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Faculty of Science, Medicine and Health - Papers: Part B

Faculty of Science, Medicine and Health

2019

# Health-related quality of life among adults living with diabetic foot ulcers: a meta-analysis

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**Abstract**

Purpose
To undertake a systematic review of the literature to investigate the HRQOL among adults living with DFUs.

Methods
A systematic search of the medical and nursing/health content databases including MEDLINE, CINAHL, and PsycINFO was conducted up to November 2018. The methodological quality of each study was assessed independently by all authors using the Joanna Briggs Institute checklist. Data analysis was conducted using the Comprehensive Meta-analysis software. All analyses were performed using random-effects models and heterogeneity was quantified.

Results
A total of 12 studies were included in the review. Overall, the HRQOL of participants in the studies was poor on four of eight subscales in the SF-36: physical functioning (mean = 42.75, SE 1.5); role physical (mean = 20.61, SE 3.4); general health (mean = 39.52, SE 1.7); and vitality (mean = 45.73, SE 2.8). In addition, presence of pain, high levels of C-reactive protein (> 10 mg/L), ulcer size > 5 cm$^2$, Ankle Brachial Index < 0.9, high glycosylated haemoglobin and body mass index > 25 kg/m$^2$ were associated with poorer HRQOL in people with DFUs.

Conclusions
This review has provided evidence indicating that people with DFUs have a significantly lower HRQOL. Evidence-based interventions to improve the HRQOL in this group of people is needed.

Keywords
quality, health-related, adults, life, among, living, meta-analysis, ulcers:, foot, diabetic

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**Keywords:** Health-related quality of life, Diabetic foot ulcers, Nursing, Meta-analysis

## Introduction

Diabetes mellitus is the most common metabolic disease and its prevalence is increasing rapidly. The International Diabetes Federation (IDF) has produced an estimate for 216 countries and territories on the prevalence rate of diabetes (IDF, 2016). In 2015, 415 million people worldwide had diabetes, and this is expected to rise to 642 million by 2040 (IDF, 2016). The World Health Organisation (WHO) have also estimated that 422 million adults have diabetes and 1.5 million deaths are caused by diabetes (WHO, 2017). The prognosis of people with diabetes mellitus remains poor due to the changes in microvascular and macrovascular circulation that occurs with poor glycaemic control (Kostev, Jockwig, Hallwachs, & Rathmann, 2014). In adults, the most common complication associated with diabetes is diabetic foot ulcers (DFU) which occur due to neuropathy and decreased peripheral circulation (Taiwo, Green, & Raghupathi, 2014). The presence of DFUs can result in permanent disability and more often amputations related to infection (Bradbury & Price, 2011).

Diabetic foot ulcers (DFUs) are a complication that affects up to 14.8% of people with diabetes mellitus and up to 5.7% of newly diagnosed diabetic patients (Kostev et al., 2014; WHO, 2017). Diabetic foot ulcers may cause nerve damage or foot deformity (Sadosky et al., 2013; Taiwo et al., 2014; WHO, 2017) leading to lower limb amputation. It is reported in the US, that more than 50% of all amputees have diabetes mellitus type

2 (Burant, 2008). Recurrence of DFU's also poses a problem with recurrence occurring in 39% of people in the first year and up to 18% and 12.8% in the second and third year, respectively (Dubský et al., 2013). Furthermore, DFUs that get infected can result in permanent disability which is associated with diabetes wound infection.

Living with DFUs has a significant impact on the health-related quality of life (HRQOL) of people with diabetes mellitus (Carlos De Meneses, Blanes, Francescato Veiga, Gomes, & Ferreirai, 2011; Holland, 2012; Hosseini Nejhad, Molavi Vardanjani, Abolhasani, Hadipour, & Sheikhzadeh, 2013). Boutoille, Feraille, Maulaz, and Krempf (2008) found that people with DFUs had more pain compared to people who had amputations for DFUs ($p = 0.0029$). Using the Iranian version of Medical Outcome Study–Short Form (SF-36), Sanjari et al. (2011) investigated the HRQOL in 54 diabetic patients with DFUs and 78 without DFUs. The results demonstrated poor physical functioning, higher bodily pain, and low HRQOL among patients with DFUs compared to those with diabetes and without DFUs (Sanjari et al., 2011). In addition, low HRQOL has been associated with poor prognosis for a variety of health conditions including diabetes complications (Idler & Benyamini, 1997; Ribu, Birkeland, Hanestad, Moum, & Rustoen, 2008).

Various demographic and clinical factors impact on the HRQOL of people with DFUs. While some studies suggest that males have poorer general health, physical function, and physical role limitation, others report contradictory findings (Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011). Age also impacts the HRQOL of people with diabetes mellitus with older people having poorer HRQOL compared to younger people (Zoungas et al., 2014). The length of time a person has had diabetes mellitus also impacts on HRQOL. People who have had diabetes mellitus for more than ten years have a poorer HRQOL compare to those with diabetes for a shorter period (Al Hayek, Robert, Al Saeed, Alzaid, & Al Sabaan, 2014). In addition, the following clinical characteristics have also

been identified as predictors of poor HRQOL among people with type 2 diabetes mellitus: high glycosylated haemoglobin ($HbA_{1c}$ > 7.5%); lower haemoglobin (Hbg < 13.8 g/dL for men and 12.1 g/dL for women); high C-reactive protein levels (>10 mg/l); and low ankle-brachial index (ABI < 0.9) (Kim et al., 2011; Ribu, Hanestad, Moum, Birkeland, & Rustoen, 2007; Yao et al., 2012).

The literature relating to the HRQOL of people with DFUs and the factors affecting the HRQOL has not been synthesised to enable the development of evidence-based strategies to improve the quality of life of these patients. The purpose of this study was to delineate more precise HRQOL impacts on adults living with DFU by undertaking a systematic review of the literature. This systematic review will enhance the understanding of factors that lead to poor HRQOL among people with DFUs with the aim of improving diabetes care. Knowledge gained from this review will enable the researcher to identify the specific components of human functioning that impact upon HRQOL among people with DFUs. This will guide the researcher to make recommendations for the development of strategies to improve the HRQOL among people with DFUs.

## Methods

This study was conducted using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analysis) guidelines (Moher, Liberati, Tetzlaff, & Altman, 2010) and the Joanna Briggs Institute's (JBI) checklist for appraising the quality of each included study (JBI, 2016a, 2016b). This systematic review followed the JBI and Cochrane guidelines (JBI, 2016a, 2016b).

**Data sources and Study selection**

To obtain the relevant published papers the databases searched included MEDLINE, CINAHL, and PsycINFO for publication in the English language up to November 2018. The search terms included: "diabet* foot ulcer" AND "quality of life" OR "QOL" OR "health-related quality of life" OR "HRQOL". An initial review of title and / or abstract was conducted to remove duplicates and exclude any articles that did not meet the inclusion criteria. The full text of the remaining papers were retrieved and read in full by the first author (SK) to determine whether the papers met the inclusion criteria. The second and third authors (JS and RF) read all papers and consensus decision-making was used to determine the final articles for inclusion in the review. The references lists of the included studies were reviewed to identify any further relevant studies.

