

## 引用文献リスト

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研究成果の刊行に関する一覧表

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# Impact of alcohol intake on total mortality and mortality from major causes in Japan: a pooled analysis of six large-scale cohort studies

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## ABSTRACT

**Objectives** Using common alcohol consumption categories, to conduct a pooled analysis of six ongoing large-scale cohort studies in Japan in order to produce concrete estimates of the quantitative contribution of alcohol consumption to all-cause and major causes of mortality in the Japanese population.

**Methods** Of the 309 082 subjects, there were 35 801 deaths during 3 832 285 person-years of follow-up. Using a random-effect model, we conducted a meta-analysis of the HRs of each alcohol consumption category in each study, thereby obtaining pooled estimates for the risk of total and major causes of mortality due to alcohol consumption.

**Results** There was a J- or U-shaped association for the risk of total and major causes of mortality in men, and the risk of total and heart disease mortality in women. Compared with non-drinkers, there was a significantly lower risk for total mortality at an alcohol consumption level of <69 g/day, cancer mortality at <46 g/day, heart disease mortality at <69 g/day and cerebrovascular disease mortality at <46 g/day in men, and for total mortality at <23 g/day in women. In addition, mortality risk increased linearly with rising alcohol dose among drinkers. It was estimated that 5% of total mortality, 3% of cancer mortality, 2% of heart disease mortality and 9% of cerebrovascular disease mortality in men, but only 0–1% of these risks in women, could be prevented by reducing alcohol consumption to <46 g/day in men and <23 g/day in women.

**Conclusion** Maintaining alcohol consumption below 46 g/day in men and 23 g/day in women appears to minimise the risks of mortality in the Japanese population.

## INTRODUCTION

A number of studies have reported the health benefits of light to moderate alcohol consumption with respect to total mortality,<sup>1 2</sup> and the risks of major causes of death such as cardiovascular disease,<sup>3 4</sup> although these findings remain controversial.<sup>5 6</sup> Heavy alcohol drinking has been found to be positively associated with cancer.<sup>7–9</sup> In addition, the net balance of risks and benefits is likely to vary in different populations.<sup>5</sup>

In Japan, alcohol drinking is now recognised as an important and preventable public health problem. Alcohol consumption and the proportion

of heavy drinkers had been increasing for decades until 1990, and have only recently reached a plateau.<sup>10</sup> New public health policies should consider both qualitative and quantitative estimation of the effects of alcohol, not only on specific diseases, but also on total and major causes of mortality in the aggregate. However, because published studies use different alcohol consumption categories, meta-analysis for the purpose of quantitative assessment based on common alcohol consumption categories is not possible.<sup>11</sup>

In the present study, therefore, we conducted a pooled analysis of six ongoing large-scale cohort studies in Japan, using common alcohol consumption categories. The main purpose of this study was to estimate the quantitative contribution of alcohol drinking to total mortality and major causes of mortality (ie, mortality from cancer, heart disease and cerebrovascular disease) in the Japanese population, to permit future estimation of the burden of major diseases attributable to alcohol consumption in Japan.

## METHODS

### Study population

In 2006, the Research Group for the Development and Evaluation of Cancer Prevention Strategies in Japan initiated a pooling project using original data from major cohort studies to evaluate the association between lifestyle and major forms of cancer in the Japanese population. This project was conducted in parallel with systematic reviews of the relevant literature.<sup>11</sup> Topics for the pooled analysis were determined from discussions of the scientific evidence and public health implications.<sup>12 13</sup> To ensure the quality and comparability of data, we established inclusion criteria for the present purpose. To be included, the study had to: (1) be a population-based cohort study conducted in Japan; (2) have started in the mid-1980s to mid-1990s; (3) have included more than 30 000 participants; (4) have obtained information on amount of alcohol consumed (g/day) using a validated questionnaire at baseline; and (5) have collected information on any-cause mortality during the follow-up period. Six ongoing studies met these criteria: (1) the Japan Public Health Center-based Prospective Study, Cohort I (JPHC-I),<sup>14</sup> (2) the Japan Public Health Center-based Prospective Study, Cohort II (JPHC-II),<sup>14</sup> (3) the Japan Collaborative Cohort

Study (JACC),<sup>15</sup> (4) the Miyagi Cohort Study (MIYAGI),<sup>16</sup> (5) the Ohsaki National Health Insurance Cohort Study (OHSAKI)<sup>17</sup> and (6) the Takayama Study (TAKAYAMA).<sup>18</sup> Four of these studies have already published results on the association between alcohol intake and mortality in each cohort.<sup>7 8 19–21</sup> For the present analysis of these cohorts, we used updated datasets with an extended follow-up period. When analysing individual results from each study, subjects with a previous history of any cancer, stroke or myocardial infarction, or with unknown alcohol drinking status were excluded. Table 1 presents selected characteristics of these studies. Each study obtained approval from a relevant institutional ethical review board, namely, that of the National Cancer Center (JPHC-I and JPHC-II), Aichi Medical University (JACC), Tohoku University Graduate School of Medicine (MIYAGI and OSAKI), and Gifu University Graduate School of Medicine (TAKAYAMA).

