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REVIEW ARTICLE

Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis†

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ABSTRACT

Diabetic foot is a severe public health issue, yet rare studies investigated its global epidemiology. Here we performed a systematic review and meta-analysis through searching PubMed, EMBASE, ISI Web of science, and Cochrane database. We found that that global diabetic foot ulcer prevalence was 6.3% (95%CI: 5.4–7.3%), which was higher in males (4.5%, 95%CI: 3.7–5.2%) than in females (3.5%, 95%CI: 2.8–4.2%), and higher in type 2 diabetic patients (6.4%, 95%CI: 4.6–8.1%) than in type 1 diabetics (5.5%, 95%CI: 3.2–7.7%). North America had the highest prevalence (13.0%, 95%CI: 10.0–15.9%), Oceania had the lowest (3.0%, 95% CI: 0.9–5.0%), and the prevalence in Asia, Europe, and Africa were 5.5% (95%CI: 4.6–6.4%), 5.1% (95%CI: 4.1–6.0%), and 7.2% (95%CI: 5.1–9.3%), respectively. Australia has the lowest (1.5%, 95%CI: 0.7–2.4%) and Belgium has the highest prevalence (16.6%, 95%CI: 10.7–22.4%), followed by Canada (14.8%, 95%CI: 9.4–20.1%) and USA (13.0%, 95%CI: 8.3–17.7%). The patients with diabetic foot ulcer were older, had a lower body mass index, longer diabetic duration, and had more hypertension, diabetic retinopathy, and smoking history than patients without diabetic foot ulceration. Our results provide suggestions for policy makers in deciding preventing strategy of diabetic foot ulceration in the future.

KEY MESSAGES

- Global prevalence of diabetic foot is 6.3% (95%CI: 5.4–7.3%), and the prevalence in North America, Asia, Europe, Africa and Oceania was 13.0% (95%CI: 10.0–15.9%), 5.5% (95%CI: 4.6–6.4%), 5.1% (95%CI: 4.1–6.0%), 7.2% (95%CI: 5.1–9.3%), and 3.0% (95% CI: 0.9–5.0%).
- Diabetic foot was more prevalent in males than in females, and more prevalent in type 2 diabetic foot patients than in type 1 diabetic foot patients.
- The patients with diabetic foot were older, had a lower body mass index, longer diabetic duration, and had more hypertension, diabetic retinopathy, and smoking history than patients without diabetic foot.

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Introduction

Diabetic foot is a severe chronic diabetic complication that consists of lesions in the deep tissues associated with neurological disorders and peripheral vascular disease in the lower limbs (1). The incidence of diabetic foot has increased due to the worldwide prevalence of diabetes mellitus and the prolonged life expectancy of diabetic patients. A previous study showed that a lower limb is amputated due to diabetes every 30 s (2), and the average annual cost of diabetic foot is $8659 per patient (3). The total medical cost for treating diabetic foot diseases in America ranges from $9 to $13 billion and is an additional cost associated with diabetes (4). Thus, the International Diabetes Foundation is increasing awareness of diabetic foot problems due to the substantial social, medical, and economic burdens (5).

Of all amputations in diabetic patients, 85% are preceded by a foot ulceration which subsequently deteriorates to a severe gangrene or infection (6). There are currently no studies investigating the global prevalence of diabetic foot ulceration despite the significance of this increasing problem. In addition, most studies evaluating the prevalence of diabetic foot ulcer were carried out in specific areas within a certain period and varied considerably in study design or

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population demographics. Thus, a contemporary and comprehensive evaluation and update of diabetic foot ulcer epidemiology worldwide is critical. The information could be used to develop a prevention and treatment strategy for diabetic foot ulcer, improve patients' quality of life, and reduce the economic burden. Here, we conducted a systematic review and meta-analysis of all available studies to calculate the current prevalence of diabetic foot ulceration.