**Criteria for inclusion papers**

To be eligible for inclusion, studies must have been published in English, used primary quantitative research methods, and include participants who were 18 years of age or older with a DFU. Studies that included participants who had diabetes but no DFUs were excluded. Additionally, if studies did not report data about DFUs separately the papers were excluded (See Figure 1).
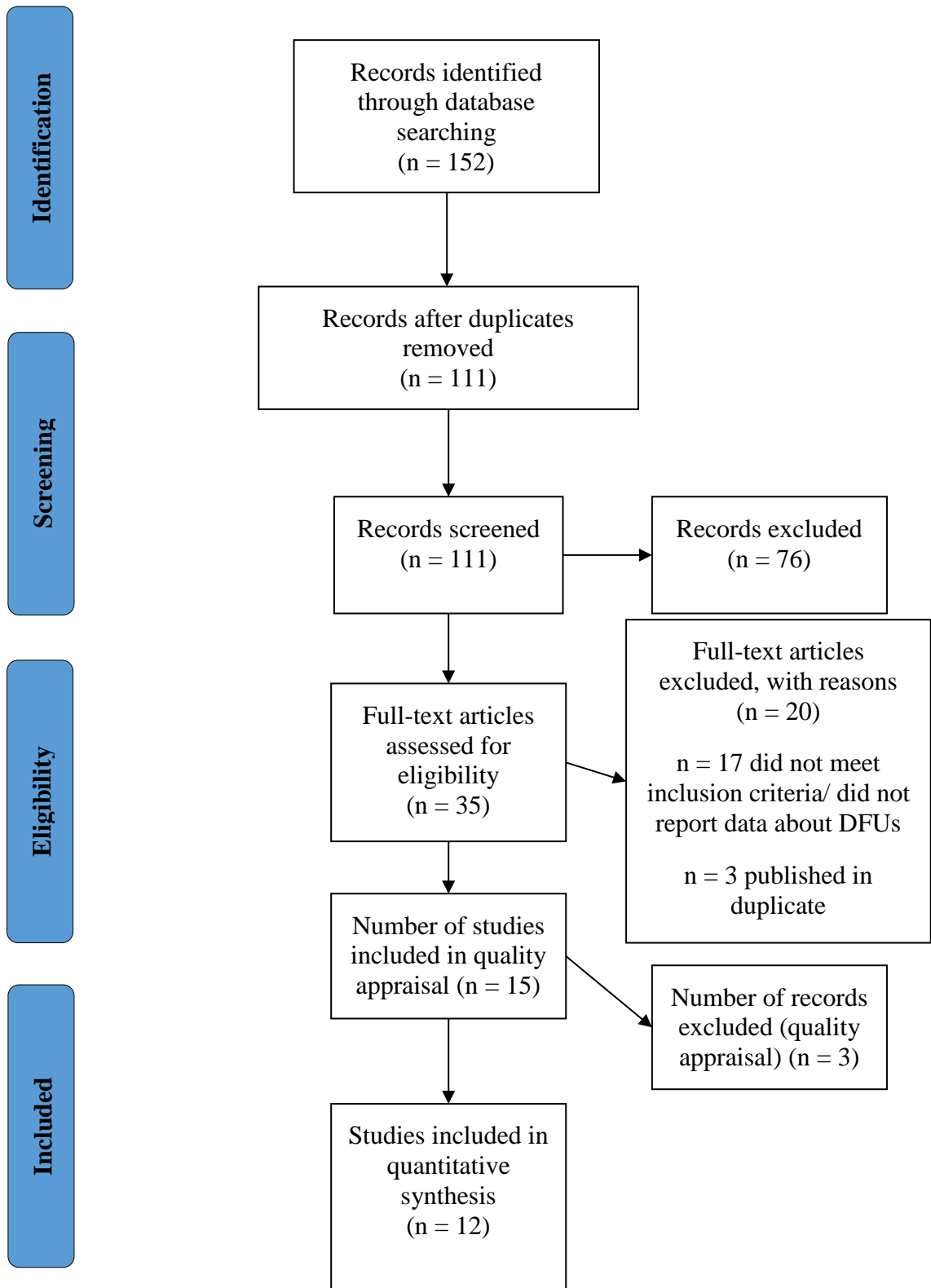
**Figure 1:** Process of paper selection – Prisma Flow diagram: Process of paper selection (modified from Moher et al. (2010))

**Quality assessment**

Critical appraisal of each article was undertaken by the first author (SK) and independently reviewed by the second (JS) and third authors (RF) using either the JBI checklist for cohort studies (11 questions) (JBI, 2016a) or the JBI checklists for cross-sectional studies (eight questions) (JBI, 2016b). Each question was allocated an outcome: yes, no, unclear, and not applicable. Only studies that had a yes response to more than 50% of the questions were included in the review. There were no disagreements in the quality assessment of the individual studies among the three authors.

**Data synthesis and analysis**

Data were extracted from each article and included specific details about the sample, demographics, tools, settings, study methods, and reason for withdrawals and dropouts, as well as any outcomes of significance to the objective of the review. Data were extracted by the first author (SK) and checked by the other authors (JS and RF).

All analysis were undertaken using the Comprehensive Meta-analysis (CMA) version 2 software (Borenstein, Hedges, Higgins, & Rothstein, 2005). Subgroup analyses according to mean age was undertaken to assess whether differences in patient characteristics affected HRQOL. Two sensitivity analysis based on study design and sample size were performed. Heterogeneity was assessed using the $X^2$ test (P < 0.1 being defined as significant heterogeneity) and quantified using the $I^2$ test.(Hedges & Olkin, 1985) $I^2$ values of 25%, 50%, and 75% represent low, moderate, and high heterogeneity (Hedges & Olkin, 1985). Given that the random-effects model is more conservative and assists in controlling for unobserved heterogeneity, all analyses were conducted using a random-effects model, even if the $I^2$ was low (Brockwell & Gordon, 2001; Kontopantelis & Reeves, 2012). To assess the potential for publication bias, the Egger's test was undertaken and funnel plots constructed for each domain to visualize possible asymmetry

(Sterne & Egger, 2001). Where meta-analysis was not appropriate the results have been presented in a narrative form.

## Results

### Study selection

One hundred and fifty-two studies were identified through the search strategy (Figure 1) and were downloaded to Endnote© Version 8. Following removal of duplicates, the title and abstract of 111 studies were reviewed for eligibility and 76 articles were excluded as they did not meet the inclusion criteria. The full text of 35 studies were obtained for further evaluation and a further twenty studies were excluded as they did not meet the inclusion criteria (n = 17) or were published in duplicate (n = 3). Following assessment of the methodological quality of the remaining 15 studies a further three studies were excluded as combining studies of poor quality with those that were more rigorously conducted could lead to a false sense of precision of the results (Lau, Ioannidis, & Schmid, 1998). A total of 12 studies were included in the final review (Figure 1).

