Summary and future perspectives
Introduction

The viruses dengue and chikungunya are a major public health threat for affected countries. In this thesis, we focused on improving health care and prevention of these diseases in two countries situated at the Caribbean Sea: Curaçao and Venezuela. We examined access to care and health seeking behaviour for dengue and fever in a community in Venezuela. Communities’ preventive practices and mosquito control practices were investigated in Venezuela and Curaçao. Furthermore, we examined the impact on QoL of chikungunya, and the influence of co-infection with dengue on these sequelae in Curaçao. The research methods from this thesis originate from various disciplines, amongst these are medical, psychological and sociological sciences.

Dengue and health behaviours in Venezuela

Venezuela faces a challenging public health situation. In the last decades, dengue has emerged in Venezuela as a result of urbanisation and insufficient mosquito control policies [1,2]. Within the same year as the major dengue outbreak of 2010 [3], a cohort study was set up in the city Maracay, to investigate epidemiological, behavioural, clinical and viral characteristics related with dengue disease and transmission [2]. The studies presented in this thesis were performed in 2013-2014 as part of one of the annual surveys. During the past years, Venezuela’s political and healthcare systems have been unstable, at a background of ongoing anti-governmental protests [4-6]. At the time the fieldwork of these studies was performed, anti-governmental protests intensified, resulting in an unsafe situation for the staff performing the fieldwork. The research team therefore had to cease the fieldwork after a sample size of 105 individuals. Hence, the results provide unique insights in attitudes and behaviours of a population facing a complex political and healthcare situation.

In Chapter 2, we examined the dynamics of health seeking behaviour (HSB) of fever and dengue, in order to find ways to improve early healthcare seeking. In Venezuela, people tend to seek care relatively late [7]. As dengue can develop into severe disease conditions, early health centre attendance is important in order to reduce the mortality rate of dengue [1,2]. We used the Health Belief Model (HBM) and the Theory of Planned Behaviour (TPB) for interpreting and analysing the results, and for providing a better understanding of social and psychological motives of intended behaviour and attitudes. We found that if people suspected a dengue infection, they would go to a doctor at day one or two. On the other hand, when they were confronted with a ‘fever’, people first provided household remedies. These are important findings, meaning that people perceive dengue as a threat, which would prompt them to go to a doctor early if they know they are having dengue. Hence, a diagnostic tool for dengue to be used at home could possibly improve prompt doctor visits and reduce the mortality rate of dengue in Venezuela. To understand the HSB decisions taken by the participants in Chapter 2, it is important to reflect on the current health system of Venezuela. In Chapter 3, we described the access to health-care in the same population in which we examined the HSB regarding dengue and fever, using qualitative and quantitative methods. The health-system of Venezuela currently encompasses a private sector and a public sector. The public sector offers healthcare free of charge and comprises traditional public health centres (primary/secondary ‘ambulatorios’ and tertiary hospitals). Since 2003, a parallel public healthcare system was set up based on an agreement with Cuba. In this agreement, Cuba offered Cuban doctors to work in Venezuela ‘inside the
slum’ (in Spanish: ‘Barrio Adentro’) in return for oil from Venezuela. Our quantitative and qualitative results revealed the complex situation that people face to obtain timely and proper healthcare in Venezuela. Most people (79-81%) preferred to firstly visit a traditional ambulatorio in the case of fever or dengue, since the doctors in the traditional HCs were trusted. However, long waiting times and a lack of diagnostic and treatment supplies at these HCs were considered as major barriers to attend traditional HCs. On the other hand, these barriers were perceived to a lesser extent in the parallel HCs. However, a prominent reason not to go to parallel HCs was distrust towards the Cuban staff working at these centres. The private HCs were perceived as giving the best care, but these HCs were only available for people with a health insurance. The perceived barriers and advantages of the different health centres made people intend to visit multiple HCs to obtain satisfactory healthcare. The results of Chapter 3 show the current challenging situation people face when they search for healthcare, and highlight the need to improve health seeking behaviour (Chapter 2) and access to healthcare (Chapter 3) in Venezuela.

