Development of health promotion model for economic evaluation in Thailand: a case study of alcohol control interventions

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1. Introduction

1.1 Health-related risk behaviour and health promotion interventions in Thailand

The magnitude of chronic non-communicable diseases (NCDs) have been gradually increasing in Thailand (Kaufman et al. 2011). In 2013, the major diseases that make Thai people lost their lives and their year of healthy lives were NDCs, for example, stroke, ischemic heart disease (IHD), diabetes, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), or liver cancer (International Health Policy Program 2015). They contributed more than 70% as causes of death of Thai people in 2014, which brought more than 350,000 deaths per year to the country (World Health Organization 2014). There were a lot of evidences showed the link between precarious lifestyles and NCDs (Doll et al. 2004; N.C.D. Risk Factor Collaboration 2016; C. D. Parry et al. 2011; Thakur et al. 2011; Wakabayashi et al. 2015; Webber et al. 2012). The data in 2010 showed that Thai male consumed pure alcohol approximately 14 litres per year. Additionally, fifty per cent of Thai male were smoking in 2011 (World Health Organization 2014).

Health promotion has become an interesting issues since 1986, where it has been defined as "a process of enabling people to increase control over, and to improve, their health"(World Health Organization 2014). Health promotion was recommended as an effective approach for decreasing and preventing NCDs (International Union for Health Promotion and Education 2011). In Thailand, health promotion has been developed and implemented for over a decade. The movement of tobacco control in Thailand had become a world leader in advocacy to establish policies, legislation and regulation to reduce and ultimately prevent the consumption of cigarettes (Galbally et al. 2012). In 2001, Thai Health Promotion Foundation (ThaiHealth) was established in order to promote and increase healthy life of Thai people by using multiple approaches: increase tobacco and alcohol taxes, promote healthy sponsorship of sports and culture, develop healthy environments, develop multisectoral support for health promotion, take a social determinants approach, and promote innovation and new knowledge. In the past decade, ThaiHealth and funded organisations achieved in modifying major health risk factors (e.g., alcohol and tobacco consumption, and road accident) through wide range of interventions for example (Galbally et al. 2012): increasing excise tax of tobacco and alcohol beverage, Tobacco Control Act and Alcohol Control Act, drink driving countermeasures and increasing penalties, controlling accessibility, reducing underage smoking and drinking, banned advertisement and social marketing e.g. the annual "No alcohol during Buddhist Lent" campaign for 3-month period, and Road Safety Campaign during annual festivals

1.2 Alcohol- related harms and impact on economic cost

The alcohol- related harms have been a public health problem in Thailand. The Thai burden of disease 2011 reported 2,204 alcohol-related deaths for males and 310 deaths for females. According to the premature deaths among those, disability-adjusted life years (DALYs) related to alcohol dependence and harmful use were 535,589 for males with highest rank and 41,083 for females (Burden of Disease (BOD) and International Health Policy Program 2014). There are many published studies of direct dose-response relationship between level of drinking and risk of morbidity and mortality (Bloss 2005; Corrao et al. 2004; Gutjahr et al. 2001; Patra et al. 2010; Rehm et al. 2010; Roerecke and Rehm 2013; Room et al. 2003). More than 200 health conditions identified by ICD-9 and ICD-10 disease and injury codes are attributable to alcohol consumption, and these conditions were categorised by the alcohol attributable fraction (AFF) (Grant et al. 2009; Jones et al. 2008; Jones and Bellis 2014). The alcohol attributable conditions are listed as follows (full detail is provided in Appendix): mental and behavioural disorder (e.g. alcohol dependence and alcohol use disorder); gastrointestinal diseases (e.g. liver cirrhosis, acute and chronic pancreatitis); cancer (e.g. oral cavity cancer, pharynx cancer, oesophageal and larynx cancer, liver cancer and breast cancer); and intentional and unintentional injuries (e.g. assault, intentional self-harm, and road traffic accident).

It has been shown that harmful alcohol use not only has health burdens for individual drinker, but also impacts on other people around the drinker e.g. family, friend, work colleagues or other people who are assaulted by drinker (Finan et al. 2015; Room et al. 2003). Furthermore, alcohol related harms impacted on country economic costs (i.e., health care direct costs, law costs, other direct cost, and indirect cost); in high income countries, its average costs was 179,859 million $ purchasing power parity (PPP) in year 2007 value equal to 2.5% gross domestic product (GDP); in middle income countries, its cost was 15,111 million $PPP equal to 2.1% GDP (Rehm et al. 2009). The alcohol- related harms have been also a public health problem in Thailand. The Thai burden of disease 2011 reported 2,204 alcohol-related deaths for males and 310 deaths for females. According to the premature deaths among those, disability-adjusted life years (DALYs) related to alcohol dependence and harmful use were 535,589 for males with highest rank and 41,083 for females (Burden of Disease (BOD) and International Health Policy Program 2014). Moreover, total economic costs of alcohol related harms was 7,903 million $PPP equal to 1.3% GDP (Rehm et al. 2009).

1.3 Alcohol intervention

Due to the impact of alcohol related harms on the whole society, the public health policy makers have shown an increasing awareness and allocated government budget to reduce alcohol-

related harms through alcohol policies and interventions (Anderson et al. 2009a; Thomas F. Babor et al. 2010; Martineau et al. 2013; Room et al. 2003). Two studies reviewed the effectiveness of policies and programmes to reduce the harm caused by alcohol (Anderson et al. 2009a; Martineau et al. 2013) classified into eight groups:

1. *Provision of information and education* (e.g. school-based education (Jones et al. 2007), parenting (Petrie et al. 2007), and social marketing4 (Janssen et al. 2013)), to raise awareness and knowledge about alcohol-related harms, is systematically reviewed, and it was concluded that such provision increases alcohol-related knowledge and improves attitudes. Nonetheless, the interventions are not an effective intervention to reduce alcohol consumption and the harms caused by alcohol.
2. *Screening and brief intervention for alcohol use disorders* is the most effective evidence-based treatment. Systematic review and meta-analysis of these programmes in different health-care settings observed the reducing alcohol consumption for non-dependent drinkers (Kaner et al. 2009; Mdege et al. 2013). However, there is no evidence to show the effectiveness of brief intervention for alcohol dependence (Saitz 2010). The review of providing pharmacologic treatments for alcohol dependence alone, and in combination with brief psychosocial therapies, showed a modest efficacy when compared with the placebo group (Miller et al. 2011).
3. *Community-based programmes* Babor et al. concluded that media advocacy can lead to a reframing of the solution to alcohol-related problems, which is a coordinated approach by relevant sectors, and results in increased attention to alcohol within political and public agendas (T. F. Babor et al. 2003). Other community-based interventions for controlling accessibility – including the environmental contexts of selling, distribution, involved enforcement of public health polices for drinking and driving, and reducing underage drinking – can reduce high-risk alcohol consumption and alcohol-related injuries resulting from motor vehicle crashes and assaults (Giesbrecht 2003; H. D. Holder et al. 2000). Although a systematic review of work-place interventions for alcohol-related problems revealed some methodological problems in included studies, this review reported statistically significant differences in measures such as a reduction in alcohol consumption, binge drinking and alcohol problems (Webb et al. 2009).
4. *Drink-driving policies* – including increased prices of alcohol, minimum purchase age laws, controls on the promotion and advertising of alcohol, and on the opening hours of sales and outlet density – supported by mass media campaigns, have been shown to be effective, or promising, in reducing impaired driving as well as other consequences related to alcohol use and the misuse of opening hours and sales (Grube and Stewart 2004). Establishment of a legal concentration of alcohol in the blood and intensive random breath-testing can reduce alcohol-related injuries and fatalities (R. A. Shults et al. 2001; Ruth A Shults et al. 2009).

