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The Economic Effects of Reduced Drinking among High-risk Drinkers in Japan

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題目：我が国の高リスク飲酒者に対する飲酒量低減治療の経済効果

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要旨

我が国の健康政策「健康日本 21」（第二次）のアルコール対策目標に、生活習慣のリスクを高める量を飲酒している者（1 日当りの純アルコール摂取量が男性 40g 以上、女性 20g 以上；本研究における「高リスク飲酒者」）の割合を 2022 年までに減少させることが挙げられているが、目標達成は容易でないとの認識もある。そこで、近年のデータを用いた国内の飲酒に関する疾病費用の推計、飲酒量低減の経済効果（飲酒量低減により回避できる、早期死亡による経済損失）の推計、さらにスクリーニング（高リスク飲酒者の特定）とブリーフ・インターベンション（飲酒量低減のための介入）の費用対効果の考察が重要と考えた。

本研究では、2012 年の国内医科診療医療費データを基に、国内の飲酒に関する疾病費用（直接費用と間接費用の合計）を国内先行研究の約 1.5 倍と推計した。また、アルコール寄与率の国内推計値を基に、アルコール関連医療費を国内先行研究の約 1.65 倍と推計した。さらに、高リスク飲酒者の飲酒量低減によりもたらされうる経済効果について、就労中の 40 歳日本人男性をモデルにした場合で年間最大約 3,631 億円、性・年齢階級を考慮した場合で約 1,946 億円、就業率も考慮した場合で約 1,584 億円と推計した。

また、国内外の文献とアルコール治療に携わる国内医師から得られた情報を基に、「健康日本 21」（第二次）の目標達成に必要な介入対象者数を算出し、2 つのレベルのブリーフ・インターベンション（“simple advice”と“extensive intervention”）と 2 つのスクリーニング実施・陽性率の組合せから成る 4 つの介入実施シナリオを設定し、費用対効果を考察したところ、いずれの介入も非介入に比べて費用対効果が良好であった。

国内の飲酒に関する疾病費用は依然として大きく、飲酒量低減による関連疾患の発症予防や進展抑制、早期死亡の回避が経済的負担の軽減に寄与することが示唆された。本研究では、介入の費用対効果が良好であることが示唆されたが、将来的には、より少ない費用での介入実施と全国的普及、飲酒量低減効果を出来るだけ長く維持させるための社会的仕組みづくりが非常に重要と考えられた。

キーワード：疾病費用、健康日本 21、SBI、飲酒量低減、費用対効果

Title: The Economic Effects of Reduced Drinking among High-risk Drinkers in Japan

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Abstract

Japan's health promotion campaign called Health Japan 21 (the second term) includes an alcohol-related goal to reduce the number of high-risk drinkers (more than 40g/day of pure alcohol consumption in men and more than 20g/day in women; "high-risk drinkers" in this thesis) by 2022. However, achieving this goal seems challenging; thus, estimating the cost-of-illness on alcohol with recent data and economic effects of reduced drinking, i.e. economic loss due to premature mortality that can be avoided by reduced drinking, and evaluating the cost-effectiveness of screening and brief intervention (SBI) in Japan were considered important.

In this study, the cost-of-illness on alcohol in Japan (sum of direct and indirect costs) was estimated to be approximately 1.5 times higher than the preceding study, based on 2012 national medical expenditure data. Moreover, medical costs associated with alcohol was approximately 1.65 times higher than the preceding study, based on alcohol-attributed fractions (AAFs) for Japan. Furthermore, annual economic effects brought by reduced drinking among high-risk drinkers were calculated as approximately 363.1 billion yen at maximum when a scenario of 40 year-old Japanese man who works until he reaches the retirement age of 65 years old was used. When the age groups and gender were considered, the economic effects were approximately 194.6 billion yen, and when the employment rates by the age groups and gender were further considered, the possible savings were calculated as approximately 158.4 billion yen.

Furthermore, the number of high-risk drinkers who need to receive SBI was calculated in line with the goal of Health Japan 21 (the second term) based on the systematic literature review and information obtained from some alcohol specialists in Japan. Then, 4 SBI scenarios which consists of 2 levels of brief intervention ("simple advice" and "extensive intervention") and 2 combinations of screening rate and screening positive rate were built to analyze the cost-effectiveness. It was found that the both levels of brief intervention were cost-effective compared to non-intervention.

The cost-of-illness on alcohol in Japan is still large, and it was suggested that the prevention of alcohol-related diseases, disease progression, and premature mortality resulted from reduced drinking contributes to decreased economic burden. In this study, the cost-effectiveness of SBI was confirmed, but further efforts to reduce SBI costs, expand SBI among high-risk drinkers in Japan, and establish a social system to maintain the effects of reduced drinking as long as possible were considered very important.

Key words: Cost-of-illness, Health Japan 21, SBI, reduced drinking, cost-effectiveness

Outline

1. Introduction p. 5

2. Study background and objectives p. 7

2.1. Background p. 7

2.2. Objectives p. 8

3. Cost-of-illness studies on alcohol in Japan and overseas p. 9

3.1. Methods p. 9

3.2. Results p. 11

4. Economic loss due to premature mortality by drinking p. 19

4.1. Methods p. 19

4.2. Results p. 20

5. Screening and brief intervention and its cost-effectiveness p. 26

5.1. Methods p. 26

5.2. Results p. 30

6. Discussions p. 41

6.1. Cost-of-illness studies on alcohol in Japan and overseas p. 42

6.2. Economic loss due to premature mortality by drinking p. 47

6.3. Screening and brief intervention and its cost-effectiveness p. 49

7. Conclusions p. 56

8. Ethical considerations p. 57

Acknowledgements

Conflict of interest statement

9. References p. 59

10. Appendix p. 70

1. Introduction

In Japan, a treatment goal for alcohol dependence has long been abstinence, but many alcohol dependent patients had faced difficulties achieving such challenging goal even with pharmacotherapy for abstinence. Recently, a concept of 'harm reduction' has gained popularity, and reduced drinking as an interim treatment goal for alcohol dependence has become accepted by many physicians and the patients. Currently, no pharmacotherapy for reduced drinking is available in Japan, thus a motivational interviewing called brief intervention is considered as an effective way to support reduced drinking among high-risk drinkers in Japan.

In this thesis, alcohol dependent patients will not be focused, because they need to stop drinking eventually and they are often managed by the clinical setting. This study will thus focus on alcohol use disorder (also known as 'harmful use' or 'alcohol abuse') and unhealthy use (also known as 'problematic drinking' or 'risky use') populations who need to reduce alcohol consumptions in terms of volume and frequency. In this thesis, both alcohol use disorder population and unhealthy use population are defined as high-risk drinkers, and brief intervention is further divided into 2 levels: "extensive intervention," which is normally multiple counseling sessions provided to the former population and "simple advice," which is a single brief advice to the latter population.

The brief intervention is usually provided in a routine clinical setting, and it shall be distinguished from the longer and more intense psychologically-based intervention which does not occur in a routine clinical setting.

The burden of disease associated with alcohol is as high as the burden of disease associated with smoking, for example, and the Japanese government has been putting continuous efforts to reduce the number of high-risk drinkers in Japan. In fact, Japan's Health Promotion campaign called Health Japan 21 (the second term) includes an alcohol-related goal to reduce the proportion of high-risk drinkers (more than 40g/day of pure alcohol consumption in men and more than 20g/day in women) in Japan by 2022.

In this thesis, after the description of study background and objectives in Section 2, cost-of-illness study methodologies on alcohol in Japan and overseas were analyzed based on the systematic literature review in Section 3, then economic loss due to premature mortality by drinking were estimated in line with the goal of Health Japan 21 (the second term) in Section 4. Since screening and brief intervention (SBI) to high-risk drinkers helps them achieve reduced drinking, its methodologies and outcomes in Japan and overseas were analyzed based on the systematic literature review, then its cost-effectiveness in Japan was considered in Section 5. The overall discussions and conclusions are described in Section 6 and 7, respectively. The most of the contents

described in Section 3, 4, 5, 6, and 7 of this thesis have been published in peer-reviewed journals by the author.

2. Study background and objectives

2.1. Background

In 2000, Japan's Ministry of Health, Labour and Welfare (MHLW) initiated a 10-year health promotion campaign called Health Japan 21 (the first term) to prevent premature mortality from non-communicable disease and injuries[1)]. Decreasing the proportion of heavy drinkers (more than 60g/day on average of pure alcohol consumption in men and women) was included in the goals, but it was not successful in that the proportion of heavy drinkers in 2010 was slightly higher (4.8% in men, 0.4% in women) than that in the baseline (4.1% in men, 0.3% in women) at the final evaluation[2)]. Thus, a goal was set continuously in Health Japan 21 (the second term) in 2010 to reduce the proportion of high-risk drinkers (more than 40g/day of pure alcohol consumption in men and more than 20g/day in women) who have high potential of developing life-style related diseases in Japan by 2022[1)].

Alcohol-related disease awareness, defined as understanding of signs, symptoms and consequences of alcohol use disorders, is low in Japan and overseas[3)] despite its high

clinical, economic, and social burden. Cost-of-illness (COI) studies are often conducted to show economic and social burden of disease to healthcare decision-makers. However, COI studies on alcohol in Japan are very limited and data used are relatively old, thus estimating alcohol-related medical and social costs with recent data and showing alcohol-attributable medical care costs possibly saved by reduced drinking in line with the goal of Health Japan 21 (the second term) are considered valuable in supporting Japan's healthcare policy.

Furthermore, importance of providing SBI to high-risk drinkers not only in the specialized alcohol treatment sites but also in the primary care sites has been discussed in Japan[4], and further expansion and cost-effective implementation of SBI are requested in Japan[5] to surely reduce the number of high-risk drinkers and to achieve the goal of Health Japan 21 (the second term) by 2022.

2.2. Objectives

The objectives of the study are following:

1) Comparative analysis of methodologies of COI studies on alcohol in Japan and overseas, and calculation of alcohol-attributable medical care costs in Japan based on recent government statistics and alcohol-attributed fractions (AAFs) for Japan

2) Estimation of economic loss due to premature mortality by drinking in line with

the goal of Health Japan 21 (the second term)

3) Considerations of feasibility and cost-effectiveness of SBI in Japan in achieving the goal of Health Japan 21 (the second term)

3. Cost-of-illness studies on alcohol in Japan and overseas

3.1. Methods

A systematic literature review was conducted in October, 2014 by searching major electronic databases PubMed and Embase to identify relevant publications in English between the years 2005-2014 (past 10 years) concerning the COI studies on alcohol. The literature searches were conducted by combining the following terms: “cost-of-illness” and “alcohol”. First, the titles and abstracts of the potentially relevant publications were assessed, and publications irrelevant to COI studies on alcohol were excluded. Then, COI studies focused on developing countries, or not written in English were excluded. Review articles were also excluded but eligible COI studies or relevant government reports were further identified by checking references of such review articles. Likewise, COI studies on alcohol in Japan were identified from the widely recognized Japanese electronic database, Igaku-Chuo-Zasshi (Ichu-shi) with the following terms in Japanese:「疾病費用」and「酒」. Since few eligible publications were expected, the year of publication

was not limited in Ichu-shi. The search and retrieval process for the literature review is described in **Figure 1.**

