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SYSTEMATIC REVIEW

Measures of health-related quality of life in diabetes-related foot disease: a systematic review

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Abstract
Aims/hypothesis Patient-reported outcome measures (PROMs) are increasingly used as key performance indicators in chronic illness. We sought to review the value of these tools in assessing health-related quality of life (HRQOL) in patients with diabetes-related foot disease and identify the impact of each foot problem on life quality.
Methods A systematic review of literature on HRQOL PROMs in diabetes-related foot disease was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. The quality of eligible studies was evaluated within pre-existing criteria.
Results 53 studies written between 1995 and 2010 met the inclusion criteria. A variety of HRQOL PROMs were used. Disease-specific tools were better than generic at quantifying temporal changes in life quality and showed greater sensitivity to ulcer/neuropathic severity. No studies have simultaneously evaluated disease-specific tools. Generic and utility HRQOL PROMs are frequently used as secondary outcome measures in randomised trials and cost–utility analysis.

HRQOL is depressed in diabetes, further impaired by the presence of foot disease. Ulcer healing is associated with improvements in HRQOL. Patients with active ulceration report poorer HRQOL than those whom have undergone successful minor lower extremity amputation (LEA) but there is a paucity of quality data on HRQOL outcomes for diabetes-related LEA.
Conclusions/interpretation No one PROM was identified as a 'gold standard' for assessing HRQOL in diabetes-related foot disease. Specific areas for further development include the most valid HRQOL PROM with disease-specific content; HRQOL outcomes in minor and major amputations and the role of HRQOL tools in routine clinical care.

Keywords Amputation · Diabetic foot disease · Health-related quality of life · Patient-reported outcome measures · Peripheral neuropathy · Ulcer

Abbreviations

CWIS	Cardiff Wound Index Scale
DFS	Diabetic Foot Ulcer Scale
DFS-SF	Diabetic Foot Ulcer Scale Short Form
DFU	Diabetic foot ulcer
DPN	Diabetes-related peripheral neuropathy
EQ-5D	EuroQOL 5D Health Utility Index
HRQOL	Health-related quality of life
LEA	Lower extremity amputation
NICE	National Institute for Health and Clinical Excellence
Norfolk QoL-DN	Norfolk Quality of Life in Diabetic Neuropathy Questionnaire
PROM	Patient-recorded outcome measure
RAND-36	Research and Development 36-item Form
SF-12	Medical Outcomes Study 12-item Short-Form Health Survey
SF-36	Medical Outcomes Study 36-item Short-Form Health Survey

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Introduction

Management of diabetes-related foot disease demands a multidisciplinary approach with treatments that are often intensive and prolonged. As a result, hospitalisations are frequent and costs are high. Evidence to support any one approach over another, in terms of conventional endpoints such as wound healing or major amputation, is thin [1]. Given the lack of clear benefit in terms of conventional outcome measures, the use of other markers of treatment success may be more appropriate.

One such marker is health-related quality of life (HRQOL). HRQOL is a subjective measure of a person's physical and psychological well-being and represents a patient's assessment of how a particular disease or intervention has affected their life. Information about a patient's HRQOL is commonly gathered using 'Patient-Reported Outcome Measures' (PROMs). These involve the patient responding to a number of questions on themes such as physical functioning, social functioning and mental well-being, and may include both generic and disease-specific questions. Responses are analysed to produce a multi-dimensional quality of life 'score' that can be measured repeatedly to help clinicians identify an improvement or deterioration in a patient's health status. The use of PROMs has been recommended in the evaluation of healthcare technologies/services and in regulatory decision-making in the UK National Health Service (NHS) [2].

The purpose of this review is to summarise and analyse the literature pertaining to HRQOL PROMs used in the spectrum of diabetes-related foot disease. Specifically, we aim to assess the validity of HRQOL PROMs and examine specific factors affecting HRQOL in patients with diabetes and foot disease.

Methods

Systematic searches using the keywords 'diabetes mellitus and foot' OR 'diabetic foot' AND 'neuropathy/ulcer/Charcot arthropathy/amputation/lower extremity amputation' AND 'health related quality of life/quality of life/QALY/patient reported outcome measure' were performed using the 'explosion technique' where possible in Medline, PubMed, EMBASE and the Cochrane Library. Articles were limited to English language, human studies and peer review publications, and included all papers identified from 1966 to 7 February 2011. Bibliographies of relevant citations were screened for further articles of relevance.

Inclusion criteria specified that studies had to assess HRQOL specifically pertaining to foot health in patients with diabetes using structured PROMs. Studies using PROMs to look at general aspects of HRQOL in diabetes were excluded, as were studies that used 'self-evaluation' (i.e. free texting/interviews without formulaic format) as a means of recording HRQOL.

HRQOL PROMs were rated according to pre-defined criteria (assessing study quality, quality of tool employed and the generalisability of outcomes) [3]. The score was adapted to ensure its relevance to diabetes-related foot disease [4] and an overall quality 'score' (range, 0–15) was assigned as a gross marker of fulfilment of the criteria—where 0 represented poorest quality and 15 best quality.

The literature review conformed to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement standards [5, 6]. Owing to heterogeneity of study design, varying methodology and PROMs used, a quantitative pooled meta-analysis was not performed.

Results

Initial search strategies revealed 203 papers. When abstracts and reference lists were scrutinised and exclusion/inclusion criteria applied, 53 studies were eligible and included (Fig. 1). The median quality 'score' [3] of the 53 included studies assessed was 10 (range 4–15) (Table 1).

PROMs used to assess HRQOL in diabetes-related foot disease

A variety of generic, summary, utility, dimension specific, disease-specific and site-specific PROMs were used to assess HRQOL in diabetes-related foot disease (Tables 1 and 2).

Generic PROMs The most frequently encountered tool, used in 27 studies, was the generic HRQOL tool: the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36) (http://www.qualitymetric.com). The SF-36 is commonly used as a 'gold standard' PROM to verify construct validity when developing disease-/site-/dimension-specific PROMs. It has shown efficacy in assessing HRQOL in diabetes-related foot disease [7–18] (Fig. 2). When evaluated alongside site-/disease-specific PROMs, the Diabetic Foot Ulcer Scale (DFS) [10–12] and the Cardiff Wound Index Scale (CWIS) [8, 19], statistically significant correlations between the assessed 'life domains' (e.g. locomotor abilities, mental wellness, personal care) make it an appropriate measure (Fig. 3).

