CHAPTER 7

General discussion
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Tobacco smoking was the second largest contributor to the global burden of diseases in 2015, after high blood pressure. (1) Tobacco-attributable disability-adjusted life years (DALYs) reached almost 150 million and globally, more than 7 million people died as a result of tobacco use in that year. The number of deaths attributable to smoking is projected to increase to 8.3 million by 2030, with the largest increase occurring in Asia. (2) Asia houses the largest producers and consumers of tobacco. (3)

After the economic transition during the 1990s in many countries in Asia, including Mongolia, cigarettes became more accessible and more available. (4) (5) As a consequence, prevalence of current smoking has been remained relatively high during the past decade in Mongolia. (6-8) While tobacco use has been significantly reduced in most of high-income countries with the implementation of effective tobacco control interventions by local authorities, tobacco companies continue to successfully penetrate the markets in many low-middle income countries in Asia resulting in about 800 thousand smokers starting each year. (9)

To support countries, WHO MPOWER measures contain a set of six tobacco control interventions consisting of Monitor tobacco use and prevention policies, Protect people from tobacco smoke, Offer help to quit tobacco use, Warn about the dangers of tobacco, Enforce bans on tobacco advertising, promotion, and sponsorship, and Raise taxes on tobacco interventions. (10) In resource limited settings, it is important to set priorities for these interventions. (11)

However, relatively few studies regarding the long term benefits and cost-effectiveness of tobacco control interventions in Asian countries have been presented, as most of the evidence regarding health-economics aspects of tobacco control interventions has been obtained in Western countries. (12-14)
AIM OF THESIS
The main goal of this thesis was to quantify the future costs and effects associated with cigarette smoking in Mongolia, and of possible tobacco control interventions. To do so, the DYNAMO-HIA (dynamic public health model structure for health impact assessment) tool was used and filled with the relevant input data from Mongolia.

The advantages and disadvantages of applying the DYNAMO-HIA in an Asian context will be discussed. The ways that the results of this thesis can be used to support decision making in tobacco control and reduce the health and economic burden of smoking in Asia, particularly Mongolia, will be explored.

Main findings
Based on region-specific relative risks of smoking to lung cancer mortality and lung cancer incidence, population-attributable fraction to tobacco smoking was found to be around 38%, which is equivalent to the annual 2600 DALYs for Mongolia as a whole. (Chapter 2) We found that there was a large discrepancy between men and women in the PAF estimates of the lung cancer DALY burden in Mongolia. In particular, among men more than 3000 DALYs were associated with lung cancer incidence and mortality compared with 150 DALYs among women annually. This provides strong evidence of the significant public health risk relating to tobacco smoking.

The inpatient costs associated with three major NCDs: COPD, IHD and Stroke, were estimated at $480, $516, $525 per patient per year, respectively in 2018. (Chapter 3) The study also revealed that per patient $172 could have been saved, if the unofficial referral path been avoided. Indeed, referral along official channels would be more efficient. On the total number of hospitalizations for these 3 NCDs, this would imply an annual saving of 6.2% of total costs for these 3 NCDs.

There was significant heterogeneity across the existing model-based economic evaluation studies used to estimate the cost-effectiveness of population-based tobacco control interventions in Asia in relation to their model structure, scope and the quality of input data used. (Chapter 5) For
our own evaluations, we chose to apply a dynamic public health model, the DYNAMO-HIA, and populated this with local input data on demographics, incidence, mortality and prevalence for six smoking-related diseases and Asian estimates for the price elasticity of demand for cigarettes based on literature reviews.

We showed that an increase in tobacco taxation of 75%, reflecting the increase needed to arrive at the policy aim of a 5% point reduction in current smoking prevalence by 2021, could indeed reduce tobacco use in Mongolia and would bring significant benefits to population health, particularly among men. (Chapter 6)

We used the same model to evaluate four of the MPOWER tobacco interventions: tobacco taxation, cessation support, mass media campaigns, and school programs. We applied, the WHO Cost-it model to estimate intervention costs. All of these interventions were shown to be ‘cost-effective’ in the current Mongolian healthcare settings, yet the school program was the only cost-saving and thus dominant intervention. (Chapter 7)

METHODOLOGICAL ISSUES

Some important factors influencing the validity of the results in this thesis should be carefully considered. The potential impact of limitations were disused in detail in chapter 2-6. Here we highlight some of the limitations that are not specific for the individual chapters.