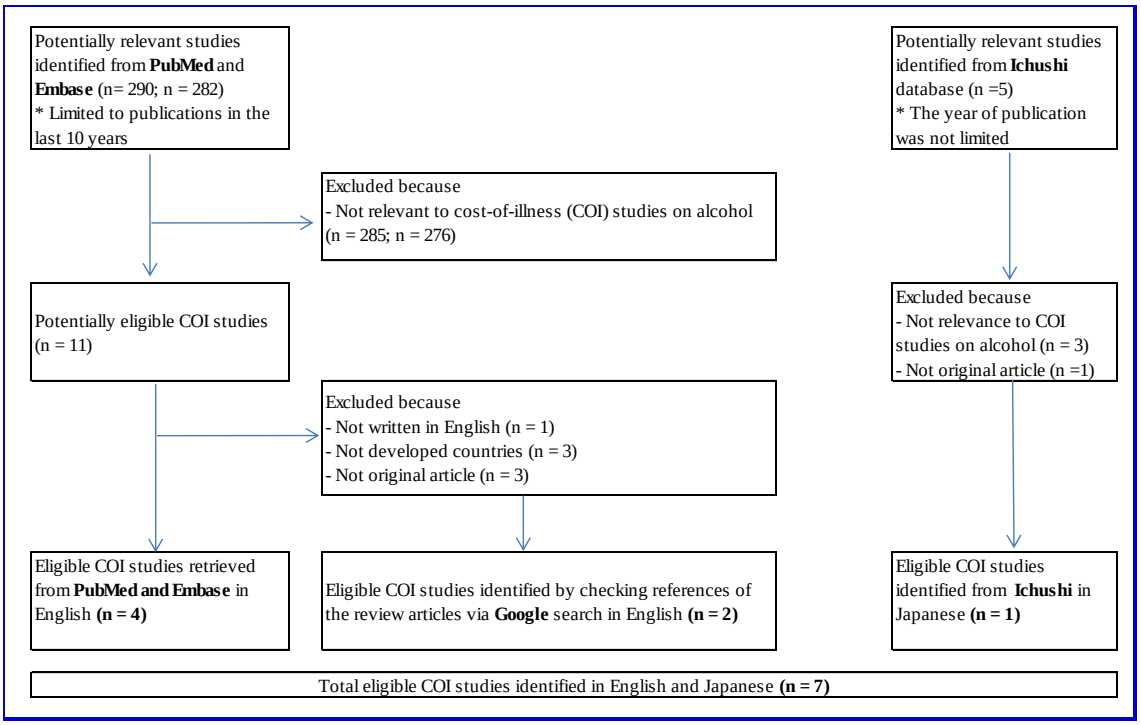

Figure 1: Search and retrieval process

Each eligible study identified from the systematic review was reviewed and summary tables were created to facilitate comparative analysis of the cost components included in the COI studies as well as total estimated costs of alcohol-attributable diseases and proportions of direct and indirect costs in Japan and other developed countries.

Furthermore, alcohol-attributable medical care costs in Japan were calculated with 2012 medical care costs data by different diagnostic disease categories (above 15 years old). The study first used the same service utilization rate as the preceding study, assuming that there is no change overtime. Then, the study exploratory used AAFs for

Japan obtained from a global burden of disease study attributable to alcohol, except for AAFs for digestive disorders for which assumption was necessary. AAFs represented the proportion of each outcome such as number of deaths or burden of disease and injury in disability-adjusted life-years (DALYs) that were attributable to alcohol. Since some diagnostic disease categories in Japan did not fully match with AAFs for Japan available, the same service utilization rate in the preceding study was used for them.

3.2. Results

The systematic literature review resulted in final retrieval of 7 original COI studies on alcohol from 7 developed countries/legal entities (Japan, US, Portugal, Sweden, Scotland, England, and Ireland) out of 572 potentially relevant studies from PubMed and Embase and 5 potentially relevant studies from Ichu-shi as shown in **Figure 1**. Irrelevant COI studies on alcohol were excluded. Then, 3 studies focused on developing countries (Estonia, South Africa, and Thailand) were excluded, given the secondary purpose of the study. Furthermore, 1 article written in Spanish except for abstract and 3 review articles were excluded, although the study by Thavorncharoensap et al.[6] provided a very good overview of international comparison.

Regarding the eligible COI studies on alcohol in Japan, only 1 article published in 1993 by Nakamura et al.[7] was identified. In this preceding study, the cost estimation was based

on 1987 medical care costs data by different diagnostic disease categories (above 15 years old), and alcohol-attributed medical costs were calculated by multiplying alcohol-attributable service utilization rate, which was estimated from the number of inpatients, average hospitalization length, and alcohol-attributable morbidity percentage based on ICD-9 (the 9th International Classification of Disease) codes.

There was another relevant Japanese study reported in 2012 based on the 2008 national survey data, but the information existed only as a conference proceeding and detailed description of the methodology was not available, thus it was excluded. Actually, the cost estimation based on the 2008 national survey data was also reported in a section of White Paper on Alcohol[8], but the methodology was based on the study conducted by Nakamura et al.[7], thus it was considered as a reference.

Table 1 provides an overview of the cost components included in the COI studies on alcohol in the 7 countries. All countries estimated the direct costs (outpatient and inpatient care including drug/service costs and hospitalization, property damage due to criminal justice, motor vehicle crashes due to drunk driving) and indirect costs (productivity loss due to premature mortality, presenteeism or "days at work but limited in performing job tasks because of health" [9]), but cost estimation on absenteeism or "days of work missed because of illness"[9] was unknown in Japan. More than 4 countries included following

direct costs (research and prevention, nursing homes, fire losses, welfare assistance/social work) and indirect costs (productivity loss due to early retirement). Only US included cost items on Fetal Alcohol Syndrome (FAS).

Sweden and England had an additional cost category called "intangible costs." According to the study which estimated economic and human costs in Sweden in 2002[10], intangible costs refer to Quality of Life (QOL) losses from alcohol consumption (pain, suffering, distress, loss of life/bereavement), and there is no appropriate methodology existing and this approach is seldom used in the COI analysis. In England, Department of Health[11] also calculated intangible costs related to alcohol, but it was limited to the costs of high-risk drinkers (more than 3-4 units of alcohol for men and 2-3 units for women per day, when 1 unit is equal to 10 ml of pure alcohol), thus it was not possible to compare with the case of Sweden, where QOL losses of relatives, friends, and crime victims were also estimated. Other countries mentioned methodological limitation for not calculating intangible costs.

The costs related to crime victims, crime victim property damage, and lost day due to incarceration were not calculated in Japan due to limited data, while they were calculated in the US[12], Portugal[13], Sweden[10], England[11], and Ireland[14].

Table 1: Cost components included in the COI studies

Cost Components		Japan (Nakamura, 1993)	US (Bouchery, 2011)	Portugal (Cortez-Pinto, 2010)	Sweden (Jarl, 2008)	Scotland (Johnston, 2012)	England (Dept of Health, 2008)	Ireland (Byrne, 2010)
Direct costs	Health care costs/outpatient care costs	○	○	○	○	○	○	○
	Hospitalization/inpatient care costs	○	○ only primary diagnosis-related	○	○	○	○	○
	Amburatory care costs	unknown	○ only primary diagnosis-related	○	unknown	○	○	○
	Fetal alcohol syndrome (FAS)	×	○	×	×	unknown	×	×
	Health insurance administration costs	○	○	unknown	unknown	unknown	unknown	unknown
	Drugs/services	○	○	○	○	○	○ Drug dispensing costs are not included	○
	Research and prevention costs	○	○	×	○	○	○	×
	Nursing homes	○	○	unknown	unknown	○	○	unknown
	Crime victims	unknown	○	○ (Thavorncharonsap, 2009)	○	unknown	○	○
	Property damanage due to criminal justice	○	○	○	○	○	○	○
	Motor vehicle crashes due to drunken driving	○	○	○	○	○	○	○
	Fire losses	○	○	unknown	○	unknown	○	unknown
	Crime victim property damage	unknown	○	○	○	×	○	○
	Special education costs on FAS	×	○	×	×	unknown	×	×
	Welfare assistance/social work	○	unknown	○	○	○	×	○
Indirect costs	Productivity loss due to premature mortality	○	○ Underage drinking and productivity loss at home are included	○	○	○	○	○ Suicide related to alcohol are included
	Presenteeism (reduced on-the-job productivity)	○	○	○	○	○	○	○
	Absenteeism (being absent from work)	unknown	○	○	○	○	○	○
	Productivity loss due to early retirememt	○	×	○	○	○	○	○
	Lost day due to crime victims and incarceration	×	○	○	○	unknown	○	unknown
	Fetal alcohol syndrome (FAS)	×	○	×	×	unknown	unknown	unknown
Intangible costs	QOL losses from alcohol consumption (pain, suffering, distress, loss of life/bereavement)	× Due to methodological limitation	× Due to methodological limitation	× Due to methodological limitation	○ Alcohol consumers, their relatives and friends, and crime victims are considered	× Despite mentioning importance	○ Only high-risk drinkers are considered (counseling fees are calculated by Willingness-to-pay approach)	× Due to methodological limitation

Table 2 shows total estimated COI on alcohol and proportions of direct and indirect costs in 5 selected countries (Japan, US, Sweden, England, and Ireland). Portugal[13] and Scotland[15] were excluded from the comparative analysis because healthcare and hospitalization costs (sum of outpatient and inpatient care costs) did not account for the largest share of direct costs, which was different from Japan.

According to Nakamura et al.[7], the total costs of inappropriate drinking in Japan were approximately 6.6 trillion yen (sum of direct costs of 1,298.9 billion and indirect costs of 5,338.7 billion yen). The proportions of direct and indirect costs in Japan were 19.6% and 80.4%, respectively, while those in other countries ranged widely from 14.0% to 83.1% for direct costs and from 16.9% to 86.0% for indirect costs. England had the lowest proportion of direct costs (14%); however, when the intangible cost (25%) was included, the proportions of direct and indirect costs were equivalent (38% and 37%, respectively). In Sweden, intangible costs accounted for as much as 83.2% of total estimated costs, lowering the proportions of both direct and indirect costs to one sixth compared to the pre-inclusion.

Table 2: Costs and proportions

	Total estimated costs and proportions	Japan (Nakamura, 1993)		US (Bouchery, 2011)		Sweden (Jarl, 2008)			England (Dept of Health, 2008)		Note: England (Cabinet Office, 2003)	Ireland (Byrne, 2010)	
		billion ¥	%	million $	%	million SEK	%	%	million £	%	%	million £	%
Direct costs	health care costs/outpatient care costs	1,174.2		10,668		1,540			167.6			1,200	
	hospitalization/inpatient care costs	Included in health care costs		5,116		1,680			Included in health care costs			Included in health care costs	
	amburatory care costs	NA		1,196		NA			Included in health care costs			Included in health care costs	
	fetal alcohol syndrome (FAS)	NA		2,054		NA			NA			NA	
	Health insurance administration costs	88.6		1,586		NA			NA			NA	
	Drugs/services	Included in health care costs		1,212		75			Included in health care costs			Included in health care costs	
	Research and prevention costs	Included in insurance administration costs		1,207		479			Included in health care costs			NA	
	Nursing homes	Included in health care costs		1,003		NA			Included in health care costs			NA	
	Crime victims	NA	**19.6**	NA	**28.9**	2,850	**37.5**	6.3	NA	**14.0**	38.0	3	**83.1**
	property damanage due to criminal justice	0.2		20,973		Included in crime victims costs			Included in health care costs			435	
	motor vehicle crashes due to drunken driving	3.5		13,718		Included in crime victims costs			Included in health care costs			526	
	fire losses	8.9		2,137		Included in crime victims costs			Included in health care costs			NA	
	crime victim property damage	NA		440		Included in crime victims costs			Included in health care costs			171	
	special education costs on FAS	NA		369		NA			NA			NA	
	welfare assistance/social work	23.5		NA		4,364			Included in health care costs			264	
Indirect costs	productivity loss due to premature mortality	923.1		65,062		8,520			1,023			277 (including suicide)	
	presenteeism (reduced on-the-job productivity)	4,257.3		74,102		1,175			Included above			197	
	absenteeism (being absent from work)	NA	**80.4**	4,238	**71.1**	4,908	**62.5**	10.5	Included above	**86.0**	37.0	330	**16.9**
	productivity loss due to early retirememt	158.3		NA		3,177			Included above			Included in presenteeism	
	lost day due to crime victims and incarceration	NA		6,329		614			NA			NA	
	fetal alcohol syndrome (FAS)	NA		2,054		NA			NA			NA	
Intangible costs	QOL losses from alcohol consumption (pain, suffering, distress, loss of life/bereavement)	NA	NA	NA	NA	145,356 (lost QALY)	NA	83.2	Unknown (thus referrd to Cabinet Office report)	NA	25.0	NA	NA

According to the global burden of disease study attributable to alcohol[16], the top 3 diseases associated with high-risk drinking in Japan were cancer, followed by unintentional and intentional injuries and liver cirrhosis. Moreover, AAFs for Japan were following: cancer (11% in men, 6% in women), unintentional and intentional injuries (18% in men, 13% in women), liver cirrhosis (70% in men, 68% in women), neuropsychiatric disorders (4% in men, 2% in women), cardiovascular diseases (4% in men, 0% in women), where 0% indicates fewer than 500 alcohol-attributable DALYs in the disease category.