The SF-36 has shown sensitivity when correlating HRQOL scores with diabetic foot ulcers (DFUs) [13] and neuropathy severity [20]. Furthermore it can show temporal changes in HRQOL [21] and has been used in a number of randomised controlled trials assessing the treatment of diabetes-related foot disease [9, 12, 22–26] in which improvements in primary outcomes (i.e. ulcer healing and

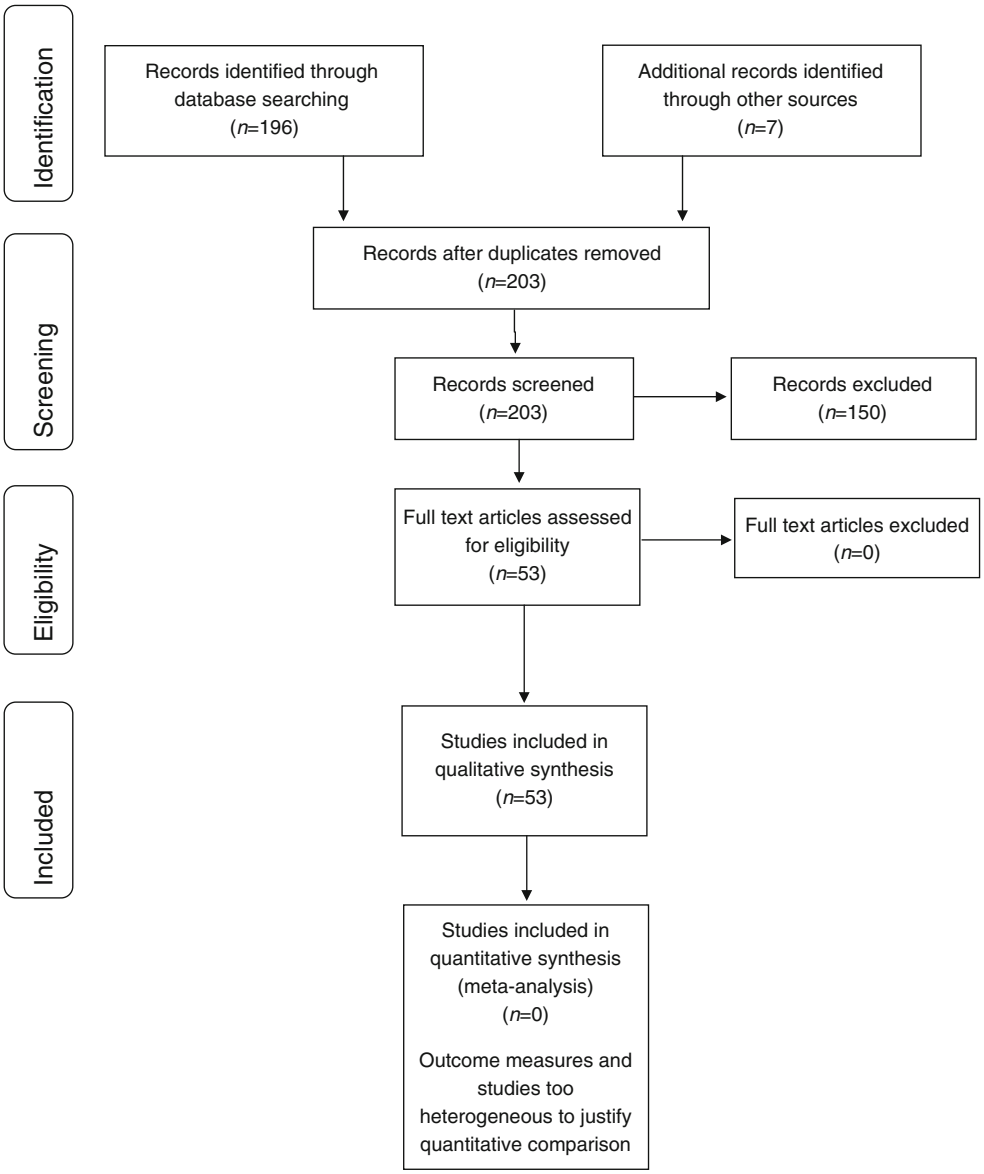

Fig. 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 flow diagram

improved pain scores) were associated with appropriate changes in HRQOL scores.

In contrast, a Nottingham-based randomised controlled trial assessing the use of different dressing types in the treatment of DFUs used the SF-36 alongside the CWIS to document HRQOL as a secondary outcome measure. Whereas the CWIS showed statistically significant improvements in HRQOL between healed and non-healed ulcers, the SF-36 failed to show any difference [27]. This poor sensitivity to ulcer healing was presumed by the study group to relate to the large volume of incomplete SF-36 questionnaires at follow-up, suggesting that it is a poorly accepted tool. Most observational studies assessed by this review have, however, reported good response rates of >70% when using the SF-36.

The SF-36 is well equipped to generate a generic measure of HRQOL and can be truncated into the Medical Outcomes Study 6D Short-Form Health Utility Index (SF-6D) for health utility analysis. However, the SF-36 lacks specificity and may be confounded by other (non-foot) complications of diabetes [13, 14].

Other generic measures of HRQOL (the Medical Outcomes Study 12-item Short-Form Health Survey [SF-12], the Research and Development 36-item Form [RAND-36], the Nottingham Health Profile, the Sickness Index Profile) show appropriate changes in HRQOL according to severity of foot disease [28–31] but remain subject to confounding factors as a result of poor specificity.

