MANAGEMENT OF ENDOCRINE DISEASE

Suicide risk in patients with diabetes: a systematic review and meta-analysis

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Abstract

Background: Previous studies investigating the risk of suicide in diabetes patients reported controversial findings. We did a systematic review and meta-analysis to comprehensively estimate the risk and incidence rate of suicide in diabetic patients.

Methods: PubMed, EMBASE and PsycINFO were searched for eligible studies. Random-effects meta-analysis was used to calculate the relative risk (RR) and the incidence rate of suicide in diabetes patients. We also calculated the proportion of deaths attributable to suicide among diabetes patients.

Results: 54 studies were finally included, including 28 studies on the suicide risk associated with diabetes, 47 studies on the incidence rate of suicide and 45 studies on the proportion of deaths attributable to suicide. Meta-analysis showed that diabetes could significantly increase the risk of suicide (RR = 1.56; 95% CI: 1.29–1.89; $P < 0.001$). Subgroup analysis showed that the RR of suicide associated with type 1 diabetes was 2.25 (95% CI: 1.50–3.38; $P < 0.001$). The pooled incidence rate of suicide in patients with diabetes was 2.35 per 10 000 person-years (95% CI: 1.51–3.64). The pooled proportions of long-term deaths attributable to suicide in type 1 diabetes patients and type 2 diabetes patients were 7.7% (95% CI: 6.0–9.8) and 1.3% (95% CI: 0.6–2.6), respectively.

Conclusion: This meta-analysis suggests that diabetes can significantly increase the risk of suicide. Suicide has an obvious contribution to mortality in diabetic patients, especially among type 1 diabetes patients. Effective strategies to decrease suicide risk and improve mental health outcomes in diabetes patients are needed.

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Introduction

Suicide is one common cause of death with almost 1 million people dying from suicide worldwide each year, and it is a serious problem for global public health (1). Identification of risk factors of suicide is very important for the development of effective prevention strategies for suicide (2). Diabetes is also a public health issue worldwide and its global pandemic is still increasing obviously (3, 4). There are over 400 million people suffering from diabetes worldwide, and its prevalence is still increasing every year (4). Diabetes is also associated with increased

risks of many subsequent diseases, such as cardiovascular diseases, cancers and chronic kidney disease (5, 6, 7, 8).

Mental diseases are common among patients with diabetes, such as depression and suicidal ideation, but mental health is still a neglected comorbidity in patients with diabetes (9, 10, 11). Recent studies have suggested possibly increased risk of externally caused death such as suicide in patients with diabetes (12, 13, 14, 15). However, the risk of suicide associated with diabetes has not received enough attention. To date, it is still unclear

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whether diabetes can result in increased risk of suicide. There was also lack of a comprehensive estimation of suicide risk associated with diabetes. Therefore, to provide a comprehensive estimation of the risk of suicide in diabetes patients, we carried out a systematic review and meta-analysis of published studies. In this meta-analysis, to appropriately evaluate the risk of suicide in diabetes patients, we investigated the risk of suicide associated with diabetes, the incidence rate of suicide in diabetic patients and the contribution of suicide to mortality in diabetic patients. This systematic review was registered at PROSPERO (CRD42016039709).

Methods

Search strategy and selection criteria

PubMed, EMBASE and PsycINFO were searched to identify eligible studies. Databases were searched from January 1980 to October 15, 2016. We updated the literature search in PubMed on February 16, 2017. We used keywords and MeSH searches with the combination of the following terms: (suicide OR suicides OR suicidal OR suicidality) AND (diabetes OR diabetic OR T1DM or T2DM OR NIDDM OR IDDM). Language restriction was not used. The reference lists of relevant articles or reviews were also retrieved to for more eligible studies.

The following predefined inclusion criteria were used: (a) cohort studies; (b) for studies assessing the risk of suicide associated with diabetes, the exposure of interest was diabetes and for studies on the rate of suicide, diabetes patients were the population of interest; (c) studies recruiting either type 1 diabetes mellitus (T1DM) patients or type 2 diabetes mellitus (T2DM) patients, or studies mixing T1DM patients and T2DM patients together were all considered eligible; (d) the outcomes of interest were the incidence rate of suicide, the proportion of deaths attributable to suicide and the risk estimates of suicide associated with diabetes, such as standardized mortality ratio (SMR), hazard ratio (HR), relative risk (RR) and odds ratio (OR); (e) reporting data on the outcomes of interests. Since a few studies did not report the risk or the incidence rate of suicide in either T1DM or T2DM patients separately, but reported outcomes in a population, which mixed T1DM patients and T2DM patients together, we thus firstly assessed the risk of suicide in diabetes patients regardless of its types. However, to make it more appropriate, we would then stratified the studies by the types of diabetes and evaluated the risk or the incidence rate of suicide in patients with either T1DM or T2DM

separately. Studies reporting suicide attempts or suicidal ideation were excluded.

