistics were not mentioned  | no specific criteria  | no specific criteria other than that analytical methods must be clearly stated   | studies excluded if information about variance or results of statistical tests was missing                            | no specific criteria other than that data must be quantitative (numeric)  |
| selection criteria for trial design                            | field trials and farm comparisons only   | field trials, farm comparisons, and shopping basket studies all included in principle, but all shopping basket studies excluded due to other criteria   | field trials, farm comparisons, and shopping basket studies all included  | field trials, farm comparisons, and shopping basket studies all included  | field trials, farm comparisons, and shopping basket studies all included unless multiple levels and types of fertilizer were included, but all shopping basket studies excluded due to other criteria      | field trials, farm comparisons, and shopping basket studies all included  | field trials, farm comparisons, and shopping basket studies all included  |
| selection criteria for plant genotype comparisons              | same cultivar <sup>a</sup> in organic and conventional treatment   | same cultivar <sup>a</sup> in organic and conventional treatment  | same Group <sup>a</sup> in organic and conventional treatment   | not clearly specified   | same cultivar <sup>a</sup> in organic and conventional treatment   | not a selection criterion, but "evaluated" the extent to which pairs were of the same Group <sup>a</sup>              | not clearly specified   |

Table 2. continued

|   | 40%  | 65%  | 33%  | 30%   | 50%   | >85% (not clearly specified)   | >90% (not clearly specified)   |
|---|--|--|--|---|---|--|--|
| percentage of publications included after application of quality criteria                                   | 40%  | 65%  | 33%  | 30%   | 50%   | >85% (not clearly specified)   | >90% (not clearly specified)   |
| handling of multiple forms of compounds   | when data on multiple forms of a compound were reported, if a "total" or "combined" value was present, only this was included in the meta-analysis; if not, only the most abundant form was used; the rest were ignored                  | when data on multiple forms of a compound were reported, the contents of the most similar forms were added to form a maximum of 6 aggregate groups of compounds per sample; no data were excluded unless they were clearly duplicated or included in other data; compounds were grouped into 7 categories (6 types of secondary metabolites + vitamin C), and each group analyzed separately and in combinations | when data on multiple forms of a compound were reported, each one was included separately; compounds were grouped into 98 categories, and categories represented by at least 10 studies were analyzed separately | not clearly specified                             | not clearly specified; however, presumably all forms of the same vitamin, mineral, or trace element were considered equivalent, because only these types of compounds were included | not clearly specified; however, 14 "vitamins and nutrients" were included, some of which presumably include multiple forms               | not clearly specified  |
| handling of multiple treatments within a study (storage duration, harvest times, storage temperature, etc.) | when multiple treatments were reported, only one was chosen for inclusion, e.g., shortest duration of postharvest, or methods representing "the most common organic and conventional treatments" (not clear if they had to be identical) | when multiple treatments were reported, the average of all treatments was calculated and used, except for multiple durations of postharvest treatments, when only the shortest duration was used   | when multiple treatments were reported, either each one was included as separate data points or the average was calculated; criteria for choosing one or the other option were not specified                     | not clearly specified                             | when multiple treatments were reported, the data from the least processed treatment and/or the maturity stage most representative of commercial maturity were used                  | data for separate treatments were presumably combined using random-effect models; this is not clearly specified                          | when multiple treatments were reported, as far as possible each one was included as separate data points |
| handling of data from studies containing more than one year/growing season                                  | when data were reported for multiple years combined, as well as for each year separately, the combined value was used, although separate values for each year were used if no combined value was reported                                | when reported in the publication or available from the author, as far as possible data for separate years were included as separate data points  | not clearly specified  | not clearly specified                             | not clearly specified, other than that "compared foods were grown in the same season"   | data for separate years were combined using random-effect models   | as far as possible data for separate years were included as separate data points                         |
| handling of data from studies containing more than one location   | when data were provided for separate locations, the average for all locations was calculated and used  | when data were provided for separate locations, the average for all locations was calculated and used  | when data were provided for separate locations, each location was included separately  | not clearly specified                             | not clearly specified, other than that "data reported as an average of multiple farms were considered as a single comparison"   | not clearly specified, but presumably treated as "samples" and therefore combined using random-effect models                             | not clearly specified  |
| handling of data from studies containing more than one genotype   | data from each cultivar <sup>a</sup> were used separately; studies where cultivar <sup>a</sup> names were not provided were excluded   | within a Group <sup>a</sup> the average of data from all cultivars <sup>a</sup> was used; studies were excluded if cultivar <sup>a</sup> names were not provided   | data from each cultivar <sup>a</sup> were used separately, except in studies (mainly shopping surveys) when only data on the average for a Group <sup>a</sup> were provided                                      | not clearly specified                             | individual cultivars <sup>a</sup> of the same food were used as separate comparisons  | not clearly specified, but presumably treated as "samples"   | not clearly specified  |
| handling of data reported on fresh weight or dry matter basis   | not clearly specified  | data reported on dry matter basis were adjusted to correspond to values on fresh weight basis by multiplying with the average ratio of dry matter content in organic and conventional produce, calculated from those studies where the dry matter content itself was reported  | no distinction made  | only data reported on fresh weight basis included | no distinction made   | not clearly specified, but subgroup analyses were done for 3 compounds (calcium, potassium, and phosphorus) showing no change in outcome | not clearly specified  |

