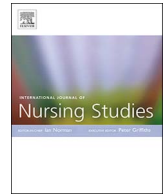




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Increasing value and reducing waste by optimizing the development of complex interventions: Enriching the development phase of the Medical Research Council (MRC) Framework



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ABSTRACT

Background: In recent years there has been much emphasis on 'research waste' caused by poor question selection, insufficient attention to previous research results, and avoidable weakness in research design, conduct and analysis. Little attention has been paid to the effect of inadequate development of interventions before proceeding to a full clinical trial.

Objective: We therefore propose to enrich the development phase of the MRC Framework by adding crucial elements to improve the likelihood of success and enhance the fit with clinical practice

Methods: Based on existing intervention development guidance and synthesis, a comprehensive iterative intervention development approach is proposed. Examples from published reports are presented to illustrate the methodology that can be applied within each element to enhance the intervention design.

Results: A comprehensive iterative approach is presented by combining the elements of the MRC Framework development phase with essential elements from existing guidance including: problem identification, the systematic identification of evidence, identification or development of theory, determination of needs, the examination of current practice and context, modelling the process and expected outcomes leading to final element: the intervention design. All elements are drawn from existing models to provide intervention developers with a greater chance of producing an intervention that is well adopted, effective and fitted to the context.

Conclusion: This comprehensive approach of developing interventions will strengthen the internal and external validity, minimize research waste and add value to health care research. In complex interventions in health care research, flaws in the development process immediately impact the chances of success. Knowledge regarding the causal mechanisms and interactions within the intended clinical context is needed to develop interventions that fit daily practice and are beneficial for the end-user.

What is already known about the topic?

- To prevent research waste, little attention has been paid to the effect of inadequate development of interventions before proceeding to a full clinical trial.
- The MRC Framework for developing and evaluating complex interventions is the most cited guidance using an iterative approach.

- A misfit between the intervention and the implementation context often hampers resulting in suboptimal treatment success.

What this paper adds

- A comprehensive development approach is proposed by combining the elements of the MRC development phase with elements from

Abbreviations: MRC, Medical Research Council

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existing guidance to enhance the fit with clinical practice.

- The proposed elements will improve the development of complex interventions, strengthen the internal and external validity, minimize research waste and add value to health care research.

1. Background

Much of the cause of ‘research waste’, estimated at 85% of research activity, has been attributed to poor question selection, insufficient attention to previous research results, inadequate reporting, and poor intervention description (Ioannidis et al., 2014). Moreover, many biomedical and public health research studies can be regarded as wasteful due to avoidable weakness in their design, conduct and analysis (Ioannidis et al., 2014; Chalmers and Glasziou, 2009). In complex intervention studies in health care, preventing these weaknesses is challenging. Complex interventions are defined as interventions with several interacting components that impact the length and complexity of the causal chain from intervention to outcome and the influence of features of the local context (Craig et al., 2008). Some argue that definitions of simple and complex interventions evolve from the question being asked in the research project rather than the intervention itself (Petticrew, 2011).

In recent years, much emphasis has been placed on better reporting of evidence-based complex interventions in health care (Glasziou et al., 2014, 2010a; Hoffmann et al., 2014). Report guidance such as the Template for Intervention Description and Replication⁶ (TIDieR) and CReDECI (Mohler et al., 2015; Möhler et al., 2012) have been developed to assist authors, editors, peer reviewers, and readers enhance transparency, replication, and the potential impact. Less attention, however, has been given to enhancing the development process of complex interventions and how the intervention can be improved before proceeding to a full clinical trial. This too often ends in trials showing results that tend to be negative or inconclusive, as demonstrated in a comprehensive analysis of treatment success of 51 funded pragmatic trials (Dent and Raftery, 2011). This could possibly be prevented when the intervention was carefully designed and tested in a feasibility or pilot study.

