



REVIEW ARTICLE

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# Telehealth and telemedicine applications for the diabetic foot: A systematic review

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## Summary

The aim of this systematic review is to assess the peer-reviewed literature on the psychometric properties, feasibility, effectiveness, costs, and current limitations of using telehealth and telemedicine approaches for prevention and management of diabetic foot disease. MEDLINE/PubMed was searched for peer-reviewed studies on telehealth and telemedicine approaches for assessing, monitoring, preventing, or treating diabetic foot disease. Four modalities were formulated: dermal thermography, hyperspectral imaging, digital photographic imaging, and audio/video/online communication. Outcome measures were: validity, reliability, feasibility, effectiveness, and costs. Sixty-one studies were eligible for analysis. Three randomized controlled trials showed that handheld infrared dermal thermography as home-monitoring tool is effective in reducing ulcer recurrence risk, while one small trial showed no effect. Hyperspectral imaging has been tested in clinical settings to assess and monitor foot disease and conflicting results on its diagnostic use show that this method is still in an experimental stage. Digital photography is used to assess and monitor foot ulcers and pre-ulcerative lesions and was found to be a valid, reliable, and feasible method for telehealth purposes. Audio/video/online communication is mainly used for foot ulcer monitoring.

## KEYWORDS

diabetic foot, telehealth, telemedicine, systematic review

## 1 | INTRODUCTION

Foot complications in patients with diabetes mellitus are worldwide a major medical, social, and economic problem, with a lifetime prevalence of foot ulcers of 19%–34%.<sup>1</sup> The most devastating and costly outcome is lower limb amputation, which is nearly always preceded by a foot ulcer or frequently an infected ulcer.<sup>2,3</sup> Healthcare expenditure on

diabetic foot care adds up to one-third of total expenditure on diabetes care,<sup>4,5</sup> and the direct costs per episode of a foot ulcer in specialized centers in Europe is €5000 to €20000.<sup>6</sup> Prevention of these lower limb complications has major positive impact on morbidity, mortality, and patient well-being, and would lead to large savings on healthcare costs.

International guidelines recommend protective pressure-relieving footwear, patient education, self-management, and integrated foot care at regular intervals to prevent a diabetic foot ulcer.<sup>7–9</sup> When a foot ulcer is present, monitoring of the ulcer is important to assess treatment efficacy, predict healing, and respond swiftly in case a

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complication such as a foot infection develops. Ulcer treatment and monitoring is most often done weekly or bi-weekly at the outpatient foot clinic. Once the foot ulcer is healed, the risk of recurrence is up to 40% in the first year and 60% within 3 years.<sup>1,10</sup> As foot ulcers generally occur outside of the clinic, self-management may help to timely identify pre-signs of ulceration and therewith contribute to a sense of self-efficacy in patients with diabetic foot disease. Self-management, however, may be hampered when patients are physically limited because of loss of protective sensation, limited joint mobility, visual impairment or obesity, or when patients lack sufficient knowledge about the disease.<sup>11-13</sup>

Telehealth and telemedicine applications may have value in self-monitoring of foot health status by diabetic patients, mainly for diagnostic, therapeutic, and educational purposes with the goal to improve efficiency and effectiveness of care and patient's well-being and autonomy in a world with rapidly changing socio-economic perspectives in healthcare.<sup>14</sup> Several applications have been developed for this purpose and include dermal thermography, foot imaging tools, and mobile phone/video or online technology. But very few applications have been implemented in diabetic foot care, which may be related to their psychometric properties, feasibility in use, or lack of effectiveness or cost-effectiveness shown. To inform the community on the current state-of-the-art and to guide development and implementation in this field, the purpose was to systematically review the peer reviewed literature on telehealth and telemedicine applications that are used for the assessment, monitoring, prevention, and treatment of diabetic foot disease.

## 2 | METHODS

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>15</sup> The population of interest (P), intervention (I), and outcomes (O) were defined, and clinical questions (PICO) were formulated and reviewed for clinical relevance by all authors. The population of interest for this systematic review was people with diabetes mellitus who have a foot ulcer or who are at risk of developing one. Risk of ulceration was defined according to the International Working Group on the Diabetic Foot risk stratification as a person with diabetes and with peripheral neuropathy, with or without foot deformities, peripheral artery disease or lower-extremity amputation and/or a history of foot ulceration.<sup>16</sup> The modalities considered were any telehealth or telemedicine application, or any medical tool that may potentially serve as telehealth or telemedicine application. We formulated four modalities: dermal thermography, hyperspectral imaging, photographic imaging, and audio/video/online communication. These are defined below.