**Follow-up**

Subjects were followed from the baseline survey to the last date of follow-up for any cause of mortality in all included studies (table 1). Residence status in each study, including survival, was confirmed by using the residential registry. Information on the cause of death was obtained from death certificates provided by the Ministry of Health, Labour, and Welfare, in which cause of death was defined according to the International Classification of Disease, 10th version (ICD-10).<sup>22</sup> Residence and death registration are required by law in Japan and the registries are believed to be complete.

**Assessment of outcome**

The outcome of the present study was all-cause mortality, including the three major causes of death in Japanese: cancer (ICD-10: C00–C97), heart disease (ICD-10: I20–I52), and cerebrovascular disease (ICD-10: I60–I69).

**Assessment of exposure**

Alcohol drinking status was assessed by self-administered questionnaires at baseline in each study. Although the style of the questions differed by study, each study calculated alcohol consumption in grams of ethanol per day for regular drinkers by collecting information on the types of beverage, frequency and amount of consumption in their questionnaires. Then, alcohol consumption was divided into categories by using identical cut-points across the studies: non-drinkers (never- and ex-drinker), occasional drinkers (<once/week), and regular drinkers (at least once/week: <23 g/day, 23–<46 g/day, 46–<69 g/day, 69–<92 g/day, ≥92 g/day for men; and <23 g/day, 23–<46 g/day, ≥46g/day for women). In Japan, '1 go' is equivalent to approximately 180 ml of Japanese sake (rice wine), or 23 g of ethanol, and is the most common unit for measuring the amount of alcohol consumed. Correlation coefficients comparing alcohol consumption estimated from the questionnaire with dietary records (crude) were 0.77 in men and 0.55 in women from JPHC-I and JPHC-II,<sup>19</sup> 0.77 in men and 0.71 in women from MIYAGI,<sup>23</sup> 0.61 in men from OHSAKI,<sup>21</sup> and 0.72 in men and 0.64 in women from TAKAYAMA.<sup>18</sup> JACC, for which information on the validation of alcohol consumption was not available, used the same questions on alcohol consumption as the MIYAGI study. Ex-drinking and never-drinking non-drinkers were analysed separately in the JPHC-II, JACC, MIYAGI and OHSAKI studies; thus, additional analyses that subdivided non-drinkers into ex-drinkers and never-drinkers were conducted among these subjects.

**Table 1** Characteristics of the six cohort studies included in the pooled analysis of the association of alcohol consumption with all-cause and major causes of mortality

Study	Population	Age (years) at baseline survey	Year(s) of baseline survey	Population size	Rate of response (%) to baseline questionnaire	Method of follow-up	Age (years)	Last follow-up time	Mean duration of follow-up (years)		Size of cohort		Number of total deaths	
									Men	Women	Men	Women	Men	Women
JPHC-I	Japanese residents of 5 public health centre areas in Japan	40–59	1990	61595	82%	Death certificates	40–59	2005	14.2	23283	26199	2412	1204	
JPHC-II	Japanese residents of 6 public health centre areas in Japan	40–69	1993–1994	78825	80%	Death certificates	40–69	2005	11.3	28344	32543	3591	1826	
JACC	Residents from 45 areas throughout Japan	40–79	1988–1990	110792	83%	Death certificates	40–79	2006	14.6	35926	51672	9061	6884	
MIYAGI	Residents of 14 municipalities in Miyagi Prefecture, Japan	40–64	1990	47605	92%	Death certificates	40–64	2004 (all causes), 2001 (cause specific)	13.4, 10.3	21552	19166	2240	887	
OHSAKI	Residents of 14 municipalities in Miyagi Prefecture, Japan	40–79	1994	52029	95%	Death certificates	40–79	2006	10.0	21552	19766	3793	1841	
TAKAYAMA	Japanese residents of Takayama, Gifu, Japan	≥35	1992	31552	85%	Death certificates	35–101	1999	6.9	13355	15724	1163	899	
Total									12.4	144012	165070	22260	13541	

JPHC, Japan Public Health Center-based prospective Study; JACC, Japan Collaborative Cohort Study; MIYAGI, Miyagi Cohort Study; OHSAKI, Ohsaki National Health Insurance Cohort Study; TAKAYAMA, Takayama Study.