

Development of a complex intervention in diabetes care to reduce the rate of clinical inertia following the Medical Research Council Framework: Clustered Randomized Trial Study Protocol.

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ABSTRACT

Background: This paper outlines the development of a study protocol of a complex intervention in diabetes care that aims at the improvement of adherence to evidence-based guidelines and a reduction of the rate of clinical inertia in primary care physicians.

Methods: The Medical Research Council (MRC) framework for the development and evaluation of complex interventions for randomized control trials (RCT) was used as a theoretical guide to designing the intervention. The Preclinical Phase included a review of the literature relating to diversity in diabetes care programs and stakeholder interviews. In the Modeling Phase program development was carried out by a multidisciplinary group of health care professionals to delineate the components of the complex intervention and the underlying mechanisms by which they influence the outcomes. In the Randomized Controlled Trial Phase a trial will be implemented to test the effectiveness of a two-arm quality improvement program in diabetes care in a primary care setting in Belgium. Outcome measures include the proportion of patients reaching the ADA-targets for three outcomes: HbA1c <7%, SBD \leq 130 mm Hg and LDL-C <100mg/dl. Secondary endpoints are constituted by the individual improvement of 12 validated parameters. The proportion of patients in every respective intervention arm who have made use of the Diabetes Care Team defines tertiary outcomes.

Results: In the Preclinical Phase a total of 21 systematic reviews were included in the review that represented a total of 185 diabetes care programs. This review led to an overview of best choice of interventions and indicators, selection of the conceptual model, major confounders and strategic design issues. The stakeholder interviews provided an overview of barriers to high quality diabetes care at the health system, the individual provider and patient level of care. The Modeling Phase resulted in a choice of best achievable

combination of intervention components and the identification of feasible and valid measures of outcomes.

Conclusion: The MRC Framework was instrumental in the development of our complex intervention in diabetes care, but it provides a methodological rather than an explanatory approach to evaluating complex interventions.

BACKGROUND

Diabetes management is a complex process requiring intervention at multiple levels (physiological, psychological and social)[1,2]. Although there is considerable evidence to support the use of pharmacological interventions in aspects of diabetes care[3,4], the best way to intervene to improve health outcomes using nonpharmacological 'complex interventions' is often unclear[5]. A growing number of complex interventions equally target improvements in patient, provider and organisational aspects of care[6]. The active components of these complex interventions all seem essential to their proper functioning and may act both independently and interdependently[7]. A conceptual model that is often used to underpin complex interventions in diabetes care is the Chronic Care Model (CCM)[8,9]. According to the Chronic Care Model (CCM), patient outcomes such as good control of risk factors should be associated with the presence of one or more interrelated components (community resources, self-management support, delivery system redesign, decision support, clinical information systems and organizational support) [8]. Despite the usefulness of the CCM to conceptualize a path to better care for people with diabetes, studies that apply CCM elements often fail to provide useful information on the 'active ingredient' of the intervention that is effective[7,10]. The latter is also referred to as 'program differentiation' indicating which elements of programs are essential, without which the program will not have its intended effect[11]. In this context, study protocols of complex intervention studies in diabetes care have often been criticized as a substantial number amongst them do not provide sufficient specifications on important features of the program such as the study population, the quality improvement interventions, the frequency/intensity of intervention activities, the implementers or change agents and features of the information imparted[10,12-16]. In case of a negative result it is sometimes not clear whether the intervention was inadequately developed (a so-called Type III error)[12,17] or applied in an inappropriate context. Other reasons for negative results of studies are sometimes related to

