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Associations of health literacy with diabetic foot outcomes: a systematic review and meta-analysis

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What's new?

- The potential role of health literacy in diabetic foot disease prevention is currently not well understood.
- The novel data from this first systematic review of the potential effects of health literacy on diabetic foot disease and its risk factors show that there are insufficient data to rule out associations between health literacy and diabetic foot disease and its risk factors, but health literacy appears unlikely to have an important role in foot self-care.

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- The contribution of low health literacy to diabetic foot disease development needs to be definitively assessed through robust longitudinal studies.

Abstract

Background People with diabetes have low health literacy, but the role of the latter in diabetic foot disease is unclear.

Aim To determine, through a systematic review and meta-analysis, if health literacy is associated with diabetic foot disease, its risk factors, or foot care.

Methods We searched PubMed, EMBASE, CINAHL, Web of Science, Scopus and Science Direct. All studies were screened and data extracted by two independent reviewers. Studies in English with valid and reliable measures of health literacy and published tests of association were included. Data were extracted on the associations between the outcomes and health literacy. Meta-analyses were performed using random effects models.

Results Sixteen articles were included in the systematic review, with 11 in the meta-analysis. In people with inadequate health literacy, the odds of having diabetic foot disease were twice those in people with adequate health literacy, but this was not statistically significant [odds ratio 1.99 (95% CI 0.83, 4.78); two studies in 1278 participants]. There was no statistically significant difference in health literacy levels between people with and without peripheral neuropathy [standardized mean difference –0.14 (95% CI –0.47, 0.18); two studies in 399 participants]. There was no association between health literacy and foot care [correlation coefficient 0.01 (95% CI –0.07, 0.10); seven studies in 1033 participants].

Conclusions There were insufficient data to exclude associations between health literacy and diabetic foot disease and its risk factors, but health literacy appears unlikely to have a role in foot care. The contribution of low health literacy to diabetic foot disease requires definitive assessment through robust longitudinal studies.

Introduction

Diabetes is a chronic disease necessitating ongoing self-care to maintain optimal glycaemic control and prevent end-stage complications. This presents a complex set of challenges for people with diabetes, with sustained efforts required for a wide spectrum of tasks. For glycaemic control, this includes glucose monitoring, administering medications and carbohydrate counting. Prevention of complications adds further complexity, demanding proficiency in managing blood pressure, as well as appropriate eye and foot care habits. For these reasons, a diagnosis of diabetes can be overwhelming because of the sheer volume of new information and lifestyle changes required [1].

Diabetic foot disease is a leading cause of hospitalization and amputation in people with diabetes [2]. Irreversible damage to peripheral nerves and arteries caused, *inter alia*, by prolonged periods of hyperglycaemia, places people with diabetes at significant risk of developing non-healing sores or wounds on their feet (ulcers), which are then prone to infection or may lead to amputation [3,4]. The prognosis for diabetic foot disease is unacceptably poor, with amputation a common outcome, and estimates of 5-year mortality rates post-amputation ranging as high as 70% [5].

International guidelines emphasize the importance of early risk factor identification and education to prevent foot ulcer development [6,7]; however, whilst routinely performed in primary care and podiatric practices, the responsibility of daily self-care rests with the individual. Activities such as regular foot inspections and good footwear and vigilant foot care can identify and prevent areas vulnerable to foot ulceration [6]. Despite this, numerous studies have reported inadequate knowledge of good foot care behaviour, as well as poor foot care practices among people with diabetes [8–10].

People with diabetes commonly struggle to translate and apply information received, and have misunderstandings about their foot health, and subsequently make poor choices about footwear or self-care [11]. The search for explanations for an individuals' non-adherence to recommended diabetic foot care regimes has led to a focus on health literacy.

