PLOS ONE

RESEARCH ARTICLE

Prevalence of diabetic foot at risk of ulcer development and its components stratification according to the international working group on the diabetic foot (IWGDF): A systematic review with metanalysis

Tania Maldonado-Valer[1], Luis F. Pareja-Mujica[1], Rodrigo Corcuera-Ciudad[2], Fernando Andres Terry-Escalante[3,4], Mylenka Jennifer Chevarría-Arriaga[3], Tery Vasquez-Hassinger[1], Marlon Yovera-Aldana[5]*

1 Universidad Científica del Sur, Lima, Peru, **2** Universidad Científica del Sur, Facultad de Ciencias de la Salud, Carrera de Medicina Humana, CHANGE Research Working Group, Lima, Peru, **3** Universidad de San Martín de Porres, Facultad de Medicina Humana. Lima, Peru, **4** Red de Eficacia Clínica y Sanitaria (REDECS), Lima, Peru, **5** Grupo de Investigación en Neurociencias, Efectividad Clínica y Salud Pública, Universidad Científica del Sur, Lima, Peru

* myovera@cientifica.edu.pe

Abstract

Aims

To determine the overall prevalence of diabetic foot at risk according to the International Working Group on the Diabetic Foot stratification.

Materials and methods

We searched PubMed/Medline, Scopus, Web of Science, and Embase. We included cross-sectional studies or cohorts from 1999 to March 2022. We performed a meta-analysis of proportions using a random-effects model. We assessed heterogeneity through subgroup analysis by continent and other characteristics.

Results

We included 36 studies with a total population of 11,850 people from 23 countries. The estimated overall prevalence of diabetic foot at risk was 53.2% (95% CI: 45.1–61.3), I2 = 98.7%, p < 0.001. In the analysis by subgroups, South and Central America had the highest prevalence and Africa the lowest. The factors explaining the heterogeneity were the presence of chronic kidney disease, diagnostic method for peripheral arterial disease, and quality. The estimates presented very low certainty of evidence.

Conclusions

The overall prevalence of diabetic foot at risk is high. The high heterogeneity between continents can be explained by methodological aspects and the type of population. However,

using the same classification is necessary for standardization of the way of measuring the components, as well as better designed general population-based studies.

Introduction

Globally, one out of every six patients with diabetes mellitus (DM) will develop an ulcer in the lower limb at some point in their lives. Likewise, 85% of the patients with lower limb amputation, presented an ulcer that could be prevented [1]. In the US, one third of the direct costs of diabetes are caused by diabetic foot problems. The investment in diabetic foot treatment is similar to the expense related to oncological diseases [2]. The high disease burden requires the installment of an early screening to decrease these outcomes.

The main risk factors for diabetic foot ulcer are peripheral neuropathy (PN), peripheral artery disease (PAD), biomechanical deformity and limited articular mobility. Diverse academic organizations established the "foot at risk" terminology, in presence of any of them or combination [3]. There are several classification systems, sharing similar categories and components. One of the most frequently used is the International Working Group on Diabetic Foot (IWGDF) classification [4]. It allows a practical and accessible evaluation in limited-resource environments. Furthermore, it has already been assessed by validation studies in prospective studies [5]. Therefore, the early detection of diabetic foot at risk, as well as an adequate follow-up and preventive measures are essential necessities [6].

According to a global systematic review of PN on patients with DM, there is a broad range of prevalence's that indirectly reflect the impact of an adequate glycemia or metabolic control on the strategies from world-wide healthcare systems in the prevention of non-transmissible diseases [7]. Outlining that developing countries are overcoming an epidemiological transition, simultaneously coexisting with infectious diseases burden [8]. Given that, we aim to estimate the global prevalence of diabetic foot at risk base on the IWGDF stratification and explain the heterogeneity of the estimated proportions through a systematic review with metanalysis.

Materials and methods

This study was conducted following the "Preferred Reporting Items for Systematic reviews and Meta-Analyses" (PRISMA) guidelines [9]. This protocol has been registered on PROSPERO database with the following code: CRD42021254275.

Literature search

The search was conducted on Medline/PubMed, Web of Science, Scopus and Embase. The temporality of the search was restricted from 2000 until the last systematic search on March 4th of 2022, given that IWGDF stratification was created in 1999.

We used the Medical Subject Headings (MeSH) terms "prevalence", "risk", "Mass screening", "Cross-Sectional Studies", "diabetic foot", "foot ulcer", "risk assessment". As well as free terms as "screen*", "cross-sectional", "prevalenc*", "transvers*", "risk", "at-risk", "diabetic foot", "foot ulcer", "diabetic feet", "International Working Group on the Diabetic Foot", "IWGDF", "classificat*" and "stratificat*". The search strategy was modified according to the compatibility of each database, and the precision of the results was verified with previous studies.

A filter for transversal studies was included with the objective to discard other types of studies. Moreover, a manual search of grey literature was performed. The bibliographic references of all the included studies were reviewed in order to identify other studies that fulfilled the eligibility criteria. The complete search strategy can be seen at **S1 Table**.

Eligibility criteria

The inclusion criteria were the following: (a) Studies that describe subjects with type 1 and/or type 2 DM (b) Diabetic foot at risk assessment according to IWGDF classification (c) Transversal or cohort studies (d) Any language. Were excluded: (a) Studies that included patients with active foot ulcer, who were not possible to exclude them (b) Studies with the same reference population (c) Other study designs: Case-control studies, letter to the editor and reviews.

Selection and extraction of data

All the phases of the data selection were performed using the Rayyan software [10]. Duplicated documents were eliminated with the Brammer method on EndNote X9 [11]. Two reviewers (TMV and LFPM) independently screened the studies by tittle and abstract. Any discrepancy was solved by a third author (MYA). Finally, the same reviewers independently assessed the full text of the study to check if they fulfilled the eligibility criteria. The disagreements were solved by a third author (MYA). The complete list of included studies can be seen at **Table 1**. The excluded studies on the full text phase are presented on the **S2 Table**.

Data extraction was independently done by two reviewers (TMV and LFPM), who collected all the variables of interest on an Excel 365 spreadsheet. The data collected from each study were author, year of publication, country, study design, type of population, total population, type of healthcare center, continent, type of DM, history of chronic kidney disease (CKD). All the extracted was coded for the posterior analysis.

Likewise, the reviewers extracted the mean and standard deviation of the age and time of DM, the number of subjects according to sex, foot at risk, PN, PAD, biomechanical deformity, ulcer history, as well as the grade 0, 1, 2 and 3, the diagnostic tests used for PN, PAD and biomechanical deformity on each study.

Risk of bias assessment

The quality of studies was assessed using the questionnaire developed by Loney [12], which evaluates the quality of the study assigning one point to each of the eight criteria grouped in 3 dimensions: validity, results and applicability. The risk of bias assessment was done by two reviewers (TMV and LFPM). All the disagreements were solved through discussion. If it was not possible to achieve consensus after an exhaustive discussion between the reviewers, the opinion of a third reviewer was considered (MYA). The majority consensus made the final decision. For this analysis, a score of seven to eight accounted for a high quality; five to six, accounted for moderate quality; three to four accounted for low quality; and two or less for very low quality. Fort the adequate sample size item, we considered a size of 373 subjects. This was calculated considering a prevalence of 41.36% reported by Lavery with a precision of 5% and a confidence level of 95% [13]. A detailed analysis of the evaluation can be seen in **S3 Table**.

Statistical analysis

We calculated the pooled foot at risk prevalence with the corresponding 95% confidence interval (CI), expressed as the percentage of diabetic subjects. The extracted data were quantitatively synthesized using metanalysis techniques. A Freeman-Turkey Double Arcsine

Table 1. Characteristics of 36 included studies of Prevalence of foot at risk of ulceration according to IWGDF stratification.

	Author (year)	Country	Design of study	Population, age, male (%), number of centers	Diabetes: type and time of disease	Sample size	Sum of foot at risk	G1/ G2/ G3	Peripheral neuropathy	Peripheral arterial disease	Biomechanical deformity	History of ulcer	Quality (total score)
1	Peters (2001)	United states	Cohort	**Population**: Hospital **Age**: 52.6 ± 10.4 **Male n (%)**: 99 (46.4) **Center**: Unicenter	**Type**: 2 **Time**: 11 ± 9.3	213	134	21/ 51/ 62	73	67	105	62	Moderate (5 points)
2	Malgrange (2003)	France	Cross-sectional	**Population**: Hospital **Age**: 56 ± 15 **Male n (%)**: 286 (51.3) **Center**: Unicenter	**Type**: 1 and 2 **Time**: 13 ± 10.4	555	151	54/ 54/ 43	150	94	117	35	Moderate (6 points)
3	Mugambi (2009)	Kenia	Cross-sectional	**Population**: Hospital **Age**: 55.9 ± 9.8 **Male n (%)**: 120 (55.0) **Center**: Unicenter	**Type**: 1 y 2 **Time**: 13.8 ± 5.4	218	94	22/ 35/ 37	92	26	98	37	Moderate (5 points)
4	Gonzalez de la Torre (2010)	Spain	Cross-sectional	**Population**: Primary **Age**: 64.35 ± 12.22 **Male n (%)**: 54 (56.2) **Center**: Unicenter	**Type**: 1 y 2 **Time**: -	96	53	14/ 25/ 14	-	16	18	14	Moderate (5 points)
5	Monteiro-Soares (2012)	Portugal	Cohort	**Population**: Hospital **Age**: 65 ± 10.6 **Male n (%)**: 177 (48.6) **Center**: Multicenter	**Type**: 2 **Time**: 17 ± 10.7	364	237	21/ 90/ 126	183	46	259	128	Moderate (5 points)
6	Shahbazian (2013)	Iran	Cross-sectional	**Population**: Hospital **Age**: 53.8 ± 10.7 **Male n (%)**: 161 (37.4) **Center**: Unicenter	**Type**: 1 y 2 **Time**: 8.1 ± 6.6	430	153	75/ 47/ 31	264	7	81	31	Moderate (5 points)
7	Bortoletto MS (2014)	Brazil	Cross-sectional	**Population**: Primaria **Age**: ND **Male n (%)**: 136 (40.3) **Center**: Multicenter	**Type**: 1 y 2 **Time**: ND	337	97	3/ 82/ 12	-	-	-	12	Moderate (5 points)
8	Alonso-Fernández (2014)	Spain	Cross-sectional	**Population**: Primaria **Age**: 68.9 ± 12 **Male n (%)**: 213 (48.0) **Center**: Multicenter	**Type**: 2 **Time**: 9.2 ± 6.4	443	93	53/ 23/ 17	38	42	64	17	Moderate (6 points)

(Continued)

Table 1. (Continued)