Several guides for developing and evaluating complex interventions have been published to enhance the performance and design of an intervention before studying its effectiveness (Conn et al., 2001a; van Meijel et al., 2004; Whittemore and Grey, 2002; Bartholomew et al., 2011) and some emphasize the importance of studying the modifiable causal or contextual factors (Wight et al., 2016; Card et al., 2011). The Medical Research Council (MRC) Framework for developing and evaluating complex interventions is well known and cited in the literature and guides the process in making appropriate methodological and practical decisions. By working with the MRC Framework and other intervention development guidance over the years, we have learned that when designing interventions using these existing models, the fit with the actual context often hampers. Additional knowledge is often needed to successfully develop a complex intervention that has a strong evidence and theoretical base and fits within the delivery context (Wight et al., 2016; Richards and Hallberg, 2015a; Wells et al., 2012).

Designing interventions that fit into practice and increase the chance of success, data are needed regarding 1) the causal mechanism between the intervention ingredients and outcomes, 2) the interactions between the proposed intervention ingredients, and 3) how the context, i.e. the receiver (recipient) and provider (professional) interact with the intervention. Thus far, to our knowledge, none of the existing guidance systematically addresses the abovementioned elements in the development or design phase. However, there are few examples, such as the process evaluation guidance by Moore et al. (2015), describing various elements that should be considered when developing interventions, although this is seldom the case. Therefore, based on published reports and our own experience, we propose a comprehensive approach by combining the elements of the development phase of the MRC

Framework with elements of existing development models to enhance the intervention design, increase value and minimize the risk of subjects being exposed to ineffective interventions. This approach may facilitate researchers, research funders, and reviewers when developing a complex intervention in a broad domain of health care research. To illustrate the methodology that can be used within the development phase, we use published examples.

2. Methods

2.1. Design

a methodological approach consisting of reviewing the literature combined with using published examples and experience to enrich the MRC development phase to enhance the design of complex interventions. This approach was chosen to illustrate the different methodological approaches that can be used to address one element within the development phase of complex interventions.

2.2. Essential principles throughout the development process

When synthesizing existing guidance, a commonality of existing models is that they aim to systematically map the path from the recognition of a relevant need or problem to the identification of a therapeutic solution (Appendix A) (Craig et al., 2008; van Meijel et al., 2004; Whittemore and Grey, 2002; Wight et al., 2016; Conn et al., 2001b; Corry et al., 2013). Essential common principles is that the intervention should be evidence-based, have a strong conceptual basis or solid theoretical rationale, and match the individual needs, capacities, and preferences of both recipients and providers as well as fit into the context of routine practice (van Meijel et al., 2004; Bartholomew et al., 2011; Conn et al., 2001b). However, different models address distinctive elements and activities that contribute to enhancing the intervention development process. In Table 1, we outline the elements within the developmental phase of several existing development models.

An iterative development approach rather than a linear-stepwise approach has been recommended (Craig et al., 2008; Richards and Hallberg, 2015a), because of the reciprocal relation between the elements in the development phase. In this reflective approach, literature reviews as well as quantitative and qualitative research are considered to be of major importance to optimizing the prototype of the intervention design (Craig et al., 2008; Lewin et al., 2009; O’Cathain et al., 2014). During this iterative process, important feedback-loops can be incorporated and researchers are challenged to consistently seek answers to fill in the knowledge gaps within each element. Considering the sustainability of the intervention a priori, and the likelihood of adoption and implementation in daily practice is crucial in the development phase (Richards and Hallberg, 2015a). A user-centred approach consisting of an interdisciplinary team of researchers and experts together with recipients and providers may enhance the feasibility, efficacy, and effectiveness of the intervention. (van Meijel et al., 2004) Multiple stakeholders can be invited to participate in the development phase and consulting them frequently regarding the when, how, what, and why of the intervention can provide important information (Glasziou et al., 2010a). An example that covers these elements and is based on our experience is provided in Box 1.

2.3. Proposed elements added to the MRC development phase

The MRC Framework describes three, non-linear elements consisting of a systematic approach of ‘*identifying the existing evidence*’, ‘*identifying or developing theory*’, and ‘*modelling process and outcomes*’ in the development phase before proceeding to feasibility and piloting phase. These elements focus primarily on gathering the existing evidence for the proposed intervention using systematic reviews and

Table 1
Overview framework and guidance for intervention development.

