In this thesis we set out to examine how health care systems in LIC can improve care for and self-management of people with diabetes, as a representative chronic disease, by making use of new opportunities. We did so in two phases. The first part is a reflection on the specificities of chronic diseases and their implications for health system organization in LIC. The second part is an empirical study in which we tested and evaluated the use of an mHealth intervention embedded in existing diabetes programs in different countries.

Summary and discussion of findings

Chronic diseases and health systems in LIC

Global transitions in epidemiology, in the institutional arrangements in society and in access to information and communication lead to the need of health system leaders to redirect their attention to the role of primary care providers and their relationship with patients. (chapter 2). Health systems in most LIC have few resources and have organizational weaknesses that hamper their potential to adjust to these changes. The rising numbers of people living with chronic diseases lead to additional needs to address this new type of burden. The successes in the scale-up of access to treatment for people living with HIV/AIDS show the feasibility of and the need for decentralization of care and the expansion of treatment through involvement of lay workers and patients, through the ‘public health’ approach. In this third chapter we explore thinking about cross-fertilization across disease-specific programs, taking new perspectives, namely that of patients in their environments, the health care organization, and the biomedical specifics of each disease. These viewpoints lead to new insights about care and self-management. Increasing self-management through involvement of patients in their own care, can be both a way to improve access to care for patients through radical decentralization, and an element of improved quality of individual care. Primary care providers can develop their specific competences and prove their relevance through a renewed focus on empowerment, to support patients in self-management.

The chronic dimension of these diseases has further implications for the organization and the quality of care. The chronic dimension forces people to incorporate a life-long disease such as HIV/AIDS or diabetes into their daily life and identity, through making physical, mental and practical adjustments. They will need access to health care services, for routine care, prevention and treatment of complications, although the needs and demands will vary according to the individual variations in the phenotype of disease and personal capabilities of the patient. Time-wise, most of chronic disease management falls under the responsibility of the patients, who make day-to-day decisions about behaviours that potentially influence the course of their illness. For the organization of health care, this implies the need for health care services that are able to follow-up on patients, to tune their services according to the differences between patients, to improve the quality of care and to improve interaction with other broader support services within the community. Ideally, people are empowered to take up the responsibility for self-management of their own health and disease, supported by peers, professionals and information and communication tools. The development of technologies such as mHealth could be a lever to stimulate this process (chapter 4).

In this part of the thesis, we demonstrated the need for and value of more and better self-management by patients with a chronic disease in LIC. We analyzed the potential to learn from HIV/AIDS control programs about how to involve patients and communities in self-management (support) and we argued that technical and social innovations can further accelerate these processes also for patients with other chronic diseases. Important knowledge gaps concern the implementation of self-management support into existing health care organizations in LIC and the implications of scaling-up such interventions for the wider health system, for instance on financing and regulation of collaboration between professional and community-based partners in chronic care. A more comprehensive implementation of the CCM in LIC requires adaptations to the health care organization, such as a clinical information system.
to track and trace patients, but also a reorientation of the role of the patient towards a well-informed and activated partner in disease management. This implies renewed attention for the quality of the interaction between health care provider and patient.

**Enhancing self-management with an mHealth intervention**

Based on the findings from the literature studies, we designed and conducted the TEXT4DSM study. The aim of this research project was to evaluate the effectiveness of a mobile phone Diabetes Self-Management Support (DSMS) intervention on top of an existing Diabetes Self-Management Education (DSME) strategy in three countries, Democratic Republic Congo (DRC), Cambodia and the Philippines, to improve health outcomes, access to care and enablement of people with diabetes. In each country 480 people with diabetes were randomised to either the standard support (self-management education) or to the intervention (additional mHealth support) arm (chapter 5). The findings from this empirical research can be categorized into findings about the existing diabetes programs, about the implementation of the intervention and about its effects.