	Author (year)	Country	Design of study	Population, age, male (%), number of centers	Diabetes: type and time of disease	Sample size	Sum of foot at risk	G1/ G2/ G3	Peripheral neuropathy	Peripheral arterial disease	Biomechanical deformity	History of ulcer	Quality (total score)
9	Tshitenge (2014)	Botswana	Cross-sectional	**Population:** Hospital **Age:** ND **Male n (%):** 46 (31.9) **Center:** Unicenter	**Type:** 2 **Time:** ND	144	22	10/ 7/5	-	-	-	5	Moderate (5 points)
10	Wu (2015)	China	Cross-sectional	**Population:** Hospital **Age:** 59.77 ± 11.83 **Male n (%):** 156 (52.7) **Center:** Unicenter	**Type:** 1 y 2 **Time:** 7.4 ± 5.78	296	192	47/ 108/ 37	196	-	80	37	Moderate (5 points)
11	Isip, (2016)	Philippines	Cross-sectional	**Population:** Hospital **Age:** 63.8 ± 9.42 **Male n (%):** 46 (27.0) **Center:** Unicenter	**Type:** 1 y 2 **Time:** -	170	107	29/ 62/ 16	97	32	53	16	Moderate (5 points)
12	Damas-Casani (2017)	Peru	Cross-sectional	**Population:** Hospital **Age:** 60.3 ±11.1 **Male n (%):** 96 (25.9) **Center:** Unicentro	**Type:** 2 **Time:** -	370	288	29/ 235/ 24	131	145	201	24	Moderate (5 points)
13	Kahn (2017)	Pakistan	Cross-sectional	**Population:** Primary **Age:** 53.82 ±9.96 **Male n (%):** - **Center:** Unicentro	**Type:** 2 **Time:** 7.87 ± 5.50	230	75	37/ 6/32	70	30	11	32	Moderate (5 points)
14	Lucoveis (2018)	Brazil	Cross-sectional	**Population:** Hospital **Age:** ND **Male n (%):** 18 (36.0) **Center:** Unicenter	**Type:** 1 y 2 **Time:** ND	50	17	8/3/ 6	-	6	11	6	Moderate (5 points)
15	Rodríguez (2018)	Peru	Cross-sectional	**Population:** Primary **Age:** ND **Male n (%):** 122 (40.5) **Center:** Unicenter	**Type:** 2 **Time:** ND	301	40	12/ 28/0	40	56	193	-	Moderate (5 points)
16	Vibha (2018)	India	Cross-sectional	**Population:** Hospital **Age:** 63.37 ±10.8 **Male n (%):** 264 (42.5) **Center:** Unicenter	**Type:** 2 **Time:** ND	620	321	194/ 74/ 53	321	67	65	53	Moderate (6 points)

(*Continued*)

Table 1. (Continued)

	Author (year)	Country	Design of study	Population, age, male (%), number of centers	Diabetes: type and time of disease	Sample size	Sum of foot at risk	G1/ G2/ G3	Peripheral neuropathy	Peripheral arterial disease	Biomechanical deformity	History of ulcer	Quality (total score)
17	Cardona (2018)	Cuba	Cross-sectional	**Population:** Primary **Age:** ND **Male n (%):** 145 (27.1) **Center:** Unicenter	**Type:** 2 **Time:** 11.88 ± 10.29	534	424	165/ 241/ 18	375	239	339	18	Moderate (5 points)
18	Tindong (2018)	Cameroon	Cross-sectional	**Population:** Hospital **Age:** ND **Male n (%):** - **Center:** Multicenter	**Type:** 2 **Time:** ND	203	39	14/ 16/9	34	23	14	9	Moderate (5 points)
19	Ramírez (2019)	Venezuela	Cross-sectional	**Population:** - **Age:** 63 ± 11 **Male n (%):** 36 (36) **Center:** Unicenter	**Type:** 1 y 2 **Time:** 13.6 ± 11.0	100	95	5/ 74/ 16	-	-	-	16	Low (4 points)
20	Cardoso (2019)	Brazil	Cross-sectional	**Population:** Primary **Age:** 59.6±12.8 **Male n (%):** 30 (35.2) **Center:** Unicenter	**Type:** 1 y 2 **Time:** 14.5 ±9.0	85	52	25/ 20/7	50	25	5	7	Moderate (5 points)
21	Banik (2020)	Bangladesh	Cross-sectional	**Population:** Primary **Age:** 51.6 ± 11.9 **Male n (%):** 445 (37.0) **Center:** Unicenter	**Type:** 2 **Time:** 6.9 ±5.9	1200	534	50/ 142/ 342	-	-	-	342	Moderate (6 points)
22	Zantour (2020)	Tunisia	Cross-sectional	**Population:** Hospital **Age:** 55.07 ± 13.54 **Male n (%):** 106 (48.1) **Center:** Unicenter	**Type:** 1 y 2 **Time:** 9.7 ± 5.19	220	60	13/ 39/8	52	81	96	8	Moderate (5 points)
23	Gonzales de la Torre (2020)	Spain	Cross-sectional	**Population:** Primary **Age:** 66.93±10.85 **Male n (%):** 102 (56.0) **Center:** Unicenter	**Type:** 1 y 2 **Time:** ND	182	60	27/ 14/ 19	40	39	4	19	Moderate (5 points)
24	Mizouri (2021)	Tunisia	Cross-sectional	**Population:** Hospital **Age:** 55.8 ± 14.22 **Male n (%):** 33 (40.24) **Center:** Unicenter	**Type:** 1 y 2 **Time** 9.98 ± 8.11	82	47	18/ 26/3	-	-	-	3	Moderate (5 points)

(*Continued*)

Table 1. (Continued)

	Author (year)	Country	Design of study	Population, age, male (%), number of centers	Diabetes: type and time of disease	Sample size	Sum of foot at risk	G1/ G2/ G3	Peripheral neuropathy	Peripheral arterial disease	Biomechanical deformity	History of ulcer	Quality (total score)
25	Castañeira (2018)	Cuba	Cross-sectional	**Population:** Hospital **Age:** - **Male n (%):** - **Center:** Unicenter	**Type:** 1 y 2 **Time:** -	111	105	27/ 17/ 61	-	-	-	61	Low (4 points)
26	Mineoka (2022)	Japan	Cross-sectional	**Population:** Hospital **Age:** - **Male n (%):** - **Center:** Unicenter	**Type:** 2 **Time:** -	469	200	150/ 38/ 12	-	-	-	12	Moderate (6 points)
27	Formiga (2020)	Brazil	Cross-sectional	**Population:** Primary **Age:** 73.3 ± 7.8 **Male n (%):** 72 (28.3) **Center:** Multicenter	**Type:** 2 **Time:** 10.1 ± 8	254	163	111/ 12/ 40	-	-	-	40	Low (4 points)
28	Elsharawy (2012)	Saudi Arabia	Cross-sectional	**Population:** Hospital **Age:** 56.9 ± 6.27 **Male n (%):** 138 (43.4) **Center:** Unicenter	**Type:** 1 y 2 **Time:** 12.4 ± 4.2	318	144	88/ 43/ 13	-	-	-	13	Moderate (5 points)
29	Álvarez (2015)	Cuba	Cross-sectional	**Population:** Hospital **Age:** 51 **Male n (%):** 123 (58.0) **Center:** Unicenter	**Type:** 1 y 2 **Time:** 9.88 ± 9.98	212	140	39/ 52/ 49	135	49	62	49	Moderate (5 points)
30	Lavery (2003)	United States	Cohort	**Population:** Primary **Age:** 69.1 ± 11.1 **Male n (%):** 838 (50.3) **Center:** Unicenter	**Type:** 1 y 2 **Time:** 11.2 ± 9.5	1666	689	98/ 411/ 180	690	205	1051	180	Moderate (6 points)
31	Ndip (2010)	London	Cross-sectional	**Population:** Hospital **Age:** 64 **Male n (%):** - **Center:** Unicenter	**Type:** 1 y 2 **Time:** -	326	286	47/ 134/ 105	232	169	93	105	Moderate (5 points)
32	Ndip (2010)	London United States	Cross-sectional	**Population:** Hospital **Age:** 60 ± 13 **Male n (%):** 247 (53.0) **Center:** Multicenter	**Type:** 1 y 2 **Time:** 20 ± 10	466	445	32/ 232/ 181	373	266	-	181	Moderate (6 points)
33	Yusuf (2016)	Indonesia	Cross-sectional	**Population:** Hospital **Age:** - **Male n (%):** 94 (42.9) **Center:** Unicenter	**Type:** 2 **Time:** -	219	129	14/ 98/ 17	-	-	-	17	Moderate (5 points)

(*Continued*)

Table 1. (Continued)

	Author (year)	Country	Design of study	Population, age, male (%), number of centers	Diabetes: type and time of disease	Sample size	Sum of foot at risk	G1/ G2/ G3	Peripheral neuropathy	Peripheral arterial disease	Biomechanical deformity	History of ulcer	Quality (total score)
34	Dòria (2016)	Spain	Cross-sectional	**Population:** Hospital **Age:** - **Male n (%):** 53 (63.8) **Center:** Multicenter	**Type:** 1 y 2 **Time:** -	83	80	18/ 32/ 30	-	-	-	30	Moderate (5 points)
35	Bañuelos (2013)	Mexico	Cross-sectional	**Population:** Primary **Age:** 58,8±12,2 **Male n (%):** 26 (29.8) **Center:** Unicenter	**Type:** 2 **Time:** 9,1 ±7,4	87	56	44/ 10/2	21	10	44	2	Low (4 points)
36	Akila (2021)	India	Cross-sectional	**Population:** Hospital **Age:** - **Male n (%):** 85 (43.3) **Center:** Unicenter	**Type:** 1 y 2 **Time:** -	196	35	34/ 1/0	-	-	10	-	Moderate (5 points)

G1: Grade 1. G2: Grade 2. G3: Grade 3.

transformation was used to stabilize the variances before applying the metanalysis [14]. Due to the high expected heterogeneity, a random effects model was employed according to the Der-Simonian and Laid method [15]. The assessment of the heterogeneity between studies was performed through a Cochrane chi-square and using the I^2 statistic to classify the heterogeneity degree (Low: <40%, Moderate: 30–60%. Substantial: 50–90%. High: 75–100%) [16].

To evaluate the sources of heterogeneity between primary studies, a subgroup analysis by continent, sex, type of DM, type of population, age group, time of DM and history of CKD was performed. We selected these factors due to their evidence from systematic reviews. The prevalence of foot at risk varies according to the prevalence of diabetes in the continent, demographic characteristics and presence of complications [3]. Additionally, a sensitivity analysis was run according to the methodological characteristics such as year of publication, type of study, number of centers, sample size and the quality score.

A meta regression was run following the Thompson and Higgins [17] recommendations to adjust the influence of potential confounding factors on the prevalence of diabetic foot at ulceration risk. The hypothesis that factors like age, sex, time of DM, continent, type of population, type of DM, history of CKD, year of publication, type of study, number of centers, sample $\geq$ 373, quality score, diagnostic method of PN, PAD and biomechanical deformity would influence on the estimation of the prevalence, was established. All the statistical analysis were run using STATA 15.1.

Publication bias

The publication bias in prevalence systematic reviews implies assessing the bias of small studies. Given that, there isn't a value that predisposes to the publication of itself, also called, bias due to positive results. The funnel plot was graphed using the effect size and the standard error from the effect size. An Egger's test was performed, considering a p-value < 0.1 to determine

the asymmetry. If the former analysis demonstrates asymmetry between included studies, the trim and fill random effects model was applied. This command imputes studies and calculates a new prevalence estimate.

Geographical assessment

We made a global representation of the prevalence of foot at risk grouped by continent, detailing the number of studies, pooled prevalence and sample size.

Evidence certainty assessment

We assessed the certainty of the diabetic foot at risk prevalence using The grading of recommendation, assessment, development, and evaluation (GRADE) approach [18]. We based our assessment on five domains, as indicated in the GRADE manual: the study limitations (risk of bias from the studies included), imprecision (sample size and CI), indirectness (generalizability), inconsistency (heterogeneity) and publication bias [16]. The prevalence estimates evaluation was adapted. The potential result was characterized as high, moderate, low or very low. The results were summarized in a "Summary of findings table (SoF)", manually adapted from the online tool GRADE [16].