Type of data Authors	Problem definition (identification & analysis)		Identifying the evidence		Identifying or developing theory		Determine the needs (recipients and/or providers)		Examine practice		Modelling process and outcomes		Intervention design	
	Literature, quantitative and qualitative studies	Literature reviews, <i>meta-analysis</i> , Individual patient data study	Literature Theory, conceptual model/ theoretical framework, qualitative studies	Literature quantitative, qualitative	Literature quantitative, qualitative, qualitative.	Literature, quantitative, qualitative.	Modelling work based on all available data sources. E.g. logic model	Modelling work leading to prototype that will be tested (feasibility, pilot)						
Craig et al. (2008)	NI ^a	Included	Included	NI	NI	Included	NI	NI	NI	NI	Included	NI	NI	
Conn et al. (2001b)	NI	Included	Included	NI	NI	NI	NI	NI	NI	NI	NI	Included	Included	
van Meijel et al. (2004)	Included	Included	NI	Included	Included	NI	NI	NI	NI	NI	NI	Included	Included	
Bartholomew et al. (2011)	NI	Included	Included	NI	NI	NI	NI	NI	NI	NI	NI	NI	NI	
Whittemore and Grey (2002)	Included	NI	NI	Included	Included	NI	Included	NI	NI	NI	Included	NI	NI	
Card et al. (2011)	NI	Included	Included	NI	NI	NI	Included	NI	NI	NI	Included	NI	NI	
De Silva et al. (2014)	NI	NI	Included	Included	Included	NI	NI	Included	NI	NI	NI	NI	NI	
Wight et al. (2016)	Included	Included	NI	NI	NI	NI	NI	NI	NI	NI	Included	NI	NI	

^a NI indicates: not included.

modelling the process and associated outcomes of the intervention before testing. A key task in this phase is to develop a theoretical understanding of the underlying processes of change (Craig et al., 2008). Based on our experience, we learned that conducting these steps is in most cases not enough to develop a state-of-the art intervention that has the highest likelihood of being effective in its specific context.

Information regarding the implementation context, the recipients, and the providers give essential information to optimize the intervention before proceeding to the next phase. Moreover, assessing the likelihood of the (cost-)effectiveness in advance may require a series of prospective studies to refine the intervention process and expected outcomes before performing a full-scale evaluation (Richards and Hallberg, 2015a). This is even more important, since ‘value for money’ is an important consideration, especially when resources are limited (Ioannidis, 2016). However, the expected added value of information is rarely analysed (Ioannidis et al., 2014). Therefore, determining whether conducting a trial is feasible and necessary and whether the costs are justified by the potential benefit of the obtained information should be considered (Soares et al., 2012a, 2012b).

Based on experience and the literature we therefore propose to add the following four elements to the MRC Framework development phase: ‘problem identification & definition’, ‘determination of recipients’ & providers’ needs’, ‘examination of current practice & context’, and ‘intervention design’ (Fig. 1). All these joint elements provide guidance to the systematic, iterative, and non-linear data collection regarding the context, the recipients, and the providers and thereby enhance the intervention design. Reviewing the literature may be necessary for each element and based on our experience we learned that it provides important information about how to proceed or whether additional data collection is needed. Hence, depending on the type of problem and the available evidence, one should decide which scientific efforts are needed within each element. Next, we more thoroughly describe all seven elements of the refined comprehensive development phase with published examples.

2.3.1. Starting point: problem identification & definition

Identifying and operationalizing the problem is an essential starting point (Aranda, 2008). An in-depth understanding of the problem, phenomenon or concern is important when developing an intervention (van Meijel et al., 2004; Conn et al., 2001b). It can be challenging to operationalize the exact nature and impact of the problem to obtain a clear picture regarding the situation as experienced by recipients and providers (van Meijel et al., 2004; Bartholomew et al., 2011). Identifying the current problem in a specific context and defining the desired situation is therefore essential and provides insights into the current gaps. The goal is to design an intervention that ‘solves’ or reduces the impact of the problem and to formulate appropriate intervention targets. Various methods and methodologies can be used to explore and define the exact problem. In particular, qualitative methods using in-depth interviews and focus groups are useful to analyse the specific nature of the problem, ascertain who is involved or affected by the problem, and how the problem is perceived from different perspectives (O’Cathain et al., 2014; Ludvigsen et al., 2013). A phenomenological approach might be useful to explore in-depth a problem. The perceptions of recipients and providers regarding the problem are highly important in this early stage and should not be underestimated. Other approaches that can be used to explore the problem are surveys, shadowing or participant observation (van Meijel et al., 2004). An example from our experience is provided in Box 2.