Methods

Search strategy and selection criteria

We searched English-language databases including PubMed, EMBASE, ISI Web of science, and the Cochrane database. The search terms used were "diabetic foot" OR "diabetic feet" OR "diabetic foot ulcer" OR "diabetic foot problem" AND "epidemiology" OR "incidence" OR "prevalence". We did not restrict the study design or the level (national or regional) of the studies. All the databases were searched from their inception until September 2015. We then reviewed references of all the included articles to identify other potentially relevant surveys.

The study inclusion criteria included the following: data were available in English, the process of identifying diabetic foot ulceration was described, and the studies provided sufficient information to estimate the pooled prevalence of diabetic foot ulceration. Prospective studies were included if the prevalence of diabetic foot at baseline could be calculated. If there was more than one article based on the same sample then only the study that provided the most complete data was included. Abstracts meet the inclusion criteria were included. Studies were excluded if only the diabetic foot ulceration incidence in follow-up years was stated or if they did not state the process of diagnosing diabetic foot ulceration. Those only focused on the prevalence of diabetic amputation were also excluded. Moreover, we excluded studies that focused on specific groups of people such as the elderly or the young. The authors of the studies without available information were contacted to obtain detailed data.

Study identification and data extraction

All identified studies were screened for inclusion by two independent investigators and any disagreements were resolved by a third reviewer. The process of study inclusion is shown in Figure 1. The investigators extracted details of each study based on a predefined protocol. The study characteristics including author name, publication year, region, population, study design and sample size, baseline participant characteristics (such as age, diabetic duration, sex ratio and type of diabetes), and the process of diagnosing diabetic foot ulcer were extracted. The qualities of the included studies were evaluated using a checklist of items for observational studies in epidemiology (STROBE Statement) (7).

Statistical analysis

A random effect or fixed effect meta-analysis was performed based on the degree of heterogeneity. We then calculated the pooled diabetic foot ulceration prevalence and its 95% confidence intervals (CI). The I^2 statistic is an indicator of the heterogeneity between studies and is characterized as low, moderate, or high heterogeneity at values of 25%, 50%, and 75%, respectively (8). We used multivariate random-effects meta-regression and subgroup analyses (including different types of study participants and different geographic areas) to examine potential sources of heterogeneity. Furthermore, we used data from seven studies to compare the characteristics between diabetic patients with or without diabetic foot. All analyses were conducted using STATA version 12.0 (StataCorp LP, College Station, TX).

Results

Figure 1(A) shows the flow chart and selection process for the global prevalence of diabetic foot ulceration. There were 67 publications including 39 cross-sectional, descriptive and observational studies (9–47), eight prospective studies (48–55), and six retrospective studies (56–61) with a total of 801,985 subjects from 33 countries eligible for the systematic review. There were no available studies found in Antarctica and South America (Figure 1(B)). The characteristics of all included studies are summarized in Supplementary Table 1 (9–75). Quality assessment of all the included studies is in supplementary files.

The pooled worldwide prevalence of diabetic foot ulceration was 6.3% (95%CI: 5.4–7.3%). As shown in Figure 2, North America had the highest prevalence of 13.0% (95%CI: 10.0–15.9%) (18,37,50,51,66). Oceania had the lowest prevalence of 3.0% (95%CI: 0.9–5.0%) (21,22,46). The prevalence in Africa was 7.2% (95%CI: 5.1–9.3%) (9,11,57,58,61,62,64,65,72,75) which was higher than Asia (5.5%, 95%CI: 4.6–6.4%) (10,12–14, 16,17,20,25,26,30,32–35,39–41,44,45,47,48,55,59,60,63,68, 69,73) and Europe (5.1%, 95%CI: 4.1–6.0%) (15,19,23, 24,27–29,31,36,38,42,43,49,52–54,56,67,70,71,74) (Figure 2).

