Scaling up cost-effective physical activity interventions in a culturally diverse setting

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List of abbreviations

DALY	Disability-adjusted life-year
GBD	Global burden of disease
GP	General practitioner
ICER	Incremental cost-effectiveness ratio
MET	Metabolic equivalent of task
NCDs	Non-communicable diseases
PAF	Population attributable fraction
RCT	Randomized controlled trial
RR	Relative risk
SPACE	Swiss physical activity cost-effectiveness
WHO	World health organization

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Preface

This PhD thesis investigated the cost-effectiveness of physical activity interventions in the culturally diverse setting of Switzerland. After an abstract and an extended summary, the first chapter of the thesis elaborates on the background. Afterwards, the specific aims are described, which are then followed by the three papers forming part of this thesis. The thesis finishes with a chapter that summarizes the main findings, includes a general discussion, shows prospects for future research and finally draws overarching conclusions.

Abstract

Before this PhD project started, evidence showed that physical inactivity causes a substantial health and economic burden globally. For Switzerland, there was research available investigating the burden of physical inactivity. However, this research estimated the burden for the entire country without differentiating between sub regions although the prevalence of physical inactivity varies significantly between the French-, German- and Italian-speaking regions. Therefore, this thesis had three aims:

1. Estimating the health and economic burden of physical inactivity in Switzerland and for the French-, German- and Italian-speaking language regions separately
2. Systematically reviewing trial-based economic evaluations of interventions to reduce physical inactivity
3. Developing a health economic model that investigates the cost-effectiveness of physical activity interventions in Switzerland and its three language regions

The thesis showed that the burden of physical inactivity in Switzerland is substantial and that the French- and Italian-speaking regions are over-proportionally affected. These two regions distinguish themselves from the German-speaking region by having a higher prevalence of physical inactivity, higher per capita health care spending, and higher disease prevalence. Due to the substantial burden of physical inactivity, interventions aiming to increase physical activity should be considered. In the systematic review we conducted, we found evidence from randomized controlled trials indicating the cost-effectiveness of some physical activity interventions for primary prevention in adults. These interventions were then further evaluated in a cost-effectiveness model built for the Swiss setting. This model showed that Swiss policy makers have cost-effective options of physical activity promotion. We recommend that individualized advice and general practitioner referral be further evaluated as interventions and that decision-making considers the specifics of the Swiss language regions. Furthermore, we judge the cost-effectiveness model to be not only relevant for Switzerland but also for other multicultural countries. Based on similar data availability, our model has the potential to be applied beyond Switzerland, primarily to high-income countries with a comparable background, as a tool to guide societal efforts in primary prevention of physical-inactivity-related diseases.

Summary

Background and aims

Before this PhD project started, evidence showed that physical inactivity causes a substantial health and economic burden globally. For Switzerland, there was research available investigating the burden of physical inactivity. However, this research estimated the burden for the entire country without differentiating between sub regions although the prevalence of physical inactivity varies significantly between the French-, German- and Italian-speaking regions. Therefore, the aim of the first publication forming part of this PhD thesis was to estimate the burden of physical inactivity in Switzerland separately for the three language regions. In a systematic review that formed the basis of the second publication of this thesis, we aimed to identify cost-effective physical activity interventions that have been investigated in randomized controlled trials (RCTs). We then moved on and used findings from the first two PhD publications to develop a health economic model that investigates the cost-effectiveness of physical activity interventions in Switzerland and its three language regions.

Publication 1: Burden of physical inactivity in Swiss language regions

We estimated the burden of physical inactivity in Swiss adults from a societal perspective with a prevalence-based top-down approach using population attributable fractions (PAFs) and the latest data available for Switzerland. The following nine diseases related to physical inactivity were included in the analysis: coronary heart disease, hypertension, ischemic stroke, type 2 diabetes mellitus, breast cancer, colorectal cancer, osteoporosis, low back pain, and depression. Total disability-adjusted life-years (DALYs), health care costs, and productivity losses of these diseases were then retrieved from the global burden of disease study and a recent study on the costs of non-communicable diseases in Switzerland. In order to analyze the fraction of this total burden that is attributable to physical inactivity, we combined estimates of the prevalence of physical inactivity stemming from the Swiss Health Survey with literature-based estimates of disease incidence in the presence vs. absence of physical inactivity and resulting relative risks. The combination of these two types of parameters allowed us to estimate PAFs, which describe the proportion of disease occurrence that can be attributed to a certain risk factor.

The burden of physical inactivity in Switzerland in 2013 was estimated at CHF 1.610 billion (95%CI CHF 1.413-1.827 billion) plus 40,433 (95%CI 34,935-46,487) DALYs. The DALYs lost due to physical inactivity represented 2.0% (95%CI 1.7%-2.2%) of total DALYs lost in Switzerland. Health care costs caused by physical inactivity were estimated at CHF 0.802 billion (95%CI CHF 0.684-0.934 billion) or at 1.2% (95%CI 1.0%-1.3%) of total health care expenditures. This was equivalent to CHF 116 (95%CI CHF 99-135) per capita. Productivity

losses were valued at CHF 0.808 billion (95%CI CHF 0.653-0.983 billion) or CHF 117 (95%CI CHF 94-142) per capita. Furthermore, we found that the French- and Italian-speaking regions, which are home to 30% of the Swiss population, contribute more than 45% to the burden of physical inactivity. Reasons include a higher prevalence of physical inactivity, higher per capita health care spending, and higher disease prevalence than the German-speaking region. In addition, the per capita burden was twice as high in the French- and Italian-speaking regions compared to the German-speaking region.

In conclusion, this study showed that physical inactivity causes a substantial health and economic burden in Swiss adults and that the French- and Italian-speaking regions are over-proportionally affected. Investments in interventions aiming to increase physical activity should therefore be considered. Such interventions should be cost-effective and this study indicates that regional differences likely influence the cost-effectiveness of physical activity interventions.

Publication 2: Systematic review of cost-effectiveness of physical activity interventions

In this systematic review, we aimed to summarize evidence from RCT-based economic evaluations of primary prevention physical activity interventions in adult populations outside the workplace setting. We included cost-effectiveness analyses in which all data (except unit costs) came from one RCT. As the studies reported different physical activity outcomes, effect measures were standardized in metabolic equivalent of task (MET)-hours gained per person per day. We further calculated the mean differences in costs and outcomes between intervention and control as a basis for estimating the incremental cost-effectiveness ratio (ICER) in US$ per MET-hour gained. A benchmark between US$0.44 and US$0.63 per MET-hour gained, which was based on the health care costs and productivity losses of physical inactivity in Switzerland, was used to assess the cost-effectiveness of interventions.

Twelve studies published between 2000 and 2018 were included in the final analysis. In these twelve studies, 22 interventions were investigated. Interventions were based on advice, goal setting and follow-up support, exercise classes, financial incentives or teaching on behavioral change. The effects and costs of the interventions varied widely and so did the ICER. Four interventions showed an ICER below the applied benchmark. These four interventions were based on individualized advice delivered in four different ways: print (postal mail) or web (website and email) and in a basic form (standard advice) or with additional environmental components (e.g., walking and cycling routes). One other intervention that was based on general practitioner (GP) referral to behavior change counseling by telephone had an ICER of US$0.64 per MET-hour gained. One pedometer-based individualized goal-setting intervention had an ICER of US$0.67 per MET-hour gained. Another intervention was based on exercise prescription and had an ICER of US$0.85 per MET-hour gained. All other interventions had an ICER above US$1.00 per MET-hour gained.

In conclusion, we found evidence from RCTs indicating cost-effectiveness of some physical activity interventions for primary prevention in adults. However, cost-effectiveness results varied widely among interventions and the majority of interventions would not be cost-effective according to the benchmark applied. Four interventions that delivered individualized advice via print or web showed the best value (physical activity gains) for money (intervention costs).