Ethics

This research did not include people, we only evaluated published studies. It was not necessary to require participan consent. We obtained authorization from the Institutional Ethics and Research Committee of thethrough the certificate 122-CIEI-CIENTIFICA-2021.

Results

Search results

During the initial systematic review, a total of 739 studies were identified, from which 299 duplicates were removed. During the screening by tittle and abstract, the potentially eligible studies quantity was reduced from 440 to 47. Posteriorly, in the full-text evaluation, 18 documents were excluded (**S2 Table**). In the manual search 7 documents were added. Finally, 36 studies were included in the analysis (**Fig 1**).

Studies characteristics

The included studies showed publication dates from 2001 to 2022. Ten studies were from Asia [19–28] and South America/Caribe [29–38], seven from Europe [39–45], five from Africa [46–50] and three from North America [13, 51, 52]. The study from Ndip et al. was conducted in the United Kingdom and United States [53]. (**Fig 2**). The most frequent population scenario was inpatient with 23 studies [19–24, 26, 27, 30, 34, 36, 37, 39, 41, 44–51, 53]. Regarding the type of DM, 23 studies [13, 19, 21, 22, 24, 26, 27, 30, 32, 33, 36–40, 43–46, 48–50, 53] didn't specify the type of DM. Only three studies included population with CKD [44, 45, 53]. According to study design, the mayority was cross-sectional [19–40, 42–50, 52, 53]. and only 7 were multicenter studies [32, 33, 35, 39, 42, 45, 48, 53]. **Table 1** shows all the descriptive information of each study, including the male population, number of centers and so on.

Risk of bias assessment on the included studies

The quality score of the included studies varied between 4 and 6. Four studies [33, 35, 37, 52] presented a low quality, and 32 studies [13, 19–32, 34, 36, 38–51, 53, 54] a moderate quality.
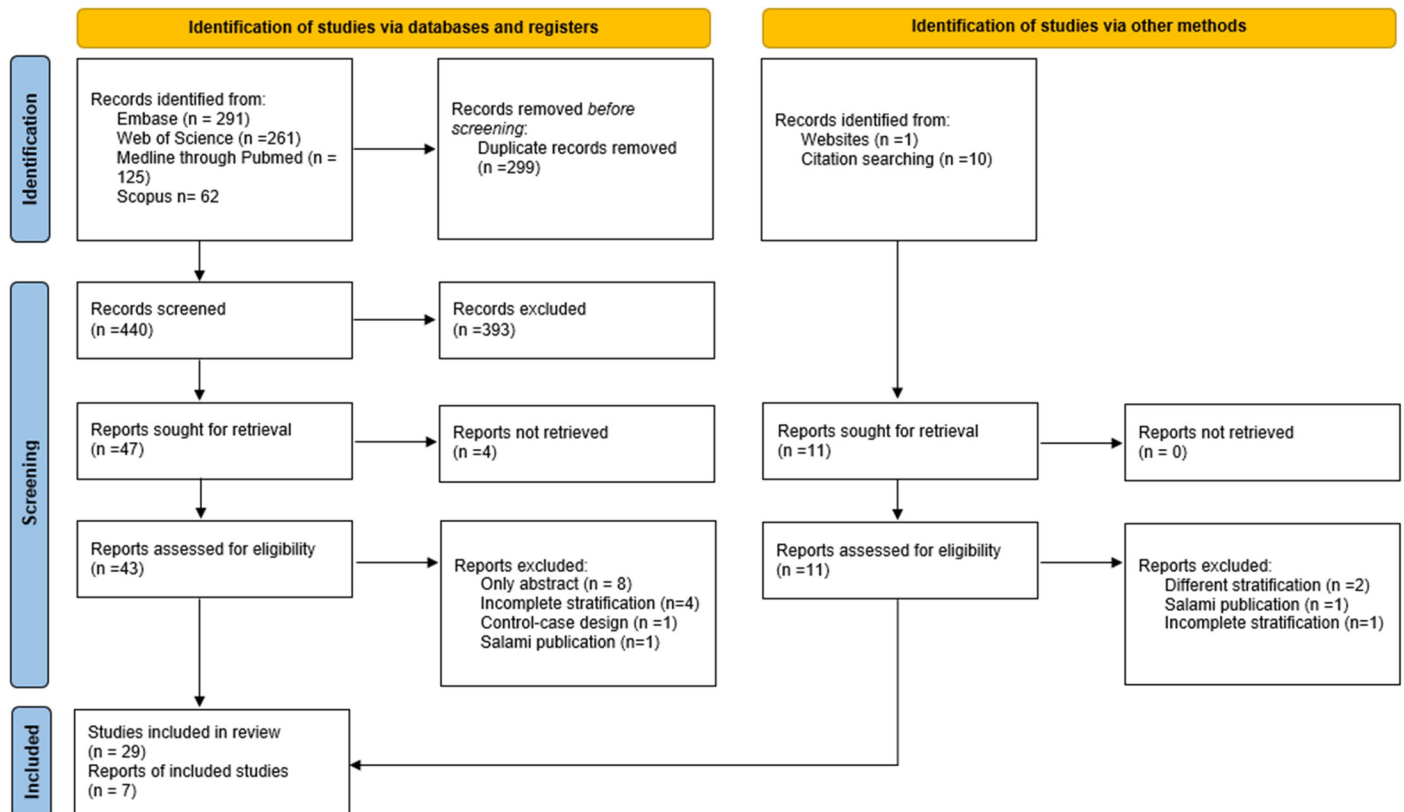
Fig 1. Flow chart for the selection of included studies. From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. The PRISMA Statement and the PRISMA Explanation and Elaboration document are distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. (http://prisma-statement.org/PRISMAStatement/CitingAndUsingPRISMA.aspx.

https://doi.org/10.1371/journal.pone.0284054.g001

Fig 2. Prevalence of foot at risk according to IWGDF stratification: characteristics and geographical location by continents of the included studies. "Continental organizations" by Sbb1413 is licenced under CC-BY 4.0/Modified from original.

https://doi.org/10.1371/journal.pone.0284054.g002

The most frequent unreached criteria were an inadequate sampling design (100%), inadequate sampling frame (100%), followed by an inadequate sample size (75%), and finally, not running a subgroup analysis (16%). All the studies presented validated criteria while using the IWGDF classification, according to the guideline standards, and adequately describing its population. The details of the evaluation can be observed at the **S3 Table.**
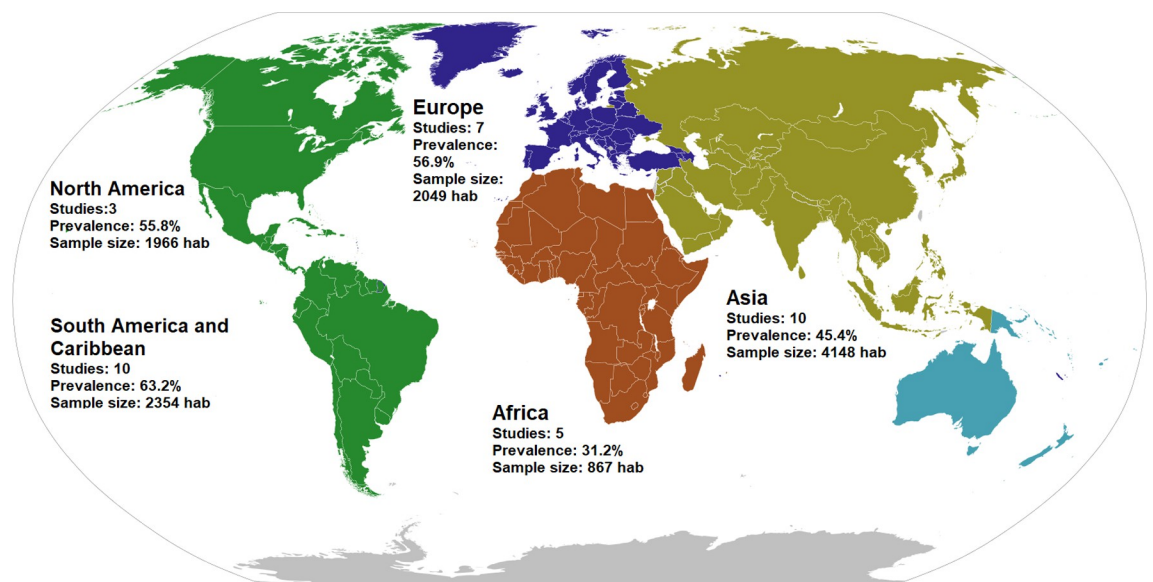
Pooled estimations and cumulative metanalysis

The pooled prevalence of diabetic foot at risk was 53.2% (95% CI: 45.1–61.3) in 36 studies (n = 11 850). A high heterogeneity was identified (I^2 = 98.7%, p <0.001) (**Fig 3**).

The pooled prevalence didn't show any defined temporal variation. The estimation of the first study in 2001 was 62.9%% (95% CI: 49.5–76.3) and in 2022 was 52.0% (95% CI: 44.6–59.3). (**Fig 4**)

The most frequent components were diabetic neuropathy (42.5%; IC 95%: 42.5–51.7) and biomechanical deformity (28.9%; 95%CI 16.6–39.3).. For those who presented foot at risk, the highest percentage corresponds to grade 2 (20.2%; 95%CI 15.2–25.6). (**Table 2**).

Subgroup analysis

In the analysis according to continent, South America and Central America (SACA) presented the highest prevalence (63.2%; 95% CI 43.9–80.6); the lowest prevalence was identified in Africa (31.3%; 95%CI 18.8–45.3).

Of the demographic variables, the highest prevalence of foot at risk was observed in those with an average age equal to or greater than 60 years. (67.0%; 95%CI 53.0–79.7) and those in which men were more than 50% (60.4%; 95%CI 41.4–78.0).

Studies carried out in hospitals or reference centers (55.6%; 95% CI 44.5–66.5), had a higher prevalence than those carried out in primary care centers (44.3%; 95% CI 33.4–55.4).

Only 13 studies specified the type of diabetes they included. The prevalence in type 2 DM was 48.9% (95%CI: 36.3–61.6). There were no studies indicating to include subjects with tipe 1 DM. In studies whose average time of diabetes was greater than 10 years, the prevalence was 66.1% CI95% 46.8–83. Population-based studies with chronic kidney disease had a prevalence of 93.4% (95% CI 87.1–97.8) (**Table 3**).

Sensitivity analysis

The pooled prevalence, by individually excluding each study, varied between 50.60% (95%CI: 43.71–57.50) and 53.12% (95%CI: 45.89–60.42). No single study influenced on the pooled evidence estimation was identified (**Fig 5**). The published studies between 1999 and 2010 presented a prevalence of 61.2% (95%CI: 37.9–82.0) and the published between 2011 and 2022 presented a prevalence of 51.2% (42.7–59.7).

The prevalence of foot at risk was higher on low-quality studies 82.0% (95%CI: 61.3–96.0), while lower to moderate quality studies 49.3% (95%CI: 45.1–57.7). We defined an adequate sample size of a prevalence study if it was greater than 373 considering an expected frequency of 42% and a precision of 5%. According to this limit, in studies with a sample size equal or greater than 373, the prevalence was 49.9%; 95%CI 34.8–64.4). (**Table 4**).