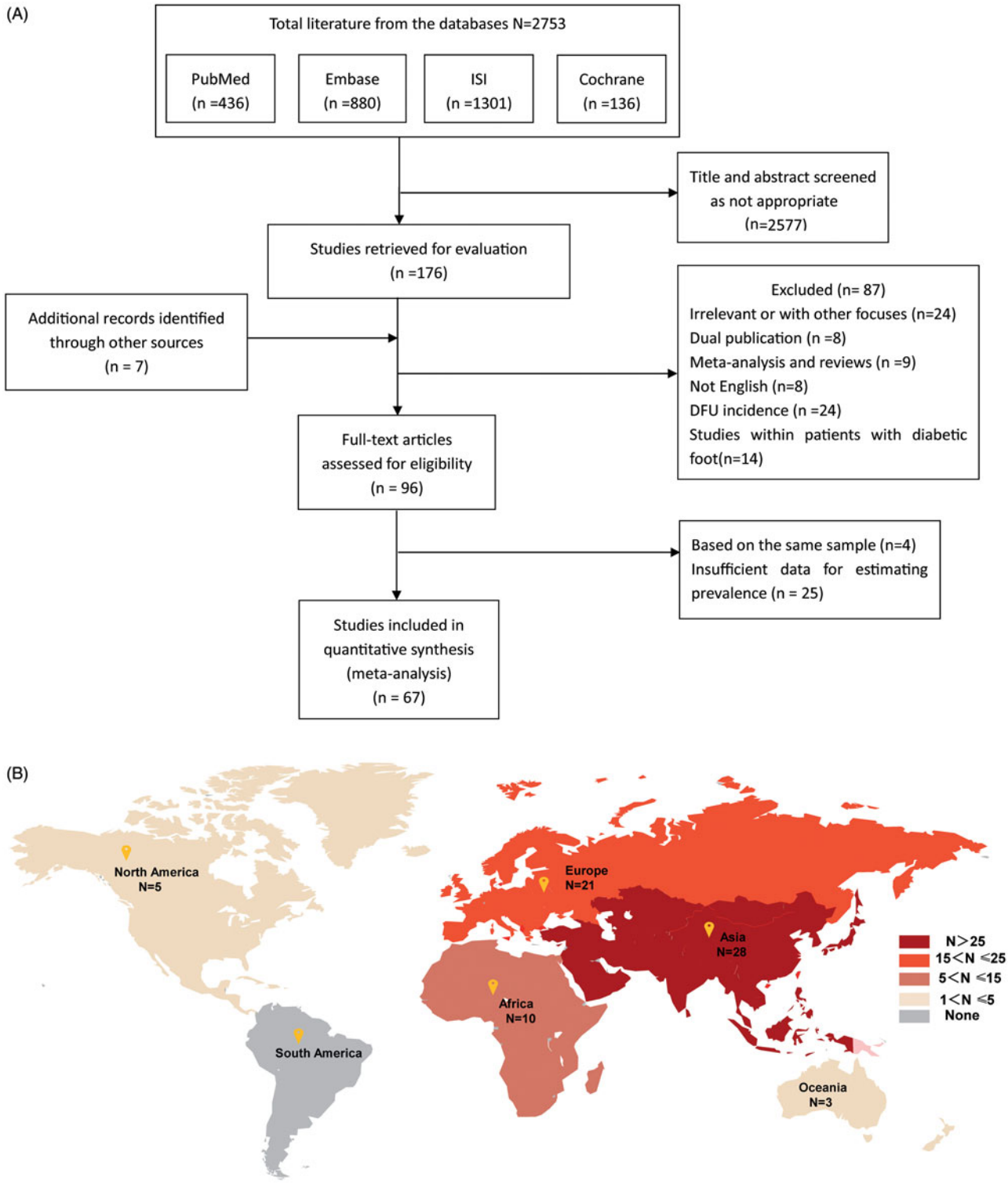

Figure 1. (A) Flow diagram of the assessment of the studies identified in the systematic review of global diabetic foot ulcer prevalence. (B) Included studies in the global diabetic foot ulcer prevalence meta-analysis by continent.

