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META-ANALYSIS

Diabetes self-management education reduces risk of all-cause mortality in type 2 diabetes patients: a systematic review and meta-analysis

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Abstract

Background Diabetes self-management education is an essential part of diabetes care, but its impact on all-cause mortality risk of type 2 diabetes patients is unclear. A systematic review and meta-analysis aiming to elucidate the impact of diabetes self-management education on all-cause mortality risk of type 2 diabetes patients was performed.

Methods Randomised controlled trials were identified though literature search in Medline, Embase, CENTRAL, conference abstracts, and reference lists. Only randomised controlled trials comparing diabetes self-management education with usual care in type 2 diabetes patients and reporting outcomes after a follow-up of at least 12 months were considered eligible. Risk ratios with 95 %CIs were pooled. This study was registered at PROSPERO with the number of CRD42016043911.

Results 42 randomised controlled trials containing 13,017 participants were included. The mean time of follow-up was 1.5 years. There was no heterogeneity among those included studies ($I^2 = 0$ %). Mortality occurred in 159 participants (2.3 %) in the diabetes self-management education group and in 187 (3.1 %) in the usual care group, and diabetes self-management education significantly reduced risk of all-cause mortality in type 2 diabetes patients (pooled risk ratios : 0.74, 95 %CI 0.60–0.90, $P = 0.003$; absolute risk difference: −0.8 %, 95 %CI −1.4 to −0.3). Both multidisciplinary team education and nurse-led education could significantly reduce mortality risk in type 2 diabetes patients, and the pooled risk ratios were 0.66 (95 %CI 0.46–0.96, $P = 0.02$; $I^2 = 0$ %) and 0.64 (95 % CI 0.47–0.88, $P = 0.005$; $I^2 = 0$ %), respectively. Subgroup analyses of studies with longer duration of follow-up (≥1.5 years) or larger sample size (≥300) also found a significant effect of diabetes self-management education in reducing mortality risk among type 2 diabetes. Significant effect of diabetes self-management education in reducing mortality risk was also found in those patients receiving diabetes self-management education with contact hours more than 10 h (pooled risk ratio: 0.60, 95 %CI 0.44–0.82, $P = 0.001$; $I^2 = 0$ %), those receiving repeated diabetes self-management education (pooled RR: 0.71, $P = 0.001$; $I^2 = 0$ %), those receiving diabetes self-management education using structured curriculum (pooled risk ratio: 0.72, $P = 0.01$; $I^2 = 0$ %) and those receiving diabetes self-management education using in-person communication (pooled risk ratio: 0.75, $P = 0.02$; $I^2 = 0$ %). The quality of evidence for the effect of diabetes self-management education in reducing all-cause mortality risk among type 2 diabetes patients was rated as moderate according to the Grading of Recommendations Assessment, Development, and Evaluation method, and the absolute risk reduction of all-cause mortality of type 2 diabetic patients by diabetes self-management education was estimated to be 4 fewer per 1000 person-years (from 1 fewer to 6 fewer).

Conclusions The available evidence suggests that diabetes self-management education can reduce all-cause mortality risk

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in type 2 diabetes patients. Further clinical trials with longer time of follow-up are needed to validate the finding above.

Keywords Diabetes self-management education · Type 2 diabetes · All-cause mortality · Meta-analysis

Introduction

Type 2 diabetes is a serious issue for public health worldwide and its global pandemic is still obviously increasing [1]. The incidence rate of type 2 diabetes in the United States was 7.1 per 1000 persons in 2012, and the estimated prevalence of type 2 diabetes among adults in the United States was 14 % in 2012, both of which had increased obvious since 1980s [2, 3]. There are approaching 400 million people suffering from diabetes worldwide, which largely results from high prevalent obesity and sedentary lifestyle changes in recent decades and has become a serious burden of public health worldwide [4]. Patients with types 2 diabetes are also at high risk of cardiovascular diseases and all-cause mortality [5–8]. High quality medical care and multifactorial risk-reduction interventions are needed to reduce the burden of microvascular and cardiovascular diseases, and improve the outcomes of types 2 diabetes patients [9, 10].

Diabetes self-management education (DSME) is an essential part of diabetes care [11, 12]. Guidelines for the treatment of diabetes recommend that all diabetes patients should take part in DSME to improve clinical outcomes and quality of life [11–13]. DSME can help types 2 diabetes patients improve the knowledge, skills, and ability of self-management in a cost-effective manner [12]. Several systematic reviews have suggested that DSME can improve patients' self-management and blood glucose control, and it should be regarded as a crucial element in the treatment of diabetes [14–20]. DSME could lead to more than 0.4 % reduction in hemoglobin A1c (HbA1c) of type 2 diabetes patients, more than 5 mg/dl reduction in total cholesterol, and more than 1 mmol/L reduction in fasting blood glucose [14–19]. However, these systematic reviews focused on short-term outcomes, but the impact of DSME on long-term outcomes, such as all-cause mortality, had not been sufficiently assessed. The impact of DSME on all-cause mortality risk in type 2 diabetes patients is critical but is still unclear. A systematic review and meta-analysis was thus carried out to elucidate this question. The aim of this systematic review was to assess the effect of DSME in reducing risk of all-cause mortality among type 2 diabetes patients compared with usual care. This systematic review was registered at International Prospective Register of Systematic Reviews (PROSPERO) with the number of CRD42016043911. This study was reported by PRISMA statement [21].

Methods

Search strategy and selection criteria

Randomised controlled trials were identified though literature search in Medline, Embase and Cochrane Central Register of Controlled Trials (CENTRAL) (from inception to June 2016). The conference abstracts from American Diabetes Association were also searched. In addition, the reference lists of relevant systematic reviews or relevant reviews were further searched [14–20, 22–31]. Both key words and Medical Subject Heading (MESH) terms were used, and the search strategies for Medline were: ("Self Care"[Mesh] OR "Health Behavior"[Mesh] OR "Education"[Mesh] OR "Behavior Therapy"[Mesh] OR self-care OR self-management OR educational OR education OR educator* OR lifestyle OR management program OR behavioral intervention* OR behavior intervention* OR case management) AND ("Diabetes Mellitus, Type 2"[Mesh] OR diabetes mellitus OR diabetes OR diabetic OR T2DM OR NIDDM) AND ("Randomized Controlled Trial" [Publication Type] OR random OR randomly OR randomized OR randomised OR double blind OR placebo controlled OR randomized controlled trial). No language restriction was applied in the literature search.

The inclusion criteria in the meta-analysis were: (1) randomised controlled trial; (2) individuals with type 2 diabetes; (3) compared DSME with usual care; (4) had a follow-up or intervention duration of at least 12 months; (5) reported events of all-cause mortality in each treatment groups. Studies were excluded if they were non-random trials, used an active comparator, used minimal intervention, compared the effect of different types of DSME, or had a follow-up of less than 12 months.