Through the analyses of the three diabetes care and self-management education programs, Kin-réseau in DRC, MoPoTsyo in Cambodia and FildCare in the Philippines, we have learned that it is possible to improve diabetes care services within a health system with few resources. The basic components of the programs are comparable, comprising an essential package of medical diabetes care and self-management education. These programs were developed taking into account contextual constraints and opportunities, which led to different choices in the delivery of services. These differences in delivery, together with the resources available, led to differences in the recruitment of patients for the programs, in the role of patients and their interaction with health care providers. The focus on self-management was largest in the MoPoTsyo program. On average, Kin-réseau program participants are older, have a longer diabetes history and are more frequently overweight than participants from the other two programs. The MoPoTsyo program includes most female, most illiterate and most lean patients compared to the other two programs. Health outcomes (HbA1c level, systolic blood pressure, diabetes foot lesions) were most favourable for patients in the MoPoTsyo programme. Diabetes-related health care expenditure was highest for patients in the FildCare program. The cross-program comparison does not allow us to make causal attributions to the differences between the outcomes of participants. But the knowledge about the natural history of disease leads us to the assumption that the duration of these programs and duration of diabetes history of their participants, and the way in which people entered the care program, have contributed to differences in the health outcomes of their participants (chapter 6).

The three programs emerged in reaction to their surrounding health system and its wider social, cultural and economic context. In order to better understand this, we studied one of them, the MoPoTsyo program in Cambodia, in more detail, focusing on its development and its perceived place within the health system. The program was created as an innovation to address a health system failure that left diabetes patients essentially without care. The program developed in three stages: a focus on diabetes self-management; a widening scope to ensure access to affordable medicines and access to other health care services; and aiming for sustainability through more integration with the Cambodian public health system and further upscaling. Despite resistance of other health system stakeholders, the organisation has been successful in reaching its goals (empowering patients to self-manage and demand services that meet their needs) and in integrating essential elements of its approach into the national health policy (chapter 7).

In these three different contexts, we implemented the DSMS intervention, which was similar in all three as to its underlying theoretical framework, its objectives and format of diabetes self-management support, the latter being Short Messaging Services (SMS) sent out on a regular basis targeting all dimensions of diabetes self-management. The implementation turned out to
be different in each country, with the main parallel being that there was a decline at each step in the process from planned intervention to effective coverage. This entailed both shortcomings at the ‘supply’ side of the program, such as delays in the formulation of new messages and technical problems with the telecommunication, and barriers at the side of the participants receiving messages. In the Philippines, the intervention did not reach the participants as planned, largely due to the discontinuation of participation of one center leading to high rates of loss to follow-up (LTFU). The freely available software we used had a very limited potential to customize the design of the intervention and it proved vulnerable to provider and network problems. One third of the phone numbers turned out to be out of reach due to breakage, loss and cancelled subscriptions. Even if phones are on, people don’t always open their in-boxes. The fierce competition in the mobile phone market, especially in Cambodia, led to people receiving frequent commercial messages overloading their phone inboxes. Coverage of the intervention was best among the participants in the Kin-réseau program, where more than half of the participants remembered having received (almost) all messages, whereas among the participants of the MoPoTsyo program, this was only 10%. This process analysis helped us to better understand the operationalization of mHealth, and the technological, contextual and participant-related barriers (chapter 8).

Our mHealth intervention did not lead to more people with controlled diabetes at the end of the intervention. More striking than the lack of effect of the intervention were the differences in the trends over time between the three programmes, comparable for both the intervention and control groups. The number of people having controlled diabetes increased among the participants in the Kin-réseau program and decreased among the MoPoTsyo program participants. The large LTFU in FildCare makes it difficult to interpret findings from this program. In the improvement of diabetes control over time among all participants of the Kin-réseau program, the DSMS intervention might have had an adjuvant role; there was a marginally larger increase in people with controlled diabetes among the participants in the DSMS intervention group than in the control group. This effect was also seen in the reduction of diabetes foot lesions among participants in the intervention group in the Kin-réseau program, as compared to the control group. Foot wounds were relatively frequent among Kin-réseau program participants and soon after the start of the intervention, foot care was improved across the board. The additional effect among participants in the DSMS intervention could point to text messages as an additional motivator on the side of the patients.

Also for intermediary and secondary outcomes, such as the knowledge and perceptions, self-management behaviour, utilisation of care and other health indicators, we were not able to demonstrate effects of the intervention: if changes were observed over time, they were observed for both the intervention and control group. For instance, the pharmaceutical management within the Kin-réseau and MoPoTsyo programs has been intensified, with more people receiving insulin and anti-hypertension treatment. The somewhat larger increase of intensified treatment among people in the intervention group suggests that the messages may have had a share in pushing this development. Also remarkable was the decrease in negative attitude towards diabetes in the Kin-réseau and FildCare programs over time, for all participants. The recognition of the link between negative emotions and diabetes control renders this a meaningful observation (chapter 9).