Publication 3: Cost-effectiveness model of physical activity interventions

The cost-effectiveness model of physical activity interventions was built as a proportional multistate life table model for the Swiss adult population over their lifetime. We named it the Swiss Physical Activity Cost-Effectiveness (SPACE) model. In the model, a comprehensive set of diseases was included, namely breast cancer, colorectal cancer, type 2 diabetes mellitus, coronary heart disease, ischemic stroke, osteoporosis, low back pain and depression. The effect of interventions on diseases was modelled with data from recent meta-analyses. Interventions analyzed were individualized physical activity advice, pedometer with individualized goal setting, GP referral to telephone-based counseling and exercise prescription. Intervention effects were taken from RCTs, and intervention costs were based on a bottom-up approach with Swiss prices. Cost-effectiveness in terms of cost per DALY averted compared to "doing nothing" as well as cost-effectiveness between interventions were analyzed on the national level and separately for the French-, German- and Italian-speaking language regions. The frequently assumed tentative willingness-to-pay threshold of CHF 100,000 per DALY was used to assess the cost-effectiveness of interventions. Interventions that led to better health and were at the same time cost-saving were categorized as "dominant".

From a societal perspective and irrespective of language region, all four interventions were cost-saving and more effective compared to "doing nothing". At the national level and in the German-speaking region, individualized advice was the preferable intervention followed by GP referral. These two interventions dominated pedometer and exercise prescription. In the French- and Italian speaking regions, GP referral was the preferable intervention that dominated the three others. From a health care payer perspective, however, individualized advice was the preferable intervention followed by GP referral. The uncertainty underlying key model input parameters led to substantial variation in the modelled results, according to the probabilistic sensitivity analysis.

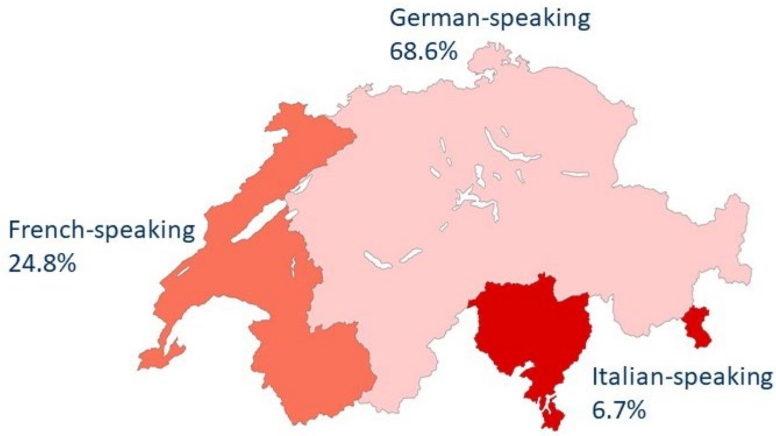
In conclusion, we hope to inform efficient resource allocation and evidence-based decision-making in primary prevention in Switzerland. We recommend that individualized advice and GP referral be further evaluated as interventions and that decision-making considers the specifics of the Swiss language regions. Furthermore, we judge the SPACE model to be not only relevant for Switzerland but also for other multicultural countries. Based on similar data availability, the SPACE model has the potential to be applied beyond Switzerland, primarily to high-income countries with a comparable background, as a tool to guide societal efforts in primary prevention of physical-inactivity-related diseases.

1. Background

1.1 Switzerland - a multilingual, multicultural country

Switzerland has a population size of about 8.5 million [4]. Influenced by its neighboring countries, there are three main language regions in this rather small country: German-speaking, French-speaking and Italian-speaking (Figure 1). The fourth national language is Romansh, which is spoken by a minority of about 0.5% of the population [5]. There are also many foreigners contributing to the linguistic diversity of Switzerland. The most commonly spoken foreign languages are English, Portuguese, Spanish, Serbian, Croatian and Albanian [5]. The relationship between language and culture has been extensively studied [6] and recent concepts suggest an interactional relationship between the two [7]. Due to its linguistic diversity, Switzerland can be considered a culturally diverse setting.

Figure 1: Switzerland and its three main language regions



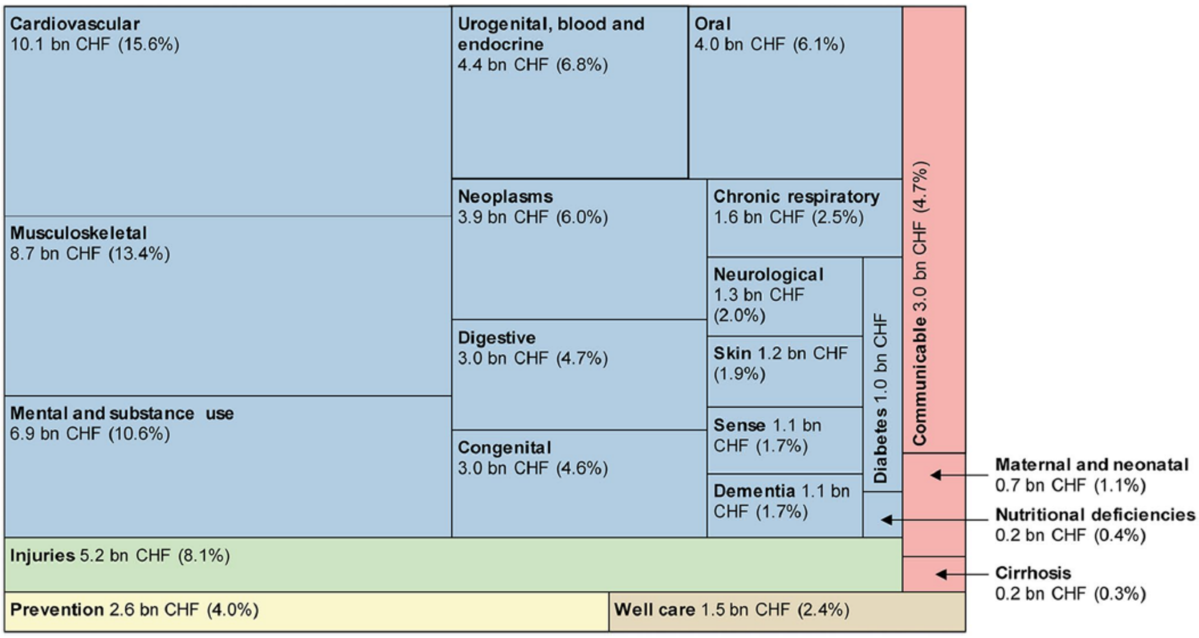
Interestingly, we see substantial differences in health behavior, self-perceived health status and health care resource use between the language regions. Examples include prevalence of smoking, alcohol abuse, unhealthy eating habits and physical inactivity that are on average higher in the French- and Italian-speaking regions compared to the German-speaking region [8]. Furthermore, self-perceived health status is highest in the German-speaking region, followed by the French-speaking and Italian-speaking regions [8]. In addition, there are more doctor's visits per year in the French- and Italian-speaking regions than in the German-speaking region [8]. Research also showed variation in the cost of care during the last year of life between Swiss language regions and highlighted the importance of cultural factors for the delivery and utilization of health care [9].

1.2 The relevance of non-communicable diseases in Switzerland

Switzerland has the second highest life expectancy worldwide, which is 84 years [10]. However, Switzerland also has the second highest health care expenditure with US$ 9836 per capita [11]. Non-communicable diseases (NCDs) such as cardiovascular diseases, musculoskeletal diseases and neoplasms cause 80% of the health and economic burden in Switzerland (Figure 2) [12, 13]. This substantial burden is the reason for the strategic initiative for the prevention of NCDs by the Swiss Federal Office of Public Health [14].

In addition to personal and environmental factors, modifiable lifestyle factors influence the incidence of NCDs and life expectancy [15-19]. Modifiable lifestyle factors include smoking, alcohol abuse, unhealthy eating habits and physical inactivity. All these lifestyle factors are common in Switzerland [8]. Furthermore, the health and economic burden due to smoking, alcohol abuse and physical inactivity has been shown to be substantial [20-22]. This PhD project focuses on one of these lifestyle factors: physical inactivity.