Data extraction and quality assessment

The primary outcome of interest was the risk ratio (RR) of all-cause mortality. The secondary outcome of interest was the absolute risk difference of all-cause mortality between two groups. Two investigators independently extracted data by using a structured form, and differences were settled by reaching consensus. Data extracted from included studies were as following: family name of first author, publication year, study design, newly-diagnosed or previously treated diabetes, types of DSME, duration of DSME, primary instructors, delivery methods (Group, individual, or mixed), communication methods (in person, through telephone, or mixed), use of structured curriculum or not, participants'

characteristics (age, sex, number, and disease duration), duration of follow-up, rate of drop-out, and events of mortality between two groups. The Cochrane Collaboration's tool was used to assess the risk of bias of those included studies, which included selection bias, detection bias, performance bias, attrition bias, reporting bias, adequacy of follow-up, and bias from other possible sources [32].

Statistical analysis

The pooled RRs or risk difference with corresponding 95 % CIs were used to compare treatment effects. Both Cochrane's Q test and I^2 test were used to evaluate the degree of heterogeneity, and $I^2 > 50$ % indicated high heterogeneity [33, 34]. For the existence of obvious heterogeneity, the random-effects model was used to pool data by DerSimonian–Laird method [35]; otherwise, the fixed-effects model was used to pool data by Mantel–Haenszel method [36]. Sensitivity analyses were performed by using alternative pooling methods, including Peto's method and random-effect model [37]. Subgroup analyses were carried out by number of participants (≥300 vs. <300), follow-up (≥1.5 years vs. <1.5 years), contact hours (≥10 vs. <10 h), primary instructors (multidisciplinary team, nurses, or others), types of diabetes (newly diagnosed vs. previously treated), delivery methods (group only, individual delivery, or mixed), communication methods (in-person, through technology, or mixed), types of DSME (repeated courses vs. single course), structured curriculum (yes vs. unclear), study design (randomised controlled trial vs. cluster randomised controlled trial). Subgroup analysis of patients with secondary diseases was also performed. Publication bias was assessed by funnel plot, Begg's test and Egger's test [37–39]. Statistical analyses were carried out using Review Manager (Version 5.1.0) and Stata (Version 12.0). P value <0.05 indicated statistically significant difference. The quality of evidence was rated from very low to high by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method, which reflected the confidence that the pooled effect estimate was correct [40].

Results

Characteristics of included studies

Of 10,559 studies identified through literature searches, 306 studies were retrieved for detailed assessment for further assessment (Fig. 1). A total of 264 full-text articles excluded, including 181 studies without outcomes on mortality, 61 studies for not relevant to DSME, 19 studies for not using usual care as control, and three studies with overlapping data (Supplementary material). Therefore, 42 randomised clinical trials were eligible for inclusion in meta-analysis [41–82]. The characteristics of these studies were described in Table 1 (Table 1). There were 37 randomised controlled trials [41–43, 45–55, 57, 59, 60, 62–77, 79–82] and 5 cluster randomised controlled trials [44, 56, 58, 61, 78] with a total of 13,017 participants (Table 1).

Among these 42 trials, 34 studies were performed in previously treated diabetes patients, five were performed in newly diagnosed diabetes patients (Table 1). The time of follow-up ranged from 12 months to 5 years, and the mean time of follow-up was 1.5 years (Table 1). 40 studies were performed in developed countries, while the other studies were performed in Argentina and India (Table 1). The sample sizes ranged from 58 to 1146, with a mean of 310. There was lack of clear definitions of "usual care" in most included studies, and there were also obvious differences in the methods of DSME interventions in different studies (Table 1). Among those 42 included trials, only 6 trials studied type 2 diabetes patients with comorbidities or diabetic complications, and the other trials included newly diagnosed or treated type 2 diabetes patients but didn't focus on type 2 diabetes patients with specific comorbidities or complications (Table 1). Most included studies used routine hypoglycemic medications to treat diabetes (Table 1). Nurses were the primary instructors in 18 trials, and

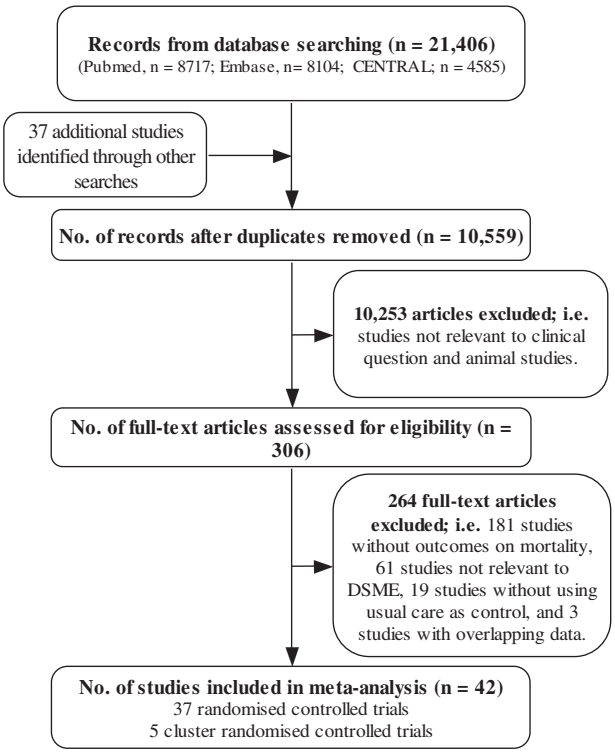

Fig. 1 Flow chart of study selection in the meta-analysis

Table 1 Characteristics of these 42 randomised controlled trials included in the meta-analysis

Study[ref.]	Design	Country	Participants (secondary diseases)	Glucose-lowering treatments	Mean age (female percentage)		Primary instructors	DSMP interventions	Follow-up	Drop-out rate
					DSMP group	Control group				
Bloomgarden ZT 1987 [82]	RCT	USA	302 insulin-treated patients with type 2 diabetes with a mean diabetes duration of 13 years (NR)	Insulin	56 years (61 %)	59 years (48 %)	Multidisciplinary team	Group education by nurse educator and nutritionist with nine education sessions and using structured materials.	1.5 years	8.3 %
Heller SR 1988 [81]	RCT	UK	87 newly diagnosed obese type 2 diabetic patients (Obesity)	Diet alone	56.5 years (44 %)	56.4 years (59 %)	Multidisciplinary team	Group education by diabetes specialist nurses and a dietitian with five 90-rnin group sessions and using structured materials.	1 year	12.6 %
Hanefeld M 1991 [42]	RCT	Germany	1088 newly diagnosed type 2 diabetic patients (NR)	Dietary treatment, insulin or oral antidiabetic drugs	46.6 years (45 %)	46.2 years (39 %)	Multidisciplinary team	Structured intensified health education by group and individual education	5 years	13.0 %
Weinberger M 1995 [80]	RCT	USA	275 previously treated type 2 diabetic patients (NR)	Oral hypoglycemic agent or insulin	63.9 years (1.5 %)	63.2 years (0 %)	Nurse	Nurse-initiated contacts were made by telephone at least monthly to provide patient education.	1 year	3.6 %
Piette JD 2000 [79]	RCT	USA	248 previously treated type 2 diabetic patients (NR)	Insulin or oral hypoglycemic medications	56 years (61 %)	53 years (56 %)	Nurse	Biweekly automated assessment and self-care education calls with telephone follow-up by a nurse educator.	1 year	10.9 %
Groeneveld Y 2001 [78]	Cluster RCT	Netherlands	246 previously treated type 2 diabetic patients (NR)	Insulin or oral hypoglycemic medications	62.7 years (66 %)	62.3 years (53 %)	Multidisciplinary team	Structured care assistance by a diabetes educator (a nurse) and a dietician	1 year	8.1 %
Piette JD 2001 [77]	RCT	USA	292 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	60 years (5 %)	61 years (1 %)	Nurse	Biweekly ATDM health assessment and self-care education calls, and a nurse educator followed up with patients based on their ATDM assessment reports	1 year	4.8 %
Taylor CB 2003 [74]	RCT	USA	169 previously treated type 2 diabetic patients (Major comorbid conditions)	Routine hypoglycemic medications	55.5 years (50 %)	54.8 years (44.7 %)	Nurse	Patients met with a nurse-care manager to establish individual outcome goals, attended group sessions once a week for up to 4 weeks, and received telephone calls to manage medications and self-care activities	1 year	18.3 %