5. *Addressing the availability of alcohol* For example, government monopolies for the sale of alcohol (H. Holder et al. 2008) and implementation of laws that set a minimum age for the purchase of alcohol, in conjunction with controls on sellers (Grube and Stewart 2004), show a reduction in alcohol-related harms and drink-driving casualties.

6. *Addressing the marketing of alcoholic beverages* Longitudinal studies have consistently suggested that exposure to media and commercial communications on alcohol is associated with the initiation of youth drinking and increased drinking amongst baseline drinkers (Anderson et al. 2009b; Snyder et al. 2006). Additionally, these findings also confirmed, by the systematic review of prospective cohort (Smith and Foxcroft 2009) and experimental studies (Engels et al. 2009), that an increased exposure at baseline led both drinkers and non-drinkers to a significant increased risk of drinking at follow-up.

7. *Pricing policy* A rise in alcohol prices leads to less alcohol consumption and less alcohol-related harm in many settings (Gallet 2007; Pan et al. 2006; Charles dh Parry et al. 2003; Wagenaar et al. 2009). A systematic review on public policies affecting the price of alcoholic beverages suggested that doubling the alcohol tax would reduce alcohol-related mortality by an average of 35%, traffic crash deaths by 11%, sexually transmitted disease by 6%, violence by 2%, and crime by 1.4% (Wagenaar et al. 2010).

8. *Harm reduction interventions* These interventions are important, because the problems that commonly harm people, rather than the drinker, and potentially averted. A published study systematically reviewed harm reduction in drinking environments (i.e. bars, nightclubs and their surrounds) and found three studies which indicated that multi-component programmes combining community mobilisation, a responsible beverage service training programme, house policies, and stricter enforcement of licensing laws, may be effective in reducing assaults, traffic crashes, and underage sales depending on the focus of the intervention (Jones et al. 2011).

As shown above, many effectiveness studies to date have tended to focus on intermediate outcomes of alcohol control programmes such as the amount of alcohol consumption, episodic binge drinking, alcohol-related knowledge and attitudes. Nevertheless, the pricing policy effectiveness could be seen the reduction of alcohol-related mortality and other harms, but its effects were estimated to the aggregate level of whole society. Only drink-driving policies were measured the final outcome in term of the reduction of alcohol-related injuries and fatalities. For these reasons, there is still a scarcity of studies on the impact of these programmes on intermediate and final outcomes among drinkers. Moreover, there is no reliable evidence that has clearly found relationship between outcomes with different periods of time, which would be used for prediction of alcohol-related consequences.

Martineau et al. (2013) concluded the key findings from appraisal of a number of systematic reviews in particular of the effectiveness of population-level interventions to reduce alcohol-related harm as presented in Table 1 (Martineau et al. 2013). There are four categories of supporting level of

evidence which will be useful for researchers and policy makers to decision about further researches and alcohol policies, especially targeting population-level interventions.

Table 1 Summary of review-level support for population-level of alcohol interventions

Interventions consistently supported across reviews
Restricting days or hours of sale, reducing alcohol outlet density, preventing privatisation of sales, minimum legal drinking ages, dram shop liability, drink-driving checkpoints, increasing police road patrols, drink-driving awareness campaigns, multi-component community drink-driving interventions, mass media campaigns, increasing taxation, graduated driver licences
Interventions with mixed or weak support across reviews
On-premises server training, school-based drink-driving programmes, family interventions, restricting alcohol advertising, school-based interventions, workplace interventions
Interventions consistently found to be ineffective across reviews
Higher education interventions
Interventions with insufficient review-level evidence
On-premises health education, toughened glassware, free driving-home service, designated driver promotion, reducing movement between bars, illicit alcohol interventions, counter-advertising, community interventions targeting young people

Source: (Martineau et al. 2013)

1.4 Previous works and needs of economic evaluation of health promotion in Thailand

The evaluation of health promotion interventions has also become increasingly important in Thailand, particularly evaluation of effectiveness and cost-effectiveness (Room et al. 2003). The past evaluations of ThaiHealth were the assessment of intermediate outcome e.g. alcohol consumption per capita, individual alcohol drinking pattern, aggregate alcohol sales, and household expenditure on alcohol (Buasai et al. 2007; Galbally et al. 2012). However, the further expected outcomes of those interventions should be changes in epidemiological measures e.g. mortality, morbidity, and health-related quality of life in population, which these are the final outcomes of interest (Martineau et al. 2013; Tones 1992). Moreover, for the purposes of economic evaluation of alcohol consumption control interventions, it is still methodological problematic to estimate that decreasing alcohol consumption could estimate the final outcomes of interest, especially measured as life years (LYs), quality-adjusted

life years (QALYs) and lifetime economic cost which are widely recommended for economic evaluation of health interventions, including recommendation of Thai Health Technology Assessment Guidelines (Chaikledkaew and Kittrongsiri 2014; ISPOR 2014; NICE 2013; Teerawattananon and Chaikledkaew 2008).

To operate health promotion programmes and support funded partners, ThaiHealth invested the annual budget around 0.75% of total national health expenditure (3,489 million baht) (Buasai et al. 2007; Galbally et al. 2012). Due to ThaiHealth's investments since 2001, ThaiHealth has been evaluated and monitored by policy makers and public sectors (Buasai et al. 2007; Galbally et al. 2012). The recommendations from the ThaiHealth's 10-Year Review referred to the demand for health economics, impact evaluation, action research and social epidemiology to strengthen ThaiHealth's evaluation efforts overall to prove that its funding decisions offer value for money (Galbally et al. 2012). Therefore, this further methodological research will develop to improve the estimation outcomes of interest, especially cost-effectiveness. The method used has been developed and validated in Scottish setting which is the alcohol policy mathematic model for predicting LYs, QALYs and lifetime health care costs. The further study will transfer the methodology of developing alcohol policy model in Scottish setting to Thai setting using country-specific data. The Thai study will demonstrate cost-effectiveness of existing alcohol policies and interventions in Thailand.

2. Conceptual framework of developing the Thai Health Promotion Intervention model for economic evaluation

To estimate a cost-effectiveness of health promotion intervention which this study is focussing on an alcohol intervention in different levels (e.g. individual and population), the economic evaluation alongside RCTs (for a source of evidence on relative effectiveness) might be limited. As a result, it would be needed the combined approaches to estimate the costs and outcomes of alcohol intervention with avoiding biased estimate. Even though the existing economic evaluation alongside RCTs were conducted to assess the intervention cost-effectiveness (Cowell et al. 2012; Crawford et al. 2014; Crawford et al. 2015; UKATT Research Team 2005), these estimates were measured within follow up period, while the consequences of alcohol intervention often become noticeable many years after implementation. Thus, the extrapolation of costs and outcomes beyond the end of the trial using observational data to link intermediate outcomes to final outcomes should be considered to extend the time horizon analysis (e.g. for the lifetime of different drinking patterns). This study will develop a health promotion policy model which is a model that can evaluate the effectiveness and cost-effectiveness of interventions to inform health policy decision makings (Lewsey et al. 2015).