The main differences of our study with other ones showing an improvement in diabetes control of mHealth interventions was the duration of the intervention (ours being longer than the average 6-12 months of other studies), the variation of patient characteristics (in most studies rather homogenous cohorts, for instance only newly diagnosed patients, or patients on oral antidiabetic therapy only, while in our study, the heterogeneity was pronounced) and the scope of the intervention (for instance linking the mHealth intervention with other internet resources being available to patients). These differences help us to partly understand the divergence. However, other explanations for our study being deviant point to the design of the study and the
implementation. Our messages were initiated by the program (or ‘dropped on patients’), not very tailored and not interactive. These features have, in some reviews, shown to affect the potential for behaviour change (1). Another confounder is the diabetes care that patients have access to, next to the text messages. Limited access to medication, like in Kin-réseau, and a decrease in support from the routine program, like in MoPoTsyo, interfere with the potential of mhealth to contribute to change. In the two successful studies, routine care was given in a tertiary centre by an endocrinologist (2,3). The poor effective coverage of the SMS intervention, especially in Cambodia and the Philippines, can also contribute a lot to explain the absence of effects (chapter 9).

Explanations for the deterioration of glycaemic control among MoPoTsyo program participants might be looked for in the changes in the routine programme, as could be suspected from the reduction in the frequency of contacts with the peer educator and in the percentage of people performing glucose monitoring. The scaling up of the routine MoPoTsyo programme within the national strategy, as described in chapter 7, has led to uncertainty among staff and patients, affecting the functioning of the programme.

Methodological considerations

The conceptualization and implementation of the TEXT4DSM study has been a lesson in itself. The strategy to develop a multi-country translational research project was ambitious. We aimed for comparable studies through a similar design and intervention, in three different countries with diverse health care systems. We anticipated differences between the programs and therefore calculated the sample size so as to be able to determine effects for each program separately. Indeed, this was justified in retrospect. The differences in the organization and implementation of the study and the difficulties in the management of the intervention in the Philippines compared to the other two countries, decreased the potential of an overall evaluation and for comparison with the two other study sites. In a multi-country study with such diversity between contexts, studying the differences can be as interesting as the evaluation of the pooled effects.

All partners had to build expertise in how to conduct a randomised controlled trial, in the technological aspects of an mHealth intervention and in the appropriation of the behaviour theory guiding the messages. These were a lot of lessons to learn in 4 years’ time, in a project with modest resources. The preparation year was used to build organisational capacity and to prepare all research materials such as the protocol, the translations, measurements, communication channels, etc., with relatively little time to test the intervention. A pilot study with a smaller group of participants in each country, before initiating a full-scale effectiveness study, might have proven useful to adjust the practicalities of implementation of the study. The pilot studies could have been embedded into a broader formative research phase, comprising qualitative research and participative planning of the intervention. Through an approach like intervention mapping, local research teams could have been facilitated better in conducting a participatory situation analysis, and a contextualised intervention development process (4). This would have provided the opportunity to link the situation analyses findings to the generic theory of change and the contextualised application of it. This potentially would have helped to develop a deeper common understanding of the intervention and its relevance for the practice among more stakeholders. Qualitative research in this phase through interviews and focus group discussions would have led to the perceptions of patients and staff about self-management behaviour and their possible determinants to be better known by all. This could in turn have guided the implementation strategy of the intervention, and have helped the country teams in the formulation of more tailored self-management support text messages.

The format of our messages was uniform for all patients in one country. Only in MoPoTsyo in the second year, messages were targeted to subgroups, such as people with hypertension or with overweight. The social determinants of behaviour are rather complex, involving system-
related determinants as well as individual variation. Newer self-management support strategies make use of a mix of uniform messages and individualised support which might prove to be more effective. With the advances in technology and the further integration of behaviour science into health research, these combinations of universal content and individualised targeting is likely to become available at a wider scale.

The implementation of the intervention required the enduring competence of the implementation organisation. The anticipated risk of contamination between the intervention and control group, through patients of both groups being in contact with each other and through contact with educators from the routine program, turned out to be realistic and was substantial. While we had considered a cluster-randomised design with enough geographical space between the clusters, the size of clusters in the Philippines made us opt for individual randomisation, in all countries. With hindsight, we could have considered a differentiated approach to optimise the design to each context, accepting the loss in potential for a pooled analysis.