### 2.1 | Dermal thermography

- Infrared thermography: technology detecting radiation in the infrared range of the electromagnetic spectrum (thermal sensors capture the emitted or reflected thermal radiation from objects).

- Liquid-crystal thermography: technology using (layers of) thermochromic liquid crystals, each changing color within a determined temperature interval which can be read and which provides information concerning the temperature distribution.
- Temperature sensors based on a thermistor, an element with an electrical resistance (resistor) whose resistance changes in response to temperature.

### 2.2 | Hyperspectral imaging

Technology that uses the near-infrared range of the electromagnetic spectrum. This can be used to quantify tissue oxygenation by measuring oxygen delivery (oxyhemoglobin) and oxygen extraction (deoxyhemoglobin) and to generate maps of microcirculatory changes at depths of up to several centimeters.

### 2.3 | Photographic imaging

Digital photography, either as stand-alone camera or integrated in a device.

### 2.4 | Audio/video/online communication

Telephone, video-telephone, videoconference modules, and interactive online communication platforms.

The main outcomes in this systematic review were validity, reliability, feasibility, effectiveness, and costs in the outcome categories of assessment, monitoring, prevention, or treatment of diabetic foot disease.

Original peer-reviewed research studies written in the English language on the population of interest were included. We included randomized controlled trials (RCTs), non-RCTs, case-control studies, cohort studies, cross-sectional studies, case series, case reports, and qualitative research; excluded were systematic reviews and meta-analyses. Conference proceedings were only included to search for full-article publications of the same study. We excluded studies on healthy subjects, on persons with other diseases than diabetes, or on persons with diabetes who were not at risk for foot ulceration. We also excluded studies that had interventions that were not considered to (potentially) be a telehealth or telemedicine approach. The literature search was performed using the MEDLINE/PubMed database on the 31st of August 2018. The search was not limited by date. The search string used is shown in Supplementary Appendix A. All included studies underwent a reference list cross check to identify studies that were not found in the initial database search. Two reviewers (CH, WadS) independently assessed all obtained records by title and abstract for eligibility. Three reviewers (CH, WadS and SB) then independently assessed full-article copies of references that were selected based on title/abstract, to determine final eligibility for inclusion. Disagreements between reviewers were discussed, and a final decision was made based on consensus.

The Scottish Intercollegiate Grouping Network algorithm for classifying study design was used to classify the studies ([http://www.sign.ac.uk/assets/study\\_design.pdf](http://www.sign.ac.uk/assets/study_design.pdf)). CH, WadS, and SB independently assessed included studies with a (non) randomized controlled study design for methodological quality (i.e., risk of bias), using scoring sheets developed by the Dutch Cochrane Centre ([www.cochrane.nl](http://www.cochrane.nl)). Reviewers resolved disagreement regarding risk of bias by discussion until consensus was reached. Risk of bias was scored for each study as ++ (very low risk of bias), + (low risk of bias) or – (high risk of bias). Data were extracted from each included study and summarized in an evidence table (Supplementary Appendix B). This included study design, characteristics of the study population, type and description of intervention/diagnostic test, outcome category (assessment/monitoring, prevention or treatment), results, conclusions, and limitations of each study. CH and WadS extracted the data, the other authors checked this for content and presentation. All authors thoroughly discussed the content of the evidence table.