Mosquito control in Curaçao and Venezuela
Severe disease conditions of dengue can be avoided by adequate HSB (Chapter 2) or by appropriate access to healthcare (Chapter 3). Nevertheless, the best remedy against the consequences of dengue remains prevention [8,9]. Prevention might include personal protection against the vector of dengue, i.e. the mosquito of the Aedes spp.. However, preventing mosquitoes from multiplying by mosquito breeding site control is more effective on the long term [10,11]. Therefore, we explored which factors influenced dengue preventive practices in our study population in Maracay, Venezuela, as described in Chapter 4. We observed good knowledge on transmission routes of dengue and a high usage of personal protection, but found mosquito breeding sites in 57% of the examined houses. Although personal protection against mosquitoes is advised, mosquito breeding site control is more important for dengue control. We concluded in Chapter 4, that dengue control campaigns in Maracay should focus on promoting mosquito breeding site control in people’s houses and yards. Furthermore, complementary to the conclusions of Chapter 4, we examined the intentions to perform ‘Mosquito Breeding Site Control’ (MBSC) in Chapter 5. In this chapter, we incorporated theories of health behaviours in each stage of research, by designing, performing, analysing and interpreting studies based on a solid theoretical framework. A multidisciplinary research project in Curaçao including 339 participants for a (quantitative) survey, and 75 participants for qualitative research was set up. The mixed-methods (qualitative and quantitative methods) of this study were highly complementary, because both methods used an integrated theoretical framework based on the Health Belief Model (HBM) [12,13] and the Theory of Planned Behaviour (TPB) [14]. The introduction of this book provides an explanation of these health behaviour theories and in Chapter 5 the theoretical framework is presented. People reported high levels of knowledge, and high performance of MBSC. However, still 37% of the study population had a lower intention to perform MBSC. We identified factors related with this lower intention and presented three possible intervention methods to improve community participation in MBSC. These interventions are: (1) Ongoing, repetitive media coverage on MBSC to remind people of the importance of MBSC. These messages should be grounded in communities’ realities. (2) Visibility of governmental MBSC practices, which might motivate people to engage in MBSC. Hence, messages to the public concerning governmental MBSC practices should be provided. However, these messages should include that people’s own MBSC remain essential, preventing that people lose their sense of responsibility
to perform MBSC. (3) Usage of local community key persons serving as ‘ambassadors’ to promote MBSC in their community. A limitation of this study was that we relied on the ‘intention’ of participants, and did not measure the actual performed MBSC practices of our study population. On the other hand, this study is unique because of its multidisciplinary approach, which led to comprehensive and applicable outcomes.

Since Chapter 4 and 5 have revealed important social and behavioural determinants of community participation in MBSC, these studies provide practical implications, which might also be useful for other countries and communities. Therefore, performing similar studies in other contexts might expose more targets to enhance MBSC and lower the burden of arboviral diseases.

The impact of chikungunya on quality of life
The research in Curaçao was set up against the backdrop of a recent chikungunya epidemic and established dengue transmission of all four serotypes [15,16]. We used mixed-methods to investigate the impact of chronic chikungunya disease on quality of life (QoL). Quantitative data was collected using the RAND-36/SF-36 QoL questionnaire as described in Chapter 6. We obtained additional in-depth insights on chronic chikungunya sequelae and its impact on QoL of infected people by applying qualitative research methods in Chapter 7. Based on the definition of health from the World Health Organisation (WHO) [17], we investigated QoL by examining physical, emotional, social and economic well-being of chikungunya infected people. These were similar QoL concepts as were measured in Chapter 6 with the RAND-36/SF-36. The coping strategies were analysed using the principles of Lazarus’ theory on coping strategies [18,19].

Chapter 6 shows that QoL-scores from chikungunya patients were reduced on emotional, social and physical domains of QoL. The people who were characterized as suffering more severe from chikungunya (‘highly affected’) scored the lowest QoL scores. The in-depth interviews and focus group discussions in Chapter 7 show that impact on QoL concerned mainly physical and emotional well-being, whereas impact on social and economic well-being was limited. Physical impact of chikungunya was caused by musculoskeletal manifestations and other symptoms, leading to pain and limited mobility. Hence, e.g. dependency, hopelessness, a change of identity, and moodiness were experienced by participants. The employed coping strategies influenced the impact on QoL. A higher uptake of medical care and higher impact on QoL where linked to problem-focused coping strategies, whereas lower impact on QoL was observed by those performing emotion-focused coping strategies (focused on acceptance of the situation). The work we present in Chapter 7 is the first qualitative assessment on this topic.

The highly complementary findings of Chapter 6 and 7 highlight the unique value of mixed-methods research in public health, by providing important generalizable and in-depth knowledge on chikungunya and may inform public health policies. As QoL is often severely reduced for years, development of effective long-term treatment for chikungunya needs to be prioritized. Meanwhile, healthy coping strategies should be promoted in order to lessen the impact of chronic chikungunya in affected populations.

Clinical manifestations of chikungunya
Chikungunya causes a major public health impact in affected countries given its long-term sequelae
responsible for significant impairment of patients’ physical and mental quality of life [20]. Nevertheless, chronic chikungunya disease still lacks a proper definition and classification. In Chapter 6, we investigated the chronic clinical presentation in a population infected by chikungunya during the epidemic of 2014/2015 in Curaçao. Based on a novel classification tool, the Curaçao Long Term Chikungunya Sequelae (CLTCS) score, we classified the participants as being ‘recovered’, ‘mildly affected’ or ‘highly affected’ by long-term chikungunya sequelae. We estimated that people had a 79% chance to remain affected for longer than one month. Furthermore, 64% of the population was estimated to remain affected after 400 days. Long-term chikungunya sequelae typically included musculoskeletal manifestations. Tiredness, sleeplessness and neurological symptoms were also commonly reported. QoL scores were decreased in those still being affected by chikungunya, particularly in the ‘highly affected’ population. Therefore, this group should be targeted in health promotion strategies and monitored by health professionals. We propose the CLTCS score as an easily applicable tool for physicians to classify chronic chikungunya sequelae and quickly estimate the need for symptom-alleviating treatment.