Gatjahr et al.[17] describes that alcohol-related negative health consequences are categorized into chronic conditions such as cancer and liver cirrhosis and acute conditions such as injuries and suicide. AAFs for chronic conditions are usually determined by combining relative risks (RRs) and prevalence data at different alcohol consumption levels, and AAFs for acute conditions are usually determined by including the cases happened under the influence of alcohol at the time of the event.

Table 3 shows calculation of alcohol-attributable medical treatment costs in Japan, based on electronic statistical data released on Oct 8, 2014 by Japan's Ministry of Health, Labour and Welfare (MHLW) and Statistics Bureau of the Ministry of Internal Affairs and Communications[18], and 2012 national medical expenditure data by diagnostic

disease category (adjusted by hospitalization status, age groups and gender). AAFs for Japan were used and the results were compared with those by Nakamura et al.[7].

Table 3: Medical care costs with AAFs

AAFs for Japan (Rehm, 2009)			AAFs-multiplied costs based on 2012 data (MHLW, 2014)		Alcohol attributable treatment costs (MHLW, 2014)
	Men	Women	Men	Women	(billion ¥)
Cancer	11%	6%	225.64	102.86	328.51
Neuropsychiatric disorders	4%	2%	35.43	19.35	54.79
Cardiovascular disorders	4%	0%	40.14	0.00	40.14
Cirrhosis of the liver	70%	68%	66.29	52.36	118.65
Digestive disorders (assumed)	52%	37%	441.95	286.97	728.92
Total	NA	NA	809.45	461.55	1271.00

Nakamura (1987 data)				Gov't Stats (2012 data) Table 13		Gov't stats (2012 data) Table 15 and AAFs
Disease Category	Total medical care costs (billion ¥) (above 15 years old)	Alcohol-attributable service utilization rate (%)	Alcohol-attributable medical care costs (billion ¥)	Total medical care costs (billion ¥) (above 15 years old)	Alcohol-attributable medical care costs (billion ¥) *When same service utilization was used	Alcohol-attributable medical care costs (billion ¥) *When AAFs-multiplied medical costs were combined
Infectious and parasitic diseases	456	16.38	74.7	557	91.2	91.2
Neoplasm	1,174	**6.30**	74.0	3,766	237.3	**328.51**
Mental disorders	1,114	**4.78**	53.2	1,853	88.5	**54.79**
Diseases of the circulatory system	3,780	**0.04**	1.6	5,780	2.4	**40.14**
Diseases of the digestive system	1,881	**34.00**	639.5	1,626	552.6	**728.92**
Diseases of the nervous system	978	1.76	17.2	1,183	20.8	20.8
Endocrine, nutritional and metabolic diseases	669	18.89	126.4	1,942	366.8	366.8
External causes of injury and poisoning	1,091	10.00	109.1	1,853	185.3	185.3
(Other disease categories)	4,673	Included in tot	NA			
Total	**15,816**		**1095.7**	**18,558**	**1,545.0**	**1,816.5**

When alcohol-attributable medical care costs were calculated based on the 2012 data using the same alcohol-attributable service utilization rates of 1987, the total amount was 1,545 billion yen (approximately 1.5 times as much as the amount in the preceding study), and when AAFs-multiplied medical costs based on 2012 data were used for the 4 disease categories that were available, the total amount was 1,816.5 billion yen (approximately 1.65 times as much as the amount in the preceding study) as shown in **Table 3**. Given Japan's total national medical care expenses of approximately 39.2 trillion yen in 2012,

these alcohol-attributable treatment costs accounted for 3.9-4.6% of the total expenses.

4. Economic loss due to premature mortality by drinking

4.1. Methods

In the previous section, alcohol-attributable medical care costs were calculated based on the Japanese government's statistical data on medical expenses in 2012 (adjusted by disease categories, age groups, and gender) and also by using AAFs for Japan for some disease groups associated with alcohol consumption. In this section, possibly saved costs by reduced drinking among high-risk drinkers in Japan were estimated by calculating salaries that could have been earned by avoiding premature mortality with a base case scenario of 40-year-old Japanese man who works until he reaches the retirement age of 65 years old. Possibly saved costs by reduced drinking among housewives/homemakers and unemployed persons were excluded from the calculation due to limited data.

Then, a scenario analysis was conducted with different age groups (40s, 50s, and 60s) and gender. Since the base case estimation initially used an assumption of 100% employment rates, different employment rates by age groups and gender reported by the Japanese government were applied to make more realistic estimation.

In order to estimate costs possibly saved by reduced drinking, the number of high-risk

drinkers in Japan who need to reduce volume and/or frequency of alcohol consumption was calculated in the ideal scenario of achieving the goal of Health Japan 21 (the second term)[19], based on the Japanese population data (as of October 1, 2012) adjusted by age groups and gender[20]. Then, additional costs incurred for additional clinical practices, i.e., costs associated with SBI, were estimated based on the data from a representative alcohol treatment facility in Japan. Decreased tax revenue from decreased purchase of alcoholic beverages was also calculated based on the 2012 government data on tax revenue[21]. The costs for SBI and decreased tax revenue were subtracted from the possibly saved costs calculation. Finally, a scenario analysis was conducted with use of parameters such as employment rates and drinking volume and frequency by age groups and gender.

4.2. Results

According to the national survey conducted in 4,153 adults in Japan (response rate of 58%) based on 2012 population data[22], a life-time prevalence of alcohol dependence was 2.1% (n = 950,000) for men and 0.2% (n = 140,000) for women, totaling 1.09 million. The national survey also reported that when more than 20 points in the Alcohol Use Disorders Identification Test (AUDIT) screening are considered as probable alcohol dependence and more than 16 points as potential alcohol dependence, 1.13 million probable and 2.63 million potential alcohol dependent persons are assumed to exist in

Japan.

Although a traditional treatment goal for alcohol dependence in Japan has been abstinence, an early intervention of reduced drinking as a mid-term treatment goal for some patients (such as diagnosed alcohol dependent patients who have difficulty in maintaining abstinence or undiagnosed high-risk drinkers) has also been discussed among both alcohol specialists and non-specialists[23], because of 'health gain' or decreased mortality rate[24], particularly among high-risk drinkers (men: >60g/day and women: >40g/day).

In 2000, the MHLW initiated a 10-year health promotion campaign called Health Japan 21 (the first term) to prevent premature mortality from non-communicable diseases and injuries[1]. Decreasing the number of heavy drinkers (more than 60g/day on average of pure alcohol consumption in men and women) was included in the objectives, but it was not successful as previously mentioned. Thus, the Japanese government has continuously set a goal in 2010 (the second term) to reduce a proportion of high-risk drinkers (men: >40 g/day and women: >20 g/day) from 15.3% to 13% in men, and from 7.5% to 6.4% in women by 2022[19]. To achieve this goal, approximately 3.05 million adults aged 20 or older need to reduce their alcohol consumption over 12 years from 2010, based on 2010 Japanese population. This means that approximately 0.2% or 254,210 adults per year need

to receive brief intervention, which is “10 to 15 minutes of counseling, with feedback about drinking, advice and goal setting, and follow-up contact (one or more discussions lasting 10 to 15 minutes with a clinician)” [25]. Since brief intervention is known to be successful in half of the patients according to the case of Kurihama Medical and Addiction Center[26], it was considered that 508,420 adults per year would need to receive such brief intervention.

Miyakawa et al. provides medical costs on alcohol treatment in Japan by following 4 categories: 1) one routine examination (visit by abnormal value found in the annual health examination), 2) preventive treatment as an outpatient for education and testing (group psychotherapy plus 5 examinations), 3) normal outpatient treatment after discharged from the hospital, and 4) hospitalization of alcohol dependent patients for 3 months[27]. The costs associated with introducing brief intervention to high-risk drinkers in Japan are related to 1) and 2), because patients for 3) and 4) are usually instructed to keep abstinence and avoid binge drinking. Assuming that one person needs to visit a medical institution 2 times for 1) and 6 times for 2), the total costs (100% costs, not out-of-pocket payment amount) per person per year would become 9,360 yen for 1) and 51,750 yen for 2). Also assuming that 254,210 adults (50%) undergo type 1) and another 254,210 adults (50%) undergo type 2), annual costs for conducting the brief intervention to 508,420 adults in

Japan would become approximately 15.5 billion yen per year, considering the optimistic 50% success rate.

Rehm and Roerecke found a reduction of 20g/day of pure alcohol consumption in heavy drinkers, who consume more than 48g/day of pure alcohol, lowered the annual mortality risk to approximately 1% in Europe[24]. Thus, it was assumed that successful reduction of 20g/day of pure alcohol consumption in 254,210 high-risk drinkers per year would save the lives of 2,542 high-risk drinkers per year in Japan. Considering the case of 40-year-old Japanese man (university graduate) with an annual salary of 6 million yen according to 2012 Basic Survey on Wage Structure[28], preventing potential loss of 25 more years of employment could save as much as 0.15 billion yen per person or as much as 381.3 billion yen per year. Moreover, given that the national tax revenue from selling alcohol in 2012 was approximately 1.35 trillion yen[21], if the 0.2% of high-risk drinkers refrained from purchasing alcohol beverages, the decreased tax revenue was estimated at approximately 2.7 billion yen. Thus, a successful reduction of high-risk drinkers in line with the goal of Health Japan 21 (the second term) on alcohol would save at least 363.1 billion yen per year, after subtracting 15.5 billion and 2.7 billion yen.

The results of the scenario analysis of possibly saved amounts of 363.1 billion yen are shown in the **Table 4**.