Data extraction and quality assessment

A standardized extraction form was used, and disagreements were resolved by discussion. Data were independently extracted by two reviewers from the full-texts of included studies. Study characteristics, such as first author's name, number of participants, demographic characteristics, the number of person-years, incident cases of suicide, time of follow-up, completeness of follow-up, method of standardization of SMR and risk estimates (SMR, HR, RR or OR), were all extracted. Newcastle–Ottawa Scale was utilized to evaluate the bias risk of observational studies with comparison groups, which assessed studies on three domains including the selection of participants, the comparability of exposure group and non-exposed group, and the ascertainment of the outcomes (16). The comparability was mainly assessed by the adjustment for confounding factors or the standardization of SMRs. Four, two and three stars were scored for those three domains, respectively. Studies with less than 6 stars were deemed to have high risk of bias, and studies with one star for the selection of participants or outcome ascertainment, or zero for any domain were all deemed to have high risk of bias (17, 18). For studies without a comparison group, which reported data on the incidence rate of suicide or the proportion of deaths attributable to suicide among diabetes patients, the risk of bias was assessed by a modified version of Newcastle–Ottawa scale proposed by Rotenstein *et al.* (19). The modified scale assessed the risk of bias of those studies without a comparison group on five items including representativeness of participants, sample size, comparability between respondents and nonrespondents, ascertainment of suicide and thoroughness of descriptive statistics. One point was scored for each item in the modified bias scoring scale, and studies were judged to have low risk of bias (≥ 3 points) or high risk of bias (< 3 points).

Statistical analysis

Meta-analyses were performed on the incidence rate of suicide, the risk estimate of suicide associated with diabetes and the proportion of deaths attributable to suicide, respectively. Because the incidence of suicide in diabetes patients was relatively low, OR and HR were approximately close to RR and were assumed to be the

same measure and a common estimate of RR, and this strategy had been used in many published meta-analyses of observational studies (20, 21, 22, 23). Besides, SMR was in line regarded as one form of RR in epidemiological researches and was thus conventionally used as the same measure of RR in the present meta-analysis. As the results were presented separately for men and women in some studies, we firstly obtained a within-study summary RR using a fixed-effect meta-analysis. The pooled estimates with 95% confidence intervals (95% CIs) were calculated using a random-effects model (24). This meta-analysis used both the I^2 statistic and the Cochran's Q statistic to evaluate the heterogeneity (25, 26). I^2 more than 50% indicated substantial heterogeneity among included studies. The proportion of deaths attributable to suicide was converted by the method of Freeman–Tukey double arcsine transformation before data synthesis, and then was back-transformed to the original pattern, and it was calculated using the METARATE command in the 'meta' package for R. The incidence rates of suicide were pooled using the 'metan' module of STATA. The commands above in detail were shown in [Supplementary Table 1](#) (see section on [supplementary data](#) given at the end of this article). Sensitivity analysis was performed by excluding studies with high risk of bias. The estimates were also stratified by gender and types of diabetes. Publication bias was evaluated by funnel plot and Egger's test (27). Meta-analysis was carried out using Stata (version 12, Stata Corp.) and R Studio (version 3.0.2). A *P* value less than 0.05 suggested statistical significance.

Results

Study selection and characteristics

1391 unique records were identified from literature search ([Fig. 1](#)). 127 articles with full-texts were screened and 54 studies were finally included into the meta-analysis (12, 13, 14, 15, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77). There were 28 studies on the suicide risk associated with diabetes (12, 13, 14, 15, 28, 29, 31, 32, 33, 34, 36, 38, 40, 41, 42, 43, 46, 47, 48, 50, 52, 54, 56, 60, 62, 63, 70, 76), 47 studies on the incidence rate of suicide in patients with diabetes (12, 14, 15, 28, 30, 31, 33, 35, 36, 37, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 70, 71, 73, 74, 75, 76, 77) and 45 studies on the proportion of deaths attributable to suicide in patients with diabetes

Figure 1

Flow chart of study selection in the meta-analysis.