Table 2. continued

| handling of data reported only in graphical form | not clearly specified  | approximate values measured manually; graphical data on a logarithmic scale were excluded                              | excluded   | not clearly specified | not clearly specified   | not clearly specified                 | not clearly specified  |
|--|--|--|--|-----------------------|---|---------------------------------------|--|
| variable used for statistical analysis           | response ratio of concentrations in organic and conventional material; also used "vote-counting" | Ln-transformed response ratio of concentrations in organic and conventional material (also used normalized difference) | normalized difference between concentrations in organic and conventional material (also re-sponse ratio) | "vote-counting"       | normalized difference between concentrations in organic and conventional material; also used "vote-counting"                                    | standardized mean difference          | normalized difference between concentrations in organic and conventional material; also used "vote-counting" |
| statistical test                                 | no test  | resampling test <sup>17</sup> (also <i>t</i> test)   | <i>t</i> test with "robust standard deviation" (no reference provided)                                   | no test               | one-sample <i>t</i> test or Wilcoxon signed rank tests for differences depending on normality of distributions; "sign test" for "vote-counting" | random-effect models and funnel plots | Wilcoxon signed rank   |

<sup>a</sup>The terms "cultivar" and "group" are used here according to the *International Code of Nomenclature for Cultivated Plants*.<sup>18</sup> The cited reviews used either "cultivar" or "variety" when describing the selection process. However, none of the reviews (or individual studies) provided a reference or correct definition of the terms they used, reflecting widespread inconsistency and lack of awareness of this issue. Therefore, the classification here is based on the actual selection outcome, specifically on whether or not a review included studies defining the genotype only at "group" level as assessed by this criterion.

advance,<sup>7</sup> and only one or two alternative methods were used to analyze the data. In every study the criteria for selection of data to include in analyses were defined solely on the basis of the authors' preferences (not sensitivity analyses), in most cases without any specific explanation for the choices of methods. Only three studies reported that sensitivity analyses were performed. Dangour et al.<sup>7</sup> and Brandt et al.<sup>6</sup> compared normalized differences with response ratios. In Brandt et al.,<sup>6</sup> additionally the outcomes were calculated with or without dry matter adjustment. In Smith-Spangler et al.,<sup>10</sup> different estimated values for sample size were explored for studies for which this value was not available, as well as subgroup analyses of differences between plant species or dry matter versus fresh weigh measurements for a few compounds. In all of these cases it was shown that the tested adjustments did not change the significance of the conclusions. This clearly indicates how a consolidated methodology for meta-analyses of agronomic/horticultural data would be beneficial.

We propose to use the same approach as used in environmental research<sup>2</sup> when a similar situation occurred regarding the effect of elevated carbon dioxide on soil carbon (four independent meta-analyses of the same type of data reported substantially different outcomes). Through the analysis of similarities and differences among the previous studies, a more robust and authoritative methodology was developed, which succeeded in resolving the question and also explaining the reasons for the discrepancies.<sup>2</sup>