Health utility PROMs Health utility PROMS have been used for the economic evaluation of foot care/treatment in diabetes with variable outcomes in terms of calculated health states (Table 2). To ensure comparability between cost–utility analyses and to guide healthcare resource allocation, the National Institute for Health and Clinical

Table 1 Eligible studies assessing HRQOL in diabetic foot disease

Reference	Study design	Study aims	PROM used	Quality score
Eckman et al, USA, 1995 [41]	Cost–utility	To determine outcomes in management of foot infection/ osteomyelitis in T2DM	SF-36	6
Carrington et al, UK, 1996 [33]	Cross-sectional	To compare the HRQOL of diabetic patients with chronic DFU, LEA and controls without foot disease	Quality of Life Ladder Foot questionnaire	7
Armstrong et al, USA, 1997 [51]	Longitudinal	To evaluate pulsed-dose electrical stimulation as an analgesic modality in patients with painful DPN (HRQOL as a secondary outcome)	10 cm VAS	7
Backonja et al, USA, 1998 [52]	Randomised controlled trial	To evaluate the use of gabapentin monotherapy in painful DPN (HRQOL as a secondary outcome)	SF-36	13
Benbow et al, UK, 1998 [28]	Cross-sectional	To assess HRQOL and pain scores in patients with DPN	Nottingham Health Profile 10 cm VAS	11
Piaggesi et al, Italy, 1998 [53]	Randomised controlled trial	To assess the surgical vs non-surgical management of DFU	10 cm VAS	5
Davies et al, UK, 2000 [48]	Longitudinal	To assess the impact of orthotic treatment on HRQOL in diabetes-related foot disease	SF-36	10
Tennvall and Apelqvist, Sweden, 2000 [43, 44]	Cross-sectional	To assess HRQOL in patients with diabetes: with current DFU, primary healed DFU, a history of minor LEA and a history of major LEA	EQ-5D with 10 cm VAS	13
Meijer et al, Holland, 2001 [29]	Cross-sectional	To compare the HRQOL of patients with and without DFU	RAND-36 Barthel Score WSQ	12
Peters et al, USA, 2001 [30]	Cross-sectional	To assess functional levels in patients with diabetes post LEA	SIP	11
Abetz et al, UK, 2002 [12]	Longitudinal	To assess validity/reliability of the DFS tool	DFS SF-36	15
Coffey et al, USA, 2002 [54]	Cross-sectional/Cost–utility	To describe the health utilities associated with diabetes and its treatments, complications and co-morbidities	QWB-SA	10
Pinzur, et al, USA, 2003 [40]	Cross-sectional	To evaluate the HRQOL of patients with Charcot arthropathy	SF-36 AAOS	8
Vileikyte et al, USA + UK, 2003 [31]	Cross-sectional	To develop and validate NeuroQoL	NeuroQoL SF-12	13
Price and Harding, UK, 2004, [8]	Focus groups, pilot study, cross-sectional	To document the development of the CWIS and to validate it	CWIS SF-36	11
Rosenstock et al, USA, 2004 [26]	Randomised controlled trial	To evaluate pregabalin in painful DPN (HRQOL as a secondary outcome)	SF-36	9
Dhahwan et al, USA, 2005 [55]	Cross-sectional multicentre	To document the development of and evaluate a Charcot arthropathy-specific HRQOL tool	AOFAS-DFQ	7
Evans and Pinzur, USA, 2005 [56]	Cross-sectional	To perform a feasibility trial using AAOS to assess HRQOL in DFU	AAOS	7
Nabuurs-Franssen et al, UK, USA and Europe, 2005 [9]	Randomised placebo-controlled trial	To assess whether ulcer healing improves HRQOL (HRQOL as a secondary outcome measure)	SF-36	13
Willrich et al, USA, 2005 [57]	Cross-sectional	To assess HRQOL and depression in DM patients with DFU, osteomyelitis, Charcot arthropathy and LEA	SF-36	8
Valensi et al, France, 2005 [11]	Cross-sectional	To compare the HRQOL of patients with diabetes with and without DFU to determine factors influencing disease-specific HRQOL in DFU	SF-36 DFS	13
Vinik et al, USA, 2005 [35]	Cross-sectional	To validate and evaluate the Norfolk QOL-DN tool	Norfolk QOL-DN	9

Table 1 (continued)

Reference	Study design	Study aims	PROM used	Quality score
Currie et al, UK, 2006 [20]	Cost–utility	To characterise symptom severity of DPN in people with diabetes, correlating with health-related utility and HRQOL	Norfolk QOL-DN SF-36	15
Davies et al, UK, 2006 [7]	Cross-sectional	To determine the prevalence and severity of painful DPN and examine its impact on HRQOL	NeuroQoL	12
Goodridge et al, Canada, 2006 [58]	Cross-sectional	To evaluate HRQOL in patients with unhealed and healed DFUs	CWIS SF-12	12
Ribu et al, Norway, 2006 [15]	Cross-sectional	To assess the prevalence and occurrence of DFU pain on HRQOL using generic and disease-specific PROMS	SF-36 DFS	9
Tarride et al, Canada, 2006 [59]	Cost–utility	To examine the 12 week cost-effectiveness of pregabalin vs gabapentin, in DPN and post-herpetic neuralgia	EQ-5D	8
Tolle et al, Europe, 2006 [60]	Cost–utility	To determine patient burden of painful DPN with respect to pain intensity, patient functioning and to characterise treatment patterns	EQ-5D	12
Casselini et al, USA, 2007 [61]	Randomised controlled double-blind placebo-controlled trial	To investigate the effects of PKC-β inhibitor ruboxistaurin on neurovascular function and other measures of DPN (HRQOL as a secondary outcome)	Norfolk QOL DN	9
Lewko et al, Poland, 2007 [62]	Cross-sectional	To determine the relationship between HRQOL and degrees of acceptance of those with and without DPN	SF-36	6
Nelson and Little, USA, 2007 [63]	Cross-sectional	To evaluate changes in HRQOL after multiple lower-extremity nerve decompressions in DPN	Sf-36	4
Rauck et al, USA, 2007 [25]	Randomised controlled trial	To evaluate effects of lacosamide on painful DPN (HRQOL as a secondary outcome measure)	SF-36	11
Ribu et al, Norway, 2007 [14]	Cross-sectional	To describe HRQOL in those with DFU compared with controls	SF-36	9
Ribu et al, Norway, 2007 [13]	Cross-sectional	To describe socio-demographic variables, clinical characteristics and treatment factors in DFU and to explore their associations with HRQOL	SF-36	9
Armstrong et al, USA, 2008 [24]	Randomised controlled trial	To compare the HRQOL of patients with diabetes with and without pressure offloading modalities to heal DFU	SF-36	11
Boutoille et al, France, 2008 [45]	Retrospective case–control	To evaluate the influence of amputation for DFU on HRQOL	SF-36	10
Happich et al, Germany, 2008 [64]	Observational cost analysis	To describe HRQOL, resource utilisation and annual costs associated with DPN	SF-12 Norfolk QoL-DN	10
Huang et al, Taiwan, 2008 [16]	Cross-sectional	To compare generic and disease-specific measures of HRQOL in the assessment of patients with diabetes (regardless of foot health)	D-39 SF-36	10
Lavery et al, USA, 2008 [65]	Randomised controlled trial	To determine the efficacy of anodyne monochromatic infrared photo energy in home treatments on improving peripheral sensation and HRQOL in patients with DM (HRQOL as a secondary outcome measure)	NeuroQoL	7
Lincoln et al, UK, 2008 [66]	Randomised controlled trial	To determine the effect of a foot care education programme in the secondary prevention of foot ulcers (assessing HRQOL as a secondary outcome)	DFS	10
Ribu et al, Norway, 2008 [10]	Longitudinal	To assess temporal changes in HRQOL	SF-36	10