Particularly, we calculated the prevalence of diabetic foot ulceration in each country. As shown in Table 1, the prevalence varied greatly in different countries, with Australia has the lowest (1.5%, 95%CI: 0.7–2.4%) and Belgium has the highest prevalence (16.6%, 95%CI: 10.7–22.4%), followed by Canada (14.8%, 95%CI: 9.4–20.1%) and USA (13.0%, 95%CI: 8.3–17.7%) (Table 1).

The prevalence of diabetic foot ulceration from hospital-based (7.1%, 95%CI: 5.4–8.8%) and public health center studies (5.6%, 95%CI: 3.5–7.6%) was higher than from population-based (4.6%, 95%CI: 3.7–5.5%) and

Table 1. Prevalence of diabetic foot ulcer in each country.

Country	No. of studies	Prevalence	95%CI	I^2
Belgium	1	16.6	10.7–22.4	NA
Canada	1	14.8	9.4–20.1	NA
USA	3	13	8.3–17.7	98
Trinidad	1	12.2	10.8–13.6	NA
India	2	11.6	6.4–16.8	90.8
Norway	1	10.4	8.8–11.9	NA
Cameroon	3	9.9	6.3–13.5	86.6
Italy	1	9.7	7.8–11.6	NA
Thailand	2	8.8	1.7–15.9	95
Iran	2	8.1	0.1–16.1	94.9
Denmark	1	7.8	5.6–10.1	NA
Pakistan	4	7.4	0.5–14.3	99
Tanzania	2	7.3	2.1–12.6	83.4
Pacific island countries	1	6.8	4.5–9.0	NA
UK	4	6.3	4.6–8.0	79.8
Egypt	2	6.2	4.1–8.2	49.8
Bahrain	1	5.9	4.7–7.1	NA
South Africa	2	5.8	3.8–7.9	0
France	1	5.6	2.4–8.7	NA
Greece	1	4.8	3.3–6.2	NA
Jordan	2	4.2	3.4–5.1	0
China	10	4.1	3.1–5.2	97.4
Uganda	1	4	1.6–6.4	NA
Ireland	1	3.9	2.3–5.5	NA
Turkey	1	3.1	1.9–4.3	NA
Spain	5	3	1.9–4.4	97
Germany	2	2.8	2.4–3.3	0
Saudi Arabia	1	2.3	2.2–2.4	NA
Japan	1	2	1.4–2.6	NA
Netherland	2	1.8	1.0–2.6	0
Korea	2	1.7	0.6–2.9	85.1
Poland	1	1.7	1.1–2.3	NA
Australia	2	1.5	0.7–2.4	58.1

NA: not available.

community-based (2.9%, 95%CI: 1.0–4.7%) studies. We also suggested that diabetic foot ulceration was more prevalent in male diabetic patients (4.5%, 95%CI: 3.7–5.2%) than female patients (3.5%, 95%CI: 2.8–4.2%) (16,19,26,27,33,38,40,45,59,71). Diabetic foot ulceration was also more prevalent in patients with type 2 diabetes mellitus (T2DM, 6.4%, 95%CI: 4.6–8.1%) than in patients with type 1 diabetes mellitus (T1DM, 5.5%, 95%CI: 3.2–7.7%) (16,19,24,30,38,74,75) (Table 2).

A meta-regression analysis suggested that geographic region was associated with significant heterogeneity between prevalence rates in Asia and North America ($p < .01$). Study type also resulted in heterogeneity between retrospective studies and cross-sectional studies ($p = .01$). Additionally, the sample size was associated with significant heterogeneity for studies with more than 800 and less than 800 subjects ($p = .02$) (Table 3).

Next, we compared the characteristics between diabetic patients with and without diabetic foot ulcer. Among all the 67 studies, nine articles provided available clinic information of these two groups of patients (12,16,19,23,38,40,45,55,59). The patients with diabetic foot ulceration had the following characteristics: older age (61.7 ± 3.7 versus 56.1 ± 3.9), longer diabetic duration (11.3 ± 2.5 versus 7.4 ± 2.2), lower body mass Index (BMI, 23.8 ± 1.7 versus 24.4 ± 1.7), higher percentage of smokers (29.1%, 95%CI: 18.3–39.8% versus 17.4%, 95%CI: 12.4–22.4%), hypertension (63.4%, 95%CI: 49.4–88.3% versus 53.1%, 95%CI: 33.8–72.5%), and diabetic retinopathy (63.6%, 95%CI: 38.8–88.3%% versus 33.3%, 95%CI: 13.8–52.7%) than patients that did not develop diabetic foot ulceration (Table 4).