Table 4: Scenario analysis of possibly saved amounts

	①	②	③ (=①x②)	④	③x④	
	Average annual salaries until retirement (yen)	Number of years until retirement	Economic loss due to premature mortality/person	Breakdown: Men 66% Women 34%		**If employment rates are100% (productivity of non-employed person= productivity of employed person)**
40 years old men	5,935,810	25	148,395,250	1,678	249,007,229,500	
40 years old women	3,781,990	25	94,549,750	864	81,690,984,000	
				2,542	330,698,213,500	**a**
50 years old men	5,798,233	15	86,973,495	1,678	145,941,524,610	
50 years old women	3,661,350	15	54,920,250	864	47,451,096,000	
				2,542	193,392,620,610	**b**
60 years old men	5,340,650	5	26,703,250	1,678	44,808,053,500	
60 years old women	3,474,750	5	17,373,750	864	15,010,920,000	
				2,542	59,818,973,500	**c**
(a+b+c)/3					**194,636,602,537**	**Appox. 194.6 billion yen**

						If employment rates are considered
40 years old men	5,269,920	25	131,748,000	1,678	221,073,144,000	
40 years old women	2,516,524	25	62,913,100	864	54,356,918,400	
				2,542	275,430,062,400	**a**
50 years old men	4,976,194	15	74,642,910	1,678	125,250,802,980	
50 years old women	2,291,084	15	34,366,260	864	29,692,448,640	
				2,542	154,943,251,620	**b**
60 years old men	4,352,630	5	21,763,150	1,678	36,518,565,700	
60 years old women	1,945,860	5	9,729,300	864	8,406,115,200	
				2,542	44,924,680,900	**c**
(a+b+c)/3					**158,432,664,973**	**Approx. 158.4 billion yen**

According to the 2014 salary census[29], average annual salaries for men and women (all academic backgrounds) were 5,570,950 yen and 3,891,350 yen, respectively in the age category of 35-44 years old (the average of age category of 35-39 and age category of 40-44 was calculated and defined as the salary of 40 years old men and women); 6,713,400 yen and 4,034,550 yen in 45-54 years old (the average of age category of 45-49 and age category of 50-54 was calculated and defined as the salary of 50 years old men and women); and 5,340,650 yen and 3,474,750 yen in 55-64 years old (the average of age category of 55-59 and age category of 60-64 was calculated and defined as the

salary of 60 years old men and women). Then, average annual salaries until retirement in **Table 4** were calculated based on these amounts. For example, the average annual salary until retirement for 40 years old men was calculated based on the following formula: (5,570,950 yen x 5 years) + (6,713,400 yen x 10) + (5,340,650 yen x 10)/25 = 5,935,810 yen.

According to the 2012 national health and nutrition survey in Japan[30], proportions of drinkers who are 20 years old or above and who are defined as high-risk drinkers (more than 40g/day of pure alcohol consumption in men and more than 20g/day in women) were 14.7% in men and 7.6% in women, which corresponds to approximately 66% in men and 34% in women. Thus, the breakdown of the annual 2,542 high-risk drinkers whose lives could be saved by reduced drinking[1] were calculated as 1,678 men and 864 women; then average salaries for men and women in their 30s, 40s, and 50s were calculated.

Moreover, according to the 2014 employment rate data in Japan[31], employment rates for men and women were 93.3% and 70.1%, respectively in the age category of 35-44 years old; 92.7% and 73.9% in 45-54 years old; and 81.5% and 56.0% in 55-64 years old. Thus, these were multiplied to the annual average salaries of men and women in their 40s, 50s, and 60s. When the employment rates for all high-risk drinkers were

considered as 100%, the possible savings by reduced drinking were approximately 194.6 billion yen in the scenario analysis. Meanwhile, when the employment rates by age groups and gender were further considered, the possible savings were calculated as approximately 158.4 billion yen.

5. Screening and brief intervention and its cost-effectiveness

5.1. Methods

A systematic literature review was conducted in February, 2015 by searching major electronic databases PubMed, Embase, and Ichu-shi to identify relevant publications in English and Japanese concerning SBI to reduce alcohol consumption and concerning cost-effective or cost-benefit analysis of SBI. The literature search was conducted by combining the following terms: “cost-effectiveness” “cost-benefit” “brief intervention” and “alcohol.” For the Japanese literature database Ichu-shi, the terms「スクリーニング」and「ブリーフ・インターベンション」were used.

First, the titles and abstracts of the potentially relevant publications including review articles were assessed, and irrelevant publications, such as those focused on SBI in the emergency department or hospitalized patients, were excluded. Then, 7 additional publications were obtained from PubMed, Embase, Ichu-shi, and Google by checking

references of the 9 relevant publications initially extracted. The search and retrieval process for the literature review is described in **Figure 2**.

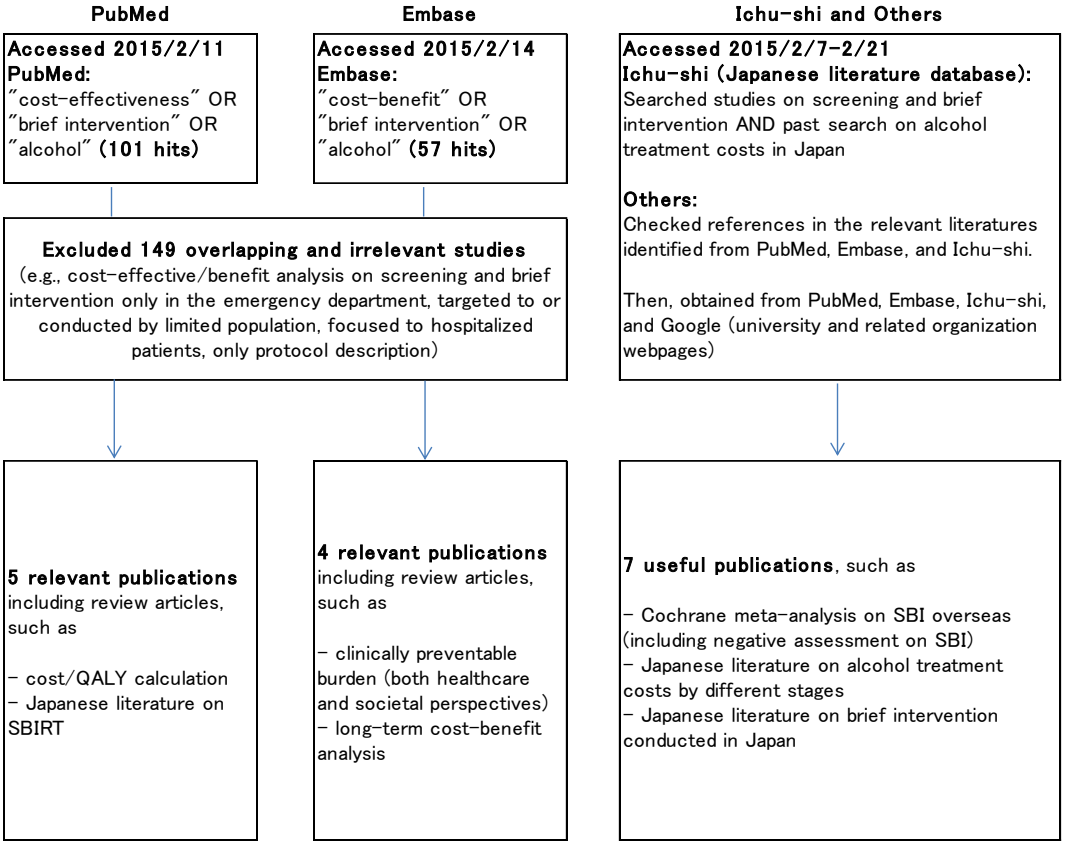

Figure 2: Search and retrieval process

Information such as who provide and receive SBI, how many times and how often provided, which screening tools or brief intervention materials are used, how the outcomes are measured, whether SBI was cost-effective or not, whether follow-up is provided or not, and others were collected from the literatures and summarized in a table.

Then, information not fully obtained from the literatures, for example information on preparation and implementation costs of SBI, hourly costs of physicians and other

healthcare provides, were identified, so that the information can be obtained from the semi-structured physician interview. An interview guide was prepared, and 5 physicians who treat alcohol dependent and/or alcohol use disorder patients including high-risk drinkers in Japan (both at specialized alcohol treatment sites and primary care sites across Japan) were interviewed from March to April, 2015 and asked about their daily SBI practices and future challenges in expanding SBI among high-risk drinkers in Japan.

Based on the findings from the literatures on SBI in Japan and overseas and the physician interviews, 4 SBI scenarios were established. The scenarios were separated by 2 levels of brief intervention: “simple advice” and “extensive intervention,” which were considered equivalent to “brief advice” for drinkers who had AUDIT scores of 8-15 and “brief advice and simple counseling, continuous intervention” for drinkers who had AUDIT scores of 16-19, respectively[32]. The scenarios were also separated by 2 sets of screening parameters (i.e., a combination of screening rate of 50% and positive screening rate of 80%, and a combination of screening rate of 30% and positive screening rate of 60%); then, SBI success rates of 20% (the average of optimistic 30% and pessimistic 10%) were applied to the 4 SBI scenarios.

Furthermore, preparation and implementation costs for 2 levels of SBI to one high-risk drinker per year in Japan were estimated based on the costs and outcomes data obtained

from the literatures and physician interviews. It was assumed that SBI was successful if the high-risk drinkers could reduce their alcohol consumption by 30% compared to baseline after one year. According to the observational study conducted in primary care in England[33], the utility values obtained from EQ-5D were 0.609 in 'high-risk drinkers' (61-100g/day of average pure alcohol consumption in men and 41-60g/day in women), 0.714 in 'medium-risk drinkers' (41-60g/day in men and 21-40g/day in women), and 0.755 in 'low-risk drinkers' (0-40g/day in men and 0-20g/day in women) as defined by World Health Organization (WHO). Thus, differences in these utility values were applied to the SBI scenario in this study. In other words, it was considered that the utility values of 0.105 and 0.041 could be obtained from the "extensive intervention" and "simple advice," respectively. Alcohol-attributed death were not considered in this study.

Finally, cost-effectiveness of 2 levels of SBI was analyzed by calculating the quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs). Then, optimistic and pessimistic case analyses were conducted in comparison to the base case analysis by changing the QALYs. Furthermore, alternative ways to expand SBI among high-risk drinkers in Japan to achieve the goal of Health Japan 21 (the second term) by 2022 were considered from the perspectives of feasibility and cost-effectiveness.

5.2. Results

Table 5 summarizes the findings from 11 relevant literatures (including 2 relevant literatures indirectly obtained from Ichu-shi and others) [34-44] on SBI target population, SBI provision methods, and the outcomes in the Unites States, Italy, Netherlands, United Kingdom, and Japan. Although the descriptions of the target population were somewhat different among countries, they were generally comparable to the SBI target, i.e. high-risk drinkers, defined in the Health Japan 21 (the second term).