Table 1 (continued)

Reference	Study design	Study aims	PROM used	Quality score
Sochocki et al, Canada, 2008 [18]	Cross-sectional	To evaluate HRQOL in patients with Charcot arthropathy and identify risk factors that contribute to poor HRQOL	SF-36	8
Vinik et al, Germany, 2008 [36]	Cross-sectional	To evaluate the German version of the Norfolk QOL-DN	Norfolk QOL-DN	6
Jeffcoate et al, UK, 2009 [27]	Randomised controlled trial	To compare the effectiveness and cost-effectiveness of three dressing products for DFU	SF-36 CWIS 10 cm VAS	14
Pakarinen et al, Finland, 2009 [17]	Cross-sectional	To evaluate the long-term effects of diabetes-related Charcot foot	SF-36	10
Rerkasem et al, Thailand, 2009 [49]	Retrospective cohort	To assess the HRQOL outcomes of DFU patients who were involved in a randomised controlled trial assessing outcomes in management according to a 'diabetic foot pathway' compared with standard care pathways	SF-36	9
Winkley et al, UK, 2009 [42]	Prospective cohort	To describe temporal changes in HRQOL in patients with their first DFU over 18 months and its association with adverse outcomes	SF-36	12
Jaksa and Mahoney, Canada, 2010 [19]	Cross-sectional	To evaluate the CWIS in a DFU population	CWIS SF-36	9
Mittlmeier et al, USA, 2010 [67]	Retrospective cohort	To evaluate outcomes in primary surgical management of Charcot joints	AOFAS Ankle Hindfoot Scale	9
Selvarajah et al, UK, 2010 [22]	Randomised controlled trial	To assess efficacy of Sativex (GW Pharmaceuticals, Salisbury, UK), a cannabis-based product, as adjuvant treatment of painful DPN (HRQOL as secondary outcome)	EQ-5D SF-36 10 cm VAS	7
Swislocki et al, USA, 2010 [23]	Randomised controlled trial	To evaluate the photon stimulations affect on pain and HRQOL in patients with painful DPN (HRQOL as secondary outcomes)	SF-36	6

AAOS, American Academy of Orthopaedic Surgeons Musculoskeletal Outcomes Measure: Foot and Ankle; ADL, activities of daily living; AKA, above-knee amputation; BKA, below-knee amputation; DM, patients with diabetes mellitus; QWB-SA, Quality of Well Being Index – Self Administered; PKC-β, protein kinase C β; T2DM, type 2 diabetes mellitus; TA, toe amputation; TMA, transmetatarsal amputation; VAS, visual analogue scale; WSQ, Walking and Walking Stairs Questionnaire

Excellence (NICE) have specified the EuroQOL 5D Health Utility Index (EQ-5D) as the preferred PROM for use in the UK [32].

Diabetic foot-specific PROMs PROMs specifically designed to assess diabetes-related foot problems include the DFS [12], NeuroQoL [31] and the Carrington foot questionnaire [33].

The DFS was developed using semi-structured interviews and focus groups of patients with DFUs and their care givers [12]. It has shown internal consistency, reliability, validity [12] and sensitivity to wound severity [11, 15] and healing [15]. A shortened version, the DFS Short Form (DFS-SF) [34] showed similar robustness and sensitivity. The DFS-SF has statistically significant regression correlations to the DFS and SF-36 and, at only 29 questions, is a more 'user-friendly' tool for everyday clinical practice.

NeuroQoL was designed to assess HRQOL in patients with diabetes complicated by peripheral neuropathy and DFUs. It has been validated against the SF-12 to show construct validity and sensitivity to neuropathic symptoms, which the SF-12 (as a generic instrument) is unable to detect. Factor analyses have demonstrated internal consistency and its brevity makes it feasible and acceptable.

NeuroQoL has proven proficient in assessing the impact of advancing neuropathy on HRQOL. It is less useful in showing the relationship between DFU severity and HRQOL. This may reflect the tool's focus on neuropathic (as opposed to ulcerative) symptoms. It could also be a consequence of diminished nociceptive responses in patients with ulcers, reducing pain scores (and thus indicating better HRQOL). However, a well-designed UK cross-sectional population study (using NeuroQoL) disputes this theory; showing more

