Clinical Nutrition 38 (2019) 1368–1372

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Frequency of alcohol consumption and risk of type 2 diabetes mellitus: A nationwide cohort study

Yun-Ju Lai [a, b, c], Hsiao-Yun Hu [d, e], Ya-Ling Lee [e, f, g], Ming-Chung Ko [h, i], Po-Wen Ku [j], Yung-Feng Yen [a, e, i, k, l, **], Dachen Chu [a, e, i, m, *]

[a] School of Medicine, National Yang-Ming University, Taipei, Taiwan
[b] Division of Endocrinology and Metabolism, Department of Internal Medicine, Puli Branch of Taichung Veterans General Hospital, Nantou, Taiwan
[c] Department of Exercise Health Science, National Taiwan University of Sport, Taichung, Taiwan
[d] Department of Education and Research, Taipei City Hospital, Taipei, Taiwan
[e] Institute of Public Health and Community Medicine Research Center, National Yang-Ming University, Taipei, Taiwan
[f] Department of Dentistry, Taipei City Hospital, Taipei, Taiwan
[g] Department of Dentistry, School of Dentistry, National Yang-Ming University, Taipei, Taiwan
[h] Department of Urology, Taipei City Hospital, Taipei, Taiwan
[i] Department of Health Care Management, National Taipei University of Nursing and Health Sciences, Taipei, Taiwan
[j] Graduate Institute of Sports and Health, National Changhua University of Education, Changhua, Taiwan
[k] Section of Infectious Diseases, Taipei City Hospital, Taipei City Government, Taipei, Taiwan
[l] Center for Infectious Disease and Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan
[m] Department of Neurosurgery, Taipei City Hospital, Taipei, Taiwan

A R T I C L E I N F O

Article history:
Received 15 January 2018
Accepted 6 June 2018

Keywords:
Alcohol
Diabetes
Epidemiology
Risk factors

S U M M A R Y

Background & aims: Alcohol consumption correlates with type 2 diabetes through its effects on insulin resistance, changes in alcohol metabolite levels, and anti-inflammatory effects. We aim to clarify association between frequency of alcohol consumption and risk of diabetes in Taiwanese population.
Methods: The National Health Interview Survey (NHIS) in 2001, 2005, and 2009 selected a representative sample of Taiwan population using a multistage sampling design. Information was collected by standardized face to face interview. Study subjects were connected to the Taiwan National Health Insurance claims dataset and National Register of Deaths Dataset from 2000 to 2013. Kaplan–Meier curve with log rank test was employed to assess the influence of alcohol drinking on incidence of diabetes. Univariate and multivariate Cox proportional regression were used to recognize risk factors of diabetes.
Results: A total of 43,000 participants were included (49.65% male; mean age, 41.79 ± 16.31 years). During the 9-year follow-up period, 3650 incident diabetes cases were recognized. Kaplan–Meier curves comparing the four groups of alcohol consumption frequency showed significant differences ($p < 0.01$). After adjustment for potentially confounding variables, compared to social drinkers, the risks of diabetes were significantly higher for non-drinkers (adjusted hazard ratio [AHR] = 1.21; 95% confidence interval [CI], 1.09–1.34; $p < 0.01$), regular drinkers (AHR = 1.19; 95% CI, 1.06–1.35; $p < 0.01$), and heavy drinkers (AHR = 2.21, 95% CI, 1.56–3.13, $p < 0.01$).
Conclusions: Social drinkers have a significantly decreased risk of new-onset diabetes compared with non-, regular, and heavy drinkers.

1. Introduction

The increasing incidence of type 2 diabetes mellitus is a universal problem, because it is one of the main cause of cardiovascular disease and mortality [1]. Further, the health expenditure of diabetes and its complications are enormous, increasing the financial burden of the national health care systems around the world [2].