Discussion and conclusions

Our systematic review included a large sample of studies involving more than 800,000 global participants from 67 studies in the past three decades. These studies included patients from five continents. We suggested that the pooled prevalence of diabetic foot ulceration was about 6.3% worldwide. Because there are no published epidemiological data of diabetic foot ulceration worldwide, our results may provide suggestive information for public health planning and management of diabetic foot ulcer.

The results suggested that the highest prevalence of diabetic foot ulceration was reported in North America (13.0%), and the lowest prevalence was reported in Oceania (3.0%). The prevalence of diabetic foot ulcer was relatively higher in Africa (7.2%) than in Asia (5.5%) and Europe (5.1%).

We observed that Belgium's prevalence was the highest among all the included studies. Although only one study from Belgium was included in our paper, which may not signify the whole country, an earlier research manifested that the incentive for prevention of this disease was low from patients' perspective because cost for prevention was paid by the patients but the cost for treatment was covered by the health care system in Belgium (76). The cause of the high prevalence of diabetic foot ulceration in North America is unclear. National surveys in the USA demonstrated that smoking was more common in white Americans (22.0%) and American Indians (32.4%) than in other ethnic groups such as black people (21.3%) and Asians (9.9%) (77). Previous studies have identified smoking as a risk factor for diabetic foot ulcers because daily tissue hypoxia may cause vascular and neuropathic disorders in the lower extremities of diabetic patients (78,79). Thus, one possible explanation for the high prevalence of diabetic foot ulcer in North America could be the relatively larger proportion of smokers. Indeed, the highest daily smoking prevalence can be seen in Belgium and Norway than other European countries (80), which might be associated with the higher prevalence of diabetic foot ulceration in these countries observed in our study.