Table 2 PROMs used in eligible studies

Instrument	Type	Domains/subscales	Scoring system	Comment	Studies using PROM
The Medical Outcomes Study 36-item Short-Form Health Survey (SF-36)	Generic	36 questions measuring eight conceptual domains: • physical functioning • bodily pain • general health perceptions • vitality • social functioning • role limitations due to physical health • role limitations due to emotional problems • mental health	Three key scores: • overall HRQOL score • mental component summary score (MCS-36) • physical component summary score (PCS-36) Overall HRQOL score 0–100 (0 indicating poorest HRQOL)	Facilitates comparison with other chronic diseases. Can be converted into SF-6D scores for health utility evaluations. Not specific to diabetes-related foot disease. The most frequently utilised tool.	[8] [9] [10] [11] [12] [13] [14] [15] [16] [17] [18] [20] [22] [23] [24] [25] [26] [27] [40] [41] [42] [45] [48] [49] [52] [62] [63]
Research and Development 36-item Form (RAND-36)	Generic	Assesses the same domains as SF-36.	As SF-36 but differs in the recommended scoring algorithm.		[29]
The Medical Outcomes Study 12-item Short-Form Health Survey (SF-12)	Generic	Abbreviated adaptation of SF-36. 12 questions measuring the eight conceptual domains of the SF-36.	Overall HRQOL score 0–100 (0 indicating poorest HRQOL)	An abbreviated version of SF-36. Its brevity lends its use to condition-specific surveys that are used in clinical trials. When converted into SF-6D scores can be used in economic evaluation.	[31] [58] [64]
Sickness Impact Profile (SIP)	Generic	136 questions assessing 12 categories of everyday activities: • sleep and rest • emotional behaviour • body care and movement • home management • mobility • social interaction • ambulation • alertness behaviour • communication • work • recreation and pastimes • eating	Scores 0–100 (Scores >20 associated with severe disability)	Known as a ‘health status score’ rather than measure of HRQOL. Infrequently used in the evaluation of diabetes-related foot disease.	[30]
Nottingham Health Profile (NHP)	Generic	Part I: 38 statements requiring yes/no responses to six domains: • energy • sleep • pain • physical mobility • emotional reactions • social isolation Part II: seven yes/no questions on daily living problems.	Parts can be used independently. Scores 0–100 (100 indicating poorest HRQOL)	Well-validated tool but infrequently used in diabetes-related foot disease.	[28]
Quality of Life Ladder (QOLL)	Summary	Life satisfaction marked on a scale.	Scores 0–10 (0 indicating poorest HRQOL)	Quick, non-specific estimate of HRQOL.	[33]
10 cm Visual analogue scale (VAS)	Summary	Pain score/HRQOL score marked on a 10 cm scale.	Scores 0–100% (0 indicating poorest HRQOL)	Quick, non-specific estimate of HRQOL. Subject to poor external consistency. Used within the EQ-5D.	[22] [27] [51] [53]
The Medical Outcomes Study 6D Short-Form Health Utility Index (SF-6D)	Utility	Based on an algorithm using a subset of 11 questions from the SF-36.	Estimates a preference based single summary score which can be used against an index of measures.	Provides a means for using the SF-36 and SF-12 in economic evaluation. Allows the analyst to obtain quality-adjusted life-years (QALYs) for cost–utility analysis. Better descriptive ability and sensitivity to change than EQ-5D.	[27]

Table 2 (continued)

				Defines 18,000 health states. Infrequently used to evaluate HRQOL in diabetes-related foot disease.	
Quality of Well Being Index – Self Administered (QWB-SA)	Utility	Participants asked to identify symptoms/problems that have affected them over last 3 days from list of 58 items based on three scales of functioning: • mobility • physical activity • social activity	Score 0–10 (0 indicating poorest HRQOL)	Used to create health utility scores. Infrequently used to evaluate HRQOL in diabetes-related foot disease.	[54]
EuroQOL 5D Health Utility Index (EQ-5D)	Utility	Five questions with three possible answers for each (1=no problem, 2= moderate problem, 3=severe problems) on: • mobility • self care • usual activities • pain/discomfort • anxiety/depression and Completion of 20 cm visual analogue scale. and Single question on current health state: Is it worse/same/better than 1 year previous?	Produces 'health state' profile comprising of a single summary score created using a formula which weighs the different domains, based on EQ-5D scores from the general population. Numeric index generated from –0.594 to 1. (Score 0 represents no quality of life; scores <0 represent states perceived by the respondent to be worse than death)	The five dimensions assessed can be transcribed into 243 possible health states. Designed as research/health utility tool – not recommended for use in routine clinical practice. Can generate QALYs from VAS. Relies on ratings from the general public to define 'normality' [68]. Recommended for use in the UK by NICE.	[20] [22] [44] [60]
Barthel Index	Dimension-specific	Ten questions on activities of daily living.	Score 0–20 (20 indicates normality)	Infrequently used to evaluate HRQOL in diabetes-related foot disease.	[29]
Walking and Walking Stairs Questionnaire (WSQ)	Dimension-specific	62 questions subdivided into four hierarchical scales.	Scores 0–100 (0 indicating poorest mobility)	Not a global assessment of HRQOL. Infrequently used to evaluate HRQOL in diabetes-related foot disease.	[29]
American Academy of Orthopaedic Surgeons – Diabetic Foot Questionnaire (AAOS–DFQ)	Disease-specific	66 question tool in five sub-sections: • demographics • health conditions • general health • foot problems • diabetes and foot care assessing six domains: • general health • physicality • emotion • worry • foot status • care	Numerous outcome measure scales: Scores 0–100 (0 indicating poorest HRQOL)	Made from pre-validated instruments but, as a whole, limited validation of AAOS-DFQ. Specific but cumbersome scoring scales. Infrequently used to evaluate HRQOL in diabetes-related foot disease.	[55]
Diabetes 39 (D-39)	Disease-specific	39 questions (seven-point Likert Scale): • energy and mobility • diabetes control • anxiety and worry • social burden • sexual functioning	Subscale scores generated with higher scores reflecting poorer HRQOL. Summary score created from subscale scores.	For HRQOL assessment in T1/T2 diabetes mellitus. Not specific to foot pathology. Infrequently used to evaluate HRQOL in diabetes-related foot disease.	[16]
Cardiff Wound Impact Schedule (CWIS)	Disease-specific	47 questions divided into four domains: • well-being • physical symptoms and daily living • social life • overall quality of life	Scores 0–100 (0 indicating the poorest HRQOL)	For all chronic wounds. Shows sensitivity to wound healing in RCT evaluating types of dressings for DFU [27]. Lacks sensitivity to ulcer severity [8].	[8] [19] [27] [58]
Norfolk Quality of Life in Diabetic Peripheral Neuropathy Questionnaire (Norfolk QoL DN)	Disease-specific	47 questions grouped into: • small fibre function • large fibre function • autonomic function • symptoms • activities of daily living	Score 0–100% (0 indicating best HRQOL)	Designed as a 'fibre-specific' tool to assess all aspects of DPN. Not specific to foot disease.	[20] [35] [36] [61] [64]

Table 2 (continued)