Table 1 continued

Study[ref.]	Design	Country	Participants (secondary diseases)	Glucose-lowering treatments	Mean age (female percentage)		Primary instructors	DSMP interventions	Follow-up	Drop-out rate
					DSMP group	Control group				
Gary TL 2003 [76]	RCT	USA	72 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	59 years (76 %)	57 years (74 %)	Nurse	Nurse case manager intervention interventions were 45-min face-to-face clinic visits and/or telephone contacts	2 years	15.3 %
New JP 2003 [75]	RCT	UK	1407 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	64 years (NR)	64 years (NR)	Nurse	Nurses provided clinics for participants, with attendance every 4–6 weeks, until targets were achieved. Lifestyle advice and titration of drug therapies were provided according to the locally agreed upon guidelines	1.5 years	12.9 %
Krein SL 2004 [71]	RCT	USA	246 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	61 years (2 %)	61 years (5 %)	Nurse	Two nurse practitioner case managers worked with patients and their primary care providers, monitoring and coordinating care for the intervention group for 18 months through the use of telephone contacts, collaborative goal setting, and treatment algorithms	1.5 years	5.7 %
Sarkadi A 2004 [70]	RCT	Sweden	77 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	66.5 years (NR)	66.4 years (NR)	Pharmacist	The intervention was a 12-month long group educational program led by specially trained pharmacists, assisted by a diabetes nurse specialist on the first two occasions	2 years	14.3 %
Goudswaard AN 2004 [72]	RCT	Netherlands	58 previously treated type 2 diabetic patients (NR)	Oral hypoglycaemic agents	62.6 years (48 %)	58.7 years (56 %)	Nurse	A 6-month educational programme by a diabetes nurse.	1.5 years	6.9 %
Clark M 2004 [73]	RCT	UK	100 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	59.5 years (NR)	59.5 years (NR)	Interventionist	Brief tailored intervention including follow-up telephone calls	1 year	6.0 %
Rothman RL 2005 [69]	RCT	USA	217 type 2 diabetic patients with poor glycemic control (NR)	Routine hypoglycemic medications	54 years (56 %)	57 years (56 %)	Multidisciplinary team	Intensive management from clinical pharmacists, as well as from a diabetes care coordinator who provided	1 year	7.8 %

Table 1 continued

Study[ref.]	Design	Country	Participants (secondary diseases)	Glucose-lowering treatments	Mean age (female percentage)		Primary instructors	DSMP interventions	Follow-up	Drop-out rate
					DSMP group	Control group				
								diabetes education, applied algorithms for managing glucose control and decreasing cardiovascular risk factors, and addressed barriers to care		
Fornos JA 2006 [68]	RCT	Spain	112 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	62.4 years (57 %)	64.9 years (57 %)	Pharmacist	Individualized program consisting of the detection and resolution of drug-related problems and diabetes education, involves patients in their own care in order to obtain maximum benefit from the medication they use	1 year	0.9 %
Adolfsson ET 2007 [67]	RCT	Sweden	101 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	62.4 years (43 %)	63.7 years (39 %)	Multidisciplinary team	The minimum number of empowerment group education sessions was four and the maximum was five (mean value: 4.7), including one follow-up session given within 7 months	1 year	14.9 %
Shibayama T 2007 [66]	RCT	Japan	134 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	61 years (35 %)	62 years (35 %)	Nurse	One-to-one lifestyle counseling by a certified expert nurse	1 year	10.4 %
Thoolen B 2007 [65]	RCT	Netherlands	227 type 2 diabetic patients (NR)	Routine hypoglycemic medications	61 years (38 %)	61 years (38 %)	Nurse	Self-management course lasted 12 weeks, including two individual sessions and four biweekly group meetings lead by a trained nurse	1 year	4.8 %
Cooper H 2008 [64]	RCT	UK	112 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	59 years (NR)	59 years (NR)	Nurse	The system of education included physical activity and exercise, relaxation, health topics, and was delivered by trained leaders, in 2 h sessions weekly for 8 weeks	1.5 years	9.8 %
Thoolen BJ 2009 [63]	RCT	Netherlands	197 newly diagnosed type 2 diabetic patients (NR)	Dietary treatment or hypoglycemic medications	62 years (36 %)	61.9 years (45 %)	Nurse	The education intervention consisted of two individual and four group sessions, spread out over 12 weeks	1 year	7.6 %

Table 1 continued

Study[ref.]	Design	Country	Participants (secondary diseases)	Glucose-lowering treatments	Mean age (female percentage)		Primary instructors	DSMP interventions	Follow-up	Drop-out rate
					DSMP group	Control group				
Piatt GA 2010 [61]	Cluster RCT	USA	119 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	66 years (57 %)	66 years (42 %)	Multidisciplinary team	6 diabetes self-management education (DSME) sessions, which were facilitated by a CDE, and held weekly, followed by monthly support groups	3 years	13.4 %
Edelman D 2010 [62]	RCT	USA	239 previously treated type 2 diabetic patients (Hypertension)	Routine hypoglycemic medications	63 years (4.5 %)	61 years (3.8 %)	Multidisciplinary team	Clinics comprised 7 to 8 patients and a care team that consisted of a primary care general internist, a pharmacist, and a nurse or other certified diabetes educator. Each session included structured group interactions moderated by the educator	1 year	8.8 %
Crasto W 2011 [41]	RCT	UK	189 previously treated type 2 diabetic patients (Microalbuminuria)	Routine hypoglycemic medications	62.6 years (25 %)	60.3 years (26 %)	Trained professional educators	Intensive intervention with structured patient education	1.5 years	5.8 %
Andrews RC 2011 [60]	RCT	UK	345 newly diagnosed type 2 diabetic patients (NR)	Dietary treatment or hypoglycemic medications	60.1 years (36 %)	59.5 years (37 %)	Multidisciplinary team	Dietary consultation every 3 months with monthly nurse support, and a pedometer-based activity programme	1 year	3.2 %
Wakefield BJ 2011 [59]	RCT	USA	200 previously treated type 2 diabetic patients (Hypertension)	Routine hypoglycemic medications	67.8 years (1 %)	67.9 years (4 %)	Nurse	A branching disease management algorithm programmed into the device and focused on diet, exercise, smoking cessation, foot care, advice for sick days, medications, weight management, preventive care, and behavior modification and lifestyle adjustments	1 year	7.5 %
Khunti K 2012 [58]	Cluster RCT	UK	824 newly diagnosed type 2 diabetic patients (NR)	Dietary treatment or hypoglycemic medications	59 years (45 %)	60 years (44 %)	Trained professional educators	A structured group education programme for six hours delivered in the community by two trained healthcare professional educators compared with usual care	3 years	8.7 %