Metaregression

The univariate meta regression models showed an association between foot at risk prevalence with age, former history of CKD, and quality of the study (p<0.05). And a marginally significant association with time of diabetes mellitus and diagnostic method employed for PN and
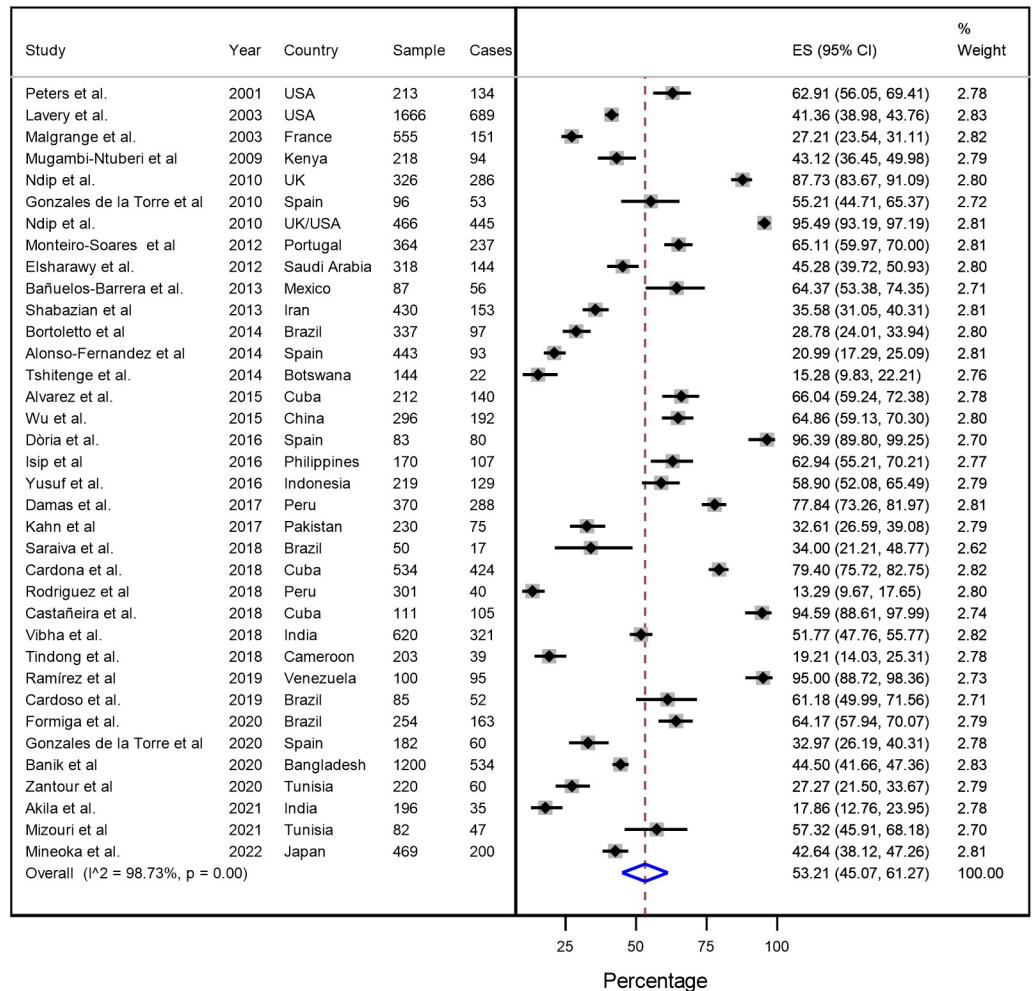
Study	Year	Country	Sample	Cases	ES (95% CI)	% Weight
Peters et al.	2001	USA	213	134	62.91 (56.05, 69.41)	2.78
Lavery et al.	2003	USA	1666	689	41.36 (38.98, 43.76)	2.83
Malgrange et al.	2003	France	555	151	27.21 (23.54, 31.11)	2.82
Mugambi-Ntuberi et al	2009	Kenya	218	94	43.12 (36.45, 49.98)	2.79
Ndip et al.	2010	UK	326	286	87.73 (83.67, 91.09)	2.80
Gonzales de la Torre et al	2010	Spain	96	53	55.21 (44.71, 65.37)	2.72
Ndip et al.	2010	UK/USA	466	445	95.49 (93.19, 97.19)	2.81
Monteiro-Soares et al	2012	Portugal	364	237	65.11 (59.97, 70.00)	2.81
Elsharawy et al.	2012	Saudi Arabia	318	144	45.28 (39.72, 50.93)	2.80
Bañuelos-Barrera et al.	2013	Mexico	87	56	64.37 (53.38, 74.35)	2.71
Shabazian et al.	2013	Iran	430	153	35.58 (31.05, 40.31)	2.81
Bortoletto et al	2014	Brazil	337	97	28.78 (24.01, 33.94)	2.80
Alonso-Fernandez et al	2014	Spain	443	93	20.99 (17.29, 25.09)	2.81
Tshitenge et al.	2014	Botswana	144	22	15.28 (9.83, 22.21)	2.76
Alvarez et al.	2015	Cuba	212	140	66.04 (59.24, 72.38)	2.78
Wu et al.	2015	China	296	192	64.86 (59.13, 70.30)	2.80
Dòria et al.	2016	Spain	83	80	96.39 (89.80, 99.25)	2.70
Isip et al	2016	Philippines	170	107	62.94 (55.21, 70.21)	2.77
Yusuf et al.	2016	Indonesia	219	129	58.90 (52.08, 65.49)	2.79
Damas et al.	2017	Peru	370	288	77.84 (73.26, 81.97)	2.81
Kahn et al	2017	Pakistan	230	75	32.61 (26.59, 39.08)	2.79
Saraiva et al.	2018	Brazil	50	17	34.00 (21.21, 48.77)	2.62
Cardona et al.	2018	Cuba	534	424	79.40 (75.72, 82.75)	2.82
Rodriguez et al	2018	Peru	301	40	13.29 (9.67, 17.65)	2.80
Castañeira et al.	2018	Cuba	111	105	94.59 (88.61, 97.99)	2.74
Vibha et al.	2018	India	620	321	51.77 (47.76, 55.77)	2.82
Tindong et al.	2018	Cameroon	203	39	19.21 (14.03, 25.31)	2.78
Ramírez et al	2019	Venezuela	100	95	95.00 (88.72, 98.36)	2.73
Cardoso et al.	2019	Brazil	85	52	61.18 (49.99, 71.56)	2.71
Formiga et al.	2020	Brazil	254	163	64.17 (57.94, 70.07)	2.79
Gonzales de la Torre et al	2020	Spain	182	60	32.97 (26.19, 40.31)	2.78
Banik et al	2020	Bangladesh	1200	534	44.50 (41.66, 47.36)	2.83
Zantour et al	2020	Tunisia	220	60	27.27 (21.50, 33.67)	2.79
Akila et al.	2021	India	196	35	17.86 (12.76, 23.95)	2.78
Mizouri et al	2021	Tunisia	82	47	57.32 (45.91, 68.18)	2.70
Mineoka et al.	2022	Japan	469	200	42.64 (38.12, 47.26)	2.81
Overall (I^2 = 98.73%, p = 0.00)					53.21 (45.07, 61.27)	100.00

Fig 3. Forest Plot (random effects model) of the diabetic foot at risk of ulceration metanalysis according to IWGDF stratification.

PAD (p<0.2). In the adjusted model with these six variables, it was associated with quality of the study OR 0.67 IC95% 0.53–0.85; p = 0.002 and CKD OR 1.48 IC95% 1.11–1.97; p = 0.010. (**Table 5**).

Publication bias

The funnel plot showed a symmetrical distribution between included studies, which indicates the lack of publication bias (small studies) (**Fig 6A**) This was confirmed by Egger's test (p = 0.351). In the "trim and fill" model, no study required "linear trimming" based imputation (**Fig 6B**).

Certainty of evidence

We classified all available evidence as very low. Thirty four out of 36 studies presented low to moderate quality of evidence, according to Loney's scale. Additionally, the category was decreased due to the high heterogeneity ($I^2 > 75\%$) in the metanalysis. (**Table 6**)
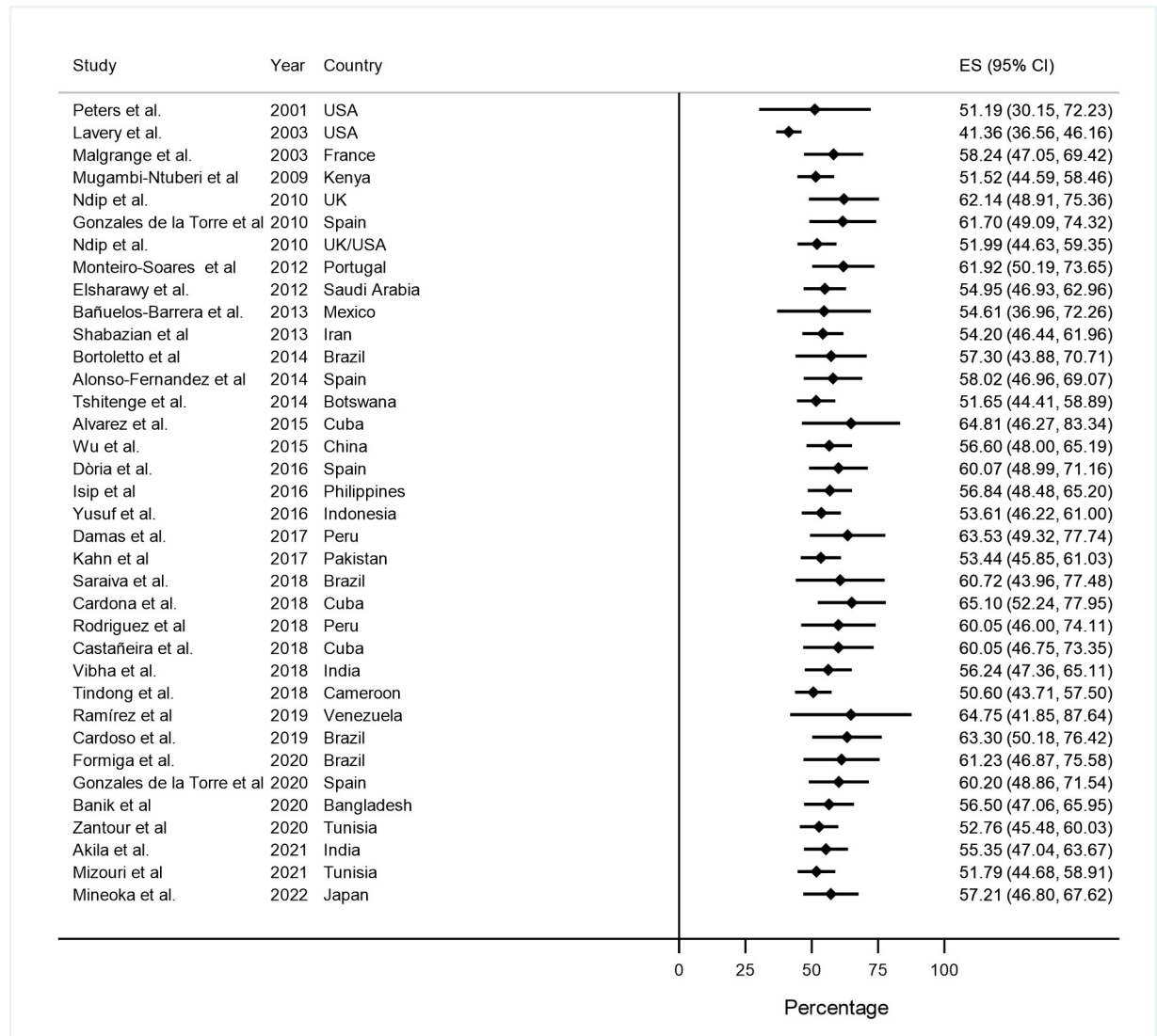
Study	Year	Country	ES (95% CI)
Peters et al.	2001	USA	51.19 (30.15, 72.23)
Lavery et al.	2003	USA	41.36 (36.56, 46.16)
Malgrange et al.	2003	France	58.24 (47.05, 69.42)
Mugambi-Ntuberi et al	2009	Kenya	51.52 (44.59, 58.46)
Ndip et al.	2010	UK	62.14 (48.91, 75.36)
Gonzales de la Torre et al	2010	Spain	61.70 (49.09, 74.32)
Ndip et al.	2010	UK/USA	51.99 (44.63, 59.35)
Monteiro-Soares et al	2012	Portugal	61.92 (50.19, 73.65)
Elsharawy et al.	2012	Saudi Arabia	54.95 (46.93, 62.96)
Bañuelos-Barrera et al.	2013	Mexico	54.61 (36.96, 72.26)
Shabazian et al	2013	Iran	54.20 (46.44, 61.96)
Bortoletto et al	2014	Brazil	57.30 (43.88, 70.71)
Alonso-Fernandez et al	2014	Spain	58.02 (46.96, 69.07)
Tshitenge et al.	2014	Botswana	51.65 (44.41, 58.89)
Alvarez et al.	2015	Cuba	64.81 (46.27, 83.34)
Wu et al.	2015	China	56.60 (48.00, 65.19)
Dòria et al.	2016	Spain	60.07 (48.99, 71.16)
Isip et al	2016	Philippines	56.84 (48.48, 65.20)
Yusuf et al.	2016	Indonesia	53.61 (46.22, 61.00)
Damas et al.	2017	Peru	63.53 (49.32, 77.74)
Kahn et al	2017	Pakistan	53.44 (45.85, 61.03)
Saraiva et al.	2018	Brazil	60.72 (43.96, 77.48)
Cardona et al.	2018	Cuba	65.10 (52.24, 77.95)
Rodriguez et al	2018	Peru	60.05 (46.00, 74.11)
Castañeira et al.	2018	Cuba	60.05 (46.75, 73.35)
Vibha et al.	2018	India	56.24 (47.36, 65.11)
Tindong et al.	2018	Cameroon	50.60 (43.71, 57.50)
Ramírez et al	2019	Venezuela	64.75 (41.85, 87.64)
Cardoso et al.	2019	Brazil	63.30 (50.18, 76.42)
Formiga et al.	2020	Brazil	61.23 (46.87, 75.58)
Gonzales de la Torre et al	2020	Spain	60.20 (48.86, 71.54)
Banik et al	2020	Bangladesh	56.50 (47.06, 65.95)
Zantour et al	2020	Tunisia	52.76 (45.48, 60.03)
Akila et al.	2021	India	55.35 (47.04, 63.67)
Mizouri et al	2021	Tunisia	51.79 (44.68, 58.91)
Mineoka et al.	2022	Japan	57.21 (46.80, 67.62)