Figure 2: Health care expenditure in Switzerland by disease group and disease (from Wieser et al. [13])



1.3 Physical activity

Physical activity is defined as bodily movement produced by skeletal muscles that results in energy expenditure [23]. Physical activity occurs for different reasons in different domains throughout the day. The four domains are occupational, transportation, household and leisure-time physical activity [24].

Physical activity is associated with a wide range of health benefits. Higher levels of physical activity lead to reduced all-cause mortality [25-29]. Furthermore, physical activity reduces the risk of several NCDs such as coronary heart disease, ischemic stroke, type 2 diabetes mellitus, colorectal cancer, breast cancer, depression and low back pain [30-32].

Due to the health-enhancing effects of physical activity, the world health organization (WHO) recommends at least 2.5 hours of physical activity with moderate intensity per week or 1.25 hours of physical activity with high intensity per week [33]. These WHO guidelines have been adopted by the Swiss Federal Office of Sports [34]. Most recent recommendations have been issued for the US [35]. The US guidelines specify higher levels of physical activity: adults should do at least 2.5 hours to 5 hours a week of moderate-intensity, or 1.25 hours to 2.5 hours a week of vigorous-intensity physical activity, or an equivalent combination of moderate- and vigorous-intensity activity. Adults should also do muscle-strengthening activities on two or more days a week. Children and adolescents should be physically active for at least one hour per day.

1.4 Physical inactivity in Switzerland

Physically inactive people do not comply with physical activity recommendations. Although physical inactivity can be considered a global pandemic, the problem is of particular concern in high-income countries. In 2016, the prevalence of physical inactivity in high-income countries was twice that in low-income countries (36.8% versus 16.2%) [36].

In Switzerland, 24.3% of the population over the age of 15 is physically inactive [8]. However, the prevalence of physical inactivity shows significant regional differences: 21.0% of the adult population in the German-speaking region is physically inactive whereas 32.6% are physically inactive in the French-speaking region and 31.5% in the Italian-speaking region. These regional differences can also be seen in children: during an average school day, 21% of the children in the German-speaking region are physically active for less than one hour whereas this number is 31% in the other two language regions [37]. People with higher education and higher income generally tend to be more active. Recent studies, however, showed that the regional differences of physical inactivity in Switzerland cannot be explained by such socio-demographic differences or differences in the built environment [38-41].

1.5 The burden of physical inactivity in Switzerland

Cost-of-illness studies estimate the burden of specific health problems at the population level in terms of losses of quality and length of life, health care resource use and productivity losses. Cost-of-illness studies are often used to demonstrate the importance of particular health problems to policy makers and the public. In these circumstances, the magnitude of a health problem is used to justify or guide resource allocation, e.g. the allocation of intervention/prevention programs or the allocation of research funding [42, 43]. Although cost-of-illness studies are of a descriptive nature, they can also be used to analyze the magnitude of a certain aspect of a health problem. In addition, cost-of-illness studies define the upper limit of resources that could be saved through interventions and therefore serve as a framework for cost-effectiveness analyses of interventions [44, 45].

The global burden of physical inactivity is substantial. In 2015, 1.6 million deaths and 34.6 million disability-adjusted life-years (DALYs) were attributable to physical inactivity [46]. Furthermore, the health problem is getting worse as deaths and DALYs attributable to physical inactivity increased by more than 17% between 2005 and 2015. The major health burden of physical inactivity has also been shown in other studies [47]. Besides the substantial health burden, physical inactivity also causes an associated economic burden worldwide [48-50].

In a recent study, we estimated health care costs due to physical inactivity at CHF 1.2 billion or at 1.8% of total health care expenditures in Switzerland in 2011 and productivity losses at CHF 1.4 billion [22]. Furthermore, 326,310 cases of disease and 1,153 deaths were attributable to physical inactivity in 2011. Although the prevalence of physical inactivity varies significantly between Swiss language regions, this study estimated costs for the entire country without differentiating between sub regions. Therefore, the aim of the first publication forming part of this PhD thesis was to estimate the burden of physical inactivity in Switzerland separately for the German-, French- and Italian-speaking regions.

1.6 Physical activity interventions

Physical activity behavior is determined by individual, social and environmental factors (Figure 3) [51]. Physical activity interventions initially were targeting individual-level health, and interventions intending to change physical activity on a population level emerged later. More recently, a systems approach that acknowledges the complex interaction of individual- and population-level interventions has been promoted (Figure 4) [52]. In accordance with this systems approach, the Global Advocacy for Physical Activity defined the following seven “best investments” for physical activity with good evidence of effectiveness and worldwide applicability: school-based interventions, transport, urban design, primary health care, public education (including mass media), community-based interventions (including workplace) and the sports system [53].

Figure 3: Adapted ecological model of the determinants of physical activity (from Bauman et al. [51])