* Corresponding author. Department of Neurosurgery, Taipei City Hospital, No. 145, Zhengzhou Rd., Datong Dist., Taipei City 10341, Taiwan.
** Corresponding author. Section of Infectious Diseases, Taipei City Hospital, Taipei City Government, No. 145, Zhengzhou Rd., Datong Dist., Taipei City 10341, Taiwan.
E-mail addresses: dam37@tpech.gov.tw (Y.-F. Yen), dad57@tpech.gov.tw (D. Chu).

https://doi.org/10.1016/j.clnu.2018.06.930
0261-5614/

Alcohol consumption is correlated with type 2 diabetes through its effects on insulin resistance, changes in alcohol metabolite levels, and anti-inflammatory effects [3,4]. People in different countries consume different beverage types and show different drinking patterns. Moreover, ethanol metabolism not only differs between males and females, but also between diverse populations due to genetic factors [5,6].

Beulens et al. analyzed data from eight European countries and reported that modest alcohol intake was related with a lower diabetes risk in women, but not in men. Besides, the correlation between alcohol and diabetes was stronger in overweight than normal-weight subjects [7]. Liang et al. similarly reported that moderate alcohol consumption associated with lower diabetes risk in middle-age and elderly Chinese men [8], whereas a meta-analysis conducted by Knott et al. showed that moderate alcohol intake associated with reduced diabetes risk only in females and non-Asian populations [9]. Another meta-analysis by Lee et al. revealed that slight and moderate alcohol consumption related with decreased diabetes risk, while heavy alcohol consumption was not related with increased diabetes risk [10].

However, the prior studies on the relation between alcohol use and the risk of diabetes were restricted to particular populations and had insufficient adjustment for potential confounders. Herein, we aimed to clarify the association between frequency of alcohol consumption and diabetes risk in Taiwanese people by using population representative data.

2. Materials and methods

2.1. Data source

The National Health Interview Survey (NHIS) was carried out by the Bureau of Health Promotion, Department of Health, and the National Health Research Institutes in 2001, 2005, and 2009 in Taiwan. The survey selected a representative sample of the Taiwanese population using a multistage sampling design. The NHIS data were gathered by regular face-to-face interviews. Information on demographic characteristics, personal and household income, body height and weight, and health behaviors such as frequency of alcohol consumption, smoking habits, and leisure time physical activity were collected. Participants who had provided consent were connected to the Taiwan National Health Insurance (NHI) claims data and the National Deaths Dataset from 2000 to 2013. The NHI claims records contain information on medical use, including ambulatory and inpatient care. The follow-up period began on the date of the interview and was terminated at the time of diagnosis of new-onset diabetes, death, or on Dec 31, 2013. If the participant was interviewed twice or more, only the information obtained from the first interview was analyzed. This study was approved by Taipei City Hospital's Joint Institutional Review Board (TCHIRB-10404118-W).

2.2. Frequency of alcohol consumption

Detailed information on frequency of alcohol consumption was gathered by face-to-face interviews. Frequency of alcohol consumption was evaluated by the questions: “How often do you drink alcohol?” and “Do you regularly get drunk?” Frequency of alcohol consumption was classified by consumption frequency and drunkenness into non-drinker, social consumption (less than once a week), regular consumption (more than once a week but not to the point of being drunk), and heavy consumption (more than once a week, to the point of being drunk) [11].

2.3. Diabetes

Comorbidity were defined by the diagnosis codes of the NHI claims records, using more than three outpatient claims or at least one inpatient admission claim, according to the International Classification of Disease, 9th Revision Clinical Modification (ICD-9-CM). The study cohort was defined as people who were free of diabetes at the beginning of the study. People who was diagnosed as having diabetes before the NHIS interview were excluded from the study. The outcome variable of this study was diabetes (ICD-9-CM code 250).

