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Association between diabetes and risk of suicide death: A meta-analysis of 3 million participants

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Abstract

Background: Results of the relationships between diabetes and the risk of suicide death are inconclusive. This meta-analysis was conducted to assess this association.

Methods: We systematically searched PubMed, EMBASE, Web of Science and the Cochrane Library up to February 29, 2016 for relevant observational studies regarding the association between diabetes and risk of suicide. Random-effects models were used to calculate summary relative risk (RR) and 95% confidence interval (CI).

Results: 6 observational studies (8 independent reports) with a total of 3,075,214 participants and 3038 suicide deaths events were included in the meta-analysis. Overall, diabetes was not associated with risk of suicide deaths, with significant heterogeneity among studies observed (Summary RR = 1.61, 95% CI: 0.91–2.83, Pheterogeneity < 0.001, I^2 = 97.2%). No publication bias was detected across studies, and both the subgroup analysis and sensitivity analysis suggested that the general result was robust.

Conclusion: Our meta-analysis based on more than 3 million participants indicates that diabetes is not associated with increased risk of suicide death. Further well-designed prospective cohort studies are needed to confirm the findings of this meta-analysis.

1. Introduction

Diabetes is a chronic disease which has become a serious worldwide public health problem. The estimated number of individuals affected by diabetes worldwide was 171 million in 2000 and it will increase to 366 million by 2030 [1]. Diabetes is associated with many adverse consequences, including reduced life expectancy, increased risk of various complications, diminished quality of life, and even deaths [2]. According to the World Health Organization (WHO), diabetes was estimated to directly cause 1.5 million deaths in 2012 [3], and it is projected to be the 7th leading cause of death in 2030 [1].

Suicide, as a very complex human behavior, has also become a serious worldwide public and mental health problem. Every year, more than 800,000 people die by suicide, with approximately 1 death every 40 s [4]. Among diverse factors, mental illness, such as depression, schizophrenia, and bipolar disorder, is well recognized to be associated with increased risk of suicide [5]. In recent years, several researchers tried to explore the relationship between diabetes and suicide [6–11]. Nevertheless, evidence on the association of diabetes with risk of suicide has not been systematically assessed. We therefore conducted a meta-analysis of observational studies to explore the effects of diabetes on risk of suicide.

Conflicts of interest: The authors declare that they have no conflicts of interest concerning this article.

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2. Methods

2.1. Search strategy

PubMed, EMBASE, Web of Science and the Cochrane Library up to February 29, 2016 were searched for relevant observational studies that regarding the association between diabetes and risk of suicide. The reference lists of all retrieved articles were also scanned to find any additional literatures. The search terms used were 'Diabetes AND Suicide'. No language restriction was applied. The Meta-Analysis of Observational Studies in Epidemiology guidelines [12] were followed to conduct this meta-analysis.

2.2. Study selection criteria

Studies were included if they met the following criteria: i.) were case–control studies or cohort studies, ii.) evaluated the association between diabetes and risk of suicide deaths, iii.) cases of suicide deaths were obtained from death certificates or death record, and iv.) reported the risk estimates such as odds ratio (OR), relative risk (RR) or hazard ratio (HR) and corresponding 95% confidence interval (CI). Non-human studies, letters, case reports, conference abstracts, and reviews were excluded.

2.3. Data extraction and quality assessment

Two reviewers independently performed data extraction with discrepancies resolved by discussion. The following information was extracted: name of the first author, publication year, study characteristics (design, location, name and follow-up duration in cohort studies), age of participants, exposure and endpoint with ascertainment methods, total number of suicide cases and study population, the most fully adjusted risk estimates with 95% CI, and confounding factors that being adjusted for. We did not contact the authors because the included studies provided sufficient information for meta-analysis.

The Newcastle–Ottawa Scale (NOS) [13] was used to assess the study quality. A maximum of 9 points could be assigned to selection of study groups (4 points), comparability of study groups (2 points), assessment of outcomes (for cohort studies) or exposure (for case–control studies) (3 points), respectively. Studies with scores 0–3, 4–6, and 7–9 were respectively regarded as low, moderate, and high quality.