Table 1 continued

Study[ref.]	Design	Country	Participants (secondary diseases)	Glucose-lowering treatments	Mean age (female percentage)		Primary instructors	DSMP interventions	Follow-up	Drop-out rate
					DSMP group	Control group				
Rygg L 2012 [57]	RCT	Norway	146 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	66 years (NR)	66 years (NR)	Multidisciplinary team	The education lasts for 15 h over three sessions with one week between each session at Hospital 1 and two weeks between sessions at Hospital 2	1 year	8.9 %
Sperl-Hillen J 2013 [52]	RCT	USA	377 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	62 years (NR)	62 years (NR)	Multidisciplinary team	The education intervention consisted of three 1 h individual sessions spaced approximately 1 month apart and were delivered by either nurse or dietitian certified diabetes educators using the conventional method of the care system	1 year	0.3 %
Mons U 2013 [53]	RCT	Germany	204 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	68 years (40 %)	67 years (38 %)	Nurse	A patient-centered supportive counseling intervention comprising monthly telephone-based counseling sessions by practice nurses over 12 months	1.5 years	5.4 %
Blackberry ID 2013 [56]	Cluster RCT	Australia	473 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	63.6 years (46 %)	61.9 years (40 %)	Nurse	Practice nurses from intervention practices received two days of training in a telephone coaching programme, which aimed to deliver eight telephone and one face to face coaching episodes per patient	1.5 years	3.0 %
Crowley MJ 2013 [55]	RCT	USA	359 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	56 years (69 %)	57 years (75 %)	Nurse	The 12-month nurse intervention provided monthly self-management support and quarterly medication management facilitation	1 year	7.0 %
Gagliardino JJ 2013 [54]	RCT	Argentina	234 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	62.2 years (38 %)	62.0 years (33 %)	Trained professional educators	Structured group education programmes were conducted by trained educators to groups of up to 10 ambulatory patients; they encouraged interaction between the educator and participants	3.5 years	19.7 %

Table 1 continued

Study[ref.]	Design	Country	Participants (secondary diseases)	Glucose-lowering treatments	Mean age (female percentage)		Primary instructors	DSMP interventions	Follow-up	Drop-out rate
					DSMP group	Control group				
Welschen LM 2013 [51]	RCT	Netherlands	154 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	60.5 years (40 %)	61.2 years (36 %)	Multidisciplinary team	The intervention group was planned to receive 3–6 cognitive behavioural treatment sessions of 30 min, which was dependent on the need of the patient	1 year	3.2 %
Hamid S 2014 [49]	RCT	USA	268 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	56 years (58 %)	54 years (66 %)	Nurse-community health worker	A nurse-community health worker behavioral intervention	1 year	3.7 %
Eakin EG 2014 [50]	RCT	Australia	302 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	57.7 years (45 %)	58.3 years (43 %)	Interventionist	A telephone-delivered behavioral weight loss and physical activity intervention	2 years	15.2 %
Perez-Escamilla R 2015 [46]	RCT	USA	211 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	55.4 years (72 %)	57.3 years (74 %)	Community health worker	A community health worker–led structured intervention comprised 17 individual sessions delivered at home over a 12-month period. Sessions addressed T2D complications, healthy lifestyles, nutrition, healthy food choices and diet for diabetes, blood glucose self-monitoring, and medication adherence	1.5 years	5.2 %
Edelman D 2015 [48]	RCT	USA	377 previously treated type 2 diabetic patients (Hypertension)	Routine hypoglycemic medications	57.8 years (55 %)	59.6 years (55 %)	Nurse	Telephone calls from a nurse experienced in diabetes and hypertension management once every two months over a period of two years, for a total of 12 calls	2 years	10.9 %
McGowan P 2015 [47]	RCT	Canada	252 type 2 diabetic patients (NR)	Routine hypoglycemic medications	64.6 years (36 %)	63.8 years (40 %)	Interventionist	Peer-led self management programs	1 year	12.3 %
Ali MK 2016 [45]	RCT	India	1146 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	54.2 years (55 %)	54.2 years (53 %)	Multidisciplinary team	The care coordinators were responsible for following up with intervention patients at least once every 3 months to set up laboratory or clinic	3 years	8.5 %

Table 1 continued

Study[ref.]	Design	Country	Participants (secondary diseases)	Glucose-lowering treatments	Mean age (female percentage)		Primary instructors	DSMP interventions	Follow-up	Drop-out rate
					DSMP group	Control group				
								appointments and contacted patients by telephone at least once a month to discuss diabetes self-management, adherence to diet plans, exercise, tobacco cessation, medication use, selfmonitoring of glucose levels, and stress management		
Johansson T 2016 [44]	Cluster RCT	Australia	337 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	62.2 years (51 %)	63.6 years (51 %)	Interventionist	Group meetings and peer supporters for for the treatment and management of type 2 diabetes, motivation, medical aspects of diabetes, nutrition, experience, and feedback	2 years	6.8 %
Odnoletkova I 2016 [43]	RCT	Belgium	574 previously treated type 2 diabetic patients (NR)	Routine hypoglycemic medications	63.8 years (40 %)	62.4 years (37 %)	Nurse	The programme consisted of five telephone sessions of a mean (range) duration of 30 (10–45) min, delivered at a mean (range) interval of 5 (3–8) weeks by a certified diabetes nurse educator after a 5-day training course	1.5 years	10.5 %

RCT randomised controlled trial, *Cluster RCT* cluster randomised controlled trial, *DSMP* diabetes self-management education, *NR* not reported

multidisciplinary team was the primary instructors in 13 trials (Table 1). The primary instructors in other studies were trained professional educators, pharmacists or community health workers (Table 1). Only 11 studies provided DSME with contact hours more than 10 h, and 18 studies reported they used structured curriculums (Table 1).

The outcomes of bias assessment of these 42 included studies were shown in Fig. 2 (Fig. 2). There was no obvious risk of selection bias (Fig. 2). However, owing to the nature of DSNE intervention, few of the interventions were blind and there was obvious risk of performance bias across most included studies (Fig. 2). In addition, some studies also had high drop-out rates (Fig. 2, Table 1). The proportion of patients lost to follow-up was reported in most studies, ranging from 0.3 to 19.7 % (Table 1).

Meta-analysis

Table 2 summarized the main findings of the meta-analysis (Table 2). There was no heterogeneity among those included studies ($I^2 = 0$ %). Mortality occurred in 159 participants (2.3 %) in the DSME group and in 187 (3.1 %) in the usual care group, and DSME significantly reduced risk of all-cause mortality in type 2 diabetes patients (pooled RR: 0.74, 95 % CI 0.60–0.90, $P = 0.003$; absolute risk difference: −0.8 %, 95 % CI −1.4 to −0.3) (Fig. 3). When using random-effect model, the pooled RR of all-cause mortality in the DSME group compared with the usual care group was 0.74 (95 % CI 0.60–0.91, $P = 0.005$). When using Peto's method, the pooled Peto's odds ratio of all-cause mortality in the DSME group compared with the usual care group was 0.72 (95 % CI 0.58–0.89, $P = 0.003$; $I^2 = 0$ %).