2.4. Confounding variables

Demographic characteristics, socioeconomic status, and health behaviors were recorded by face-to-face interviews. Comorbidities, including hypertension (ICD-9-CM codes 401-405) and hyperlipidemia (ICD-9-CM code 272) were recognized from the diagnosis codes of the NHI claims records [12]. Body weight and height were self-reported by the study subjects. Body mass index was categorized as underweight (<18.5 kg/m^2), normal (18.5–23.9 kg/m^2), overweight (24–26.9 kg/m^2), and obesity (≥ 27 kg/m^2) [13]. Information on fruit and vegetable consumption was collected by the questions “How many days do you eat fruit in a week?” and “How many days do you eat vegetables in a week?” Leisure-time physical activity was evaluated by the question: “Did you participate in any leisure-time physical activities during the last two weeks?” Weekly energy expenditure (kcal) of physical activity was calculated by the following equation: activity intensity code (kcal/min) $\times$ frequency per week (times) $\times$ duration for each time (minutes) [14].

2.5. Statistical methods

Kaplan–Meier curves with the log-rank test were employed to demonstrate and investigate the differences in the development of diabetes during the study period among the four groups of alcohol consumption frequency. Baseline characteristics of participants across alcohol categories were compared by t test and chi square test. A univariate Cox proportional regression model was applied to compare baseline characteristics among the study cohort. A multivariate Cox proportional regression model was applied to investigate the independent associations of alcohol consumption frequency with the incidence of diabetes. Stratified analysis by sex was performed, as previous studies have revealed sex disparities in the association between frequency of alcohol consumption and risk of diabetes [9,15]. Sensitivity analysis was carried out by excluding incident diabetes cases during the first one and two years after the NHIS interview. All analyses were performed using SAS software v.9.4.

3. Results

A total of 48,604 people aged more than 18 years were included in the 2001, 2005, and 2009 NHIS. Subjects with a history of diabetes ($n = 3685$), subjects who did not respond to the alcohol consumption frequency questions ($n = 1918$), and subjects with missing data of sex ($n = 1$) were excluded. Thus, data of 43,000 people were finally analyzed in our study. The mean (SD) age of the study population was 41.79 (16.31) years, and 50.35% of the subjects were women. During 357,908 person-years of follow-up, 3650 subjects developed new-onset diabetes.

Kaplan–Meier curves comparing the four groups of alcohol consumption frequency revealed a statistical significance (p-value of log-rank test <0.01; Fig. 1). During the 5–13 years of follow-up, incident diabetes was recognized in 2399 (9.20%) non-drinkers, and in 573 (5.32%), 636 (10.74%), and 42 (19.0%) subjects with social, regular, and heavy alcohol consumption, respectively (Table 1).

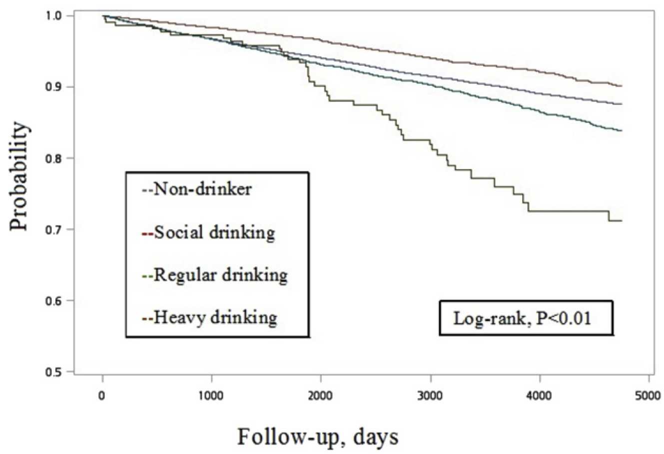

Fig. 1. Kaplan–Meier survival curve estimates for incident diabetes in a random community sample in Taiwan.

As compared with subjects with social alcohol consumption, non-drinkers and individuals with regular and heavy consumption had higher risks of incident diabetes (non-drinkers: hazard ratio [HR], 1.47; 95% confidence interval [CI] 1.34–1.61, $p < 0.01$; regular consumption: HR, 1.82, 95% CI 1.62–2.03, $p < 0.01$; and heavy consumption: HR, 3.27, 95% CI 2.39–4.48, $p < 0.01$) (Table 2). Other factors associated with the development of diabetes were older age, male sex, overweight or obesity, widowed/divorced/separated, smoking, hypertension, and hyperlipidemia. Alternatively, higher education level, higher household income, and moderate physical activity were negatively associated with incidence of diabetes (Supplementary Table 1).