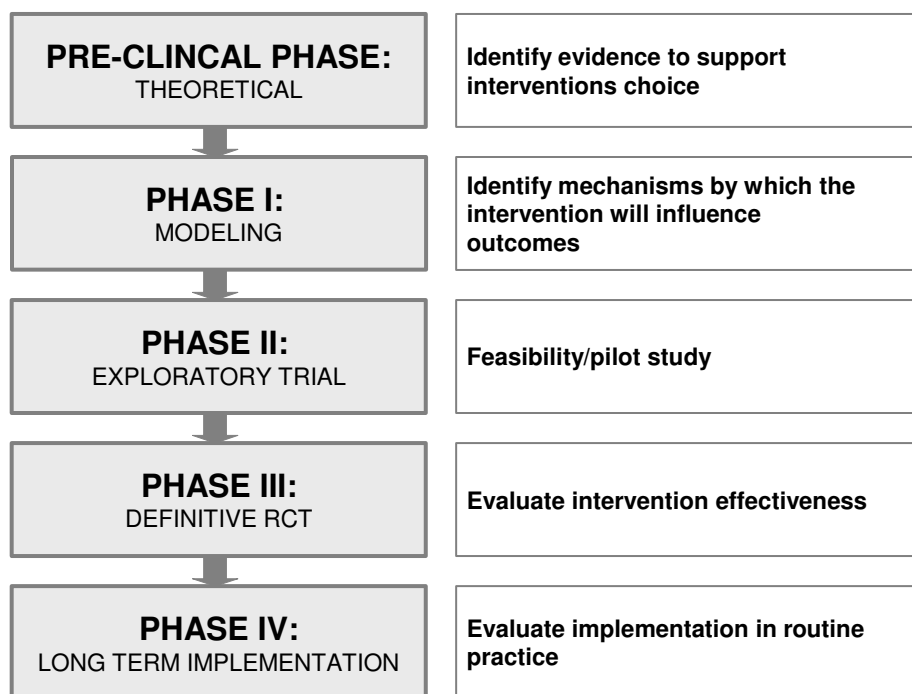
the use of an inappropriate design, comparison groups or outcomes. In case of a positive effect it can be hard to judge how the results of the trial might be applied to a different context[18]. For the aforementioned reasons, the careful modeling of complex interventions at an early stage in the development of hypothesis and in the design of projects is increasingly advocated[16,19,20]. A number of models exist to assist in developing and evaluating of complex interventions with the aim of improving intervention quality[21-24]. The UK Medical Research Council[6] (MRC) Framework outlines five key phases for intervention development in randomized controlled trials for complex interventions. It also recognizes that the organizational and technical processes of implementing and delivering a complex intervention require attention and understanding, and that these should also be a focus of evaluation[25]. The Framework does not prescribe specific research methods to be used in intervention development but does recommend specific questions to be addressed in each phase in order to ensure that studies are well designed[26]. Although previous studies have started to use this Framework to guide the development of complex interventions in primary care[16,25,27-31] and diabetes care in particular[32,33], this paper is to our knowledge the first to describe the use of the MRC framework for the development of a quality improvement program in diabetes care aiming at the improvement of adherence to evidence-based guidelines and a reduction of the rate of clinical inertia in primary care physicians.

METHODS

The study protocol of the Diabetes Project Leuven is based on the MRC framework as it allows for the development of a high quality study design, execution and generalizability of the results. Although our project is not set up as a controlled trial, but as an open pragmatic before/after study with cluster randomization, we find it useful to outline our study protocol according to the MRC framework since it includes sequential stages of a continuum of

increasing qualitative and quantitative evidence of complex interventions. Stages refer to a preclinical/theoretical phase, a modeling phase, a phase of exploratory trials prior to the randomized controlled trial and the phase of long-term implementation[18]. All phases, except Phase 3 (Exploratory Trial Phase) and Phase 4 (Long-term Implementation Phase) are examined in-depth. A schematic overview of the different phases of the MRC Framework is presented in Figure 1.

Figure 1: Phases of the MRC Framework for developing complex interventions



Below we outline the content of every respective phase of the MRC Framework. A detailed overview is also provided in table 1.

- **Preclinical phase of the MRC framework**

According to the preclinical or theoretical phase of the MRC framework, relevant theory and evidence was explored to ensure best choice of underlying hypotheses, conceptual model, interventions and indicators. For this purpose a review of systematic reviews was

conducted[34]. A total of 21 systematic reviews (1989-2006) were included in the review that represented a total of 185 diabetes care programs. Conceptual backgrounds, goals, settings, type of programs, type and number of interventions, type and number of indicators and (cost) effectiveness were evaluated in both the 21 systematic reviews and the individual diabetes care programs.

Besides the exploration of relevant theory and evidence, the local context in terms of existing national/regional governmental policies, characteristics of the region and perceived barriers to high quality diabetes care were extensively studied with regard to their impact on the content and execution of the study protocol. For this purpose stakeholder interviews were organised including a representative group of 18 thought leaders and experts in diabetes care[35].

- **Modeling phase of the MRC framework**

In the modeling phase we delineated the components of our complex intervention and the underlying mechanisms by which they influence the outcomes. We tried to understand the pathways by which the problem is caused and sustained, including all barriers to high quality diabetes care. We also explored whether the pathways were amenable to change, and if so, at which points. In this context, the potential for improvement in both process and primary outcomes was estimated. The aforementioned actions resulted in a choice of best achievable combination of intervention components, implementation strategies and intensities of care delivery as well as the identification of feasible and valid measures of outcomes.