### Objectives of the Review.

- To systematically collect all primary data on paired comparisons of contents of vitamins, minerals, macronutrients, and secondary metabolites in plant foods grown using organic or conventional production methods.
- To carry out relevant sensitivity analyses of the methods used for selection of studies of appropriate quality, to determine the advantages and disadvantages of each of the methods, and to assess the effect of the outcomes of using more or less optimal methods for this purpose.
- To carry out relevant sensitivity analyses of the methods used for selection and adjustment of data from those studies to include in meta-analyses, to determine the advantages and disadvantages of each of the methods, and to assess the effect of the outcomes of using more or less optimal methods for this purpose.
- To carry out relevant sensitivity analyses of the methods used for comparison of these data, to determine the advantages and disadvantages of each of the methods, and to assess the effect of the outcomes of using more or less optimal methods for this purpose.
- To determine the significances and magnitudes of differences found using selected combinations of methods including those considered to be optimal on the basis of the sensitivity analysis.

## MATERIALS AND METHODS

**Inclusion Criteria.** The paper will include all original studies that compare primary data on the content of vitamins, minerals, macronutrients, and secondary metabolites in plant foods grown using organic or conventional production methods. Studies published on paper or electronically (including, e.g., Ph.D. thesis repositories and Web-only

Table 3. Information to be Extracted from the Identified Publications

| type of information  | predefined categories  | essential information |
|--|--|-----------------------|
| <b>General Information about the Publication</b>   |  |                       |
| source of publication  | electronic database searches, hand searches of reference lists of reviews and original publications, direct contact with the authors                           | no                    |
| author names (at least one)  |  | yes                   |
| title  |  | no                    |
| year of publication  |  | no                    |
| type of publication  | journal article, conference paper, conference proceedings, book chapter, report, thesis, other   | yes                   |
| name of journal or book series when relevant   |  | no                    |
| country of the first author  |  | no                    |
| research unit of the first author  |  | no                    |
| e-mail address of corresponding author   |  | no                    |
| language of publication  |  | no                    |
| availability of English abstract   | yes, no (assumed no if not specified)  | N/A <sup>c</sup>      |
| information if the data presented in the publication were duplicated in other study  | yes, no (assumed no if not specified)  | N/A                   |
| <b>Potential Study Quality Indicators (For Sensitivity Analysis)</b>   |  |                       |
| peer-reviewed  | yes, no (assumed no if not specified in publication, publisher's Web site or other available information)  | N/A                   |
| funding source   | public, organic industry, conventional industry, other   | no                    |
| type of study  | shopping basket study, farm comparison, controlled experiment  | yes                   |
| no. of experimental years  |  | yes                   |
| location as country; if available, also province/state/county and town   |  | yes                   |
| plant species and, if relevant and available, Group(s) <sup>a</sup>  |  | yes                   |
| no. of plant cultivars <sup>a</sup> included   |  | no                    |
| production system (as defined by author)   | organic, biodynamic, conventional, integrated  | yes                   |
| if products are certified (both for organic and conventional treatments)   | yes, no (assumed no if not specified)  | N/A                   |
| name of certifying body  |  | no                    |
| if inputs are specified  | yes, no  | N/A                   |
| if specified inputs are compatible with organic standards  | yes <sup>b</sup> , no <sup>b</sup>   | N/A                   |
| <b>Data Recorded for Each Paired Value</b>   |  |                       |
| plant species and, if relevant and available, Group <sup>a</sup>   |  | yes                   |
| product analyzed   |  | yes                   |
| plant cultivar <sup>a</sup> name   |  | no                    |
| compd name   |  | yes                   |
| unit of measurement  |  | no                    |
| name of analytical method or "no method provided"  |  | N/A                   |
| value for concentration for each data point  |  | yes                   |
| value reported on fresh weight basis   | yes, no (assumed yes if not specified)   | N/A                   |
| standard error of the mean (SEM) or standard deviation (SD) of the value   |  | no                    |
| no. of full replications of each system in terms of growing sites or field plots   |  | no                    |
| Number of technical repetitions within each replication  |  | no                    |
| if difference between systems was reported by author as significant  | yes, no  | N/A                   |
| dry matter %   |  | no                    |
| data source  | numeric, graphical   | N/A                   |
| limit of detection (LOD) and/or limit of quantification (LOQ)  |  | no                    |
| all "treatments" distinguishing separate sets of paired data found in the publication, which are replicated for at least one organic and one conventional sample, to ensure that all relevant data points from the publication are included in as much detail as available | preservation method, sampling/harvesting time/method, year, season, irrigation method, maturity stage at harvest, precrop, seed rate, storage conditions, etc. | N/A                   |
| data control status  | confirmed or corrected by author, updated or extended by author, confirmed or corrected without input from author  | N/A                   |

<sup>a</sup>"Group" and "cultivar" defined according to ref 18 (as in Table 2). <sup>b</sup>Assessed by study staff based on available input lists, if not explicitly stated in publication. <sup>c</sup>N/A, not applicable.

conference proceedings) after January 1958, in all languages, both peer-reviewed and non-peer-reviewed, will be included initially.