We used a multivariate Cox regression model to determine the factors associated with incident diabetes (Table 2 and Supplementary Table 2). After adjusting for the subjects' demographics, health behaviors, and comorbidities (age, sex, BMI, marriage, education, household income, smoking status, vegetable and, fruit intake, physical activity, hypertension, and hyperlipidemia), non-drinkers and subjects with regular and heavy alcohol

Table 1
Baseline characteristics of participants classified according to frequency of alcohol consumption (N = 43,000; 3650 incident diabetes cases).

Characteristics	Non-drinker n = 26,090	Social n = 10,769	Regular n = 5920	Heavy n = 221	p-value
Age in years, mean (SD)	43.02 (17.43)	37.69 (13.96)	43.80 (13.86)	42.53 (12.19)	<0.01
Gender					
Female	16,632 (63.75%)	4001 (37.15%)	988 (16.69%)	29 (13.12%)	<0.01
Male	9458 (36.25%)	6768 (62.85%)	4932 (83.31%)	192 (86.88%)	
BMI (kg/m^2)					
Underweight (<18.5)	2095 (8.52%)	641 (6.04%)	197 (3.5%)	10 (5.05%)	<0.01
Normal weight (18.5–23.9)	13,910 (56.54%)	5791 (54.54%)	2681 (47.6%)	103 (52.02%)	
Overweight (24–26.9)	5288 (21.5%)	2578 (24.28%)	1639 (29.1%)	42 (21.21%)	
Obesity (≥27)	3307 (13.44%)	1608 (15.14%)	1115 (19.8%)	43 (21.72%)	
Marriage status					
Married/cohabiting	15,745 (60.36%)	5776 (53.65%)	4050 (68.41%)	127 (57.47%)	<0.01
Never married	7515 (28.81%)	4285 (39.8%)	1222 (20.64%)	60 (27.15%)	
Widowed/divorced/separated	2826 (10.83%)	706 (6.56%)	648 (10.95%)	34 (15.38%)	
Education					
Low (elementary or below)	7057 (27.07%)	1145 (10.63%)	1463 (24.73%)	62 (28.18%)	<0.01
Moderate (junior/senior high)	11,046 (42.38%)	4760 (44.21%)	3473 (58.72%)	138 (62.73%)	
High (college or above)	7964 (30.55%)	4863 (45.16%)	979 (16.55%)	20 (9.09%)	
Household income					
<US$952/month	5853 (23.91%)	1578 (15.79%)	1449 (25.7%)	91 (42.92%)	<0.01
US$952–2222/month	10,744 (43.89%)	4313 (43.17%)	2536 (44.98%)	71 (33.49%)	
>US$2222/month	7885 (32.21%)	4100 (41.04%)	1653 (29.32%)	50 (23.58%)	
Smoking status					
Never	21,631 (82.95%)	6128 (56.91%)	1614 (27.3%)	36 (16.36%)	<0.01
Current	3545 (13.59%)	3611 (33.54%)	3761 (63.61%)	167 (75.91%)	
Former	902 (3.46%)	1028 (9.55%)	538 (9.1%)	17 (7.73%)	
Vegetable					
<5 days/week	3630 (13.93%)	1581 (14.69%)	893 (15.09%)	55 (25%)	<0.01
5–7 days/week	22,429 (86.07%)	9182 (85.31%)	5024 (84.91%)	165 (75%)	
Fruit					
<5 days/week	9073 (34.82%)	4029 (37.43%)	2880 (48.67%)	143 (65%)	<0.01
5–7 days/week	16,985 (65.18%)	6734 (62.57%)	3037 (51.33%)	77 (35%)	
Physical activity					
0 kcal/week	12,041 (47.35%)	4636 (43.46%)	3363 (57.49%)	145 (65.91%)	<0.01
0–800 kcal/week	7207 (28.34%)	3300 (30.93%)	1213 (20.74%)	52 (23.64%)	
>800 kcal/week	6182 (24.31%)	2732 (25.61%)	1274 (21.78%)	23 (10.45%)	
Hypertension					
No	19,109 (73.24%)	8874 (82.4%)	4194 (70.84%)	136 (61.54%)	<0.01
Yes	6981 (26.76%)	1895 (17.6%)	1726 (29.16%)	85 (38.46%)	
Hyperlipidemia					
No	21,476 (82.32%)	9333 (86.67%)	4823 (81.47%)	181 (81.9%)	<0.01
Yes	4614 (17.68%)	1436 (13.33%)	1097 (18.53%)	40 (18.1%)	
Diabetes					
No	23,691 (90.8%)	10,196 (94.68%)	5284 (89.26%)	179 (81%)	<0.01
Yes	2399 (9.2%)	573 (5.32%)	636 (10.74%)	42 (19%)	