Conceptual background

The program is built on principles of integrated care. As there is no unambiguous definition of integrated care at this stage, we have further build on the definitions of Ellrodt and colleagues[36], Mur-Veeman and colleagues[37] and the Disease Management Association of America (DMAA) [38]. We consider integrated care as 'an organizational process of

continuous coordination of evidence-based and relevant interventions across the entire health care delivery system and care continuum that seeks to maximize quality of care tailored to the needs of every individual patient while minimizing costs'. Literature on integrated diabetes care programs provides a growing body of evidence with regard to the effectiveness of such programs on patient and process outcomes of care[39]. These programs mostly cover a few, and more in particular those dimensions of the Chronic Care Model for which there exists substantial evidence that they will improve care for individuals with diabetes. Typical examples of such interventions are clinician education and dissemination of guidelines[40,41], feed-back on performance[42], patient education[43,44], care management [45,46] and diabetes care teams to support primary care physicians[47-49]. These interventions have also proven their effectiveness to improve adherence to guidelines and to reduce 'clinical inertia' [50-52]. This is particularly important in the management of chronic disease where patients are surveilled on an ongoing basis and specific values for elevated blood glucose, blood lipids and blood pressure are used that trigger for changes in treatment. Clinical inertia is defined as a lack of treatment initiation or intensification in a patient not at evidence-based goals of care[53]. Failure to intensify therapy in these patients fits the definition of medical errors given by the Institute of Medicine[54,55]. Clinical inertia will inexorably lead to adverse events in a high proportion of patients, but it may take years for the consequent adverse event to declare itself[56]. Numerous authors, including those who report on clinical inertia, have defined three principal sources for non-adherence to evidence-based guidelines and clinical inertia including; 1) physician factors, 2) patient factors and 3) office system and organizational factors [57-59]. Physician factors that contribute to clinical inertia are e.g. an overestimation of care actually delivered, a failure to identify and manage comorbid conditions, disagreement with evidence-based goals of care and the use of "soft reasons" to avoid intensification of therapy (e.g., patient refusal)[60,61]. Patient factors that contribute to clinical inertia are limited motivation or resistance to adopting lifestyles that support optimal

disease care, which stresses the importance of patient empowerment as a cornerstone to high quality diabetes[62,63]. Office system and organizational factors that contribute to clinical inertia are e.g. a lack decision support and a team approach to care. These three sources interact in complex ways and interventions to reduce clinical inertia therefore need to be multifactorial in nature.

An overall goal of our program is to improve adherence to evidence-based guidelines and more in particular to reduce the rate of clinical inertia in primary care physicians and, in this context, to improve the management of glycemic control and cardio-vascular risk factors in persons with diabetes.

In a first intervention arm a set of 'usual' quality improvement interventions (UQIP) will be implemented with the aim to improve adherence to evidence-based guidelines and to reduce the rate of clinical inertia in primary care physicians (PCP's). The term 'usual' is applied since these interventions address the principal factors contributing to clinical inertia (physician, patient and office system factors) and represent standard requirements for what is considered quality of diabetes care in most health care systems according to international clinical guidelines [64] and theoretical frameworks on quality of diabetes care in particular [65]. The first intervention arm is innovative to the Belgian healthcare system and adds to available insights from international literature on how to address clinical inertia in diabetes care.

In addition to interventions as defined in the UQIP, PCP's and their patients of the second intervention arm will receive supplementary and more experimental interventions that we refer to as 'advanced' quality improvement interventions. The interventions of this Advanced Quality Improvement Program (AQIP) aim at improvements in adherence to evidence-based guidelines and a reduction of the rate of clinical inertia in PCP's by means of an extended focus on behavior changes in patients and providers. Interventions that focus on the patient aim at a more active involvement of the patient in his/her treatment regimen with a special focus on lifestyle attitude changes. For this purpose the AQIP offers supportive tools,

patient-oriented actions including e.g. structured educational materials and group sessions and the availability of both nurse educators at home/in the PCP practice and a health psychologist. It is expected that improvements in “patient empowerment” will lead to greater reduction in the rate of clinical inertia by increasing the patient’s willingness to intensify his/her treatment[66,67]. Interventions that target the provider (PCP’s) focus on improvements in communication patterns with patients, interdisciplinary shared care and the involvement of PCP’s in community campaigns. For this purpose CME and peer review sessions based on the Transtheoretical Model of Change[68] will be organized. Further on, PCP’s will receive feedback including summaries of clinical performance of diabetes care delivered to individual patients and active reminders to implement a shared care protocol recommending referral of patients in case treatment targets are not reached. Finally, PCP’s will be invited to participate in community campaigns that focus on lifestyle changes such as smoking cessation and physical exercise. By this multiple focus on patient, provider and organisational aspects of care our quality improvement program is fully in line with the latest insights and findings on what is considered high quality chronic care, and high quality diabetes care in particular[9,10,48,69-75]. The differences between the AQIP and the UQIP will now be further outlined below. A detailed overview is provided in table 2.

Advanced Quality Improvement Program (AQIP) versus Usual Quality Improvement Program (UQIP)

To operationalize all six dimensions of the CCM we made use of two classification schemes. Quality improvement interventions that are linked to the different dimensions of the CCM were chosen from the classification scheme from Shojania and colleagues[76] who defined eleven distinct categories of quality improvement interventions adapted from the Cochrane Effective Practice and Organization Of Care (EPOC) group[77]. These categories are: patient education, promotion of self-management, clinician education, audit and feed-back, case

management, team changes, electronic patient registry, clinician reminders, facilitated relay of clinical information to clinicians, patient reminder systems and continuous quality improvement. Five interventions were not included in the service program as they are either integrated in other interventions of the program (patient reminder system is integrated with physician reminder system) or because of reasons of complexity in the Belgian primary health care system (case management, audit, electronic patient registry and facilitated relay of clinical information to clinicians). The different implementation strategies that were used were derived from an overview by Grol and Wensing[78] who have summarized thirteen important theories and models related to the implementation of change to improve diabetes care, including important factors and lessons for improving diabetes care. These theories/models relate to individual professionals/patients, the social context and the organizational and economic context.