(12, 14, 15, 28, 30, 31, 33, 35, 36, 37, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77).

[Table 1](#) described the main characteristics of those 28 studies on the suicide risk associated with diabetes ([Table 1](#)). Most studies were from North America and Europe, and all studies were published in English ([Table 1](#)). The mean or median time of follow-up ranged from 4.4 years to 28.7 years ([Table 1](#)). 14 studies reported SMRs of suicide in patients with diabetes, 6 studies reported HRs of suicide associated with diabetes and the other 8 studies reported RRs of suicide associated with diabetes ([Table 1](#)). 13 studies mixed T1DM patients and T2DM together and did not assess the risk of suicide in T1DM patients and T2DM patients separately ([Table 1](#)). Among those 28 studies, 11 studies reported data on risk estimates of suicide associated with T1DM, and 7 studies reported data on risk estimates of suicide associated with T2DM. According to the Newcastle–Ottawa scale, 24 studies had low risk of bias, while the other 4 studies had high

Table 1 Characteristics of 28 cohort studies assessing the relative risk of suicide associated with diabetes.

Study	Country	Type of diabetes	Participants	Follow-up (years)	Suicide	Outcomes	Confounding factors or variables used to standardize SMR	Bias risk
(76)	UK	T2DM	T2DM: 187 968; Control: 908 016	5	805	HR	Age, sex, ethnicity, deprivation, calendar year	Low risk
(28)	Norway	T1DM	7871 patients	16.8	20	SMR	Age	Low risk
(15)	Japan	Mixed	105 408: Normal; 4898: with diabetes	19.4	618	RR	Age, area, alcohol-drinking, BMI, cohabitation, employment status, hours of sleep, frequency of physical exercise, stress level, and history of major physical illnesses	Low risk
(14)	Australia	T2DM	1413: T2DM adults 5660: non T2DM	13.1	14	HR	Age, gender	High risk
(29)	Denmark	Mixed	1849 110 older adults	20	4792	RR	Period, age group, conjugal status, income level, comorbidity, psychiatric disorders	Low risk
(13)	Sweden	Mixed	252 191: Diabetic 1260214 non-diabetic	Unclear	1126	RR	Age, sex, county of birth	Low risk
(31)	Sweden	Mixed	7 140 589 adults	8	8721	HR	Age, marital status, country of birth, education, employment status, income and urban/rural status, psychiatric and somatic disorders	Low risk
(32)	UK	Mixed	4005 640	Unclear	626	RR	Age, region of residence and deprivation score associated with patients' area of residence	Low risk
(33)	Denmark	Mixed	4734 703	11	1013	RR	Age, calendar year, diagnosis of severe mental illness	Low risk
(36)	Australia	T1DM	1309: T1DM; 6451: age- and sex-matched controls	7.6	6	SMR	Age	Low risk
(34)	USA	Mixed	4005 662	8	10 169	HR	Age, gender, BMI, psychiatric comorbidity, medical comorbidity	Low risk
(38)	UK	T2DM	849 434	NA	75	RR	Age, smoking status, hypertension, dyslipidemia	Low risk
(40)	Korea	T2DM	1 329 525	14	472	HR	Exercise, smoking status, alcohol consumption, body mass index, height, blood pressure blood cholesterol	Low risk
(41)	USA	Mixed	1 053 831 adults	26	464	RR	Age, education, BMI, smoking, alcohol intake, vegetable intake, red meat intake, physical activity, aspirin use	Low risk
(42)	Finland	T1DM	17 306	21.4	110	SMR	Age	Low risk
(43)	Sweden	Mixed	879: patients; 837 control	15	2	HR	Gender, age	High risk
(46)	Taiwan	Mixed	1792 patients	7	2	SMR	Age	High risk
(47)	UK	T1DM	4246 patients	12	6	SMR	Age	Low risk
(48)	13 countries	T1DM	28887 patients	7.6	11	SMR	Age	Low risk
(50)	Norway	T1DM	1906 patients	24	13	SMR	Age	Low risk
(52)	Sweden	T1DM	10200 patients	8	7	SMR	Age, gender	Low risk
(54)	Taiwan	Mixed	256 036 patients	4.4	361	SMR	Age	Low risk
(56)	Sweden	Mixed	4097 patients	5	10	SMR	Age	Low risk
(60)	Finland	T2DM	11 215 patients	5	77	SMR	Age	Low risk
(62)	Sweden	T1DM	91: T1DM	28.7	2	RR	None	High risk
(63)	UK	Mixed	5783	15.7	17	SMR	Age	Low risk
(12)	Denmark	T1DM	1682: patients	13	12	SMR	Age	Low risk
(70)	USA	T1DM or T2DM	1200: T1DM; 1772: T2DM	8.5	5	SMR	Age, gender	Low risk

