Chapter 1. General introduction
Health systems in low income countries and chronic diseases

Health systems all over the world face the continuous challenge of how to adapt to changes in context, such as newly emerging diseases, rapid urbanisation and technological innovations (1). In many Low Income Countries (LIC), health systems have structural problems and function poorly. Available resources are limited and there is inadequate capacity to organise the supply and distribution of these resources. The capacity for leadership and organisational management is constrained by weak governance and overly centralised institutional arrangements, little communication and information, dependence on donor funding and few incentives to improve performance (2,3). Already fragile, it is much more difficult for these health systems to adapt to new health problems and other changes (4).

A health system comprises “all organizations, institutions and resources devoted to producing actions whose primary intent is to improve health” (5), one of their central tasks being to facilitate and/or organise the delivery of health services, health care in particular (6). Health care in LICs is often characterised by a general shortage of means, lack of qualified and motivated professional staff, fragmentation of services and inconsistent quality of care. The importance of the central role of primary care in health service organisation is recognised for all health systems: health systems oriented towards primary care have better access to health care, better and more equitable health outcomes at lower costs (7–10). But while the definition of primary care contains high ambitions recognised in well-resourced settings (the first entry point into and the coordinating hub of the health care system, person-focused care over time for all but the most uncommon conditions (11), the reality in LIC is usually different. There, primary care is selectively focused on traditionally highly prevalent health problems, such as mother and child health and infectious diseases, and organised to deliver episodic care for a limited period of time, with little attention for patient-provider interaction (12–14).

Environmental, demographic and epidemiological transitions have led to a rapid increase of chronic conditions, such as HIV/AIDS, cardiovascular diseases and diabetes mellitus (15), also in LIC. The chronic nature of these conditions, in the absence of effective measures to prevent the emergence of new cases, leads to an increasing burden for health care systems. Present global estimates amount to 422 million people living with diabetes (16), 1 billion people with hypertension (17) and 15 million people living with HIV/AIDS (18), most of them in LIC. In the absence of screening programmes, people are usually diagnosed in an advanced stage of disease. Poor quality of care without attention for long-term follow-up leaves many patients on their own once the diagnosis is made and the acute problems have been stabilised. At the next episode, people return or try their luck somewhere else, be it the local pharmacy, another doctor or a traditional healer, mostly paying out of pocket (19). The consequences are poor health outcomes for patients with chronic conditions, an increase in catastrophic health care expenditure, and potentially a breakdown in trust between health care providers and patients (13).

The studies in this thesis aim to contribute to how health care systems in LIC can better address the needs of people with chronic conditions in this changing context.

Chronic disease management in LIC

In order to respond to the needs of people with chronic conditions, countries need to address “multiple gaps in health systems related to access to basic technologies and medicines, the health workforce, service delivery, health information, and referral, with a special focus on primary care” (20).

Lessons can be learned from the way health systems have faced and responded to the increasing numbers of patients with HIV/AIDS. To scale up the response, health systems simplified and decentralised treatment, and they expanded the delivery of treatment through involvement of lay workers and patients. This is called the ‘public health approach’, ‘prioritizing large-scale
access to treatment over maximizing individual treatment” (21).

Apart from integrating yet another group of diseases into the package of services and activities to be delivered through the health system, the chronic dimension of these diseases inevitably leads to rethinking the role of the patient, the patient-provider relationship and the health care organisation around it. People with a chronic disease live their life almost all the time without professional support. Many challenges, unforeseen problems and questions appear in daily life, but not during the consultation with the health care providers. People find a way to incorporate a chronic disease into their life and identity, to combine the requirements of disease management with their being a truck driver, father or volleyball player. The long duration of the condition and the relatively big influence patients have on its course are an opportunity for patients to gain knowledge and expertise in their condition and its management (19).

The Chronic Care Model (CCM) was the first and, until now, the most dominant framework to prescribe how care for chronic patients can be best organised (22). It illustrates how the health (care) system and the community both need to be well-organised in order to contribute to productive interactions between a health care provider (team) and the patient, who should be well-informed and take an active role (figure 1).

