This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 774548.

EC Framework Programme for Research and Innovation

Horizon 2020

H2020-SFS-2017-2-RIA-774548-STOP:

Science & Technology in childhood Obesity Policy

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Methodological Considerations for Conducting Systematic Reviews of Nutrition-related Policy Actions

Start date of project: 1st June 2018 Duration: 48 months

D9.1: Peer-reviewed publication on methods for the systematic review and synthesis of evidence of the effectiveness of policies

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Version: Final

Preparation date: 25/06/20

Science and Technology in childhood Obesity Policy

Abbreviation	Definition
WHO	World Health Organisation
ICD	International Classification of Diseases
NCD	Noncommunicable diseases
FAO	Food and Agriculture Organization of the United Nations
SDGs	Sustainable Development Goals
ICN2	Second International Conference on Nutrition
UNGA	UN General Assembly
STOP	Science and Technology in childhood Obesity Policy
NFS	Department of Nutrition and Food Safety
NUGAG	WHO Nutrition Guidance Expert Advisory Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
NRS	Non-randomised studies
EPOC	The Cochrane Effective Practice and Organization of Care
ROBINS-I	Risk Of Bias In Non-randomised Studies-of Interventions
EtD	Evidence-to-decision

Dissemination Level

PU	Public	☒
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

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1 Background

The global nature of the obesity epidemic was formally recognized by the Expert Consultation held by the World Health Organization (WHO) in 1997 (WHO 2000), which highlighted obesity as a disease in its own right while it is also a major determinant of various noncommunicable diseases (NCD), such as type 2 diabetes, coronary heart disease and stroke and increases the risk of several types of cancer, gallbladder disease, musculoskeletal disorders and respiratory symptoms. The Expert Consultation also noted the advent of childhood obesity as great concern.

WHO's recognition of obesity as a disease goes back to its establishment in 1948. WHO was then entrusted to review and update the International Classification of Diseases (ICD) and the 6th version of ICD (ICD-6) set out by WHO had already classified obesity as a disease. In 1989, the WHO Study Group on Diet, Nutrition and Prevention of Chronic Diseases which established population nutrient intake goals for prevention of diet-related noncommunicable diseases (NCD) reviewed both adults and childhood obesity issues and their risk factors, highlighting the need to modify the population's environmental circumstances to reduce susceptibilities of people to become overweight and obese (WHO 1990). It was the first time when the analysis of prevalence of childhood obesity was conducted using the available data from over 30 countries.

In 1992, the International Conference on Nutrition (ICN), the first global intergovernmental conference on nutrition, examined the magnitude and extent of malnutrition in all its forms which included obesity and diet-related NCDs, established targets and intervention strategies to address them. The WHO Expert Committee on Physical Status held in 1993 also reviewed overweight and obesity issues both in adults and children extensively including biological, sociocultural behavioural determinants and consequences as part of the process for establishing and updating the anthropometric measurements, references and cut-off points.

But malnutrition in all its forms remains a global public health challenge, with almost all countries of the world currently faced with one or more forms of malnutrition, such as stunting, wasting, overweight and obesity (UNICEF, WHO and WB 2020), as well as micronutrient deficiencies, such as aneamia. The world has taken significant steps towards improving nutrition over recent decades which has resulted in declining of stunting (i.e. 144 million in 2019 comparing to almost 200 million in 2000), except in Africa where the number of stunted children has risen (UNICEF, WHO & WB 2020).

However, since the end of the millennium development goals in 2015, the Food and Agriculture Organization of the United Nations (FAO) has reported an increase in the number of people without access to adequate calories (FAO 2017). What appears to be a reversal of decades of progress is also marked by an increase in the number (~50 million) of chronically undernourished people in the world (FAO 2018). Furthermore, wasting still impacts the lives of far too many young children (i.e. 47 million in 2019) (UNICEF, WHO & WB 2020) and as the COVID-19 pandemic continues, it is expected that food insecurity will rise, access to health services including essential nutrition services will be reduced and social protection programmes will be undermined, leading to estimated 10 – 50% increases in childhood wasting (Roberton et al 2020).

On top of this, the global burden of NCDs and the associated risk factors continues an unprecedented rise with over 1 billion adults living with hypertension and 422 million adults with diabetes (2020 Global Nutrition Report). Furthermore, almost 700 million adults are obese and 40 million children under 5 years of age are overweight (2020 Global Nutrition Report; UNICEF, WHO & WB 2020).

Thus, all forms of malnutrition persist at unacceptably high levels on a global scale and intensified efforts and actions are needed to achieve the 2025 global nutrition and diet-related NCD targets. To meet this challenge, world leaders have established in 2015 the Sustainable Development Goals (SDGs) with one of the key targets aimed at ending malnutrition in all its forms (target 2.2). There are also several parallel and closely linked initiatives aimed at tackling global nutrition and diet-related NCD issues. In November 2014, WHO, jointly with the Food and Agriculture Organization of the United Nations (FAO), organized the Second International Conference on Nutrition (ICN2). ICN2 adopted the Rome Declaration on Nutrition and Framework for Action, recommending a set of policy options and strategies to promote diversified, safe and healthy diets at all stages of life. Furthermore, in April 2016, the UN General Assembly (UNGA) declared a UN Decade of Action on Nutrition (2016-2025), recognizing the role of nutrition in achieving the 2030 Agenda on Sustainable Development and the Sustainable Development Goals (SDGs). The Decade calls for eradicating hunger and preventing all forms of malnutrition worldwide, particularly stunting, wasting, and overweight in children under five years of age; and anaemia in women and children among other micronutrient deficiencies; as well as for reversing the rising trends in overweight and obesity and reducing the burden of diet-related NCDs in all age groups. Therefore, the goal of the Decade is to increase action at the national, regional and global levels in order to achieve commitment of the Rome Declaration adopted at ICN2, through implementing policy options included in the Framework for Action and evidence-informed programme actions.

Achievement of global nutrition and diet-related NCD targets and related SDGs all hinges on the successful implementation of evidence-informed interventions in multiple sectors (e.g. health agriculture, education, and trade) to address risk factors. As also highlighted in the Rome Declaration on Nutrition (FAO & WHO 2014b), addressing all forms of malnutrition requires clear and definitive evidence-informed guidance to provide a roadmap on how complex multisectoral approaches can work effectively.