### 3 | RESULTS

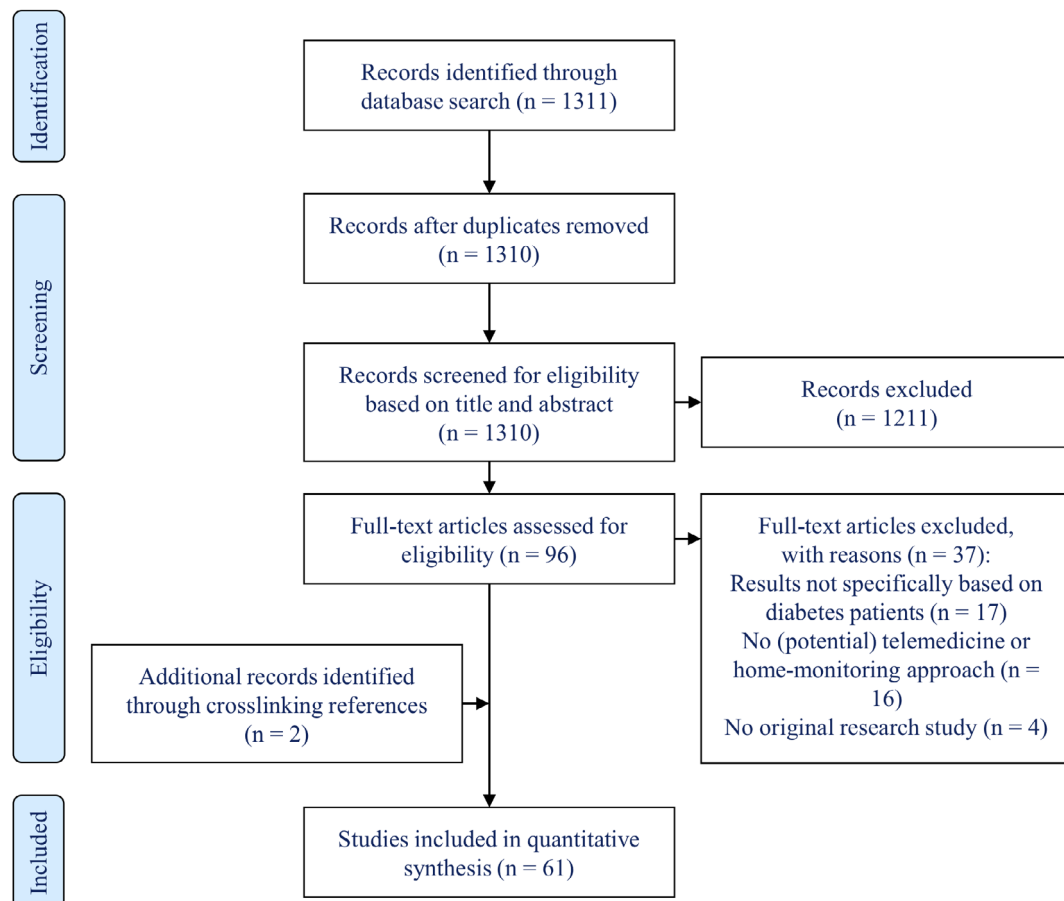
A total of 1311 references were identified in the database search, of which 96 were considered eligible for inclusion based on the assessment

of title and abstract. After full-article review, 61 original peer-reviewed research articles were selected for final inclusion. Figure 1 shows the PRISMA flow diagram. Table 1 shows the distribution of included articles across different types of telehealth and telemedicine approaches and different outcome categories. Risk of bias was evaluated for seven included (non-)RCTs (Table 2). Detailed results from the 61 included articles are summarized in Supplementary Appendix B.

#### 3.1 | Dermal thermography

In one case series and two cross-sectional studies, a significantly higher temperature was measured in the foot with an ulcer or Charcot arthropathy than in the contralateral foot.<sup>17-19</sup> These results were confirmed in one other cross-sectional study<sup>20</sup> and case report.<sup>21</sup> A small cross-sectional study detected latent inflammation at sites of callus in patients with diabetes using dermal thermography in combination with ultrasonography.<sup>22</sup>

In each of four RCTs identified on the use of infrared dermal thermography to prevent ulcer recurrence, patients randomized to the intervention group measured their plantar foot temperatures at home on a daily basis at six locations per foot. In case a temperature difference  $>4^{\circ}\text{F}$  ( $2.2^{\circ}\text{C}$ ) between corresponding locations on the left and



**FIGURE 1** PRISMA 2009 flow diagram

**TABLE 1** Distribution of included studies in the systematic review across type of telehealth and telemedicine approaches and outcome category