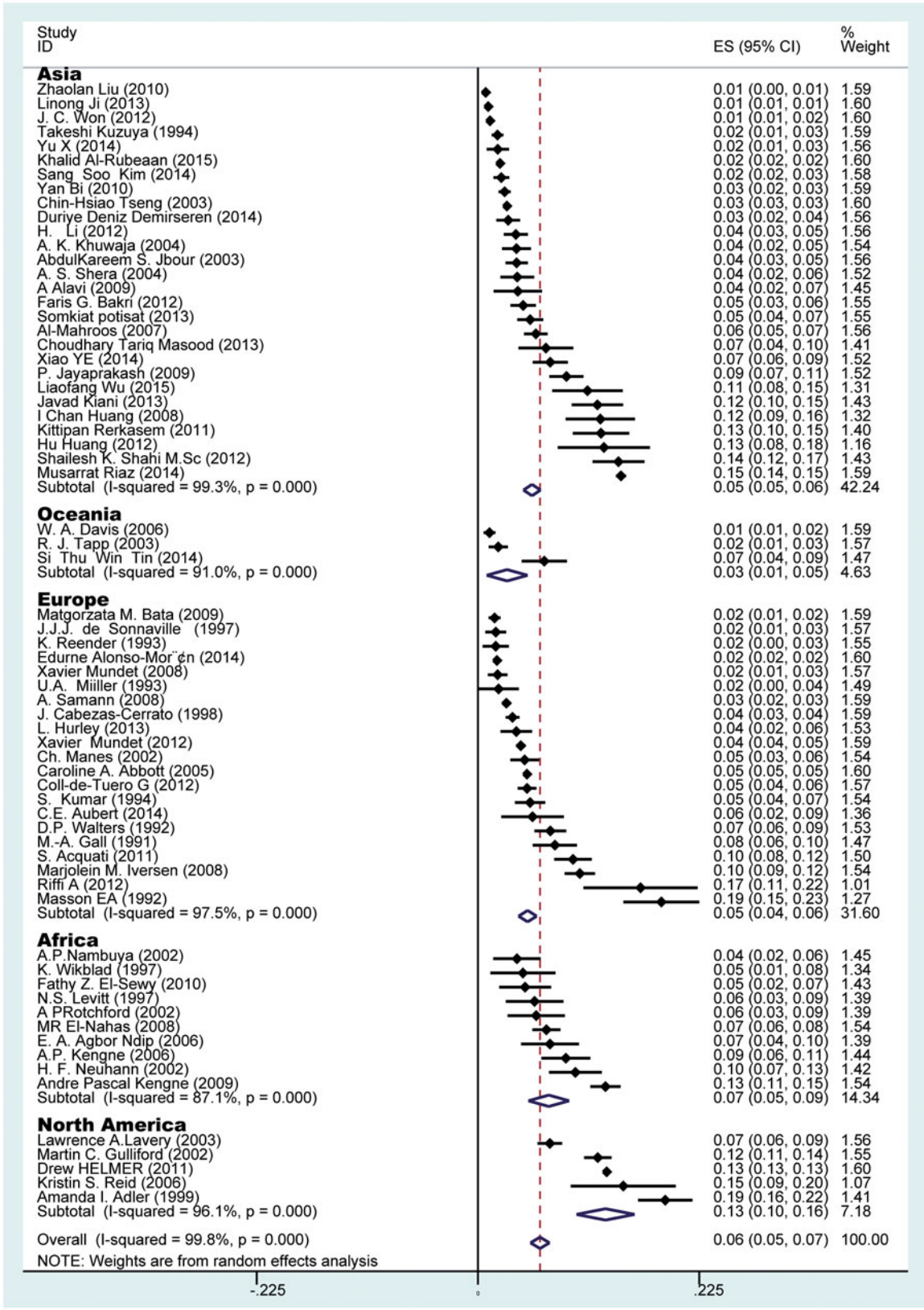

Figure 2. Forest plot of the prevalence of studies of diabetic foot ulcer all over the world.

The prevalence of diabetic foot ulceration in Oceania was the lowest, and the prevalence in Australia was lower than in the Pacific Island countries based on the three included studies from Oceania (21,22,44). This observation may be associated with a poor screening process of diabetic foot in Australia

Table 2. Subgroup analysis in global prevalence of diabetic foot ulcer.

Category	Subgroup	No. of studies	Total	Cases	Pooled estimate (95%CI)	Heterogeneity I^2 (%)	p value
Total			801,985	47208	6.3 (5.4–7.3)	99.8	.000
Source of population	Population based	13	48,456	2058	4.6 (3.7–5.5)	95.0	.000
	Hospital based	44	611,226	42051	7.1 (5.4–8.8)	99.9	.000
	Community based	2	1158	34	2.9 (1.0–4.7)	72.1	.06
	Public health center	8	141,145	3065	5.6 (3.5–7.6)	97.8	.000
Types of diabetes	T1DM	7	3841	168	5.5 (3.2–7.7)	84.4	.000
	T2DM		63,388	1754	6.4 (4.6–8.1)	96.9	.000
Gender	Male	10	234,897	3985	4.5 (3.7–5.2)	98.7	.000
	Female		210,834	3098	3.5 (2.8–4.2)	98.3	.000

Table 3. Multivariate meta-regression of included studies.