Meta-analysis of 20 trials with longer duration of follow-up (≥1.5 years) also suggested that DSME could obviously reduce all-cause mortality risk in type 2 diabetes patients (pooled RR: 0.72, 95 % CI 0.57–0.92, $P = 0.007$; absolute risk difference: −1.1 %, 95 % CI −1.8 to −0.3) (Fig. 4, Table 2). Meta-analysis of 13 studies with larger sample size (≥300) further suggested that DSME was obviously associated with decreased mortality risk in type 2 diabetes patients (pooled RR: 0.73, 95 % CI 0.56–0.96, $P = 0.02$; absolute risk difference: −0.8 %, 95 % CI −1.6 to −0.1) (Fig. 4, Table 2).

Both multidisciplinary team education and nurse-led education could reduce mortality risk, and the RRs were 0.66 (95 % CI 0.46–0.96; $P = 0.02$; $I^2 = 0$ %) and 0.64 (95 % CI 0.47–0.88; $P = 0.005$; $I^2 = 0$ %), respectively (Fig. 4, Table 2). Further subgroup analyses revealed significant effects of DSME in reducing all-cause mortality risk among type 2 diabetes patients receiving DSME with contact hours more than 10 h (pooled RR: 0.60, 95 % CI 0.44–0.82; $P = 0.001$; $I^2 = 0$ %), repeated DSME (pooled RR: 0.71, 95 % CI 0.57–0.87; $P = 0.001$; $I^2 = 0$ %), DSME using structured curriculum (pooled RR: 0.72, 95 % CI 0.55–0.93; $P = 0.01$; $I^2 = 0$ %), or DSME using in-person communication (pooled RR: 0.75, 95 % CI 0.58–0.96; $P = 0.02$; $I^2 = 0$ %) (Fig. 4, Table 2).

There were only two randomised controlled trials reporting risk of cardiovascular mortality [41, 42], and there was no heterogeneity between those two studies ($I^2 = 0$ %). Meta-analysis suggested that DSME was not significantly associated with reduced risk of cardiovascular mortality (pooled RR: 0.56, 95 % CI 0.19–1.65, $P = 0.29$).

The shape of funnel plots did not show evidence of asymmetry (Fig. 5). The P values of Begg's test and Egger's test in the meta-analysis of total 42 studies were 0.34 and 0.11, respectively. In the subgroup analysis of 13 studies with larger sample size (≥300), the P values of Begg's test and Egger's test were 0.99 and 0.67, respectively. Therefore, there was no obvious risk of publication bias.

Most studies did not report mortality as primary outcomes of interest and there was possible risk of performance bias (Fig. 2). In addition, since the mean time of follow-up was 18 months, the rates of mortality in patients receiving DSME or usual care were 2.3 and 3.1 % respectively, which were relatively low. Taking into account the above factors, the quality of evidence for the effect of DSME in reducing all-cause mortality risk among type 2 diabetes patients was rated as moderate according to GRADE method. The incidences of all-cause mortality in patients receiving DSME and those receiving usual care were 12 and 16 events per 1000 person-years, respectively. The absolute risk reduction in all-cause mortality in type 2 diabetes by DSME was estimated to be 4 fewer per 1000 person-years (from 1 fewer to 6 fewer).

Discussion

DSME is believed to be an essential element of diabetes care, but its impact on all-cause mortality risk in type 2 diabetes patients has not been systematically assessed. We thus did a systematic review and meta-analysis to elucidate the impact of DSME on all-cause mortality risk in type 2 diabetic patients. This study systematically reviewed 42 randomised controlled trials comparing DSME with usual care in type 2 diabetic patients. There was no heterogeneity among those included studies ($I^2 = 0$ %). Meta-analysis of total 42 trials suggested that DSME significantly reduced risk of all-cause mortality more than usual care in type 2 diabetes patients (pooled RR: 0.74, 95 % CI 0.60–0.90; $P = 0.003$; $I^2 = 0$ %) (Fig. 3). Subgroup analyses of studies with longer duration of follow-up (≥1.5 years) or larger sample size (≥300) also found a beneficial effect of DSME in reducing mortality risk among type 2 diabetes (Table 2, Fig. 4). Significant effect of DSME in reducing mortality