### Study characteristics

The review included nine cross-sectional and two cohort studies. The studies were conducted in: Brazil, Belgium, Czech Republic, Denmark, Germany, Italy, Slovenia, Spain, Sweden, Netherlands, London, Iran, Canada, England, and China. The age of the participants ranged between 45 years (Ribu et al., 2008) and 70 years (Goodridge et al., 2006). The number of participants in each study ranged from 9 (Boutoille et al., 2008) to 1,232 (Siersma et al., 2013) The majority of the studies were carried out in European countries and were conducted primarily in clinical settings such as diabetes clinics.

**Quality of included studies**

The quality scores for the two cohort studies were eight and nine, respectively (maximum score obtainable is 11) and all nine cross-sectional studies obtain the maximum score of eight indicating high quality. The appraisal score for each study is documented in the methods column of Table 4. In all included studies, the exposure to the disease and the outcomes were measured in a valid and reliable way. The follow-up time was reported and ranged between six months (Siersma et al., 2017) and 18 months (Winkley, Stahl, Chalder, Edmonds, & Ismail, 2009) which was long enough for outcomes to occur. Appropriate statistical analysis was used in all included studies.

**HRQOL assessment instruments**

The HRQOL was measured using Medical Outcome Short Form (SF-36) in eight studies (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Ribu et al., 2007; Ribu et al., 2006; Sanjari et al., 2011; Winkley et al., 2009; Yao et al., 2012). One study used both the Cardiff Wound Impact Scale (CWIS) and the Medical Outcome Short Form (SF-12) (Goodridge et al., 2006), one study used the SF-36 and the Diabetic Foot Ulcers Scale (DFS) (Valensi, Girod, Baron, Moreau-Defarges, & Guillon, 2005). The WHOQOL-BREF (Nemcová et al., 2017) and Euro-Qol-5D questionnaire (EQ-5D) (Siersma et al., 2013) were used in one study each (see Table 1). All HRQOL instruments used had satisfactory reliability and validity, and are accepted measures for assessing quality of life (Hogg, Peach, Price, Thompson, & Hinchliffe, 2012).

**Table 1:** Summary Table

| Reference | Country | Methods (quality score) | Sample size | | | Results Mean (SD) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *HRQOL measured using SF36* | | | | | | | | | | | | |
| | | | | | **BP** | **GH** | **MH** | **PF** | **RE** | **RP** | **SF** | **VT** |
| Boutoille et al. (2008) | France | Retrospective cohort study (9/11) | 9 | | 33 (17) | 35 (18) | 62 (9) | 62 (18) | 63 (42) | 25 (28) | 53 (19) | 59 (14) |
| Carlos De Meneses et al. (2011) | Brazil | Cross-sectional study (8/8) | 15 | | 40.40 (14.80) | 44.90 (24.76) | 49.3 (26.69) | 52.3 (29.02) | 20.50 (26.93) | 13.30 (26.50) | 49.90 (26.38) | 43.00 (26.38) |
| Garcia-Morales et al. (2011) | Spain | Cohort study (8/8) | 163 | | 62.17 (31.97) | 42.36 (18.09) | 55.77 (22.28) | 44.47 (24.68) | 67.68 (44.04) | 28.22 (40.45) | 61.73 (29.45) | 45.52 (21.86) |
| Sanjari et al. (2011) | Iran | Cross-sectional study (8/8) | 54 | | 34.9 (26.4) | 40.1 (16.2) | 47.5 (22.1) | 41.1 (22.6) | 21.6 (31.1) | 21.7 (31.1) | 45.3 (24.6) | 36.6 (19.6) |
| Yao et al. (2012) | China | Cross-sectional study (8/8) | 131 | | 55.83 (28.02) | 35.82 (19.93) | 57.24 (19.73) | 40.59 (25.12) | 62.75 (41.66) | 15.13 (26.28) | 56.62 (21.76) | 46.93 (19.66) |
| Ribu et al. (2007) | Norway | Cross-sectional study (8/8) | 127 | *Patients with HbA1c ≥ 8.3* | 54.7 (32.0) | 38.5 (25.2) | 67.9 (20.2) | 48.1 (32.5) | 50.0 (46.6) | 21.4 (34.5) | 61.4 (27.8) | 41.1 (26.2) |
| | | | | *Patients with CRP(mg/l) >10* | 44.6 (29.1) | 43.1 (29.1) | 68.2 (21.3) | 38.2 (27.7) | 40.4 (44.6) | 13.5 (26.1) | 62.5 (31.9) | 45.7 (27.5) |
| | | | | *Patients with ABI < 0.9* | 42.9 (27.3) | 38.1 (21.8) | 64.3 (21.2) | 39.2 (27.2) | 38.1 (42.3) | 14.3 (29.2) | 54.9 (26.4) | 39.1 (23.6) |

| Reference | Country | Methods (quality score) | Sample size | | | Results | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ribu et al. (2006) | Norway | Cross-sectional study (8/8) | 127 | *No pain* | *Patients with no pain While walking / standing* | 85.09 (23.27) | 57.06 (25.41) | 75.71 (21.83) | 58.57 (31.60) | 72.73 (39.49) | 45.45 (42.60) | 80.36 (22.75) | 56.47 (25.55) |
| | | | | | *During the night* | 76.06 (31.25) | 56.16 (25.33) | 78.67 (16.15) | 58.47 (29.62) | 72.46 (38.69) | 39.89 (41.59) | 82.65 (19.23) | 56.25 (23.18) |
| | | | | *Pain A little / some of the time* | *While walking / standing Mean (SD)* | 53.95 (28.68) | 47.11 (25.75) | 73.38 (17.40) | 54.59 (27.78) | 53.66 (38.64) | 21.25 (32.79) | 67.86 (27.35) | 50.60 (23.82) |
| | | | | | *During the night Mean (SD)* | 47.61 (23.90) | 41.84 (22.46) | 65.77 (18.26) | 50.40 (30.41) | 41.13 (39.45) | 17.39 (28.32) | 55.47 (26.91) | 45.61 (24.74) |
| | | | | *Pain Most or all of the time* | *While walking / standing Mean (SD)* | 33.87 (18.31) | 34.13 (19.96) | 62.82 (17.48) | 42.46 (28.48) | 41.67 (45.54) | 14.67 (28.66) | 56.25 (24.12) | 37.50 (21.05) |
| | | | | | *During the night Mean (SD)* | 32.48 (16.01) | 33.57 (23.07) | 63.37 (22.19) | 42.66 (27.54) | 46.91 (47.38) | 15.18 (32.16) | 59.91 (27.42) | 33.57 (20.18) |
| Winkley et al. (2009) | England | Prospective cohort study (11/11) | 253 | Physical component score: 35.79 (12.89) | | | | | Mental component score: 45.71 (15.71) | | | | |
| Valensi, Girod, et al. (2005) | France | Cross-sectional study (8/8) | 239 with DFUs and 116 without DFUs (Total 355) | HRQOL was significantly lower among those with DFUs in all SF-36 domains (p= 0.0001) | | | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| ***HRQOL measured using SF12*** | | | | | | | | |
| Goodridge et al. (2006) | Canada | Cross-sectional study (8/8) | 104 | Physical component score: 35 (8) | | | Mental component score: 50 (10) | |
| ***HRQOL measured using CWIS*** | | | | | | | | |
| Goodridge et al. (2006) | Canada | Cross-sectional study (8/8) | 104 | Well-being     35 ± 6<br>Physical Symptom and Daily Living     58 ± 5<br>Social Life     53 ± 6 | | | | |
| ***HRQOL measured using DFS*** | | | | | | | | |
| Valensi, Girod, et al. (2005) | France | Cross-sectional study (8/8) | 239 with DFUs and 116 without DFUs (Total 355) | Scores for DFS domains ranged from 41.2 (SD 28.0) for Daily Activities to 79.7 (SD 21.1) for Family Life<br>Age was significantly associated with several DFS domains including Daily Activities, Physical Health and Dependence.<br>An independent inverse relationship was found between good HRQOL in DFS domain of leisure and Wagner grade as well as the number of DFUs.<br>The more severe the Wagner grade, the poorer HRQOL on DFS domains of leisure (p=0.03); Side Effect (p=0.016); Daily Activities (p=0.009); Emotions (p=0.002); and Treatment (p=0.033) | | | | |