Table 5: Target population, provision methods, and outcomes of SBI

Database	Embase	Embase	Embase	Embase	PubMed	PubMed	PubMed	PubMed	PubMed	Ichu-shi and Others	Ichu-shi and Others
Authors, year published	**Bray, et al. 2012**	**Solberg, et al. 2008**	**Bray, et, al. 2014**	**Fleming, et al. 2002**	**Angus, et al. 2014**	**Tariq, et, al. 2009**	**Cowell, et al. 2010**	**Purshouse, et al. 2013**	**Ino and Cho, 2013**	**Muto, et al. 2013**	**Ito, et al. 2015**
Country, Research setting	US: Literature review	US: Literature review	US: original research	US: TrEAT RCT 48-month efficacy and cost-benefit analysis	Italy: ICER vs do nothing scenario	Netherlands: primary care	UK: NICE view on different types of HE evaluations	UK: BI in primary care Established a new model to satisfy study purposes a) seek optimal BI implementation (providers, time, frequency, etc.) and b) national applicability	Japan: Literature review on SBIRT (SBI, Referral to Treatment) at a specialized alcohol treatment site (to support physician fees)	Japan：Medical records of Hizen Psychiatric Center satellite outpatients were analyzed (diagnosis, treatment goal, treatment outcome, etc.)	Japan： Effectiveness of SBI to heavy-drinking employees of 6 large companies（each company hiring more than 1,000 employees）. Total 304 drinkers were randomized to BI group, BI group with drinking diary, and control.
Type of analysis		cost-effective analysis (CEA)		cost-benefit analysis (CBA)	CEA with Sheffield Alcohol Policy Model	cost-effective analysis (CEA)			CEA, CBA, etc.		
Perspectives (healthcare, societal, patients)	focused on implementation costs of SBI (resource costs for delivery)	cost-saving both healthcare and societal		healthcare and society		healthcare perspective, focusing on health benefits and health care costs					
SBI target population	hazardous drinkers and at risk of alcohol dependence (primary care outpatients)			who drink more than 2-3 drinks per day		High risk groups defined more than 40g/day for men and 20g/day for women who do not meet dependency criteria of DSM-IV		16 years or older Next GP registration AND next GP consultation		Those who visited satellite (94 patients) excluding patients who consulted their family or who are treated for alcohol dependence/use disorders	Heavy drinkers who are 19 years or older and under 60 years old (weekly pure alcohol comsumption: more than 210g in men, more than 140g in women, OR drink more than 60g/day more than once/week)
SBI providers	primary care physician, nurse, social workers									Mainly physicians	Occupational physicians, nurses
Level of intervention	median $3.8 per screen (2 min), median $47.87 per BI (13.75 min) – activity based costs		mean $1.50-4.33 (1.5-3.5 min) outpatient setting for screening, and mean $6.22-8.66 (7.5-13.9 min) for BI		AUDIT-C screening then 10 min BI for patients screened positive (mean 12.3% reduction after 24.9 min intervention)					Set abstinence or reduced drinking as a tretmant goal of patients who were diagnosed as alcohol dependence or use disorders, then follow up by telephone or letters.	SBI group: 15 min counseling at baseline and 4 weeks later; SBI with diary group: baseline, 4 weeks, plus 3 months. Drinking volume and frequency were observed.
Costs on SBI	calculation is based on the wage of the provider and service delivery time								Listed cost components such as personnel costs and medical site costs before and after providing SBIRT		

Table 5: Target population, provision methods, and outcomes of SBI

Database	Embase	Embase	Embase	Embase	PubMed	PubMed	PubMed	PubMed	PubMed	Ichu-shi and Others	Ichu-shi and Others
Authors, year published	**Bray, et al. 2012**	**Solberg, et al. 2008**	**Bray, et, al. 2014**	**Fleming, et al. 2002**	**Angus, et al. 2014**	**Tariq, et, al. 2009**	**Cowell, et al. 2010**	**Purshouse, et al. 2013**	**Ino and Cho, 2013**	**Muto, et al. 2013**	**Ito, et al. 2015**
Outcomes related to SBI (and evaluation timing if available)	Good if conducted short time	cost-effectiveness ratio of $1755/QALY saved from health-system perspective	positive detected in screening: 15-39% of total, of which 40-68% people due to heavy drinking (five or more drink in one setting)	Past research (Wallace et al.) showed 10-30% reductions over 12 months in the total alcohol consumption volume and frequency of binge drinking. This study followed-up for 48 months and showed brief physician advice is associated with reduced drinking and associated direct costs ($43,000 reduction of health care costs for every $10,000 investment in early intervention). $56,263 reduction for every $10,000 from the societal perspective. Rate of self-reported problem drinking in past 7 days decreased by 57% from baseline at 12 month. There were consistent 15-20% treatment across following 4 outcome measures: reduced alcohol use over 48 months: mean drinks per week, any binge drinking in the past month, excessive drinking episode in the last month, and in the past week) in both men and women *10% effect was considered enough w this model.	Model: 10 year programme of SBI, and 30 year follow-up of health outcomes (per week mean alcohol consumption change from baseline by different age and sex groups) 590 Euro/QALY at next GP consultation.	Calculation from Table 1: Among people screened positive in the AUDIT screening, 67.6% received BI and 6.7% of those received BI reduced or stopped drinking. Approx.. 8.5% of total Dutch populations aged 20-65 years old were identified positive in screening Model: dynamic model for entire Dutch populations (RIVM Chronic Disease model) 5400 Euro/QALY gained (incremental costs)	NICE concludes the evidence is premature	Setting the base case scenario of 12.3% reduction in the first year follow-up and 5.9% reduction in 5 min short intervention (p183) Next consultation (same GP) assuming that 71-89% of hazardous and harmful drinkers receive BI (compared to changing GP/next registration: 33-40% receiving BI)	Primary care: Drinkers who received succeeded in reducing drinking volume and frequency. Alcohol-related spending also decreased. General hospital ward: Effectiveness of SBI among hospitalized patients were limited, compared to primary care outpatients and emergency department patients.	Out of 77 diagnosed alcohol dependent patients, 21patients set reduced drinking as a treatment goal, of whom 15 patients were successfully maintaining reduced drinking at re-visit (4-10 weeks after the inital visit) Out of 12 alcohol use disorder patients, 10 patients set reduced drinking as an intermediary treatment goal, of whom 6 patients were successfully maintaining reduced drinking. * Details of reduction goal: Set an upper drinking volume limit, set drink-free days (so called liver holidays), stop habitual drinking and only allow opportunity drinking, avoid drinking strong alcohol, mix water when drinking, etc.	Outcome assessment: Observe outcomes at baseline, 3 months, and 12 months, using TLFB (see below) 1) drinking volume in the past 7 days, 2) number of binge drinking(more than 60g pure alcohol per day) and liver holidays in the past 28 days Results: Compared to baseline, the above-described outcomes at 3 and 12 months improved (in particular, drinking volume in the past 7 days and 12 months improved in all 3 groups)
Whether or not SBI is recommended	Recommended				cost-neutral than cost-saving for policy makers (similar conclusion as Solberg and Tariq)				Recommended (provision and expansion of SBI are both recommended)	Recommended	Recommended
Additional information	SBI is supported by US policy (Grade B preventive service), Reimbursed by Medicaid and Medicare only more than 30 min intervention		Demerit: discontinuous patient flow and high initial program costs (fixed costs) causes annual operating costs to exceed the service provision costs	Two 15 min physician intervention (one month apart), then 2 nurse follow-up call 2 weeks after physician visit (primary care setting)					Obstructive factors against expanding SBIRT: lack of intervention knowledge and skills, lack of time, worry for breaking physician-patient relationship, stigma toward disease, access to medical sites, etc.	Since it is difficult for one physician to instruct abstinence and also provide brief intervention, and relationship with patients tends to be broken, collaboration and coordination with co-medical staff is essential for physicians who instruct abstinence or reduced drinking.	In this study, no significant difference was observed between SBI group and SBI with diary group in intervention effects. The fact that no follow-up (intervention) by the counselor was provided was considered as the cause.
SBI Feasibility	suggesting 15.75 min is not practical				Model is linear but alcohol consumption and relative risk of acute alcohol-related harms may not be linear thus overestimating the benefit of the SBI in the model (Sensitivity analysis assumed the effect of intervention lasts only 3 years)	Wutzuke et al. conclude SBI is no longer effective after 10 years			To expand SBIRT in Japan, it is necessary to introduce the physician fees, conduct training to SBI providers, and strengthen coordination among medical sites, support legislation, etc.	It is important to maintain satellite outpatient department for potential alcohol use disorder patients. It is also important to inform the existence/availability of such satellite outpatient department to the general public and other medical sites.	In the future, advantages of internet-based intervention (protection of patient privacy, improved quality of response on drinking status, etc.) are expected.
SBI-related costs				Use of self-help booklet, checking of the drinking goal, diary cards to record alcohol intake, and (referral to a counselor)		All waiting-room patients were asked by GP assistant to fill in the AUDIT then scores were assessed by physician, if more than score 8, follow-up at 6 and 12 months.		Recommending AUDIT score more than 6 (despite 8 in Tariq)	Training costs for providing SBI, fee for using AUDIT, costs of preparing materials for patients, SBIRT program preparation and implementation costs, costs for patient follow-up.		

Regarding the screening tool for possible alcohol dependence or alcohol use disorders, many studies have used AUDIT or AUDIT-C (short version). Providers of SBI varied from physicians only to the combination of physicians and other healthcare professionals such as nurses, social workers, and assistant or staff, depending on the countries. The time for providing SBI also varied from 1.5 to 10 minutes per single time to 13.75 to 24.9 minutes per single time. The outcomes of providing SBI, i.e. achievement rates for reduced drinking, were higher when the healthcare professionals other than physicians have conducted a follow-up by telephone between the previous visit and next physician appointment.

In overseas, SBI is mainly conducted in primary care, and a positive screening rate was around 15-40%. In Japan, screening for possible alcohol dependence or alcohol use disorders is mainly conducted in specialized alcohol treatment sites or general hospitals or clinics which have alcohol-related outpatient departments; thus, the positive screening rate was higher than that in overseas. The achievement rates for reduced drinking were reported at around 10% overseas, but the time point of measuring the outcomes differed greatly. In fact, the time points varied from several months after the brief intervention to 6 months, 1 year, and 2 years, and in the case of providing any follow-up after the brief intervention, observation period was as long as 4 years, 10 years, and 30 years. Moreover,

the study by Fleming et al.[37] described the volume of alcohol consumption that needs to be reduced in order to judge that the brief intervention was 'successful'. For example, 10-30% reduction of total alcohol consumption volume and binge drink frequency in the past 12 months or longer has been reported.

In addition, some negative assessments on SBI included the following: a meta-analysis of 22 RCTs enrolling 7,619 participants[45] showed that BI was effective in reducing alcohol consumption of mean 38g/week than the control group after one year or longer, but the sub-group analysis enrolling 2,307 participants confirmed that BI was effective only in men. Another study[46] reported that physicians found it difficult to establish rapport with patients and ensure compliance with BI, and some physicians also felt lack of confidence in their abilities to counsel patients effectively on lifestyle-related issues.

Table 6 describes 4 SBI scenarios and expected results in Japan which were built based on 2 levels of brief intervention and 2 sets of screening parameters obtained from the literatures and physician interviews.