The integration of a long-term health intervention and a study to test its effectiveness into a diabetes care and self-management program required quite an organisational capacity. There is a substantial risk for LTFU due to death, migration and people having other priorities. Since this loss is not only relevant for research, but also for the organisation of health care and self-management programs for people with chronic life-long conditions in general, it is important to better understand the reasons for LTFU and to address these. Retention studies and strategies in HIV/AIDS programmes suggest that home visits and community health worker involvement reduce LTFU rates (5). This overcomes transport problems for patients and addresses the challenges that people who are too sick or otherwise vulnerable face to come to the clinic. More broadly, the organisation of health care services is usually based on a bureaucratic and technocratic rationale, not taking into account why and how people choose to make use of them. More involvement of users into this process could be a way of better addressing their perceived needs, thereby increasing the chance of better utilisation of and engagement with these services (6).

An additional lesson from our study for researchers on chronic diseases is the factor progression. In the design of a longitudinal study for a progressive disease like diabetes, it is sensible to take into account the rate of deterioration and the stage of disease of participants at baseline, in order to make realistic estimates about the losses due to death and adjust the sample size, duration of the study and intervals between data collection rounds accordingly. In settings with high migration rates, researchers could include ‘intention to stay’ in their inclusion criteria.

Lastly, an important aim of a cross-country study is to learn lessons across contexts and to give researchers from each context the opportunity to learn from each other. This requires explicit planning of this learning, through regular exchange, on theoretical and methodological issues and on implementation challenges, for instance in communities of practice that combine virtual and face-to-face contact. We had two consortium meetings, in the preparation phase and in the midst of the implementation phase, and one cross-site visit, where the program manager of Kin-réseau went to see the MoPoTsyo program. The common analysis of baseline data and paper writing stimulated scientific reflection among all involved. This has strengthened the research capacity at institutional and individual level in all three countries. Dissemination of the experiences and findings in each country can further stimulate this process of reflection, learning and action.

Lessons for chronic disease management

Our empirical study provides a warning against high expectations of mobile phone applications as a game changer to improve the organisation of care for chronic diseases in LIC. The range of applications of this technology varies and so may the underlying mechanisms through which
these applications can be successful – or not. The simple sending of text messages in our study had been conceptualised as behaviour support, through which we aimed to influence behaviour, thereby improving health outcomes. We experienced a lack of coverage by the intervention, a lack of quality of the messages, a flaw in the theoretical causal relationships between the intervention, behaviour and outcomes, or by the interference of other factors, such as the care program, the context and the disease characteristics. Managers contemplating to add mHealth interventions into a chronic care management program, need to be well aware of the additional function of this mHealth intervention (e.g. facilitating self-care, stimulating behaviour change or decrease access to care), and adjust both content and format of the messages accordingly. Subsequently, they need to strive for an optimal integration of the intervention in the context, taking into account technical barriers, health service characteristics and the local mobile phone market.

**Lessons for health care organization in LIC**

We started our research with the Chronic Care Model (CCM) as the main reference to improve care for chronic conditions. Our research focused on two elements of the CCM, namely improving self-management support and the health care delivery system.

Self-management and care are two sides of the same coin. Both are needed and ideally reinforce each other. Interventions to improve chronic disease management should be directed to providers (care provision) and to patients directly (self-management). In the organisation of care, access to an essential package of care for the most common chronic diseases is a prerequisite, such as availability of first line medication, diagnostic equipment and a registration and communication system for the follow-up of patients. Taking into account the low level of qualified staff at public primary care facilities in many LIC, this means, realistically, that improvements will most often start at the referral level (e.g. district hospital), where part of this package is already in place. In order to improve access for more people, further decentralisation through task-shifting and ensuring more resources is an obvious next step for the local level health system managers. The efficiency of the health care organisation could be improved by a system in which stable patients can be differentiated from patients in need of intensified care, diversifying the attention of different cadres of staff. Apart from the ‘hardware’ essentials, there is a dire need to experiment with the improvement of the ‘software’ of care, meaning the way health providers interact with patients with chronic conditions, not only to educate them in self-management, but also to support them to increase coping capacity and motivation for optimal self-management behaviour.