| ***HRQOL measured using WHOQOL-BREF*** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Nemcová et al. (2017) | Slovakia, Czech Republic, and Poland | Cross-sectional study (8/8) | 525 | WHOQOL-BREF domains | Total sample (n= 525) Mean (SD) | Slovakia (n= 129) Mean (SD) | Czech Republic (n= 102) Mean (SD) | Poland (n= 165) Mean (SD) | Hungary (n= 129) Mean (SD) |
| | | | | Physical | 11.32 (2.48) | 11.31 (2.79) | 11.80 (1.9) | 12.35 (1.84) | 9.64 (2.42) |
| | | | | Psychological | 12.86 (2.76) | 13.33 (2.68) | 13.82 (2.6) | 13.59 (2.14) | 10.68 (2.54) |
| | | | | Social | 13.10 (3.03) | 13.60 (2.88) | 13.92 (2.36) | 14.02 (2.91) | 10.77 (2.57) |
| | | | | Environmental | 12.83 (2.52) | 12.70 (2.57) | 13.25 (2.23) | 13.80 (2.34) | 11.40 (2.24) |

| ***HRQOL measured using Euro-Qol-5D*** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Siersma et al. (2013) | Belgium, Czech Republic, Denmark, | Cross-sectional study (8/8) | 1,232 | EQ-5D index score: Mean 0.58, SD 0.33 | | | | |
| | | | | Mobility (n=1132) | Self-care (n=1124) | Usual activities (n=1123) | Pain/ discomfort (n=1127) | Anxiety / depression (n=1128) |

| | Germany, Italy, Slovenia, Spain, Sweden, Netherlands, United Kingdom | | | None 31.9%<br>Some 62.6%<br>Severe 5.5% | None 70.7%<br>Some 22.9%<br>Severe 6.4% | None 48.7%<br>Some 39.0%<br>Severe 12.3% | None 35.5%<br>Moderate 52.6%<br>Extreme 11.9% | None 58.9%<br>Moderate 35.5%<br>Extreme 5.7% |
|---|---|---|---|---|---|---|---|---|

**Abbreviations:**

HRQOL: Health-related Quality of Life; SF – 36 = Medical Outcome Short Form – 36; DFS = Diabetic Foot Ulcer Scale; DFUs = Diabetic Foot Ulcers; CWIS = Cardiff Wound Impact Scale; SF-36 domains (BP = Bodily Pain, GH = General Health, MH = Mental Health, PF = Physical Functioning, RE = Role Emotional, RP = Role Physical, SF = Social Functioning, VT = Vitality); $HbA_{1C}$ = Glycosylated Haemoglobin; CRP = C-reactive Protein; ABI = Ankle-brachial Index; EQ-5D = Euro-QoL-5D Health Utility Index; SF-12 = Medical Outcomes Short Form – 12. WHOQOL-BREF = World Health Organization Quality-of-Life Scale

**HRQOL**

The results from the meta-analysis component of this systematic review are reported using the SF-36 domains. The SF-36 has eight domains and each domain has a minimum score of 0 and maximum of 100. Where meta-analysis was possible, study results were pooled and presented using means, standard estimates (SE) and forest plots. Forest plots for each of the eight domains are presented in Figure 2. For all other studies a narrative summary of results is provided.

*Physical functioning – quality of life*

Seven studies assessed physical functioning using the SF-36 instrument (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Sanjari et al., 2011; Valensi, Girod, et al., 2005; Winkley et al., 2009; Yao et al., 2012). Two studies (Valensi, Girod, et al., 2005; Winkley et al., 2009) did not provide data relating to Standard Deviation (SD) and were not included in the meta-analysis. Pooled data for five studies demonstrated a mean physical function score of 45.58 (SE 2.70; $I^2 = 70.4$ %). Subgroup analysis was undertaken which revealed that in studies that had patients with a mean age of greater than 65 years the mean physical function score was 50.56 (SE 10.68; $I^2 = 91.1$%) and those involving patients with a mean age of less than 65 years, the mean physical function score was 43.89 (SE 1.75; $I^2 = 7.94$%). Sensitivity analysis by study design indicated high heterogeneity among cohort studies ($I^2 = 87.1$%) and low heterogeneity among cross-sectional studies ($I^2 = 11.6$%). Further sensitivity analysis by sample size revealed low heterogeneity ($I^2 = 18.3$%) when one study(Boutoille et al., 2008) with a small sample was removed. Hence, data for the four studies with large samples were pooled using a random-effects model which demonstrated a mean physical function score of 42.75 (SE 1.5) (See Figure 2).

Narrative analysis of the studies not included in the meta-analysis demonstrated significantly poorer HRQOL as indicated by lower mean scores on all SF-36 domains among those with DFUs compared to those without DFUs (Valensi, Girod, et al., 2005; Winkley et al., 2009). In the study using the SF-12 and CWIS instruments (n = 104), a mean score of 37 ± 10 for physical health of participants and a mean score of 58 ± 5) for physical symptoms and daily living was identified (Goodridge et al., 2006). One study that used the WHOQOL-BREF in 525 participants reported a mean score of 11.32 ± 2.48 for physical health (Nemcová et al., 2017). In the study that used the Euro-QoL-5D to assess HRQOL, 68.1% of the people had mobility limitations and 29.3% had self-care problems due to DFUs (Siersma et al., 2014).

*Bodily pain – quality of life*

Six studies investigated bodily pain using the SF-36 among people who had DFUs (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Ribu et al., 2007; Sanjari et al., 2011; Yao et al., 2012). Five studies (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Sanjari et al., 2011; Yao et al., 2012). were pooled in the meta-analysis; however, the results demonstrated high heterogeneity ($I^2$ = 93.5%). Subgroup analysis by age, and sensitivity analysis by study design and sample size also revealed high heterogeneity ($I^2 > 92\%$). Therefore, using a random effect model, data from the five studies were pooled together which demonstrated a mean bodily pain score of 45.75 (SE 5.7).

An additional study examined the impact of pain severity during walking-/ standing or during the night on participants with DFU and found that pain had a significant impact ($p < 0.05$) on quality of life (Ribu et al., 2006). Another study assessed pain and discomfort using the Euro-QoL-5D and reported a high prevalence (84.5%) of pain and discomfort among people with DFUs (Siersma et al., 2014).