To take into account the range of related risk factors that would likely affect to hospitalisations and death, developing health promotion intervention model is focussing on the association between related risk factors and harms (i.e., morbidity and mortality) to predict LYs and QALYs of different health risk profiles. Those risk factors were identified i.e., pattern and level of alcohol consumption, socioeconomic status (Jones et al. 2015; Probst et al. 2015) as well as other factors, which were found a relationship with alcohol drinking, smoking status (Aekplakorn et al. 2008; De Leon et al. 2007; Falk et al. 2006; Harrison et al. 2008; McKee et al. 2010), physical activity (Kendzor et al. 2008), and body mass index or BMI (Hart et al. 2010). This study examines whether the selected risk factors would accurately predict the hospitalisations and death. Then, the policy model would be developed to estimate LYs, QALYs and lifetime healthcare costs, and those outcomes would be presented in different risk profiles. Moreover, the findings could be used for the evaluation of intervention that aims to change those selected risk factors, and it could show the association between the modified risk factors (intermediate outcome) and the health outcomes.

To evaluate the effect of alcohol intervention in long-term period using an intermediate outcome, a conceptual model of the relationship of biomarkers, surrogate endpoints, and the process of evaluating therapeutic interventions can be applied (Biomarkers Definitions Working Group 2001; Buyse et al. 2010). The biomarker measurements (as compared to risk behaviour in this study) can help explain empirical results of clinical trials by investigating the relationship between the effects of interventions on molecular and cellular pathways and overall clinical responses. The biomarkers that represent highly sensitive and specific indicators of disease pathways have been used as substitutes for final outcomes in clinical trials when evidence indicates that they predict clinical risk or benefit. Figure 1 presents a conceptual framework of the development of the Thai Health Promotion Intervention model adapted from the Biomarkers Definitions Working Group 2001(Biomarkers Definitions Working Group 2001; Buyse et al. 2010). A health promotion intervention would have direct and indirect effects to wide ranging modifiable risk factors of individual, for example, an alcohol consumption control intervention could change alcohol drinking pattern and other related risk behaviour (e.g. cigarette per day). Consequently, a mathematical analyses will examine that subset of those risk factors, represented in the figure by a quadrant, could achieve surrogate endpoint status in term of accuracy (correlation of measure) and precision (reproducibility) which is required to be reasonably likely to predict the endpoints in term of morbidity and mortality. These final outcomes could be converted to LYs, QALYs and lifetime costs, and then a cost-effectiveness of intervention would be estimated.

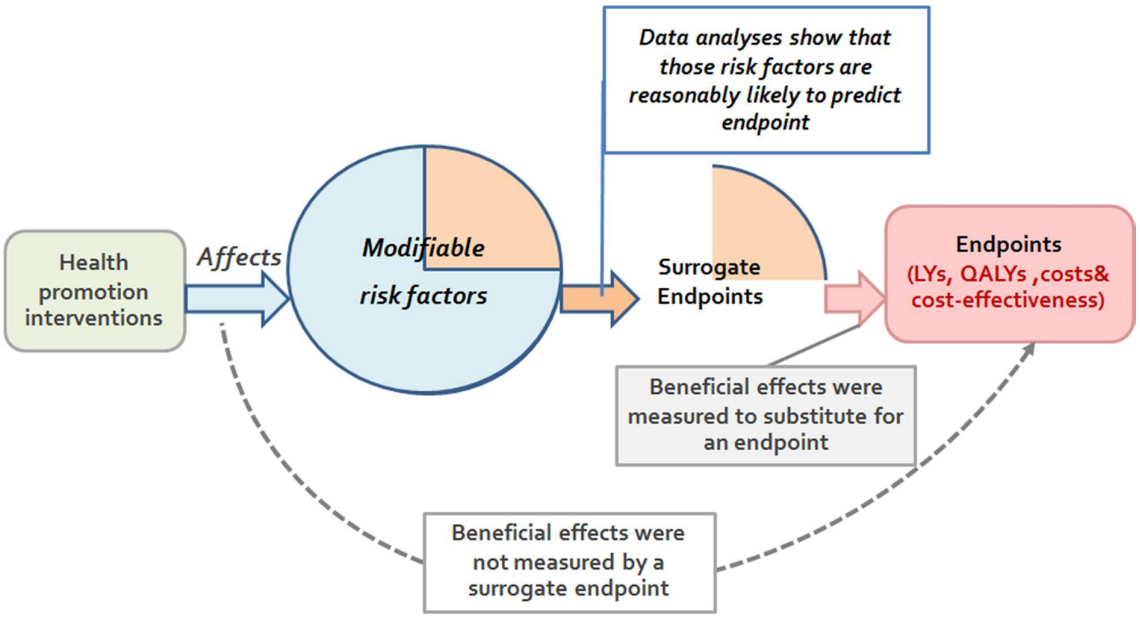


Figure 1 A conceptual framework of developing health promotion policy model

*adapted from the (Biomarkers Definitions Working Group 2001)

3. The objectives of this study

1) To develop the Thai Health Promotion Intervention model which could be used for economic evaluation of health promotion interventions.

2) To demonstrate the usefulness of Thai Health Promotion Intervention model by conduct an economic evaluation of selected existing alcohol intervention.

4. Methods

Based on the literature review about the effectiveness of interventions to reduce the harm caused by alcohol consumption, a stakeholder consultation meeting will be conducted to discuss about two main purposes as follows: 1) selecting alcohol intervention for economic evaluation that public health policy decision makers would be interested in Thai context and 2) discussing the appropriateness of approach used for development of Thai Health Promotion intervention model. To demonstrate the usefulness of the model, this study will apply a mathematical approach which was primarily developed to evaluate the alcohol intervention in Scottish setting, namely the Scottish alcohol policy model (Appendix 3). The Scottish model was structured using a health state transition model to characterise the plausible consequences (i.e. hospitalisation and death) of different drinking behaviours (Figure 2),

and the Scottish model was well validated and calibrated (Appendix 3). The model is consistent with the key features of the economic evaluation, such as perspective, time horizon, and measured costs and outcomes (A. Briggs et al. 2006a; Drummond MF et al. 1997; Gray et al. 2011a).

Then, LYs, QALYs and lifetime economic costs can be estimated categorised by alcohol drinking patterns. Those outcomes and costs of different drinking behaviours suggest that in case of an alcohol intervention can change alcohol consumption; then, how its benefit in lifetime horizon can be shown in term of cost-effectiveness i.e. LY gained, QALY gained, lifetime economic costs and incremental cost-effectiveness ratio (ICER). Therefore, the Scottish alcohol policy model will be applied for developing Thai Health Intervention model, since the estimated outcomes and costs are suitable for the purpose of health economic evaluation, and those outcomes are widely recommended for the purposes of economic evaluation of health interventions, including recommendation of Thai HTA guidelines to inform policy decision making in Thai context (Chaikledkaew and Kittrongsiri 2014; ISPOR 2014; NICE 2013; Teerawattananon and Chaikledkaew 2008). Initially, The Thai Health Intervention model will introduce the model for the economic evaluations of alcohol interventions.