Abbreviations: SD, standard deviation.

Table 2
Univariate and multivariate Cox proportional hazards analysis of risk factors for incident diabetes mellitus.

Alcohol consumption frequency	HR	(95% CI)	p-value	AHR	(95% CI)	p-value
Non-drinker	1.47	1.34–1.61	<0.01	1.21	(1.09–1.34)	<0.01
Social	Ref			Ref		
Regular	1.82	1.62–2.03	<0.01	1.19	(1.06–1.35)	<0.01
Heavy	3.27	2.39–4.48	<0.01	2.21	(1.56–3.13)	<0.01

Abbreviations: HR, hazard ratio; AHR, adjusted hazard ratio; CI, confidence interval. Multivariate Cox proportional hazard analysis was adjusted for age, sex, BMI, marriage, education, household income, smoking status, vegetable and fruit intake, physical activity, hypertension, and hyperlipidemia.

consumption significantly associated with increased risks of incident diabetes (non-drinkers: HR, 1.21; 95% CI 1.09–1.34, $p < 0.01$; regular consumption: HR, 1.19, 95% CI 1.06–1.35, $p < 0.01$; and heavy consumption: HR, 2.21, 95% CI 1.56–3.13, $p < 0.01$).

The results of the sex-stratified analysis are given in Table 3. Social consumption was associated with a decreased risk of incident diabetes in all subgroups. Next, sensitivity analysis was performed by excluding incident diabetes cases within the first and second years of the study period. There were 476 and 937 new-onset diabetes cases within one and two years after the NHIS interview, respectively. Multivariate Cox proportional hazards analysis was adjusted for age, sex, BMI, marriage, education, household income, smoking status, vegetable and fruit intake, physical activity, hypertension, and hyperlipidemia. As a result, social consumption remained significantly associated with decreased risks of incident diabetes in the sensitivity analysis (non-consumption: HR, 1.17; 95% CI 1.04–1.31, $p = 0.01$; regular consumption: HR, 2.45, 95% CI 1.02–1.35, $p = 0.03$; and heavy consumption: HR, 2.45, 95% CI 1.68–3.56, $p < 0.01$).

4. Discussion

Our study investigated the association between alcohol and diabetes risk in the general Taiwanese population, and the results showed that people with social alcohol consumption had significantly decreased risk of incident diabetes compared with non-drinkers and those with regular or heavy alcohol consumption. The present study illustrates the U-shape relationship between frequency of alcohol consumption and risk of incident diabetes in both men and women.

The finding of our study that social alcohol consumption is associated with lower diabetes risk was compatible to the findings of previous studies. Several studies have reported the biological mechanisms to explain the lower risk of development of diabetes in people with modest alcohol consumption. Alcohol may improve insulin resistance by inhibiting gluconeogenesis, which leads to decreased risks of the development of diabetes mellitus [16,17]. In addition, the so-called anti-inflammatory theory was also reported, which suggests that alcohol may positively change the expressions of inflammatory proteins such as adiponectin and interleukin-1b involved in metabolic processes [18–20]. Alcohol may also motivate the synthesis of high-density lipoprotein [19].