*Social functioning – quality of life*

Five studies investigated social functioning using the SF-36 among people who had DFUs (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Sanjari et al., 2011; Yao et al., 2012). Pooled data for five studies demonstrated a mean social functioning score of 54.09 (SE 3.2; $I^2$ = 77.2%). Subgroup analysis revealed high heterogeneity ($I^2$ = 88.4%) in studies that had patients with a mean age of less than 65 years. Sensitivity analysis by study design indicated high heterogeneity ($I^2$ = 77.7%) among cross sectional studies and moderate heterogeneity among cohort studies ($I^2$ = 40.4%). Further sensitivity analysis by sample size revealed high heterogeneity ($I^2$ = 82.6%) when one study (Boutoille et al., 2008) with a small sample was removed. Hence, data were pooled for all five studies using a random-effect model.

One study that used the WHOQOL-BREF reported a mean score of 13.1 ± 3.03 for social health (Nemcová et al., 2017). In the study that used the CWIS, 30% of participants with DFUs had a decreased ability to enjoy their usual social life (Goodridge et al., 2006).

*Role emotional – quality of life*

Five studies investigated role emotional using the SF-36 among people who had DFUs (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Sanjari et al., 2011; Yao et al., 2012). Pooled data for the five studies demonstrated high heterogeneity ($I^2$ = 96.1%). Subgroup analysis revealed high heterogeneity ($I^2$ = 97.7%) in studies that had patients with a mean age of less than 65 years. Sensitivity analysis by study design indicated high heterogeneity ($I^2$ = 96.9%) among cross-sectional studies and low heterogeneity among cohort studies ($I^2$ = 0%). Further sensitivity analysis by sample size revealed high heterogeneity ($I^2$ = 97.0%) when the study with the small sample size (Boutoille et al., 2008) was removed. Hence, data were pooled for all

five studies using a random-effects model which demonstrated a mean social functioning score of 46.67 (SE 11.1).

*Mental health – quality of life*

Seven studies (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Ribu et al., 2007; Ribu et al., 2006; Sanjari et al., 2011; Yao et al., 2012) investigated mental health in people with DFUs. Five studies (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Sanjari et al., 2011; Yao et al., 2012) were pooled in the meta-analysis, demonstrating a mean mental health score of 55.26 (SE 2.2; $I^2$ = 70.3%). Subgroup analysis revealed high heterogeneity ($I^2$ = 66.9%) in studies that had patients with a mean age of less than 65 years. Sensitivity analysis by study design indicated high heterogeneity among cross-sectional ($I^2$ = 76.5%) and cohort studies ($I^2$ = 69%). Further sensitivity analysis by sample size revealed high heterogeneity ($I^2$ = 65.8%) when one study (Boutoille et al., 2008) with a small sample was removed. Hence, data were pooled for all five studies using a random effects model.

One study assessed the impact of unhealed foot ulcers on mental health using the SF-12 instrument and CWIS tool. The mean score for mental health was $50 \pm 10$ (SF-12) and $35 \pm 6$ (CWIS) (Goodridge et al., 2006). Patients with unhealed ulcers were frustrated with healing and had anxiety about their wounds resulting in a marked negative impact on average well-being (Goodridge et al., 2006). One study that used the WHOQOL-BREF reported a mean score of 12.9 $\pm$ 2.76 for psychological domain (Nemcová et al., 2017). The final study (Siersma et al., 2014) assessed anxiety and depression using the Euro-Qol-5D and reported that 41.2% of participants had anxiety and depression due to DFUs.

*Vitality – quality of life*

Five studies investigated vitality using the SF-36 among people who had DFUs (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Sanjari et al., 2011; Yao et al., 2012). Pooled data for the five studies included in the meta-analysis revealed a mean vitality score of 45.73 (SE 2.8; $I^2 = 80.3\%$). Subgroup analysis by age ($I^2 > 74\%$) and sensitivity analysis by study design and sample size also indicated high heterogeneity ($I^2 > 81\%$). Hence, data were pooled for all five studies using a random-effects model.