**Figure 1. The Chronic Care Model, developed by Wagner (22)**

[Image of the Chronic Care Model]

Having been implemented in high income countries, the CCM and similar models have also been widely propagated as useful for LIC (23,24). Although this model includes a system-based approach, addressing various levels of health care organisation at the same time, most initiatives in LIC are limited to the implementation of one or a few components. Self-management support has been most widely picked up as an innovation. Self-management got recognised as inevitable and intrinsically valuable. It relates to the day-to-day decisions people with chronic diseases make, regarding what they eat, their medications, physical exercise and other aspects of life influencing their disease (25). Self-management support delivered via peers has proven an attractive strategy (26). A number of LIC have experimented with peer support...
strategies to improve self-management mainly through education or psychosocial support (27,28). More encompassing initiatives to implement a CCM approach have been seen in the response to the HIV/AIDS epidemic, in which there has been quite some attention and resources for the improvement of individual care, through counselling, family support, adherence support, and community- or home-based care (29).

**Diabetes mellitus as an example**

In this thesis we focus on diabetes mellitus. Its characteristics are highly representative of many other chronic diseases. It is a lifelong progressive disease, which requires a diagnosis and biomedical treatment ranging from simply routine to complex care, and its course is greatly influenced by lifestyle behaviours such as eating and physical activity, thus having a large impact on daily life.

Globally, there are 422 million people living with diabetes, which is a result of the increase in prevalence rates, from 4.3% in 1980 to 9.0% in 2014 for men, and from 5.0% to 7.9% for women. This increase is most striking in low and middle income countries (LMIC). Age-standardized prevalence rates doubled in many Sub Saharan African and Asian countries. In the top-10 list of countries with the highest absolute numbers of adults with diabetes, there are seven LMIC (30). The causes for the increase in these countries are complex and varied. There are ethnic differences in genetic susceptibility and phenotypic variations. This is illustrated by, for instance, the observations that diabetes develops at an earlier age in Asian than in Caucasian populations, and that ketosis-prone atypical diabetes is mostly recorded in people of African origin. Also the thrifty phenotype hypothesis, which links β-cell dysfunction to inadequate foetal and childhood nutrition and growth, falls under these explanations (31). Demographic and environmental transitions also contribute: ageing and rapid urbanisation coincide with a decrease in physical activity and a change in diet (32,33). The early onset of diabetes in LIC, the late diagnosis and the lack of access to quality care lead to many more people with diabetes in an advanced stage, suffering from long-term complications.

**Pathophysiology of diabetes mellitus**

Diabetes can be classified into different categories, the most common ones being type 1, type 2, gestational and specific types due to other causes (34). Type 2 diabetes represents roughly 90% of all cases and thus is numerically the biggest burden for health systems, also in LIC; hence our focus is on this type. Pathophysiology of type 2 diabetes is multifactorial – encompassing genetic and lifestyle-related risk factors.

In a normal situation, the β-cells in the pancreas secrete insulin, the amount being regulated in response to the plasma glucose concentration. The effect of insulin is to reduce glucose output by the liver, enhance glucose uptake by the skeletal muscles and to suppress fatty acid release from fat tissue. Insulin sensitivity is the degree in which the body is able to react on insulin. People with well-functioning β-cells and a normal insulin sensitivity react with subtle upturns of insulin secretion in reaction of increasing blood glucose concentration, small amounts of insulin being sufficient to downregulate blood glucose. Pathophysiology begins when insulin sensitivity decreases (also termed insulin resistance) and/or the function of the β-cells is diminished. The pancreas can compensate with upregulating the insulin secretion, up to a certain level. Insulin resistance is associated with obesity and inversely associated with physical activity, but several other factors interact with the development of diabetes, as indicated in figure 2 (35,36).

Once the β-cells fail to secrete more insulin in response to excessive glucose levels, we speak of β-cell failure and impaired insulin secretion (figure 2). Glucose in itself is toxic, affecting β-cell function. This catalyses the vicious cycle of hyperglycaemia, hyperinsulinemia and increasing resistance. This vicious cycle partly explains the progression of the disease in most patients, most patients ending with a form of insulin deficiency after about 10 years of diabetes (35).