2.4. Data analysis

RR was used as a measure of the association between diabetes and risk of suicide to combine the results. HR and OR were directly considered as RR considering that suicide was very rare. Heterogeneity was assessed using the Cochrane Q statistic (significance level at $P < 0.10$) and the I^2 statistic [14,15]. We used random effect model to calculate the pooled RR as this model takes into account both study sample size and between-study variation [16]. Sensitivity analysis was conducted to explore the potential influence of each individual study on overall results. Additionally, subgroup analyses were performed according to study location (Asian countries/non-Asian countries), study design (cohort/case–control), sex (male/female), number of factors for adjustment (<10/≥10). The Begg's test [17] and Egger's test [18] were used to detect publication bias. Data analysis was conducted using Stata version 11.0 (Stata Corporation). The statistical tests were all two-sided with a significance level of 0.05, unless otherwise specified.

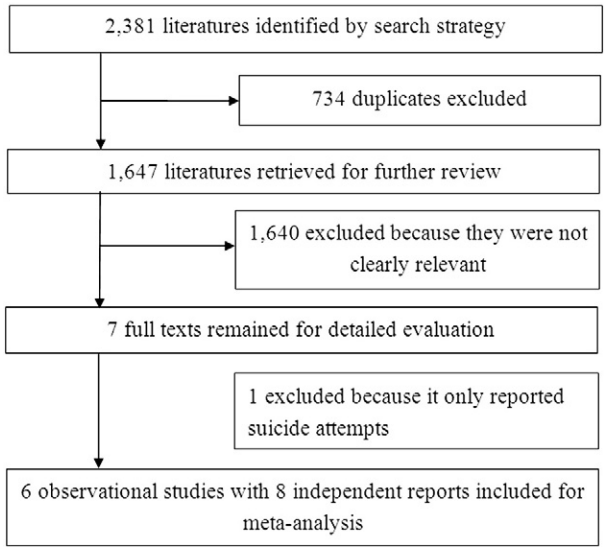

Fig. 1. Selection flow of studies included in the meta-analysis.

3. Results

3.1. Literature search

Fig. 1 presents the study selection flow. In brief, we totally identified 2381 articles using the search strategy. After removal of duplicates and screening of titles or abstracts, we excluded 2375 articles. By reading the full text of the remained 7 articles, we further excluded 1 article [19] as it used suicide attempt as endpoint. In the study of Batty et al. [6] and Yamauchi et al. [11], the results of male and female were presented separately, so we treated it as two separate reports. Finally, we included 6 observational studies with 8 independent reports.

3.2. Study characteristics

Table 1 lists the characteristics of included studies. There were 5 cohort studies [6,9–11] and 1 case–control study [8], which were respectively conducted in Korea [6], Australia [7], Canada [8], U.K. [9], Sweden [10] and Japan [11]. The sum number of suicide deaths was 3038 with a total of 3,075,214 participants involved. The exposure of 4 studies [8–11] was diabetes mellitus with any type while 1 study [6] focused on type 2 diabetes. The exposure and endpoint was generally ascertained by record linked dataset or register.

Table 1
Characteristics of observational studies of diabetes and suicide deaths included in the meta-analysis.

Author	Location	Design (follow-up years)	Age	Type of diabetes	Ascertainment of diabetes	Ascertainment of suicide[a]	Case/Total	Risk estimate[b] (95%CI)	Confoundings
Quan 2002 [8]	Canada	Case–control	≥55	Unspecified	Record linkage, verified by Medical Examiner's records	Record linkage, verified by Medical Examiner's records; ICD-9	822/1766	OR 0.84 (0.57,1.23)	Age, sex, marital status, race, income, residence, employment, history of disease (cancer, ischemic heart disease, cerebrovascular disease, chronic pulmonary disease, peptic ulcer, prostatic disorder, depression and other psychiatric illness)
Batty 2011 [6]	Korea	Cohort	30–95	Type 2	Fasting serum glucose test, with self-report of either physician diagnosis or medication usage	Death certificates; ICD-10	472/1,234,927	HR M: 2.55 (1.30,5.00) F: 3.64 (1.12,11.86)	Exercise, smoking status, alcohol consumption, body mass index, height, blood pressure and blood cholesterol
Singhal 2014 [9]	UK	Retrospective cohort	≥10	Unspecified	Linked dataset	Death record; ICD-9, ICD-10	626/213,635	RR 1.0 (0.9,1.1)	Age in five-year bands, time period in single calendar years, region of residence and deprivation score associated with patients' area of residence in quintiles
Webb 2014 [10]	Swedish	Retrospective cohort	Median 69.3	Unspecified	National Register	Death Register; ICD-9, ICD-10	482/1,512,405	RR 3.36 (2.99, 3.79)	Age, sex, and county of birth
Yamauchi 2015 [11]	Japan	Cohort	51.2 ± 7.9	Unspecified	Self-report of physician diagnosis or medication usage at baseline	Death certificates; ICD-10	618/105,408	RR M: 1.2 (0.9,1.8) F: 1.5 (0.7,3.0)	Age at study entry, public health center area, smoking, alcohol-drinking, body mass index, cohabitation, employment, hours of sleep, physical exercise, stress level and history of major physical illnesses (cancer, stroke, heart disease)
Devis 2015 [7]	Australia	Cohort	62.3 ± 12.7	Type 1	Identified from clinic and inpatient lists, local physician referrals, allied health facilities, pharmacies, opticians, advertising in local media and word of mouth	Death certificates; NA	18/7073	HR 1.16 (0.38–3.51)	Age and sex