Two separate groups are randomly defined. The first group receives an advanced quality improvement program (AQIP-program) whereas a second group receives a usual quality improvement program (UQIP-program). Physicians can make use of the services of the programs on a voluntary basis.

LEVEL I: PATIENT

- Patient education/promotion of self-management

Both patients in the AQIP and UQIP-program can be referred by their primary care physician to a Diabetes Care Team (DCT) to receive a medical assessment by an internist as well as to receive patient education, dietary advice and examinations with an ophthalmologist. This core membership of internists, nurse educators, dieticians and an ophthalmologist reflects the basic requirements of diabetes treatment: nutrition, medication, self-monitoring, self-management and the management of risk factors[79]. Physicians from both the AQIP en UQIP program can rely on internists/diabetologist for advice on complex patient cases, with or without referral of the patient. Educational services and promotion of self-management to

patients of the AQIP and UQIP program are only provided upon referral of the physician. Nurse educators have followed a post-graduate one-year training program on diabetes nursing care. The nurse educator applies individual patient counseling, didactic goal setting and situational problem solving as key educational methods to patients of the AQIP-program, whereas patients from the UQIP-program receive services close to regular care, i.e. individual patient counseling. Physicians from both the AQIP en UQIP program can consult dieticians for complementary dietary advice or can refer their patients to discuss information on meal algorithms, dietary strategies and tailoring food intake to meet patients' lifestyle, motivation and specific needs[79]. Education on lifestyle changes, identification of barriers to diabetes self-management and stress management will be provided by a health psychologist to patients of the AQIP-program, and after referral of the physician.

Additional services including group educational sessions for both patients and relatives, education at home or at the physician's practice (provided by a flying educator), structured and printed educational materials from the DCT and community organizations, and free tools for self-monitoring of blood glucose levels are reserved to patients of the AQIP.

LEVEL II: PROFESSIONAL

- Clinician education

Interventions for clinician education comprise the promotion of an increased understanding of principles guiding clinical care or awareness of specific recommendations for the patient population by means of a treatment and shared care protocol as well as four post-graduate educational sessions. During a first session at the start of the project physicians will be trained on the use of evidence-based guidelines and the principles of shared care. A second and a third session will focus on the use of insulin and patient-centered counseling. A fourth session will be set up as a peer review session. Educational messages are delivered, for most part, by a locally well-known diabetologist ('opinion leader') using techniques of group academic detailing[80]. The provision of clinical leadership from secondary care is

considered highly important for primary care physicians working in an unstructured and thus non-integrated health care environment.

Only the first two types of sessions are offered to physicians of the UQIP program, whereas physicians from the AQIP program will be invited to participate at all sessions. Physicians from the AQIP program will also receive extended educational materials. Both physicians from the AQIP and UQIP receive accreditation points for their participation at the educational sessions.

- **Feed-back**

Feed-back interventions, provided by a program manager to the physicians, will include both summaries of clinical performance of diabetes care delivered to individual patients over a three-month period and benchmarking feed-back (for physicians from the AQIP program). Physicians from the UQIP program will only receive benchmarking feed-back at the start and at the end of the project.

Feed-back includes percentage of a physician's individual patients who achieve target levels for glycosylated haemoglobin (HbA1c), LDL, total cholesterol and triglycerides, systolic/diastolic blood pressure, eye and foot examination, aspirin and statine prescription, anti-hypertensive medication, smoking status and weight loss.

- **Clinician reminders**

Clinician reminders for physicians of the AQIP program are combined with the provision of three-monthly feed-back by the program manager and reminders to make use of the DCT in case treatment targets are not met. Physicians are asked to remind their patients about upcoming appointments. Patients in their turn are asked by the physicians to make use of a diabetes passport in which the appointments are noted down together with important treatment results. Physicians of the UQIP program do not receive clinician/patient reminders nor do they receive reminders on the use of the DCT.