Health literacy refers to the 'cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand, and use information in ways which promote and maintain good health' [12]. Several studies have shown that people with diabetes have low health literacy [13,14], and although the literature is relatively sparse, correlations have been established between poor health literacy and other diabetes-related complications, such as retinopathy and cerebrovascular disease [15,16]. Conceptually, people with diabetes require an understanding of the diabetes process, its consequences and how to prevent them to be able to engage successfully in activities necessary for diabetes management; however, the link between health literacy and foot care or foot disease remains unclear. The aim of the present review, therefore, was to synthesize current evidence to determine the associations between health literacy and foot self-care and foot outcomes in people with diabetes.

Participants and methods

A protocol for this systematic review was registered with PROSPERO (CRD42015014985) (available at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015014985). We report the systematic review and meta-analysis in accordance with the guidelines for Meta-Analyses and Systematic Reviews of Observational studies (MOOSE).

Data sources and searches

Study investigators searched six electronic databases up to 1 June 2016: Embase; PubMed; CINAHL; Web of Science; Scopus; and Science Direct. Searches were limited to the categories of medical, health and social sciences, and to studies published as full-text in English. There were no limits on publication year. The detailed search strategy used for PubMed and replicated for all other databases is provided in Appendix S1.

In addition, we subscribed to the search performed in PubMed to alert us to potential new articles published after our initial search date.

Study selection

We included all quantitative studies on adults with diabetes mellitus (excluding gestational diabetes) that used valid and reliable measures of health literacy and included one or more of the following foot disease outcome measures: amputation; foot ulceration; ischaemic gangrene or necrosis and cellulitis (primary review outcomes); risk factors for these outcomes (peripheral neuropathy, peripheral arterial disease and foot deformity); and frequency of foot self-care. Health literacy measures were considered appropriate if there was publication of or reference to statistical descriptors of validity and reliability (Cronbach's α).

Studies measuring only general literacy or levels of education were excluded. To maximize the use of available data, we did not initially exclude studies in which measures of health literacy and foot outcomes were assessed but tests of associations between these variables were not reported. Instead, we sought to obtain any such unpublished data from study authors. An email was sent to authors of articles without published correlations or data that

could be used in a meta-analysis, with a courtesy follow-up email 1 month later. If such data were not available, the studies were then excluded from the meta-analysis.

Assessment of potential studies against the inclusion criteria was performed independently by two researchers (P.C. and S.E). All disagreements between reviewers were resolved by consensus.

Alerts from the subscription to PubMed were monitored and evaluated by one person (P.C.).

Data extraction and quality assessment

Data extraction was also performed independently by P.C. and S.E., with disagreements resolved by consulting a third researcher (T.W.). Data were extracted on study characteristics [authors, year(s) of study, study design and if applicable, periods of follow-up] and participant characteristics (number, setting, diabetes diagnostic criteria, age, sex, country, comorbidities, socio-economic data and ethnicity). With regard to health literacy, the measurement tool, validity data and categories of health literacy and/or health literacy scores were extracted.

For dichotomous outcomes (presence or absence of risk factors for foot disease) we extracted odds ratios of outcomes across health literacy categories, or the number of individuals with and without exposure and outcome measures in a 2×2 table, or mean and SD of health literacy levels in people with and without the outcome of interest. For continuous outcomes (number of days/week foot care is performed) we extracted the result of the test of association reported for that outcome, e.g. Pearson's or Spearman's correlation, or β coefficients from linear regressions.

In the case of studies in which health literacy and an outcome of interest were both measured but no test of association was reported, we attempted to contact the authors to acquire such data.

All included studies underwent an assessment of quality, also independently by P.C. and S.E. This was carried out using a standardized set of criteria previously used in systematic reviews of observational studies for musculoskeletal disorders, which we modified for use in the present review [17]. A study was considered of high quality if the score was greater than the median score of all included studies. Description of the quality assessment tool is available in Appendix S2. Where unpublished data were obtained from the author contact process, items 19–21 were scored as being not applicable.

Data synthesis and analysis

To account for differences in methods and study characteristics we used random effects models to calculate pooled odds ratios, standardized mean differences (SMDs) and correlation coefficients, with 95% CIs. For all analyses, a two-tailed *P* value of < 0.05 was taken to indicate statistical significance.