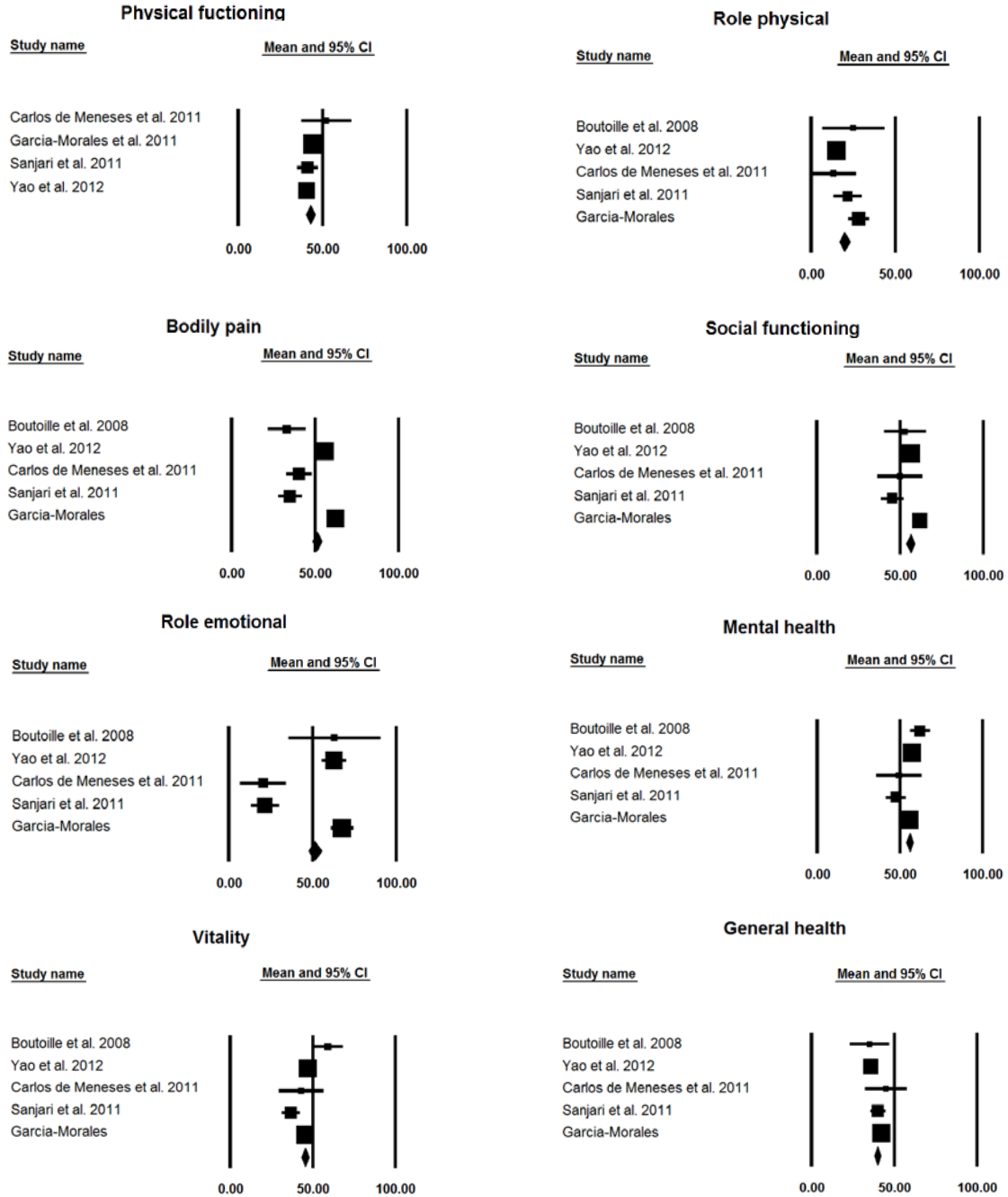*Role physical – quality of life*

Five studies investigated role physical using the SF-36 among people who had DFUs (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Sanjari et al., 2011; Yao et al., 2012). The mean role physical score in the five studies included in the meta-analysis was 20.61 (SE 3.4; $I^2 = 68.3\%$). Subgroup analysis by age indicated low heterogeneity in studies that had patients with a mean age of greater than 65 years and high heterogeneity in patients with a mean age of less than 65 years ($I^2 = 55.5\%$). Sensitivity analysis by study design indicated low heterogeneity in both the cohort studies ($I^2 = 0\%$) and cross-sectional studies ($I^2 = 3.8\%$). Further sensitivity analysis by sample size revealed high heterogeneity ($I^2 = 75.6\%$) when one study (Boutoille et al., 2008) with a small sample was removed. Hence, data were pooled for all five studies using a random-effects model.

*General health – quality of life*

Six studies (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Ribu et al., 2007; Sanjari et al., 2011; Yao et al., 2012). reported on general HRQOL. Pooled data for five studies (Boutoille et al., 2008; Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Sanjari et al., 2011; Yao et al., 2012) demonstrated a mean general health score of 39.52 (SE 1.7;

$I^2$ = 59.1%). Subgroup analysis by age demonstrated no heterogeneity. Sensitivity analysis by study design demonstrated low heterogeneity ($I^2 < 50\%$) and by sample size demonstrated high heterogeneity ($I^2 = 67.1\%$). Hence, data from all five studies were pooled using a random-effects model.

In the study by Goodridge et al. (2006) mean scores for the well-being component was 35.5 (SD = 6). In addition, the study by Nemcová et al. (2017) used the WHOQOL-BREF and reported that the mean score for environmental domain was 11.8 ± 2.52.

## Physical fuctioning

Study name      Mean and 95% CI

Carlos de Meneses et al. 2011
Garcia-Morales et al. 2011
Sanjari et al. 2011
Yao et al. 2012

0.00      50.00      100.00

## Role physical

Study name      Mean and 95% CI

Boutoille et al. 2008
Yao et al. 2012
Carlos de Meneses et al. 2011
Sanjari et al. 2011
Garcia-Morales

0.00      50.00      100.00

## Bodily pain

Study name      Mean and 95% CI

Boutoille et al. 2008
Yao et al. 2012
Carlos de Meneses et al. 2011
Sanjari et al. 2011
Garcia-Morales

0.00      50.00      100.00

## Social functioning

Study name      Mean and 95% CI

Boutoille et al. 2008
Yao et al. 2012
Carlos de Meneses et al. 2011
Sanjari et al. 2011
Garcia-Morales

0.00      50.00      100.00

## Role emotional

Study name      Mean and 95% CI

Boutoille et al. 2008
Yao et al. 2012
Carlos de Meneses et al. 2011
Sanjari et al. 2011
Garcia-Morales

0.00      50.00      100.00

## Mental health

Study name      Mean and 95% CI

Boutoille et al. 2008
Yao et al. 2012
Carlos de Meneses et al. 2011
Sanjari et al. 2011
Garcia-Morales

0.00      50.00      100.00

## Vitality

Study name      Mean and 95% CI

Boutoille et al. 2008
Yao et al. 2012
Carlos de Meneses et al. 2011
Sanjari et al. 2011
Garcia-Morales

0.00      50.00      100.00

## General health

Study name      Mean and 95% CI

Boutoille et al. 2008
Yao et al. 2012
Carlos de Meneses et al. 2011
Sanjari et al. 2011
Garcia-Morales

0.00      50.00      100.00

**Figure 2:** HRQOL according to the SF-36 domains

**Predictors of HRQOL**

*Demographic characteristics*

*Age*

Three (Goodridge et al., 2006; Ribu et al., 2007; Valensi, Le Devehat, et al., 2005) studies reported on demographic characteristics and HRQOL. In the three studies that reported on age, one study(Goodridge et al., 2006) reported that age was not a predictor of overall physical or mental health. In contrast, Ribu et al. (2007) found that participants aged 67 years and above were more likely to have a lower role emotional score ($p < 0.05$) than those aged 40 to 66 years. Similarly, increased age was also a predictor of lower HRQOL relating to daily activities, physical health and dependence (Valensi, Girod, et al., 2005) as well as psychological and social well-being (Nemcová et al., 2017).

*Gender*

Gender as a predictor of HRQOL was examined in four studies (Carlos De Meneses et al., 2011; Garcia-Morales et al., 2011; Goodridge et al., 2006; Ribu et al., 2007). Gender was not a predictor of overall physical or mental health in one study (Goodridge et al., 2006). In contrast, the study by Carlos De Meneses et al. (2011) reported that women had a significantly higher overall HRQOL compared to men, however, there was no significant difference between the genders for subscales relating to role physical, social functioning, role emotional and physical functioning. In the remaining two studies, women had significantly lower score for vitality and mental health (Ribu et al., 2007) and overall quality of life (Garcia-Morales et al., 2011).

*Marital status*

Marital status was not a predictor of HRQOL in participants with DFUs (Goodridge et al., 2006). In one study, (Goodridge et al., 2006) marital status was not a predictor of HRQOL in participants

with DFUs. However, in the second study, participants living with a partner had significantly higher HRQOL in the psychological and environmental domains (Nemcová et al., 2017).

*Body Mass Index (BMI)*

Higher Body Mass Index (BMI) was associated with lower scores in HRQOL relating to the mental health, general health (Ribu et al., 2007; Yao et al., 2012) and the physical domains (Nemcová et al., 2017).

*DFU characteristics*

Six studies (Garcia-Morales et al., 2011; Goodridge et al., 2006; Ribu et al., 2007; Ribu et al., 2006; Valensi, Girod, et al., 2005; Yao et al., 2012) investigated the association between DFU characteristic and HRQOL in people with DFUs. The duration of time that a person had a DFU was a significant predictor of decreased physical health (Garcia-Morales et al., 2011; Goodridge et al., 2006) and increased financial burden (Valensi, Girod, et al., 2005). Severity of the DFU using the Wagner scale (Wagner, 1979) was also a significant predictor of overall HRQOL in one study (Yao et al., 2012) and social functioning in another study (Valensi, Girod, et al., 2005). Ulcer size greater than 5 cm$^2$ was significantly associated with poorer domain scores for physical functioning, role physical, role emotional, and mental health domains (Ribu et al., 2007). Two studies (Nemcová et al., 2017; Ribu et al., 2006). investigated HRQOL among those who had pain related to their DFUs. The results demonstrated significantly lower HRQOL in all domains including physical, social, emotional, psychological and general health among those who had pain (Nemcová et al., 2017; Ribu et al., 2006).