LEVEL III: ORGANISATIONAL

- Team changes

Team changes are operationalized in three separate ways. At first, a Diabetes Care Team (DCT) will be actively installed at two locations in primary care facilities that are run by primary care physicians. The DCT's will be intensively supervised by a diabetologist from the academic hospital in the project region who provides clinical leadership to the team. All DCT members will receive a 60 hours in-house training program on the use of a shared care protocol, communication skills and team dynamics. Key elements of the interdisciplinary team include shared leadership with common goals, shared professional identity, and collaborative, rather than consultative, relationships among members[81]. Team members are expected to engage and learn from each other and to attend scheduled meetings. An experienced counselor and a member of the academic project team will provide the training program. The DCT's operate in support of the primary care physicians and actively promote referral towards physicians of the AQIP in case the treatment targets are not met[82]. Bi-weekly interdisciplinary meetings will be organized between the members of the Diabetes Care Team who can invite individual physicians from the AQIP program in case of complex patient conditions.

Nurse educators, dieticians and the health psychologist will meet their colleagues from a university hospital-based diabetes team and the supervising diabetologist on a three-monthly basis to exchange experiences and to discuss complex patient cases. Internists will meet the supervising diabetologist on a two-monthly basis to discuss individual patient cases.

Structured and extensive reports will be provided by members of the DCT to the physicians of the AQIP program since primary care physicians rank standardized, structured correspondence very high[83,84]. Physicians of the UQIP program will only receive standard communication forms.

A second way in which team changes will be realized is through the active promotion of a diabetes program manager who operates as the central point of referral to the physicians. The program manager will be selected for the project based on the following criteria: strong interpersonal communication skills, the ability to create trust, knowledge of diabetes and organizational capabilities. The program manager will provide physicians from the AQIP program with extended (logistic) support. These services include physician reminders, the provision of feed-back, liaison activities between the DCT and the physicians, the organization of group educational sessions and responses to questions on the study or diabetes related topics. A logistic support service that is accessible for both physicians of the AQIP and UQIP program is a project website.

A third way in which team changes will be operationalized is through the involvement of independent pharmacists in the study. Pharmacists are asked to provide the physicians of the AQIP program with medication schemes of their patients upon request. As such pharmacists can play a more active role in patient monitoring or adjusting medication regimens[85-87].

- **Continuous quality improvement**

Continuous quality improvement will be assured by an iterative process for assessing quality problems in the implementation of the project, developing solutions to those problems, testing their impacts, and then reassessing the need for further action. For this purpose an Interdisciplinary Quality Assurance Team will be established including a diabetologist, four primary care physicians, two nurses, internists, dieticians and pharmacists. The Quality Assurance Team will be asked to monitor the implementation of the project as well as the evaluation of outcome indicators of the project. Meetings will be organized on a regular basis with individual members of the Quality Assurance Team.

- **Randomized Controlled trial phase of the MRC Framework**

Aims

The aim of the study is to evaluate the effectiveness of a two-arm intervention quality improvement program (AQIP and UQIP) on process and outcome indicators in diabetes care. Three hypotheses were developed following our background reading. A first hypothesis is that an advanced quality improvement program (AQIP) significantly improves clinical outcomes in persons with type 2 diabetes compared to a usual quality improvement program (UQIP). The second hypothesis is that persons with type 2 diabetes who make use of a Diabetes Care Team (DCT) have significant better patient related outcomes compared to non-users of the DCT. A third hypothesis is that primary care physicians who participate in the AQIP implementation program have better process outcomes compared to physicians who participate in the UQIP.

Program development was carried out by a multidisciplinary group of health care professionals including primary care physicians as well as academic experts in diabetes care, family medicine, implementation strategies, program management and members of the scientific project team. The early involvement of and collaboration with primary care physicians was considered important since it has shown to enhance the development of interventions targeted to their needs[88].

Design

The study is an open pragmatic cluster randomized trial with before/after measuring. A 'clustered' design is necessary since randomization is performed on practice level, the intervention happens on physician level, but a large part of the data are analyzed at the patient level. The implementation period of the trial is 18 months. All 379 primary care physicians (PCP's) that actively execute their profession in the project region are invited to participate. These PCP's work in a semi-rural setting with 357.000 inhabitants in Belgium

and predominantly serve Caucasian patients with diabetes mellitus type 2. Primary care physicians provide care for approximately 80% of patients with type 2 diabetes, and are often the sole providers of care. The only inclusion criterion for the providers is the agreement to bring in all their known patients with type 2 diabetes mellitus. Diabetes is defined in accordance to the 2003 ADA criteria[89].

After the recruitment period, using computer-generated numbers, a researcher not involved the study and blind to the identity of the practices will perform a randomization stratified by practice size (solo/duo/group practice) and the presence/absence of an electronic medical recording system. The financier to the project imposes a sample size of minimal one third of the potential PCP's. Using the calculator of the university of Aberdeen, sample size for cluster trials was computed[90]. This study size gives a 80% power (type II error: 0.20) to detect a 20% of relative difference between the intervention arm I and II in the proportion of patients achieving a 10% improvement in any one of the following: blood pressure, total cholesterol, or HbA1c (type I error: 0.05; assumed Intra Cluster Coefficient 0.6). No blinding is possible at physician level, but patients don't know to which intervention arm their physician belongs.