Exposure measures of the Rapid Estimate of Adult Literacy in Medicine (REALM), Test of Functional Health Literacy in Adults (TOFHLA) and the Diabetes Numeracy Test (DNT) have reasonable congruence with the functional subscaIe of the Functional, Communicative and Critical Health Literacy Scale (FCCHLS) [18], so studies using these measures were pooled.

For the dichotomous outcome of diabetic foot disease, studies reported health literacy in categories. We considered foot ulceration and amputation as being at the end of the diabetic foot disease spectrum with similar aetiologies, so these outcomes were pooled. Odds ratios were calculated if a 2×2 table of raw data was provided, and pooled thereafter. For outcomes of risk factors for foot ulceration (peripheral neuropathy and peripheral arterial disease), most studies reported health literacy as the mean (SD) of scores in the groups with and without each risk factor. We pooled SMDs between those with and without the outcomes of interest, which made it possible to combine results from different health literacy scales. For those studies reporting odds ratios [14,19], these were converted to SMDs to enable pooling of results [20].

Where studies had both health literacy and outcome measures as continuous measures (for the outcome measure of frequency of foot self-care), correlation coefficients, Pearson's correlations, Spearman's correlations and standardized β-coefficients were pooled. These were the most commonly published measure of association, and the use of standardized β-coefficients has previously been identified to be equivalent to direct correlation coefficients despite the inclusion of other variables [21,22].

Where other measures of association were reported, we contacted the authors for additional data, and if no additional data were obtained, calculations were made from the available information. If mean and *P* values of frequency of foot care behaviour across health literacy groups were published, we used this to calculate a *t*-value and SD, from which an SMD was obtained. Using a formula from Borenstein *et al.* [20], correlation coefficients and variance values were calculated which were subsequently used in meta-analysis.

On three occasions, sensitivity analyses were required. The first instance was for the study by Ferguson *et al.* [24], which reported mean (SD) values of frequency of foot self-care across three categories of health literacy measured using the REALM. We combined the categories of 'sixth grade or below' and 'seventh to eighth grade' levels of literacy *a priori* as we considered these to be most consistent with the short-form version of the TOFHLA (S-TOFHLA) categories of inadequate and marginal health literacy, respectively. We repeated the analysis combining the 'seventh to eighth grade' and 'high school and above' categories instead as a sensitivity analysis.

The second instance was with the two studies [15,22] reporting on ulceration as an outcome with health literacy as a categorical exposure. One [15] categorized participants into having inadequate or adequate health literacy, omitting participants with marginal health literacy, which was included in analysis by the second study [22]. Unpublished data were obtained from Morris *et al.* [19], who similarly omitted individuals with marginal health literacy, to match categories in the study by Schillinger *et al.* [14] for use in meta-analysis. Sensitivity analyses were performed using alternative calculations combining the marginal health literacy group from the study by Morris *et al.* [19] with the inadequate and then the adequate groups.

In the third instance, in two papers, peripheral neuropathy was reported from medical records [25,26], whereas the unpublished data we obtained from Morris *et al*. [19] used self-reported peripheral neuropathy. The former used the FCCHLS and the latter the S-TOFHLA as exposure measures. Our primary analysis pooled data from only the first two sources using the functional subscale of the FCCHLS. Two sensitivity analyses were performed; first

including self-reported peripheral neuropathy as the outcome, the second using the full FCCHLS score rather than the functional subscale.

Publication bias was only assessed for the outcome of foot self-care as this was the only outcome with data available from sufficient studies. We used the trim-and-fill method, proposed by Duval and Tweedie [27,28], which is based on suppression of the most extreme results on one side of the funnel plot, and amplifying the effects of the remaining studies. This was followed by a weighted regression test using the standard error as the predictor [29].

Statistical analyses were performed using the *metafor* package in R version 3.3.2 [29]. Meta-analyses were conducted using random effects modelling, with heterogeneity calculated using the restricted maximum likelihood estimator.