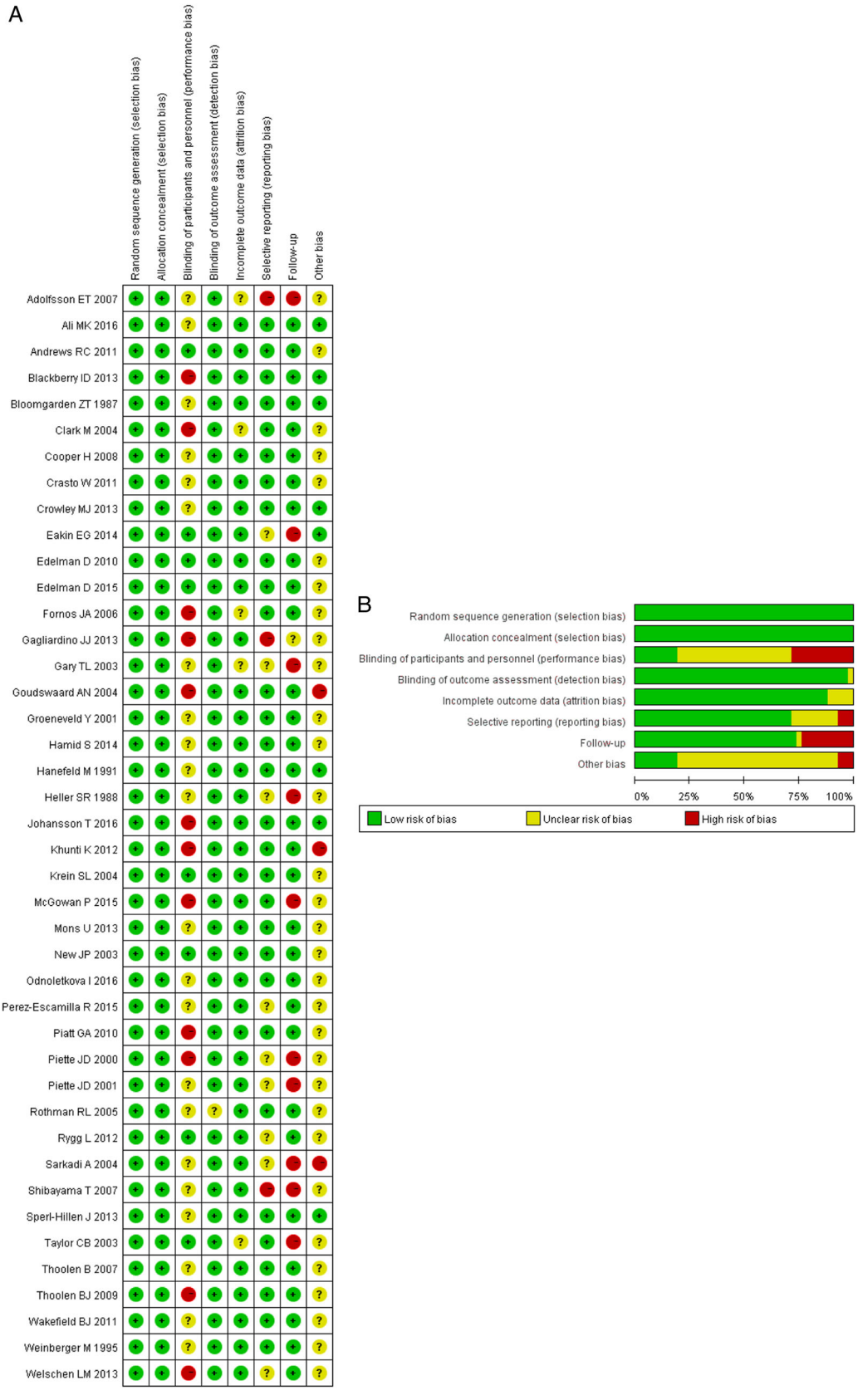

Fig. 2 Risk of bias assessment of these 42 included studies in the meta-analysis. **a** Judgment about each risk of bias item for each included study. **b** Judgment about each risk of bias item presented as percentages across all included studies

Table 2 Effect of DSME in reducing risk of all-cause mortality in type 2 diabetes patients

Comparison groups	No. of studies	Events/ Participants	RR (95 % CI)	*P* values	P_h	I^2 (%)
Total studies	42	346/13,017	0.74 (0.60, 0.90)	0.003	0.96	0
Participants (≥300)	13	202/7831	0.73 (0.56, 0.96)	0.02	0.87	0
Participants (<300)	29	144/5186	0.75 (0.54, 1.02)	0.06	0.86	0
Follow-up (≥1.5 years)	20	266/8272	0.72 (0.57, 0.92)	0.007	0.88	0
Follow-up (<1.5 years)	22	80/4745	0.78 (0.51, 1.18)	0.23	0.82	0
Contact hours (≥10 h)	11	156/4284	0.60 (0.44, 0.82)	0.001	0.89	0
Contact hours (<10 h)	31	190/8733	0.86 (0.65, 1.13)	0.27	0.93	0
Multidisciplinary team education	13	112/4487	0.66 (0.46, 0.96)	0.02	0.63	0
Nurse-led education	18	151/5624	0.64 (0.47, 0.88)	0.005	0.94	0
Previously treated diabetes	34	269/9860	0.75 (0.59, 0.95)	0.01	0.90	0
Newly diagnosed diabetes	5	41/2461	0.76 (0.48, 1.21)	0.24	0.52	0
Patients with secondary diseases	6	26/1261	0.85 (0.40–1.78)	0.66	0.84	0
Delivery by group only	13	100/3229	0.99 (0.68, 1.45)	0.96	0.69	0
Individual delivery	21	172/7520	0.66 (0.49, 0.89)	0.006	0.88	0
Combing group with individual	8	74/2268	0.62 (0.39, 0.98)	0.04	0.98	0
Communication through in-person	26	231/7763	0.75 (0.58, 0.96)	0.02	0.81	0
Communication through technology	11	83/4450	0.72 (0.47, 1.09)	0.12	0.73	0
Combing in-person with technology	5	32/804	0.67 (0.33, 1.33)	0.25	0.87	0
Repeated DSME	41	320/12,193	0.71 (0.57, 0.87)	0.001	0.96	0
Single DSME	1	26/824	1.21 (0.56, 2.60)	0.62	–*	–*
Using structured curriculum	18	207/6642	0.72 (0.55, 0.93)	0.01	0.83	0
No definite structured curriculum	24	139/6375	0.76 (0.55, 1.05)	0.10	0.87	0
Randomised controlled trial	37	288/11,016	0.72 (0.58, 0.90)	0.005	0.98	0
Cluster randomised controlled trial	5	58/1999	0.80 (0.48, 1.33)	0.39	0.13	44

NA not applicable, *RR* risk ratio, *95 % CI* 95 % confidence interval, P_h the *P* value of Cochrane's *Q* test, I^2, the value of I^2, * not available

risk was also found in those patients receiving DSME with contact hours more than 10 h, those receiving repeated DSME, those receiving DSME using structured curriculum and those receiving in-person communication (Table 2, Fig. 4). Therefore, the findings from the meta-analysis suggest that DSME can reduce risk of all-cause mortality in type 2 diabetes patients when compared with usual care, which supports the practice of DSME in type 2 diabetes to improve patients' outcomes.

DSME is a cost-effective intervention which can help types 2 diabetes patients improve their self-management, and the short-term effect of DSME on HbA1c and BMI has been well established [14–18]. The finding from our study suggests that DSME can also effectively reduce mortality risk in type 2 diabetes patients. The absolute risk reduction in all-cause mortality by DSME was estimated to be 4 fewer per 1000 person-years (from 1 fewer to 6 fewer). The finding above is important, because DSME is a cost-effective method of reducing mortality risk in diabetes patients. Our findings also suggest the necessity and importance of DSME in the medical care for type 2 diabetes patients. Guidelines for the treatment of diabetes also recommend that all diabetes patients should take part in DSME to improve clinical outcomes and quality of life [11–13]. However, recent studies have shown that a large part of diabetes patients do not receive any diabetes education, and fewer than 50 % have participated in DSME, which is a serious problem that should be avoided [83, 84]. Therefore, to achieve better self-management and improve patients' survival, it's urgent for all diabetes patients to receive