NeuroQoL	Disease-specific	28 questions (five-point Likert Scale) assessing two domains: 1. Physical factors • painful symptoms • reduced feeling • diffuse sensorimotor symptoms 2. Psychosocial factors • disruption of daily activities • interpersonal-emotional burden and Overall question asking patients to rate overall QOL.	Two scale scores: physical symptom and psychosocial functioning. Overall HRQOL measured by one-item measure from NeuroQoL.	Validation has shown high degrees of internal consistency and robust test–retest reliability. Poorly sensitive to ulceration severity [31]. The neuropathic disability score was used to assess neuropathy severity in the development of this tool, but no such tool was used to grade ulceration.	[7] [31] [65]
Foot Questionnaire	Site-/region-specific	12 pairs of opposites reported on a seven point scale. Participants mark on a line how they feel about their foot at that time.	Higher scores indicating more positive attitude towards feet.	Not validated.	[33]
Diabetes Foot Ulcer Scale (DFS)	Site-/region-specific	58 questions assessing factors specific to DFUs in 15 subscales: • leisure • physical health • daily life • dependence • family and friends • treatment compliance • positive relationship • financial burden • side effects • diet • compliance • medical complications • satisfaction	Scores 0–100 (0 indicating poorer HRQOL)	Assessed against SF-36: assumed superior as more reliable in discriminating between healed and current DFU [10, 12–14].	[11] [12] [15] [66]
Diabetes Foot Ulcer Scale-Short Form (DFS-SF)	Site-/region-specific	29 questions based on six subscales: • leisure • physical health • dependence/daily life • negative emotions • worry about ulcer/feet • impact of ulcer care	Scores 0–100 (0 indicating poorer HRQOL)	Well validated against DFS. Brevity enhances acceptability.	[69]
American Academy of Orthopaedic Surgeons Musculoskeletal Outcomes Measure: Foot and Ankle (AAOS)	Site-/region-specific	Clinical based outcomes from nine questions on three subscales: • pain • function • alignment	Produces outcome measure scales. All scales with scores from 0–100: • co-morbidity scale • individual co-morbidity subscales • physical health and pain (aka SF-36) • treatment expectations • satisfaction with symptoms • global foot and ankle scale (GFAS) • shoe comfort scale (SCS)	General health system includes SF-36 item set. Not one HRQOL score produced – numerous scales. Not validated against any other HRQOL tools.	[40] [56] [67]
American Academy of Foot and Ankle Surgeons – Ankle/Hindfoot Scale (AOFAS–Ankle/Hindfoot Scale)	Site-/region-specific	Five subscales each containing nine items: • pain • appearance • functional capacities • radiographic evaluation • musculoskeletal	Overall scores 0–100 (0 indicating greatest disability)	Subjective scores of pain and function provided by the patient. Objective scores based on the surgeon's physical examination of the patient, making it not a 'true' PROM. Infrequently used to evaluate HRQOL in diabetes-related foot disease.	[67]

severe neuropathy to be associated with a higher prevalence of pain and a poorer HRQOL [7]. NeuroQoL's poor sensitivity to DFUs may therefore be related to its failure to assess ulcer-related therapies (e.g. non-weight-bearing regimens, dressing changes and antibiotic therapy).

The Norfolk Quality of Life in Diabetic Neuropathy Questionnaire (Norfolk QoL-DN) was designed to assess all aspects of diabetes-related neuropathic disease. It is intended for use as a diagnostic aide as well as for disease monitoring and treatment evaluation [20, 35]. Despite robust validation, the Norfolk QoL-DN [35, 36] lacks specificity for peripheral neuropathy, limiting its use in assessing the impact of diabetes-related foot disease.

Disease-specific tools for diabetes-related peripheral neuropathy (DPN) have shown sensitivity to symptom severity but no attempts have been made to evaluate their

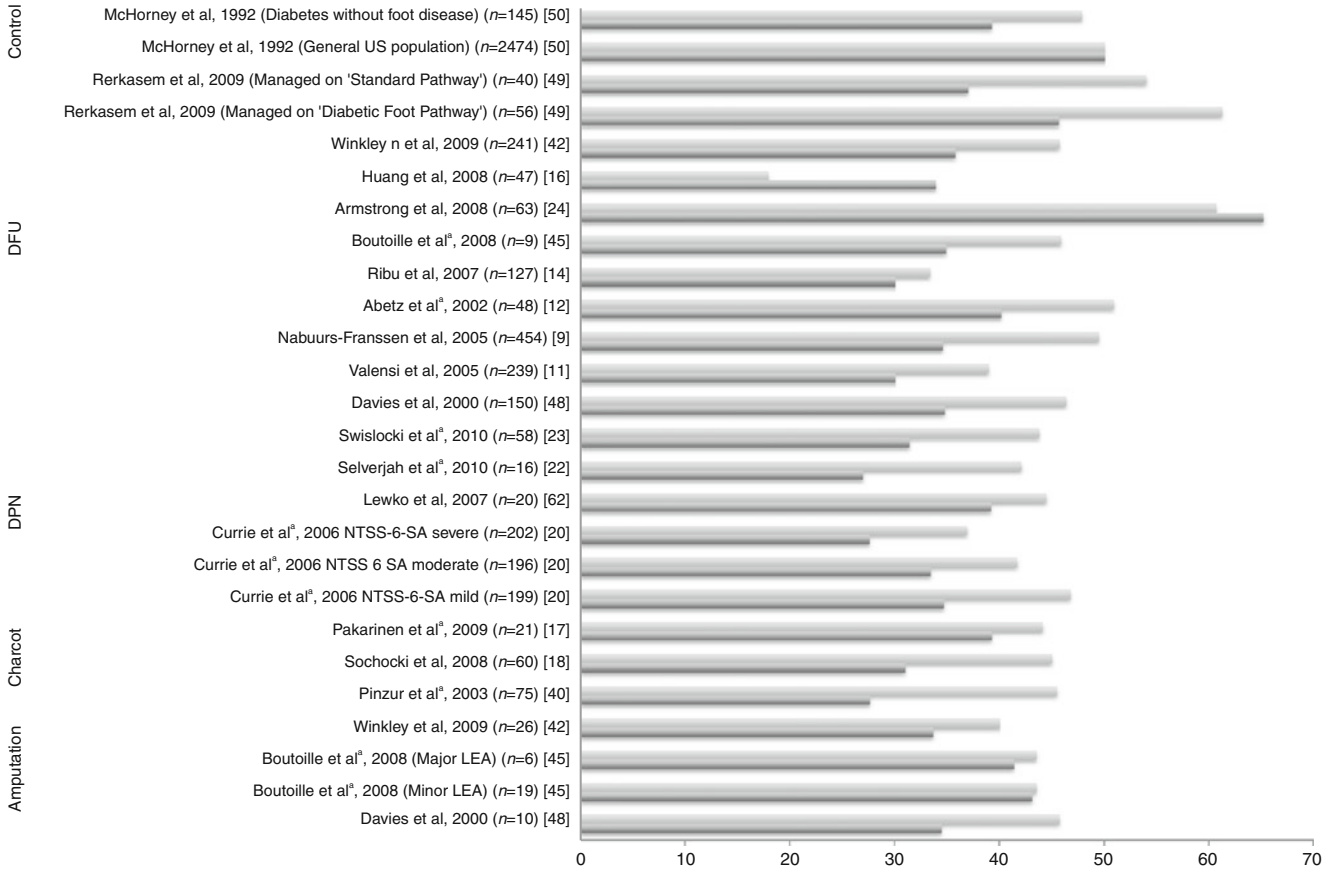

Fig. 2 Comparison of SF-36 physical component scores (PCS, dark grey bars) and mental component scores (MCS, light grey bars) from studies using the SF-36 to record HRQOL in diabetes-related foot disease. Scores compared to those from patients with diabetes without foot disease and the general US population [50]. Scores as stated in respective studies. [a]Studies in which component scores were not stated in text. PCS and MCS calculated from subscores at SF-36, PCS, MCS and NBS Calculator, available at www.sf-36.org/nbscalc/index.shtml, accessed 1 November 2010 NTSS-6-SA, Neuropathic total symptom score—self-administered

