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Challenges and lessons from systematic literature reviews for the Australian dietary guidelines

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Abstract

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Abstract

In 2009-2010 the Dietitians Association of Australia conducted a series of systematic reviews for the National Health and Medical Research Council to generate evidence statements to inform the revision of the Dietary Guidelines for Australians. In total 202 body of evidence statements were constructed and assigned a grading detailing the certainty with which each could be used to inform policy. This paper describes some of the challenges and insights gained from the process, specifically related to: study type, study quality assessment, the lack of quantified data, diet exposure, definition of a healthy population, generalisability and applicability, and resource allocation. It is clear that there is still a need for further refinement of the methods for evaluating evidence for nutrition policy, but the current dietary guidelines are now much more robustly evidence-informed than ever before.

Keywords: systematic review, evidence-based health care, dietary guidelines

Introduction

Evidence-informed public health is a practice model that builds on the success of evidence-based medicine (Kohatsu *et al*. 2004) and is now being applied to public health nutrition. The Cochrane Collaboration has begun to include reviews of the benefits of whole foods (Priebe *et al* 2008, The Cochrane Collaboration 2010 and 2013) and in the US there have been calls to incorporate an evidence-based approach to establishing dietary guidelines (King 2007). The 2010 revision of the US dietary guidelines was informed by a series of systematic literature reviews, which are now available on line (US Department of Agriculture 2010). However the theoretical framework for knowledge translation in public health is still being developed and it is clear that beyond the scientific evaluation of evidence, the concepts of applicability and transferability must form part of any evidence-based public health policy (Armstrong *et al*. 2006, Brownson *et al*. 2009).

It is currently common practice to use formal systematic literature reviews to underpin the development of clinical practice guidelines (Cook *et al.* 1997). In Australia, the National Health and Medical Research Council has published guidelines for assessment and application of scientific evidence to support such guidelines, which have been widely used (NHMRC 2000). However a number of writers have noted that there are difficulties in applying these guidelines in the field of nutrition (Mann 2010, Truswell 2005, Truswell 2001). The Australian and New Zealand Food Authority (now Food Standards Australia New Zealand) used the NHMRC levels of evidence in the background papers for its committee on scientific substantiation of health claims for food, but decided that the levels should be revised due to the fact that RCTs are relatively rare among studies on diet and disease, and that food intake data from cohort studies may be more reliable (Truswell 2002). The World Cancer Research Fund has also developed a different systematic approach to the review of evidence linking dietary intake and cancer risk (World Cancer Research Fund and American

Institute for Cancer Research 2005), which relies less on RCTs and rates evidence as "convincing" through to "substantial effect on risk unlikely" (Wiseman 2008).

However, whilst the methodology for an evidence-based approach for nutrition recommendations is still being refined, the development of national nutrition guidelines, aimed to promote health and reduce the risk of diet-related conditions and chronic disease, continues (NHMRC 2011a). In 2009-2010 the Dietitians Association of Australia (DAA) was contracted by the NHMRC to conduct a series of targeted systematic reviews and generate evidence statements to support the latest revision of the Dietary Guidelines for Australians. The full report of the systematic reviews has been published (NHMRC 2011b). Searches for the project yielded 54920 papers for review; data was extracted from 2981 papers to prepare a total of 202 evidence statements. The project involved more than 35 people (approximately 8.8 full-time equivalents) over a period of one year.

The purpose of this paper is to reflect on the experience and process of conducting this project and to highlight some of the specific challenges that arise when undertaking reviews in the field of nutrition in order to inform public health recommendations.