The levels of glucose can be directly measured in plasma or capillary blood. These
measurements provide information about the current concentration of glucose (glycaemia), which varies over the day and the time since the last meal taken. The long-term complications of diabetes are the result of chronic hyperglycaemia. A complementary method to monitor diabetes control is the measurement of glycated haemoglobin (HbA1c), which is a component of red blood cells that is slowly formed from haemoglobin and glucose, proportionally to the ambient glucose concentrations. The HbA1c level provides information about the average glucose concentrations over the past 120 days, the average lifespan of an erythrocyte. HbA1c is measured as its relative proportion as compared to unglycated haemoglobin (unit being %) or in absolute concentrations (unit mmol/mol). In persons without diabetes, the normal variation is 4-6% of 20-44 mmol/mol (37).

Figure 2. Pathophysiology of hyperglycemia and increased circulating fatty acids in type 2 diabetes (35)

Even when treated, diabetes is characterized by natural progression, reflected by the ‘coefficient of failure’, a roughly 1% increase in HbA1c per 2 years (figure 3)(38). The lack of capacity of the body to adequately respond to changes in blood glucose levels implies acute and chronic danger. The most frequent acute complications are hypo- or hyperglycemia, which can be caused by a mismatch of glucose intake and medication or by concurrent infections which raise glucose levels. In severe untreated cases, both can lead to coma and death. The continuously high levels of glucose lead to complications, mostly vascular. Diabetes leads to a two-fold excess risk for macrovascular diseases, mainly coronary heart disease and stroke (39). Microvascular complications entail nephropathy, retinopathy, neuropathy, in particular leading to diabetic foot problems. Other complications are weight gain (especially for people on insulin treatment) (40). Once complications arise, these affect glycaemic control and remaining β-cell function. The comorbidity of diabetes with other diseases, such as cardiovascular diseases but also, in LMIC, with tuberculosis or HIV/AIDS, further complicates the course of diabetes (41).
Management of diabetes and access to diabetes care in LIC

The global objective in glycaemic control for people with diabetes is to reach average plasma glucose levels below 6.5 mmol/l or 115 mg/dl, which corresponds with a HbA1c level of 7.0% or 53.0 mmol/mol, although there is growing recognition for individual goal setting and adaptations of targets, taking into account age and co-morbidity. The most commonly used medications to lower glucose levels in patients with type 2 diabetes are the oral anti-diabetes agents metformin and sulfonylurea (usually glibenclamide), and insulin, usually added to the treatment regimen in this sequence. Among other functions, metformin increases the sensitivity to insulin and reduces the increased production of glucose by the liver. Sulfonylureas stimulate the pancreas to secrete more insulin. Exogenous insulin, injected subcutaneously, parallels the function of endogenous insulin, except for the amount being administrated not being regulated by the body itself. There is a wide range of other anti-diabetes agents, but their availability in LIC is very limited.

Several diabetes management guidelines have been developed for resource constrained settings (45,46). Apart from the organisational elements (such as the establishment of a patient register, patient cards and case detection methods, and inpatient care), this basic package advises the following targets and methods for glucose monitoring and control: glucose monitoring targets of HbA1c <7.0% (53 mmol/mol), a fasting glycaemia <6.5 mmol/l (115 mg/dl) or a postprandial glycaemia <9.0 mmol/l (160 mg/dl), self-monitoring for people on insulin, pharmacotherapy through metformin, sulfonylurea and insulin. An annual assessment of the patient, his control and risk factors is advised (blood pressure, lipids, renal function, foot examination, sensory examination and – two-yearly – eye examination) and the addition of antihypertensive medication, statins and the treatment of complications such as peripheral neuropathic pain and
retinopathy, if indicated. Lifestyle management education should include nutritional
counselling. There is explicit mention of awareness of psychosocial problems affecting diabetes
self-management and the potential to involve community-based partners to assist patients.

Access to diabetes care and management is problematic in most LIC. Diabetes care is often only
available at secondary care level (for instance, a district hospital), and even there, quality of care
is hampered by a lack of (use of) guidelines, short supplies of test strips, insulin and oral anti-
diabetic medication (32,47,48). The private sector, if present, might offer some of it, at a
patient’s own cost (49).