	Number of Studies	References
Type of Approach/Technology		
Dermal thermography		
Infrared	19	17-34,37
Thermistor	2	35,36
Liquid-crystal	3	38-40
Hyperspectral imaging	11	41-51
Photographic imaging	13	52-61,63-65
Dermal thermography + photographic imaging	1	62
Audio/video/online communication	12	66-77
Outcome		
Ulcer prevention	15	22-26,31-37,39,48,65
Ulcer assessment/monitoring	27	17,20,27-29,40-47,50-61,63,64
Ulcer prevention + assessment	4	18,19,38,49
Ulcer treatment	12	66-77
Assessment of infection	3	21,30,62

right foot occurred for two consecutive days, participants were instructed to contact the study nurse and reduce their ambulatory activity until temperatures normalized. The control group in these four RCT's had standard follow-up and treatment, which did not include foot temperature monitoring. Lavery *et al* reported in 85 patients a 6-month ulceration rate after of 2% in the intervention group versus 20% in the control group ( $P = 0.01$ , odds ratio [OR] = 10.3).<sup>23</sup> In Armstrong *et al*,<sup>24</sup> assessing 225 patients, 18-month ulcer recurrence rates were 4.7% and 12.2% for the intervention and control group, respectively ( $P = 0.038$ , OR = 3.0). In Lavery *et al*,<sup>25</sup> assessing 173 patients, 15-month ulcer recurrence rates were 8.5% for the intervention group and 29.3% for controls ( $P = 0.008$ , OR = 4.48). In the fourth and most recent RCT, Skafjeld *et al* found in a small sample of 41 patients that self-monitoring of skin temperature is feasible, but does not result in a significant reduction in 12-month ulcer recurrence rate compared to performing daily inspection of their feet 39% versus 50% ( $P = 0.532$ ).<sup>26</sup>

Van Netten *et al* demonstrated in a cross-sectional study that diabetic foot complications can be distinguished using infrared temperature profiles, with feet without complications showing left-to-right temperature differences  $<1.5^{\circ}\text{C}$ , those with local complications (e.g. abundant callus or neuropathic ulcer)  $>2^{\circ}\text{C}$ , and those with diffuse complications (e.g. Charcot foot, infected ulcer)  $>3^{\circ}\text{C}$ .<sup>27</sup> A subsequent study by van Netten *et al* found the most optimal cut-off temperature difference ( $2.2^{\circ}\text{C}$ ) to detect diabetes related complications to be 76% sensitive and 40% specific.<sup>28</sup> Liu *et al* demonstrated a sensitivity of 85% and a specificity of 98.4% for computer-based

automated detection of foot complications (e.g. callus, blisters, redness or ulceration) using asymmetric analysis of thermal images in combination with color imaging.<sup>29</sup> Surprisingly, a large cohort study of 362 patients with a foot ulcer and a concomitant infection showed no significant change in left-to-right foot temperature difference.<sup>30</sup>

Mori *et al*, presented in a cross-sectional study more variable thermographic patterns of the foot in patients with diabetes compared to healthy controls.<sup>31</sup> This was explained by the individual regularity of blood supply at the angiosome level (due to stenosis of arteries or A-V shunt between angiosomes).<sup>31</sup> Gatt *et al* found in two cross-sectional studies that the mean temperatures of the toes and forefoot were significantly higher in patients with foot complications (neuropathy, neuro-ischemia, peripheral arterial disease, and neuro-ischemic toe ulceration) compared to patients with no foot complications and healthy individuals.<sup>32,33</sup> The counterintuitive results regarding higher foot temperature in ischemic feet are suggested by the authors to be the result of an altered thermoregulation that is affected by both neuropathy and peripheral arterial disease.<sup>32</sup>

Najafi *et al* tested Smart Socks, an optical-fiber-based textile that measures plantar foot temperature, plantar pressure and toe range of motion. They found a moderate agreement ( $r = 0.58$ ) in foot temperature changes between Smart Socks and an infrared thermal camera.<sup>34</sup> Frykberg *et al* used a wireless thermometric foot mat with temperature sensors based on a thermistor to assess plantar temperature profiles and asymmetries in 132 patients.<sup>35</sup> In 34 weeks, a total of 53 non-traumatic diabetic foot ulcers developed in 37 (28.7%) patients, and using a temperature asymmetry threshold of  $2.22^{\circ}\text{C}$  the system correctly identified 97% of these ulcers with an average lead time of 37 days. A false-positive rate of 57% was reported (sensitivity 97%, specificity 43%).<sup>35</sup> A case report also showed that foot ulcers were preceded by thermal asymmetry using this thermometric foot mat.<sup>36</sup>