2.3.2. Identifying the evidence base

As proposed by the MRC, a thorough identification of the available evidence, ideally by systematic reviews or meta-analyses, must be conducted. The effectiveness of existing interventions targeting the identified problem, including contextual variations of the problem and the intervention, acceptability and feasibility of the intervention, and

Box 1

Developing with stakeholders: an example.

During the development of a proactive, multicomponent, community-based, nurse-led intervention to preserve daily functioning in older adults, a multidisciplinary team of older adults, nurses, general practitioners (GPs), researchers, and experts were involved from the beginning (Bleijenberg et al., 2013a). The research team consulted a group of older adults regularly regarding the content of the intervention and asked which geriatric conditions were most important to them. Evidence-based care plans were developed for these conditions that were considered relevant and were used by the nurses during the home visits. Geriatric experts as well as GPs and nurses, i.e. the providers, were consulted to validate these care plans. As a result, the intervention was perceived feasible in clinical practice by older adults and the providers (Bleijenberg et al., 2015, 2013b). The development of the intervention has been described in detail to enhance replication (Bleijenberg et al., 2013a).

mechanisms of interactions should be studied (Craig et al., 2008). This information provides answers regarding the potential effectiveness of the intervention (Petticrew et al., 2013). The goal is to identify what works, what works in whom, which assessments are valid and reliable, and what determinants are modifiable within the causal pathway. Several systematic literature reviews regarding various questions may therefore be conducted to reduce the chance of exposure to non-effective interventions or use of invalid outcome measurements (Richards and Hallberg, 2015a). Van Meijel et al. recommend identifying existing literature on similar interventions and methods to evaluate them (van Meijel et al., 2004). Each aspect of evidence that contributes to the design of the proposed intervention should be reviewed (van Meijel et al., 2004). However, critical appraisal of the methodological quality of the systematic reviews remain important since poorly prepared and conducted systematic reviews might present biased results and therefore, add to research waste (Roberts and Ker, 2015). The results of the various literature reviews can provide information regarding the effectiveness of existing interventions, contextual variation, relevant outcome measures, acceptability, feasibility, and mechanisms of action (Richards and Hallberg, 2015a). An example from our experience is described in Box 3.

2.3.3. Identifying or developing theory

The identification and development of theory that underpins the

proposed intervention is crucial; (Petticrew et al., 2013) however, the underlying theory is often not clearly described. Multiple theories may explain the proposed mechanism and actions within the causal chain. If a theory is lacking, defining one using a grounded theory approach might be crucial step to undertake. By understanding the causal mechanism, the key components of the intervention can be defined based on the knowledge gained from other elements in the development phase such as the systematic reviews. The rationale for the intervention, its components, and the expected outcomes are reflected by the identified modifiable determinants and requires an in-depth understanding of the causal mechanisms. For example, one may examine the relationship between the symptoms of a disease and the intervention that can lead to a desired clinical outcome, including the identification of moderating variables (Richards and Hallberg, 2015b). A theoretical framework provides information on how the possible intervention influences the causal chain. Furthermore, a theoretical method needs to be translated to practical applications, for example the translations of behaviour change methods into practical intervention elements that fit the intervention context and target population characteristics. When theoretical parameters are not properly translated into practice, the effectiveness of a method can be undermined or counter intuitive. For example, the International Classification of Functioning (ICF) framework is widely used (WHO, 2001). When this framework shows gaps, new theoretical ideas can be gained by conducting quantitative (i.e., cross-sectional,