Results

Study selection

A total of 8399 articles were obtained from the six databases. We identified 2009 duplicates, with the remaining 6390 articles undergoing title and abstract screening. Of these, 6276 articles were excluded. The main reasons for exclusion were inclusion of a study population without diabetes or the article not specifically addressing health literacy. A total of 114 full-text articles were assessed for eligibility; of these, 98 were excluded. Ten articles met the inclusion criteria of valid health literacy and outcome measures, but were excluded as they did not publish data on associations (eight articles) or published data that could not be used in our analyses (two articles). In the latter case, the studies published data with health literacy as part of a structural equation modelling pathway [30,31], which was statistically incompatible for pooling, and thus were excluded. The remaining articles were excluded because of a lack

of exposure or outcome measure (84 articles) or for including a population without diabetes (four articles). Initial agreement between both reviewers was 98.1%, and of the 1.9% disagreed upon (160 articles), all but three articles were resolved by consensus and the rest were adjudicated by the third reviewer.

Sixteen studies were included in the systematic review, of which 11 were also included in the meta-analyses (Fig. 1). The five articles not included in the meta-analyses included single publications on the particular outcome of interest, namely foot ulcer healing [32] and intermittent claudication [33]. The other three reported on foot care, with two providing unstandardized β-coefficients in regression analysis [34,35], and one using low health literacy as a reference group [36]; these studies were statistically incompatible for pooling and were excluded at the meta-analysis stage.

No additional relevant articles were identified from our subscription to the search terms in PubMed.

Characteristics of included studies

The characteristics of studies included in the systematic review are shown in Table 1 [14,19,23–26, 32–37]. Eleven studies provided published data, one provided both published and unpublished data and four provided only unpublished data on request from the present authors. Eleven studies (68.8%) were of cross-sectional design; there was one (6.3%) randomized controlled trial where only baseline data were used. Two studies (12.5%) were designed to validate new health literacy assessment tools. There were also two prospective observational studies (12.5%) in which baseline cross-sectional data were used. We omitted longitudinal results as the prospective components of the prospective studies were not focused on foot outcomes. Twelve studies were based in the USA, and the mean sample size was 321.

The most commonly reported measure of health literacy was the TOFHLA, or the 30-item abbreviated version S-TOFHLA (eight studies, 50%). Three articles (18.8%) used the REALM, and the same number of studies utilized FCCHLS. One study (6.3%) reported on the DNT and one (6.3%) used the Health LITT scale.

Three studies reported on health literacy and diabetic foot disease outcomes of ulceration [19], amputation [14] and the log healing rate of chronic ulcers [32].

Four studies measured risk factors for foot disease. Three assessed peripheral neuropathy by self-report [19] or diagnosis and documentation in medical records [25,26], with health literacy measured using the FCCHLS [25,26] as well as the S-TOFHLA [19]; we obtained unpublished data or sought clarification on data published from the authors of all of these studies. One study assessed intermittent claudication (a symptom of peripheral arterial disease) with S-TOFHLA as the exposure measure. Both studies using the FCCHLS were based in Japan, whereas those using S-TOFHLA were based in the USA.

Ten studies reported on frequency of foot self-care, but in none of these was foot care the primary outcome. Nine had published data and for one we obtained unpublished data from Hahn *et al.* [37]. Exposure measures consisted of the REALM (three articles), TOFHLA or S-TOFHLA (four articles), and one each using the Health LITT tool, FCCHLS and DNT. All articles used the foot care component of the Summary of Diabetes Self Care Activities as outcome measures.

The overall quality of all included studies was high, and the mean score was 90.3%. Studies often fell short where adjustments for covariates were not performed in analyses. There were disagreements on three items requiring further input from a third author.

Associations between health literacy and outcomes of interest

End-stage diabetic foot complications

Two studies of 1278 participants reported on diabetic foot disease; namely, lower limb amputation [14] and self-reported 'ulcers or sores on the foot or leg' [19]. Individuals with inadequate health literacy had almost twice the odds of developing foot disease than those with adequate health literacy [odds ratio 1.99 (95% CI 0.83, 4.78)], but this was not statistically significant (P=0.12).