Description of the process to conduct the systematic reviews

Several documented methods of conducting systematic reviews exist (eg, Eden *et al.* 2011; The Joanna Briggs Institute, 2011; The Cochrane Collaboration, 2010; Cook *et al.* 1997) but, given that the project was conducted for the NHMRC, the methods of that organisation were used as the basis of the reviews in this project (National Health and Medical Research Council 2000 & 2009). The NHMRC defined the food-health relationships to be examined, and then the PECO framework (population, exposure, comparison, outcome) was used to refine specific questions to be investigated (Bowker 2008). For example, "*In healthy free-living women aged 31-50 years (population), does a particular intake of vegetables (exposure and comparison) affect the risk of hypertension (outcome)?"*

A detailed process manual was developed to ensure a standardised and rigorous methodological approach was consistently applied across all reviews. It is available on the DAA website (Williams *et al.* 2009) and explains the process used to develop the final evidence statements. For each study question a body of evidence (BOE) matrix was assembled which summarised the breadth and consistency of the evidence, clinical impact, generalisability and applicability.

Each of these five criteria was graded as Excellent, Good, Satisfactory or Poor. For example, for the evidence base to be rated as Excellent, the NHMRC guidelines state that there should be several systematic reviews or RCTs with a low risk of bias. For a Good rating one or two RCTs or a systematic review of cohort or case control studies are required. A Satisfactory rating is assigned to cohort and case control studies with a low risk of bias, but those that are biased or have a study design such as pre- and post-test are considered Poor evidence (NHMRC 2000).

The matrix was then used to make a summarizing evidence statement and to define which of four gradings of recommendation were applied to the evidence statement, ranging from A (sufficient to guide practice in all cases) to having D (insufficient evidence to make any practice recommendations) (NHMRC 2009). Figure 1 gives an example of one evidence matrix, showing the final evidence statement and summary of the findings of the systematic literature review about egg consumption and the risk of coronary heart disease.

The wording of evidence statements depended on the types of studies in the evidence base. RCTs can show that an intervention directly results in changes in a clinical indicator or disease state eg: “substitution of polyunsaturated fat for saturated fat *decreases* LDL cholesterol”. However if the BOE was informed by a limited number cohort or case control studies then while an association could be demonstrated, the statement could not imply causation, eg: “consumption of coffee *is associated with* a decreased risk of type 2 diabetes”. If the evidence base and the clinical impact indicated that a particular quantity of a food was associated with the outcome then this amount was included in the statement.

Although an individual study may have met inclusion criteria, evidence statements can only be made if there is a sufficiently extensive body of evidence. In this project a decision was taken to only make an evidence statement if it could be informed by five or more relevant primary studies. This number is somewhat arbitrary, but was considered appropriate given the scope of the project, and was endorsed by the NHMRC project team. However, relevant studies that were not included in BOE statements because of the small number of studies were still briefly summarised in the full evidence report (NHMRC 2011b).

It should be noted that the main focus of this project was to review the evidence relating food consumption and health impacts. While some brief narrative reviews about the intersections

of food choice and environmental issues were developed, they did not systematically examine the primary research in this area and are not considered in this paper. Nonetheless the issue continues to be one of significant attention and debate (Selvey and Carey 2013) and poses its own methodological challenges.

What was learnt from the process of conducting the systematic reviews

The experiences of those contributing to the dietary guidelines review highlighted seven issues to consider when undertaking systematic reviews in food and nutrition.

1) Study type

The published NHMRC methods for literature reviews are primarily designed to assess the evidence of the effectiveness of medical interventions, usually relying on RCTs or diagnostic tests. In the case of diet-health relationships, there is a notable dearth of evidence from Level I and Level II studies, as evidenced in the previous editions of the Dietary Guidelines for Australians (NHMRC 2003), with much of the cited scientific evidence being observational, especially from prospective cohort studies. This poses particular challenges in translating the evidence into public health conclusions and there is an urgent need to develop evaluation standards and protocols for use in circumstances where RCTs are not appropriate (Victora *et al* 2004).

It is rarely possible to conduct blinded intervention studies with whole foods or diets, and very few trials are conducted for long enough periods to assess long-term health outcomes. Furthermore, in the food and nutrition areas, RCTs often cannot be ethically conducted (for example, examining the protective effect of fruit and vegetables on cancer development), so systematic reviews of cohort studies may be the most appropriate and highest level of evidence available. Cross-sectional studies are not generally considered appropriate when trying to determine causation, because the study factor should not be measured at the same time point as outcome. In this project, the NHRMC requested that these types of studies be excluded.