An example of consolidated efforts to bring together the multi-disciplinary policy-relevant evidence base and generate effective and sustainable policies to prevent and manage rapidly increasing childhood obesity – one of the most dramatic features of the global obesity epidemic with long-term consequences on health and socioeconomic outcomes – can be seen in the Science and Technology in childhood Obesity Policy (STOP) project which was initiated in 2018 and is being implemented in the European Union. The STOP project builds on and expand the work undertaken by various partners, including international organizations such as WHO and OECD, in the past decade, aiming at producing quantitative and qualitative syntheses of evidence from evaluations of various policy actions, including fiscal policies, nutrition labelling policies, policies to regulate marketing of food and non-alcoholic beverages to children, policies to promote consumer behaviour change, reformulation policies, policies to promote physical activities, and health care management policies. These policy analyses will rely on several key components, one of which would be systematic reviews of existing evidence.

This paper aims to provide practical considerations for methodological approaches in the conduct of systematic reviews on nutrition-related policy actions, including those being conducted in the STOP project or in the WHO Guideline Development process. It also discusses challenges which may be faced when using or translating evidence from systematic reviews on policy actions and interventions in the guideline development process.

2 WHO Guideline Development Process

In accordance with the Organization-wide transformation in strengthening WHO's role in developing evidence-informed public health guidance which was implemented in 2010, the Department of Nutrition and Food Safety (NFS)has strengthened its role and leadership in providing evidence-informed policy and programme guidance to Member States for promoting healthy diets and nutrition throughout the lifecourse. WHO's commitment to strengthen its normative work was also reiterated in the *13th General Programme of Work (2019 – 2023)* endorsed by the World Health Assembly in May 2018, which states that "Setting norms and standards is a unique function and strength of WHO" and WHO "will reinforce its science- and evidence- based normative work".

To implement the strengthening of evidence-informed nutrition guidance, NFS established in 2010 the WHO Nutrition Guidance Expert Advisory Group (NUGAG) guided by the WHO Steering Committee for Nutrition Guidelines Development, which includes representatives from all Departments in WHO with an interest in the provision of recommendations in promoting healthy diets and nutrition. Membership in NUGAG includes experts from various WHO Expert Advisory Panels as well as experts from a larger roster including those identified through open calls for experts, taking into consideration a balanced mix of genders, breadth in areas of expertise, and representation from all WHO Regions.

Updating of the dietary goals for the prevention of obesity and diet-related NCD has been the focus of the work of the NUGAG Subgroup on Diet and Health since its creation in 2010. After completing the work on updating the guidelines on sodium intake (WHO 2020), potassium intakes (WHO 2012) and sugars intake (WHO 2015), the NUGAG Subgroup on Diet and Health had been working on the updates of the intake of total fat, saturated fatty acids, *trans*-fatty acids, polyunsaturated fatty acids, non-sugar sweeteners and carbohydrates. The draft guidelines on saturated fatty acids and *trans*-fatty acids were completed, launched for public consultation in May 2018, and are currently being finalized for release in 2020. The draft guidelines on the intake of total fat, polyunsaturated fatty acids, non-sugar sweeteners and carbohydrates are currently being prepared for public consultation before the end of 2020. Over the past several years, the NUGAG Subgroup on Diet and Health also began reviewing the issues related to dietary patterns, in which interest and concern are growing as a result of rapidly changing food environments. Furthermore, prompted by the increasing requests from various Member States for WHO's guidance on effective policy measures to develop enabling food environment for promoting healthy diets and nutrition, in 2017 the NUGAG Subgroup on Policy Actions was establish to initiate the development of WHO guidelines on policy actions, such as nutrition labelling policies, fiscal policies, policies to restrict marketing of food and non-alcoholic beverages to children, and school food and nutrition policies.

WHO guidelines are developed in ways consistent with internationally recognized best practices, emphasizing the appropriate use of systematically reviewed available evidence. The robust guideline development process being implemented by WHO is described in detail in the *WHO Handbook for guideline development* (WHO 2014). Undertaking of systematic reviews follows the Cochrane methodology (Higgins 2011) and are used to assess the evidence for outcomes that are critical for decision-making. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology is used to assess the overall quality of evidence and establish the strength of the recommendations, considering four main factors, such as values and preferences related to the outcomes of an intervention, the balance of benefits and harms, and costs (i.e. resource implications) (Guyatt 2011; Guyatt 2011a; Guyatt 2008; WHO 2014). In addition, when formulating nutrition or public health policy recommendations, considering several other factors may also be

important. These include the importance or priority of the problem being addressed (i.e. burden of disease, disease prevalence or baseline risk), equity and human rights, acceptability, and feasibility (WHO 2014).

The WHO decision making, and guideline development process often depends heavily on evidence derived from systematic reviews (WHO 2014). But particularly when developing guidelines on nutrition policies and programme interventions, careful attention needs to be paid to equity, human rights principles, gender and other social determinants of health as the effects of recommended policies and programme interventions may manifest in the different forms of health outcomes across different population groups or cause unintended consequences due to complex interactions among various factors.

WHO is, therefore, conducting separate reviews on additional decision criteria, i.e. other factors – values and preferences, the balance of benefits and harms, costs/resource implications, the importance or priority of the problem, equity and human rights, acceptability, and feasibility, to be considered when moving from evidence to recommendations (WHO 2014). The reviews also include some sub-criteria part of the WHO-INTEGRATE Evidence to Decision framework (Rehfuess et al 2018) as considered relevant following discussions at the meeting of the NUGAG Subgroup on Policy Actions. These include the impact of the policy action on, or the policy action's *interaction* with, existing health and food systems.

3 Key Considerations

3.1 Developing a logic model

In systematic review methodology, there has been increased recognition of the need to evaluate not only what works, but the theory of why and how an intervention works. It is even more critical to consider the wider context and system in which policy interventions are implemented and how these factors may contribute to the effectiveness of a policy. A logic model is a graphical representation of intervention processes, and outcomes linked by arrows indicating the direction of effect, which are developed into chains of cause-and- effect relationships (Kneale, 2018). Engaging the research team in coming up with the pathways to impact of a policy should be a first step when conducting systematic reviews of nutrition-related policy actions. This process offers a framework to help the review authors think conceptually during the review. The logic model should bring together the understanding of the knowledge users and the expert knowledge of the review team. The well thought out logic model can provide guidance at several stages of the systematic review process (Kneale 2015). In this paper we will examine the usefulness of the logic model for policy action systematic reviews at the following stages: 1) defining the intervention, 2) developing the search strategy, 3) identifying relevant outcomes, 4) identifying implementation factors and 5) communicating review findings. By their nature, policy actions in nutrition are complex and usually include interrelated strategies. such as direct nutrition support, or indirect mechanisms related to trade, education, agriculture, and economic empowerment (Mozaffarian 2018). Within the logic model, each mechanism of the policy action can be outlined which facilitates not only definition of the intervention, but also refining the review question. In a review conducted by Kristjansson and colleagues (2019), interventions to improve community food security in developed countries were examined and a logic model was used to map the scope of the review (see Table 1).