**Diabetes Self-Management**

Self-management refers to “a set of skilled behaviours to manage one’s illness” (50). They
comprise healthy lifestyle behaviours, adhering to recommended treatment, monitoring
markers of health and disease and acting upon those, and coping with the effects of illness on
daily life and on oneself. For diabetes, these behaviors have been well-eliminated: healthy
eating, being physically active, monitoring physical markers such as blood glucose and body
weight, taking medication, reducing risks for long-term complications, problem solving and
developing coping strategies (51). The development of programmes of diabetes education and
support programmes especially in the United States have been geared towards a standardised
package of content and principles of patient-centred care, with a particular focus for each
critical time in the course of disease, such as time of diagnosis, annual check-up and occurrence
of complications (52,53). The variety of types of interventions to improve self-management is
large, ranging from education, to psychological, practical or social support (54–57). The
implementation of these professional-based strategies has been described mostly in high
income settings with sophisticated health care delivery systems. The effects of such strategies
on clinical outcomes and on self-management behaviour vary, depending on the behaviour
targeted and the approach chosen. Meta-analyses suggest a generally positive (temporary)
effect of self-management education strategies on diabetes control (55).

Also in LIC, the importance to strengthen a patient in his/her self-management of diabetes is
recognised (45). Strategies to improve diabetes self-management usually have a much more
narrow focus on nutrition, physical exercise and foot care (58). The approach in the
professional guidelines is predominantly based on education – often in group sessions, less on
the behavioural processes underlying self-management. The support of self-management
through another channel, namely peer support, is better documented (59–61). These peer
support programmes comprise elements of daily management for instance through cooking
workshops, social and emotional support through telephone contact or home visits and linking
to health facilities. The education strategies in the guidelines and the peer support strategies
from the studies show that diabetes self-management can be stimulated through both facility-
based and community-based interventions.

**Mobile health as a new opportunity**

While there are still many health system barriers for better diabetes management in LIC, there
are also new opportunities. The rapid increase in access to and use of mobile phones by people
in LIC has a strong potential to connect health care providers and patients, to distribute
information among large groups of people and thus, theoretically, to strengthen the self-
management capacity of people living with a chronic disease such as diabetes. The term mobile
Health (mHealth) refers to the use of mobile communication technologies to promote health by
supporting healthcare practices (62).
The body of research on mHealth has started to develop, still mostly with small-scale projects which address only one or few elements of the health care delivery process, and results are mixed (63–66). Reviews have analyzed the effectiveness of mHealth interventions on the adoption of healthy behaviors and improved disease management (67), the effect of direct mHealth interventions on diabetes control (65,66) and the effect of mHealth interventions in Sub Saharan Africa (64). Most of the implemented mHealth interventions include Short Messaging Service (SMS) and a number of studies, especially in developing countries, demonstrated a positive impact of SMS-based strategies on HbA1c levels (68,69).

The revolution in communication and technology will continue its expansion into LIC and its further innovation in techniques and applications. This will probably lead to some of the present barriers to disappear within a foreseeable future, such as limited network connectivity and lack of possibilities to link the mHealth messages directly with the medical care process through electronic medical records.

**Testing an mHealth intervention: the TEXT4DSM Study**

The central problem in this thesis is how health care systems in LICs can improve the care for and self-management of people with chronic diseases, with diabetes as an example, making use of new opportunities such as mobile phone technologies. To answer this question, the TEXT4DSM study was set up. For this study, we developed a mobile phone intervention embedded in an existing diabetes care and self-management education programme in three developing countries, to improve diabetes self-management. The study took place in 2012 to 2015, with an intervention duration of 2 years in each country.

A theoretical framework was developed to understand relationships between care, self-management and health outcomes. Diabetes Self-Management Education (DSME) is defined as "the on-going process of facilitating the knowledge, skills, and ability necessary for diabetes self-care". The overall objectives are "to support informed decision making, self-care behaviours, problem solving and active collaboration within the health care team and to improve clinical outcomes, health status and quality of life" (52). Diabetes Self-Management Support (DSMS) is defined as "activities to assist people with diabetes to implement and sustain the on-going behaviours needed to manage their illness. It includes activities such as education, reminders and behavioural support" (70).