[a] ICD: International Classification of Diseases; NA: not available.
[b] OR: odds ratio, RR: relative risk, HR: hazard ratio, F: female, M: male.

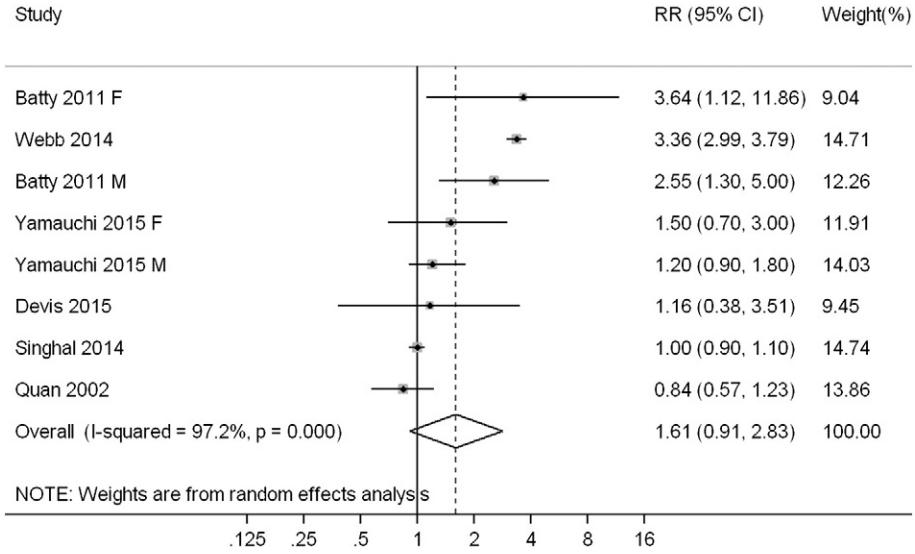

Fig. 2. A forest plot of the association between diabetes and risk of suicide death. Random-effects model was used to pool the overall relative risks (RRs) and 95% confidence intervals (CIs). The diamond represents the pooled RR and, the squares and the horizontal lines respectively represent the RR and 95% CI of each individual study.

Result from NOS indicated that all included studies were in high quality, with an average score of 7.5 (Table S1).

3.3. Main analysis

Fig. 2 shows a forest plot presenting individual and summary results. Overall, meta-analysis by random-effects model suggested that diabetes was not associated with increased risk of suicide death (overall RR = 1.61, 95% CI: 0.91–2.83). High statistically significant heterogeneity was found across studies (Pheterogeneity < 0.001, I^2 = 97.2%).

3.4. Subgroup and sensitivity analysis

Table 2 shows the effects of diabetes on suicide risk in subgroup analysis. Greater summary RRs were observed in studies which were conducted in Asian countries (versus in non-Asian countries), or had a cohort design (versus case–control design). In addition, the females with diabetes were found to have higher risk of suicide death than diabetic males. However, only the result pooled from studies conducted in Asia was statistically significant (RR = 1.75, 95% CI: 1.09–2.80). For sensitivity analysis, the pooled RR was not substantially influenced by any individual study, with a range from 1.23 (95% CI: 0.94–1.62) when omitting Webb et al.'s study [10] to 1.78 (95% CI: 0.96–3.33) when excluding Quan et al.'s study [8].

3.5. Publication bias

There was no evidence of publication bias in studies of diabetes and suicide risk, as indicated by the Begg's and Egger's test (all $P > 0.05$).

4. Discussion

To our knowledge, the present study is the first meta-analysis of observational studies to assess the

Table 2
Summary risk estimates of the association between diabetes and suicide deaths.