*Clinical bio-markers*

Two studies (Ribu et al., 2007; Yao et al., 2012) reported data on clinical bio-markers as predictors of HRQOL in people with DFUs. A C-reactive protein (CRP) greater than 10 mg/l was significantly associated with lower scores on the following SF-36 domains: physical functioning, role physical, bodily pain, social functioning, and role emotional (Ribu et al., 2007). Ankle-Brachial Index (ABI) less than 0.9 was associated with lower scores in physical functioning, bodily pain, and social functioning domains (Ribu et al., 2007). Higher HbA$_{1C}$ levels were associated with lower scores on the vitality and general health domains (Yao et al., 2012).

**Publication bias**

No evidence of funnel plot asymmetry was found for the majority of the HRQOL domains (Egger's test: physical functioning $p = 0.28$, social functioning $p = 0.20$, role emotional $p = 0.29$, mental health $p = 0.29$, vitality $p = 0.43$, role physical $p = 0.36$ and general health $p = 0.42$). Significant plot asymmetry was found only for bodily pain (Egger's test $p = 0.03$) which could be due to the small number of studies (see Figure 3).
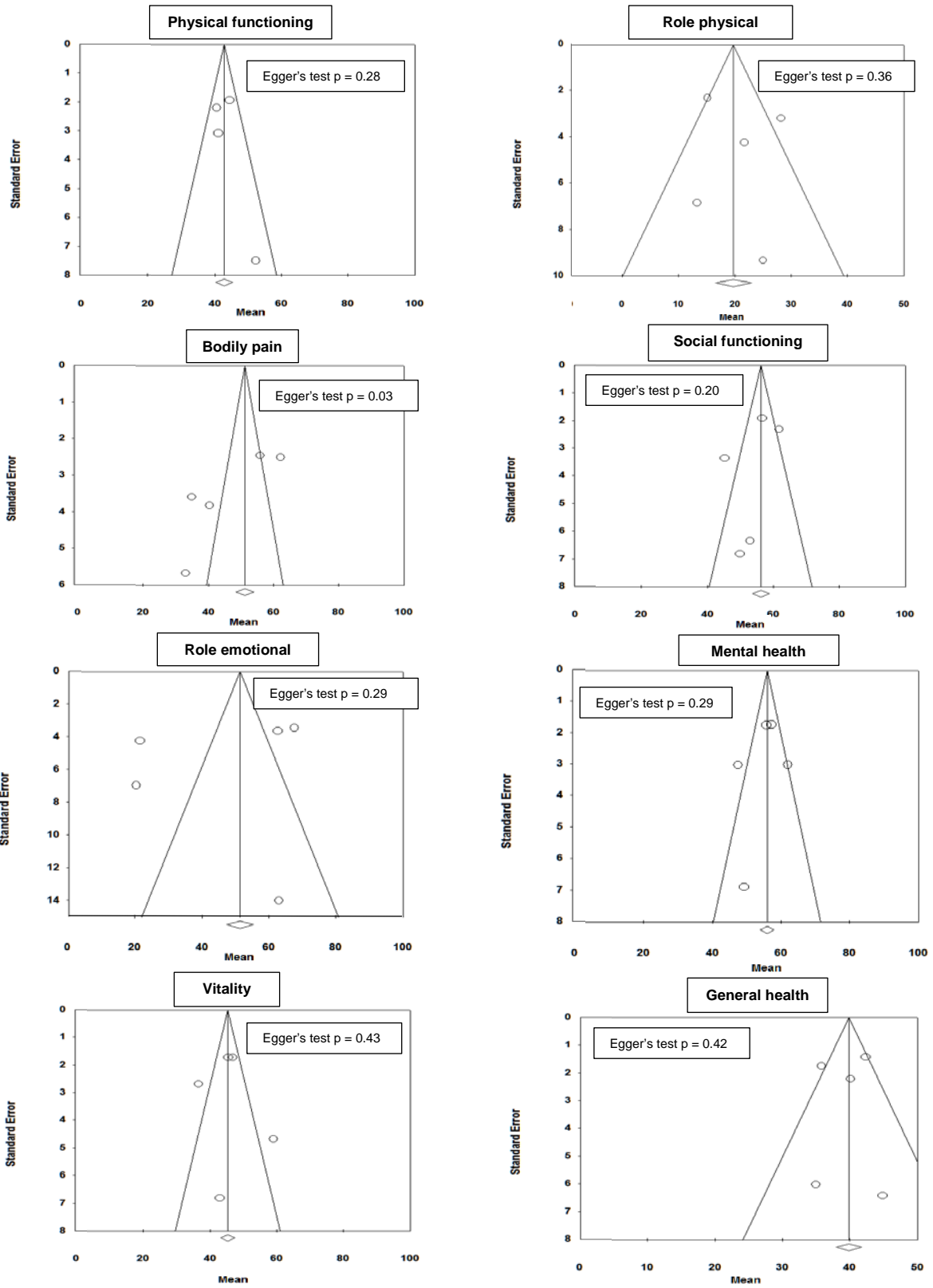
**Figure 3:** Funnel plot of standard error by mean score of SF-36

## Discussion

Diabetic foot ulcers are a major complication of diabetes mellitus and have an impact on the HRQOL of people living with the disease. Following an extensive search of the literature, twelve studies that investigated the HRQOL of people with DFUs were included in the review. The studies included in the review used valid and reliable HRQOL instruments such as the SF-36, SF-12, Euro-Qol-5D, DFS and CWIS. However, the majority of the studies used the SF-36 instrument which is a generic instrument to measure a person's HRQOL and does not specifically focus on HRQOL for people with a DFU. The use of a disease-specific validated tool for people with DFUs such as the DFS or DFS-SF should be used in future studies to assess the HRQOL of people with DFUs.

All studies included in the review reported low scores for HRQOL in all domains for people with DFUs which is congruent with the literature on HRQOL of people with chronic venous leg ulcers (Lopes, Marcondes, Aline Medeiros, Larissa Marques Barreto Mello, & Valdeci Carlos, 2013; Wachholz, Masuda, Nascimento, Taira, & Cleto, 2014). The low scores for HRQOL could be due to various factors such as pain, severity of the ulcers, location of ulcers and foot deformation (Siersma et al., 2013). In this review, people with DFUs had increased bodily pain indicating poor HRQOL. This finding is consistent with the literature where pain has been reported as a predictor of poor HRQOL in people with chronic wounds (Gonzalez-Consuegra & Verdu, 2011; Hopman, Buchanan, VanDenKerkhof, & Harrison, 2013; Obilor & Adejumo, 2015).

A high prevalence (84.5%) of pain and discomfort among people with DFUs was also identified in this review (Siersma et al., 2014). This result is not unusual given that people with DFU have diabetic neuropathy that often results in significant pain (Martin, Albers, Pop-Busui, & Group,

2014). The intensity of pain was also identified as having a significant impact on the quality of life of people with DFUs.