**Exclusion Criteria.** The study will not include publications containing data from only one production system. In case of duplicates of primary data, the least detailed version will be excluded. Studies will be excluded if the essential information (see Table 3) is missing from the published description and

cannot be obtained by contact with the author. Specific languages may be excluded if it is not possible to locate sufficiently qualified assistance within the project group and its affiliates to allow extraction of the essential information.

**Literature Search.** Papers will be identified through an initial search of the literature with Web of Knowledge and Scopus, followed by further hand search of reference lists of identified reviews and original publications. Corresponding

authors of the identified publications will also be contacted by e-mail and asked to provide further relevant publications.

**Search Terms for Electronic Databases.** Titles of publications will be identified through the search of the literature using the search term structure: (organic\* or ecologic\* or biodynamic\*) and (conventional\* or integrated) and (names of 72 relevant crops and foods) and (names of 51 relevant compounds and constituents) for the period 1958 through the present.

**Data Extraction.** Information from the identified publications will be extracted to an MS Access database as detailed in Table 3. A set of paired values is defined as the values provided for the concentration of one “compound” in the same product from the same variety (or cultivar if variety name is unavailable) and treatment. A “compound” can be a chemically defined entity (e.g., iodine) or several chemically related compounds measured together (e.g., “sugars” or “hydroxycinnamic acids”). For initial data collection, each “compound” will be recorded as defined by the author, although when more than one synonym is used for the same “compound” in different papers, the most frequently used name will subsequently be applied for the data from all papers. Some of the subsequent analyses will involve the grouping of “compounds” according to the different principles used in each of the published meta-analyses (see “handling of multiple forms of compds” in Table 2). Data presented in graphical form on arithmetic scales will be recorded manually, whereas graphical data presented on logarithmic scales will be excluded.

**Quality Control.** For most publications the data will be extracted by one person. To reduce the risk of spelling errors (including errors in the publications), for data recorded as a limited number of repeated words or phrases (author names, research units, names of compounds, analysis methods, etc.), each new occurrence of such a word or phrase will be added to a list, whereas repeated occurrences will be copied from the list. After completion of the data extraction, an initial test for outliers will be used to find and correct obvious errors. Those authors whose work has been included in the review may then be contacted and asked to check whether the extracted information is accurate and also invited to provide additional information if relevant. In particular, this will be done in cases when information is missing or unclear in the publication, including data presented only as graphics or only as averages of factors such as years. For such publications, if the response is insufficient or not received, the data will be checked by repeated extraction by a different person.

Once the meta-analysis data have been published, the full extracted data sets will be made available online, allowing any interested party to check and reproduce all of the published calculations. The Web site will include a facility for reporting of errors or additional data. If errors in data or calculations are reported, which may affect the conclusions of the meta-analyses, the affected analyses will be repeated and the corrected results presented on the Web site.

**Comparison of Analysis Methods.** The methods used by each of the previous authors (see Table 2) will be compared using iterative sensitivity analysis, changing one element of a method at a time when feasible, in those cases when the description is sufficiently detailed to allow it to be replicated. Methods from other studies on related topics, such as the paper by Seufert et al.<sup>14</sup> on comparison of crop yields in organic and conventional agriculture, will also be considered and included when relevant. Specifically, in this paper the variable used was

the ln-transformed response ratio weighted by the inverse of the mixed-model variance, excluding studies with only one data pair. In contrast, another recent review by Hoefkens et al.<sup>15</sup> with a meta-analysis of composition of organic and conventional vegetables, used a fundamentally different set of methods, which we probably will not be able to compare with the other meta-analyses. This study was to a large extent based on primary data from studies on composition of vegetables from only one production system (“unpaired” data), and rather than assessing the physiological responses of the plants to the production methods, the aim was described as to investigate the scientific validity of nutrition claims such as “no vegetable/potato has higher amounts of nutrient X than organic vegetables/potatoes”. This study’s methods are so different from the other reviews that it was not possible to include them in Table 2.