The process of selection of existing diabetes care programmes for the study started at a workshop on chronic care in LICs in 2009 in Belgium, where three programmes were identified for their offering of care, self-management education and support to diabetic patients, and for their willingness to participate in the study.

In the Democratic Republic of Congo (DRC), the diabetes care programme is embedded in an established network of 60 primary care centres for diabetes care in Kinshasa, 'Kin-réseau', in which specialised nurses, referred to as educators, act to implement the DSME programme. Five centres have been purposively selected to recruit study participants. Similar to other countries in Sub-Saharan Africa, the public health care system is built upon governmental and faith-based primary care facilities with referral hospitals. Diabetes care is delivered at the better functioning facilities in this system (71).

The programme in Cambodia is facilitated through community-based peer educator networks, which began in 2005 as a relatively new development. Peer educators are responsible for the DSME programme for patients who live in their area, supported by a non-governmental organisation based in the capital Phnom Penh, which has also organised access to medical care. Nine peer educators have been purposively selected from one urban network and 6 rural networks in 2 provinces (Kampong Speu province, Takeo province).

The DSME programme FildCare in the Philippines is provided by a number of specially trained 'Barangay' or community health workers and/or nursing aids/midwives as educators in Quezon
City (Metro Manila), in the City of Batac (Ilocos Norte Province), and in the municipality of Pagudpud (Ilocos Norte Province). Health systems in Asian countries have a long-standing tradition of such community health workers in the delivery of primary care.

Because of differences in the existing DSME programmes in each country, the numbers of diabetes patients cared for by one educator were different in DR Congo, Cambodia and the Philippines. The purposive selection of participating centres in each country was based on patient group sizes being comparable, the quality of the DSME given, the willingness of staff to be part of a research project, and convenience factors such as travel distance. Patients in the intervention group received additional DSMS through automated Short Messages Services (DSMS) on a mobile phone, which they were provided with at the start of the project. Figure 4 shows how the study is implemented in each country. A more detailed description of the programmes is presented in chapter 6 of this thesis.

**Figure 4. The TEXT4DSM study: routine programme and DSME, study sites and randomisation to the DSMS intervention in each country**

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**Scope and aim of this thesis**

In summary, we have seen that health care systems in LIC have not been adapted to organise chronic care for people with lifelong conditions, which is an urgent problem given the rise of the numbers of people with diabetes and other chronic diseases.

The aim of this thesis is to increase knowledge on improvement of care for chronic diseases in LIC, with a particular focus on the potential value of mHealth interventions in addition to existing diabetes care and self-management programmes. To reach this goal, several questions will be addressed throughout the thesis:

1. What are the challenges of health care systems in LIC to meet the health care needs of people with chronic diseases?
2. How have the existing diabetes programmes developed in their own context and what are their strengths and differences?
3. How feasible is the implementation of mHealth interventions in different contexts?
4. What is the added effect of the mHealth intervention on the health outcomes, utilisation of care and self-management of people with diabetes in the different programmes?

**Outline of the thesis**

The first part of the thesis (chapters 2-4) addresses the challenges of health care systems in LIC to meet the health care needs of the growing number of people with a chronic disease. The second part of the thesis (chapters 5-9) focuses on the TEXT4DSM study.
Chapter 2 presents an overview of the challenges for primary health care in LIC in the 21st century and the particular problem of the rise of chronic conditions and the implications for the relationship between health care providers and patients. Chapter 3 examines whether lessons can be learned from how health care systems in LIC have managed to organise care for HIV/AIDS patients, through a literature review. In chapter 4, we reflect on the conceptual specificities of chronic diseases and how health systems could better respond to these, making use of new opportunities such as mHealth.

Chapter 5 describes the design of the TEXT4DSM study. In chapter 6, we analysed the biomedical care and approach to self-management in the three study settings before the intervention. In chapter 7, we explore in more detail one of the three, the MoPoTsyo programme in Cambodia, taking a health system’s perspective. In chapter 8, we present a process analysis of the TEXT4DSM intervention in all three settings. In chapter 9, we analyse the effects of the intervention and the differences between contexts.

In chapter 10, we summarise and discuss the main findings, put these in a broader perspective and present implications for further research.

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