In a small case series of 20 patients who measured their plantar foot temperature at six locations four times a day over 6 days follow-up, Wijlens *et al* found single-day temperature differences  $>2.2^{\circ}\text{C}$  in 8.5% of all cases.<sup>37</sup> This reduced to 0.3% with confirmation of a temperature difference  $>2.2^{\circ}\text{C}$  the subsequent day, and with individually corrected temperature thresholds, this reduced further to 0.2%.<sup>37</sup>

Using liquid-crystal thermography, Stess *et al* found higher mean foot temperatures in patients with diabetes and a foot ulcer (history) compared to healthy individuals, but no temperature differences between active ulcer locations and the corresponding site on the contralateral foot.<sup>38</sup> Benbow *et al* found a significantly higher mean plantar foot temperature in neuropathic diabetic patients who went on to develop a plantar foot ulcer, compared to patients who did not develop an ulcer.<sup>39</sup> Roback *et al* found that 74% of areas classified as clinically large problem areas were identified by measured temperature differences between the feet.<sup>40</sup>

### 3.2 | Hyperspectral imaging

Studies used hyperspectral imaging to assess tissue oxygenation at or near the ulcer according to measured oxyhemoglobin and

**TABLE 2** Assessment of risk of bias in the included (non)randomized controlled trials

	Randomization	Independent assignment	Patient /care provider blinded	Outcome assessor blinded	Similarity groups	Withdrawal / drop-out acceptable (<20%)	Intention-to-treat	Patients treated equally except for intervention	Selective reporting ruled out	Free from commercial interest	Score
<b>Thermography</b>											
Lavery et al 2004 <sup>23</sup>	?	?	-	?	+	+	+	+	+	+	6/10
Armstrong et al 2007 <sup>24</sup>	+	+	-	+	+	?	?	+	+	+	7/10
Lavery et al 2007 <sup>25</sup>	+	+	-	?	+	+	+	+	+	+	8/10
Skafeld et al 2015 <sup>26</sup>	+	?	-	?	-	+	-	+	+	+	5/10
<b>Audio/Video/online communication</b>											
Wilbriht et al 2004 <sup>69</sup>	-	-	-	?	-	?	?	-	-	+	1/10
Rasmussen et al 2015 <sup>70</sup>	+	+	-	?	+	+	-	+	+	+	7/10
Smith-Strøm et al 2018 <sup>73</sup>	+	+	-	?	+	+	+	+	+	+	8/10

deoxyhemoglobin levels. From these levels, a healing index was calculated to determine the potential for healing. Two case-control studies monitored the healing of 21 and 73 diabetic foot ulcers and reported sensitivity levels of 93% and 80%, specificity levels of 86% and 74%, and positive predictive values of 93% and 90% for ulcer healing in 6 months and 24 weeks, respectively.<sup>41,42</sup> Another case-control study monitored the healing of 24 diabetic foot ulcers and reported a sensitivity of 0.9, specificity of 0.86 and a positive predictive value of 82% for ulcer healing in 4 weeks.<sup>43</sup> Four case-control studies observed a significant reduction in oxyhemoglobin level prior to ulcer closure in those ulcers that healed, compared to unchanged oxyhemoglobin levels in ulcers that did not heal.<sup>44-47</sup> A negative slope in the rate of change of oxyhemoglobin concentration was indicative for healing in all foot ulcers.<sup>44-47</sup>

One case series analyzed 21 sites that had ulcerated during follow-up and showed that the occurrence of these ulcers could be predicted using hyperspectral imaging with a sensitivity of 95% and specificity of 80% in a mean of 58 days before skin breakdown became apparent.<sup>48</sup> The same research group reported in a case report that an increase in epidermal thickness (callus) was associated with a decrease in oxyhemoglobin concentration prior to ulceration.<sup>49</sup> Liu *et al* showed that with hyperspectral imaging callus, ulcers, and healthy skin spots could be automatically discriminated with a sensitivity of 97% and a specificity of 96%.<sup>50</sup> In contrast with previous studies,<sup>41,42</sup> data from Jeffcoate *et al* showed a significantly lower baseline oxygenation level in those 26 of 50 diabetic foot ulcers that healed in 12 weeks compared to the other 24 that did not heal.<sup>51</sup>