Patient identification and data collection

In order to avoid patient selection bias, physicians must bring in all their patients with type 2 diabetes mellitus. In addition, participants will be asked to screen more systematically for new type 2 diabetes mellitus patients during 7 months after the start of the registration period. Practices have no pre-existing registers. Patients with type 2 diabetes mellitus will be identified using physician's memory, electronic searching in computerized records and laboratory lists of patients with increased glycaemia or registered glycated haemoglobin. The final decision about the diagnosis of type 2 diabetes of each individual is let to the physician. Baseline data will be collected over a seven-month period. Physicians will be asked to perform a complete examination including a blood analysis at patient's first visit during the

registration period in order to fill in a paper form. Identified patients without a visit during the three first months will be invited to present themselves. The completeness of data capture will be double-checked by a data monitor. Final data will be collected over a seven-month period. Again, patients who do not spontaneously appear will be called back.

Primary and secondary endpoints

The primary endpoints of the study are the proportion of patients reaching the ADA-targets for three bio-clinical outcomes: (1) HbA1c < 7%; (2) SBP \leq 130 mm Hg; (3) LDL-C < 100mg/dl. Secondary endpoints are individual improvements of 12 validated parameters, i.e. HbA1c, LDLC, HDL-C, Total Cholesterol, SBP, Diastolic Blood Pressure (DBP), weight, physical exercise, healthy diet, smoking status, statin and anti-platelet therapy.

Statistical analysis

Endpoints will be analyzed according to the intention-to-treat principle. Linear and generalized linear mixed models will be used to account for the clustered nature of the data, i.e., patients clustered within PCP's, and repeated assessments clustered within patients. Such models not only allow to study how outcomes change over time within patients, but they also allow to study how these longitudinal changes depend on patient and/or PCP's characteristics, such as the intervention program, or the use of the diabetes care team (DCT). 'Use of the DCT' is defined as having at least one consultation with a member of the team, with exception of the health psychologist and the flying educator because those were only available for the patients of the AQIP.

Subgroup analyses permit to distinguish the effect of the program in the two intervention arms using different cut-off values. Concerning HbA1C, 3 subgroups are defined: patients with HbA1c < 7%; with HbA1c \geq 7% and < 8% and with HbA1c \geq 8%. Concerning SBP, 4 subgroups are defined: patients with SBP \leq 130 mmHg; with SBP > 130 mmHg and \leq 140 mmHg; with SBP > 140 mmHg and \leq 160 mmHg and with SBP > 160 mmHg. Concerning

LDL-C, four subgroups are defined: patients with LDL-C < 100 mg/dl; with LDL-C \geq 100 mg/dl and < 115 mg/dl; with LDL-C \geq 115 mg/dl and < 130 mg/dl and with LDL-C > 130 mg/dl.

DISCUSSION

Trials of complex interventions are of increasing importance because of the drive to provide the most cost effective health care[7]. In this, randomized controlled trials are recognized as the "gold standard" methodology in quantitative research. Health care interventions are, however, often complex in themselves and are always implemented in complex health care settings[16,91-93]. Complex interventions often have particular characteristics making them less likely to succeed when evaluated using randomized controlled trials (RCT) methods, such as multiple components, aiming to target multiple outcomes, being difficult to implement or evaluate, or aiming to achieve outcomes which are notoriously difficult to influence[26]. In this context it is even argued that the complexity of an intervention presents a substantial barrier to its adoption[94]. Complex interventions have greater scope for variation in their delivery, and are more vulnerable to one or more components not being implemented as they should[95]. The application of the MRC framework demonstrated the difficulty of balancing optimum study design with designing interventions that are practical enough to be applied in family practice. In this context we must recognize the limitations of the MRC Framework as it provides a methodological rather than an explanatory approach to evaluating complex interventions. This means that in order to fully understand and predict problems of workability and integration of complex interventions the additional use of sociological and psychological models is important in the design and evaluation of complex interventions.

What we consider a limitation to our study protocol is we do not apply qualitative or quantitative methods within the context of a pilot trial that can help to interpret the results of such trial by clarifying process and outcome results. This shortcoming is however

compensated by a stakeholder analysis from which we derived our understanding of existing barriers to high quality diabetes care. What we consider a particular strength of the study is it generates new hypotheses on innovative types of change interventions (such as interdisciplinary teams operating on the primary-specialty care interface and educational strategies which target change in professional practice and improvements in patient empowerment)[96]. These hypotheses will be tested using a large group of physicians and patients during an 18-month period. Most quality improvement programs reduce the intervention period to six months and are limited to smaller groups. A six-month period is short considering the Hawthorne effect that probably has not been washed out. Another strength of our study is that the primary and specialty care interface is strongly valued and considered an important attribute to high quality diabetes care[97]. More specific, the clinical leadership and coaching provided by a diabetologist to both the primary care physicians and the diabetes care team is of particular importance in fragmented systems of care, including the one from Belgium. Another strength of the study is the explicit project focus on multiple cardiovascular risk factors. A systematic review published in 2001 observed that most interventions did not pay enough attention to patient outcomes and if so, only changes in glycemic control were evaluated[98]. A last strength of the study is the use of all six dimensions of the Chronic Care Model (CCM), which is to our knowledge the fourth study in the field of diabetes care to do so [9,99,100]. The use of all six dimensions of the CCM allows for an evaluation how some of the CCM components are associated with improved outcomes and thus it provides evidence to support the validity of this model. In this context, it is important to mention that the different implementation strategies that relate to every respective dimension of the CCM are explicitly described. Implementation strategies in complex interventions are rarely described[101], even in large-scale implementation studies, which limits the understanding of why an intervention is or is not locally successful[29].