The baseline differences between the three diabetes programs suggest that involving patients themselves is promising, as was seen, for instance, in the very high degree of medication adherence and lower LTFU in the MoPoTsyo program compared to the Kin-réseau program (7). The combination of relatively strong patient engagement and good health outcomes in the routine program of MoPoTsyo at baseline supports the argument to steer health service organisation more around people (8). In order to move towards more self-management by patients, they need access to resources, such as medication and possibilities to get feedback about their health status, for instance through glucose monitoring. These resources need organisation, usually within health services. The case study of MoPoTsyo suggests that such services can start outside the health system, but in order to be sustainable, a more formalised link between the mainstream health system and such programs needs to be established.

While adequate self-management is intrinsically valuable, our studies illustrate that it is not self-evident for people in LIC to engage in self-management, nor to demonstrate the added contribution to health outcomes. The natural course of the disease and the quality of medical care are both important confounders. People in advanced stages of disease might have little health gain to expect from maximising their self-management capacity. Health care providers should be honest towards patients about the benefits and the limitations of any medication or
lifestyle advice, and about their own unknowns. If not, they might not only lose the trust of their patients, but also it might affect their self-confidence, contribute to deception and decrease their quality of life. It is a challenge for doctors to learn that their profession does not only entail curing patients, but also assisting them in building “resilience or capacity to cope and maintain and restore one’s integrity, equilibrium, and sense of wellbeing” (9).

Chronic disease management, ideally, is a partnership effort, in which the strength of each partner and the reciprocity of the relationship can vary from person to person and over time. The quality of the interaction between providers and patients is shaped by psychosocial characteristics of the persons involved, but is also heavily influenced by the institutional, organisational and cultural environment. Many interventions try to improve the health service organisation context, through training of health providers or providing counselling environments. Other strategies focus more on empowering patients for instance through peer support groups. It will be interesting to examine mechanisms to increase mutual connectivity between patients, providers and their support systems.

What we learned about diabetes care and self-management holds lessons for care for other chronic diseases. Cardiovascular disease and diabetes share similar needs for life-style adjustments and parallels in their long-term progression. In many countries, these families of diseases are treated in the same clinics, by the same professionals. Indeed, there are many efficiency gains possible. The variation in epidemiology of other chronic diseases, such as respiratory diseases, cancers and mental diseases, is large among LIC. While the generic health system lessons about quality of chronic care and partnerships with patients and community organisations hold true for most of these diseases, it is probably more pragmatic to analyse the specific disease characteristics and health service requirements and the personal and environmental dimensions of each disease, to provide strategic advice on the way forward. This still entails the plea for a generically trained cadre, especially at the primary care level, that can provide care for the most common diseases, including the attention for their chronic dimension.

**Lessons for future research**

The rise of chronic diseases has led to a refocused attention of three scientific domains, clinical research, behavioural science and health systems research. Clinicians have become more aware of their need for knowledge about the reasons of behaviour (change). It has refocused the attention of health systems researchers to the importance of quality of care and to the role of people not only as patients or consumers but also as agents of care and self-management. The growing attention for behaviour and lifestyle determinants leads to knowledge from the domain of health promotion gradually trickling down to the more clinically oriented domain of health care - gradually, and not yet very widely so in LIC. Too often still, risks for chronic diseases are addressed as if being one basket of similar behaviours (smoking, overeating, drinking alcohol), having uniform effects on all people. The influence of particular disease characteristics and other genotypic and phenotypic elements is only starting to receive attention.

While each scientific domain still has a wide area of research to deepen on its own, the more complex and interesting questions and solutions are found in the inter- or transdisciplinary collaboration: research to understand how biochemical characteristics of disease interact with disease management, and how health systems can facilitate adequate behaviour and support people in making informed decisions about self-management. A research agenda for the coming ten years could include the following topics: 1) improvement of the quality of care in primary care facilities in LIC, including the integration of behavioural dimensions into routine care; 2) clinical studies among patients with different varieties of the same disease (e.g. diabetes), to better understand these differences and the reciprocal influence of behaviour and other determinants on them; 3) redesign of local (district) level health systems towards a better linking of health care facilities, organisations in the community and patients and their families to better identify and share responsibilities in disease management; and 4) proper evaluation of
such experiments to understand the mechanisms of success or failure, so as to be able to transfer to other contexts and possibly go to scale.

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