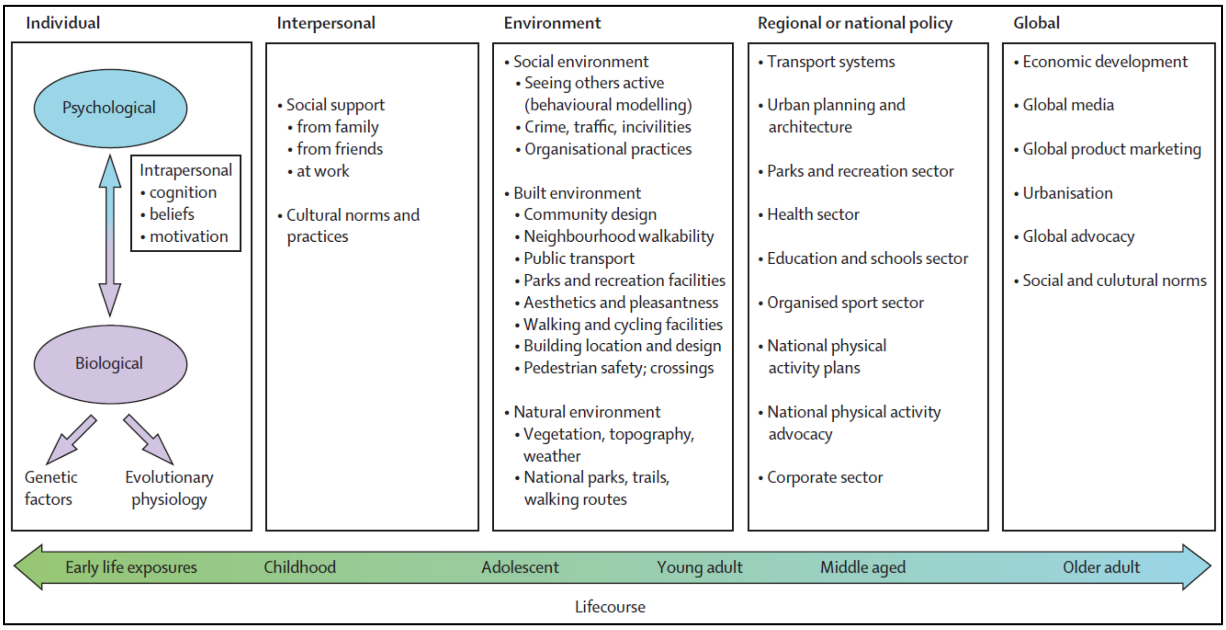


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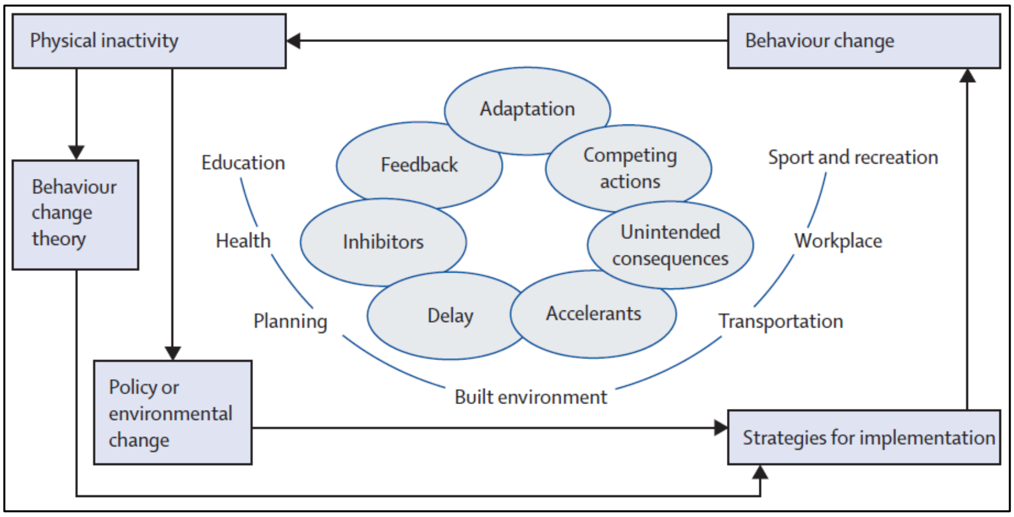
Figure 4: Systems approach to physical activity (from Kohl et al. [52])



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There are hundreds of primary studies investigating the effectiveness of physical activity interventions, and it is not surprising that systematic reviews are also numerous [54-71]. However, with limited resources available, policy makers are interested in interventions that provide best value for money. Therefore, interventions aiming to increase physical activity should not only prove effectiveness in terms of health outcomes but also cost-effectiveness.

1.7 Cost-effectiveness analyses

Cost-effectiveness analyses compare costs and outcomes of an intervention with a comparator and are also called full economic evaluations [72]. In full economic evaluations, costs can be reported from different perspectives, e.g. intervention costs, health care costs offset due to interventions or productivity losses offset due to interventions. There are also different outcome measures that can be used such as MET-hours per week gained, DALYs averted or quality-adjusted life-years (QALYs) gained (strictly, the latter two would be named cost-utility analyses instead of cost-effectiveness analyses). The difference in costs between intervention and comparator is divided by the difference in the effect between intervention and comparator to estimate the incremental cost-effectiveness ratio (ICER). The ICER describes how much it would cost to gain one MET-hour per week, how much it would cost to avert one DALY or how much it would cost to gain one QALY. This ICER can then be compared between interventions in order to find the most cost-effective one. Some countries also know an ICER threshold and if the ICER of an intervention lies above this threshold, the intervention is no longer considered to be cost-effective. Consequently, cost-effectiveness analyses investigate value for money. However, there is a second relevant question in economic evaluations and that is the one about affordability. Affordability is investigated in budget impact analyses. Budget impact analyses estimate expected changes in health care expenditure after the introduction of a new intervention [73]. However, a budget impact analysis can also be useful for budget or resource planning.

There are two different approaches in economic evaluations: trial-based economic evaluations and model-based economic evaluations [74]. However, the transition between the two is smooth. In a trial-based economic evaluation, costs are measured alongside a clinical trial investigating the effect of the intervention [75-78]. In a model-based economic evaluation, data on the effect and the costs from different sources are combined in a decision-analytic model [79, 80]. Both methodological approaches have strengths and weaknesses [81-85]. The main strengths of a trial-based economic evaluation are related to the methodological strength of randomized controlled trials (RCTs), i.e. the exclusion of potential biasing factors [80]. However, RCTs have weaknesses when directly used for policy making that are related to the efficacy versus effectiveness discussion [80]: areas of potential concern include choice of comparator, protocol-driven costs and outcomes, artificial environment, intermediate versus final outcomes, inadequate participant follow-up, and selected patient and provider populations [80]. Model-based economic evaluations have the strength that they can synthesize the best evidence available in case relevant head-to-head clinical trials are missing, costs were not measured within trials, intermediate endpoints were captured or trial follow-up was short-term [74]. Nevertheless, inappropriate use of clinical data, bias in observational data, difficulties of extrapolation and concerns about transparency or validity of models are major problems [74]. These strengths and weaknesses make it evident that for policy-making reasons the two methods are better used complementarily than alternatively [81].

Several systematic reviews have investigated the cost-effectiveness of physical activity interventions [86]. Most reviews focused on specific settings (e.g. school, workplace, community) and did not pay much attention to the methodological approaches (trial-based or model-based) chosen in the identified economic evaluations [86]. The availability of trial-based economic evaluations of physical activity interventions seems to be limited [54, 60, 87, 88], and to the best of our knowledge, no systematic review has focused on this topic. Consequently, the second publication forming part of this PhD thesis aimed to systematically review trial-based economic evaluations of interventions to increase physical activity.

1.8 Modelling cost-effectiveness of physical activity interventions

Policy makers have to make decisions on a national or even regional level and cost-effectiveness of physical activity interventions may differ between regions. This could be specifically the case in Switzerland where the prevalence of physical inactivity but also health care resource use substantially differs between language regions. Therefore, policy makers need to know the cost-effectiveness of physical activity interventions regionally in order to allocate resources efficiently. Health economic modelling can support decision-making, particularly in the absence of region-specific data [74, 79].

A variety of model structures have been presented for the economic evaluation of public health interventions for NCDs [89]. Previous models investigating the cost-effectiveness of physical activity interventions include decision trees [90, 91], Markov models [92-96], microsimulation models [97, 98] as well as multistate life table models [99-102]. Most models were built for the UK [90-94, 97-99, 103-108], Australia [100, 102, 109-111] and the USA [96, 112-114]. However, no such model is yet available for Switzerland. Therefore, the aim of the third publication forming part of this PhD thesis was to develop a health economic model that investigates the cost-effectiveness of physical activity interventions in Switzerland and its three language regions.

To the best of our knowledge, all previous models investigating physical activity interventions were built from a health care payer perspective. Therefore, our aim was to develop a model not only from a health care payer perspective but also from a societal one, meaning we also included productivity losses [115]. Furthermore, we aimed to account for the fact that the use of certain resources does not increase when scaling up the interventions (fixed costs) [115]. The term ‘scaling up’ describes “the ambition or process of expanding the coverage of health interventions, but can also refer to increasing the financial, human and capital resources required to expand coverage” [116] and it originates from the time when the HIV/AIDS pandemic was the most relevant public health issue. Nowadays, physical inactivity is also seen as a pandemic and it is not surprising to see similar considerations regarding scaling up of interventions in this field [52, 117, 118]. It is suggested that cost-effective and financially feasible interventions should be considered for scaling up [119-121].

2. Aims

The aims of this PhD project were:

1. Estimating the health and economic burden of physical inactivity in Switzerland and for the French-, German- and Italian-speaking language regions separately
2. Systematically reviewing trial-based economic evaluations of interventions to reduce physical inactivity
3. Developing a health economic model that investigates the cost-effectiveness of physical activity interventions in Switzerland and its three language regions

3. Publication 1: Physical inactivity caused economic burden depends on regional cultural differences

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4. Publication 2: Physical activity interventions for primary prevention in adults: a systematic review of randomized controlled trial-based economic evaluations

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5. Publication 3: Cost-effectiveness analysis of physical activity interventions in a multicultural setting: a modelling study

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6. Discussion

Before this PhD project started, evidence showed that physical inactivity causes a substantial health and economic burden globally [47, 49]. For Switzerland, there was research available investigating the burden of physical inactivity [22]. However, this research estimated the burden for the entire country without differentiating between sub regions although the prevalence of physical inactivity varies significantly between Swiss language regions [8]. Therefore, the aim of the first publication forming part of this PhD thesis was to estimate the burden of physical inactivity in Switzerland separately for the German-, French- and Italian-speaking regions [1]. As this first PhD publication showed a substantial burden of physical inactivity in the Swiss language regions, we investigated interventions aiming to increase physical inactivity in a systematic review that underlies the second publication forming part of this PhD thesis [2]. We then moved on and used findings from the first two PhD publications to develop a health economic model that investigates the cost-effectiveness of physical activity interventions in Switzerland and its three language regions [3]. The cost-effectiveness model has recently been submitted for publication. This chapter summarizes the main findings of the two publications forming part of this PhD thesis and the paper that has been submitted for publication, discusses them and provides prospects for future research.