BMI, body mass index; HR, hazard ratio; NA, not available; RR, relative risk; SMR, standardized mortality ratio; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

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risk of bias (Table 1). The scores for each term were shown in detail in Supplementary Table 2. Table 2 described the main characteristics of 47 studies on the incidence rate of suicide in diabetic patients (Table 2). According to the modified version of Newcastle–Ottawa scale, 37 studies had low risk of bias, while the other 10 studies had high risk of bias, which was shown in detail in Supplementary Table 3. Table 3 described the main characteristics of 45 studies on the proportion of deaths attributable to suicide in patients with diabetic patients (Table 3). According to the modified version of Newcastle–Ottawa scale, 36 studies had low risk of bias, while the other 9 studies had high risk of bias, which was shown in detail in Supplementary Table 4.

Meta-analysis

Meta-analysis of 28 studies reporting risk estimates of suicide associated with diabetes showed that diabetes could significantly increase the risk of suicide (RR=1.56; 95% CI: 1.29–1.89; $P<0.001$, $I^2=93.2\%$) (Fig. 2). After excluding studies with high risk of bias, there was still an obvious association between diabetes and increased risk of suicide (RR=1.56; 95% CI: 1.27–1.91; $P<0.001$, $I^2=94.3\%$). Subgroup analysis by gender showed that diabetes was significantly associated with increased risk of suicide in both men (RR=1.39; 95% CI: 1.23–1.57; $P<0.001$, $I^2=54.6\%$) and women (RR=1.36; 95% CI: 1.10–1.69; $P=0.004$, $I^2=63.7\%$). Subgroup analysis by types of diabetes showed that the RR of suicide associated with T1DM was 2.25 (95% CI: 1.50–3.38; $P<0.001$, $I^2=69.3\%$) (Fig. 3). However, there was a possible association between T2DM and increased risk of suicide (RR=1.65, 95% CI: 0.95–2.85; $P=0.07$, $I^2=95.0\%$). There was no obvious risk of publication bias in the meta-analysis of 28 studies reporting risk estimates of suicide associated with diabetes ($P_{\text{Egger's test}}=0.48$).

Meta-analysis of 47 studies on the incidence rate of suicide showed that the pooled incidence rate of suicide in patients with diabetes was 2.35 per 10000 person-years (95% CI: 1.51–3.64; $I^2=98.8\%$). After excluding studies with high risk of bias, the pooled incidence rate of suicide in patients with diabetes was 1.81 per 10000 person-years (95% CI: 1.13–2.90; $I^2=99.0\%$). Subgroup analysis by types of diabetes showed that the pooled incidence rate of suicide in T1DM and T2DM patients was 2.25 per 10000 person-years (95% CI: 1.66–3.05; $I^2=76.5\%$) and 2.56 per 10000 person-years (95% CI: 1.56–4.19; $I^2=90.4\%$),

respectively. Subgroup analysis by gender showed that the pooled incidence rates of suicide in male diabetic patients and female diabetic patients were 2.34 per 10000 person-years (95% CI: 1.06–5.17; $I^2=99.3\%$) and 0.94 per 10000 person-years (95% CI: 0.38–2.30; $I^2=98.5\%$) respectively.

Meta-analysis of 45 studies on the proportion of deaths attributable to suicide in diabetes patients showed that the pooled proportion was 3.5% (95% CI: 2.6–4.8; $I^2=97\%$). After excluding studies with high risk of bias, the pooled proportion of deaths attributable to suicide in diabetes patients was 3.5% (95% CI: 2.5–4.8; $I^2=98\%$). Subgroup analysis by types of diabetes showed that the pooled proportions in T1DM patients and T2DM patients were 7.7% (95% CI: 6.0–9.8; $I^2=67\%$) and 1.3% (95% CI: 0.6–2.6; $I^2=94\%$) respectively (Fig. 4). Subgroup analysis by gender showed that the pooled proportions of long-term deaths attributable to suicide in male diabetic patients and female diabetic patients were 2.9% (95% CI: 1.9–4.5; $I^2=98\%$) and 1.3% (95% CI: 0.8–2.2; $I^2=97\%$) respectively.