Dimensions of	Use of the logic model	Detailed example

the systematic review		
Defining the intervention	Understanding the intervention. Coming up with the multiple components of the intervention.	Three levels of intervention were identified. 1) interventions to improve: food supply, such as agricultural policy, programmes to create or sustain markets for local agricultural/farm products and storage programmes. 2) interventions to improve access and availability such as macroeconomic interventions, economic development, advocacy and food recovery programmes. 3) interventions to improve access such as social policies, food subsidies, food delivery programmes, programmes to transport people to food outlets and strategies targeting increase in knowledge or skills of recipients of the intervention.
Developing the search strategy	Identifying exclusion criteria based on components of the intervention. Scoping the range of search databases relevant to the interventions.	The review team was able to narrow the specific interventions components which allowed for coming up with inclusion/exclusion criteria. Given the nature of policy interventions the logic model also highlighted important contextual and implementation factors that were used in refining the search 'concepts'. Additionally, by identifying the core components of the interventions, it made clear that search databases should include those in the social sciences, biomedical, agriculture, policy, etc.
Refining outcomes	Identifying both intermediate and long-term outcomes	Changes in the population and its behavior usually results long after policy actions are taken. However conceptually mapping the review with relevant stakeholders helps with elucidating the various pathways to distal outcomes. In this review the author team created intermediate outcomes such as changes in availability or accessibility at the consumer level. The understanding of how these may relate to outcomes further downstream allowed for coming up with long term outcomes such as changes in household food security and health and well-being.
Identifying implementation factors	Understanding what works and why.	Policy interventions are influenced by many contextual and implementation factors operating at the level of the intervention and outcome. The logic

		model for community food security highlighted the role of community assets, the political and organizational context and how this contributes to how the intervention influences changes in outcomes. Identifying the implementation factors *a priori* informs the analysis such as defining key subgroups, but also helps with describing both mediators and moderators in the pathway to impact in the review. A key factor including in this domain of the model was quality of food which is important in explaining the 'why or why not' of the intervention when looking at distal outcomes.
Communicating review findings	A framework for analysis and reporting the findings of the review.	The logic model provides the grounded basis for systematically examining putative relationships in the causal chain. From this framework, review authors conducted analysis and reported on the most important sub-chains of the causal chain. For example, the review reports on how subsidies impact the change dietary changes in the economic circumstances of the population which may be influenced by reach and intensity of the intervention.

Table 1. Use of logic model for interventions to improve food security in developed countries: a nutrition policy relevant systematic review

While it is not the intention of this paper to provide the details of how to develop a logic model, as this is available in elsewhere (Kneale 2015; Funnel and Rogers 2011; Rohwer et al. 2017), a brief overview from the perspective of conducting policy action reviews is outlined. Start with the end in mind by engaging those external stakeholders (i.e. policy users, consumers, content expert and methodologists) who can play an integral role in forming a sound logic model (Kneale 2015). Developing the logic model follows an iterative backward process of identifying expected and intended outcomes of the intervention under study, and their potential mediating factors. Looking at existing logic models may be useful as a starting point to conceptually frame the logic model or use as a template (Rohwer et al. 2017). Having identified some components of the logic model, the goal is then to create links between the intervention and distal outcomes. These linkages should take into account intermediate outcomes contextual factors and implementation factors that may be operating at the intervention and outcome level simultaneously. See Figure 1 for an example of the community food security logic model.

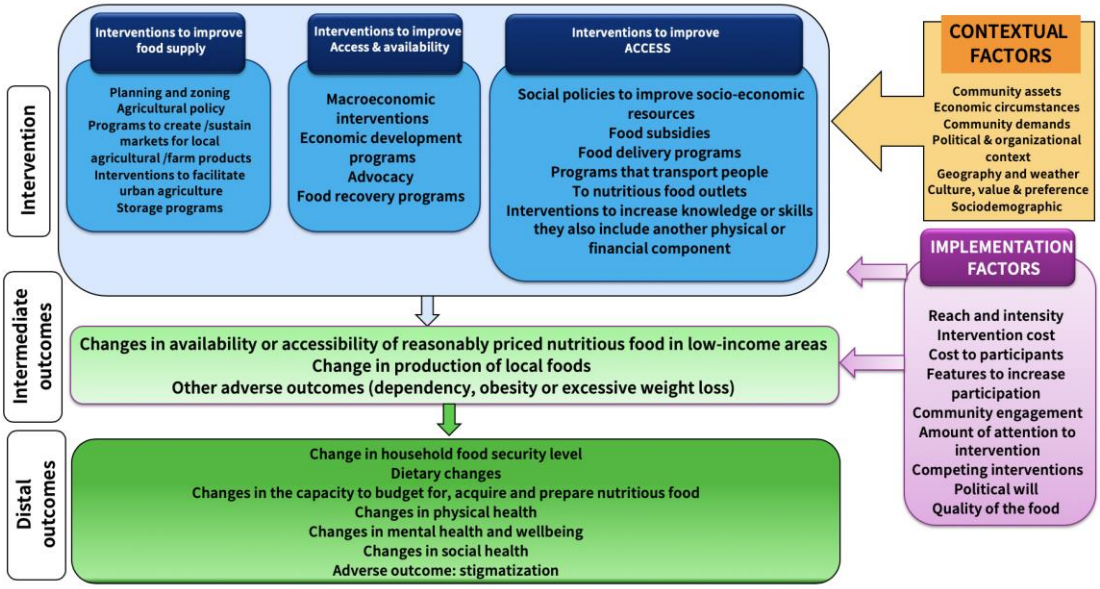

Figure 1. Interventions to improve community food security in developed countries: what works & why?
Source: Kristjansson 2019

It is useful to share the logic model with a steering group not directly involved in undertaking the review as this allow for fresh insights. Intervention outputs can also be identified after identifying outcomes, those necessary pre-conditions to reach outcomes. but not necessarily goals in themselves (Kneale 2018). Throughout several iterations of the logic model, additional contextual factors may be theorized. It is expected that there might be unexplained areas in the causal chain which may be better understood through the review synthesis.