6.1 Summary of findings

6.1.1 Aim 1: Burden of physical inactivity in Swiss language regions [1]

We estimated the burden of physical inactivity in Swiss adults from a societal perspective with a prevalence-based top-down approach using population attributable fractions (PAFs) and the latest data available for Switzerland. The following nine diseases related to physical inactivity were included in the analysis: coronary heart disease, hypertension, ischemic stroke, type 2 diabetes mellitus, breast cancer, colorectal cancer, osteoporosis, low back pain, and depression. Total DALYs, health care costs, and productivity losses of these diseases were then retrieved from the global burden of disease (GBD) study and a recent study of the costs of NCDs in Switzerland. In order to analyze the fraction of this total burden that is attributable to physical inactivity, we combined estimates of the prevalence of physical inactivity stemming from the Swiss Health Survey in 2012 with literature-based estimates of disease incidence in the presence vs. absence of physical inactivity and resulting relative risks (RRs). The combination of these two types of parameters allowed us to estimate PAFs, which describe the proportion of disease occurrence that can be attributed to a certain risk factor.

The burden of physical inactivity in Switzerland in 2013 was estimated at CHF 1.610 billion (95%CI CHF 1.413-1.827 billion) plus 40,433 (95%CI 34,935-46,487) DALYs. The DALYs lost due to physical inactivity represented 2.0% (95%CI 1.7%-2.2%) of total DALYs lost in Switzerland. Osteoporosis contributed 34.4% of the DALYs, low back pain 17.7%, cardiovascular diseases 21.9%, and depression 8.3%. Health care costs caused by physical inactivity were estimated at CHF 0.802 billion (95%CI CHF 0.684-0.934 billion) or at 1.2% (95%CI 1.0%-1.3%) of total health care expenditures. This was equivalent to CHF 116 (95%CI CHF 99-135) per capita. Of these health care costs, 35.4% were attributed to cardiovascular diseases (coronary heart disease, ischemic stroke, and hypertension), 20.9% to low back pain, 17.5% to depression, and the remaining 26.2% to osteoporosis, type 2 diabetes mellitus, colorectal cancer, and breast cancer. Productivity losses were valued at CHF 0.808 billion (95%CI CHF 0.653-0.983 billion) or CHF 117 (95%CI CHF 94-142) per capita and were mainly caused by low back pain (38.2%), depression (20.0%), and cardiovascular diseases (17.9%).

Furthermore, we found that the French- and Italian-speaking regions, which are home to 30% of the Swiss population, contribute more than 45% to the burden of physical inactivity. Reasons include a higher prevalence of physical inactivity, higher per capita health care spending, and higher disease prevalence than the German-speaking region. In addition, the per capita burden was twice as high in the French- and Italian-speaking regions compared to the German-speaking region. In the German-speaking region, we estimated per capita health care costs due to physical inactivity at CHF 87, productivity losses at CHF 96, and DALYs per 1,000 persons at 4.5. Health care costs in the French-speaking region were estimated at CHF 179 per capita, productivity losses at CHF 164, and DALYs at 8.9 per 1,000 persons. In the Italian-speaking region, per capita health care costs were valued at CHF 172, productivity losses at CHF 153, and DALYs per 1,000 persons at 8.6.

In conclusion, this study showed that physical inactivity causes a substantial health and economic burden in Swiss adults and that the French- and Italian-speaking regions are over-proportionally affected. Investments in interventions aiming to increase physical activity should therefore be considered. Such interventions should be cost-effective and this study indicates that regional differences likely influence the cost-effectiveness of physical activity interventions. Furthermore, this study showed that low back pain and depression substantially add to the burden of physical inactivity. Consequently, future studies should consider these two diseases when estimating the burden of physical inactivity.

6.1.2 Aim 2: Systematic review of cost-effectiveness of physical activity interventions [2]

In this systematic review, we aimed to summarize evidence from RCT-based economic evaluations of primary prevention physical activity interventions in adult populations outside the workplace setting. We included cost-effectiveness analyses in which all data (except unit costs) came from one RCT. As the studies reported different physical activity outcomes, effect measures were standardized in metabolic equivalent of task (MET)-hours gained per person per day. We further calculated the mean differences in costs and outcomes between intervention and control as a basis for estimating the ICER in US$ per MET-hour gained. A benchmark between US$0.44 and US$0.63 per MET-hour gained, which was based on the health care costs and productivity losses of physical inactivity in Switzerland, was used to assess the cost-effectiveness of interventions.

Twelve studies published between 2000 and 2018 were included in the final analysis. In these twelve studies, 22 interventions were investigated. Interventions were based on advice, goal setting and follow-up support, exercise classes, financial incentives or teaching on behavioral change. The effects and the costs of the interventions varied widely and so did the ICER. Four interventions showed an ICER below the applied benchmark. These four interventions were based on individualized advice delivered in four different ways: print (postal mail) or web (website and email) and in a basic form (standard advice) or with additional environmental components (e.g., walking and cycling routes and physical activity possibilities and initiatives in participants' own neighborhood and home exercises). One other intervention that was based on behavior change counseling by telephone had an ICER of US$0.64 per MET-hour gained. One pedometer-based individualized step-related goal setting intervention had an ICER of US$0.67 per MET-hour gained [39]. Another intervention was based on face-to-face advice, goal setting, follow-up face-to-face meeting and follow-up telephone counseling [36]. This intervention had an ICER of US$0.85 per MET-hour gained. All other interventions had an ICER above US$1.00 per MET-hour gained.

In conclusion, we found evidence from RCTs indicating cost-effectiveness of some physical activity interventions for primary prevention in adults. However, cost-effectiveness results varied widely among interventions and the majority of interventions would not be cost-effective according to the benchmark applied. Four interventions that delivered individualized advice via print or web showed best value (physical activity gains) for money (intervention costs). Our study also showed that trial-based evidence on the cost-effectiveness of physical activity interventions is relatively scarce. Therefore, we recommend that future studies investigating the efficacy or effectiveness of interventions aimed at increasing physical activity consider costs as an additional outcome and assess cost-effectiveness.

6.1.3 Aim 3: Cost-effectiveness model of physical activity interventions [3]

The cost-effectiveness model of physical activity interventions was built as a proportional multistate life table model for the Swiss adult population over their lifetime. We named it the

Swiss Physical Activity Cost-Effectiveness (SPACE) model. In the model, a comprehensive set of diseases was included, namely breast cancer, colorectal cancer, type 2 diabetes mellitus, coronary heart disease, ischemic stroke, osteoporosis, low back pain and depression. The effect of interventions on diseases was modelled with data from recent meta-analyses. Interventions analyzed were individualized physical activity advice, pedometer with individualized goal setting, general practitioner (GP) referral for telephone-based counseling and exercise prescription. Intervention effects were taken from RCTs and intervention costs were based on a bottom-up approach with Swiss prices. Cost-effectiveness in terms of cost per DALY averted compared to "doing nothing" as well as cost-effectiveness between interventions were analyzed on the national level and separately for the French-, German- and Italian-speaking language regions. The frequently assumed tentative willingness-to-pay threshold of CHF 100,000 per DALY was used to assess the cost-effectiveness of interventions. Interventions that led to better health and were at the same time cost-saving were categorized as "dominant".

From a societal perspective and irrespective of language region, all four interventions were cost-saving and more effective compared to "doing nothing". At the national level and in the German-speaking region, individualized advice was the preferable intervention followed by GP referral. These two interventions dominated pedometer and exercise prescription. In the French- and Italian speaking regions, GP referral was the preferable intervention that dominated the three others. From a health care payer perspective, however, individualized advice was the preferable intervention followed by GP referral. The uncertainty underlying key model input parameters led to substantial variation in the modelled results, according to the probabilistic sensitivity analysis.