For the sensitivity analyses, we combined groups of individuals with marginal and adequate health literacy, and individuals with inadequate and marginal health literacy from data obtained from Morris *et al.* [19], which produced similar odds ratios of 1.97 (95% CI 0.80, 4.84; P=0.14) and 1.96 (95% CI 0.82, 4.67; P=0.13), respectively.

A third study in 22 participants [32] reported no statistically significant association between foot ulcer size and duration of S-TOFHLA score. From contacting the authors, we obtained a correlation coefficient of 0.09 between S-TOFHLA score and log healing rate of chronic ulcers. These data were not pooled with foot ulcer incidence and amputation data as these outcomes were not sufficiently clinically similar and there lacked a P value or CI to do so.

A summary of the data is available in Table 2.

Risk factors for diabetic foot disease

There was no statistically significant difference in health literacy levels between people with peripheral neuropathy identified from medical records and those people without (two studies in 42 participants with and 357 participants without peripheral neuropathy; SMD –0.144 (95% CI –0.47, 0.18; *P*=0.38 [Table 2]).

A sensitivity analysis in which unpublished data on self-reported peripheral neuropathy were included was also not statistically significant but yielded a slightly higher SMD [three studies in 330 participants with and 1008 participants without peripheral neuropathy; SMD –0.35 (95% CI –0.70, 0.0003); *P*=0.052]. In a second sensitivity analysis using the full FCCHLS score, health literacy was significantly lower in people with than without for medical record-identified peripheral neuropathy [SMD –0.38 (95% CI –0.70, -0.05); *P*=0.02].

For the risk factor of peripheral arterial disease, a single study measured intermittent claudication in the Self-Administered Comorbidity Questionnaire in 998 people with heart failure and diabetes. It did not report any published associations, but we obtained unpublished data from the authors. In people with intermittent claudication (*n*=88) health literacy was lower than in people without claudication [*n*=915; mean (SD) S-TOFHLA score 26.66 (11.48) and 30.03 (9.30) respectively, SMD –0.35 (95% CI –0.57, –0.14); *P*=0.001].

Foot self-care in people with diabetes

The meta-analysis pooled one standardized β coefficient, five sets of Pearson's correlations and one Spearman's correlation. There was no association between health literacy and foot self-care [correlation = 0.01 (95% CI –0.07, 0.10); *P*=0.73 (Fig. 2)]. There was substantial heterogeneity [heterogeneity/variability ratio (I^2) = 44.76%].

In the present analysis, we used the *a priori* combination of 'sixth grade and below' with 'seventh or eighth grade' based on the publication by Ferguson *et al*. [24]. As a sensitivity analysis, we combined the groups of 'seventh or eighth grade' with 'high school and above', and the result was similar [correlation =0.006 (95% CI –0.08, 0.09); *P*=0.89].

The findings of the article omitted from the meta-analysis described earlier [36], which published data using low health literacy as the reference group, was consistent with the meta-analysis findings in that there was no statistically significant association (β =0.54 for marginal and 0.21 for adequate vs inadequate health literacy; both *P* >0.05). The other two papers that were excluded from the meta-analysis because standardized β-coefficients were unable to be calculated were also similar with the pooled analysis with no effect (unstandardized β-coefficient = –0.3 [35] and 0.138 [34]; both *P*>0.05).

Visual inspection of funnel plots (Fig. 3) suggested no bias towards publication of statistically significant positive associations. This was confirmed statistically by the trim-and-fill method and by absence of funnel plot asymmetry(*P*=0.06).