3.2 Study Designs – going beyond trials

Methodological research suggest randomized control trials are the best way to avoid bias introduced by systematic differences between groups in a study (Schunemann 2013). However, policy interventions are usually implemented at the population level and are not often amendable to randomised control trials. Therefore, systematic reviews of policy interventions should consider non-randomized and quasi-randomized studies as either ‘replacement’ or ‘sequential’ to RCTs where RCTs already exist (Schunemann et al. 2013). When deciding what studies are to be included in the systematic reviews, consider the fit for purpose for each study design in line with the review question (Petticrew and Roberts 2003). Non-randomised studies (NRS) may be most suited to provide direct evidence and contextual information about whether or not the intervention works.

NRS include studies where assignment to the intervention is based on other known rules such as self-selection by participants or on program criteria with comparison group. The most common

NRS include the controlled before-after studies in which allocation to comparison groups are not made by investigator. The outcomes of interest are measured in both intervention and control groups before the intervention is introduced and again after the intervention has been introduced. Other designs include the interrupted time series design where data are collected at multiple intervals before and after the interventions. Controlled prospective cohort studies may also be considered particularly if other studies don't exist. The Cochrane Effective Practice and Organization of Care (EPOC) group has suggested an algorithm for including non-randomized studies in complex systematic reviews which might be relevant for policy action reviews in public health (see Figure 2).

Is it ever okay to consider other designs?

Traditionally, health interventions are concerned with a treatment effect, but in contrast policy interventions have a larger focus on behavior change. In addition to evaluating if an intervention works, for example, smoking reduction and incidence of lung cancer, a systematic review of policy interventions may well be more concerned with understanding the process of changing behavior. For example, does taxation and banning tobacco use in public places leads to a reduction in smoking? The latter might require evidence from non-randomized qualitative studies which could provide complementary information on contextual and implementation factors. It must be noted that the principles underpinning systematic review methodology can be applied to answer a range of different questions and include the synthesis of a range of different types of evidence, including qualitative evidence (Petticrew & Roberts 2006; Gough et al. 2012). However, while the need for these studies might be clear to the investigator, the obvious limitations should also be considered. Non-randomized uncontrolled studies are insufficient to show causation and inherently more at risk for bias and indirectness (Schunemann 2013). One approach in making the decision to include other types of evidence such as non-randomized uncontrolled studies is to consider whether high or moderate quality evidence from RCT or more robust NRS covers all the PICO elements defined in the review protocol. Where gaps exist, then non-randomized uncontrolled studies are likely to add complementary, sequential or replacement information. Available evidence from the suggested designs (RCTs and NRS) may also be graded as low quality, an issue to be addressed later in this paper, in which case it might be appropriate for review authors to consider whether or not the non-randomized uncontrolled studies literature can provide complementary evidence. This is plausible where non-randomized uncontrolled studies and RCTs and NRS are consistent in terms of the direction and magnitude of the effect, in which case the non-randomized uncontrolled studies evidence provides support that an effect possibly exists.

Systematic reviews use comprehensive methods that often assess whether an intervention is effective as well as identify some of the determinants for implementation of the intervention. The

latter, which is of paramount importance in informing nutrition-related policy actions, usually requires extensive data on process as well as outcome, in order to conduct causal chain analysis (Kneale 2018). This is often a limitation of systematic reviews that focuses on narrow questions and restrict inclusion only to randomized study designs. It is relevant for systematic reviews for nutrition-related policy actions to include studies that incorporate programmatic experiences of implementation and other process outcomes. It has been recognized that non-randomized studies can be considered as complementary (i.e. providing additional information on whether or not an intervention works in different populations and possible interaction effects); sequential (i.e. data are not available from RCTs on complex or long term outcomes); or replacement (i.e. providing higher quality evidence than RCTs or providing the best available evidence in the absence of RCTs) to randomized studies (Schunemann 2013). More systematic reviews on nutrition interventions now includes non-randomized studies, but there are gaps in the methodological guidance for such reviews.