In conclusion, we hope to inform efficient resource allocation and evidence-based decision-making in primary prevention in Switzerland. We recommend that individualized advice and GP referral be further evaluated as interventions and that decision-making considers the specifics of the Swiss language regions. Furthermore, we judge the SPACE model to be not only relevant for Switzerland but also for other multicultural countries. Based on similar data availability, the SPACE model has the potential to be applied beyond Switzerland, primarily to high-income countries with a comparable background, as a tool to guide societal efforts in primary prevention of physical-inactivity-related diseases.

6.2 General discussion

6.2.1 Diseases related to physical inactivity

The following five diseases can be considered the “core set of diseases related to physical inactivity” as they are frequently used in health economic studies investigating physical activity [96, 97, 100]: breast cancer, colorectal cancer, type 2 diabetes mellitus, coronary heart disease and ischemic stroke. Osteoporosis, low back pain and depression have been taken into account less frequently [94, 122, 123]. However, it has recently been shown that physical activity reduces incidence of these three diseases [31, 32, 122]. Consequently, we included them in the first PhD paper (burden of physical inactivity) as well as in the third (cost-effectiveness model of interventions). In the first paper, we showed that all three diseases substantially add to the burden of physical inactivity. In the third paper, these three diseases had a substantial influence on the cost-effectiveness of interventions. Consequently, it can be suggested that future studies investigating the burden of physical inactivity include osteoporosis, low back pain and depression. In addition, the inclusion of the three diseases can be recommended for cost-effectiveness models investigating physical activity interventions.

While we included hypertension in the first PhD paper, we no longer considered it in the third paper. Hypertension is modelled as a disease in its own right in some studies [97, 124] or as part of cardiovascular diseases [125] or as a risk factor for cardiovascular diseases [126]. As the impact of hypertension on the burden of physical inactivity was rather small in the first PhD paper and we did not specifically model other risk factors for the diseases included, we did not consider hypertension in the cost-effectiveness model.

Obesity was also not included as a specific primary disease in either the first or the third PhD paper, as the main burden related to obesity was considered to be caused by cardiovascular diseases and type 2 diabetes mellitus. Therefore, obesity was considered a risk factor rather than a disease on its own. This is in line with many other health economic studies investigating physical inactivity [90-97, 99, 100, 102].

Although we tried to be comprehensive with diseases related to physical inactivity, there may be other diseases for which physical inactivity will be established as a risk factor such as dementia and Alzheimer’s disease [127-130]. Due to conflicting evidence, however, these diseases were not included in our work [131]. A recently-published, very extensive scientific report also found strong evidence that greater amounts of physical activity are associated with reduced risk of developing bladder cancer, endometrial cancer, esophageal cancer, gastric cancer, renal cancer, and anxiety disorders [24]. These diseases may be included in future studies investigating the health economic aspects of physical inactivity.

6.2.2 Cost-effectiveness evaluation of physical activity interventions

The cost-effectiveness evaluation of physical inactivity interventions is subject to several challenges. For example, the ICER benchmark applied in the second PhD paper (between US$0.44 and US$0.63 per MET-hour gained, which is equal to CHF 0.53 and CHF 0.76 per MET-hour gained for 2018) was based on 2.5 hours of moderate intensity physical activity (at 3 METs) per week and the per capita costs of physical inactivity in Switzerland. As approximately one quarter of the Swiss population is physically inactive, the cost per capita for the physically inactive ones is four times higher than for the total population. Therefore, the benchmark for an intervention targeting specifically the inactive people would be approximately four times higher, i.e. between CHF 2 and CHF 3 per MET-hour gained. Consequently, there is no particular benchmark to use for the cost-effectiveness evaluation of physical activity interventions. Furthermore, the outcome will depend on the different types of costs considered for the intervention under evaluation (intervention costs, health care costs offset, productivity losses offset). Further aspects that influence the cost-effectiveness include: the target population (e.g. general population or specifically the inactive ones), the population reached (e.g. 1%, 3%, 5%), and the time horizon considered. As some of these aspects cannot be evaluated in trials, health economic modelling will always play an important role for the evaluation of the cost-effectiveness of physical activity interventions. Therefore, the combination of within-trial cost-effectiveness analysis and beyond-trial modelling, as recently published by Harris et al. [132], may become a widely used method in the future. Modelling also allows for a relatively simple estimation of DALYs averted (or QALY gained). Such more generic outcomes, in comparison to a physical activity specific outcome like MET-hours gained, make it possible to compare interventions between different risk factors for NCDs (e.g. smoking, diet, etc) or compare interventions with other treatments for primary or secondary prevention.

6.2.3 Cost-effectiveness studies run the risk of favoring interventions that only add small benefit

Wu et al. [88] showed previously that some interventions that increased physical activity levels only by small amounts, such as stair climbing prompts, may be very cost-effective due to the very low intervention costs. This finding was supported by the results from the second PhD publication where the intervention investigated by Golsteijn et al. [133] that provided individualized advice delivered via web and included additional environmental components was the most cost-effective. The intervention itself had a negative effect of -0.06 MET-hours gained per person per day when comparing physical activity at the one-year follow-up with baseline. However, compared to the "doing nothing" control group, the incremental effect was 0.26 MET-hours gained per person per day, which is equivalent to approximately 5 min of moderate physical activity per person per day. Although this is a positive effect, it can be considered a relatively low incremental physical activity gain that is not sufficient to lead to substantial health benefits [35]. The annual intervention costs were US$25.14 per person. This led to an ICER of US$0.27 per MET-hour gained, which was below the benchmark of between US$0.44 and US$0.63 per MET-hour gained applied in this study. Therefore, the intervention was considered cost-effective although the physical activity gain can be considered insufficient to lead to substantial health benefits. These findings were also confirmed in the third PhD paper, where we also included the intervention by Golsteijn et al. [133]. Consequently, relying on cost-effectiveness alone might favor interventions that are unable to add substantial health benefits. Therefore, we recommend that the specifics of each intervention should be considered and additional criteria such as minimal clinically-relevant effectiveness thresholds might be used in future physical activity policy decision-making.

6.2.4 Regional differences in physical inactivity and their consequences for policy making

In Switzerland, 24.3% of the population over the age of 15 is physically inactive [8]. However, the prevalence of physical inactivity shows significant regional differences: 21.0% of the adult population in the German-speaking region is physically inactive whereas 32.6% are physically inactive in the French-speaking region and 31.5% in the Italian-speaking region [8]. Due to this difference in the prevalence of physical inactivity and other differences such as per capita health care spending and disease prevalence, we showed in the first PhD paper that the per capita burden of physical inactivity is twice as high in the French- and Italian-speaking regions as in the German-speaking region [1]. Furthermore, the cost-effectiveness of physical activity interventions differed between language regions, as investigated in the third PhD paper [3]. In this paper, we showed that in regions with higher prevalence of physical inactivity, more costly interventions can still be cost-effective. These findings suggest that physical inactivity is tackled language-region specifically in Switzerland. This may also be the case for other risk factors for NCDs as they also show substantial regional variation [8].

6.2.5 Summary of strength and limitations

This PhD thesis has a number of strengths, but also some limitations that should be considered. One major strength is the societal perspective chosen for the cost assessment, i.e. the incorporation of productivity losses. Previous studies mainly focused on health care costs, while Briggs et al. [99] also included social care costs for ages above 75 years. A further strength of this thesis was the comprehensive set of diseases included. Besides the “core set of diseases related to physical inactivity” (breast cancer, colorectal cancer, type 2 diabetes mellitus, coronary heart disease and ischemic stroke), we also considered osteoporosis, low back pain and depression. These three additional diseases substantially added to the burden of physical inactivity and influenced the cost-effectiveness of interventions. An additional strength of the thesis is the language-region-specific analyses made. While the study by Roux et al. [112] analyzed cost-effectiveness separately for different age groups, many other models investigating physical activity interventions focused on entire countries without analyzing subgroups. In Switzerland, where the prevalence of physical inactivity substantially differs between language regions, the regional analysis was shown to be crucial to allocate resources efficiently. Furthermore, we considered fixed and variable intervention costs separately when assessing the cost-effectiveness of physical activity interventions to account for the fact that the use of certain resources is independent from the number of people receiving the intervention [115]. Our findings showed that the separation of fixed and variable intervention costs may substantially influence cost-effectiveness when the scale of the intervention substantially differs.