4.1 Health state transition model structure

The overall purpose of a health state transition model structure is to characterise the plausible consequences in a way that is appropriate for state decision problem and the boundaries of the model (A. Briggs et al. 2006a; Drummond MF et al. 1997; Gray et al. 2011a). The study cohort will be general population who had never experienced an alcohol-related hospitalisation. To estimate alcohol-related harms of different drinking, there are the alcohol attributable hospitalisations and deaths identified by alcohol attributable fraction (AFF) (Grant et al. 2009; Jones et al. 2008; Jones and Bellis 2014) i.e. wholly alcohol-attributable conditions (AFF=1) and partly alcohol-attributable conditions (0<AFF<1). Moreover, other non-alcohol related hospitalisations and deaths will be taken into account to be the competing risk of first events after entering date, and these events will be subordinate states as emergency admission and cardiovascular diseases-CVD (Appendix 1) due to focussing on the association between alcohol consumption and CVD (excluded CVD categorised to be partly alcohol-attributable conditions), which has been controversial between its risks and benefits to CVD (Rehm et al. 2010).

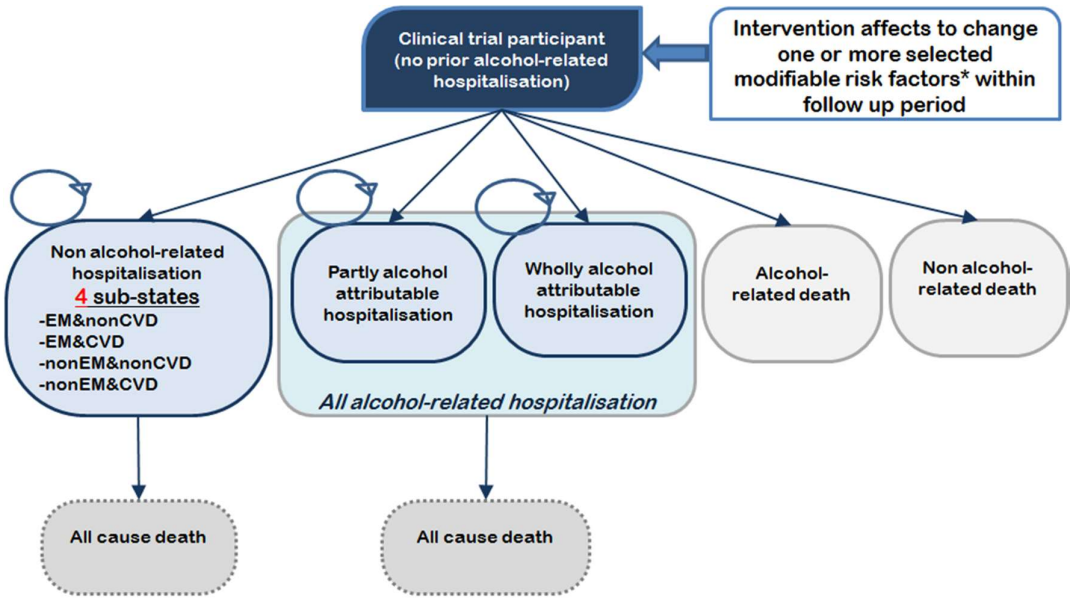


Figure 2 Structure of health state transition model

Figure 2 presents a modelling health state of alcohol-related hospitalisation and death of no prior alcohol-related hospitalised cohort. There are five competing first events classified by the ICD-9 and ICD-10 (Grant et al. 2009; Jones et al. 2008; Jones and Bellis 2014) of primary diagnosis (Appendix 1) as follows: 1) wholly alcohol-attributable hospitalisation (21 conditions); 2) partly alcohol-attributable hospitalisation (26 conditions); 3) alcohol-related death, which is defined as an alcohol-related hospitalised patient died within 28 days; 4) non-alcohol related death, which is defined as a non-alcohol related hospitalised patient died within 28 days; and 5) non-alcohol related hospitalisation divided into four admission types: non-emergency (EM) admission and non-CVD; non-EM admission with CVD; EM admission and non-CVD; and EM admission with CVD.

4.2 Estimating risk of hospitalisation and death among difference drinking pattern

To develop such an analytical model for predicting LY, QALY, and lifetime costs, an extensive individual linked health data set between baseline risk behaviours measured from health surveys and administrative data set (i.e. hospitalisation and death record) after survey date have been required. In Thailand, there has been a scarcity of linked dataset between national health surveys and national hospitalisation and death records, so this seems to be an importance limitation of developing Thai Health Intervention model using the same method as Scottish model (Appendix 3). One alternative is

to adapt the well-validated model using longitudinal data derived from other setting (Daniel Mullins et al. 2014; Stout et al. 2009). , all data set will be used to calibrate the cause-specific hazard model derived from Scottish setting, and a multiplying factor will be derived for adjusting linear predictor of the original equation. Then, the calibrated model will be applied for estimate risks of hospitalisation and death (as shown in Figure 2). There are four existing data that will be investigated as listed below:

1) National Health Examination Survey V (2013) conducted by National Health Examination Survey Office, which alcohol consumption and Alcohol Use Disorder Identification Test (AUDIT) were collected

2) National Household Survey for Substance and Alcohol Use year 2007 (N=26,633) including information on pattern of alcohol consumption, AUDIT and consequences of drinking

3) The national survey of willingness to pay for selected health promotion programmes under ThaiHealth conducted by HITAP in 2012, which measured modifiable risk factors including alcohol consumption, smoking, physical activity, and socioeconomic status (N=7,311)

4) Baseline morbidity and mortality of alcohol-related condition reported by Thai Burden of Diseases (BOD)

After approved data access requirement, to analyse the administrative data, all researcher need to correspond to the safe use of individual patient data with good practice methods and awareness patient data protection. Thus, all researchers who will access individual patient data and produce the report need the Safe Researcher Training (http://www.adls.ac.uk/safe-researcher-training/) to have the basic knowledge to treat administrative data in a responsible manner. Additionally, the study protocol has been approved by Institute for the Development of Human Research Protections (IHRP) as shown in Appendix 2.

4.2 Cost-utility analysis (CUA)

To estimate a cost-effectiveness of an intervention which aims to modify the selected risk factors, two scenarios are performed for each individual risk profile. The first scenario models to estimate lifetime costs and health outcomes (i.e. LYs and QALYs) of baseline risk profiles. The second scenario estimates those costs and outcomes of changes risk behaviours (e.g. reduction of alcohol consumption) that the intervention affects these modifiable risk factors leading to changes of first hospitalisation and death risks as well as health care costs and QALY. Next, the estimated lifetime hospitalisation costs and health outcomes are compared between baseline and intervention effect

scenarios, and incremental-cost effectiveness ratio (ICER) that is the additional cost per additional unit of effect (i.e. QALY) from a new intervention, so the ICER of CUA is the incremental cost per QALY gained (Briggs et al., 2006c, Drummond MF et al., 1997, Gray et al., 2011b). Then, ICER of the intervention would be compared to the threshold ICER at 160,000 THB per QALY gained recommended by the Thai Subcommittee for Development of the NLEM and the Subcommittee of the Development of Benefit Package and Service System, NHSO.