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS CONTRIBUTIONS'

BL, GG, VDBC participated in the study design and drafted the manuscript.

MC, AB, VG, CA, IA, GR and HJ participated in the study design.

All authors have read and approved the final manuscript.

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Table 1: The MRC Framework applied for the development and evaluation of a complex intervention in diabetes care.

PHASES			
PHASE I- PRECLINICAL-THEORY (Why should the intervention work?)			
CONTENT	METHODS	RESULTS	PUBLICATIONS
Collecting evidence on the effectiveness of multifaceted diabetes intervention programs	Review of systematic reviews on diabetes care programs in primary care, outpatient, community and hospital settings to identify: <ul style="list-style-type: none"> ▪ Conceptual backgrounds of programs ▪ Goals ▪ Settings ▪ Type of program ▪ Type of interventions ▪ Type of indicators ▪ (Cost) effectiveness of programs and interventions 	<ul style="list-style-type: none"> - Overview of best choice of interventions and indicators - Selection of conceptual model - Overview of major confounders - Overview of strategic design issues - Overview of barriers to high quality diabetes care at the macro, meso and micro level 	[34]
Identification of evidence on appropriate outcome indicators			
Influence of local context			
PHASE II- MODELING (How does the intervention work?)			
CONTENT	METHOD	RESULTS	PUBLICATIONS
Understanding of the pathways by which the problem is caused and sustained (barriers to high diabetes care at the macro, meso and micro level)	<ul style="list-style-type: none"> ▪ Stakeholder interviews to identify and understand barriers to high quality diabetes care in the Belgian health care system ▪ Multidisciplinary team meetings to discuss program development 	<ul style="list-style-type: none"> - Definition a multifaceted intervention/implementation strategy and outcome-indicators - Local adaptation of the treatment protocol 	[35]
Exploration of whether the pathways are amenable to change and, if so, at which points			
Quantification of the potential for improvement (estimates of likely effect size)			
Program development (best achievable combination of intervention components and intensities + identification of feasible and valid measures of outcomes)			

PHASE III- EXPLORATORY TRIALS		
Not performed		
PHASE IV – RANDOMIZED CONTROLLED TRIAL		
The Diabetes project Leuven	- Clustered Randomized Trial	
PHASE IV – LONG TERM IMPLEMENTATION		
Not performed		

Table 2: Overview of components of the Usual Quality Improvement Program (UQIP) and Advanced Quality Improvement Program (AQIP).

PATIENT		
<u>Lack of adhere to treatment regimen and clinical inertia related to:</u>		
→ E.g. Limited motivation or resistance to adopting lifestyles that support optimal disease care.		
	USUAL QUALITY IMPROVEMENT PROGRAM (UQIP)	ADVANCED QUALITY IMPROVEMENT PROGRAM (AQIP)
Patient education	<ul style="list-style-type: none"> Medical assessments and education upon referral of the PCP's by diabetologist or Diabetes Care Team = internist, nurse educator, dietician and ophthalmologist	<ul style="list-style-type: none"> Medical assessments and education upon referral of the PCP's by diabetologist or Diabetes Care Team (DCT) = internist, nurse educator, flying educator, dietician, ophthalmologist and health psychologist
Promotion of self-management	----	<ul style="list-style-type: none"> Education of patients in practice (by flying educator)
	----	<ul style="list-style-type: none"> Education at patient's home (by flying educator)
	----	<ul style="list-style-type: none"> Counseling by health psychologist
	----	<ul style="list-style-type: none"> Structured educational materials from DCT
	----	<ul style="list-style-type: none"> Structured educational materials from community organizations
	----	<ul style="list-style-type: none"> Group educational sessions for patients and family members
	----	<ul style="list-style-type: none"> Free access to blood monitoring tools for self-management