The main limitation of the thesis is the uncertainty arising from the use of secondary data sources. For example, the RR we used for our calculations are not based on a standardized definition and measurement of physical activity and a standardized assessment of confounding. We also assumed equal RR across gender and age-groups. In addition, intervention effect measures were standardized to MET-hours gained per person per day. Although this method was used in previous studies, it may have some limitations when applied to broad outcomes such as step gains or proportions of populations meeting physical activity guidelines [88, 134]. Moreover, many studies did not report sufficient statistical detail and, therefore, we were not able to properly address the uncertainty of effect measures.

A further limitation is that response in the Swiss Health Survey was non-random. For instance, responders were of higher average socioeconomic status and reported better subjective health than non-responders [135]. This may have affected our estimates of prevalence of physical activity categories as well as MET-minutes assigned to each physical activity category. Furthermore, we may have underestimated the prevalence of physical inactivity as the Swiss Health Survey investigates self-reported activity levels. According to a recent study from Switzerland, time spent physically active was 4.2 times higher when self-reported compared to measurements with accelerometers [136]. Several other studies also showed substantial differences between self-reported physical activity and objective measurements [137]. Our estimates are consistent in at least the sense that both prevalence and RR were based on self-reported physical activity levels.

As a further limitation, the productivity losses estimated were based on limited data available from the literature. For some domains such as presenteeism, early retirement and informal care, values were not reported in the literature. Therefore, we likely underestimated the true productivity losses due to morbidity and informal care.

Regarding the language-region-specific analyses, the following aspects were considered in the model: population counts, prevalence of physical activity categories, disease costs, productivity losses and fixed intervention costs. Other aspects were assumed to be the same, mainly due to lack of region-specific data: intervention effect, variable intervention costs, disease incidence, disease-specific mortality and disability weights.

Furthermore, we focused on interventions that can be implemented on a population-level and therefore excluded studies investigating the workplace setting. However, some interventions focusing on the workplace setting have been previously shown to be cost-effective [138]. By limiting the study design to RCTs, we also excluded interventions targeting the built environment [88, 134, 139, 140]. As we excluded studies that did not report specific physical activity outcomes, we did not include studies only reporting quality-adjusted life-years as part of pure cost-utility analyses [125, 141, 142]. These studies showed varying results in terms of cost per quality-adjusted life-years gained by physical activity interventions.

In regard to the burden of physical inactivity, it is also noteworthy that we only investigated the impact of physical activity on primary prevention. There are several diseases in which physical activity is an effective modifier of the course of clinical disease, and one could argue that there is an additional burden related to inactive patients [143]. In addition, we did not consider costs of myocardial infarctions occurring during physical activity and costs of sport injuries. However, there is evidence that sport injuries especially happen to people that are not regularly active [144].

6.3 Prospects for future research

First of all, Switzerland would benefit from a Swiss burden of disease study. Such a study is suggested as we detected discrepancies between GBD data and data coming directly from Switzerland. Alternatively, Switzerland could further develop the collaboration with the GBD study to increase data consistency. However, the understanding of the true burden of disease in Switzerland is considered fundamental to adequately assess the burden of risk factors for diseases and the cost-effectiveness of interventions tackling those risk factors. Furthermore, DALYs have been confirmed as a very valuable complementary measure to number of deaths (mortality) and money (economic burden). In a society where quality of life is a very important good, it is time to make this measure more common. Another measure that goes even beyond morbidity, mortality and economic burden is well-being [145]. Well-being may be investigated as an additional, separate outcome in future studies.

In addition, it is recommended to refine SPACE in such a way that it allows for a cost-effectiveness evaluation of all behavioral risk factors for NCDs (i.e. smoking, alcohol abuse, dietary risks and physical inactivity) in Switzerland. Multistate life table models like SPACE have already been used to assess interventions against smoking and unhealthy diet [146-155]. This would allow for a comprehensive understanding of NCDs and the cost-effectiveness of interventions tackling their risk factors. Such future models may not only address single risk factors but also multiple risk factor behavior [156-158].

The SPACE model currently contains data for the population from 15 to 100 years old. Consequently, children are excluded and the model does not allow for a holistic life course approach. Although different physical activity trajectories have been observed, the majority of the population seems to follow a persistent one [159]. In addition, better cardiovascular health indicators have been found in children who engage in higher levels of physical activity during early childhood [160]. This may influence cardiovascular health in adulthood. A holistic life course perspective may be taken in future models, which then would allow us to also analyze the cost-effectiveness of interventions targeting children.

Although there is currently no agreement over the most appropriate approach, several studies suggest the consideration of equity in the economic evaluations of public health interventions [161]. Therefore, future versions of SPACE may also implement equity considerations.

Last but not least, the SPACE model could serve as a template for estimating the cost-effectiveness of physical activity interventions from a societal perspective in other multi-cultural countries.

6.4 Conclusions

This thesis had three aims:

1. Estimating the health and economic burden of physical inactivity in Switzerland and for the French-, German- and Italian-speaking language regions separately
2. Systematically reviewing trial-based economic evaluations of interventions to reduce physical inactivity
3. Developing a health economic model that investigates the cost-effectiveness of physical activity interventions in Switzerland and its three language regions

The thesis showed that the burden of physical inactivity in Switzerland is substantial and that the French- and Italian-speaking regions are over-proportionally affected. These two regions distinguish themselves from the German-speaking region as they have a higher prevalence of physical inactivity, higher per capita health care spending, and higher disease prevalence. Due to the substantial burden of physical inactivity, interventions aiming to increase physical activity should be considered. In the systematic review we conducted, we found evidence from RCTs indicating the cost-effectiveness of some physical activity interventions for primary prevention in adults. These interventions were then further evaluated in a cost-effectiveness model built for the Swiss setting. This model showed that Swiss policy makers have cost-effective options of physical activity promotion. We recommend that individualized advice and GP referral be further evaluated as interventions and that decision-making considers the specifics of the Swiss language regions. Furthermore, we judge the cost-effectiveness model to be not only relevant for Switzerland but also for other multicultural countries. Based on similar data availability, our model has the potential to be applied beyond Switzerland, primarily to high-income countries with a comparable background, as a tool to guide societal efforts in primary prevention of physical-inactivity-related diseases.

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Appendix: Curriculum vitae

Personal information

Date of birth 8 October 1981

ORCID-ID https://orcid.org/0000-0002-8118-1776

Education

2016 - to date	PhD student, University of Basel Topic: "Scaling up cost-effective physical activity interventions in a culturally diverse setting" Supervisors: Prof. Nicole Probst-Hensch, Prof. Arno Schmidt-Trucksäss, Prof. Matthias Schwenkglenks, Prof. Simon Wieser PhD programs: PhD Program Health Sciences (PPHS) University of Basel, SSPH+ PhD Program in Public Health, PhD Program in Public Health Sciences for Universities of Applied Sciences (SSPH+ UAS)
2013	Certificate of Advanced Studies in Health Economics, Zurich University of Applied Sciences (ZHAW), Winterthur
2011	Master of Advanced Studies in Business Administration, Zurich University of Applied Sciences (ZHAW), Winterthur
2006	Master in Human Movement Science, Swiss Federal Institute of Technology (ETH), Zurich

Employment history

2018 - to date	Head of the HTA and Health Economic Evaluation Group, Zurich University of Applied Sciences (ZHAW), Winterthur Institute of Health Economics, Winterthur
2017 - to date	Lecturer and Project Manager, Zurich University of Applied Sciences (ZHAW), Winterthur Institute of Health Economics, Winterthur