4.3 Input parameters

This stage describes the input parameters required for the model-based economic evaluation to estimate LYs, QALYs, and lifetime costs of the selected alcohol intervention which would be derived from expert consultation meeting. This analysis will perform the estimated costs and health outcomes of two scenarios as providing intervention and baseline scenarios. The base-case scenario estimated the lifetime consequences of baseline risk behaviours (i.e. drinking and related-behaviours). For the second scenario of the intervention, the effect of intervention on modifying risk behaviours (e.g. stopping drinking) will result in the changes of morbidity and mortality risks from baseline leading to the difference of estimated lifetime costs and health outcomes compared to base case.

Intervention effectiveness

To apply a recommended framework of evaluating the public health impact of health promotion interventions (Glasgow et al. 1999), namely RE-AIM framework, the intervention effectiveness should be assessed 5 dimensions as follows:

1) Reach: proportion of the target population that participated in the intervention
2) Efficacy: success rate if implemented as in guidelines; define as positive outcomes minus negative outcomes
3) Adoption: proportion of settings, practices, and plans that will adopt the intervention
4) Implementation: extent to which the intervention is implemented as intended in the real world
5) Maintenance: extent to which the intervention is sustained overtime

These dimensions can be evaluated at multi-levels e.g. individual, health care setting, community or population.

To analyse a cost-effectiveness of health promotion intervention, the intervention effectiveness should take into account those dimensions in the analytical model. Firstly, the coverage rate and acceptance rate of the intervention should be defined to estimate the proportion of the target population and the proportion of setting that would adopt the intervention (Glasgow et al. 1999).

Secondly, the efficacy of intervention on modifying selected risk behaviours (as shown in Figure 2) within follow-up period should be collected from individual who participated in a RCT or as well as an evidence synthesis of RCTs and observational studies, which the target population should be clearly described and relevant to the population of the intervention under evaluated. Thirdly, since the effect of a health promotion intervention could change overtime (Green and Tones 1999), the lag time of partial and full effects of intervention should be defined and taken into account in modelling effectiveness of the intervention. Moreover, the lag time of those effects would be captured either within study (short-term period) e.g. change of risk behaviours or in longer-term period e.g. changes of morbidity and mortality (Holmes et al. 2012). Finally, to examine long term maintenance of behaviour change due to the intervention, the duration of intervention effect should be also taken into account, and the extent to which intervention is implemented in real-world situation (Glasgow et al. 1999). This study will explore the intervention affected on alcohol consumption in the first year of implementation, duration of maintenance participant's risk behaviours, percent coverage rate and acceptance rate in Thai context. All effectiveness parameters will be verified by alcohol expert panel.

In addition, to generate QALYs, the baseline utility will be derived from EQ-5D-5L measurement. The existing data were collected by the national epidemiological survey of mental health 2013-2014 (N~5,000) conducted by Department of Mental Health, Ministry of Public Health using Composite International Diagnostic Interview or CIDI, which an alcohol abuse and alcohol dependence were diagnosed, as well as EQ-5D-5L of respondents were also collected. The EQ-5D-5L measurement will be converted to utility score using Thai EQ-5D-5L preference (Pattanaphesaj and Thavorncharoensap 2015). The impact of hospitalisation will be estimated as utility decrements which will be collected from alcohol-relate hospitalised patients. For non-alcohol related hospitalisation, the utility decrements of specific diseases will be derived from literature review using Thai HTA research database (http://db.hitap.net/). The utility decrements will be then applied to decrease the baseline utility for hospitalise health state. Moreover, the annual probabilities of readmission will be estimated until lifetime horizon. To calculate overall QALYs using Kaplan-Meier Sample Average (KMSA) estimator approach (Gray et al. 2011a), the sum of survival time in each health state weighted by utility index adjusted by probabilities of readmission and utility decrements will be calculated over 100-year cycle.

Intervention costs

The economic evaluation will be conducted using societal perspective, so lifetime costs will take into account direct medical care cost, direct non-medical care costs (i.e. transportation, meal, and accommodation related to medical care), and cost of productivity loss due to sick leave for hospitalised

patients as well as costs of reduced productivity related to alcohol drinking (Thavorncharoensap et al. 2010). The estimating each cost parameter is described as follows:

1) the intervention costs will be collected which consists of the cost of development and implementation in setting, and then the cost of full implementation to other settings should be estimated to reflect the real world situation of adopted intervention (Kruger et al. 2014).

2) The direct medical care costs: the NHSO hospitalisation data that covered around 70% of Thai population will be analysed during year 2001-2015, the administrative hospitalisation data set including diagnosis-related group (DRG) of each episode will be used to model average annual cost due to 1-year cycle length of health state transition model. Firstly, the modelling costs of yearly hospitalisation classified by ICD-9 and ICD-10 (Appendix 1) will be estimated. According to the plausible range and distribution of cost data, the generalised linear model (GLM) framework will be applied for modelling health care cost using gamma family and log-link function (Dobson and Barnett 2008; McCullagh and Nelder 1989). For alcohol drinkers who is no hospitalisation, the costs of reduced productivity related to alcohol drinking will be applied (Thavorncharoensap et al. 2010). The costs will be assumed constant until aged 60 years or retired. The lifetime costs of intervention will be affected by intervention effectiveness leading to change alcohol drinking behaviour related to the risk of hospitalisation.

4.4 Discounting

As recommended by Thai HTA guidelines to inform policy decision making in Thai context (Chaikledkaew and Kittrongsiri 2014; ISPOR 2014; NICE 2013; Teerawattananon and Chaikledkaew 2008), since public health interventions usually show their effect over the long term, the guideline has been decided to use discounting rate at 3% annually for all costs and outcome, and then the rate will change to 4% for cost and 1.5% for outcome in 30^{th} year onward (Permsuwan et al. 2014).

4.5 Uncertainty analysis

A probabilistic sensitivity analysis (PSA) will be conducted to assess the uncertainty surrounding input parameters of the analytical model that will be mostly derived from multivariate regression analyses which these parameters are correlated with others (A. H. Briggs 2000). Thus, the uncertainty analysis will perform using variance-covariance matrix of those parameters to show the covariance relationship, and an applied approach, namely Cholesky decomposition, can be employed to generate correlated draws random parameters from the multivariate standard normal distribution (A. Briggs et al. 2006c). The next stage, a Monte Carlo simulation performed in Microsoft Excel 2010 (Microsoft

Corp., Redmond, WA) will be employed to generate 5,000 iterations to demonstrate a range of plausible lifetime costs, health outcomes (LYs and QALYs), and ICERs.

The result of the analysis will be plotted in a cost-effectiveness plane (Black 1990; A. Briggs et al. 2006b), which shows the difference (intervention minus base case) in effectiveness (△E) per patient on horizontal axis versus the difference in cost (△C) per patient on vertical axis. The slope of graph is equal to ICER =△C/△E. When the ICER simulations compared to the cost-effectiveness (CE) threshold at 160,000 THB per QALY gained (recommended by the Thai Subcommittee for Development of the National List of Essential Medicine and the Subcommittee of the Development of Benefit Package and Service System, National Health Security Office), these simulations which are lower slope than the threshold line are considered to be cost-effective. Moreover, to summarise uncertainty by considering how many of the ICER simulations on the cost-effectiveness plane fall below and to the right of different thresholds, a cost-effectiveness acceptability curve (CEAC) will be illustrated (A. H. Briggs 2000; A. Briggs et al. 2006b; Fenwick et al. 2001; van Hout et al. 1994). The results will be further analysed for a relationship between the different values of the threshold and the likelihood of being cost-effective option compared between base case and the selected intervention using a net monetary benefit framework. The net monetary benefit (NMB) employs the cost-effectiveness decision rule (ICER< ceiling threshold referred as λ) by rearrangement as follows:

$$\frac{\Delta C}{\Delta E} < \lambda$$

$$\Delta E \times \lambda - \Delta C > 0$$

The intervention is considered cost-effective, if its NMB is positive at any value of ceiling threshold. Using the results of Monte Carlo simulation (5,000 iterations), each iteration of the intervention can be calculated its NMB compared to base case at the specific threshold, and the proportion of these iterations being cost-effective (NMB>0) then can be plotted on (CEAC).