Table 6: 4 SBI scenarios and expected results in Japan

Assumption: To achieve the goal of Health Japan 21 (second term) i.e. reduction of high-risk drinkers, approximately 0.35 million high-risk drinkers per year need reduced drinking.									
		Annual number of drinkers who visit physicians or undergo health examinations	**Intends to conduct intervention to all "screen positive" drinkers**			**optimistic scenario 30% (Wallace, et al)**	⟷	**pessimistic scenario 10% (Wallace, et.al)**
Brief intervention level ① (AUDIT score 8-15, medium risk)		Number of drinkers who visit physicians (or undergo health examinations) **70%**	Screening rate **50%** (assumed)	Positive screening rate **80%** (assumed)	**Simple advice (1a)**	Success rate: **30%**	**Average**	Success rate: **10%**
Estimated number of drinkers based on 2012 Japanese population	11,370,000	7,959,000	3,979,500	3,183,600		955,080	636,720	318,360
【Assumed patient characteristics】 Patients treated by internists or gastroenterologists due to alcohol-related diseases, or patients who was pointed out alcohol-related diseases at annual health examinations **⇒ Alcohol use disorders (not alcohol dependent) whose final treatment goal is reduced drinking**		Number of drinkers who visit physicians (or undergo health examinations) **70%**	Screening rate **30%** (assumed)	Positive screening rate **60%** (assumed)	**Simple advice (1b)**	Success rate: **30%**		Success rate: **10%**
		7,959,000	2,387,700	1,432,620		429,786	286,524	143,262
Brief intervention level ② (AUDIT score 16-19, high risk)		Number of drinkers who visit physicians (or undergo health examinations) **70%**	Screening rate **50%** (assumed)	Positive screening rate **80%** (assumed)	**Extensive intervention (2a)**	Success rate: **30%**		Success rate: **10%**
Estimated number of drinkers based on 2012 Japanese population	1,500,000	1,050,000	525,000	420,000		126,000	84,000	42,000
【Assumed patient characteristics】 Patients treated by psychiatrists, internists or gastroenterologists specialized at alcohol treatment due to alcohol-related diseases **⇒ Possible alcohol dependent or alcohol use disorders whose final treatment goal is abstinence (reduced drinking as a mid-term goal)**		Number of drinkers who visit physicians (or undergo health examinations) **70%**	Screening rate **30%** (assumed)	Positive screening rate **60%** (assumed)	**Extensive intervention (2b)**	Success rate: **30%**		Success rate: **10%**
		1,050,000	315,000	189,000		56,700	37,800	18,900

In **Table 6**, the estimated numbers of adult drinkers (20 years old or above) targeted for 2 levels of brief intervention in Japan were based on the results of the national survey reported in 2013[47]: 14 million male and female adult drinkers had the AUDIT scores of 8 or above; 2.94 million had the scores of 15 or above; 2.63 million had the scores of 16 or above; and 1.13 million had the scores of 20 or above. Moreover, the assumption that approximately 0.35 million high-risk drinkers per year need reduced drinking in Japan was based on the target reduction rates (3.4%) of high-risk drinkers in one of the alcohol-related goals of Health Japan 21 (the second term).

Furthermore, SBI preparation and implementation costs per target drinker per year in Japan were summarized in **Table 7**.

Table 7: SBI preparation and implementation costs per target drinker per year

Preparation of information for patients (alcohol conversion table), confirmation of procedures for AUDIT screening and simple advice	Initial investment (annual)	Assumed: 1doctor hour + 1staff hour (1 doctor hour 20,000 yen, 1staff hour 2,000 yen)	22,000
Intervention by physician + by healthcare professionals other than physician (5 min + 5 min)	Assumed: 4 times per year per person receiving SBI	Assumed: 0.33 doctor hours + 0.33 staff hours (1 doctor hour 20,000 yen, 1staff hour 2,000 yen)	7,260
Fee for using AUDIT per person and fee for printing materials	Assumed: 400 yen per year per person receiving SBI		400
Total costs of level ① intervention (simple advice)			**29,660**
Fee for using AUDIT per person and fee for printing materials + Preparation of information for the patients (alcohol conversion table, drink diary, etc.) + Fee related to DVD	Initial investment (annual)	300,000 yen + 600,000 yen (costs related to DVD) /30 medical sites* ＊Assumed extensive interventions are regularly conducted at 30 medical sites all over Japan	30,000
Fee for SBI trainings	Training fee: 20,000 yen per session (physicians, other healthcare professionals) x 2= 40,000 yen per year per person Time spent: 16 hours/day x 2 days = 32 hours per person	Total training fee and time costs for 1 physician and 1 healthcare professional: 432,000 yen/10 ＊ ＊Assumed that 1physician and 1 healthcare professional provide extensive intervention to 30 patients per day across Japan (since 1 patient receives 3 interventions, total fee for SBI training was divided by equivalent of 10 patients)	43,200
Intervention by physician + by healthcare professionals other then physician (10 min + 15 min)	Assumed: 2 sessions (6 visits) per year per person receiving SBI	Assumed: 1doctor hour + 1.5 staff hours (1 doctor hour 20,000 yen, 1staff hour 2,000 yen)	23,000
Follow-up by healthcare professionals other than physician (15 min)	Assumed: 2 times (1follow-up/session x 2 sessions) per year per person receiving SBI	Assumed: 0.5 staff hours	1,000
Coordination fee to refer patients to alcohol specialists	General investment per site (annual)	3 doctor hours(60,000 yen)/30 medical sites＊ ＊Assumed extensive interventions are regularly conducted at 30 medical sites all over Japan	2,000
Total costs of level ② intervention (extensive intervention)			**99,200**

Cost items related to SBI preparation and implementation were listed by 2 levels of SBI, and hourly costs of physicians and other healthcare professionals were set as 20,000 yen and 2,000 yen, respectively. Initial investment was estimated per medical site. It was calculated that the annual costs for preparing and providing SBI to one target drinker were 29,660 yen for the "simple advice" and 99,200 yen for the "extensive intervention." In the "extensive intervention," costs for multiple brief intervention sessions (1 patient receives a series of 3 brief intervention sessions at separate physician visits) and follow-up between the physician visits, as well as coordination fee with the alcohol specialists were included. It was assumed that each combination of 1 physician and 1 healthcare professional who received an annual SBI training provide the "extensive intervention" to 10 different patients per year. Materials that can be downloaded free of charge from the internet was not included, but the licensing fees for using AUDIT screening or DVD materials were included. Various assumptions on healthcare resource use shown in the table were mainly based on the input from the physicians experienced in preparing and providing SBI in Japan.

An annual spending calculated by multiplying the SBI target population per year in the scenarios 1b ("simple advice") and 2a ("extensive intervention") in **Table 6** to the annual costs for the SBI preparation and implementation per drinker was approximately 70.8

billion yen in the scenario 1b and 52 billion yen in the scenario 2a.

Given that the average life expectancy of 40-year-old man is 40 years, QALY obtained when continuing reduced drinking for the remaining 40 years would be 4.2 years in the "extensive intervention" and 1.64 years in the "simple advice." On the other hand, costs necessary for providing such brief intervention for the remaining 40 years would be 3,968,000 yen (99,200 yen x 40) and 1,186,400 yen (29,660 yen x 40), respectively. Therefore, costs per 1 QALY gained were calculated as 944,762 yen for the "extensive intervention" and 723,415 yen for the "simple advice".

Furthermore, ICERs for the "simple advice" to 'medium-risk drinkers' and the "extensive intervention" to 'high-risk drinkers' in comparison to no intervention (no SBI), were calculated as shown in **Table 8**:

Table 8: ICERs for conducting "simple advice" and "extensive intervention"

For high-risk drinkers

	Extensive intervention	No intervention	⊿ (Extensive-No intervention)
Cost (Yen)	99,200	0	99,200
QALYs	0.714	0.609	0.105
ICER			**944,762**

For medium-risk drinkers

	Simple advice	No intervention	⊿ (Simple advice-No intervention)
Cost (Yen)	29,660	0	29,660
QALYs	0.755	0.714	0.041
ICER			**723,415**

Compared to no intervention, both "extensive intervention" and "simple advice" were cost-effective with ICERs being below 1 million yen, and the difference between

"extensive intervention" and "simple advice" was relatively small.

The following 2 simulations with different QALYs (based on assumptions) indicated that "extensive intervention" becomes more cost-effective if conducted to more severe alcohol use disorders patients, including possible alcohol dependent patients. Similarly, "simple advice" becomes more cost-effective if conducted to mild to moderate alcohol use disorders patients who are more willing to improve their drinking behaviors thus likely to have higher QALYs gained, as shown in **Table 9A**. On the other hand, if the QALYs gained by "simple advice" and "extensive intervention" are smaller, it becomes less cost-effective as shown in **Table 9B**.

Table 9A: ICERs for conducting "simple advice" and "extensive intervention"

	Extensive intervention	No intervention	⊿ (Extensive-No intervention)
Cost (Yen)	99,200	0	99,200
QALYs	0.714	**0.559**	0.155
ICER			**640,000**

	Simple advice	No intervention	⊿ (Simple advice-No intervention)
Cost (Yen)	29,660	0	29,660
QALYs	**0.805**	0.714	0.091
ICER			**325,934**

Table 9B: ICERs for conducting "simple advice" and "extensive intervention"

	Extensive intervention	No intervention	⊿ (Extensive-No intervention)
Cost (Yen)	99,200	0	99,200
QALYs	0.714	**0.659**	0.055
ICER			**1,803,636**

	Simple advice	No intervention	⊿ (Simple advice-No intervention)
Cost (Yen)	29,660	0	29,660
QALYs	**0.735**	0.714	0.021
ICER			**1,412,381**

6. Discussions

In this thesis, the COI study methodologies on alcohol were analyzed, and costs components and cost categories and their proportions were identified. In the preceding study on Japan, intangible costs had not been measured, and the patients' perspectives were less focused compared to some European countries. It was also learned that there is no standardized methodologies for the COI studies in Japan and overseas; however, the core cost components need to be predefined ideally, to allow comparison among countries.

In the recalculation of alcohol-attributable medical care costs, the service utilization rates of the preceding study was used. Since the exact methods and data source were not fully clear, it was not possible to update the service utilization rates. In that regard, the exploratory use of AAFs for some diagnostic disease categories may have contributed to the update of the medical care costs calculation.

The following section of this thesis focused on possibly saved costs by reduced drinking, and this possible savings were calculated based on the salaries of employed persons that could have been earned by avoiding premature mortality by drinking. If the possible savings by reduced drinking among housewives/homemakers and unemployed persons were included, the amount would have been much larger. Despite the limitation, the need for achieving the goal of Health Japan 21 (the second term) was reconfirmed by

understanding the great economic burden to the Japanese society.

Thus, considering the ways to expand SBI among high-risk drinkers in Japan as well as evaluating the cost-effectiveness of SBI in the following section of this thesis were considered valuable, given that no pharmacotherapy for reduced drinking is currently available in Japan.

The following are more detailed discussions of the pre-described 3 sections.

6.1. **Cost-of-illness studies on alcohol in Japan and overseas**

Major cost components included in the observed COI studies were medical treatment and drug costs, premature mortality costs, absenteeism, and presenteeism due to inappropriate consumption of alcohol. This is in line with the study which estimated costs of alcohol in Canada in 2002; “indirect costs or productivity losses were the largest cost category (61%), followed by health care (22%) and law enforcement costs (14%)” [48]. In addition to these direct and indirect costs, England and Sweden also included intangible costs, thus a great variation was seen in the proportions of direct, indirect, and intangible costs. In Japan, direct and indirect cost proportions were approximately 20% and 80%, based on 1987 data. The calculation with 2012 data in this study showed approximately 1.5 times higher direct costs related to alcohol in Japan. This was understandable given the increased Japanese population who suffer from diseases attributable to alcohol over

the past 25 years. Although the indirect costs could not be estimated with new data, assuming that the same proportions of direct and indirect costs are applied, the total costs of alcohol abuse in Japan can be estimated to be approximately 9.9 trillion yen. Further indirect costs data collections are necessary in the future COI studies on alcohol in Japan.

In the calculation of alcohol-attributable medical care costs, the main difference from the previous study[7] is the use of AAFs for Japan obtained from the Comparative Risk Assessment of the Global Burden of Disease study for 2002 for chronic disease categories[16], except for AAFs for digestive disorders. Since AAFs for liver cirrhosis in England (78% in men and 52% in women) were comparable to those in Japan (70% in men, 69% in women), it was considered reasonable to estimate AAFs for digestive disorders in Japan (52% in men and 37% in women) by calculating the average AAFs of following 3 relevant disease categories in England and then rounding the numbers off to the nearest integer values: acute and chronic pancreatitis (30% in men, 13% in women), gastro-oesophageal laceration-haemorrhage syndrome (47% in men and women), and oesophageal varices (78% in men, 52% in women) for all ages above 16 years old[11].