efficacy in assessing temporal changes in HRQOL in individuals with DPN. As a result their use in disease monitoring is currently limited.

Wound-specific PROMs The CWIS has validity in assessing chronic wounds but is not specific to DFUs [8, 19]. Evaluation alongside the SF-36 showed significant correlations in all domains [8, 19] but sensitivity to severity of DFUs was lacking when CWIS HRQOL values were compared against ulcer severity (as determined by the University of Texas Wound Classification system) [19]. The CWIS is able to discriminate between healed and unhealed ulcers [8, 27]

Combined generic and disease-specific PROMs Combining generic and disease-specific PROMs produces more useful information on outcomes [4]. Different measures provide complementary evidence, with disease-specific tools offering specific clinical information and reflecting treatment effects and generic measures collecting information more transferrable to the service provider and highlighting unforeseen intervention effects. There are no 'combined PROMs' in use in diabetes-related foot disease.

The impact of foot complications on HRQOL in patients with diabetes

Foot monitoring and podiatry Individuals with diabetes without foot disease have a lower HRQOL compared with the general population (Fig. 2) [7, 8, 11, 12, 14, 28, 29, 33, 35, 36]. This may relate to the general lifestyle/complications of diabetes but may also reflect the commitment needed to preserve foot health. Patient focus groups have shown that preventative foot care practices (regular visits to the podiatrist, having to wear restrictive footwear, daily foot care regimens and restrictions on activities, etc) negatively impacts HRQOL [8, 37].

DPN DPN may be asymptomatic but when painful impacts on HRQOL. Functional problems (disturbed balance; reduced foot sensation; disturbed sleep; limitations in footwear) and

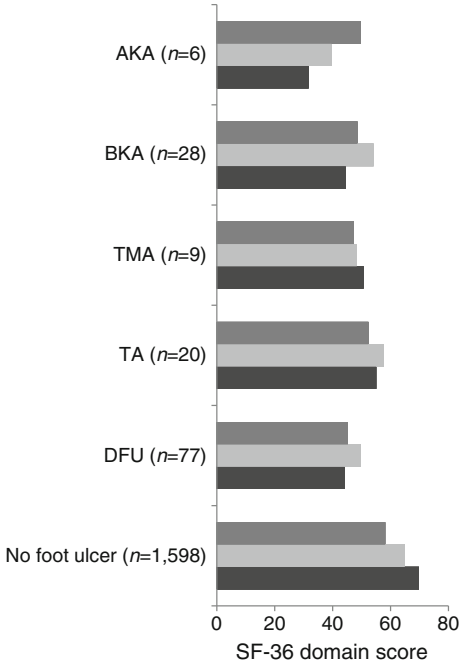

Fig. 3 Comparison of mean SF-36 domain scores in patients with type 2 diabetes and DFU undergoing amputation vs medical management. Scores compared with patients with diabetes without foot disease [41]. Scores range from 0 to 100 with a score of 0 reflecting poorest life HRQOL. Mid-grey bars, General Perception of Health; light grey bars, Pain Score; dark grey bars, Physical Functioning. AKA, above-knee amputation; BKA, below-knee amputation; TMA, transmetatarsal amputation; TA, toe amputation

psychological fears of advancing disease, ulceration and amputation often exist together. DPN is difficult to study in terms of impact on HRQOL as the classical view is that less advanced neuropathy is associated with more pain [38]. In advanced foot disease (e.g. ulceration), it is difficult to determine the exact impact of neuropathy in isolation.

Ulceration Ulcer healing has a positive impact on HRQOL scores whilst persisting ulcers have a progressively negative effect on life quality [8–10, 12]. HRQOL scores in patients who have undergone successful minor amputation for DFUs are significantly superior to those with persisting ulcers [30, 33] (although definitions of successful amputation are vague). Those who undergo major lower extremity amputation (LEA) have worse HRQOL scores than those with active DFUs [30, 33].

One study assessing variables that determine HRQOL in DFUs showed: presence of infection, co-existing peripheral arterial disease and ulcer size to be the most important [14]. When evaluating the influence of pain on HRQOL in DFUs, the same group reported that larger persisting ulcers (>5 cm) were less painful than smaller ulcers of shorter existence [15], but were associated with poorer HRQOL due to 'non pain related' factors. Indeed focus groups have found that HRQOL in DFUs most closely relate to the impact of treatments (regular dressing changes, poorer mobility caused by non weight bearing regimens, prolonged antibiotic therapy), anxieties around possibilities of future amputation, financial losses secondary to medical incapacity and the day to day disruption on social and family life rather than the ulcer size or duration [39].

Charcot arthropathy Few studies formally assessed HRQOL in patients with diabetes and Charcot disease [17, 18, 40]. Of those studies that identified Charcot arthropathy as a separate subgroup, it was suggested (using the American Academy of Orthopaedic Surgeons – Diabetic Foot Questionnaire [AAOS–DFQ] and SF-36) that the health status in these patients was comparable to that following minor LEA [40]. However these studies were small and a more detailed analysis of a broader spectrum of patients at different stages of Charcot arthropathy is required.

Amputation Outcomes in amputation have focused on functional status and mobility rather than HRQOL. A large cost–utility analysis performed in USA used three components of the SF-36 to assess HRQOL in patients with diabetes [41]. Those with active ulcers had significantly lower HRQOL scores for 'physical functioning' than those who had undergone successful toe or transmetatarsal amputations. Physical functioning in below knee amputation was no different to that in DFUs, but above knee amputation scores were worse (Fig. 4). Despite the large overall size of this cross-sectional analysis, the subgroups of interest were small and amputation groups poorly representative. Only patients who had undergone successful operations were included in this study (although 'success' was poorly defined), with no account for amputation related morbidity and mortality.