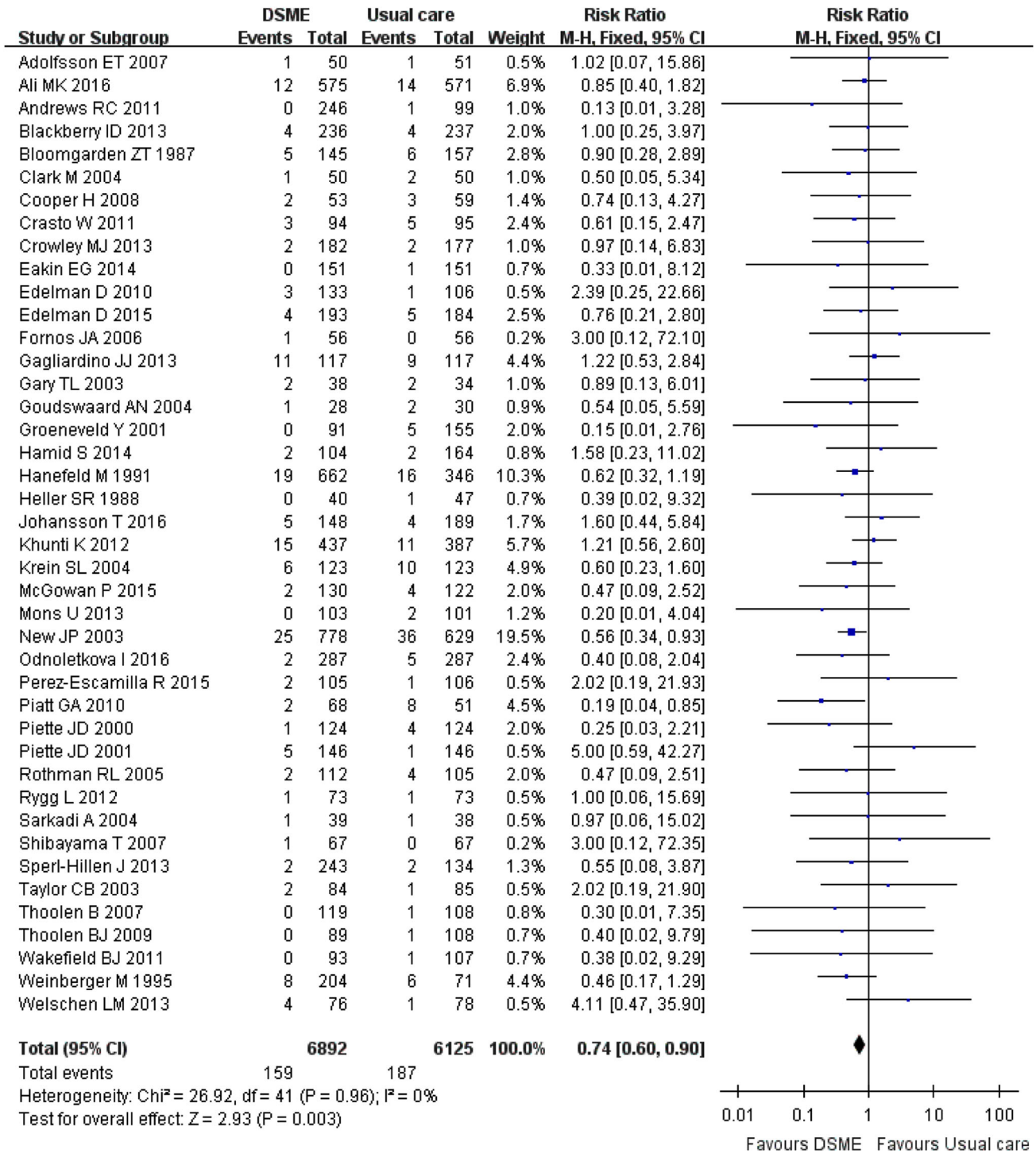

Fig. 3 Effect of DSME in reducing risk of all-cause mortality in type 2 diabetes patients

effective and structured DSME. In addition, quality improvement strategies aiming to increase access to DSME for type 2 diabetes patients are also needed in clinical practice [85, 86].

There is also some evidence from observational studies which supports the effect of DSME in reducing all-cause mortality risk among type 2 diabetes. Wong et al. performed a propensity-matched observational study of 27,278 type 2 diabetes patients and found that participants receiving structured diabetes education had a lower risk of all-cause mortality (Hazard ratio [HR]: 0.564, $P < 0.001$) [87]. Kornelius et al. also carried out a propensity-matched

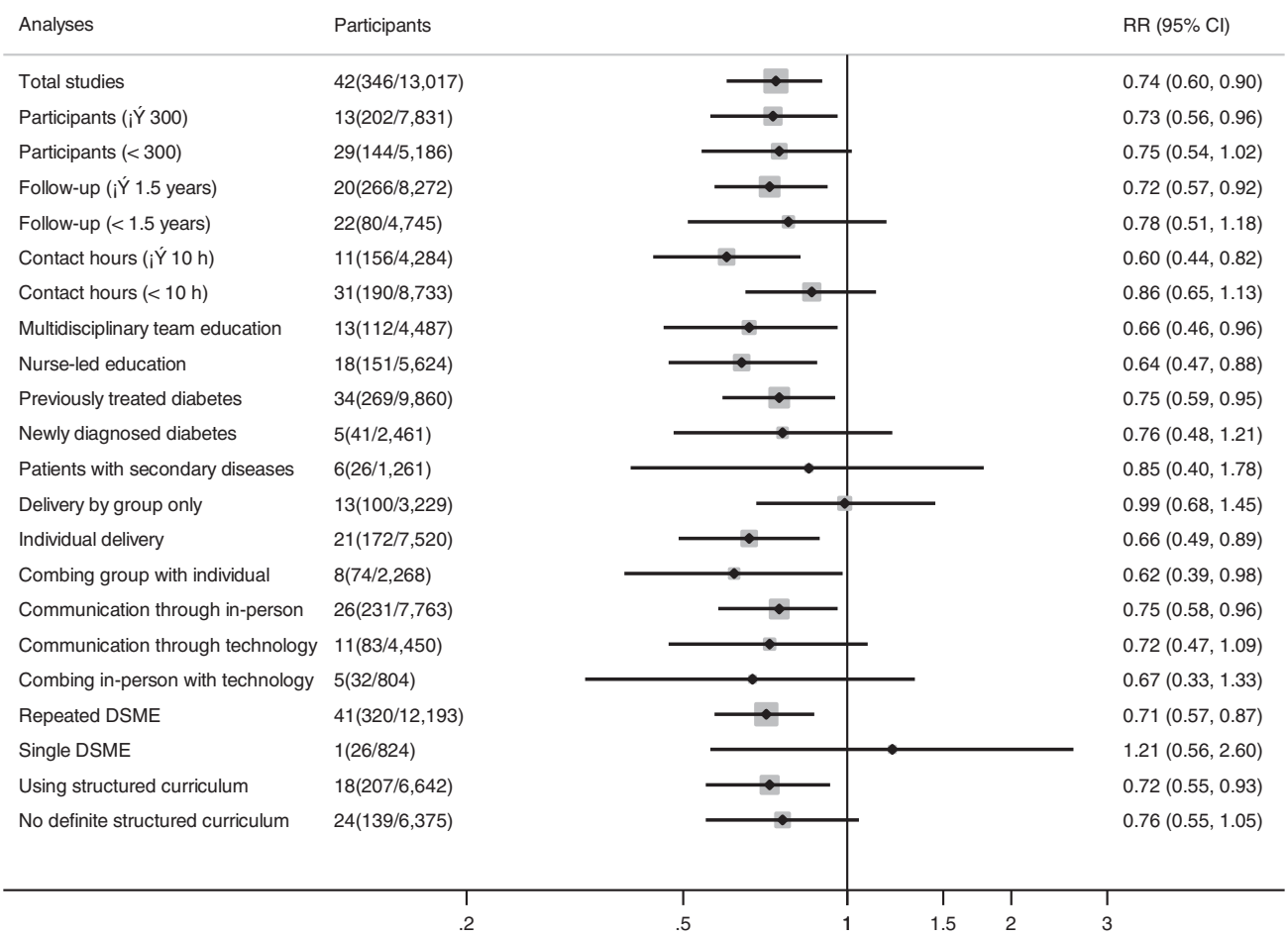

Fig. 4 Effect of DSME in reducing risk of all-cause mortality in type 2 diabetes patients in the subgroup analyses