AAFs for cancer and cardiovascular disorders in Japanese men in 2012 were much higher than the corresponding alcohol-attributable service utilization rates used 25 years ago[7]. This is not so surprising given the fact that 2012 medical costs for treating cancer

(disease category name: Neoplasm) and cardiovascular disorders (disease category name: Diseases of the circulatory system) were 3.2 and 1.5 times higher, respectively.

In this study, AAFs for Japan were newly and exploratory applied to calculate alcohol-attributable medical care costs with more recent data; however, the combination with service utilization rate in the preceding study may not have been the best option given the difference in data source and data collection timing. Despite this limitation, the use of AAFs has contributed to better understand the latest COI on alcohol in Japan. Other limitations are that if genetic variations in alcohol metabolism were considered, the estimated AAFs for Japan may have been somewhat underestimated. Moreover, given that AAFs are expected to change each year based on the actual level of drinking, some overestimation or underestimation shall be noted, though this is also true for the service utilization rate used in the preceding study.

The calculation of indirect costs in Japan, like other countries, often faces methodological challenges due to limited data. This is not unique to the study on alcohol. For example, a recent study which estimated the costs of schizophrenia in Japan states "no reliable data in Japan are available with regard to absenteeism, presenteeism, treatment-related time off work, unwanted job changes, loss of opportunities for promotion and education, and loss of unpaid production while ill"[49], thus the study

included only unemployment costs in the morbidity costs. For the quality improvement of future COI studies in Japan, a use of health-related QOL scales such as widely used WPAI-GH (Work Productivity and Activity Impairment Questionnaire: General Health) is recommended.

Regarding the calculation of productivity loss due to premature mortality, a scenario of 40 year-old Japanese man who works until he reaches the retirement age of 65 years old was used. In a case of 40-year-old Japanese woman, the amount was considered approximately 20% lower because of the average annual salary difference. Furthermore, the calculation did not consider an unemployment rate; thus, an overestimation was considered. This point is further analyzed in the later section.

In the comparative analysis of COI among 7 developed countries/legal entities, costs as percent GDP adjusted by purchasing power parity (PPP) were not calculated because the amount itself was not the main focus of this study, though the study which reviewed cost drivers associated with alcohol abuse, heavy drinking, and alcohol dependence in high-income countries reported that "the cost due to heavy drinking and/or alcohol dependence as percent GDP (PPP) was estimated to be 0.96%" [50]. Similarly, a discount rate of 2% recommended in a cost-effectiveness or long-term analysis according to the "Guideline for economic evaluation of healthcare technologies in Japan" was not

applied[51].

Moreover, morbidity costs and unrelated medical and non-medical costs possibly saved by reduced drinking were not estimated. If the morbidity costs saved by reduced drinking had been estimated, the total amount possibly saved would have been greater; thus, the estimation of morbidity costs based on a Markov model may be interesting for the future research.

There are general limitations in the COI studies on alcohol. As described in the International guidelines for estimating the costs of substance abuse[52], even if the patients successfully reduced drinking, "there would still be morbidity and mortality effects from the physiological damage of" past drinking, due to time-lag between the change of drinking behaviors and its clinical outcomes. The difficulty is that the length of time-lag often varies, depending on the types of diseases attributable to alcohol.

Another limitation is causality. It is almost impossible to determine whether or not a person lost job or work productivity truly due to alcohol. The same is true for a crime or car accident. A person may have committed a crime anyway regardless of alcohol consumption, or a person may have caused a car accident due to concomitant diseases not associated with alcohol or due to adverse drug reactions or illegal drug use.

Despite these limitations often seen, it is still worth estimating related costs with

available data than doing nothing, as also described in the international guidelines for the estimation of the avoidable costs of substance abuse by Collins et al.[53], because it will provide some evidence for making better decisions on healthcare budget and resource use.

6.2. Economic loss due to premature mortality by drinking

The estimation of possible savings by promoting reduced drinking among high-risk drinkers in Japan, which is based on the calculation of avoidable economic loss due to premature mortality by drinking, suggested significantly decreased alcohol-related medical and social costs in Japan. It was estimated that achieving the goal of Health Japan 21 (the second term) would save approximately 158.4 billion yen per year.

In the scenario analysis, the number of high-risk drinkers (total of men and women) in their 40s, 50s, and 60s were considered at the ratio of 1:1:1; thus, high-risk drinkers in their 20s, early 30s, and above 65 years old were not included. However, the number of high-risk drinkers in these age groups, especially men and women in their 20s and early 30s, and men in their 70s and above cannot be ignored[30], because approximately 70 to 90% of the Japanese men in their 50s to 80s do fall in the category of high-risk drinkers; they are actually heavy drinkers or binge-drinkers, who are often more risky than high-risk drinkers. Although the employment rates[31] of these drinkers in their 60s, 70s, and 80s are low, direct and indirect costs associated with their unfavorable drinking behaviors

cannot be ignored. Moreover, not only the economic effects by avoiding premature mortality but also costs related to absenteeism (missed work because of illness) and presenteeism (productivity loss at workplace because of illness) as well as costs for visiting hospitals or clinics and opportunity costs of high-risk drinkers' families and caregivers accompanied by hospitalization and care must be considered for all age groups and gender. In this respect, the maximum estimation of possible savings of 363.1 billion yen per year may be somewhat reasonable.

In the previously conducted COI studies[1)], a single scenario of 40 year-old Japanese man who works until he reaches the retirement age of 65 years old was used to calculate the possible savings by achieving the goal of Health Japan 21 (the second term). In this analysis, an employment rate was assumed to be 100%; high-risk drinkers were assumed to work until the retirement age of 65 years old; and the lives of 2,542 high-risk drinkers were assumed to be saved annually. Thus, the annual savings of as much as 363.1 billion yen were possibly overestimated. In the scenario analysis, average annual salaries and employment rates by age groups and gender were considered in the calculation of possible savings, without changing the assumption that the high-risk drinkers work until the retirement age of 65 years old. Then, the scenario analysis has suggested that the possible savings would become approximately 49-58% lower than

those with the single scenario of 40-year-old man. In this study, the possible savings of approximately 158.4 billion yen were considered more realistic, despite variations in the assumptions and input variables used.

Although the study has highlighted the importance of expanding SBI among the high-risk drinkers in Japan, the optimistic 50% success rate seemed to be appropriate only in a specialized alcohol treatment setting in Japan. In other words, if brief intervention was newly conducted to new high-risk drinkers in a primary care setting, the success rate could be more or less 25%, and the annual costs for conducting brief intervention to 508,420 adults in Japan could possibly become twice as much, which is approximately 31 billion yen per year.

6.3. Screening and brief intervention and its cost-effectiveness

According to the relevant literatures obtained, most studies have concluded that SBI was effective. Since healthcare system is different in each country, the results of cost-effective or cost-benefits analysis conducted overseas cannot be applied directly to Japan. However, following factors were considered important to bring success to SBI particularly in primary care: each high-risk drinker visits the same medical site regularly; a follow-up such by email or telephone call is done by next physician visit; AUDIT screening is conducted in a waiting room of the medical site before seeing the physician,

then the physician explains the results and provides brief guidance; and physicians promote modest drinking behaviors to their patients by providing supportive information (such as alcohol conversion table, drinks diary, and useful websites) and help them understand the benefits of reduced drinking and burden of continuing high-risk drinking.

In addition, it was considered important to define criteria for assessing the outcomes of SBI in future studies. For example, the following criteria need to be defined: how do we know that a particular SBI was successful?; how much should the average daily alcohol consumption be reduced?; and how long should the reduced drinking level be maintained? In this study, no specific criteria were set regarding the assessment of outcomes for reduced drinking, but it was considered possible to say that SBI was successful when pure alcohol consumption per day has decreased by approximately 10-20g in male and female drinkers (or 20-30% reduction from baseline) and it was maintained for one year.

Furthermore, AUDIT screening cut-off varies by countries and also by researchers in Japan, thus common understanding needs to be established at the national level in the future. In this study, it was assumed that drinkers whose AUDIT scores are 8 or more are subjected to receive SBI. According to some physicians treating alcohol-related diseases in Japan, AUDIT scores of 10 or more are considered a reasonable cut-off for SBI. When

AUDIT screening is conducted in the clinical setting, patients often tend to underevaluate their drinking status; thus, setting the cut-off scores a little lower makes sense to capture high-risk drinkers who need to receive brief intervention. The same thinking may apply to other screening tools such as Kurihama Alcohol Screening Test (KAST).

The negative assessments on SBI from the literature overseas seemed to have highlighted the importance of providing as minimal SBI as possible to avoid a potential risk of losing opportunities to continuously provide brief intervention to high-risk drinkers, because they are usually not willing to change their drinking behaviors thus may no longer visit physicians. During the physician interview, this concern was also mentioned indirectly, and importance of providing interventions not only in the clinical setting but also in the social setting (family and friends, schools, patient groups, etc.) and occupational setting (advice from occupational physicians, advice from general physicians in the annual health examinations, etc.) seemed to play an important role in promoting changes in drinking behaviors among high-risk drinkers in Japan.

Among 4 SBI scenarios described in **Table 6**, the combination of scenario 1b ("simple advice": screening rate of 30%, screening positive rate of 60%) and scenario 2a ("extensive intervention": screening rate of 50%, screening positive rate of 80%) were considered more realistic compared to the other scenarios. The rates of successful brief

intervention shown in the range of 10-30% were also considered realistic according to the interviewed physicians' experience in Japan. If SBI is conducted under the scenarios of 1b and 2a in Japan, 370,524 high-risk drinkers would be able to reduce their drinking per year. Since approximately 250,000 to 300,000 high-risk drinkers need to reduce their drinking per year to achieve one of the goals of Health Japan 21 (the second term), implementation of SBI with the suggested scenarios would contribute to the achievement of the goal.

The fee for SBI trainings listed in **Table 7** are based on the assumption that each combination of 1 physician and 1 healthcare professional who received an annual SBI training provide the "extensive intervention" to 10 different patients per year. This number is considered realistic, because it is known from the physician interview for this study as well as a working group memo[54)] that only 1 in 5 of high-risk drinkers who would need to receive the "extensive intervention" actually receive some kind of brief intervention (more likely to be the "simple advice") when they visit physicians due to alcohol-related diseases. This means that more or less 6,000 patients annually receive some kind of brief intervention by more or less 500 alcohol specialists (mostly psychiatrists, and some internists, gastroenterologists, and cardiologists[3)]) estimated to exist in Japan.

It was calculated that the costs per 1 QALY gained in the case of 40-year-old man who would live 40 more years were 944,762 yen for the “extensive intervention” and 723,415 yen for the “simple advice” as shown in **Table 8**. According to the previously mentioned observational study in England[33], the costs per 1 QALY gained were 5,204 pounds (936,720 yen when 1 pound is equivalent to 180 yen), and the cost/QALY threshold of less than 20,000 pounds was considered cost-effective. Thus, 2 levels of SBI analyzed in this study were also considered cost-effective. The ICERs calculated for the “simple advice” and “extensive intervention” and their simulations with different QALYs in **Table 9A** and **Table 9B** have also confirmed the cost-effectiveness of 2 levels of SBI, given that the cost/QALY threshold in Japan is around 6 to 7 million yen[55].

Moreover, it highlighted the importance of considering individual patients’ willingness or readiness to improve their drinking behaviors and severity of clinical symptoms. The higher their willingness or readiness to improve, the better the “simple advice” seems to work.