Model data

In line with findings from our literature review we aimed to use local input data as much as possible. However, some parameters were not available for Mongolia. Estimates for the price elasticity of demand, the relative risk of smoking, and the intervention effects were collected from published international studies. (14)(15) Study types deemed suitable were classified based on the hierarchy of evidence recommended by the guidelines for economic evaluation studies. (16)
Subsequently, eligible studies were ranked based on their design as well as setting, prioritizing LMIC in Asia over any country in Asia, and higher ranking studies over lower ranked designs. (17) Finally for price elasticity, we used estimates from Asian comparison studies, with an estimated value of -0.4. (18-20) Given the wide range of cigarette prices in Mongolia, the true level of price elasticity of demand could be different, with smokers switching to cheaper brands rather than quitting. (21)

In addition, affordability could play a role for those with a lower income. (22) To compensate for this uncertainty, we included a sensitivity analysis using a wide range of values for the price elasticity of demand, -0.2 to 1.0 for adults and -0.56 to -0.96 for youth based on published sources for LMIC. (18) (23)(24)

For relative risks, data were taken from Asian cohort studies, sourced in an individual-level data meta-analysis based on more than one million participants in 21 Asian cohort studies. (15)(25) As an example, the relative risk of lung cancer for current smokers was 4.8 in men and 3.53 in women in Asia. (15) In contrast, the relative risks used in the original DYNAMO-HIA study for lung cancer was 23 for men and 12 for women for current smoker based on data from Western countries. (26) While the Asian risk figures seem more appropriate, they yield lower estimated health benefits for tobacco-control policies. The low relative-risk levels reflect the comparatively short history of the smoking epidemic in Asia. (27) Over time, therefore, the relative risk for many smoking related diseases in Mongolia and other Asian countries will likely increase. (28) This particularly applies to individuals who have smoked since their youth as they grow older-unless smoking decreases drastically in the nearby future. Our projections may thus be overly conservative in this respect.

Intervention effects were sourced in Cochrane reviews. These reviews take a very systematic approach to gather all relevant published effectiveness trials, and select on predetermined criteria. However, for school programs, the actual content of the programs was very different, while also school systems vary a lot globally. (29) Hence, we decided to select two Chinese studies with
programs judged transferable to the Mongolian setting and re-estimated the effect size based on these two studies only. The resulting effect on initiation rate was closer mean value; 0.90 (0.37-2.19) when compared to the original Cochrane review 0.89 (0.73-1.08). Similarly for nicotine replacement therapy and cessation support, 17 out of 53 studies were selected based on their longer abstinence rate (12 month) combined with consultation support and reported 95% CI. (30) The re-estimated relative risk was 1.47 (1.30-1.66) compared to Cochrane 1.55(1.49-1.61) for any type of NRT.

When local data were not available, published sources have been carefully selected and additional sensitivity analyses performed. Nevertheless we recommend additional studies to support estimates of RRs, price elasticity of demand and intervention effects which reflect local circumstances such as population structure, economic condition, smoking behavior in Mongolia. (5) (4)

**Model structure**

In two chapters, we compared the future health benefits of tobacco interventions using a DYNAMO-HIA model. Dynamic simulation model in public health research is useful to predict and address questions relating to long term population impact.

The DYNAMO-HIA model, a population-based public health model with a state-transition structure, was used to project the future level of smoking prevalence associated with various tobacco control interventions and to simulate smoking-related disease burden over time. (31)(32)

The conceptual framework of DYNAMO-HIA is to follow the real population structure over time, which is important when predicting the long-term health impact of prevention. Depending on the age group affected by the intervention, the effect of the intervention in terms of the total prevented number of smokers could be different. For instance, when the number of young people who smoke is expected to grow rapidly, the effect of an intervention would be much higher than when these age groups were expected to increase.

As a drawback these types of models require relatively detailed data on
three sets of input parameters: demographic data consist of population size, births, all-cause mortality, smoking-prevalence data with three categories never smoking, current smoking and former smoking, smoking behavior (initiation rate, quit rate and relapse rate) and smoking-related diseases specific incidence, mortality and prevalence numbers epidemiological data (lung cancer, oral cancer, oespagus cancer, COPD, Stroke, IHD). All of the data applied are stratified by gender and age (based on one-year age categories up to the age of 95 years). For our studies, the model was populated with local input data, in order to provide a proper reflection of the demographic situation in Mongolia. Demographic and epidemiological data are gathered by the government authority named Center for Health Development in Mongolia and National Statistic Office, resulting in good quality data and accessible with aggregated level. (33)(34)

However, in Mongolia, health indicator data reports have as the highest age group up to 70 years old. To run DYNAMO-HIA, smoking-related diseases specific data for age groups over 70 years old were extrapolated using the chronic disease model (DisMod) tool, applying assumptions about stability over age categories. (35) Since the overall number of people in these age categories was quite small, the effects on total outcomes will be limited. However, when considering effects in age categories separately, results for the elderly should be considered with caution.