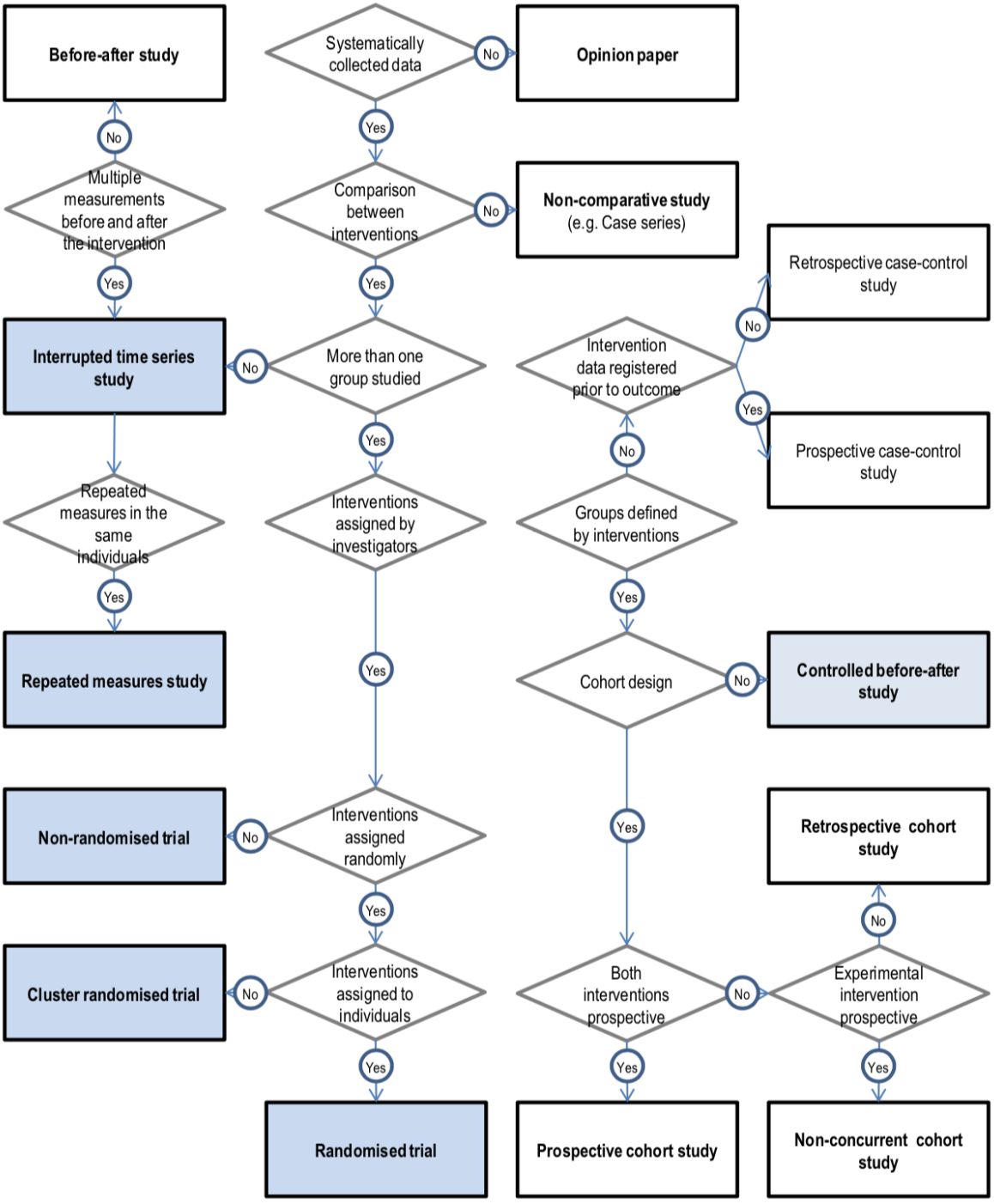

Figure 2: Study designs for evaluating the effects of healthcare interventions

3.3 Approaches to appraising bias

Systematic reviews of policy interventions predominantly include non-randomised studies. NRS are widely recognized and used to evaluate the effects of interventions aimed at long term outcomes in populations and settings relevant to real-world practice (Shmidt 2017). But much consideration has been given to the methodological approach to evaluate the strength and weaknesses of these studies. The robust assessment of the quality of evidence from these studies are particularly important since these reviews are often used for clinical and policy guidelines. The two foremost approaches that will be discussed in this paper are the Risk Of Bias In Non-randomised Studies-of Interventions (ROBINS-I) (Sterne, et al. 2016) and Cochrane EPOC suggested risk of bias criteria (EPOC 2017). Both approaches utilize domain-based assessments where different types of bias are sequentially examined.

The ROBINS-I evaluates all non-randomised studies as a 'target trial", a hypothetical pragmatic randomised trial, conducted on the same participant group without putting it at risk of bias. It is proposed that the such a trial would ideal approach to answering the question addressed by the NRS (Sterne, et al. 2016). The detail application of ROBINS-I is described elsewhere (Sterne 2016) but in brief follows a six-step process which includes:

1) Specify the research question through consideration of a target trial
2) Specify the outcome and result being assessed
3) For the specified result, examine how the confounders and co-interventions were addressed
4) Answer signaling questions for the seven bias domains
5) Formulate risk of bias judgements for each of the seven bias domains, informed by answers to the signaling questions
6) Formulate an overall judgement on risk of bias for the outcome and result being assessed.

Steps one through three are considered at the pre-intervention stages of the study being assessed. In particular, step three addresses the issue of bias due to confounding as well as selection bias in studies that have a control group. The signaling questions included in the assessment framework facilitate judgments on risk of bias for each of the seven domains covered in the tool. Evolving from the options of "Yes", "No" or "Unclear" risk, the response options are "Yes"; "Probably yes"; "Probably no"; "No"; and "No information". Some questions are answered only if the response to a previous question is "Yes" or "Probably yes" (or "No" or "Probably no"). Responses of "Yes" are intended to have similar implications to responses of "Probably yes" (and similarly for "No" and "Probably no") but allow for a distinction between something that is known and something that is likely to be the case. Along with the responses to thee signaling questions for each domain of the risk of bias, quoted text from the study or free-text should be documented to support the judgement. As it relates to the seven bias domains, the ROBINS-I appropriately categorizes them into, 1) pre-intervention, 2) at intervention and 3) post-intervention). Critical to non-randomize studies the first three domains address bias due to confounding, bias in selection of participants into the study and bias in classification of interventions.

The ROBINS-I has answered many of the gaps in assessing risk of bias in NRS, however there are still limitations in the approach. For one, NRS of interventions cannot always be treated at "target trials" as in most cases RCTs are either not feasible or inappropriate for implementing policy interventions. The idea then that arriving at overall risk of bias judgement for NRS on the basis of how well it corresponds to the risk of bias in a high quality randomised trial is flawed. While the approach is suitable for non-randomised trials and perhaps even controlled before-after studies, it has limited applicability for specific NRS designs such as, self-controlled designs, interrupted time series studies and studies based on regression discontinuity and instrumental variable analyses.

The Cochrane EPOC suggested risk of bias criteria treats studies with a separate control group (randomized trials, non-randomised trials and controlled before-after studies) differently from the interrupted time series design (EPOC, 2017). Since the ROBINS-I adequately addresses the

former designs, it might be useful to consider EPOC suggested risk of bias criteria for interrupted time series (ITS) designs. ITS studies have been traditionally used for policy interventions (Windsor 1986; Cook & Campbell 1979) mainly due to their applicability to real world practice. There are seven standard criteria used for all interrupted time series studies and are described in Table 2.

Criteria	Description	Possible judgement
Intervention independent of other changes	Examines whether the intervention occurred independently of a plausible rival hypothesis. Whether study outcomes were affected by other confounding factors over the study period.	Low risk or High risk
Shape of the intervention effect pre-specified	The point of analysis is the point of intervention and where there is deviation from this principle a logical explanation is provided in the study.	Low risk or High risk
Intervention unlikely to affect data collection	The sources and methods of collection are consistent over time and are not likely to affect the data collected. Changes in source(population) or method of data collection may introduce bias.	Low risk or High risk
Knowledge of the allocated interventions adequately prevented during the study	Primary outcomes are those variables which correspond to primary hypothesis or question defined by study authors. These outcomes should also be objective as blind assessment is often not feasible.	Low risk or High risk
Incomplete outcome data	The level of attrition or missing data is similar in pre- and post-intervention period, making it unlikely to bias the results.	Low risk or High risk
Selective outcome reporting	Relevant outcomes are pre-specified and reported on in the results section regardless of finding. Where important outcomes are not reported this may introduce bias or if important outcomes are not prespecified or reported assessing risk of bias may be difficult.	Low risk, Unclear risk or High risk
Other risk of bias	Issues such as seasonality in time of data collection or outcome assessment for pre- and post-intervention may lead to spurious effect.	Low risk or High risk

Table 2: Risk of bias for interrupted time series studies

Source: EPOC, 2017

As no one tool may comprehensively address the assessment of risk of bias for non-randomised studies it may require flexibility on the part of the reviewer to use both the ROBINS- I and EPOC criteria. The principle of 'triangulating' findings across studies to arrive at an overall risk of bias should therefore be extended to moving from one instrument to the next dependent on the specific NRS design and research question being addressed.