Development Phase

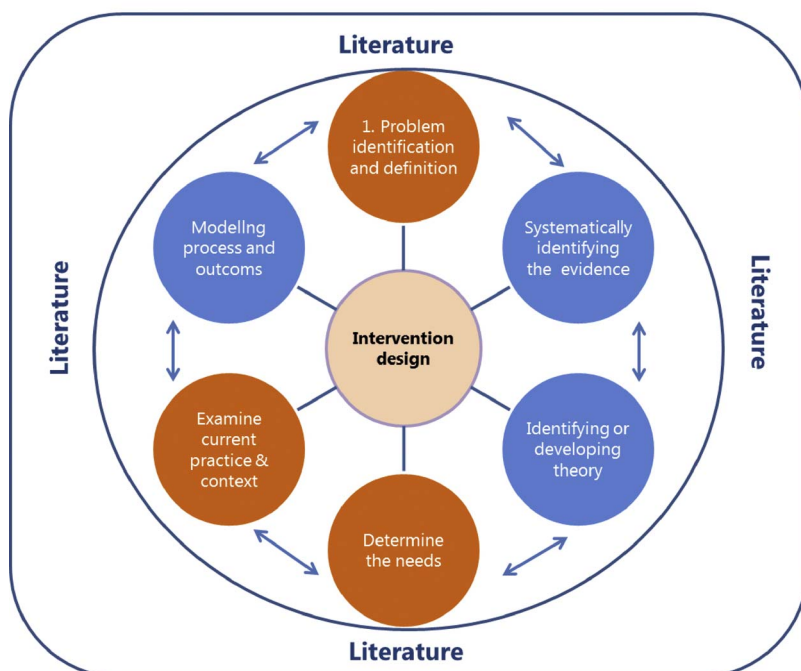


Fig. 1. Adapted MRC Development phase. Blue elements are from the original MRC Framework (Craig et al., 2008). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Box 2

Identifying the problem: an example.

A qualitative phenomenological study was conducted to explore and describe the experiences of eating and eating-related difficulties in stroke survivors living at home (Klinke et al., 2014). The study showed that eating difficulties may lead not only to serious consequences such as malnutrition but also to losses in the existential, social, and cultural lives of stroke survivors and that the ability to consume food and taking pleasure in eating are essential parts of life (Klinke et al., 2014). The authors argued that the long-term losses people experience in existential, social, and cultural life are not reflected in conventional screening tools and interventions. This information is valuable for strategies and interventions within early-stage rehabilitation intervention programmes.

prospective cohort) or qualitative studies explaining how the (individual) intervention components may lead to the desired outcome parameters. The results contribute to better elucidate on the possible causal mechanism. Howick et al. (2009) described an approach to reconsider several factors before concluding causation based on a re-examination of the Bradford Hill criteria of evidence: *direct, mechanistic and parallel* (Howick et al., 2009). This revised guideline can be helpful for researchers when RCTs are unfeasible (Howick et al., 2009). Another example is provided in Box 4.

2.3.4. Determine the needs

A thorough understanding of the needs, perceptions, preferences, and capacities of the recipients as well as the providers is a fundamental element that needs to be incorporated in the development process. The ultimate goal is to develop a (cost-)effective intervention that addresses a (clinical) problem, is highly feasible, can be replicated, and fulfils the needs of its users. Therefore, investigating the (care) needs and perceptions of the recipients and providers regarding the identified problem, on the one hand, and the preferences and capacities with regard to the proposed solution, on the other hand, is crucial. It provides important information about which parts of an intervention are most likely to be adopted, e.g., due to preferences and capacities, and how the proposed intervention can be tailored regarding content, dose, and intensity. Exploring the needs from multiple perspectives to increase external validity can be particularly valuable since the effectiveness of the intervention is determined by the extent to which the needs, perceptions, preferences, and capacities of recipients and providers are taken into account (van Meijel et al., 2004). For example, qualitative methods using for example a phenomenological or grounded theory approach are valuable for exploring the complex, often interrelated, diversity of needs, perceptions, preferences, and capacities to better understand the individual barriers and needs (Ludvigsen et al., 2013). An example based on our experience is provided in Box 5.

2.3.5. Examine practice

To optimize the successful delivery of an intervention within its context, identifying the existing intervention practice is extremely valuable during the development process (van Meijel et al., 2004). It aims to thoroughly explore the context in which the intervention will be implemented by identifying barriers and facilitators regarding the

Box 3

Identifying the evidence-base: two examples.