Discussion

This is the first systematic review to assess the potential impact of health literacy on diabetic foot outcomes. The strongest evidence from seven studies with 1033 participants was for foot self-care, with there being no association between health literacy and self-reported foot care, suggesting that this may not be a major mediator of the effects of health literacy on foot health outcomes. Data for other outcomes were too limited to be conclusive. Unpublished data from a single study suggested that health literacy could have an impact on peripheral arterial disease. The presence of associations of health literacy with peripheral neuropathy

and diabetic foot disease cannot be excluded with these limited data. In particular, a sensitivity analysis for peripheral neuropathy, using a measure of health literacy that was broader than functional health literacy, demonstrated a statistically significant lower level of health literacy in people with peripheral neuropathy compared to those without. Nonetheless, there is an urgent need for robust longitudinal data to properly elucidate whether health literacy has an impact on diabetic foot disease and its risk factors, which, in turn, will assist in deciding whether interventions targeting health literacy should be developed and tested as a way of reducing diabetic foot disease.

Low health literacy is established as an independent risk factor for poorer health outcomes. These include increased risk of hospitalization [38–40], inappropriate medication use, and poorer knowledge of disease processes and outcomes in chronic diseases such as diabetes and hypertension [14,41]. Qualitative studies suggest that health literacy is an important contributor to foot disease development in diabetes [11,42], but unbiased assessment of the overall evidence, until the present review, has been lacking. Our primary analysis of the association of diabetic foot disease with health literacy found a non-statistically significant, but potentially clinically important doubling in the odds of foot disease in individuals with inadequate as compared with adequate health literacy; however, the available data were limited, as there were only two cross-sectional studies with only small numbers of events, so the effects of health literacy on diabetic foot disease cannot be ruled out.

Because of the substantial limitations in the data available, we were also unable to rule out associations between health literacy and risk factors for diabetic foot disease. There are no data investigating associations of health literacy with foot deformity. With regard to peripheral neuropathy, in our primary analysis, there was no evidence of an association

between functional health literacy levels and peripheral neuropathy, but in a sensitivity analysis using the full FCCHLS score there was a larger, statistically significant difference, with health literacy being lower in people with peripheral neuropathy. The latter suggests that aspects of health literacy beyond functional health literacy might be important for preventing peripheral neuropathy. This could potentially apply to diabetic foot disease and other risk factors. Individuals with intermittent claudication had lower health literacy than those without intermittent claudication, but these were unpublished data from a single study in people with diabetes and heart failure and so must be interpreted cautiously in the context of the broader population of people with diabetes.

Nonetheless, the results of the present review, taken in context with the literature about the impact on health literacy on other diabetes complications, indicate that the role of health literacy in the development of diabetic foot disease and its risk factors requires urgent investigation. Initially, longitudinal studies with objective measures of foot disease and its risk factors, and with adequate power and comprehensive measures of health literacy, are required. If these provide stronger evidence that poor health literacy has a role in diabetic foot disease development, randomized controlled trials or intervention studies addressing poor health literacy should follow to substantiate the role of health literacy in foot disease prevention.

The presence of foot ulcer risk factors alone is insufficient to cause ulceration. A significant event, such as trauma, usually from ill-fitting footwear, or repetitive stress, often precipitate injury, which leads to ulceration and non-healing [43,44]. Strong recommendations exist, therefore, for people with diabetes to have annual foot health checks at a minimum, to be aware of their foot risk status, and to participate in a foot protection programme including regular podiatric care [6]. Daily foot inspections are also strongly encouraged to ensure any

potentially pre-ulcerative lesions or injury can be identified and treated [6,45]. These preventative actions can be complex, and require understanding of diabetic foot health; however, our meta-analysis has shown no differences in frequency of self-care between groups of individuals with adequate and inadequate health literacy. Of our three analyses, the meta-analysis included the most available published data, and results across primary and sensitivity analyses were all consistent. This was unexpected, given the detrimental associations of low health literacy with peripheral neuropathy, peripheral arterial disease and diabetic foot disease. A possible explanation for this is that that the effects of peripheral neuropathy and arterial disease on foot health may be largely independent of frequency of foot self-care and perhaps more dependent on other factors, such as overall glycaemic control. Alternatively, the two questions encompassing the outcome measure may not be a sufficiently comprehensive measure of self-care. The foot care section of the Summary of Diabetes Self Care Activities asks respondents to indicate on how many of the last 7 days they checked their feet, or inspected the inside of their shoes [46]. These two questions, whilst an important component of self-care, may be too basic and may not accurately represent the spectrum of more complex and demanding self-care actions. More thorough questionnaires, incorporating scales identifying knowledge of correctly identifying footwear, or requiring demonstration of understanding of legitimate concerns or injuries to the feet may capture aspects of foot self-care more likely to be influenced by health literacy.