Percentage: 0 25 50 75 100

Fig 4. Cumulative metanalysis of the diabetic foot at ulceration risk according to IWGDF stratification.

https://doi.org/10.1371/journal.pone.0284054.g004

Discussion

The diabetic foot is one of the most expensive complications in diabetes mellitus. Identifying and following the patients with foot at risk is a priority to decrease the burden of this disease. In this systematic review with meta-analysis, we estimated a global foot at risk prevalence of 53.2% (CI95%: 45.0 to 61.2). No time-cumulative prevalence tendency of foot at risk of ulceration was identified. The main sources of heterogeneity related to a major prevalence were the time duration of DM and former history of chronic kidney disease (CKD). Drawing of the high heterogeneity and high risk of bias, the included evidence was considered of very low certainty.

The IWGDF scale, designed in 1999, determined risk of ulceration if at least one had peripheral neuropathy. In 2008 the classification was re-evaluated and they divided stages 2 and 3. Stage 2 in 2A (PN + deformity) and 2B (just PAD). Likewise, stage 3 in in 3A (former ulcer history) and 3B (former amputation history) [54]. In our study, five reports [28, 41, 43, 50, 51] used this last stratification. But this modification didn't change the percentage of

Table 2. Prevalence of grades and components of diabetic foot at risk of ulceration according to IWGDF stratification.

	N	Prevalence	95% IC	I²
Grade				
Grade 0	36	44.4%	36.3–52.7	98.8%
Grade 1	36	14.6%	11.1–18.4	96.8%
Grade 2	36	20.2%	15.2–25.6	98.0%
Grade 3	36	11.3%	7.9–15.2	97.4%
Components				
Peripheral neuropathy	22	42.5%	33.5–51.70	98.6%
Peripheral artery disease	23	20.8%	14.7–27.7	98.0%
Biomechanical deformity	24	28.9%	19.6–39.3	99.0%
Previous history of ulcer	36	11.3%	7.9–15.2	97.4%
Diagnostic method of peripheral neuropathy				
Monofilament or diapason or other diagnostic method	11	44.6%	29.3–60.5	98.3%
Two objective tests	9	51.9%	39.4–64.2	98.2%
Three or more tests	16	59.8%	46.9–72.1	98.7%
Diagnostic method or peripheral artery disease				
Pulses palpation or former history	14	46.0%	30.9–61.4	98.8%
Ankle-Brachial Index	17	53.7%	45.6–61.6	97.5%
Ankle-Brachial Index and another method	5	70.8%	43.2–92.0	99.3%

patients at risk. In 2019, the classification presents another modification. The minimum requirement to be at risk was to have PN or PAD. This change will increase the frequency of standing at risk [4]. In a Latin-American serie, frequency increased from 37.4% to 54.3% with these new criteria [55].

There are multiple methods to diagnose peripheral neuropathy. The Toronto Consensus classified accuracy according to the methods used.. Possible PN when symptoms can be identified or there is an objective test. Probable PN when two objective tests were run. Confirmed PN when abnormal nervous conduction test with a sign or symptom. Subclinical PN when there is only abnormal nervous conduction test [56]. A systematic review of peripheral neuropathy, which included studies that didn't describe the measuring method, obtained a prevalence of 30% of PN (IC95% 25–34%); I2 = 99.5%; <0.001 [7]. Another SR in SACA, which specified just including studies with at least two objective tests obtained a prevalence of 46.5% IC95% 38–55%; I2 = 98.2%; p<0.001 [57]. In our systematic review, 69% of included studies employed two or more objective tests, which makes data quality to be acceptable..

For screening of peripheral arterial disease, clinical guidelines recommend pulse palpation, ankle brachial index, and arterial waveform analysis. Arterial calcification interferes with an adequate interpretation of the ABI. We obtain high ITB values (greater than 1.4). However, this is due to arteriosclerosis that causes difficulty in arterial obliteration [58]. In our systematic review, 61% of the studies performed the ABI, furthermore, five of them performed a second confirmatory test. Considering good quality data as well.

The greatest prevalence was found on SACA, followed by NA and Europe on the same percentage. While the lowest prevalence was observed in Africa. Factors that might influence are the local diabetes prevalence, proportion of subjects with diabetes who are unaware of having the disease, the incidence rate, government strategies to prevent complications, if the subjects were from centers of reference or the general population. mong other.

According to the International Diabetes Federation, Africa has the lowest prevalence of DM [59], however, it will have the highest DM percentage increase and also the highest

Table 3. Subgroup analysis of the prevalence of diabetic foot at risk of ulceration according to IWGDF stratification meta-analysis.

	N	Prevalence	95% CI	% Weight	I²
Continent					
North America	3	55.9%	38.4–72.6	8.3	.
South and Central America	10	63.2%	43.9–80.6	27.6	98.9%
Europe	7	56.9%	33.2–79.1	19.4	99.1%
Asia	10	45.4%	38.1–52.8	28.00	95.5%
Africa	5	31.3%	18.8–45.3	13.8	94.5%
More than one continent	1	95.5%	45.1–61.3	2.8	.
Age					
< 60 years	14	45.6%	37.8–53.6	38.9	96.1%
≥60 years	14	67.0%	53.0–79.7	39.0	99.0%
Undetermined	8	41.4%	20.8–63.8	22.2	99.1%
Diabetes time					
< 10 years	11	46.6%	38.4–54.9	30.6	96.9%
≥10 years	9	66.1%	46.8–83.0	25.1	99.1%
Undetermined	16	50.2%	36.0–64.3	44.3	98.7%
Male					
<50%	22	49.2%	39.7–58.7	61.0	98.4%
≥50%	9	60.4%	41.4–78.0	25.0	99.2%
Undetermined	5	57.7%	28.0–84.6	13.9	99.2%
Type of population					
In-patient	23	55.6%	44.5–66.5	63.9	98.7%
Primary care	12	44.3%	33.4–55.4	33.4	98.4%
Any population	1	95.0%	88.7–98.4	2.7	.
Type of DM					
Unspecified	23	55.7%	44.7–66.4	63.7	98.8%
Type 2	13	48.9%	36.3–61.6	36.3	98.7%
Chronic kidney disease (CKD)					
No	33	48.7%	41.7–55.7	91.7	98.1%
Yes	3	93.4%	87.1–97.8	8.3	.

proportion of undiagnosed DM for 2045. Despite its low current prevalence, it can become one of the first ranked continenets in the near future. The high prevalence of SACA, NA and Europe may be due to the predominance of hospital-based studies. Where glycemic and metabolic control is often inadequate. Hospital series show that only 30 to 50% of the subjects achieve a glycated hemoglobin level of less than 7% and only one subject out of eight also controls blood pressure and lipids.. North America and Europe, mainly the USA, despite having the largest health budgets in the world, the inequity in health does not allow consistent results for the entire population.. There are no representative studies of the Western Pacific area, which have the highest prevalence in the world. We could speculate that they have much higher prevalences of foot at risk than those described [59].