Regarding the future expansion of SBI in Japan, an early provision of SBI in a primary care setting is considered important from the perspective of clinical and economic benefits to both high-risk drinkers and healthcare providers. However, the rates of successful brief intervention are normally higher in more severe patients to whom the

“extensive interventions” are rather applied. Therefore, it is very important for physicians and other healthcare professionals who provide SBI in a primary care setting to acquire skills for effectively communicating and interacting with high-risk drinkers who are not so much aware of the need for changing their drinking behaviors anytime soon.

It is also important to continuously devise alternative ways to reduce SBI preparation and implementation costs such by effective use of IT (self-screening via internet, automatic reminder message sent to one’s private email address to keep modest drinking, free access to online educational materials related to alcohol) or by coordinating more closely with occupational physicians in the industrial setting or with general physicians and other healthcare professionals in the annual health examinations who have longer time to talk with an individual drinker. For mild to moderate drinkers who are normally more willing and ready to change/improve their drinking behaviors would be the best fit for the “simple advice” scenario whether the SBI is provided face-to-face or via IT. In fact, the combination of face-to-face and web/email-based provision of SBI is very important, and it should be noted that web/email-based provision of SBI cannot replace the face-to-face provision, because the face-to-face provision ‘pushes’ patients to recognize their problematic drinking behaviors and reduce drinking while the web/email-based provision ‘pulls’ the patients’ willingness or needs to reduce drinking and maintain

good drinking behaviors, as commented by Rooke et al[56]. The web/email-based provision would be useful to high-risk drinkers who have difficulty visiting physicians on a regular basis due to limited access or any other reasons.

Furthermore, it would be useful especially in the patient follow-up at 6 month, because a study which evaluated the effect of cognitive-behavioral therapy on relapse (re-initiation of drinking) in alcohol dependent patients in Japan showed unstable drinking outcomes after 6 months[57]. Therefore, associations between the high-risk drinker's level of readiness to change and outcomes related to reduced drinking in both short-term (6 months to 1 year) and long-term (1 to 3 years) may be worth investigating in the future, because maintaining appropriate drinking behaviors for one's entire life is more important, and it greatly impacts Japan's healthcare spending related to high-risk drinking.

Moreover, cost-effective and smooth implementation of referral to treatment (RT) both from alcohol specialists to non-specialists and from non-specialists to alcohol specialists is worth investigating in the future, especially when SBI further expands across Japan, because RT is often discussed with SBI as SBIRT, or more recently as SBIRTS in which the last S refers to 'self-help group support'. Early provision of SBI and more comprehensive support as described in the Basic Plan to Promote Measures against Alcohol-related Health Harm[58] will bring both clinical and socio-economic benefits to

the high-risk drinkers and their families.

For the “extensive intervention,” initiation timing seems to have a certain impact on the brief intervention outcome, especially among hesitant high-risk drinkers. In relation to this, further investigation on QOL losses due to craving for alcohol or dissatisfaction with reduced drinking seems quite interesting.

7. Conclusions

In this thesis, high burden of disease associated with alcohol in Japan was reconfirmed by recalculating the alcohol-attributable medical care costs with more recent data, the 2012 medical care costs data and with use of AAFs for Japan, based on the observed COI study methodologies in Japan and overseas.

It was suggested that reduced drinking among high-risk drinkers in line with the goal of Health Japan 21 (the second term) would bring great clinical, economic, and social benefits to the Japanese society. Therefore, improving the feasibility and cost-effectiveness of SBI is very important, although the evaluation of 2 levels of SBI in this study were cost-effective.

This thesis showed the current status and future challenges of COI studies on alcohol and highlighted the need for further expansion of SBI among high-risk drinkers in Japan.

Regarding the COI studies, standardized methods for collecting and analyzing data shall be established to allow comparison among different studies in a single or multiple countries. This is particularly true for the indirect costs. For the nationwide expansion of SBI, not only the goal of Health Japan 21 (the second term) but also the collaboration among various healthcare professionals is expected to become stronger in Japan.

8. Ethical considerations

This study does not involve use of human tissues or human subjects. The interviews to the physicians were conducted as part of the company project for which the author was responsible. The use of findings from the interview as the secondary data has been approved by the company and physicians mentioned in the ***Acknowledgements***.

The ethical committee at the International University of Health and Welfare reviewed the study plan and concluded that no special ethical consideration was necessary.

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Conflict of interest statement

The author is an employee of Amgen Astellas BioPharma K.K. and used to be an employee of Lundbeck Japan K.K. when the study was completed. No financial support was received for this study and for the University. The contents described in this thesis are based on the author's personal views, thus do not represent official views of the companies or organizations to which the author belongs or used to belong.

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10. Appendix

List of questions to physicians on screening and brief intervention in Japan

Background questions on screening：

- 現在の診療において、AUDIT screening を実施しているか？
  - Yes：誰が、どのくらいの時間で実施し、患者にフィードバックしているか？
  - No：今後実施可能か？

- 飲酒量低減の指導は AUDIT 何点以上が対象か？（過少評価の可能性も考慮）
  - 国内外文献では AUDIT 10 点以上が危険な飲酒群、その他の試験では 12 点以上と 16 点以上をカットオフにしている。
  - BI 対象者は飲酒量低減を要する人で依存がない人、SBI は依存症専門家でなく、ヘルスケア従事者により行われるべき。
  - Screening をどの様に実施すべきか？対面式（診察時）または非対面式（待合室）？

- どのような受療環境の患者に SBI を実施すべきか（positive screening rate）？
  - 内科・消化器科、精神科クリニックに通院している外来患者？
  - アルコールに関連した救急外来患者？
  - 健康診断や職域？

- SBI 実施者は複数（医師とコメディカル）、または 1 人（医師またはコメディカル）？
  - 実施者の違いによる実施・継続率への影響の有無？

- SBI の実施は 1 回または複数？
  - 1 回の場合、時間と実施方法？
  - 複数回の場合、それぞれ何週間後がよいか？（Happy program の場合、1 ヶ月目と 3 ヶ月目に飲酒状況の把握と目標の再設定（＋専門医への照会）
  - 各セッションの所要時間は？（Happy program の場合、90 分セッション×3 回）？

- 準備コストはいくらか？
  - 準備費用（含める場合）：テキストと飲酒日記作成費用（医師の消費時間数）？
  - 初期費用：提供者（医師、看護師、コメディカル）の事前教育・訓練費用（時間給）？

- 実施コストは？
  - 実施費用：実施シナリオ別（異なる提供者、回数・時間、集団または個人）
    - ✧ 資料の使用料（必要な場合はどれくらい）？

- BI 後のフォローアップ実施？
  - 誰がどの様にフォローアップするのが効果的か？
    - ✧ 媒体：電話？DM？メール？その他？
    - ✧ フォローアップの時間？
    - ✧ サポート資料（記録表や飲酒日誌）の使用は？

- アルコール専門医及びプライマリケア医による SBI の実施可能性はどれくらいか？
    - ✧ 阻害要因はあるか（Yes：例えば）？

- 国内の何%の対象者にスクリーニングができ、うち何%が extensive BI の対象と考えられるか？
  （国内研究:アルコール依存症と診断された 94 名（全体の 82%）のうち、21 名（22.3%）が飲酒量低減を治療目標とした。また、有害な使用者（全体の 12.8%）のうち、10 名（10.6%）が飲酒量低減を治療目標とした。つまり、全体の 94.8%が screen positive で、うち 32.9%が飲酒量低減の対象者。）
  - アルコール専門外来以外（消化器科、内科、精神科、総合診療科）で受診する患者のうち、screen positive は何%いると推測されるか？

- 治療目標（節酒、断酒）は患者が決める？医師が決める？（両方？）
  - 再来院は何週間後？
  - 指導内容は？（例：飲酒日記の使用促進）

- 継続して良好なアウトカム（定義？）がどのくらいの期間（半年後？1 年後？）みられたら、良いと判断するか？
  - （上記定義に基づく）短期成功率と長期成功率はそれぞれ何%くらいか？

メモ）WHO AUDIT 使用マニュアルの 2 モデル：

① **AUDIT8-15 点の中リスク群→「簡単なアドバイス」（簡易介入）**（想定：健康診断で毎年飲酒量低減を指摘されているが、専門施設は未受診または AD/AUD 未診断の者）

② **AUDIT16-19 点の高リスク群→「簡易カウンセリングと継続的観察」**
（20 点以上の AD 疑いは断酒が目標となるので除外）

AUDIT (10-item self-rated screening test)

1．あなたはアルコール含有飲料をどのくらいの頻度で飲みますか？

0．飲まない　1．1 カ月に 1 度以下　2．1 カ月に 2 ～ 4 度　3．1 週に 2 ～ 3 度　4．1 週に 4 度以上

2．飲酒するときには通常どのくらいの量を飲みますか？

ただし、日本酒 1 合＝ 2 ドリンク、ビール大瓶 1 本＝ 2.5 ドリンク

ウイスキー水割りダブル 1 杯＝ 2 ドリンク、焼酎お湯割り 1 杯＝ 1 ドリンク

ワイングラス 1 杯＝ 1.5 ドリンク位、梅酒小コップ 1 杯＝ 1 ドリンク

（ 1 ドリンク＝純アルコール 9 ～ 12 g ）

0．1 ～ 2 ドリンク　1．3 ～ 4 ドリンク　2．5 ～ 6 ドリンク位　3．7 ～ 9 ドリンク　4．10 ドリンク以上

3．1 度に 6 ドリンク以上飲酒することがどのくらいの頻度でありますか？

0．ない　1．1 カ月に 1 度未満　2．1 カ月に 1 度　3．1 週に 1 度　4．毎日あるいはほとんど毎日

4．過去 1 年間に、飲み始めると止められなかったことが、どのくらいの頻度でありましたか？

0．ない　1．1 カ月に 1 度未満　2．1 カ月に 1 度　3．1 週に 1 度　4．毎日あるいはほとんど毎日

5．過去 1 年間に、普通だと行えることを飲酒していたためにできなかったことが、どのくらいの頻度でありましたか？

0．ない　1．1 カ月に 1 度未満　2．1 カ月に 1 度　3．1 週に 1 度　4．毎日あるいはほとんど毎日

6．過去 1 年間に、深酒の後体調を整えるために、朝迎え酒をせねばならなかったことが、どのくらいの頻度でありましたか？

0．ない　1．1 カ月に 1 度未満　2．1 カ月に 1 度　3．1 週に 1 度　4．毎日あるいはほとんど毎日

7．過去 1 年間に、飲酒後罪悪感や自責の念にかられたことが、どのくらいの頻度でありましたか？

0．ない　1．1 カ月に 1 度未満　2．1 カ月に 1 度　3．1 週に 1 度　4．毎日あるいはほとんど毎日

8．過去 1 年間に、飲酒のため前夜の出来事を思い出せなかったことが、どのくらいの頻度でありましたか？

0．ない　　1． 1 カ月に 1 度未満　　2． 1 カ月に 1 度　　3． 1 週に 1 度　　4．毎日あるいはほとんど毎日

9．あなたの飲酒のために、あなた自身か他の誰かがけがをしたことがありますか？

0．ない　　2．あるが、過去 1 年にはなし　　4．過去 1 年間にあり

10．肉親や親戚、友人、医師、あるいは他の健康管理にたずさわる人が、あなたの飲酒について心配したり、飲酒量を減らすように勧めたりしたことがありますか？

0．ない　　2．あるが、過去 1 年にはなし　　4．過去 1 年間にあり

http://www.kurihama-med.jp/alcohol/audit.html (accessed 2015.5.31)