3.4 Synthesis

Following a systematic approach to conducting the review will provide much of the basis for the type of synthesis that is required. It is therefore important to have a well formulated question, comprehensive search strategy, objective selection of studies, robust appraisal of methodological quality and unbiased data extraction. The synthesis of included studies in the systematic review can be done quantitively using a meta-analysis or using a narrative approach. The term narrative approach/synthesis is used differently in disciplines, but the narrative approach used in this paper refers to a text-based approach to combining evidence from the various study designs included in the systematic review. Though this approach is often mistaken as inferior, it avoids statistical heterogeneity and adds to the interpretation of the evidence (Thomas et al. 2012). The narrative synthesis lends itself to bringing together studies that answers the question of effectiveness (i.e. experimental and quasi-experimental designs) and those deigns that answer questions such as 'why" an intervention works (or not) as well as the process issues underpinning effectiveness (Snilstveit at al. 2012; Petticrew & Roberts 2006).

The choice of method of synthesis for systematic reviews of policy actions is largely influenced by the nature of the evidence. Often it can include a mixed method approach, meaning, a meta-analysis and a narrative synthesis. Methods for meta-analysis are less debated and sufficiently described (Hedges & Olkin 1985; Chalmers, Hedges & Cooper 2002; Higgins et al. 2011). More recently, Popay and colleagues (2006) provided a framework for narrative synthesis of evidence on effectiveness of interventions and factors determining the implementation of interventions. The guidance on the suggested tools and techniques is briefly described in Table 3.

Element of synthesis	Suggested tools and techniques
Developing a theory of how the intervention works, why and for whom?	No specific tools or techniques identified. However, it is noted that tools and techniques suggested for other elements of the synthesis can contribute to developing the theory of change.

Developing a preliminary synthesis of findings of included studies.	Textual description of studies, groupings and clusters, tabulation, transforming data into a common rubric, vote counting as a descriptive tool, thematic and content analysis for translating data.
Exploring relationships in the data.	Graphs, frequency distributions, funnel plots, forest plots and L'Abbe plots; moderator variables and sub-group analyses; idea webbing and conceptual mapping; reciprocal and refutational translation; qualitative case descriptions; investigator/moderator triangulation; conceptual triangulation.
Assessing the robustness of the synthesis.	Weight of evidence (for example, Harden and Gough 2012); best evidence synthesis; validity assessment (for example, the CDC approach); reflecting critically on the synthesis process; checking the synthesis with authors of primary studies.

Table 3. Tools and techniques for narrative synthesis

Source: Popay et al., 2006

3.5 Recommendations and Guideline Development – GRADE

The decision-making process is complex and relies on inputs from different public health stakeholders, following a broad range of decision criteria. An important part of this process involves translating evidence from well conducted systematic reviews to support decisions or recommendations. Evidence from systematic reviews, such as those conducted on nutrition-related policy actions provides guidance for the development of policy recommendations (Zhang Y 2018; WHO 2010; Guyatt 2010). The basis of most recommendations are judgments which centres on the quality of evidence, tradeoff between benefits and harms, values and preferences and resource use. In order to ensure credibility of decisions based on judgements, the decision-making process should be transparent and based on the best available evidence (Moberg 2018). The multifaceted process of making decisions or recommendation in health require structured approaches. One such approach is the GRADE evidence-to-decision (EtD) framework (Moberg 2018; Coello 2016). This framework facilitates transparent, systematic decision-making through structured use of evidence and careful consideration of other factors, such as context and setting. The central tenet of EtD framework is the proposed decision criteria which guides the process from the development of the relevant policy question to grading the certainty of the evidence across priority outcomes.

The GRADE EtD framework is relevant to systematic reviews on nutrition-related policy actions primarily in developing the summary of findings and creating the evidence profile which includes rating the quality of evidence for each outcome. The systematic reviews provide the necessary information to develop the GARDE evidence profile which is a summary of estimate of effect for all

relevant outcomes for a given question. It also provides information about the body of evidence (e.g. number of studies), the judgments about the underlying quality of evidence, key statistical results, and the quality of evidence rating for each outcome. A detail approach to this method is documented in the GRADE Handbook (Schünemann 2015).

Systematic reviewers should consider the determinants of quality for evidence generated by the systematic reviews. There are eight considerations that relate to both randomized and observational studies that are included in the systematic reviews on nutrition-related policy actions. There are five factors that can lower the quality of the evidence primarily for randomized control trials which on the basis of its design starts off as high quality (⊕⊕⊕⊕). These factors include limitation in design or execution of the study (risk of bias), heterogeneity within and across studies, indirectness, imprecision and publication bias (Schünemann 2015). Systematic reviews on nutrition-related policy actions will largely include non-randomized or observational studies which due to inherent limitation in design is assumed to be at low quality (⊕⊕◯◯). The GRADE approach suggests three factors that can increase quality in these studies which relates to large magnitude of effect, plausible residual bias or confounding and the presence of a dose response (Schünemann 2015). It is important to note that large observational studies may be upgraded to high quality. For this reason, judgements for each decision on quality rating included in the summary of findings table of the systematic review should be supported by an explanation in the footnote of the table. Finally, systematic reviewers should report on all primary outcomes in the summary of findings table even when a meta-analysis was not conducted. A narrative approach may be used to report on the estimate of effect and a quality rating provided.