In a systematic review, information regarding possible non-pharmacological interventions for post-stroke depression patients was described (Man-van Ginkel et al., 2010). The authors explored the role of nurses within these interventions and learned which type of intervention components (e.g., information provision, motivational interviewing, or physical exercise) reduced the occurrence or severity of depressive symptoms (Man-van Ginkel et al., 2010). Another example comes from an individual patient data (IPD) analysis that examined the effectiveness of self-management interventions in heart failure (HF) patients and whether subgroups of patients responded differently (Jonkman et al., 2016). The authors included 21 studies representing 5624 patients and found beneficial effects of self-management interventions on time to HF-related hospitalization or all-cause mortality, hospitalization alone, and improvement in HF-related quality of life. While the findings did not advocate limiting the intervention to specific subgroups, a different intervention approach should be considered among depressed patients due to the increased mortality in this group (Jonkman et al., 2016).

proposed intervention among recipients and providers to enhance the workability of the intervention that closely fits the current practice (Moore et al., 2015). Careful identification of the implementation route and estimations of the impact on recipients and providers are needed. Both interviews and focus groups with recipients and providers can be conducted using a grounded theory approach. Evidence, documents (i.e., grey literature), guidelines, policy documents, and national registries can provide important knowledge to understand the context in which the intervention will be executed and financed. Considerations regarding timing, dose, and intensity, e.g., how, what, when, were, and by whom the intervention is used, (Glasziou et al., 2010b) are crucial. Additionally, important information can be obtained regarding the required competences of providers (whom) and how they should be trained or prepared in delivering the intervention (Conn et al., 2008). The question ‘what needs to be done to implement a new intervention?’ might be answered with a theoretical model. For example, the Normalization Process Theory (NPT) can help to understand implementation of complex interventions because it focuses on action rather than attitudes (May et al., 2009; May, 2013). Understanding the dynamics of the implementation context and gaining insight into how the intervention will be operationalized in practice is needed, (May, 2013), especially when developing the intervention. Box 6 provides an example from our work of how investigating current practice affects the intervention design.

2.3.6. Modelling process and outcomes

In this element, we can start modelling the active components of the intervention by synthesizing the knowledge gathered from the previous elements. Ideally, cumulative evidence from the previous elements provides insight into the modifiable determinants that influence the pathway, the extent to which these determinants are susceptible for change, and the strength of the association between the determinants and outcome. Modelling the prototype of the intervention within a multidisciplinary team including the recipients and/or providers is a complex process that is likely to increase the applicability of the intervention in practice (Hardeman et al., 2005). A modelling approach provides a rational guide to appropriate measures, intervention points and intervention techniques, and can be tested quantitatively (Hardeman et al., 2005). A useful method is a logic model to synthesize and describe the complex pathways within the intervention (Baxter

Box 4

Developing a theory: an example.

The following example is a qualitative study by Ockhuysen et al. (2014) aimed at generating a theory to better understand the likely process of change (Ockhuijsen et al., 2014). The authors tested the applicability of the existing coping theory from Folkman & Lazarus (1988) among 24 women during a waiting period after IVF and early pregnancy. The women were interviewed during a subsequent pregnancy after having a miscarriage to gain insight into the emotions and coping strategies during miscarriage, conception, and early pregnancy waiting period [49]. Three themes and one overarching theme were identified: 1) “Facing loss during the miscarriage period”, 2) “Dealing with waiting during the conception period” and 3) “Handling mixed emotions during the pregnancy period”. The overarching theme “balancing between loss of control and searching for control” relates the themes of the miscarriage, conception, and pregnancy period. Although the women realized they lost control and that there was little they could do to influence the outcome of their efforts, they searched for strategies to increase the feeling of control. The authors concluded that these results are valuable for developing or refining existing interventions to support women undergoing IVF during the conception, miscarriage, and pregnancy periods (Ockhuijsen et al., 2014).

Box 5

Determine the needs: an example.