	Variable	Coef	SE	t	p	95% CI
Geographic area	Asia[a]	–	–	–	–	–
	Oceania	0.009	0.02	0.53	.601	−0.025, 0.043
	Europe	0.009	0.02	0.48	.634	−0.029, 0.048
	Africa	0.003	0.03	0.10	.924	−0.056, 0.062
	North America	0.109	0.03	4.03	.000	0.055, 0.016
Diagnosis of diabetic foot	≥Wagner 1[a]	–	–	–	–	–
	Self-reported	−0.028	0.02	−1.74	.088	−0.061, 0.004
	Medical record	−0.014	0.02	−0.54	.593	−0.062, 0.036
	Others	−0.024	0.02	−1.59	.119	−0.055, 0.006
Study population	Population based[a]	–	–	–	–	–
	Hospital based	0.004	0.016	0.27	.787	−0.027, 0.036
	Community based	0.028	0.034	0.82	.417	−0.052, 0.025
	Public health center	−0.034	0.020	−1.67	.102	0.014, 0.094
Study type	Cross-sectional[a]	–	–	–	–	–
	NA	−0.007	0.013	−0.50	.619	−0.033, 0.020
	Prospective	−0.134	0.019	−0.70	.488	−0.052, 0.025
	Retrospective	0.054	0.019	2.72	.009	0.014, 0.094
Sample size	<800[a]	–	–	–	–	–
	≥800	−0.025	0.010	−2.42	.019	−0.046, −0.004

CI: confidential interval; NA: not available.
[a]Reference group.

because less than 50% of the diabetic population was reported to have a regular foot examination (81), which was much less than the 80% screening target established by the National Diabetic Foot Disease Management Program of Australia (82).

In addition to the identified smoking risk, we suggested differences in age, diabetic duration, BMI distribution, hypertension, and diabetic retinopathy between patients with diabetic foot and patients without diabetic foot ulceration based on available data from nine papers.

The contribution of obesity to the risk of diabetic foot ulceration is inconclusive. Previous studies have revealed that obesity might be associated with diabetic foot ulcers (83,84). However, there are also prospective studies showing that BMI has no significant correlation with diabetic foot ulcer (85,86). A recent study demonstrated that the association between BMI and diabetic foot was J-shaped, and patients with BMI $<25\,kg/m^2$ and BMI $\geq 45\,kg/m^2$ were correlated with higher risk of developing diabetic foot ulceration (87). The correlation between diabetic foot ulcer and BMI ranging from 25 to $45\,kg/m^2$ remains unknown. Our analysis suggested that patients with diabetic foot ulceration had lower BMIs than patients without diabetic foot, and most BMI levels in our study ranged from 25 to $30\,kg/m^2$. These results suggested that the association between BMI ranging from 25 to $30\,kg/m^2$ and diabetic foot ulcer requires further research.

Diabetic retinopathy was present in 63.3% of diabetic foot ulceration patients and in 33.3% of non-diabetic foot ulceration patients. A recent study also revealed that retinopathy was associated with diabetic foot ulceration in elderly diabetic patients (44). It has been shown that impairment of the microcirculation in diabetic patients may lead to secondary complications in the lower extremity due to dysfunctional vasodilation (88). There were studies observed that diabetic foot patients with retinopathy had higher levels of diabetic biomarkers such as plasma uric acid and ceruloplasmin (89–91), and ceruloplasmin was an independent predictor for the progression of diabetic nephropathy in type 2 diabetic patients (92). These results implied that there is a link between retinopathy and diabetic foot ulceration.

Our data suggested that diabetic foot was more common in male diabetic patients than female patients. One explanation of this gender difference might be the involvement in increased physical work in males (93). The results further suggested that diabetic foot ulcer

Table 4. Characteristics between diabetic foot ulcer and non-diabetic foot ulcer patients.