Pain was also reported to have a negative impact on social functioning and engagement in leisurely activities (Ribu et al., 2008). This result is congruent with the evidence obtained from the literature on people with chronic wounds where presence of pain due to leg ulcers prevented people from going out and staying in contact with friends and relatives (Hopman et al., 2013). It is clear from this review that presence of pain has a significant impact on the HRQOL of life of people with DFUs. Therefore, pain management strategies should be implemented for improving HRQOL among people with DFUs. To improve HRQOL and mobility, people with DFUs should consult with an appropriate healthcare professional to provide foot care devices such as off-loading insoles that may minimise pain and discomfort while walking. In addition, pharmacological and non-pharmacological treatments for pain relief may be required to support people with DFUs to maintain mobility and improve HRQOL.

The review also identified low scores for social functioning among people with DFUs which is congruent with the literature (Herber, Schnepp, & Rieger, 2007). A possible explanation for the low scores could be due to the person focusing on their DFU and its treatment hence not feeling able to socialise. Alternate reasons could be that these people are restricted in their work capacity hence not able to make social contacts. Irrespective of the reasons, it is vital that strategies are implemented to prevent people with DFUs from becoming socially isolated. Social support combined with family support can be effective in reducing social isolation among people with DFU's (Khunkaew, Tungpunkom, Sim, & Fernandez, 2018; Peker & Karaöz, 2017). Health-care professionals should support people with DFUs to remain active in their community.

The presence of pain, poor physical health and social isolation can often lead to poor psychological well-being of the person with DFU. In this review, the scores for HRQOL relating to mental health were low indicating poor mental health. This result is congruent with the published research indicating that poor physical functioning is directly related to the psychological well-being of people with chronic conditions (Pols et al., 2017; Swardfager et al., 2016; Tušek-Bunc & Petek, 2016). Given that people with DFUs have poor mental health, access to psychosocial interventions both in the short and long term remains a priority for health services. Peer support groups have been effective in some cultures (Heisler, 2009) and psychological support services may also be a useful strategy for some people with DFUs. Most services supporting people with DFU's do not have direct access to psychological support services but this type of service may be warranted given the poor mental health scores evident in this population.

Only three studies included in this review investigated if age was a predictor of HRQOL. The results on age identified contradictory findings with one study reporting that age was not a predictor (Goodridge et al., 2006) and the remaining two indicating that older age was a predictor of lower HRQOL relating to physical health and role emotional. This result may be due to factors related to ageing rather than diabetes and DFUs. Similarly, the evidence from this review surrounding gender differences in HRQOL remains inconclusive given that in one study females were identified to have lower HRQOL compared to males (Garcia-Morales et al., 2011) and in another males were identified to have a poorer HRQOL (Carlos De Meneses et al., 2011). Marital status was not a predictor of HRQOL. Targeted programs to address HRQOL in specific demographic groups could be created to provide appropriate strategies to support people with DFUs. An example of such strategies could include peer to peer support groups for people with

DFUs who are experiencing difficulty in healing and have had DFUs for a longer period of time (Heisler, 2009).

In addition to the presence of pain, demographic factors and ulcer characteristics, ABI, and high levels of biomarkers such as CRP and $HbA_{1c}$ have also been reported to be associated with low HRQOL in people with DFUs. This is consistent with the findings in this systematic review. Given these findings, it is important for nurses to be aware of these biomarkers and their association with HRQOL among people with DFUs. This knowledge may assist them to focus care and plan interventions that improve HRQOL.

**Limitations**

Several potential limitations in this review should be acknowledged. The limited amount of data reported in some studies prevented the inclusion of all studies in the meta-analysis. Second, publication bias may be present due to the inclusion of only studies published in the English language. In addition, some studies had a small sample size which may have impacted upon the results. Lastly, although the HRQOL was assessed using validated instruments, the information was obtained using self-administered questionnaires and hence is susceptible to social desirability bias. Further large multi-centre research using the interview method for data collection is warranted to identify the HRQOL and the predictors of HRQOL in people with DFUs.

**Implications for planning nursing care**

Understanding the impact of the clinical characteristics of people with DFUs on their HRQOL is important for planning nursing care. High levels of CRP, ulcer size $> 5$ $cm^2$, $ABI < 0.9$, high levels of $HbA_{1C}$ and $BMI > 25$ $kg/m^2$ were associated with poorer HRQOL in people with DFUs (Ribu et al., 2007).

Currently there are no universally accepted systems for the classification of DFUs, however, the Wagner's DFU Grade Classification system (Fonseca & Fonseca, 2006) or the University of Texas DFU Classification system (Noor, Zubair, & Ahmad, 2015) are commonly used in the busy clinical settings. The routine use of either of these validated scales for classifying the severity of the DFU should be implemented in practice for the detection and monitoring of DFUs. Management of DFUs should include wound care management that aims to promote healing and minimise the length of time a person has a DFU. Wound care management is an important nursing strategy to improve HRQOL and validated scales for classifying DFU's can assist with monitoring progress in wound healing. It is important for health care professionals to implement strategies to improve the HRQOL of people with DFUs. These strategies could include conducting regular follow-ups and assessment of the clinical factors to prevent deterioration in HRQOL among individuals who have these clinical characteristics. A multidisciplinary-focused education programme for people with DFUs on the importance of maintaining glycaemic control and implementing self-care strategies is pivotal to improving care for people with DFUs and decreasing the impact DFUs have on HRQOL.

Focused programs are also required to prevent development of DFUs. This education should include targeted information relating to the importance of improving glycaemic control and HbA$_{1C}$ levels and implementing regular self-care management of their feet. In addition, it would also be beneficial if other healthcare professionals such as occupational therapists or physiotherapists could assess the patients' ability to undertake foot care management particularly as obesity and ageing may reduce mobility and flexibility and thus their ability to carry out these tasks even though they have the requisite knowledge to do so. When a person has a DFU, education and skill development are required to reduce ulcer size and prevent infections. The presence of infection

particularly in the deep plantar spaces of the foot can cause pain and increase the time taken for the DFU to heal (Ribu et al., 2006). This is particularly important given that the findings of this review indicate a negative association between duration of time the person has a DFU and poorer HRQOL and a positive association between pain and poorer HRQOL. Promotion of HRQOL among patients who have a DFU should be part of routine care for this group of patients. It is evident from this systematic review that people with DFUs have a poorer HRQOL. Hence, this systematic review suggests that further research needs to be undertaken to investigate effective strategies to promote HRQOL in this group of people with DFUs.

## Conclusion

Evidence obtained from this systematic review indicates that people with DFUs have a significantly lower HRQOL than those without DFUs. Using disease-specific instruments to examine HRQOL (for example the DFS or CWIS) is recommended. Disease-specific HRQOL instruments can assist the healthcare provider to make individualised decisions about care, identify the need for additional professional education and training, and help people with DFUs to recognise their own improvements / decline over time. Agreement on the most appropriate disease-specific tool in this group of people would enable future research to pool and / or compare data so that conclusions can be made about the most effective interventions. Implementation of evidence-based interventions focussing not only on the underlying pathology but also on the quality of life in this group of people is needed.

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