A systematic review was conducted to determine barriers and motivators of adherence to prophylactic treatment in haemophilia (Schrijvers et al., 2013). The authors concluded that determinants of adherence to prophylaxis were age, symptoms, beliefs, and the relationship with the health care provider and that this information is a valuable first step towards a tailored adherence intervention (Schrijvers et al., 2013). Next, the researchers developed a grounded theory using a qualitative study to unravel adherence from a recipient’s perspective, and found that adherence was determined by the position of prophylaxis in life. Four main positions emerged that will be used to design a tailored intervention to promote adherence (Schrijvers et al., 2015). The example shows that the literature review combined with careful mapping of patients’ perspectives provided insights that strengthened the tailoring of the intervention and thus the chances of success.

Box 6

Examine practice: an example.

In testing the PREDOCS programme in a mixed-methods multicentre study on its feasibility, data from interviews and the continuous data registry at three hospitals were used. Results showed that only 70 of the 114 eligible patients completed the intervention and provided full data. Although the patients were equally satisfied with the usual care and the PREDOCS programme and the involved nurses were satisfied with the tools for guiding patients to reduce their risk of postoperative complications and considered the PREDOCS programme as complementary to usual care, integrating the PREDOCS programme into current hospital structures appeared to be difficult. Both patients and nurses indicated that the additional consult was tiresome for the patient. The researchers subsequently concluded that the PREDOCS programme was feasible to use in clinical practice but, should be built into the hospital’s cardiac surgery pathway or applied in home care, which should have been taken into account in the development phase (Hardeman et al., 2005).

Box 7

Modelling process and outcomes: an example.

An example of logic modelling is provided in the systematic review exploring factors affecting the implementation of Lay Health Workers (LHW) programmes for maternal and child health (Glenton et al., 2013). LHW perform functions related to health care delivery, have no formal professional or paraprofessional certificate of tertiary degree and received some level of training. A synthesis of qualitative evidence was carried out alongside the Cochrane review of the effectiveness of LHWs for maternal and child health. The findings were integrated in a logic model that enabled researchers to identify hypotheses for subgroup analyses (Glenton et al., 2013).

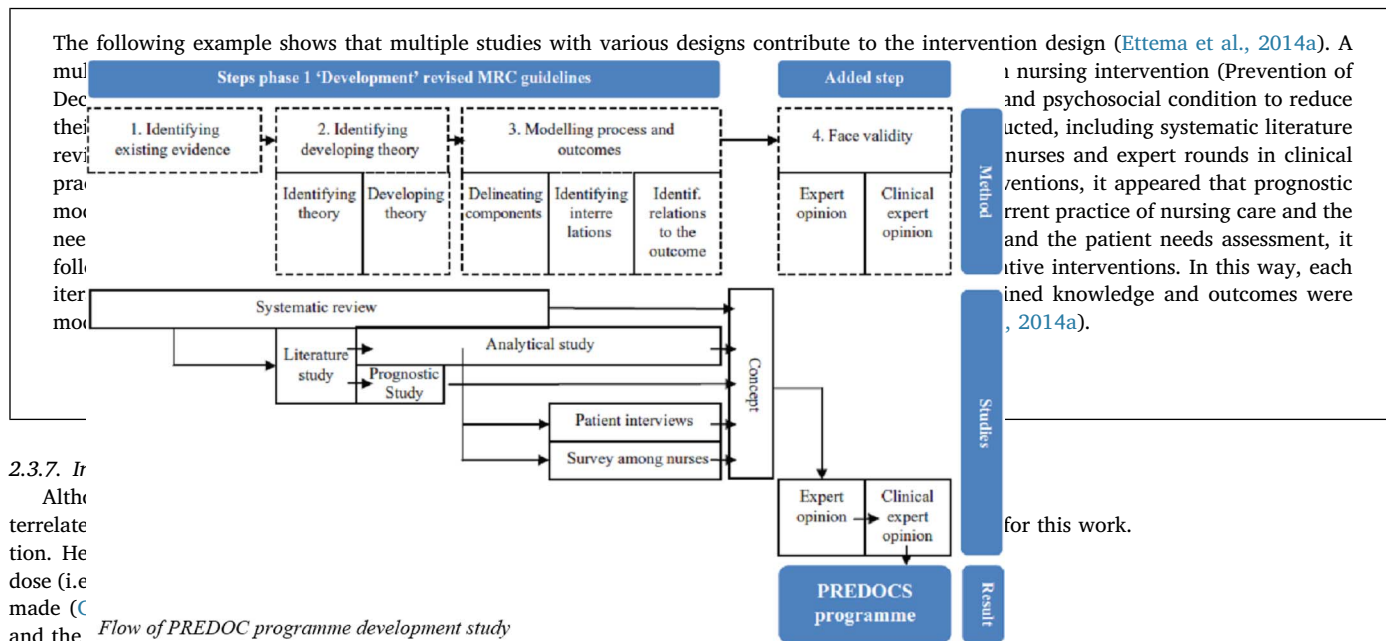
et al., 2014). A logic model can help clarify causal assumptions by depicting the intervention. It illustrates the chain of reasoning underpinning how interventions lead to immediate (or short term) and long-term outcomes and impacts (Baxter et al., 2014). There is no uniform template for developing logic models, although the most common approach involves identifying a logical flow that starts with specific planned input and activities and ends with specific outcomes or impacts, often with short-term and intermediate outcomes (Box 7) (Glenton et al., 2013).