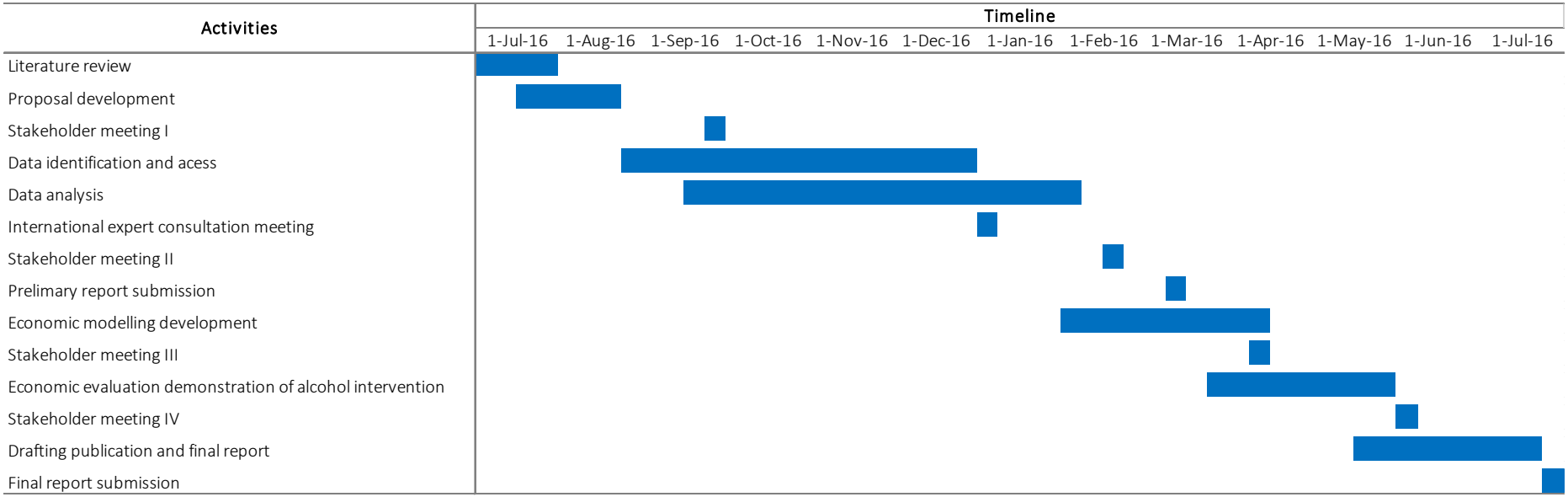
5. Outputs

Objectives	Outputs
1) To develop the THPP model which could be used for economic evaluation of health promotion interventions.	The THPP model that can estimate the final outcomes of health promotion interventions, in which the outcomes will be predicted by the set of surrogate outcomes including selected modifiable risk factors.
2) To demonstrate the usefulness of THPP model by conduct an economic evaluation of selected existing alcohol intervention.	The estimated of cost-saving and QALY-gained from the implementation of selected alcohol interventions in Thailand, which can be modified by using characteristics and life-style detail of individuals.

6. Expected outcomes

The study can be useful for monitoring and evaluating the indicators, for both surrogate and final outcomes, that normally used to monitor and evaluate the results of implementing THPP, e.g. the change of population morbidity and mortality as well as lifetime economic costs. This study also demonstrates an economic evaluation of alcohol intervention in Thailand using the THPP model which will be developed by country-specific information, so this model would be suitable for the purpose of health promotion intervention evaluation to inform policy decision making whether the intervention under evaluation shows its cost-effectiveness in the Thai context. As a result, it is, indeed, fundamental, not only for justifying the public's investment in health promotion, but also in enabling public health managers or healthcare workers to monitor the progress or success of their works. As mentioned above, the economic evaluation has been the demand research for health promotion interventions in Thailand.

7. Study timeline



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Appendix 1

Alcohol conditions and International Classification of Diseases (ICD-9 and -10) codes

	ICD-9 codes	ICD-10 codes
Wholly attributable conditions		
Mental and behavioural disorders due to use of alcohol	291, 303, 305	F10
Degeneration of nervous system due to alcohol		G31.2
Alcoholic polyneuropathy	357.5	G62.1
Alcoholic myopathy		G72.1
Alcoholic cardiomyopathy	425.5	I42.6
Alcoholic gastritis	535.3	K29.2
Chronic (incl.) alcoholic liver disease	571.0-571.5, 571.8, 571.9	K70 K73, K74.0-K74.2, K74.6
Alcohol-induced chronic pancreatitis	577.1	K86.0
Excessive blood level of alcohol	790.3	R78.0
Toxic effect of alcohol (Ethanol&Metanol poisoning)	980	T51.0, T51.1, T51.9
Accidental or intentional poisoning by and exposure to alcohol	E860.0, E860.9	X45 X65
Poisoning by and exposure to alcohol, undetermined intent	9805	Y15
Evidence of alcohol involvement determined by blood alcohol level		Y90
Evidence of alcohol involvement determined by level intoxication		Y91
Alcohol-induced acute pancreatitis (2014)	577	K85.2
Alcohol rehabilitation (excluded 2014)	V57	Z50.2
Alcohol deterrents (excluded 2014)	E947.3	Y57.3
Alcohol abuse counselling and surveillance (excluded 2014)		Z71.4
Alcohol use (excluded 2014)		Z72.1
Partly attributable-chronic conditions		
Malignant neoplasm of lip, oral cavity and pharynx	140,141-146,148-149	C00-C14
Malignant neoplasm of oesophagus	150,151	C15
Malignant neoplasm of colon	153	C18, C19, C21
Malignant neoplasm of rectum	154	C20
Malignant neoplasm of liver and intrahepatic bile ducts	155	C22
Malignant neoplasm of larynx	161	C32
Malignant neoplasm of breast	174	C50
Diabetes mellitus (type II)	250	E11

Epilepsy and Status epilepticus	345	G40-G41
Hypertensive diseases	401-405	I10-I15
Ischaemic heart disease	410-414	I20-I25
Cardiac arrhythmias	427.0,427.2,427.3	I47-I48
Haemorrhagic stroke	430-438	I60-I62, I69.0-I69.2
Ischaemic stroke		I63-I66, I69.3-I69.4
	ICD-9 codes	ICD-10 codes
Partly attributable-chronic conditions (cont.)		
Oesophageal varices	456.0-456.2	I85
Unspecified liver disease	571.5-571.9	K73, K74
Cholelithiasis	574	K80
Acute and chronic pancreatitis	577, 577.1	K85, K86.1
Spontaneous abortion	634, 656.5	O03
Tuberculosis	10-18	A15-A19
Pneumonia	480.8, 481, 482.41, 482.8, 484, 486, 487	J10,J11,J12-15, J18
Partly attributable-acute consequences		
Road/ Pedestrian traffic accidents	E810-E819, E826,E829	§
Fall injuries	E880-E888	W00-W19
Other unintentional injuries	E980-E989	§§
Drowning	E910	W65-W74
Fire injuries	E890-E899	X00-X09
Intentional self-harm/Event of undetermined intent	E950-E959	X60-X84, Y10-Y34,Y87,Y87.2
Poisoning	X40-X49	E860-E869, V15.6
Assault	E960,E965,E966,E968,E969	X85-Y09, Y87.1