Study	No. DF/non-DF	Age		Duration		BMI		Smoking		Hypertension		Diabetic retinopathy	
		DF	Non-DF	DF	Non-DF	DF	Non-DF	DF	Non-DF	DF	Non-DF	DF	Non-DF
Ye et al. (59)	61/768	63.9 ± 10.5	55.3 ± 11. 8	7.0 ± 5.9	5.7 ± 5.5	NA	NA	NA	NA	35	330	46	364
Riaz et al. (12)	2638/15481	53.5 ± 10.6	50.0 ± 12.4	15.8 ± 7.8	12.6 ± 7.7	26.7 ± 5.3	27.6 ± 5.6	759	2127	2799	10869	NA	NA
Al-Rubeaan et al. (16)	1404/60610	63.0 ± 12.7	56.7 ± 13.5	20.0 ± 8.0	13.0 ± 8.0	29.2 ± 6.4	30.7 ± 6.4	157	4076	766	28223	603	10296
Iversen et al. (19)	155/1339	67.2 ± 14.0	65.6 ± 13.6	10.0	6.0	29.3 ± 5.3	28.9 ± 4.8	70	674	NA	NA	NA	NA
De Sonnaville et al. (23)	11/598	63.8 ± 11.7	64.9 ± 12.2	6.2 ± 7.2	4.0 ± 5.4	28.2 ± 4.8	28.9 ± 5.0	38	111	NA	NA	NA	NA
Jayaprakash et al. (55)	94/950	54 ± 9.6	53.1 ± 12.0	11.0 ± 7.6	6.7 ± 6.8	24.0 ± 4.46	25.2 ± 5.3	21	115	62	450	69	338
Shahi et al. (45)	97/581	55.3 ± 12.1	47.8 ± 8.38	11.5 ± 5.7	7.6 ± 4.9	NA	NA	21	86	NA	NA	NA	NA
Sämann et al.(38)	138/4640	69.5 ± 9. 7	65.0 ± 11.7	12.4 ± 10.5	8.5 ± 8.1	29.1 ± 5.1	29.6 ± 5.3	65	1890	NA	NA	NA	NA
Hu et al. (40)	25/170	68.2 ± 12.3	57.0 ± 14.5	11.1 ± 6.0	6.7 ± 5.8	22.9 ± 3.5	23.6 ± 3.7	NA	NA	NA	NA	NA	NA
Total	4623/85137	4.1 (2.8–5.4)[a]		5.8 (3.8–7.8) [a]		0.8 (−1.3∼−0.4) [a]		29.1% (18.3–39.8%)[b]	17.4% (12.4–22.4%)[b]	63.4% (49.4–77.4%)[b]	53.1% (33.8–72.5) %[b]	63.6% (38.80–88.3%)[b]	33.3% (13.8–52.7%)[b]

DF: diabetic foot; non-DF: diabetic patients without diabetic foot; NA: not available.
[a]Weighted mean difference.
[b]Pooled prevalence.

prevalence was higher in T2DM (6.4%) patients than in T1DM (5.5%) patients, which was consistent with the results of previous studies (93). However, the underlying mechanisms have not been elucidated. Besides, there was limited evidence concerning diabetic foot ulcer epidemiology in type 1 diabetes. Thus, additional studies are warranted in the future.

This study had several limitations. First, there was high heterogeneity (more than 90%) in the meta-analysis. This heterogeneity might be attributed to the different sources of patient populations and geographic regions. Indeed, heterogeneity remains high even within the same country. This study compromised four different kinds of population (population based, hospital based, community based and public health center), and 611,226 of 801,985 participants included in this study were from hospital, which may not represent the general population. Hence the difference in prevalence between population based and hospital based studies may also explain the high heterogeneity. Other possible reasons including implementation measures and study design features such as sampling scheme, sample size, and quality control can influence the heterogeneity of pooled results. Also, 60,610 subjects did come from one study (16), which accounted for a relatively high weight when using random effect model to calculate the pooled prevalence, this may also resulted in the high heterogeneity. Thus, well-controlled nationwide multicenter studies are needed with a large population to obtain more reliable data on diabetic foot ulcer prevalence. Second, the prevalence in South America could not be estimated because there were no available English language articles from that continent.

To summarize, we reported the global prevalence of diabetic foot ulceration and its updated epidemiologic characteristics. The data suggest that it is important to screen and control the prevalence of diabetic foot ulceration, especially in North America. Our study offered a reference for the future management and prevention of diabetic foot ulceration and may help to reduce the medical and economic burden of this disease. Future studies should be devoted to defining the social and economic burden of the diabetic foot ulceration.

Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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