As stated before, chikungunya and dengue both circulate in Curaçao and are transmitted by the same mosquito. Therefore, it is not unlikely that co-infections of these diseases occur in Curaçao. Nevertheless, concomitant dengue and chikungunya infection are not abundantly examined. We analysed acute and chronic disease manifestations of chikungunya mono-infections vs. chikungunya with preceding dengue in Chapter 8. We found a high prevalence of chikungunya with preceding dengue infection in our study population (36.3%). Furthermore, we found that preceding dengue infection at disease onset predicted an aggravated chronic disease. An important limitation of this study concerned the classification criteria of preceding dengue infection. Dengue was mainly based on a positive IgM, and therefore, dengue should be considered as ‘dengue infection preceding chikungunya’. Notwithstanding the limitations of this study, the association of preceding dengue and aggravated chronic disease is a new finding in the field of co-infections, with important implications for public health and research on (pathophysiology of) co-infections. Many areas are currently facing simultaneous dengue and chikungunya transmission [21]. In the light of the results of Chapter 8, the impact of the diseases in these areas might be bigger than previously thought.

Future perspectives
In this thesis, we investigated ways to improve HSB of dengue-infected patients in Venezuela. At the time the fieldwork was performed (2013-2014), Venezuela already faced an instable political situation with deterioration of the health system [4-6]. Though Chapter 2, 3 and 4 offer valuable recommendations for health authorities in Venezuela, the political situation became even more unstable in the following years. Prioritizing prevention of (severe) dengue infection and improving access to care might currently not be feasible in Venezuela, given the political instability and other major public health concerns Venezuela confronts. Based on this thoughts it is very difficult to come out with future perspectives. However, if Venezuela overcomes these challenges, the results of Chapter 2, 3 and 4 could aid in shaping new health policies.

Since after intensive mosquito control policies the Aedes spp. re-emerged in the Americas [22], there is a growing consensus that mosquito control will only be sustainable if relying on mutual efforts of both communities and governments [23]. As reflected upon in Chapter 4, it remains difficult to engage a
community in mosquito breeding site control (MBSC). Chapter 5 revealed several practical interventions that could potentially enhance community participation in MBSC. New techniques in mosquito control are being developed. Because exact efficacy of these techniques are not yet known, it remains important that community mobilization in MBSC is fostered. Currently, and possibly in the future as well, this is one of the most efficient and sustainable components of mosquito control. Though there is still much to improve in policies aimed at enhancing community participation in MBSC, a start can be made by applying the principles presented in this thesis (Chapter 5).

Chikungunya remains a neglected tropical disease. In the last years, outbreaks of chikungunya have been overshadowed by other global health concerns, in particular by Zika and its association with microcephaly [24]. The WHO defined this threat as ‘a public health emergency of international concern’ [25]. Consequently, researchers focused on Zika, but at that time chikungunya received considerably less attention. Therefore, still relatively little is known about chikungunya. The novel classification method presented in Chapter 6, the first qualitative study on impact of chikungunya on QoL (Chapter 7) and the novel finding that suggest that dengue infection preceding chikungunya predicts severe chronic sequelae (Chapter 8), which are all presented in this thesis, reflect the lack of research regarding chikungunya. Moreover, it suggests that the findings of this thesis are just the tip of the iceberg when it concerns knowledge on chikungunya. Since chikungunya causes major long-term impact on QoL of its patients and there is no efficient treatment available yet, we recommend to foster chikungunya research. There is still much to unravel in pathophysiology (of co-infections) and to improve in the treatment and prevention of this devastating disease.

A call for intervention-focused research

Lastly, we would like to stress the importance of performing applicable health research. Health is defined by the WHO as ‘a state of complete physical, mental, and social well-being not merely the absence of disease’ [17]. In clinical sciences, research is often limited to ‘curing diseases’, thereby neglecting the mental, social and cultural determinants of health. Health interventions will result in poorer promotion of health, when one of these determinants of health is overlooked.

This thesis reflects that a holistic (and multidisciplinary) view provide comprehensive insights in health problems. Chapter 5 demonstrates that mixed- methods based on health behaviour theories aid substantially in unravelling the complex dynamics of human behaviour (in this thesis: MBSC practices of communities). Furthermore, Chapter 6 and 7 demonstrate how quantitative and qualitative research on health-related QoL complement each other, by giving both in-depth and generalizable results. These chapters have all let to new and important implications for public health policies (as was discussed before). It is important to mention here, that at all stages of research (design, collection, analyses and interpretation of results) theory and practice of the different disciplines were applied.

Therefore, to achieve applicable and sustainable health interventions, researchers from different disciplines (e.g. epidemiologists, biologists, sociologists and psychologists) should bundle their strengths. A multidisciplinary effort is needed to move from attaining absence of disease to an all-encompassing ‘physical, mental and social well-being’.
References


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