Prioritizing, reducing, selecting, and refining the components and ingredients are important in this element. The goal is seeking the delicate balance between the most optimal ingredients, components, and

costs to achieve maximum (treatment) success, on the one hand, and the best fit with current practice and the context on the other. Various approaches can be used to better understand the black-box of the intervention, why it works, and how it works. Conceptual or theoretical models are used to develop, understand, and stimulate complex interventions (Sermeus, 2015). Descriptive or graphical methods can be used to synthesize the large amount of information and to visualize the design of a system, ‘the big picture’. Mind maps, flowcharts, activity diagrams, process diagrams, and network diagrams can be helpful to structure the information and unravel the modifiable determinants and successful components (Sermeus, 2015).

Box 8

Designing the intervention: an example.



2.3.7. It

Although... relate... tion. He... dose (i.e... made (C... and the

Flow of PREDOC programme development study

provider. An example from our work is provided in Box 8. While details regarding the choices made during the development process of complex interventions are seldom reported, this is highly important to be able to understand the success of the intervention and to enable replication. After careful design and piloting of a complex intervention, estimates regarding the (cost-) effectiveness and value for money can be made. Based on these aspects, the decision can be made to evaluate and implement the intervention in.

3. Conclusion

Improving the development of complex interventions will reduce research waste and enhance the likelihood of success. Based on the literature we propose a comprehensive approach by combining the elements of the MRC development phase with elements of existing development models to enhance the intervention design. The included elements of problem identification, systematic identification of evidence and theory, determination of needs, examination of current practice modelling process and outcomes resulting in the intervention design gives developers a better chance of producing an intervention that is well-adopted, fits its context, is effective and ready for piloting and trialling.

Investing in the development phase of complex interventions is costly and time consuming; however, it is an opportunity to improve the intervention that cannot be skipped before executing a full trial. Reconsidering the investments made in the different phases of the development and testing of complex interventions adds to the value of science for practice. Maximum effort is needed from researchers, research funders, and reviewers in this task to reduce research waste, add value, and enhance the effectiveness of the intervention's implementation (Ioannidis et al., 2014; Glasziou et al., 2010a).

Authors' contributions

NB, JM, JT and MS initiated the project. NB, RE, CS, NH, DR, TH, JM, JT and MS were involved in the discussion and critically revised the manuscript for intellectual content. All authors read the final draft of this manuscript and approve its submission for publication.

The following example shows that multiple studies with various designs contribute to the intervention design (Ettema et al., 2014a). A nursing intervention (Prevention of and psychosocial condition to reduce...), including systematic literature reviews, it appeared that prognostic... current practice of nursing care and the... and the patient needs assessment, it... tive interventions. In this way, each... ined knowledge and outcomes were... (2014a).

for this work.

Availability of data and materials

No additional data are available.

Competing interest

The authors declare that they have no competing interests.

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Appendix A. Supplementary data

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