Discussion

Both diabetes and suicide are complex global health problems, and an accurate estimate of suicide risk associated with diabetes is crucial. However, the risk of suicide in diabetic patients is still not well understood and has not been comprehensively assessed. We therefore did a systematic review and meta-analysis to comprehensively estimate the risk and the incidence rate of suicide in diabetes patients. Our study is the first systematic review and meta-analysis investigating the risk of suicide in patients with diabetes. 54 studies were finally included, including 28 studies on the suicide risk in patients with diabetes, 47 studies on the incidence rate of suicide in patients with diabetes and 45 studies on the proportion of deaths attributable to suicide in diabetes patients. The findings suggested that diabetes was significantly associated with increased risk of suicide (RR=1.56; 95% CI: 1.29–1.89; $P<0.001$) (Fig. 2). The association was more profound in T1DM patients, and the RR of suicide associated with T1DM was 2.25 (95% CI: 1.50–3.38; $P<0.001$). The pooled incidence rate of suicide in patients with diabetes was 2.35 per 10000 person-years (95% CI: 1.51–3.64). The pooled proportions of deaths attributable to suicide in T1DM patients and T2DM patients were 7.7% (95% CI: 6.0–9.8) and 1.3% (95% CI: 0.6–2.6), respectively (Fig. 4).

Table 2 Characteristics of 47 cohort studies investigating the incidence rate of suicide in patients with diabetes.

Study	Country	Type of diabetes	Participants, n	Follow-up (years)	Suicide	Bias risk
(76)	UK	T2DM	187 968	5	88	Low risk
(77)	Taiwan	Mixed	92 546	12	327	Low risk
(28)	Norway	T1DM	7871	16.8	20	Low risk
(15)	Japan	Mixed	4898	19.4	41	Low risk
(14)	Australia	T2DM	1413	13.1	4	Low risk
(30)	USA	T1DM	1441	27	7	Low risk
(31)	Sweden	Mixed	7 140 589	8	8721	Low risk
(33)	Denmark	Mixed	4 734 703	11	1013	Low risk
(36)	Australia	T1DM	1309: T1DM; 6451 age- and sex-matched controls	7.6	6	Low risk
(35)	USA	T2DM	4128	10	6	Low risk
(37)	Japan	T1DM	1324	35	7	Low risk
(39)	Finland	T1DM	4174	9	6	Low risk
(40)	Korea	T2DM	42 082	14	38	Low risk
(41)	USA	Mixed	52 655	26	113	Low risk
(42)	Finland	T1DM	17 306	21.4	110	Low risk
(43)	Sweden	Mixed	879	15	2	High risk
(44)	USA	T1DM	1075	32	8	Low risk
(45)	USA	T2DM	4184	4.4	4	Low risk
(46)	Taiwan	Mixed	1792	7	2	High risk
(47)	UK	T1DM	4246	12	6	Low risk
(48)	13 countries	T1DM	28 887	7.6	11	Low risk
(49)	USA	T2DM	123	4.3	1	High risk
(50)	Norway	T1DM	1906	24	13	Low risk
(51)	Sweden	T1DM/ T2DM	6771	8.5	17	Low risk
(52)	Sweden	T1DM	10 200	8	7	Low risk
(53)	Italy	T1DM or T2DM	31 264	9	28	Low risk
(54)	Taiwan	Mixed	256 036	4.4	361	Low risk
(55)	Germany	T1DM	3674	10	22	Low risk
(56)	Sweden	Mixed	4097	5	10	Low risk
(57)	USA	T2DM	710	22	2	Low risk
(58)	UK	T1DM	1854	9.3	1	Low risk
(59)	France	T2DM	237	5	2	High risk
(60)	Finland	T2DM	11 215	5	77	Low risk
(61)	Austria	T1DM	1185	6	1	High risk
(62)	Sweden	T1DM	91	28.7	2	High risk
(63)	UK	Mixed	5783	15.7	17	High risk
(64)	UK	T1DM	845	17	2	Low risk
(65)	Sweden	T1DM	4919	7	1	Low risk
(12)	Denmark	T1DM	1682	13	12	Low risk
(66)	USA	T2DM	353	8	1	Low risk
(67)	Sweden	T1DM or T2DM	1467: T1DM; 334: T2DM	2.6	3	Low risk
(68)	UK	T1DM	310	8	1	High risk
(71)	Norway	T1DM	1908	10	2	Low risk
(70)	USA	T1DM or T2DM	1200: T1DM; 1772: T2DM	8.5	5	Low risk
(73)	Japan	Mixed	62	0.5–10	3	High risk
(75)	UK	T1DM	45	18	2	High risk
(74)	USA	Mixed	21 447	26	44	Low risk