As compared to a dynamic model structure, static models need less specific data, but hold the assumption that the introduction of a population-based tobacco intervention would immediately reduce the number of premature deaths. Such models have been applied in several previous studies in Asia. (20)(36) This type of model ignores demographic changes and disease epidemiology. It prohibits the use of discount rates for incorporating time preferences within estimates of costs and benefits. (37) Also, effects on morbidity rather than mortality are ignored. Although these static models were associated with rich outcome measures for income distribution relating to additional tax revenues, averted treatment costs, averted out-of-pocket payments, and poverty prevention resulting from tobacco control interventions,
they do not yield any insights into the timing or delay of intervention effects and savings over time.

Furthermore, most (5 out of 9) of the model-based studies in our review did at most present results of univariate sensitivity analyses. Extensive sensitivity analyses are important to assess the robustness of model outcomes and to examine the uncertainty around key parameters. The preferred approach to do so is probabilistic sensitivity analysis (PSA). For DYNAMO-HIA, however, at the time of performing these analyses, a PSA could only be possible by running the model through the batch mode which requires adequate technical knowledge. A more easily operable tool through the model interface would enhance the applicability of uncertainty analysis and improve quality of model-based analyses.

REFLECTIONS ON THE FINDINGS

There is a lack of further studies reporting on the PAF of smoking on lung cancer for Mongolia. The global burden of disease studies did report on Mongolia, but they did not apply country specific data like our study did. Their relative risks for instance were based on US studies. As a result, the proportion of tracheal, bronchus and lung cancer death rate attributable to tobacco was higher than the results we found for Mongolia; 91% for men and 74% for women in other studies compared to 58% for men and 9% for women in our study.

Furthermore, especially in Mongolia, air pollution is an environmental cause that affects many diseases which is also associated with tobacco smoking. Air pollution poses a major threat to public health in Mongolia. Especially in the capital city, the annual average concentrations of particulate matter 2.5 (PM2.5) was 75 mg/m3, seven to eight times higher than the WHO air quality guidelines. Previous local evidence highlighted that 9.7% of total deaths in the city were attributable to air pollution. This might explain why the number of lung cancer cases among women appears relatively high, even if they hardly smoke.

There is greater focus in policy on cancer treatment than cancer
prevention, hence only 5% of healthcare resources have been spent on prevention in contrast to 85% for inpatient care. (45) The model-based analyses show how proper prevention policy may reduce future healthcare costs. (20)(46) As quantified in Chapter 2, more efficient referral paths could also contribute to immediately reduce costs of inpatient care and save money that might for instance be directed towards prevention.

Effective tobacco control policies were addressed for the first time in 2005 in Mongolia. (4) As part of the ‘Action Plan for prevention and control of NCDs’, reducing tobacco control was addressed in a total of 17 policy documents including law on tobacco control, WHO-FCTC, National tobacco control strategy, WHO Country Cooperation Strategy for Mongolia, Health Sector Master Plan, and Universal Health Coverage. (47) In 2012, tobacco control law was adopted a relatively progressive set of tobacco control measures that have been implemented; including large pictorial warnings on packages, smoke-free places both indoor and outdoor, prohibitions to sell tobacco through the internet or within 500m from school areas, a minimum age limit for buying tobacco of 21 years and a ban on advertising, promotion and sponsorship. (48) However, the level of excise tobacco taxes on the retail price of a pack of cigarettes was 38% in 2018, which is not sufficient to reach the 70% target recommended by the WHO FCTC. The taxation level still seems quite low as highlighted in our study in Chapter 5. Raising tobacco taxes can be highly effective, especially among young people in preventing tobacco uptake. (49)

However, it requires strong and persistent policy to implement legislation and law enforcement to restrict tobacco use. Furthermore, recent evidence from Mongolia indicates that there is no or only limited relationship between tobacco tax and illicit cigarette trade in Mongolia. (50) For this reason, increasing tobacco tax appears to be a promising strategy to improve the effectiveness of policy to reduce smoking prevalence and promote favorable health outcomes in Mongolia.