4 Discussion

With the implementation of the new guideline development process in 2010, WHO guidelines are being developed consistent with internationally recognized best practices, through undertaking systematic reviews and based on transparent process for evaluating the certainty of evidence and the strength of recommendations through use of GRADE. This robust evidence-informed guideline development process which is guided by the *WHO handbook for guideline development* (WHO 2014) has increased the transparency of WHO's guideline development process and therefore the credibility of the WHO guidelines and their uptaking by the national governments and the international community in recent years. This was a timely transformation of the way WHO provides its guidance on diet and nutrition as the political momentum for food and nutrition in the public health agenda was increasing, also prompted by the increasing attention on NCDs, and this has challenged WHO to ensure that its guidance and recommendations are informed by the best available evidence.

But at the same time, some debates have started about the use of the methodology which is based on clinical trials, not only in the field of nutrition, but also in other fields which do not necessarily fit in using such the methodology, such as environmental health (Lawrence et al 2016; Temple 2016; Bero 2018; Morgan et al 2018; Bero 2019). Some challenges and suitability of the use of GRADE methodology for evaluating the quality of evidence deriving from nutrition and dietary studies were discussed and debated at different fora, including the Cochrane Collaboration and the Campbell Collaboration, as well as the GRADE Working Group.

In 2016, Cochrane Nutrition with a view to: 1) increase coverage, quality and relevance of Cochrane nutrition reviews; 2) increase the impact of Cochrane nutrition reviews across all stakeholders; and 3) contribute to strengthening methods for conducting nutrition systematic reviews. Increasing attentions and efforts are being made to continuously improve methods and reform evidence use in nutrition, and in nutrition-related policy actions, to increase flexibility and adapt to the available evidence (i.e. the use of observational data), so as to be more relevant and responsive to the needs of decision-makers and programme managers in developing and implementing effective national policies to improve health and nutritional well-being of the populations globally. Also there may be some learning from the way in which the environmental health research community is introducing the innovation in systematic review methods to evaluate and synthesise evidence and applying GRADE to environmental health topics as well (Morgan et al 2016).

The experience of WHO in supporting countries to develop and implement effective policy actions has been that, even when political commitment is present, there is little 'buy-in' from senior officials and significant capacity gaps in understanding and responding to the increasing complexity of food and nutrition policy development. In addition to more fully understanding this complexity, they will need the capacity to critically analyse existing or proposed nutrition-related policy actions. An important part of this capacity will be the effective use and application of evidence and advocacy and negotiation skills to present evidence-informed guidance and recommendations on nutrition-related policy and programme interventions. The engagement of public health agencies and academic agencies in synthesizing and translating evidence, taking into consideration of various contextual factors and country contexts, such as being done in the STOP project, provides a valuable opportunity to contribute to this required capacity as well as to further developing methodologies for evaluating and synthesising evidence. To support these actions, innovative and flexible approach may be required in adapting existing best practice methodologies to transform them to 'fit for the purpose' in evaluating and synthesising evidence while developing more suitable and relevant methodologies are being investigated.

5 References

1. 2020 Global Nutrition Report: Action on equity to end malnutrition. Bristol, UK: Development Initiatives, 2020.
2. Bero L, Chartres N, Diong J, et al. The risk of bias in observational studies of exposures (ROBINS-E) tool: concerns arising from application to observational studies of exposures. *Syst Rev* 2018;7:242. 10.1186/s13643-018-0915-2 30577874
3. Bero L, Norris S, Lawrence M. Making nutrition guidelines fit for purpose. BMJ 2019;365:l1579 doi: 10.1136/bmj.l1579.
4. Chalmers, I., Hedges, L. V., & Cooper, H. (2002). A Brief History of Research Synthesis. Evaluation & the Health Professions, 25(1), 12–37. https://doi.org/10.1177/0163278702025001003
5. Cochrane Effective Practice and Organisation of Care (EPOC). Suggested risk of bias criteria for EPOC reviews. EPOC Resources for review authors, 2017. Available at: http://epoc.cochrane.org/resources/epoc-resources-review-authors
6. Cook, T. D. and Campbell, D. T. (1979) *Quasi-Experimentation: Design & Analysis Issues for Field Settings.* Houghton Mifflin, Boston, MA.
7. Cook, T. D., Shadish, W. R., & Wong, V. C. (2008). Three conditions under which experiments and observational studies produce comparable causal estimates: New findings from within-study comparisons. *Journal of Policy Analysis and Management, 27*, 724–750.
8. Diet, nutrition and the prevention of chronic diseases: report of a WHO Study Group. Geneva: World Health Organization; 1990 (http://www.who.int/dietphysicalactivity/publications/trs916/intro/en/
9. FAO. World hunger on the rise again, reversing years of progress. 2017. Available at: http://www.fao.org/news/story/en/item/902489/icode/ (accessed 21 November 2019).
10. FAO, IFAD, UNICEF, WFP and WHO. 2018. The State of Food Security and Nutrition in the World 2018. Building climate resilience for food security and nutrition. Rome, FAO. 2018. Available at: http://www.fao.org/3/I9553EN/i9553en.pdf (accessed 21 November 2019).
11. FAO and WHO. Framework for Action. Second International Conference on Nutrition (ICN2). Rome, Food and Agriculture Organization of the United Nations, 2014a. Available at: http://www.fao.org/3/a-mm215e.pdf (accessed 22 June 2020).
12. FAO and WHO. Rome Declaration on Nutrition. Second International Conference on Nutrition (ICN2). Rome, Food and Agriculture Organization of the United Nations, 2014b. Available at: http://www.fao.org/3/a-ml542e.pdf (accessed 22 June 2020).
13. Framework for Action. Second International Conference on Nutrition. Rome: Food and Agriculture Organization of the United Nations/World Health Organization; 2014.
14. Funnell, S.C. and Rogers, P. J. (2011) Purposeful program theory: effective use of theories of change and logic models. San Francisco: Jossey-Bass/Wiley.
15. Guideline: Potassium intake for adults and children. Geneva: World Health Organization; 2012.
16. Guideline: Sodium intake for adults and children. Geneva: World Health Organization; 2012.
17. Guideline: Sugars intake for adults and children. Geneva: World Health Organization; 2015.
18. Handbook for guideline development 2nd Ed. Geneva: World Health Organization; 2014 Available at: http://apps.who.int/medicinedocs/documents/s22083en/s22083en.pdf (accessed 22 June 2022).
19. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from http://handbook.cochrane.org.
20. Guyatt G et al. GRADE guidelines 1. Introduction-GRADE evidence profiles and summary of findings tables. J. Clin. Epidemiol. 2011; 64(4):383–94.