Understanding the diabetic foot as a continuum, a systematic review of the presence of foot ulcers globally found an estimated prevalence of 6.3%.The highest prevalence was identified at North America with 13%, followed by Africa with 7.2%, Asia 5.5% and Europe 5.1%. The report didn't include any studies from South America, because of not finding publications in the English language. Given the high diabetic foot at risk rate on SACA, it is expected to be one of the highest in the world. Africa went from lowest standing at risk to second most likely to have cold sores, probably due to limitations in its overall health service. The high prevalence
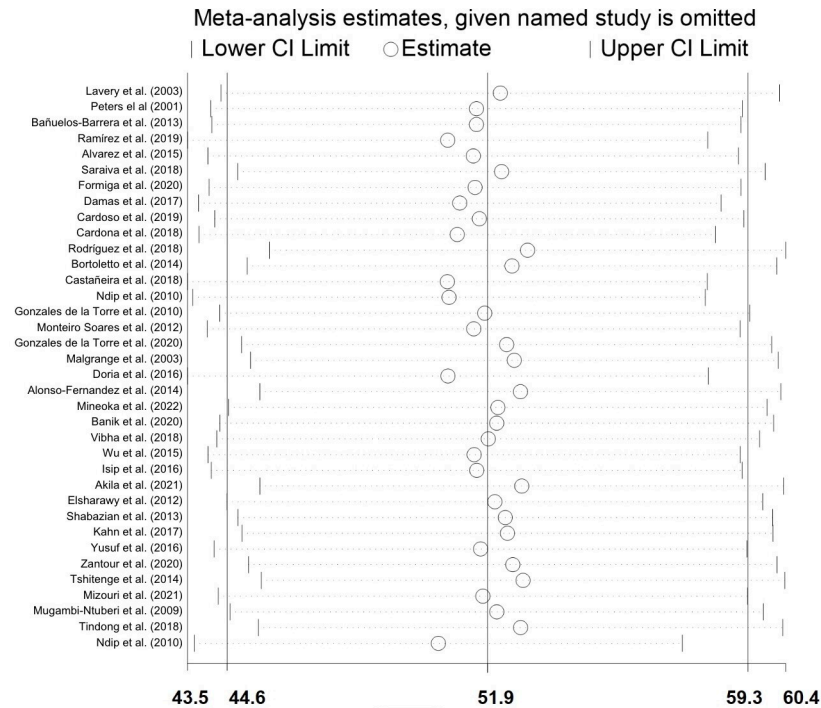
Fig 5. Sensitivity metanalysis by the consecutive exclusion of the 36 included studies.

of NA, with data mainly from the USA, would be made up of a population with limited access to health, despite having the health system with the largest budget [60].

A longer period of diabetes and presence of diabetic complications are associated with a higher probability of having a foot at risk. The chronic kidney disease (CKD) exacerbates the oxidative stress, inflammation, and endothelial distress [61]. Increases the occurrence of PAD by 2.5 times. and 90% of the dialysis population has peripheral neuropathy [62]., debuting as

Table 4. Sensitivity analysis of the prevalence of diabetic foot at risk of ulceration according to IWGDF stratification meta-analysis.

	N	Prevalence	95% CI	% Weight	I²
Year					
1999–2010	7	61.2%	37.9–82.0	19.6	99.4%
2011–2022	29	51.2%	42.7–59.7	80.4	98.4%
Study design					
Transversal	33	52.9%	43.7–62.1	91.6	98.9%
Cohort	3	56.4%	38.6–73.4	8.4	.
Number of centers					
Single center	29	53.3%	45.6–61.0	80.5	98.2%
Multicenter	7	52.8%	24.9–79.7	19.5	99.5%
Sample size ≥ 373 subjects					
No	27	54.3%	44.1–64.4	74.6	98.3%
Yes	9	49.9%	34.8–65.1	25.4	99.3%
Quality score					
Low	4	82.0%	61.3–96.0	11.0	96.5%
Moderate	32	49.3%	45.1–57.7	89.0	98.7%

Table 5. Meta regression model of the prevalence of diabetic foot at risk of ulceration according to IWGDF stratification.

		Crude			Adjusted		
	N	OR	95% CI	p-value	OR	95% CI	p-value
Continent							
North America	3	1.00					
South and Central America	10	1.06	0.79–1.44	0.694			
Europe	7	0.98	0.72–1.35	0.932			
Asia	10	0.91	0.66–1.23	0.518			
Africa	5	0.79	0.56–1.11	0.170			
More than one continent	1	1.49	1.33–2.27	0.130			
Age							
Mean <60 years	14	1.00			1.00		
Mean ≥ 60 years	14	1.20	1.01–1.43	0.041	1.04	0.85–1.27	0.689
Undetermined	8	0.95	0.77–1.17	0.642	0.94	0.74–1.19	0.591
Time of diabetes							
Mean <10 years	11	1.00			1.00		
Mean ≥ 10 years	9	1.18	0.95–1.47	0.128	1.16	0.98–1.39	0.088
Undetermined	16	1.02	0.84–1.24	0.805	1.09	0.88–1.36	0.415
Male							
< 50% of the sample	22	1.00					
≥ 50% of the sample	9	1.08	0.89–1.32	0.394			
Undetermined	5	1.06	0.83–1.36	0.634			
Type of population							
In-patient	23	1.00					
Primary care	12	1.10	0.93–1.31	0.248			
Any population	1	1.65	0.99–2.78	0.056			
Type of DM							
Both	23	1.00					
Type 2	13	1.04	0.88–1,24	0.626			
Chronic kidney disease (CKD)							
No	33	1.00			1.00		
Yes	3	1.56	1.21–2.03	0.001	1.48	1.11–1.97	0.010
Year							
1999–2010	7	1.00					
2011–2022	29	0.92	0.74–1.13	0.403			
Type of study							
Transversal	33	1.00					
Cohort	3	1.05	0.78–1.41	0.758			
Number of centers							
Single center	29	1.00					
Multicenter	7	0.97	0.79–1.19	0.763			
Sample size ≥ 373							
No	27	1.00					
Yes	9	0.97	0.79–1.15	0.634			
Quality score							
Low	4	1.00			1.00		
Moderate	32	0.73	0.57–0.95	0.020	0.68	0.54–0.85	0.002
Diagnostic method of PN							
Just one test	11	1.00			1.00		

(Continued)

Table 5. (Continued)

		Crude			Adjusted		
	N	OR	95% CI	p-value	OR	95% CI	p-value
Two objective tests	9	1.09	0.88–1.37	0.403	1.14	0.91–1.45	0.231
Three or more tests	16	1.17	0.96–1.42	0.114	1.15	0.94–1.41	0.155
Diagnostic method of peripheral artery disease (PAD)							
Just pulses or former history	14	1.00			1.00		
Ankle-Brachial Index	17	1.08	0.91–1.29	0.350	1.02	0.84–1.22	0.846
Ankle-Brachial Index and another method	5	1.26	0.98–1.62	0.066	1.03	0.81–1.32	0.780

Adjusted by age, diabetes time, kidney disease, quality of the study, diagnostic method of PN and PAD

loss of sensation, weakness and pain [63]. For these reasons, prevalence of foot at risk of ulceration in patients with CKD is much higher than in patients without CKD (93.44% vs 48.68%). Likewise, poor control of diabetes is also a factor for the development of PN and PAD [64]. Glycemic control is lost over time, despite intensive use of secretagogues and metformin. We must avoid therapeutic inertia and start insulin or drugs with other non-insulin secretagogue action mechanisms to improve metabolic control and therefore the components of the foot at risk [65].The population has many myths about the use of insulin that we must manage properly to improve metabolic control [66].

Impact in public health

The IWGDF criteria has been validated to establish the risk of ulcer, and this starts the downstream cascade that will end on a major amputation event. The risk determination is just the first step. It was run with limited resources or with sophisticated equipment. This must be followed by a follow-up schedule according to the identified risk, as well as the treatment of altered factors by a multidisciplinary team. Finally, the patient must achieve discipline in self-healthcare [67]. Initially harmless events like an inadequate cut foot nail, lack of foot hydration,
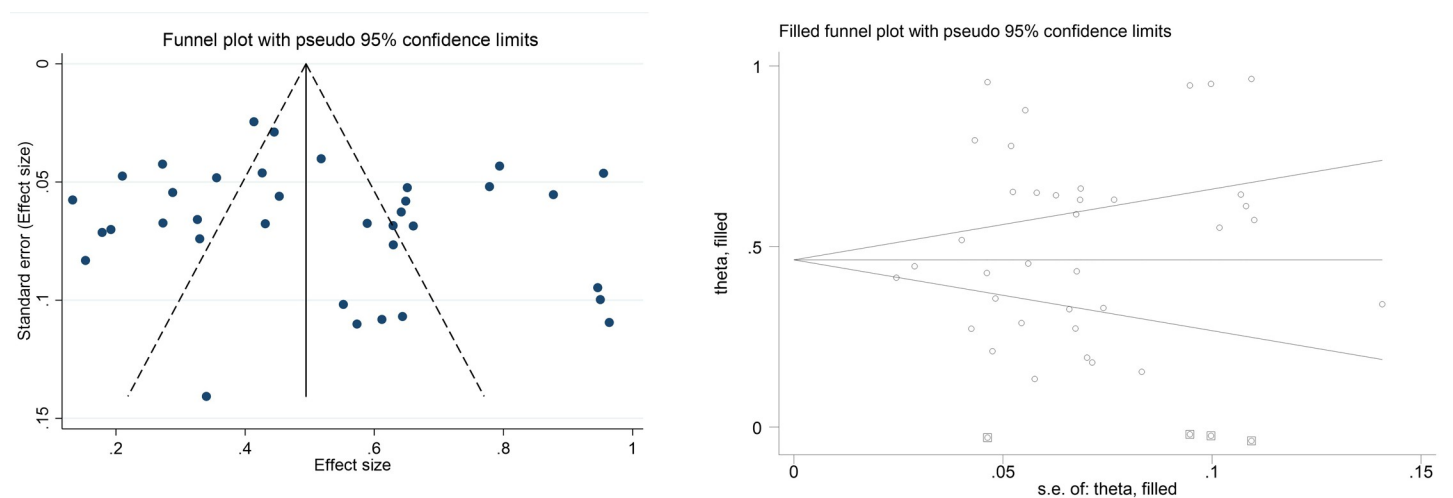
Fig 6. A. Diabetic foot at risk of ulceration according to IWGDF stratification of the 36 included studies Funnel Plot. A—Classic Funnel Plot. B. Diabetic foot at risk of ulceration according to IWGDF stratification of the 36 included studies Funnel Plot. B–Funnel Plot trimmed studies.

Table 6. Quality of the body of evidence according to GRADE: Summary of findings.

Results	Anticipated absolute effects (95% CI)		№ of participants	Certainty of evidence
	Pooled frequency (%)	IC 95%	(Studies)	(GRADE)
Prevalence of diabetic foot at risk of ulceration according to IWGDF stratification	53.2	45.1–61.3	11850 participants on 36 studies	⊕○○○[a,b,c,d] Very low

CI, Confidence interval; IWGDF, International Working Group on the Diabetic Foot

a The grade of certainty starts on a low certainty because no population-based studies were included

b High risk of bias was detected (low and moderate quality according to Loney scale) in 36 studies

c High inconsistency of the metanalysis was detected. The calculated I2 was > 75%

d No imprecision due to adequate sample size and narrow confidence interval

https://doi.org/10.1371/journal.pone.0284054.t006

using a compressive shoe, walking shoeless, loss of protective sensibility, will increase the likelihoods of developing an ulcer in these patients.

Evidence show that PAD is as important as PN for ulcer development. The higher life expectancy increased the prevalence of the former factors. By knowing the importance of doing this screening and the time invested in evaluating all the components, the Canadian Diabetes Society have designed and validated a reduced but complete version that can be applied in 60 seconds. This with the aim of screening the greatest number of patients possible [60]. The primary care services should be capable of providing the patients with the screening and follow-up. However, they are usually overcrowded to face this condition. Government strategies are required to face the classic infectious problems and emergent non-transmissible diseases simultaneously.

Limitations

This study presents some limitations. Only 23 countries were included out of a total of 195 countries in the world. The worst represented continent was Africa. Many studies were excluded for not having free access, even after contacting the corresponding authors. Furthermore, the data was based on series of inpatient or primary care patients, with limited external generalization because no general population study was included. The extrapolation of this data must be performed with precaution. Despite using the same criteria for diabetic foot at risk, many authors used different forms of measuring neuropathy or peripheral artery disease. As method to maintain the quality, we only included studies that described the methods used. We outline that 70% of included studies used an adequate method for peripheral neuropathy (two or more methods) and 60% used the Ankle-Brachial Index for peripheral artery disease. At last, some studies didn't present data on sex, age, time of diabetes mellitus disease, thus, the effect of these factors might be underestimated.