In the absence of quality health technology assessment (HTA) studies, evidence-based decision making remains a challenge. Therefore, decision
makers tend to focus more on cancer treatment than cancer prevention. Moreover, there is limited awareness on the use costs-effectiveness analysis to inform policymakers.(5) While HTA has been actively advocated by the WHO as part of the universal health coverage program, adaptation of HTA in Asia has been slower, with the notable exceptions of South-Korea, China and Japan. (51)(52) However, Asian countries are at different stages to adapt HTA within their health care systems, and face different challenges for implementation. (53) The efforts are mainly focused on using HTA in support of medicine pricing and reimbursement decisions, rather than to support decision making concerning population level prevention policy. Since prevention policy brings large potential health gains, more cost-effectiveness studies of this type of policy could support Mongolia.

FUTURE STUDIES

Mongolia is moving forward in developing the digitalization of public services in a way that is designed to be open, transparent and efficient.(54) Particularly, Mongolian Statistical Information service allow researchers to access disaggregated and aggregated level data which have been collected electronically in Mongolia already for quite some years.(55) This offers ample opportunity for evidence-based health economic decision modeling to support cost-effectiveness studies with local relevance by using locally available data.

There are a number of research issues have not yet been addressed in this thesis which could be investigated in future. For example, DYNAMO-HIA was instrumental to simulate the long-term health impact of tobacco control. It could also serve to evaluate a range of scenarios on multiple risk factors such as alcohol use, diet, and physical activity, which will allow more comprehensive insights into the level of preventable NCDs and the effect of lifestyle modification on the population health of Mongolia. Understanding the combination of multiple risk factors can help to prioritize prevention policies to prevent NCD burden and co-morbidities in Mongolia.

Additionally, given the large proportion of men who smoke in Mongolia,
investigating the effect of second-hand smoking in lung cancer among non-smokers can support our findings that effective tobacco control policy needs to be addressed in Mongolia.

Another area of further study is examining inpatient costs associated with smoking-related diseases from a broader perspective, including inpatient records from private hospitals and adding the costs covered by out-of-pocket payments. This will help to further assess the efficiency of healthcare-resource use in Mongolia. Moreover, inpatient records could be linked with outpatient records through health-info databases, in order to stratify the costs by severity of disease and complexity of diagnosis.

We have examined a one-time 75% price increase scenario in Mongolia, since this is the increase required to arrive at the aim of a 5% reduction in smoking prevalence by 2021. However, in practice, a 75% price increase will be difficult to implement; therefore it is worthwhile to compare the long-term health benefits of repeated increases in tobacco taxes in Mongolia to further support our finding that tobacco taxation can reduce tobacco use in Mongolia. For such an analysis, further information is needed about waning effects from people getting used to new price-levels and whether these differ between one-time large increases and several small price increases.

As shown in this thesis, tobacco control interventions not only impact on population health and health care costs but also on tax revenues, out of hospital treatment costs, out-of-pocket payments, as well as produce income effects, when people do not buy tobacco anymore. Particularly, the distributional cost-effectiveness of tobacco control interventions on age (income) may be important to further understand the harmful effects of tobacco smoking in Mongolia.

More local studies related to the price elasticity in the demand of tobacco products, the relative risks of smoking associated with smoking-related disease, and smoking-related costing information would contribute to improved local evidence on cost-effectiveness of tobacco control interventions in Mongolia and similar countries in Asia. The impact of major risk factors to NCDs (e.g. tobacco, alcohol and diet) can be examined in monetary terms to compare
avoidable costs in the exposed compared to unexposed group can help to formulate public health prevention policy.

CONCLUDING REMARKS

Considerable health losses may be prevented with effective anti-smoking policies. A gender-specific tobacco control policy may be worthwhile because of the large gender differences in smoking exposure in Mongolia. For instance, this could be taken into consideration for mass media campaigns and school program interventions. Reducing the uptake of smoking among young people could be a particularly worthwhile benefit of tobacco-tax increases. For the current demography of Mongolia, this could lead to large population-wide health benefits in the future.

Our findings provide essential foundational information to develop evidence-based and cost-effective interventions aimed at health promotion, prevention and service delivery. In the absence of more extensive tobacco control and prevention policy, the burden associated with tobacco use will continue to increase, and impose extra costs on the healthcare system.

More data is needed to provide high-quality evidence regarding the cost-effectiveness of tobacco control policies in Asia. Strong evidence at the country level hinges on the availability of accurate estimates of the effects of the interventions, the relative risks of smoking, and the price elasticity of the demand for tobacco. Simple transfers of models built in Western populations do not suffice.
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