21. Guyatt GH et al.; GRADE Working Group. GRADE guidelines: 9. Rating up the quality of evidence. J. Clin. Epidemiol. 2011a;64(12):1311–16.
22. Guyatt GH et al., for the GRADE Working Group. Rating quality of evidence and strength of recommendations GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ, 2008;336:924–6.
23. Harden, A. and Gough, D., 2012. Quality and relevance appraisal. *In*: D. Gough, S. Oliver, and J. Thomas, eds. *An introduction to systematic reviews*. London: Sage, 153–178.
24. Hedges, L. V., & Olkin, I. (1985). *Statistical methods for meta-analysis*. San Diego, CA: Academic Press.
25. Henry, D., Tolan, P., Gorman-Smith, D. et al. Prev Sci (2017) 18: 671. https://doi.org/10.1007/s11121-016-0706-8
26. Kneale D, Thomas J, Harris K (2015) Developing and Optimising the Use of Logic Models in Systematic Reviews: Exploring Practice and Good Practice in the Use of Programme Theory in Reviews. PLOS ONE 10(11): e0142187. https://doi.org/10.1371/journal.pone.0142187.
27. Kneale D, Thomas J, Bangpan M, Waddington H, Gough D, 2018 Causal Chain Analysis in Systematic Reviews of International Development Interventions CEDIL Inception Paper 4: London.
28. Lawrence M et al. A call to action to reshape evidence synthesis and use for nutrition. 2016;(11):ED000118https://doi.org/10.1002/14651858.ED000118
29. Morgan RL, Thayer KA, Bero L, etal . GRADE: Assessing the quality of evidence in environmental and occupational health. *Environ Int* 2016;92-93:611-6. 10.1016/j.envint.2016.01.004 26827182
30. Morgan RL, Thayer KA, Santesso N, et al. Evaluation of the risk of bias in non-randomized studies of interventions (ROBINS-I) and the 'target experiment' concept in studies of exposures: Rationale and preliminary instrument development. *Environ Int* 2018;120:382-7. 10.1016/j.envint.2018.08.018 30125855
31. Mozaffarian Dariush, AngellSonia Y, Lang Tim, Rivera Juan A. Role of government policy in nutrition—barriers to and opportunities for healthier eating BMJ 2018; 361 :k2426
32. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation. Geneva, Switzerland: World Health Organization, 2000. (WHO technical report series 894).
33. Popay, J., *et al*., 2006. *Guidance on the conduct of narrative synthesis in systematic reviews* [online]. Version 1: April 2006, ESRC Methods Programme. Available from: http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.178.3100&rep=rep1&type=pdf [Accessed 21 March 2019].
34. Petticrew, M. and Roberts, H., 2006. *Systematic reviews in the social sciences – a practical guide*. Oxford: Blackwell Publishing.
35. Rehfuess EA, Stratil JM, Scheel IB, Portela A, Norris SL, Baltussen R. The WHO-INTEGRATE evidence to decision framework version 1.0: integrating WHO norms and values and a complexity perspective. BMJ Global Health 2018;0:e000844.
36. Roberton T et al. Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study. The Lancet, 2020, 8: e901 – 908.
37. Rohwer A, Pfadenhauer L, Burns J, Brereton L, Gerhardus A, Booth A, Oortwijn W, Rehfuess E, Series: Clinical Epidemiology in South Africa. Paper 3: Logic models help make sense of complexity in systematic reviews and health technology assessments, *Journal of Clinical Epidemiology*, Volume 83, 2017, Pages 37-47, ISSN 0895-4356, https://doi.org/10.1016/j.jclinepi.2016.06.012.
38. Rome Declaration on Nutrition. Second International Conference on Nutrition. Rome: Food and Agriculture Organization of the United Nations/World Health Organization; 2014.
39. Schünemann, H. J., Tugwell, P. , Reeves, B. C., Akl, E. A., Santesso, N. , Spencer, F. A., Shea, B. , Wells, G. and Helfand, M. (2013), Non-randomized studies as a source of complementary, sequential or replacement evidence for randomized controlled trials in

systematic reviews on the effects of interventions. Res. Syn. Meth., 4: 49-62. doi:10.1002/jrsm.1078

40. Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from guidelinedevelopment.org/handbook.
41. Snilstveit B, Oliver S, & Vojtkova M, (2012) Narrative approaches to systematic review and synthesis of evidence for international development policy and practice, Journal of Development Effectiveness, 4:3, 409-429, DOI: 10.1080/19439342.2012.710641
42. Temple NJ. How reliable are randomised controlled trials for studying the relationship between diet and disease? A narrative review. *Br J Nutr* 2016;116:381-9.10.1017/S0007114516002129 27267302
43. Thirteenth general programme of work, 2019–2023. Geneva: World Health Organization; 2018.
44. Thomas, J., Harden, A., and Newman, M., 2012. Synthesis: combining results systematically and appropriately. *In*: D. Gough, S. Oliver, and J. Thomas, eds. *An introduction to systematic reviews*. London: Sage, 179–226.
45. United Nations Children's Fund (UNICEF), World Health Organization, International Bank for Reconstruction and Development/The World Bank. Levels and trends in child malnutrition: Key Findings of the 2020 Edition of the Joint Child Malnutrition Estimates. Geneva: World Health Organization; 2020
46. Schmidt W. P. (2017). Randomised and non-randomised studies to estimate the effect of community-level public health interventions: definitions and methodological considerations. *Emerging themes in epidemiology*, *14*, 9. doi:10.1186/s12982-017-0063-5
47. Sterne Jonathan AC, Hernán Miguel A, Reeves Barnaby, Savović Jelena, Berkman Nancy D, Viswanathan Meera et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions *BMJ* 2016; 355 :i4919
48. WHO Global Targets 2025 Tracking Tool (version 3 – May 2017): Global Progress Report. 2017a. Available at: http://www.who.int/nutrition/trackingtool/en/ (accessed 21 November 2019);
49. WHO. Global Health Observatory data repository: Prevalence of overweight among adults, BMI ≥ 25, age-standardized. Estimates by country, 2017b. Available at: http://apps.who.int/gho/data/node.main.A897A?lang=en (accessed 21 November 2019).
50. WHO. Use of systematic reviews of the evidence in public health nutrition. Proceedings of an informal consultation held 18 October 2011 in Geneva, Switzerland. Geneva: World Health Organization; 2013.
51. Windsor, R. A. (1986) The utility of time series designs and analysis in evaluating health promotion and education programs. *Advances in Health Education and Promotion*, **1**, 435–465.