People in different countries consume different beverage types and show different drinking patterns. Ethanol metabolism also differs in different populations and between the sexes [5,6]. Previous studies have demonstrated that wine associates with reduced risks of developing diabetes compared with beer or spirits [7,21,22]. However, as for the associations of drinking frequency and quantity with diabetes risks, the results differ between males and females. A meta-analysis of 38 epidemiology studies reported that the decreased diabetes risk associated with moderate alcohol consumption is limited to females and non-Asian populations. However, it is possible that the observed risk reductions may be due to overestimation by using a reference group contaminated by those who had quit consumption [9]. Another meta-analysis of the associations on alcohol with insulin sensitivity and blood glucose concentrations revealed that modest alcohol consumption may reduce fasting insulin and HbA1c levels in subjects without diabetes. Further, alcohol consumption may increase females' insulin sensitivity, but generally do not do so in men [15]. A European study reported that moderate alcohol consumption associated with decreased risk of type 2 diabetes in females only, which was speculated to be due to the differences in fat distribution between the sexes. In fact, in the same study, the association between alcohol and incident diabetes was stronger in overweight compared with normal-weight people [7]. Cullmann et al. reported that heavy alcohol consumption increases the risk of abnormal glucose regulation in males aged 35–56 years. However, in females, low or medium alcohol intake associated with a decreased diabetes risk, whereas heavy alcohol intake related to an increased risk [23]. Rasouli et al. analyzed data from Norway and reported that moderate alcohol use associated with a decreased risk of type 2 diabetes, although this protecting effect may be restricted to males only. Besides, heavy alcohol consumption did not increase the diabetes risk in that study [22]. Liang et al. reported that moderate alcohol intake associated with decreased type 2 diabetes risk among Chinese men aged 40–74 years [8]. A significant negative dose–response relationship between alcohol intake and incident diabetes was reported from a prospective cohort study of 8423 Japanese male workers [24]. Another study of 2500 male laborers in Korea revealed that moderate and heavy alcohol consumption were associated with increased risks of the development of diabetes in obese males [25]. The impact of alcohol consumption on the risk of diabetes varies across different population and genders. Our study also revealed differences in diabetes incidence according to sex, especially in regard to regular alcohol consumption. A majority of women in Taiwan were non-drinkers. The unequal distribution across the four groups of alcohol consumption frequency may cause decreased power in the analysis.

The current study has some limitations that should be mentioned. First, the information of the participants, including their weight, height, income, smoking habit, and frequency of alcohol consumption was self-reported, which may result in recall bias. Second, while there were only a few subjects who refused to provide consent to link their information to the health insurance dataset, bias due to selective missing should still be considered. Third, this study only collected information on the frequency and extent of alcohol consumption; however, detailed information of the beverage type and amount was not available in the questionnaires. Besides, detailed information about quality of diet and smoking was

Table 3
Subgroup analysis of the association of alcohol consumption frequency with incidence of diabetes according to sex.

Alcohol consumption frequency	Female (n = 21,650) AHR (95% CI)	Male (n = 21,350) AHR (95% CI)
Non-drinker	1.13 (0.95–1.34)	1.25 (1.10–1.41)
Social	Ref	Ref
Regular	0.99 (0.74–1.33)	1.26 (1.10–1.44)
Heavy	2.91 (1.07–7.91)	2.21 (1.52–3.22)

Abbreviations: AHR, adjusted hazard ratio; CI, confidence interval.
Multivariate Cox proportional hazards analysis was adjusted for age, BMI, marriage, education, household income, smoking status, vegetable and fruit intake, physical activity, hypertension, and hyperlipidemia.

not available in the NHIR dataset. Our questionnaires were also unable to separate never and former drinkers, which were pooled together as non-drinkers. Former drinkers are particularly noteworthy, because they may have worse health condition and higher morbidity and mortality than never-drinkers [26]. Thus, it should be taken into consideration that the non-drinker group was contaminated by less healthy former drinkers. Fourth, the alcohol consumption pattern was recorded only at baseline, and whether the consumption pattern changed over time was not assessed. Finally, laboratory data were not available in the dataset and the diagnosis of diabetes relied on the ICD-9-CM codes and medication history. However, the possibility of misclassification of the outcome was low, because the NHI covers >97% of the Taiwanese population and records all health insurance information [27].