The present meta-analysis has some limitations. There were few studies reporting diabetic foot disease outcomes and peripheral neuropathy, and only a single study reporting on peripheral arterial disease, which limits the precision and robustness of the findings. Numbers were also insufficient to perform subgroup analyses or meta-regression to look at study-level variables that might have affected the findings. No studies reported on the third major risk factor of foot deformity.

Publication bias is also a possibility; however, there was little evidence of publication bias for studies of foot self-care, suggesting this may not be an issue for other outcomes. Our search was last formally updated in June 2016 because of our intensive seeking of unpublished data to maximize the data available for the review. While we cannot rule out the possibility that more recent studies have been published, to our knowledge from subscribing to alerts of newly published journal articles with search terms used for this review in PubMed, no relevant studies have been published since our exhaustive search in June 2016. Finally, we limited search results to full-text articles in English; this was a practical decision because of the large number of search terms and articles returned and our limited capacity to translate articles not written in English.

We acknowledge that pooling the outcomes of ulceration and lower limb amputation may be questioned, although they could be considered as being at different points of the spectrum of diabetic foot disease and are likely to be related. Although both are considered end-stage complications of diabetes, prompt multidisciplinary care is effective in facilitating ulcer healing and preventing amputations [7], but there is a paucity of literature in preventing ulcer occurrence in people with diabetes [7]. Assessing the effect of health literacy on these outcomes separately might provide a better indication as to the potential value of health literacy interventions in preventing each condition, but this was not possible because of the dearth of appropriate studies. We also note that the study on peripheral arterial disease was undertaken in the context of heart failure [33], so this finding may not be generalizable to people with diabetes who do not have heart failure. Moreover, most studies were based in the USA (10 articles), with the others based in different countries in Asia, which could limit the generalizability of findings to other countries and different healthcare systems. Nevertheless,

health literacy is recognized as important for health outcomes globally [40], and this should not negate the importance of the present findings.

Whilst all exposure measures of health literacy used in the studies in the present review have established validity and reliability, they focus on the functional aspect of health literacy, and have been criticized as having narrow underlying constructs and content, failing to encompass the entire scope of health literacy. This is critical; a key failing of these tests is that none fully measure an individual's ability to seek, understand and use health information [47]. This is illustrated by our sensitivity analysis for peripheral neuropathy in which there was a larger effect size when using available data on full FCCHLS score compared with the subscale for functional health literacy alone. In future studies, adding recently developed health literacy measures, such as the Health Literacy Questionnaire [48], which assess wider aspects of health literacy may contribute to a better understanding of the relationship between health literacy and diabetic foot outcomes.

Finally, although the cross-sectional nature of the studies included in the present review prohibits attribution of causation, it is plausible that improving health literacy in people with diabetes may help prevent the development or progression of risk factors for diabetic foot disease. Nonetheless, these findings require confirmation in longitudinal studies.

In summary, the present systematic review clearly shows that data from the current literature are insufficient to exclude associations between health literacy and diabetic foot disease and its risk factors, but that health literacy appears unlikely to have an important role in foot self-care. With a lifetime incidence of foot disease of up to 25% [49] in people with diabetes, this is an important evidence gap, the filling of which could influence and improve patient

education and potentially prevent foot disease development. With the growing burden of diabetic foot disease [2], targeting health literacy and improving delivery of diabetic foot care education should be viewed as potentially instrumental in retarding progression of this important, expensive and debilitating consequence of diabetes. This review supports the need for the contribution of low health literacy to diabetic foot disease development to be definitively assessed through robust, adequately powered, longitudinal studies using comprehensive measures of health literacy. This is imperative to provide stronger evidence of health literacy contributing to the causal pathway for diabetic foot disease and to provide evidence to support randomized controlled trials to assess the efficacy of health literacy interventions for preventing the development of risk factors for end-stage complications and indeed end-stage disease itself.