Factors	No. of reports	No. of participants	Summary adjusted RR (95% CI)	Heterogeneity I^2 (%)
Total	8	3,075,214	1.61 (0.91, 2.83)	97.2
Location				
Non-Asian countries	4	1,734,879	1.37 (0.59, 3.20)	98.8
Asian countries	4	1,340,335	1.75 (1.09, 2.80)	51.2
Design				
Cohort	7	3,073,448	1.78 (0.96, 3.33)	97.5
Case–control	1	1766	0.84 (0.57, 1.23)	NA
Sex				
Male	2	839,389	1.65 (0.80, 3.43)	73.7
Female	2	500,946	2.06 (0.90, 4.73)	36.3
No. of factors for adjustment				
<10	5	2,968,040	2.03 (0.92, 4.49)	98.3
≧10	3	107,174	1.08 (0.80, 1.50)	27.8

association between diabetes and suicide deaths. Based on a study population as large as more than 3 million participants, the pooled result suggested that diabetes was not associated with an increased risk of suicide deaths.

Many mechanisms are plausible to explain a possible link between diabetes and suicides. First, mental disorders (in particular depression) are well recognized risk factors for suicide. However, diabetes is one of the most psychologically demanding chronic diseases which require strict daily management of the treatment by the patients themselves [20]. Numerous epidemiological studies have demonstrated that diabetes was associated with increased prevalence of depressive disorders and anxiety disorders [21–24]. Second, poor diabetes control can lead to serious complications including cardiovascular disease, damage of kidneys and nerves, and blindness [25]. Nevertheless, these complications might cause or aggravate depression and reduce quality of life [26]. Third, the long turn treatment of diabetes and its complications reduces family income and can even lead to poverty [27]. However, poverty is thought to play an important role in heightened suicide rates [28]. In addition, diabetic patients in low-income families tend to have higher risk of poor diabetes control [29]. Despites all above mechanisms, our study failed to find an association between diabetes and risk of suicide death.

Our meta-analysis has strengths. First, this is the first meta-analysis of observational studies assessing the association between diabetes and suicide death. Second, this meta-analysis included a large sum number of participants, with more than 3 million subjects and 3038 cases of suicide deaths.

There are still several potential limitations. First, although all included studies controlled several factors, such as age, sex, race, smoking, drinking, and etc., the possibility that other potential confounders might interfere the possible association of diabetes and suicide could not be excluded, especially considering that only one study [8] adjusted for depression which is a major risk factor for suicide. However, because adjusting for depression will only attenuate the possible association between diabetes and suicide, the null association indicated by our result seems to be more reliable.

Second, high statistical heterogeneity was observed across included studies. The heterogeneity might be generated from the differences of study designs, study location, study population and other clinical or methodological factors. Nevertheless, both sensitivity analysis and subgroup analysis suggested that the general result of this meta-analysis was rather robust.

Third, 3 included studies used retrospective design [8–10], which totally involved more than 1.7 million participants. It was therefore inevitable that recall bias existed in the collection of information on exposure or confounding factors. Moreover, diabetes was self-reported without validation in one study [11], and there was a possibility that it may lead to misclassification of diabetes status. However, the validity and accuracy of diabetes self-reports were confirmed both in Western and Asian countries [30,31].

Fourth, it has been reported in different jurisdictions that official suicide rates are most often higher than true suicide rates [32]. Misclassification of suicide deaths may exist as some true suicide cases may be recorded as deaths due to other death causes, like accident, disease or other reasons. The unbalanced underestimation of true death rate in exposure group and control group may lead to biased result. In addition, the ascertainment of suicide death used different criteria which also may cause bias. For instance, Quan et al. [8] used International Classification of Diseases, 9th revision (ICD-9) and Yamauchi et al. [11] applied International Classification of Diseases, 10th revision (ICD-10), while Singhal et al. [9] and Webb et al. [10] both used ICD-9 and ICD-10. Therefore, the result of this meta-analysis should be interpreted with caution.

Finally, although both the Begg's and Egger's test indicated no evidence of publication bias, the power to detect publication bias may be limited due to the small number of included studies [33]. Thus, the possibility of publication bias cannot be fully excluded.

In conclusion, our meta-analysis of observational studies indicates that diabetes is not associated with increased risk of suicide death. However, given the limited number of included studies, further well-designed prospective cohort studies are needed to confirm the findings of this meta-analysis.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.comppsych.2016.08.006.

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