This study also had a number of important strengths. First, the retrospective cohort study design could avoid the problems of control selection in case–control studies and vague timing in cross-sectional studies. Second, we investigated the NHIS dataset, which is a national representative sample of the whole Taiwanese population. Our study thus had good generalizability. Third, several important confounding variables were adjusted for, including demographic characteristics, socioeconomic status, diet, physical activities, smoking status, and comorbidities. Lastly, the study cohort had a total follow-up period of 9 (range, 5–13) years, providing sufficient time to obtain a confident level of statistical power.

In summary, the present study suggests that those with social alcohol consumption have a reduced risk of incidence of diabetes compared with non-drinkers and regular or heavy drinkers. Further studies are necessary to evaluate the effect of different beverage types and the quantity of alcohol on the risk of development of diabetes.

Funding sources

This work was supported by a research grant from the Department of Health, Taipei City Government (TPCH-104-005).

Author contributions

Chu, Hu, Ku, and Lee collected the data. Lai, Yen, and Ko performed data analysis. All authors reviewed and revised the manuscript.

Conflict of interest

None declared.

Acknowledgements

The authors thank the participants in the National Health Interview Survey. We also appreciated the research and administrative staff of National Health Interview Survey and National Health Insurance Research Database for their great contributions in data collection and management.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.clnu.2018.06.930.