The strengths were that exhaustive systematic search to incorporate all the studies, without language nor year of publication restrictions. Moreover, to decrease the measurement heterogeneity, despite existing multiple diabetic foot at risk scales [5], we used one scale with external validation and with a world-wide application. Meta-analysis techniques to assess the sources of heterogeneity were used. Finally, an exhaustive assessment of quality and certainty of evidence of the calculated estimates was performed, in order to guide the design of future studies.

Recommendations for research

Given the multiple forms of evaluation of neuropathy. Comparing possible versus probable neuropathy according to the Toronto Consensus in ulcer development is important. Likewise,

we generally find 30% arterial calcification in the ABI that limits the determination of flow. Therefore, we must validate adding the evaluation of the arterial waveform by portable vascular Doppler for ulcer occurrence.

Carrying out studies based on the hospital population is more feasible. But we should know the frequency of foot at risk in the general population, where the prevalence is lower, and we find people with better diabetes control or less access to health services.

Conclusion

The overall prevalence of foot at risk is high on worldwide. We identified high between-study heterogeneity and significant limitations (e.g limited countries, heterogeneous definitions, hospital-based studies, low certainty level of evidence). We need upgraded research using standardized and population-based studies and urgent action against preventable causes of diabetic foot.

Supporting information

S1 Checklist. Prisma checklist of items include reporting a systematic review.
(DOCX)

S1 Table. Search strategy.
(DOCX)

S2 Table. Studies that were evaluated in full-text and were excluded.
(DOCX)

S3 Table. Evaluation of the quality of prevalence studies.
(DOCX)

Acknowledgments

Author Contributions

Conceptualization: Tania Maldonado-Valer, Luis F. Pareja-Mujica, Marlon Yovera-Aldana.

Data curation: Fernando Andres Terry-Escalante, Mylenka Jennifer Chevarría-Arriaga, Marlon Yovera-Aldana.

Formal analysis: Rodrigo Corcuera-Ciudad, Marlon Yovera-Aldana.

Investigation: Tania Maldonado-Valer, Luis F. Pareja-Mujica, Rodrigo Corcuera-Ciudad, Fernando Andres Terry-Escalante, Mylenka Jennifer Chevarría-Arriaga, Marlon Yovera-Aldana.

Methodology: Tania Maldonado-Valer, Marlon Yovera-Aldana.

Project administration: Tania Maldonado-Valer, Marlon Yovera-Aldana.

Resources: Tania Maldonado-Valer, Luis F. Pareja-Mujica, Marlon Yovera-Aldana.

Supervision: Tania Maldonado-Valer, Marlon Yovera-Aldana.

Validation: Tery Vasquez-Hassinger, Marlon Yovera-Aldana.

Visualization: Tery Vasquez-Hassinger, Marlon Yovera-Aldana.

Writing – original draft: Tania Maldonado-Valer, Luis F. Pareja-Mujica,
   Rodrigo Corcuera-Ciudad, Fernando Andres Terry-Escalante,
   Mylenka Jennifer Chevarría-Arriaga, Marlon Yovera-Aldana.

Writing – review & editing: Tania Maldonado-Valer, Tery Vasquez-Hassinger,
   Marlon Yovera-Aldana.

References

1. Boulton AJM, Vileikyte L, Ragnarson-tennvall G, Apelqvist J. The global burden of diabetic foot disease. Lancet. 2005; 366: 1719–1724. https://doi.org/10.1016/S0140-6736(05)67698-2 PMID: 16291066

2. Armstrong DG, Swerdlow MA, Armstrong AA, Conte MS, Padula W V, Bus SA. Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer. J Foot Ankle Res. 2020; 13: 16. https://doi.org/10.1186/s13047-020-00383-2 PMID: 32209136

3. Monteiro-Soares M, Boyko EJ, Ribeiro J, Ribeiro I D-RM. Predictive factors for diabetic foot ulceration: a systematic review. Diabetes Metab Res Rev. 2012; 28: 574–600. https://doi.org/10.1002/dmrr.2319 PMID: 22730196

4. Schaper NC, van Netten JJ, Apelqvist J, Bus SA, Hinchlife RJ, Lipsky BA et al. IWGDF Guidelines on the Prevention and Management of Diabetic Foot Disease. Wound Pract Res. 2019. https://doi.org/10.33235/wpr.27.3.144

5. Morgado A, Couceiro R, Ribeiro R, Dias V, Moreira M, Mourão P. Diabetic foot ulcer development risk classifications' validation: A multicentre prospective cohort study. Diabetes Res Clin Pract. 2017; 127: 105–14. https://doi.org/10.1016/j.diabres.2017.02.034 PMID: 28340359

6. Bus SA. A shift in priority in diabetic foot care and research: 75% of foot ulcers are preventable. Diabetes Metab Res Rev. 2016; 32: 195–200. https://doi.org/10.1002/dmrr.2738 PMID: 26452160

7. Sun J, Wang Y, Zhang X, Zhu S, He H. Prevalence of peripheral neuropathy in patients with diabetes: A systematic review and meta-analysis. Prim Care Diabetes. 2020; 14: 435–44. https://doi.org/10.1016/j.pcd.2019.12.005 PMID: 31917119

8. Victoria M, Sebastian A, Weinschelbaum F. The rise of noncommunicable diseases in Latin America and the Caribbean: challenges for public health policies. Lat Am Econ Rev. 2015; 24: 11. https://doi.org/10.1007/s40503-015-0025-7

9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. The BMJ. 2021. p. n71. https://doi.org/10.1136/bmj.n71 PMID: 33782057

10. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev. 2016; 5: 210. https://doi.org/10.1186/s13643-016-0384-4 PMID: 27919275

11. Bramer WM, Giustini D, De Jong GB, Holland L, Bekhuis T. De-duplication of database search results for systematic reviews in endnote. J Med Libr Assoc. 2016; 104: 240–243. https://doi.org/10.3163/1536-5050.104.3.014 PMID: 27366130

12. Loney PL, Chambers LW, Bennett KJ, Roberts JG SP. Critical appraisal of the health research literature: prevalence or incidence of a health problem. Chronic Dis Can. 1998; 19: 170–6. PMID: 10029513

13. Lavery LA, Armstrong DG, Wunderlich RP, Tredwell J BA. Diabetic foot syndrome: evaluating the prevalence and incidence of foot pathology in Mexican Americans and non-Hispanic whites from a diabetes disease management cohort. Diabetes Care. 2003; 26: 1435–8. https://doi.org/10.2337/diacare.26.5.1435 PMID: 12716801

14. Murray FF JW. Transformations Related to the Angular and the Square Root. Ann Math Stat. 1950; 21: 607–611.

15. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986; 7: 177–188. https://doi.org/10.1016/0197-2456(86)90046-2 PMID: 3802833

16. Schünemann H, Brożek J, Guyatt G OA. GRADE handbook for grading quality of evidence and strength of recommendation. 2013.

17. Thompson SG, Higgins JPT. How should meta-regression analyses be undertaken and interpreted? Stat Med. 2002; 21: 1559–1573. https://doi.org/10.1002/sim.1187 PMID: 12111920

18. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. 2011; 64: 401–406. https://doi.org/10.1016/j.jclinepi.2010.07.015 PMID: 21208779

19. Akila M, Ramesh RS KM. Assessment of diabetic foot risk among diabetic patients in a tertiary care hospital, South India. J Educ Heal Promot. 2021; 10: 14. https://doi.org/10.4103/jehp.jehp_407_20 PMID: 33688523

20. Mineoka Y, Ishii M, Hashimoto Y, Yamashita A, Takemura T, Yamaguchi S, et al. Nutritional Status Assessed with Objective Data Assessment Correlates with a High-Risk Foot in Patients with Type 2 Diabetes. J Clin Med. 2022; 11. https://doi.org/10.3390/jcm11051314 PMID: 35268404

21. Isip JDJ, De Guzman M, Ebison A, Narvacan-Montano C. Footwear appropriateness, preferences and foot ulcer risk among adult diabetics at makati medical center outpatient department. J ASEAN Fed Endocr Soc. 2016; 31: 37–43. https://doi.org/10.15605/jafes.031.01.07

22. Elsharawy MA, Hassan K, Alawad N, Kredees A, Almulhim A. Screening of diabetic foot in surgical inpatients: A hospital-based study in Saudi Arabia. Int J Angiol. 2012; 21: 213–216. https://doi.org/10.1055/s-0032-1330230 PMID: 24293979

23. Yusuf S, Okuwa M, Irwan M, Rassa S, Laitung B, Thalib A, et al. Prevalence and Risk Factor of Diabetic Foot Ulcers in a Regional Hospital, Eastern Indonesia. Open J Nurs. 2016; 6: 1–10. https://doi.org/10.4236/ojn.2016.61001

24. Shahbazian H, Yazdanpanah L, Latifi SM. Risk assessment of patients with diabetes for foot ulcers according to risk classification consensus of international working group on diabetic foot (IWGDF). Pakistan J Med Sci. 2013; 29: 730–734. https://doi.org/10.12669/pjms.293.3473 PMID: 24353617

25. Khan A, Junaid N. Prevalence of diabetic foot syndrome amongst population with type 2 diabetes in Pakistan in primary care settings. J Pak Med Assoc. 2017; 67: 1818–1824. PMID: 29256523

26. Wu L, Hou Q, Zhou Q, Peng F. Prevalence of risk factors for diabetic foot complications in a Chinese tertiary hospital. Int J Clin Exp Med. 2015; 8: 3785–3792. PMID: 26064275

27. Vibha SP, Kulkarni MM, Kirthinath Ballala AB, Kamath A, Maiya GA. Community based study to assess the prevalence of diabetic foot syndrome and associated risk factors among people with diabetes mellitus. BMC Endocr Disord. 2018; 18: 1–9. https://doi.org/10.1186/s12902-018-0270-2 PMID: 29940924

28. Banik PC, Barua L, Moniruzzaman M, Mondal R, Zaman F, Ali L. Risk of diabetic foot ulcer and its associated factors among Bangladeshi subjects: A multicentric cross-sectional study. BMJ Open. 2020; 10: 1–10. https://doi.org/10.1136/bmjopen-2019-034058 PMID: 32114471

29. Rodríguez Alonso D, Mercedes Chávez F, Rodríguez Díaz D, Polo López T, Rivera Begazo Á, Guzmán Yparraguirre EM. Prevalencia moderada de pie en riesgo de ulceración en diabéticos tipo 2 según IGWDF en el contexto de la atención primaria. Horiz méd. 2018; 18: 9–18. https://doi.org/10.24265/horizmed.2018.v18n4.02

30. Lucoveis M do LS, Gamba MA, Paula MAB de, Morita ABP da S. Degree of risk for foot ulcer due to diabetes: nursing assessment. Rev Bras Enferm. 2018; 71: 3041–3047. https://doi.org/10.1590/0034-7167-2017-0189 PMID: 30517410

31. Cardona CC, Zaldivar IE, Álvarez I, Rodríguez A. Pie de riesgo en personas con diabetes mellitus de tipo 2 en la Atención Primaria de Salud durante 2016. MediSan. 2018; 21: 226.