### 3.3 | Photographic imaging

Two cross-sectional studies showed a strong association between ulcer area measurements from photographs and those from live assessments based on ulcer boundary drawings, with correlation coefficients >0.95.<sup>52,53</sup> Two other cross-sectional studies showed an inter-observer variation in ulcer area measurements from photographs of 16% and 11.9%, compared to 27% based on live assessments<sup>54,55</sup>; intra-observer variation showed to be 3.3%.<sup>55</sup> Wang *et al* found a correlation of 0.68 between computer-based wound area determination and to manual annotation.<sup>56</sup> Using support vector machines, they could determine the wound boundaries even more accurately.<sup>57</sup> Van Netten *et al* found that assessment of diabetic foot ulcers using a mobile phone compared to live assessment (as reference), gave strong support for the decision for per-wound debridement, but low inter-observer reliability [ $\kappa$  (k) = 0.09-0.49] and a moderate intra-observer reliability (k = 0.47-0.64) for assessing the presence of ischemia, infection, granulation, slough, tracking or tunneling, moist or an exuding wound, cellulitis, or erythema.<sup>58</sup>

Bus *et al* showed that with using a photographic foot imaging device intended for home use, a good agreement between live and photographic assessment (>74%) and between repeated photographic assessments (>82%) could be obtained for assessing the presence of abundant callus, ulceration and for the absence of signs.<sup>59</sup> This was

further elaborated on by Hazenberg et al who showed good agreement between assessment from photographs and live assessment for the presence of ulcers ( $k = 0.87$ ) and for absence of any sign ( $k = 0.83$ ), and moderate agreement for the presence of abundant callus ( $k = 0.61$ ).<sup>60</sup> Outcomes were also reliable between repeated photographic assessments ( $k = 0.70$ – $1.00$ ).<sup>60</sup> Good feasibility of using the photographic foot imaging device in the home environment was also shown: patient adherence was high, referrals based on photographic assessment justified, and perceived usability was good.<sup>61</sup> The same authors also showed in a cross-sectional study that diagnosis of foot infection is valid and reliable using photographic imaging in combination with infrared thermography, taking clinical diagnosis as reference (sensitivity  $>60\%$ , specificity  $>79\%$ ), and better than with using each modality on its own.<sup>62</sup> In two case series, Foltynski et al assessed the feasibility of at-home use of the TeleDiaFoS system for ulcer monitoring, and included: total number of assessed ulcer pictures, the length of the monitoring period, and change in ulcer area after four and 12 weeks follow-up.<sup>63,64</sup> A total 256 images from ten patients were successfully sent to the Central Clinical Server and observed by the treating physician, who found changes in wound area after 12 weeks or at the end of monitoring ranging from  $-94.5\%$  to  $+83.8\%$ .<sup>64</sup> Furthermore, patients perceived the usability of the system between moderate and good.<sup>63</sup>

Most recently, Yap et al investigated an application for a tablet to standardize acquisition of digital images for assessing and monitoring the diabetic foot, and they found a high intra- and interobserver reliability for both capturing the image of feet of diabetic patients and control feet.<sup>65</sup>

### 3.4 | Audio/video/online communication

Two small case series assessed the feasibility of using a mobile phone to connect the physician and home visiting nurse to support ulcer treatment.<sup>66,67</sup> Clemensen and Larsen et al reported that patients were satisfied with the treatment support because it was timesaving, nurses were capable of handling the technical skills, and physicians found the equipment easy to use and feasible for distance-treatment.<sup>66</sup> Furthermore, patients were satisfied and felt safe with this remote treatment support, the visiting nurse felt supported, and physicians felt a good basis for decisions with using the tool.<sup>68</sup> In a non-RCT, Wilbright et al reported no significant difference in ulcer healing between weekly telemedicine consultations using video interaction and face-to-face treatment: in 12 weeks, 75% of ulcers healed in the telemedicine group versus 81% ( $P = 0.546$ ) in the face-to-face treatment group.<sup>69</sup>