References

[1] Martin-Timon I, Sevillano-Collantes C, Segura-Galindo A, Del Canizo-Gomez FJ. Type 2 diabetes and cardiovascular disease: have all risk factors the same strength? World J Diabetes 2014;5:444–70.
[2] Zhang P, Zhang X, Brown J, Vistisen D, Sicree R, Shaw J, et al. Global healthcare expenditure on diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010;87:293–301.
[3] Davies MJ, Baer DJ, Judd JT, Brown ED, Campbell WS, Taylor PR. Effects of moderate alcohol intake on fasting insulin and glucose concentrations and insulin sensitivity in postmenopausal women: a randomized controlled trial. J Am Med Assoc 2002;287:2559–62.
[4] Bonnet F, Disse E, Laville M, Mari A, Hojlund K, Anderwald CH, et al. Moderate alcohol consumption is associated with improved insulin sensitivity, reduced basal insulin secretion rate and lower fasting glucagon concentration in healthy women. Diabetologia 2012;55:3228–37.
[5] Mumenthaler MS, Taylor JL, O'Hara R, Yesavage JA. Gender differences in moderate drinking effects. Alcohol Res Health 1999;23:55–64.
[6] Goedde HW, Agarwal DP, Fritze G, Meier-Tackmann D, Singh S, Beckmann G, et al. Distribution of ADH2 and ALDH2 genotypes in different populations. Hum Genet 1992;88:344–6.
[7] Beulens JW, van der Schouw YT, Bergmann MM, Rohrmann S, Schulze MB, Buijsse B, et al. Alcohol consumption and risk of type 2 diabetes in European men and women: influence of beverage type and body size the EPIC-InterAct study. J Intern Med 2012;272:358–70.
[8] Shi L, Shu XO, Li H, Cai H, Liu Q, Zheng W, et al. Physical activity, smoking, and alcohol consumption in association with incidence of type 2 diabetes among middle-aged and elderly Chinese men. PLoS One 2013;8, e77919.
[9] Knott C, Bell S, Britton A. Alcohol consumption and the risk of type 2 diabetes: a systematic review and dose-response meta-analysis of more than 1.9 million individuals from 38 observational studies. Diabetes Care 2015;38:1804–12.
[10] Li XH, Yu FF, Zhou YH, He J. Association between alcohol consumption and the risk of incident type 2 diabetes: a systematic review and dose-response meta-analysis. Am J Clin Nutr 2016;103:818–29.
[11] Lin HH, Chang HY, Chiang YT, Wu MS, Lin JT, Liao WC. Smoking, drinking, and pancreatitis: a population-based cohort study in Taiwan. Pancreas 2014;43:1117–22.
[12] Lai YJ, Hu HY, Lin CH, Lee ST, Kuo SC, Chou P. Incidence and risk factors of lower extremity amputations in people with type 2 diabetes in Taiwan, 2001-2010. J Diabetes 2015;7:260–7.
[13] Pan WH, Lee MS, Chuang SY, Lin YC, Fu ML. Obesity pandemic, correlated factors and guidelines to define, screen and manage obesity in Taiwan. Obes Rev 2008;9(Suppl 1):22–31.
[14] Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, et al. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc 2000;32:S498–504.
[15] Schrieks IC, Heil AL, Hendriks HF, Mukamal KJ, Beulens JW. The effect of alcohol consumption on insulin sensitivity and glycemic status: a systematic review and meta-analysis of intervention studies. Diabetes Care 2015;38:723–32.
[16] van de Wiel A. Diabetes mellitus and alcohol. Diabetes/Metab Res Rev 2004;20:263–7.
[17] Fueki Y, Miida T, Wardaningsih E, Ito M, Nakamura A, Takahashi A, et al. Regular alcohol consumption improves insulin resistance in healthy Japanese men independent of obesity. Clin Chim Acta; Int J Clin Chem 2007;382:71–6.
[18] Akash MS, Rehman K, Chen S. Role of inflammatory mechanisms in pathogenesis of type 2 diabetes mellitus. J Cell Biochem 2013;114:525–31.
[19] Brien SE, Ronksley PE, Turner BJ, Mukamal KJ, Ghali WA. Effect of alcohol consumption on biological markers associated with risk of coronary heart disease: systematic review and meta-analysis of interventional studies. BMJ (Clinical research ed) 2011;342, d636.
[20] Szabo G, Mandrekar P, Catalano D. Inhibition of superantigen-induced T cell proliferation and monocyte IL-1 beta, TNF-alpha, and IL-6 production by acute ethanol treatment. J Leukoc Biol 1995;58:342–50.
[21] Marques-Vidal P, Vollenweider P, Waeber G. Alcohol consumption and incidence of type 2 diabetes. Results from the CoLaus study. Nutr Metabol Cardiovasc Dis: NMCD 2015;25:75–84.
[22] Rasouli B, Ahlbom A, Andersson T, Grill V, Midthjell K, Olsson L, et al. Alcohol consumption is associated with reduced risk of Type 2 diabetes and autoimmune diabetes in adults: results from the Nord-Trondelag health study. Diabet Med 2013;30:56–64.
[23] Cullmann M, Hilding A, Ostenson CG. Alcohol consumption and risk of pre-diabetes and type 2 diabetes development in a Swedish population. Diabet Med 2012;29:441–52.
[24] Teratani T, Morimoto H, Sakata K, Oishi M, Tanaka K, Nakada S, et al. Dose-response relationship between tobacco or alcohol consumption and the development of diabetes mellitus in Japanese male workers. Drug Alcohol Depend 2012;125:276–82.
[25] Roh WG, Shin HC, Choi JH, Lee YJ, Kim K. Alcohol consumption and higher incidence of impaired fasting glucose or type 2 diabetes in obese Korean men. Alcohol (Fayetteville, NY) 2009;43:643–8.
[26] Tsubono Y, Yamada S, Nishino Y, Tsuji I, Hisamichi S. Choice of comparison group in assessing the health effects of moderate alcohol consumption. J Am Med Assoc 2001;286:1177–8.
[27] Lee YC, Huang YT, Tsai YW, Huang SM, Kuo KN, McKee M, et al. The impact of universal National Health Insurance on population health: the experience of Taiwan. BMC Health Serv Res 2010;10:225.