Therefore Level III prospective cohort studies sometimes provided a greater amount of evidence to inform the dietary guidelines reviews, due to their greater number and quality, than Level I evidence, which sometimes consisted of smaller short-term RCTs. The NHMRC guidelines also acknowledge that "lack of Level I or Level II evidence does not preclude a rigorous approach to the assessment of available evidence when developing practice guidelines" (National Health and Medical Research Council 2000, p13). In some cases when summarising the overall evidence base and grading the evidence statements, a rating of Excellent was still given when the best available evidence was Level III studies.

2) Study quality assessment

There are a number of different systems available to rate the quality of individual scientific studies. Three of the most relevant for systematic reviews in nutrition are:

a) SIGN

The Scottish Intercollegiate Guidelines Network (SIGN) develops evidence based clinical guidelines for the UK National Health Service and has published a grading system (GRADE) that has been widely used and is recommended by the Cochrane collaboration (Harbour and Miller 2001; Grade Working Group 2004). It has a very comprehensive set of checklists, with different ones for each of the four article types: reviews, RCTs, cohort studies and case-control studies, each with up to 23 questions (Scottish Intercollegiate Guidelines Network, 2011).

b) NHMRC and DAA

The Australian NHMRC publication on "*How to use the evidence; assessment and application of scientific evidence*" lists a number of quality criteria to consider when

evaluating individual studies or reviews (NHMRC 2000) which are reproduced in the DAA manual on the endorsement process for evidence-based dietetic practice guidelines (DAA 2009). However while these can be used to rate the study design level and guide the synthesis of evidence matrices, they do not define a process to apply a specific quality rating to an individual study.

c) American Dietetic Association

The American Dietetic Association (ADA) Evidence Analysis Manual (ADA 2008) includes detailed quality criteria checklists (with up to 50 questions), and separate checklists for Primary Research or Review articles, along with guidelines for the most important considerations for nine different study designs.

The ADA system results in a three category rating scale: Positive, Neutral or Negative, depending on answers to ten validity checklist questions covering:

1. The research question being clearly stated
2. Bias of study or subject selection
3. Comparability of study groups
4. Handling of subject withdrawals
5. Blinding
6. Descriptions of the study interventions
7. Outcomes and measurement tools
8. Statistical analysis methods used
9. Conclusions supported by evidence
10. Study sponsorship or funding.

For this project, the ADA system was used to rate individual nutrition studies, because it is one of the few that explicitly requires consideration of the validity of the dietary assessment methods. However, even this tool does not provide a detailed methodology, and development

of more specific algorithms or checklists to assess quality of dietary intake methods would be valuable.

3) Lack of quantified data

For many of the evidence statements it was not possible to quantify exposure due to limitations in the dietary methodologies used in studies or the inadequate level of detail reported. For example, in some cohort studies quantiles of exposure were reported in relation to health outcomes, but absolute intakes in terms of amounts or consumption frequencies of specific foods were not reported for the highest and lowest intake levels being compared (eg, te Velde *et al.* 2007). This makes it impossible to be specific about the relationship between amount of food intake (exposure) and specific health outcomes. When intakes are specified in serves per day or week, it is particularly important to check the definition of the serve size, since these can vary between countries (eg, a serve of bread may be one slice in the US and two in Australia).

4) Diet exposure

Since the aim of the reviews was to develop recommendations about foods rather than nutrients, studies conducted with isolated food extracts or nutritional supplements were normally excluded. However, there were some occasions when studies with purified components (eg, oils) could be used to support recommendations about whole foods (eg, margarines).

5) Definition of a healthy population

Usually nutrition reviews that are undertaken to develop public health recommendations consider only studies conducted in the general population and would exclude those conducted in particular clinical populations such as dialysis patients. However, it may be appropriate to

include studies where some or all of the subjects have a range of chronic conditions found commonly in the community (eg, overweight, hypertension, impaired glucose tolerance or hyperlipidaemia), since there are often very few studies in populations free of any chronic condition. After discussion with the NHMRC, this approach was adopted in the dietary guidelines reviews.