Prior to this step, the authors of all the meta-analysis studies will be contacted to ask if they are interested in providing additional information about the methodology they used, as well as if they have additional suggestions for which methods we should include in the comparison. The methods used as the reference in these comparisons will be the ones used in the study by Brandt et al.<sup>6</sup> Comparisons will be done in groups of elements, first comparing the methods for extraction and analysis of the data, then the methods for selection of publications to include, and, finally, combinations of relevant methods in each group.

#### Examples of Sensitivity Analyses.

- Quality criteria for the publications included, for example, peer-reviewed papers only versus both peer-reviewed and non-peer-reviewed or large sample size versus low or unreported sample size.
- Handling of data from studies with different designs: for example, data for separate years included as separate data points versus data for separate years averaged; with or without weighting based on standard variation; multiple cultivars treated as separate samples or as single samples.

#### ■ EXPECTED RESULTS AND DISCUSSION

The study will develop and implement concepts from other research areas<sup>2,3,16</sup> to provide a comprehensive meta-analysis of the effects of production systems on the composition of plant foods regarding contents of vitamins, minerals, macronutrients, and secondary metabolites, incorporating the new original data published since the most recent reviews covering each of these types of compounds, as well as the accumulated experience with different approaches for such meta-analyses. In addition, the multiple sensitivity analyses and subgroup comparisons will provide systematic information about the consequences of using different methods for selection of publications, extraction of information from them, and analysis of the data obtained.

We expect that the primary reason different methods have caused different outcomes is that the number of independent primary studies is relatively low, with a variety of different design principles and potentials for within-study correlations. Therefore, over time, as more independent original studies are published, the differences between the overall outcomes caused by using the different methods will be reduced, as found in other comparable areas.<sup>3</sup> If this is confirmed, it also means that the (combinations of) methods that are best able to estimate the overall outcome from relatively small data volumes (for

example, using reduced timespans or limited selections of crop species) are objectively better than other methods, thus providing a concept for unbiased ranking of the quality of the methodologies.

We therefore aim to derive a set of objectively justified general guidelines for future meta-analyses, which will be used for future updates to include new original data in the specific area. They may also turn out to be useful to analyze other types of external effects (e.g., climate) on other qualities of cultivated plants (e.g., resistance to diseases), when experimental designs show the same types of variations as for studies comparing organic and conventional crops.

The outcome of the present study will also provide objectively justified guidelines for the design and reporting of future primary studies. It will quantify and illustrate the importance of multiyear recordings, appropriately replicated experiments, meticulous experimental protocols, and reporting of relevant statistical outcomes, providing evidence that can be used by educators and journal editors to encourage best practice whenever possible. However, it will also demonstrate appropriate exploitation of the data resource provided by multiple independent nonreplicated experiments, each of which is often insufficient to justify publication on its own, and may thus encourage initiatives to make more good-quality unpublished data sets available for secondary research.

## AUTHOR INFORMATION

### Corresponding Author

\*Phone: +44 0191 222 5852. Fax: +44 0191 222 6720. E-mail: [kirsten.brandt@ncl.ac.uk](mailto:kirsten.brandt@ncl.ac.uk).

### Notes

The authors declare no competing financial interest.