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Competing interests

None declared.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Search Strategy in PubMed MEDLINE, replicated for use in other databases.

Appendix S2. List of criteria for assessment of the methodological quality for cohort, cross-sectional and case–control studies.

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Fig. 2 Forest plot of meta-analysis of association of health literacy with frequency of foot care in people with diabetes.

Fig. 3 Funnel plot of articles publishing on associations of health literacy with frequency of foot self-care.

Table 1 Description of included studies

Author, year	Country	Design	Exposure measure	Outcome measure	Participants, *n*	Quality, %
Morris, 2006 [19]	USA	Cross-sectional	S-TOFHLA	Foot ulceration (self-reported), peripheral neuropathy (self-reported) *	1002	81.8
Schillinger, 2002 [14]	USA	Cross-sectional	S-TOFHLA	Amputation (foot or leg)	408	100
Margolis, 2015 [32]	USA	Cross-sectional and prospective cohort	S-TOFHLA	Foot ulcer wound size, duration and healing	41 (cross-sectional) 22 (cohort)	29.4
Inoue, 2013 [25]	Japan	Cross-sectional	FCCHLS	Peripheral neuropathy*	269	100
Ishikawa, 2008 [26]	Japan	Validation of FCC HLS	FCCHLS	Peripheral neuropathy*	138	100
Bains, 2011 [23]	USA	Cross-sectional	REALM	Foot care component of SDSCA	125	100
McCleary-Jones, 2011	USA	Cross-sectional	REALM	Foot care component of SDSCA	50	90.9
White, 2011	USA	Validation of Diabetes Numeracy	DNT-Latino	Foot care component of SDSCA	146	100

		Test				
Lai, 2012	Singapore	Cross-Sectional	FCC HLS	Foot Care component of SDSCA	63	90.9
White, 2013 [35]	USA	Cross-sectional	TOFHLA	Foot Care component of SDSCA	140	100
Kim, 2004	USA	Prospective observational	S-TOFHLA	Foot Care component of SDSCA	77	90.9
Eyuboglu, 2016 [34]	Turkey	Cross-sectional	S-TOFHLA	Foot Care component of SDSCA	167	90.9
Ferguson, 2015 [24]	USA	Cross-sectional component of RCT	REALM	Foot Care component of SDSCA	280	81.8
Hahn, 2015* [37]	USA	Cross-sectional	Health LITT	Foot Care component of SDSCA	295	100
Laramee, 2007 [33]	USA	Cross-sectional	S-TOFHLA	Intermittent Claudication	998	87.5
Walker, 2014 [36]	USA	Cross-sectional	S-TOFHLA	Foot care component of SDSCA	615	100

*Denotes additional data (unpublished) obtained from authors.

DNT, Diabetes Numeracy Test; FCCHLS, Functional Communicative and Critical Health Literacy Scale; REALM, Rapid Estimate of Adult Literacy in Medicine; SDSCA, Summary of Diabetes Self Care Activities; S-TOFHLA, short-form Test of Functional Health Literacy in Adults.

Table 2 Associations of health literacy with diabetic foot disease and its risk factors

Outcome	Number of studies	Number of participants	Measure	Effect size (95% CI)	Heterogeneity
Diabetic foot disease	2	1278	Odds Ratio	1.99 (0.83, 4.78)	64.5%
Peripheral neuropathy	2	399	SMD*	–0.14 (–0.47, 0.18)	0%
Intermittent claudication	1	998	SMD*	–0.35 (–0.57, –0.14)*	NA

NA, not applicable; SMD, standardized mean difference.

*Denotes statistically significant (P<0.05).