6) Generalisability and Applicability

Concepts of applicability and transferability of evidence form a crucial part of any public health planning (Wang et al 2006; Armstrong et al 2006). As explained in the NHMRC guidelines, generalisability largely refers to the study populations in which the studies have been conducted and asks how well the participants and settings used to form the BOE match those of the target population for which the evidence will be used. In our reviews, this was for the Australian population. Results from a wide range of countries and settings increases generalisability.

Applicability refers to how likely it is that an overall benefit would apply to an individual patient (NHMRC 2000). In nutrition reviews that aim to support advice to the general community, applicability is more related to the typical diet patterns of the population. For example, very high rice intakes have been found to be associated with increased risk of ischemic stroke in a Chinese population (Liang *et al.* 2010), but even the lowest quartile of intake in that study was above the mean intakes in Australia, and the highest intakes (2450g/week) were more than eight times higher than mean adult Australian intakes (McLennan and Podger 1999), and so the results are unlikely to be applicable to a local context.

7) Time and Resources

Since no other project of this type and scope had been undertaken in Australia previously, there were considerable challenges estimating time and resource requirements in advance. The individual reviews were carried out by a team of 32 reviewers, led by 3 members of the review leadership team, assisted by 2 medical librarians and 2 project managers (for details see NHMRC 2011b). Allocation of reviewers was based on informed assessments by the leadership team of the likely size of the literature related to each research question. Our experience was that the review and extraction of a single study could take from 0.5-2.0 hours, depending on the complexity of the study, the reviewer's experience in the conduct of reviews, and their familiarity with the topic. It was apparent that reviews carried out by people who were familiar with the topic area tended to be completed more efficiently. The total time for the project was not formally recorded but it is estimated that it required over eight full-time equivalent person-years.

The size of this project, and its strict timelines and budget, precluded using two reviewers per topic. Final quality checking of each review was undertaken independently by two members of the leadership team, who had experience in the systematic review process. However, in line with best practice, those undertaking similar projects of this magnitude in future should ideally try to secure sufficient resources to employ two reviewers.

In order to limit the literature searches to a manageable number of references, only articles published since the release of the previous edition of the Dietary Guidelines for Australians were considered (ie 2002 to 2009). In many cases, some of the most important literature had been published before 2002 and thus was not included in these reviews. Therefore the evidence grades for some of the diet-disease relationships were lower than would be anticipated with a time unlimited literature review (eg, for sugar and dental caries, where the diet disease relationship was well established prior to 2002). Thus decisions about search

strategies and the resources required for large reviews need to be informed by the strength of evidence already available.

Conclusion

The ability to conduct high quality systematic reviews is critical to the philosophy of building evidence into public health nutrition practice. The issues identified here should provide some guidance to others who plan similar reviews in the future and may have relevance to many other areas of public health policy. However, unique challenges within the field mean that the evidence base may sometimes be of a lower grading than is possible for pharmaceutical trials. It would be valuable if there were a standard register developed of systematic reviews in nutrition, along the lines of the registers of RCTs, which would enable ready searches and synthesis of findings by researchers in the future.

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Figure 1. Example of evidence matrix for vegetables and coronary heart disease

Does a particular intake of vegetables affect the risk of coronary heart disease?		
Evidence Statement		**Consumption of each additional daily serve of vegetables is associated with a reduced risk of coronary heart disease.**
Grade		**B**
Component	**Rating**	**Notes**
Evidence Base	Good	Level III evidence from two meta-analyses each with 9 cohort studies (with most studies in common and medium risk bias) plus two cohort studies (low risk bias) and one case-control and one RCT (medium risk bias)
Consistency	Good	Meta-analyses and case-control and RCT studies show protective effect (and in each study) but two recent cohort studies show no effect.
Clinical impact	Good	15 to 25% reduction with additional serve
Generalisability	Good	US and European studies
Applicability	Excellent	Australian adults of both sexes.