32. Bortoletto MSS, De Andrade SM, Matsuo T, Haddad MDCL, González AD, Silva AMR. Risk factors for foot ulcers—A cross sectional survey from a primary care setting in Brazil. Prim Care Diabetes. 2014; 8: 71–76. https://doi.org/10.1016/j.pcd.2013.04.003 PMID: 23639609

33. Ramírez KNC, González MC, Rengel D, Bermúdez V. Evaluación de la neuropatía periférica y el riesgo de ulceración en pacientes diabéticos según los criterios del Grupo Internacional de trabajo sobre pie diabético. Rev Latinoam Hipertens. 2019; 14: 609–615.

34. Damas-Casani VA, Yovera-Aldana M, Seclén Santisteban S. Clasificación de pie en riesgo de ulceración según el Sistema IWGDF y factores asociados en pacientes con diabetes mellitus tipo 2 de un hospital peruano. Rev Medica Hered. 2017; 28: 5–12. https://doi.org/10.20453/rmh.v28i1.3067

35. Formiga NPF, Firmino PRA, De Cássia Félix Rebouças V, Oliveira CJ, MFM De Araújo, Alencar AMPG. Estratificação de risco para pé diabético numa população de idosos acompanhados na atenção primária. Rev Baiana Enferm. 2020; 34: e34097. https://doi.org/10.18471/rbe.v34.34097

36. Álvarez Seijas E, Mena Bouza K, Faget Cepero O, Conesa González AI, Domínguez Alonso E. El pie de riesgo de acuerdo con su estratificación en pacientes con diabetes mellitus. Rev Cuba Endocrinol. 2015; 26: 158–171. Available: http://scielo.sld.cuhttp//scielo.sld.cu

37. Castañeira Jorge E, Vázquez Díaz O, García Herrera AL, Febles Sanabria R, García Cabrera Y, Salgado Mendoza A. Caracterización del riesgo de presentar pie diabético. Servicio Provincial de Angiología de Matanzas. 2014–2015. Rev medica electron. 2018;40: 1487–1506. Available: http://scielo.sld.cu/scielo.php?script=sci_arttext&amp%0Apid=S1684-18242018000501487

38. Cardoso HC, Zara ALDSA, Rosa SDSRF, Rocha GA, Rocha JVC, Araújo MCE De, et al. Risk Factors and Diagnosis of Diabetic Foot Ulceration in Users of the Brazilian Public Health System. J Diabetes Res. 2019; 2019: 5319892. https://doi.org/10.1155/2019/5319892 PMID: 31612148

39. Malgrange D, Richard JL, Leymarie F. Screening diabetic patients at risk for foot ulceration. A multi-centre hospital-based study in France. Diabetes Metab. 2003; 29: 261–268. https://doi.org/10.1016/s1262-3636(07)70035-6 PMID: 12909814

40. González De La Torre H, Perdomo Pérez E, Quintana Lorenzo ML, Fernández AM. Risk stratification in diabetic foot. Gerokomos. 2010; 21: 172–182. Available: http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S1134-928X2010000400006&lng=es

41. Monteiro-Soares M, Vaz-Carneiro A, Sampaio S, Dinis-Ribeiro M. Validation and comparison of currently available stratification systems for patients with diabetes by risk of foot ulcer development. Eur J Endocrinol. 2012; 167: 401–407. https://doi.org/10.1530/EJE-12-0279 PMID: 22740504

42. Alonso-Fernández M, Mediavilla-Bravo JJ, López-Simarro F, Comas-Samper JM, Carramiñana-Barrera F, Mancera-Romero J, et al. Evaluación de la realización del cribado del pie diabético en Atención Primaria. Endocrinol y Nutr. 2014; 61: 311–317. https://doi.org/10.1016/j.endonu.2014.01.007 PMID: 24582291

43. Gonzalez-de la Torre H, Quintana-Lorenzo ML, Lorenzo-Navarro A, Suarez-Sanchez JJ, Berenguer-Perez M V-SJ. Diabetic foot self-care and concordance of 3diabetic foot risk stratification systems in a basic health area of Gran Canaria. Enferm Clin. 2020; 30: 72–81. https://doi.org/10.1016/j.enfcli.2019.07.027 PMID: 31500959

44. Ndip A, Rutter MK, Vileikyte L, Vardhan A, Asari A, Jameel M, et al. Dialysis treatment is an independent risk factor for foot ulceration in patients with diabetes and stage 4 or 5 chronic kidney disease. Diabetes Care. 2010; 33: 1811–1816. https://doi.org/10.2337/dc10-0255 PMID: 20484126

45. Dòria M, Rosado V, Pacheco LR, Hernández M, Betriu À, Valls J, et al. Prevalence of diabetic foot disease in patients with diabetes mellitus under renal replacement therapy in Lleida, Spain. Biomed Res Int. 2016; 2016: 7217586. https://doi.org/10.1155/2016/7217586 PMID: 27190996

46. Mugambi-Nturibi E, Otieno CF, Kwasa TOO, Oyoo GO, Acharya K. Stratification of persons with diabetes into risk categories for foot ulceration. East Afr Med J. 2009; 86: 233–239. https://doi.org/10.4314/eamj.v86i5.54195 PMID: 20084992

47. Tshitenge S, Ganiyu A, Mbuka D, Shama JM. The diabetic foot risks profile in Selebi Phikwe Government Hospital, Botswana. African J Prim Heal Care Fam Med. 2014; 6: 6–10. https://doi.org/10.4102/phcfm.v6i1.610 PMID: 26245411

48. Tindong M, Palle JN, Nebongo D, Aminde LN, Mboue-Djieka Y, Mbarga NTF, et al. Prevalence, Clinical Presentation, and Factors Associated With Diabetic Foot Ulcer in Two Regional Hospitals in Cameroon. Int J Low Extrem Wounds. 2018; 17: 42–47. https://doi.org/10.1177/1534734618764252 PMID: 29564949

49. Zantour B, Bouchareb S, El Ati Z, Boubaker F, Alaya W, Kossomtini W, et al. Risk assessment for foot ulcers among Tunisian subjects with diabetes: A cross sectional outpatient study. BMC Endocr Disord. 2020; 20: 128. https://doi.org/10.1186/s12902-020-00608-2 PMID: 32831070

50. Mizouri R, Belhadj M, Hasni Y, Maaroufi A, Mahjoub F, Jamoussi H. Relationship between level of education and podiatry risk in diabetic patients. Tunis Med. 2021; 99: 277–284. Available: /pmc/articles/PMC8636960/%0A/pmc/articles/PMC8636960/?report=abstract%0Ahttps://www.ncbi.nlm.nih.gov/pmc/articles/PMC8636960/ PMID: 33899199

51. Peters EJG, LA L. Effectiveness of the diabetic foot risk classification system of the International Working Group on the Diabetic Foot. Diabetes Care. 2001; 24: 1442–1447. https://doi.org/10.2337/diacare.24.8.1442 PMID: 11473084

52. Bañuelos-Barrera P, Arias-Merino ED, Banuelos-Barrera Y. Risk factors of foot ulceration in patients with Diabetes Mellitus type 2. Artigo. 2013; 31: 442–449. Available: http://search.ebscohost.com/login.aspx?direct=true&db=c8h&AN=2012409060&site=ehost-live

53. Ndip A, Lavery LA, Lafontaine J, Rutter MK, Vardhan A, Vileikyte L, et al. High levels of foot ulceration and amputation risk in a multiracial cohort of diabetic patients on dialysis therapy. Diabetes Care. 2010; 33: 878–880. https://doi.org/10.2337/dc09-2007 PMID: 20067975

54. Lavery L, Peters E, Williams J, Murdoch D, Hudson A, Lavery D. Reevaluating the way we classify the diabetic foot: restructuring the diabetic foot risk classification system of the International Working Group on the Diabetic Foot. Diabetes Care. 2008; 31: 154–156. https://doi.org/10.2337/dc07-1302 PMID: 17934155

55. Yovera-Aldana M, Pérez-Cavero S, Pinedo-Torres I, Zubiate-López C. Prevalence of Foot At-Risk and its Associated Characteristics among Outpatients with Diabetes Mellitus in a Peruvian Public Hospital. Rev Diabet Stud. 2022; 18: 1–9. https://doi.org/10.1900/RDS.2022.18.1 PMID: 35300751

56. Tesfaye S, Boulton AJM, Dyck PJ, Freeman R, Horowitz M, Kempler P, et al. Diabetic neuropathies: Update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care. 2010; 33: 2285–2293. https://doi.org/10.2337/dc10-1303 PMID: 20876709

57. Yovera-Aldana M, Velasquez-Rimachi V, Huerta-Rosario A, More-Yupanqui MD, Osores-Flores M, Espinoza R, et al. Prevalence and incidence of diabetic peripheral neuropathy in Latin America and the Caribbean: A systematic review and metaanalysis. PLoS One. 2021; 16: 1–29. https://doi.org/10.1371/journal.pone.0251642 PMID: 33984049

58. Criqui MH, Matsushita K, Aboyans V, Hess CN, Hicks CW, Kwan TW, et al. Lower Extremity Peripheral Artery Disease: Contemporary Epidemiology, Management Gaps, and Future Directions: A Scientific Statement from the American Heart Association. Circulation. 2021; 144: E171–E191. https://doi.org/10.1161/CIR.0000000000001005 PMID: 34315230

59. International Diabetes Federation. IDF Diabetes Atlas 10th Edition. 2021.

60. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis. Ann Med. 2017; 49: 106–116. https://doi.org/10.1080/07853890.2016.1231932 PMID: 27585063

61. Valdivielso JM, Rodríguez-Puyol D, Pascual J, Barrios C, Bermúdez-López M, Sánchez-Niño MD, et al. Atherosclerosis in chronic kidney disease: More, less, or just different? Arterioscler Thromb Vasc Biol. 2019; 39: 1938–1966. https://doi.org/10.1161/ATVBAHA.119.312705 PMID: 31412740

62. Krishnan A V, Kiernan MC. Neurological complications of chronic kidney disease. Nat Rev Neurol. 2009; 5: 542–551. https://doi.org/10.1038/nrneurol.2009.138 PMID: 19724248

63. Krishnan A V, Pussell BA, Kiernan MC. Neuromuscular disease in the dialysis patient: An update for the nephrologist. Semin Dial. 2009; 22: 267–278. https://doi.org/10.1111/j.1525-139X.2008.00555.x PMID: 19386072

64. Lim JZM, Ng NSL, Thomas C. Prevention and treatment of diabetic foot ulcers. J R Soc Med. 2017; 110: 104–109. https://doi.org/10.1177/0141076816688346 PMID: 28116957

65. Khunti S, Khunti K SS. Therapeutic inertia in type 2 diabetes: prevalence, causes, consequences and methods to overcome inertia. Ther Adv Endocrinol Metab. 2019; 10: 1–11. https://doi.org/10.1177/2042018819844694

66. Ellis K, Mulnier H, Forbes A. Perceptions of insulin use in type 2 diabetes in primary care: A thematic synthesis. BMC Fam Pract. 2018; 19: 1–21. https://doi.org/10.1186/s12875-018-0753-2 PMID: 29788908

67. Bus SA, van Netten JJ, Lavery LA, Monteiro-Soares M, Rasmussen A, Jubiz Y et al. IWGDF guidance on the prevention of foot ulcers in at-risk patients with diabetes. Diabetes Metab Res Rev. 2016; 32: 16–24. https://doi.org/10.1002/dmrr.2696 PMID: 26334001