## REFERENCES

- (1) Stroup, D. F.; Berlin, J. A.; Morton, S. C.; Olkin, I.; Williamson, G. D.; Rennie, D.; Moher, D.; Becker, B. J.; Sipe, T. A.; Thacker, S. B. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA, J. Am. Med. Assoc.* **2000**, *283*, 2008–2012.
- (2) Hungate, B. A.; van Groenigen, K. J.; Six, J.; Jastrow, J. D.; Luo, Y. Q.; de Graaff, M. A.; van Kessel, C.; Osenberg, C. W. Assessing the effect of elevated carbon dioxide on soil carbon: a comparison of four meta-analyses. *Global Change Biol.* **2009**, *15*, 2020–2034.
- (3) Leimu, R.; Koricheva, J. Cumulative meta-analysis: a new tool for detection of temporal trends and publication bias in ecology. *Proc. R. Soc. B–Biol. Sci.* **2004**, *271*, 1961–1966.
- (4) Poiroux-Gonord, F.; Bidet, L. P.; Fanciullino, A. L.; Gautier, H.; Lauri-Lopez, F.; Urban, L. Health benefits of vitamins and secondary metabolites of fruits and vegetables and prospects to increase their concentrations by agronomic approaches. *J. Agric. Food Chem.* **2010**, *58*, 12065–12082.
- (5) Benbrook, C.; Zhao, X.; Davies, N.; Andrews, P. *New Evidence Confirms the Nutritional Superiority of Plant-Based Organic Foods*; The Organic Center: Washington, DC, 2008; pp 49.
- (6) Brandt, K.; Leifert, C.; Sanderson, R.; Seal, C. J. Agroecosystem management and nutritional quality of plant foods: the case of organic fruits and vegetables. *Crit. Rev. Plant Sci.* **2011**, *30*, 177–197.
- (7) (a) Dangour, A. D.; Dodhia, S. K.; Hayter, A.; Allen, E.; Lock, K.; Uauy, R. Nutritional quality of organic foods: a systematic review. *Am. J. Clin. Nutr.* **2009**, *90*, 680–685. (b) Dangour, A. D.; Allen, E.; Lock, K.; Uauy, R. Methodologic flaws in selecting studies and comparing nutrient concentrations led Dangour et al. to miss the emerging forest amid the trees Reply. *Am. J. Clin. Nutr.* **2009**, *90*, 1701–1701.
- (8) Heaton, S. *Organic Farming, Food Quality and Human Health. A Review of the Evidence*; Soil Association: Madison, WI, 2001; pp 88.
- (9) Hunter, D.; Foster, M.; McArthur, J. O.; Ojha, R.; Petocz, P.; Samman, S. Evaluation of the micronutrient composition of plant foods produced by organic and conventional agricultural methods. *Crit. Rev. Food Sci. Nutr.* **2011**, *51*, 571–582.
- (10) Smith-Spangler, C.; Brandeau, L. M.; Hunter, G. E.; Bavinger, J. C.; Pearson, M. Are organic foods safer or healthier than conventional alternatives? A systematic review. *Ann. Intern. Med.* **2012**, *157*, 348–366.
- (11) Worthington, V. Nutritional quality of organic versus conventional fruits, vegetables, and grains. *J. Alternative Complementary Med.* **2001**, *7*, 161–173.
- (12) Moher, D.; Liberati, A.; Tetzlaff, J.; Altman, D. G. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* **2009**, *6*, e1000097.
- (13) Petticrew, M.; Roberts, H. *Systematic Reviews in the Social Sciences: A Practical Guide*. Blackwell Publications: Oxford, UK, 2006; p xv, 336 pp.
- (14) Seufert, V.; Ramankutty, N.; Foley, J. A. Comparing the yields of organic and conventional agriculture. *Nature* **2012**, *485*, 229–232.
- (15) Hoefkens, C.; Vandekinderen, I.; De Meulenaer, B.; Devlieghere, F.; Baert, K.; Sioen, I.; De Henauw, S.; Verbeke, W.; Van Camp, J. A literature-based comparison of nutrient and contaminant contents between organic and conventional vegetables and potatoes. *Br. Food J.* **2009**, *111*, 1078–1097.
- (16) Quemada, M.; Baranski, M.; Nobel-de Lange, M. N. J.; Vallejo, A.; Cooper, J. M. Meta-analysis of strategies to control nitrate leaching in irrigated agricultural systems and their effects on crop yield. *Agric., Ecosyst. Environ.* **2013**, in press.
- (17) Hedges, L. V.; Gurevitch, J.; Curtis, P. S. The meta-analysis of response ratios in experimental ecology. *Ecol. Soc.* **1999**, *80*, 1150–1156.
- (18) Brickell, C.; Alexander, C.; David, J. C.; Hettterscheid, W. L. A.; Leslie, A. C.; Malecot, V.; Jin, X.; Cubey, J. J. *International Code of Nomenclature for Cultivated Plants: (ICNCP or Cultivated Plant Code) Incorporating the Rules and Recommendations for Naming Plants in Cultivation: Adopted by the International Union of Biological Sciences, International Commission for the Nomenclature of Cultivated Plants, 8th ed.*; Brickell, C. D., et al., Eds.; ISHS: Leuven, Belgium, 2009.