NA, not available; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

The above findings suggest an obvious risk of suicide in patients with diabetes.

Diabetes is a chronic metabolic disease, and there are about 400 million people with diabetes worldwide (4, 5, 78). This meta-analysis suggests that the incidence rate of suicide in patients with diabetes

is 2.35 per 10 000 person-years, which indicates that there are about 94 000 completed suicides occurring in diabetes patients worldwide every year. In addition, the high proportion of deaths attributable to suicide in diabetes patients also shows a high risk of suicide in diabetes patients.

Table 3 Characteristics of 45 cohort studies investigating the proportion of deaths attributable to suicide in patients with diabetes.

Study	Country	Type of diabetes	Participants, <i>n</i>	Follow-up (years)	Number of all deaths (suicide)	Bias risk
(76)	UK	T2DM	187 968	5	40 286 (88)	Low risk
(77)	Taiwan	Mixed	92 546	12	327	Low risk
(28)	Norway	T1DM	7871	16.8	241 (20)	Low risk
(30)	USA	T1DM	1441	27	107 (7)	Low risk
(33)	Denmark	Mixed	4734 703	11	55 424 (1013)	Low risk
(36)	Australia	T1DM	1309: T1DM; 6451: age- and sex-matched controls	7.6	20 (6)	Low risk
(35)	USA	T2DM	4128	10	1217 (6)	Low risk
(37)	Japan	T1DM	1324	35	223 (7)	Low risk
(39)	Finland	T1DM	4174	9	455 (6)	Low risk
(41)	USA	Mixed	52 655	26	38 559 (113)	Low risk
(42)	Finland	T1DM	17 306	21.4	1338 (110)	Low risk
(43)	Sweden	Mixed	879	15	29 (2)	High risk
(44)	USA	T1DM	1075	32	279 (8)	Low risk
(45)	USA	T2DM	4184	4.4	581 (4)	Low risk
(46)	Taiwan	Mixed	1792	7	156 (2)	High risk
(47)	UK	T1DM	4246	12	108 (6)	Low risk
(48)	13 countries	T1DM	28 887	7.6	141 (11)	Low risk
(49)	USA	T2DM	123	4.3	110 (1)	High risk
(50)	Norway	T1DM	1906	24	103 (13)	Low risk
(51)	Sweden	T1DM/ T2DM	6771	8.5	120 (17)	Low risk
(52)	Sweden	T1DM	10 200	8	78 (7)	Low risk
(69)	UK	T1DM	Unclear	Unclear	98 (12)	Low risk
(53)	Italy	T1DM or T2DM	31 264	9	6749 (28)	Low risk
(54)	Taiwan	Mixed	256 036	4.4	16015 (361)	Low risk
(55)	Germany	T1DM	3674	10	251 (22)	Low risk
(56)	Sweden	Mixed	4097	5	58 (10)	Low risk
(57)	USA	T2DM	710	22	476 (2)	Low risk
(58)	UK	T1DM	1854	9.3	26 (1)	Low risk
(59)	France	T2DM	237	5	12 (2)	High risk
(60)	Finland	T2DM	11 215	5	11 215 (77)	Low risk
(61)	Austria	T1DM	1185	6	6 (1)	High risk
(62)	Sweden	T1DM	91	28.7	12 (2)	High risk
(63)	UK	Mixed	5783	15.7	3090 (17)	Low risk
(64)	UK	T1DM	845	17	44 (2)	Low risk
(65)	Sweden	T1DM	4919	7	33 (1)	Low risk
(12)	Denmark	T1DM	1682	13	168 (12)	Low risk
(66)	USA	T2DM	353	8	67 (1)	Low risk
(67)	Sweden	T1DM or T2DM	1467: T1DM; 334: T2DM	2.6	10 (3)	Low risk
(68)	UK	T1DM	310	8	7 (1)	High risk
(71)	Norway	T1DM	1908	10	20 (2)	Low risk
(70)	USA	T1DM or T2DM	1200: T1DM; 1772: T2DM	8.5	1004 (5)	Low risk
(72)	USA	Mixed	Data from death certificates	Unclear	233 (5)	Low risk
(73)	Japan	Mixed	62	0.5–10	25 (3)	High risk
(75)	UK	T1DM	45	18	7 (2)	High risk
(74)	USA	Mixed	21 447	26	2474 (44)	Low risk