PROFESSIONAL		
<u>Lack of adherence to guidelines and clinical inertia related to:</u>		
→ E.g. Overestimation of care actually delivered, a failure to identify and manage comorbid conditions, unawareness or disagreement with evidence-based goals of care and 'soft reasons' to avoid intensification of therapy.		
	USUAL QUALITY IMPROVEMENT PROGRAM (UQIP)	ADVANCED QUALITY IMPROVEMENT PROGRAM (AQIP)
Clinician education	<ul style="list-style-type: none"> Distribution of treatment protocol 	<ul style="list-style-type: none"> Distribution of treatment protocol
	<ul style="list-style-type: none"> Two post-graduate educational sessions <ul style="list-style-type: none"> Evidence based guidelines The use of insulin 	<ul style="list-style-type: none"> Four post-graduate educational sessions provided by diabetologist (opinion leader): <ul style="list-style-type: none"> Evidence-based guidelines and principles of shared care The use of insulin Patient-centered counseling Peer review
	<ul style="list-style-type: none"> Standard educational materials 	<ul style="list-style-type: none"> Extended educational materials

	----	<ul style="list-style-type: none"> Inviting PCP's during DCT meetings to discuss patient cases
	----	<ul style="list-style-type: none"> Providing structured communication forms to PCP's by DCT
	----	<ul style="list-style-type: none"> Distribution of shared care protocol + referral indication
Feed-back	<ul style="list-style-type: none"> At start and end of project: summary of clinical performance 	<ul style="list-style-type: none"> Every 3 months: summaries of clinical performance
	----	<ul style="list-style-type: none"> Every three months: benchmarking feed-back
Reminders	<ul style="list-style-type: none"> Clinical reminders at start and end of project 	<ul style="list-style-type: none"> Every three months: Clinical reminders
	----	<ul style="list-style-type: none"> Every three months: Shared care reminders
ORGANISATIONAL		
<u>Lack of office system support and organizational aspects of care related to clinical inertia:</u>		
→ E.g. Lack of decision support and a team approach to care.		
	USUAL QUALITY IMPROVEMENT PROGRAM (UQIP)	ADVANCED QUALITY IMPROVEMENT PROGRAM (AQIP)
Team changes	<ul style="list-style-type: none"> Diabetes Care Team operating close to regular care 	<ul style="list-style-type: none"> Active installment of Diabetes Care Team operating under supervision of a diabetologist from a University Hospital
	----	<ul style="list-style-type: none"> Diabetes Program manager providing logistic support to PCP's
	----	<ul style="list-style-type: none"> Introduction of shared care protocol Active encouragement by DCT and scientific team of PCP's to use shared care protocol
	----	<ul style="list-style-type: none"> Referral arrangements Active encouragement by DCT and scientific team to adhere to referral arrangements
	----	<ul style="list-style-type: none"> Liaison activities by DCT towards in-hospital diabetes care team in secondary care
	----	<ul style="list-style-type: none"> Involvement of independent pharmacists
Continuous quality improvement	<ul style="list-style-type: none"> Quality Assurance Team 	<ul style="list-style-type: none"> Quality Assurance Team

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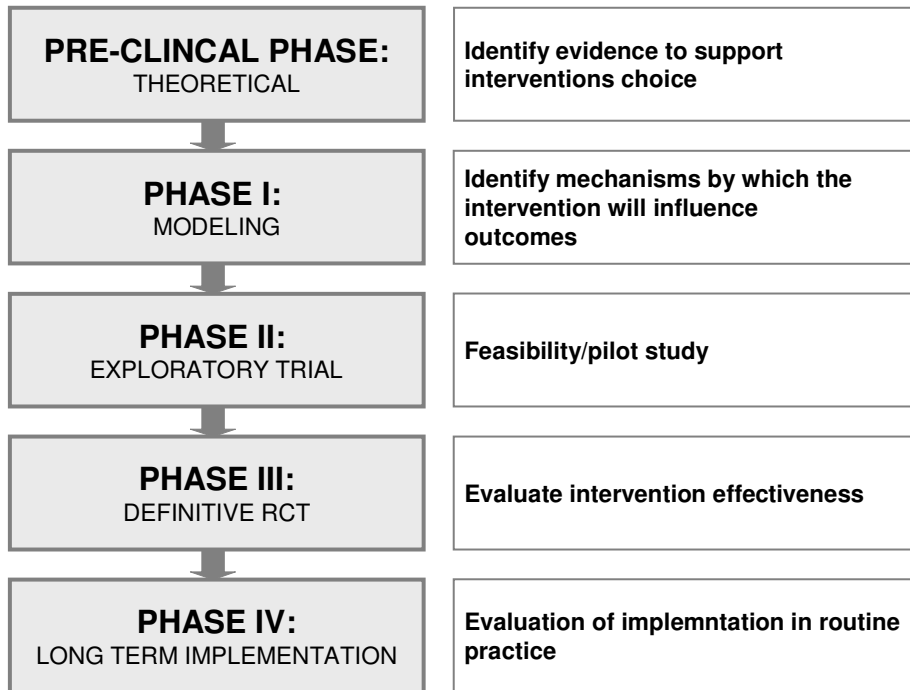
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Figure 1: Phases of the MRC Framework for developing complex interventions



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Additional file 2: implementation science table 2.pdf, 40K

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