§ = V021-V029, V031-V039, V041-V049, V092, V093, V123-V129, V133-V139, V143-V149, V194-V196, V203-V209, V213-V219, V223-V229, V233-V239, V243-V249, V253-V259, V263-V269, V273-V279, V283-V289, V294-V299, V304-V309, V314-V319, V324-V329,V334-V339, V344-V349, V354-V359, V364-V369, V374-V379, V384-V389, V394-V399, V404-V409, V414-V419, V424-V429, V434-V439, V444-V449, V454-V459, V464-V469, V474-V479, V484-V489, V494-V499, V504-V509, V514-V519, V524-V529, V534-V539,V544-V549, V554-V559, V564-V569, V574-V579, V584-V589, V594-V599, V604-V609, V614-V619, V624-V629, V634-V639, V644-V649, V654-V659, V664-V669, V674-V679, V684-V689, V694-V699, V704-V709, V714-V719, V724-V729, V734-V739, V744-V749,V754-V759, V764-V769, V774-V779, V784-V789, V794-V799, V803-V805, V811, V821, V830-V833, V840-V843, V850-V853, V860-V863, V870-V878, V892

§§ = V01, V090, V091, V099, V100-V109, V110-V119, V120-122, V130-132, V140-V142, V150-V159, V160-V169,V170-V179, V180-V189, V191-V193, V20-V28: 0.1–0.2; V290-V293, V30-V38: 0.1–0.2; V390-V393, V40-V48: 0.1–0.2; V490-V493, V50-V58: 0.1–0.2; V590-V593, V60-V68: 0.1–0.2; V690-V693, V70-V78: 0.1–0.2; V790-V793, V800, V801, V806–V809, V810, V812–V819,V820, V822–V829,

V834–V839, V844–V849, V854–V859, V864–V869, V879, V88, V890, V891, V893–V899, V90-V94, V95-V97, V98-V99, W20-W52, W75-W84, W85–W99, X10-X19, X20-X29, X30-X33, X50-X57, X58, X59, Y40-Y84 Y85, Y86, Y88, Y89

Source:

1. Jones L, Bellis MA. Updating England-Specific Alcohol-Attributable Fractions. Liverpool: Centre for Public Health, Liverpool John Moores University 2013.

2. Jones L, Bellis MA, Dedman D, Sumnall H, Tocque K. Alcohol-Attributable Fractions for England. Liverpool: Centre for Public Health, Liverpool John Moores Universitythe and North West Public Health Observatory 2008.

3. Grant I, Springbett A, Graham L. Alcohol attributable mortality and morbidity: alcohol population attributable fractions for Scotland. Edinburgh: Information Services Division, NHS National Services Scotland 2009.

Cardiovascular disease International Classification of Diseases (ICD-9 and -10) codes

(Excluded CVD attributable to alcohol consumption)

	ICD-9 codes	ICD-10 codes
Cardiovascular diseases	390-409, 415-429, 440-459	I10-I19, I26-I59, I70-I74

Appendix 2

Ethics Committee

Institute for the Development of Human Research Protections (IHRP)

Building 8 Floor 7 Room 702 Department of Medical Science Ministry Public Health Nonthaburi Thailand 11000

Certificate of Approval

Title of Project: Development and validation of alcohol-related harms prediction model for monitoring and evaluation of alcohol consumption control programmes. (Version 1/291057)

Principal Investigator: Pattara Leelahavarong

Responsible Organization: Health Intervention and Technology Assessment Program

The Ethics Committee of Institute for the Development of Human Research Protections (IHRP) had reviewed the research proposal. Concerning on scientific, ICH-GCP and ethical issues, the committee has approved for the implementation of the research study mentioned above.

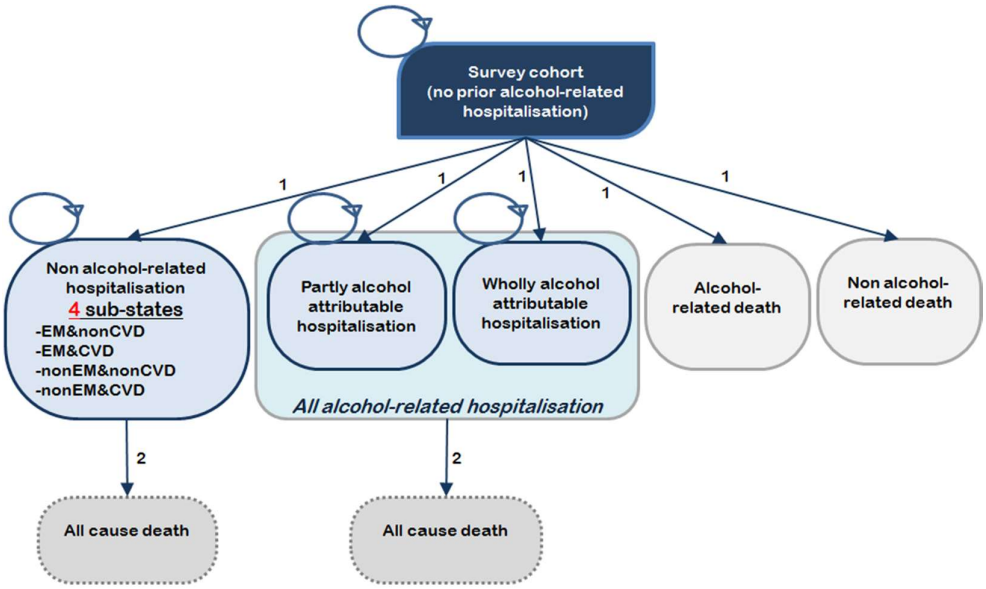
(Dr.Vichai Chokevivat)	(Dr.Pramote Stienrut)
Chairman	Committee and Secretary

Date of First Meeting: November 27, 2014

Date of Approval: November 27, 2014

Appendix 3

Development of the Scottish Alcohol Policy Model



Equation 1: Function (age at survey date, alcohol drinking status at survey date i.e. AUDIT (0-40) & binge drinking (Y/N), cigarette per day, CVD condition (Y/N), diabetes (Y/N), physical activity, BMI, socioeconomic status) subgroup by gender
Equation 2: Function (age at first hospitalisation, CVD condition (Y/N), diabetes (Y/N), socioeconomic status) subgroup by gender

EM: Emergency admission, CVD: Cardiovascular disease

Figure Model structure of Scottish alcohol policy model

Figure presents a modelling health state of alcohol-related hospitalisation and death of no prior alcohol-related hospitalised participant at SHeS survey date (cohort size of 46,230, 20,729 males and 25,501 females). There are five competing first events (equation 1) after survey date classified by the ICD-9 and ICD-10 (Grant et al. 2009; Jones et al. 2008; Jones and Bellis 2014) of primary diagnosis (**Error! Reference source not found.**) as follows: 1) wholly alcohol-attributable hospitalisation (21 conditions); 2) partly alcohol-attributable hospitalisation (26 conditions); 3) alcohol-related death, which is defined as an alcohol-related hospitalised patient died within 28 days; 4) non-alcohol related death, which is defined as a non-alcohol related hospitalised patient died within 28 days; and 5) non-alcohol related hospitalisation divided into four admission types: non-emergency (EM) admission and non-cardiovascular disease (CVD); non-EM admission with CVD; EM admission and non-CVD; and EM

admission with CVD. The follow up time for each participant was defined as the time from interviewed date until either the date of occurring first events or until 31st December 2013 (censoring date).