NA, not available; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

There are several possible explanations for the increased risk of suicide associated with diabetes. Depressive symptoms and suicidal ideation are common in patients with diabetes, both of which are associated with increased risk of completed suicide (10, 11, 79). Apart from depression,

other mental health problems are also common in diabetes patients, which can also lead to increased risk of suicide (80, 81). In addition, patients with diabetes usually have functional disabilities and comorbidity, and as a result of these impairments, the low quality of life

Figure 2

Meta-analysis showed that diabetes could obviously increase the risk of suicide. 95% CI, 95% confidence interval; RR, relative risk; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

can further increase the severity of depression and the risk of suicide. However, the mechanism underlying the association between diabetes and suicide risk has not been well understood, and more studies are needed to further explore it.

This systematic review and meta-analysis has important implications for the management of diabetes. Given the increasing prevalence of diabetes worldwide and the increased risk of suicide associated with diabetes, it is urgent for us to develop effective solutions to decrease the suicide risk in diabetes patients, especially for T1DM patients. However, current guidelines for the treatment of diabetes provide few recommendations on

the psychological monitoring and suicide prevention in diabetes patients. The findings from our meta-analysis suggest a great need to identify high-risk patients, and effective psychological support is necessary to decrease suicide risk among those patients (1, 2, 82, 83). Increased awareness of suicide risk associated with diabetes is also needed in clinical practice (11, 84). In addition, more studies are needed to develop effective strategies to decrease suicide risk and improve mental health outcomes in diabetes patients.

There is possibility of misclassification bias in the meta-analysis. Most included studies did not report whether they classified poisoning mortality into

Figure 3

Forest plot in the subgroup analysis by types of diabetes. 95% CI, 95% confidence interval; RR, relative risk; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

suicide, and some of those deaths listed as poisoning or drug overdose may be suicides, which may lead to an underestimation of the suicide risk in diabetes patients. The true proportion of deaths attributable to suicide in diabetes patients was also likely to be underestimated, because some suicide deaths may not be properly classified but were reported as poisoning or drug overdose in death certificates. Therefore, more population-based studies with high-quality data are urgently needed to estimate the magnitude of suicide risk in diabetes patients.

This meta-analysis had several other limitations. Firstly, there was obvious difference in the methodology across those included studies, which resulted in obvious between-study heterogeneity. Considering the obvious heterogeneity, the pooled estimates should be interpreted with caution. Secondly, the number of included studies was still relatively small in some subgroup analyses by

types of diabetes or gender. More future studies with large number of participants are needed. Thirdly, deaths from suicide are usually difficult to ascertain. Misreporting of suicide deaths from families and relatives are also possible, which may result in imprecise estimates of suicide risk in diabetes patients (85). Finally, the outcomes from the subgroup analysis by types of diabetes showed that the risk of suicide associated with diabetes was likely to be more profound in T1DM patients, while there was a possible association between T2DM and increased risk of suicide (RR=1.65, 95% CI: 0.95–2.85; $P=0.07$). The non-significant association between T2DM and suicide risk may result from the small number of available studies, and more epidemiological studies are needed to further evaluate this association.

This meta-analysis suggests that diabetes can significantly increase risk of suicide. Suicide has an

Figure 4

Meta-analysis of data on the proportion of deaths attributable to suicide in T1DM patients. 95% CI, 95% confidence interval; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

obvious contribution to mortality in diabetic patients, especially among T1DM patients. The findings from our meta-analysis suggest a great need to identify high-risk patients, and effective psychological support is necessary to decrease suicide risk among those patients. In addition, more epidemiological studies are needed to further evaluate the association between T2DM and suicide risk.

Supplementary data

This is linked to the online version of the paper at <http://dx.doi.org/10.1530/EJE-16-0952>.

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this review.

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