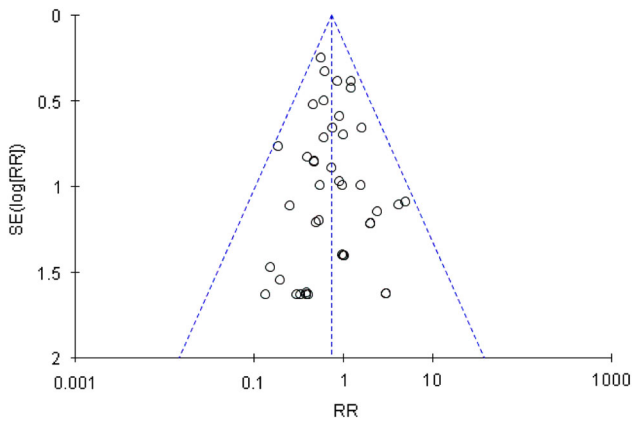

Fig. 5 Funnel plot assessing risk of publication bias in the meta-analysis of total 42 trials

observational study of 8916 type 2 diabetes patients and found that participants receiving integrated diabetes education had a significantly lower risk of all-cause mortality (HR 0.78, 95 % CI 0.63–0.95) [88]. However, another propensity-matched observational study of 16,520 type 2 diabetes patients failed to find a beneficial effect of DSME in reducing all-cause mortality risk among patients (HR 0.97; $P = 0.48$) [89]. A retrospective cohort study by Perman et al. found that patients attending self-management education workshop had 33 % lower risk of all-cause crude mortality, but the effect estimate decreased after adjustment (HR 0.82; 95 % CI: 0.61–1.08) [90]. Despite there was obvious heterogeneity among those four observational studies [87–90] ($I^2 = 89$ %), meta-analysis of those four studies using random-effect model suggested that DSME was independently associated with decreased risk of all-cause mortality in type 2 diabetes patients (Pooled HR: 0.778, 96 % CI 0.607–0.998; $P = 0.048$). Therefore, there is also evidence from observational studies which supporting the effect of DSME in reducing all-cause mortality risk in type 2 diabetes, and DSME can be a significant contributor to long-term positive outcomes. The findings from observational studies also further validate the results of our meta-analysis of randomised controlled trials.

GRADE is a well-known system for rating the quality of evidence and strength of recommendations [40]. In present meta-analysis, GRADE was also used to assess the quality of evidence for the effect of DSME in reducing all-cause mortality risk among type 2 diabetes. Generally, there was moderate quality evidence for the effect of DSME in reducing mortality risk in type 2 diabetes patients, and the reasons for the decrease of evidence quality from high to moderate were the possible of risk of performance bias and the short time of follow-up in most included studies. Risk of performance bias is ineluctable because blinding of participants and personnel with respect to study design is almost impossible in clinical trials involving behavioral interventions. However, it's feasible for clinical trials to prolong the duration of DSME or time of follow-up. Therefore, randomised controlled trials with a longer time of follow-up are urgently needed to identify the long-term beneficial effect of DSME in reducing mortality risk in type 2 diabetes patients [20, 22, 91].

Previous studies and meta-analyses have shown that DSME can improve patients' self-management and blood glucose control when compared to usual care, and it has been considered a crucial element in the treatment of type 2 diabetes [14–20]. However, there is little evidence regarding the potential effect of DSME in reducing the risks of complications and mortality among type 2 diabetes patients. As is reported, our meta-analysis of 42 randomised controlled trials provides some evidence for the benefit of DSME in reducing the risk of mortality among type 2 diabetes patients, which further proves the importance of delivering a structured DSME to type 2 diabetic patients. Owing to the limited number of randomised controlled trials providing data on the impact of DSME on diabetic complications in type 2 diabetes patients, we didn't perform a meta-analysis to assess the impact of DSME on diabetic complications in type 2 diabetes patients. However, several cohort studies have found that DSME may have a positive impact on the prevention of diabetic complications [22, 92, 93]. Therefore, DSME may also be an essential tool to reduce the occurrence of complications in type 2 diabetes patients [22]. On the contrary, an omission in delivering DSME in type 2 diabetes patients may have negative effects on the occurrence of complications and mortality [22].

There are a wide variety of self-management education programs for patients with chronic diseases [94–99], and it is the same with for DSME in type 2 diabetes patients [11, 16, 100]. At the moment, the ideal characteristics of DSME to provide the best benefit in type 2 diabetes patients have not been well defined [20, 22]. Structured DSME involving multiple topics usually provide more comprehensive interventions and benefits when compared with other simple DSME [12, 22]. However, although guidelines for the treatment of diabetes recommend structured DSME to type 2 diabetes patients, it is not always perceived by both health professionals and diabetes patients. In addition, there are many good models for DSME, but which type of DSME is the best cost-effectiveness intervention is still unclear and need future studies [12, 22]. In present meta-analysis, there were obvious variations in educational interventions used among included studies (Table 2).

In the subgroup analyses, significant effect of DSME in reducing all-cause mortality risk among type 2 diabetes was found in those patients receiving DSME with contact hours more than 10 h, those receiving repeated DSME, those receiving DSME using structured curriculum, and those receiving DSME using in-person communication (Table 2, Fig. 4). In structured DSME involving more or longer sessions, diabetes patients will have more opportunities to learn useful messages and gain more benefits from DSME, which may explain the significant findings in above subgroup analyses. On the contrary, DSME with shorter intervention durations or fewer topics may provide little benefit for type 2 diabetes patients.

There were several limitations in the meta-analysis. Firstly, there was lack of clear definitions of "usual care" in most included studies, and there were also obvious differences in the methods of DSME in different studies. Despite the obvious differences in the diabetes care provided for those patients involved in different trials, it's no doubt that patients allocated to DSME groups received more diabetes education than those in control groups. Secondly, primary instructors in most included studies were multidisciplinary team or nurses. This non-significant finding in the subgroup analysis of studies involving other diabetes educators, such as community health workers and pharmacists, didn't imply that interventions led by those educators were ineffective. It may arise from the limited number of included trials involving community health workers or pharmacists. Thirdly, the finding in the meta-analysis may not be generalized to all type 2 diabetes patients. The eligibility criteria for recruiting type 2 diabetes patients were different among those included studies, and there were obvious differences in the background of type 2 diabetes patients among those included in trials. Though we performed subgroup analysis by newly-diagnosed diabetes or previously treated diabetes, we were unable to performed further subgroup analyses by more characteristics in details, such as diabetes duration, diabetic complications, education levels, and socioeconomic status. The effect of DSME on risk of mortality in type 2 diabetes patients with specific secondary diseases is also interesting, but few relevant studies are available now. More studies are needed to further assess the effect of DSME in mortality risk in type 2 diabetes patients with different disease duration, diabetic complications, comorbidities, glycemic control status, education levels, and socioeconomic status, and find who will

benefit more from DSME and who should receive it. Fourthly, the cost-effectiveness of DSME in type 2 diabetes patients has not been well evaluated, and future studies are also needed to determine the most effective and cost-effective model of DSME. Finally, our meta-analysis only assessed the impact of DSME on mortality risk, but the impact of DSME on risks of cardiovascular mortality, cardiovascular diseases, infectious diseases and diabetic complications is still unclear. The impact of DSME on life quality in type 2 diabetes patients also has not been well studied. More clinical trials with a large number of recruited patients and longer time of follow-up are needed to solve these unanswered questions.

In conclusion, the available evidence suggests that DSME can reduce risk of all-cause mortality in type 2 diabetes patients. Further clinical trials with outcomes of longer time of follow-up are needed to validate the finding above and to determine the most cost-effective format of DSME in type 2 diabetes patients. Such clinical trials will provide clinicians with a stronger evidence for the clinical practice of DSME in type 2 diabetes patients.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

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