For estimating LYs and QALYs, this analysis also took into account all causes deaths after patients experienced the first hospitalisations (equation 2) divided into two groups: 1) hospitalised patients who had the first alcohol-related hospitalisation after survey date (either wholly or partly alcohol-attributable hospitalisation); and 2) hospitalised patients who had the first non-alcohol related hospitalisation after survey date. Thus, the follow up time for each hospitalised patient was defined as the date of first hospitalisation until either the date of death or until 31st December 2013 (censoring date). Males and females were modelled separately for all analyses.

Modelling stage I: estimating risk of having first events

During the follow-up period, Cox proportional hazard model (Cox 1972) or a semi-parametric method was used to model the cause-specific hazard functions of the five competing first events as mentioned above (presented as equation 1 in Figure 9-2), for extrapolation beyond the period of follow-up, parametric proportional hazard models (Gompertz regression) was also used (Cleves et al. 2010; Gray et al. 2011a). For differentiated cause of hospitalisations and deaths, ICD-9 and ICD-10 listed (Appendix1) defined wholly and partly alcohol attributable conditions (Grant et al. 2009; Jones et al. 2008; Jones and Bellis 2014). The selected risk factors used for modelling the first events were age at survey date, alcohol drinking status at survey date i.e. AUDIT (0-40) and binge drinking (Y/N), cigarette per day, CVD condition (Y/N), diabetes (Y/N), physical activity (no activity/low activity/medium activity/high activity), BMI(underweight/normal or BMI<25, overweight or BMI 25- <30, obesity or BMI≥30), socioeconomic status, subgroup by gender. All statistical analyses were performed using STATA program version 12 (StataCorp. 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP). Two sides test with P value less than 0.05 was considered statistically significant.

Modelling stage II: estimating life expectancy following hospitalisations

Gompertz model was also used to model the hazard functions of deaths following the first hospitalisations (presented as equation 2 in Figure 2). To classify the cause of deaths to be alcohol-related and non-alcohol related death, ICD-9 and ICD-10 listed (see Appendix 1) defined the alcohol attributable conditions (Grant et al. 2009; Jones et al. 2008; Jones and Bellis 2014). The covariates for modelling the cause- specific deaths were age at first hospitalisation, CVD condition (Y/N), diabetes (Y/N), and socioeconomic status, subgroup by gender. A predicted survival curve of different drinking

status was extrapolated until the probability of surviving beyond the follow-up time point being zero, classified by gender and age at first admission. The area under the predicted survival curve was used to estimate the remaining life expectancy using the trapezoidal rule with half cycle correction (Gray et al. 2011a).

Modelling stage III: estimating life years

The health state transition model with a 1-year cycle period for 100 years or lifetime horizon was developed using Microsoft excel® (Microsoft Corp., Redmond, WA). At the end of a model cycle, an individual risk profile can either remain in no event state or move to one of the first eight competing events i.e. hospitalisation or death states. There were three stages to estimate overall life expectancy of individual risk profile. Firstly, the health state transition model estimated life years remaining upon entering model (after survey date) in particular of each competing event occurring. For incurring first event cohort, to calculate remaining life years after survey date, the analysis model sums the survival time before the first events (derived from Modelling stage I), and the survival time of following first hospitalisations (derived from Modelling stage II). Secondly, the probability of having each first event within an annual cycle was estimated using the cause specific hazard models. This is noted that the sum of those estimated probabilities across all 100 cycles is always equal to 1. Thirdly, the remaining life years of each health state derived from the first stage were weighted by the probabilities of having particular event from the second stage, and the predicted additional life years after survey date were calculated. To estimate the overall life expectancy of survey cohort in particular of risk profile, the additional life years were combined with age at survey date.

Modelling stage IV: Estimation QALY

This stage describes how these estimations are input into the alcohol policy model to estimate QALYs using HRQoL adjusting survival (Billingham et al. 1999; Billingham and Abrams 2002). This approach combines the amount of time patients spend in a number of different health states with weights reflecting the HRQoL of those health states to create a composite measure of quality (referred to as utility) and quantity of life (Billingham and Abrams 2002). Based on the population level approach, the HRQoL of different health states which were derived from modelling stage I were combined with the survival function in each health state as represented by (Billingham and Abrams 2002; Gray et al. 2011b):

$$QALY\ (T) = \int_0^T Q(t)S(t)$$

where $S(t)$ is the proportion of cohorts that survive to time *t* and $Q(t)$ is the average HRQoL score of those survivors, which is then integrated between zero and fixed time *T* . Hence, the quality-adjusted survival curve is formed by plotting against time *t*, the product of the mean HRQoL score of patients alive at time *t*, and the probability of surviving to time *t*.

There are four stages of the alcohol policy model for predicting QALYs. Firstly, starting cohort without prior alcohol-related event was assigned the baseline utility by age at survey date, gender, socioeconomic status, and drinking bahaviour measured by AUDIT. Secondly, the survival cohort who remains to be no hospitalisation was adjusted by only baseline HRQoL until death. For having first hospitalised cohort after survey date, the reduction of HRQoL (utility decrement) was taken into account in the year of life when experienced the first hospitalisation classified by hospitalisation conditions (derived from modelling stage I). Thirdly, the hospitalised patient had the risk of incurring subsequent admissions (derived from modelling stage II), so the effect of these hospitalisations on HRQoL and the annual risk of having following admissions were used for adjusting life year. Finally, the sum of quality-adjusted survival of each annual cycle in different health states was calculated over 100 cycles and presented by remaining QALYs.

Modelling stage V: Assessment of model performance

The developed model is considered to be a theoretical representation of the complex problem and hence undergo a validation process that includes measuring how accurately the model can represent 'real world' patterns. This important validation step helps build confidence in the structure and predictions of a model. For discrimination of the cause specific hazard model, Harrell's C statistic was assessed (Steyerberg 2009), which were proposed as measures of the general predictive discrimination of a survival regression model by Harrell et al. (Harrell et al. 1982; Harrell et al. 1996). The Harrell's C statistic estimates the probability of concordance between predicted and observed responses. A value of 0.5 indicates no predictive discrimination and a value of 1.0 indicates perfect separation of study population with different outcomes (Harrell et al. 1982; Harrell et al. 1996). Notably, this study could assess discrimination where observed events were occurred before censored survival time to compare with the model predicted events. Thus, this analysis would not know how well our model discriminated in the extrapolated period. Predicted life expectancies were obtained from the policy model where the risk factors are provided by average values from the SHeS-NSS/NRS linkage

data. These predicted life expectancies were compared with the Scottish life table (National Records of Scotland 2014). The calibration factors were calculated for adjusting the linear predictors of models.