2014 - 2018	Deputy head of the Health Economics Research Group, Zurich University of Applied Sciences (ZHAW), Winterthur Institute of Health Economics, Winterthur
2012 - 2016	Research Associate, Zurich University of Applied Sciences (ZHAW), Winterthur Institute of Health Economics, Winterthur
2011 - 2012	Market Access and Health Economics Manager, Zimmer GmbH, Winterthur
2008 - 2011	Clinical Research Associate, Zimmer GmbH, Winterthur
2006 - 2007	Human Movement Scientist, Sport Clinic, Sport Biomechanics, Zurich

Institutional responsibilities

Zurich University of Applied Sciences (ZHAW): Head of HTA and Health Economic Evaluation at Winterthur Institute of Health Economics

Approved research projects (selected)

Projects assessing costs and epidemiology of diseases in Switzerland:

- Physical inactivity / tobacco / cystic fibrosis / schizophrenia
- Economic impact of levothyroxine dose adjustments in Switzerland
- Inpatient costs and reimbursement of patients with acute myelotic leukemia
- Inpatient hospital costs of febrile neutropenia as a consequence of chemotherapy for breast cancer and Non-Hodgkin lymphoma

Projects assessing cost-effectiveness and cost-benefit of interventions / health technology assessments (HTA) in Switzerland:

- Economic evaluation of oral versus parenteral iron therapy for iron deficiency without anemia
- HTA on Dynamic Intraligamentary Stabilization (DIS) for the rupture of the anterior cruciate ligament: Implant system Ligamys®
- HTA on four spinal implant procedures for Switzerland
- HTA on interspinous process devices for Switzerland

Projects developing payment systems for Switzerland:

- Prospective payment system for inpatient rehabilitation

Supervision of junior researchers at graduate and postgraduate level

Supervision of MAS theses in health economics: Ueli Peter, Flurina Meier

Teaching activities

- Health Economic Evaluations
- Health Technology Assessment
- Health Economic Modelling

Prizes, awards, fellowships

2017	SSPH+ PhD Abstract Award «Disability and early deaths attributable to physical inactivity in Switzerland in 2015»

Journal publications

Mattli R, Farcher R, Syleouni ME, Wieser S, Probst-Hensch N, Schmidt-Trucksäss A, Schwenkglenks M. Physical Activity Interventions for Primary Prevention in Adults: A Systematic Review of Randomized Controlled Trial-Based Economic Evaluations [published online ahead of print, 2019 Nov 21]. Sports Med. 2019;10.1007/s40279-019-01233-3. doi:10.1007/s40279-019-01233-3

Mattli R, Wieser S, Probst-Hensch N, Schmidt-Trucksäss A, Schwenkglenks M. Physical inactivity caused economic burden depends on regional cultural differences. Scand J Med Sci Sports. 2019;29(1):95–104. doi:10.1111/sms.13311

Pletscher M, Mattli R, von Wyl A, Reich O, Wieser S. The Societal Costs of Schizophrenia in Switzerland. J Ment Health Policy Econ. 2015;18(2):93–103.

Oral conference presentations

Mattli R, Wieser S, Probst-Hensch N, Schmidt-Trucksäss A, Schwenkglenks M. The burden of physical inactivity in Switzerland in 2017. 12. SGS-Jahrestagung, Sportwissenschaftliche Gesellschaft der Schweiz. 2020. Basel, Switzerland

Mattli R, Farcher R, Dettling M, Syleouni M, Wieser S. Die Krankheitslast des Tabakkonsums in der Schweiz: Schätzung für 2015 und Prognose bis 2050. 17. Deutsche Konferenz für Tabakkontrolle. 2019. Heidelberg, Germany

Mattli R, Wieser S, Probst-Hensch N, Schmidt-Trucksäss A, Schwenkglenks M. Disability and early deaths attributable to physical inactivity in Switzerland in 2015. Swiss Public Health Conference, The Swiss Society for Public Health. 2017. Basel, Switzerland

Mattli R, Wieser S, Schwenkglenks M. The burden of physical inactivity in Switzerland and the influence of cultural differences. 12th World Congress on Health Economics, International Health Economics Association. 2017. Boston, USA

Mattli R, Schmidt M, Wirz M, Dettling M, Wieser S. Design of a prospective payment system for inpatient rehabilitation in Switzerland. 12th World Congress on Health Economics, International Health Economics Association. 2017. Boston, USA

Mattli R, Hess S, Maurer M, Eichler K, Pletscher M, Wieser S. The social cost of physical inactivity in Switzerland in 2011. 11th World Congress on Health Economics, International Health Economics Association. 2015. Milan, Italy

Mattli R, Hess S, Maurer M, Eichler K, Pletscher M, Wieser S. The social cost of physical inactivity in Switzerland in 2011. Active Living Research Annual Conference. 2015. San Diego, USA

Mattli, R.; Hess, S.; Maurer, M.; Eichler, K.; Pletscher, M.; Wieser, S. The social cost of physical inactivity in Switzerland in 2011. 10th Annual Meeting and 5th Conference of HEPA Europe. 2014. Zurich, Switzerland

Mattli R, Pletscher M, von Wyl A, Reich O, Wieser S. The social cost of schizophrenia in Switzerland. Swiss Public Health Conference, The Swiss Society for Public Health. 2014. Olten, Switzerland

Poster presentations

Hess S, Brunner B, Mattli R, Bruegger U, Eichler K. Dynamic intraligamentary stabilisation for the treatment of the anterior cruciate ligament rupture: A health technology assessment for Switzerland. HTAi 12th Annual Meeting. 2015. Oslo, Norway

Mattli R, Pletscher M, Eichler K Wieser S. Inpatient hospital costs of febrile neutropenia as a consequence of chemotherapy for breast cancer and Non-Hodgkin lymphoma in Switzerland. ISPOR 16th Annual European Congress. 2013. Dublin, Ireland

Mattli R, Balliere A, Menzie AM. Comparing the economic impact of prosthesis choice in unicompartmental knee arthroplasty procedures: development of an economic model. ISPOR 15th Annual European Congress. 2012. Berlin, Germany

Graduate education

Course	Institution	ECTS
Epidemiology		
Systematic Reviews and Meta-Analysis: a Practical Approach	SSPH+, University of Bern	1
GIS in public health	SSPH+, University of Basel	1
Biostatistics	University of Basel	2
Advanced methods in (Network) Meta-Analysis – A Practical Course in R (Swiss Epidemiology Winter School)	SSPH+, University of Bern	2
Social and Behavioral Science in Health Research		
Evidence-based Public Health using the GRADE approach	SSPH+, University of Bern	2
Ein Public-Health-Problem erkennen und lösen	SSPH+, University of Zürich	2
Health System Research		
Gesundheitsökonomische Modellierung – Hands-on	SSPH+, University of Basel	3
Ökonomische Evaluation im Gesundheitswesen	SSPH+, University of Zurich	3
Health Economics for Public Health Decision-Making (SSPH+ International Doctoral Courses and Seminars in Health Economics and Policy)	SSPH+, University of Lausanne	3
Other (Soft Skills etc.)		
Writing a Journal Article – and Getting it Published	SSPH+, University of Bern	1
Introduction to the Statistical Software R	SSPH+, University of Basel	1
Raus mit der Sprache! - Stimme und Körpersprache als Erfolgsfaktoren (Transferable Skills)	University of Basel	1
Self-Branding and Self-Promotion (Transferable Skills)	University of Basel	1
Storytelling for Science (Transferable Skills)	University of Basel	-

Active participation at an international conference with presentation, 1 ECTS in total (applicable for SSPH+): Mattli, R.; Wieser, S.; Schwenkglenks, M. (2017). The burden of physical inactivity in Switzerland and the influence of cultural differences. Oral presentation at the 12th World Congress on Health Economics, International Health Economics Association. (7-11 July). Boston, USA	1
Total ECTS	**24**