In the UK, a prospective cohort study used the SF-36 to chart HRQOL outcomes in patients with their first

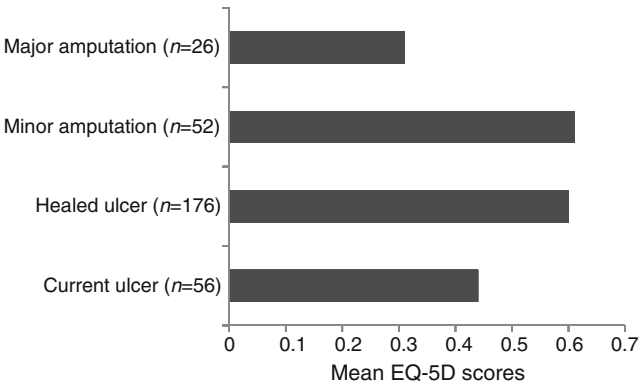

Fig. 4 Mean EQ-5D scores for patients with active ulceration/healed ulcers/minor amputation/major amputation. Possible scores range from –0.594 to 1. A score of 0 represents no life quality; scores <0 reflect a perceived life quality worse than death; a score of 1 indicates best possible life quality [43, 44]

diagnosis of DFUs. No significant deterioration in HRQOL scores was found (when adjusted for confounders) in those who went on to amputation [42]. Similarly, observational studies in Sweden [43, 44] and France [45], using the EQ-5D and SF-36, respectively, found (with the exception of major amputation, where scores were considerably lower) poorer HRQOL scores in those with active DFUs compared with patients who had undergone successful minor amputations. The Swedish group showed no difference in scores for minor amputation and primary ulcer healing (Fig. 4). Two other small observational studies [30, 33] have shown similar patterns.

Of key importance, all the studies identified that evaluate HRQOL in patients post amputation were of poor quality with small, highly selected patient groups (i.e. well healed rather than amputation stumps with complications).

Environment, delivery and modality of care A supportive multi-disciplinary team (MDT) for diabetes care is associated with improved self-management and health-related outcomes [46–48]. Using generic and disease-specific PROMs (SF-36 and DFS), a French observational study [11] found better HRQOL outcomes for patients managed in tertiary centres, with less deterioration in physical health scores, less irritation due to ulcer appearance, shorter durations of foot ulcer care, greater closeness with partners and friends and greater satisfaction with overall medical care. These results were echoed by patients cared for by a devoted MDT in Thailand [49].

Discussion

Generic, diabetes foot-specific, utility, complication-specific, summary, site-specific and combination PROMs all have validity in measuring HRQOL in patients with diabetes-related foot disease. However, each has its limitations and none can be considered a suitable tool in every study or complication setting. Of the generic tools, the SF-36 shows sensitivity to foot disease and has been used most frequently but lacks NICE approval for use in utility studies (who favour the EQ-5D). Of the disease-specific tools, the DFS and NeuroQoL are the most validated, but no studies have compared them simultaneously and, as their titles suggest, they fail to encompass the full spectrum of diabetes-related foot disease. The CWIS shows promise in assessing HRQOL in active ulceration, but is non-specific for DFUs and may fail to capture aspects of this disease. Using a combination of generic and disease-specific PROMs should produce the most meaningful outcomes, but as indicated by the poor response rate in one randomised trial, the use of two instruments (e.g. CWIS and SF-36) may be cumbersome and unfeasible in clinical practice [27].

Generic HRQOL tools are limited in their abilities in identifying the factors reducing HRQOL (for example, a low score on ‘role performance’ may result from retinopathy rather than foot disease). Their advantage is that they can be compared against pre-existing figures from the general population and translated into cost–utility analysis making these tools more amenable to the research setting.

Disease-specific tools (DFS, NeuroQoL) offer greater insight into specific issues impairing health status. They show greater sensitivity to changing foot health/disease severity and are subject to fewer confounders, offering greater insights into lifestyle factors that may be improved by the MDT. Limitations include validation in smaller numbers of studies, exclusivity to disease state (cannot be given to a disease free control group) and narrow focus (they may miss unexpected aspects of impaired HRQOL, e.g. gastrointestinal side effects from antibiotics used to treat osteomyelitis that would not exist with surgical management). In contrast, these tools offer more use in the clinical setting for disease monitoring.

The quality of studies available was variable. The assessment of test-retest reliability and use of comparable HRQOL tools to assess construct validity of PROMs was often lacking and should be encouraged when validating any PROM. The ‘quality score’ used in this review is a gross estimate of ‘quality’ pertaining to the correct use of a PROM [3]. However, a well designed RCT that uses a single PROM as a secondary outcome measure may have a poor quality score due to a number of issues such as an ungeneralisable patient group, lack of re-test validation and lack of discussion of HRQOL domains, etc. The score is therefore more useful in observational studies designed to evaluate PROMs.

HRQOL PROMs have shown the negative impact of advancing foot disease on quality of life. Where uncertainty lies is in outcomes post LEA, where only a small number of poorly generalisable studies have assessed patient reported HRQOL using PROMs [7, 30, 33, 41–43, 45]. The suggestions from these studies (that HRQOL after successful minor amputation is superior to that of active ulceration) could form a large paradigm shift in clinical approach and management of DFUs. However, patient HRQOL after unsuccessful or complicated LEA is a neglected area of study and given that amputations are associated with significant peri-operative and late morbidity, more work in this area is required before any direct conclusions can be made.

Studies indicate that patient-reported HRQOL in DFUs is superior in patients managed by an MDT [11, 49]. There is no data to suggest whether MDT management would improve HRQOL in patients with less severe foot disease.

Preserving HRQOL in patients with diabetes-related foot disease is of high importance and should be measured accurately in order to guide appropriate management of these

patients. Using HRQOL PROMs can offer valid insights into this complex and ever increasing disease; shaping service provision and ensuring cost effective patient care.

This review has demonstrated that a number of tools exist to assess HRQOL in patients with foot-related complications of diabetes. There is no one ideal PROM from which to assess HRQOL and each tool has its limitations. Clinicians and researchers should be aware of these limitations before implementation in individual settings.

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Duality of interest The authors declare that there is no duality of interest associated with this manuscript.

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