The RCT by Rasmussen et al compared the effectiveness on ulcer healing of either two telephone or online consultations in addition to one outpatient clinic visit or three outpatient clinic visits and found no significant difference in hazard ratio for healing or amputation between these two interventions. Remarkably, they found a significantly higher mortality in the telemedicine group ( $P = 0.0001$ ,  $HR = 8.68$ , 95%CI: 6.93–10.88).<sup>70</sup> In a cost-effectiveness analysis

based on this RCT, Færevold et al reported that the average ulcer treatment cost per patient for the telemedicine group was €12 346 and for the control group €14 395, which was not a statistically significant difference.<sup>71</sup> In a qualitative sub-analysis of their RCT, Rasmussen et al concluded that the involved visiting nurses are empowered by telemedicine and that a key factor for implementing telemedicine was training of these nurses.<sup>72</sup> However, concerns were raised regarding lack of multidisciplinary wound care teams, patient responsibility and lack of patient interaction with the physician.<sup>72</sup>

Recently, Smith-Strøm et al found in a cluster randomized controlled noninferiority trial that weekly telemedicine consultations of the community nurse via an interactive Web-based ulcer record and a mobile phone that enabled counseling and communication with the healthcare specialist in addition to outpatient clinic every 6 weeks, was non-inferior to visiting the outpatient clinic every second week for ulcer treatment on time to healing (mean difference  $-0.43$  months [95%CI:  $-1.50$  to  $0.65$ ]).<sup>73</sup> A lower proportion of patients with an amputation was found in the telemedicine group ( $-8.3\%$ , 95%CI:  $-16.3$  to  $0.5\%$ ).<sup>73</sup> Based on this RCT, four qualitative studies investigated the value of focus groups and individual semi-structured interviews of both patients and healthcare professionals.<sup>74–77</sup> Patients from both the telemedicine and the control group mentioned that the best wound care depends on a combination of competence and professional skills in wound management and continuity of care.<sup>75</sup> Telemedicine enabled healthcare professionals to approach their patients with more knowledge, better wound assessment skills and heightened confidence.<sup>74</sup> Four key factors for success that were identified in using telemedicine were: technology and training must be user-friendly, the presence of someone in the work setting who can facilitate the intervention, the need for support of committed and responsible leaders and effective communication at organizational level.<sup>76</sup> In the patient's home setting, it is also important for the community nurse to have good access to the ulcer record and adequate equipment with sufficient consultation time for ulcer assessment and treatment.<sup>77</sup>

## 4 | DISCUSSION

This systematic review discusses the peer-reviewed literature on telehealth and telemedicine applications for the diabetic foot. The findings of this review show that there are several technologies available that may be of value in the assessment/monitoring, prevention, and/or treatment of diabetic foot disease. However, they require a larger scientific base of effectiveness and/or feasibility or are still at an early stage of development and require a technically and economically more efficient approach before they can be widely deployed in the patient's home as telehealth or telemedicine tool.

### 4.1 | Dermal thermography

Three RCTs showed that home monitoring of foot temperatures using infrared thermography is highly effective in reducing diabetic foot



ulcer recurrence incidence.<sup>23-25</sup> These well-designed RCTs at low risk of bias were from the same research group covering the same geographical region in the United States.<sup>78</sup> A more recent small RCT from Norway did not confirm the positive findings of the three US trials, but this study was underpowered with a small sample size.<sup>26</sup> Two recent systematic reviews suggest that the home monitoring of foot temperature is an effective way to predict and prevent diabetic foot ulcer recurrence.<sup>78,79</sup> Effect sizes found were large, among the largest of any intervention that aims to prevent foot ulcer recurrence in diabetes.<sup>1,7,8</sup> It is therefore quite surprising to observe that such home-monitoring is not adopted in clinical practice. This may be because of issues regarding the usability and applicability of such foot temperature monitoring at home, and specifically the use of handheld infrared thermography. Several non-contact infrared skin thermometers have large measurement errors.<sup>80</sup> Also the TempTouch® (Xilas Medical Inc., San Antonio, TX, USA) as used in the RCTs may show operational errors in case of presence of abundant callus or dry skin.<sup>81</sup> Another issue is the burden on patients of performing these measurements on a daily basis, at multiple, sometimes hard to reach, locations on the foot, and including the recording and calculation of temperatures and differences between the left and right foot. One RCT reported reasons for withdrawal from the study, with 'too much to do' in the home-monitoring group being the main reason.<sup>25</sup> This is also the experience in the ongoing DIATEMP trial from the Netherlands.<sup>81</sup> Technological advancements in monitoring foot temperature, for example, through intelligent handheld infrared thermometers, temperature monitoring through the use of special socks,<sup>82</sup> other Smart Sox devices<sup>34</sup> or a thermometric foot mat<sup>35</sup> may reduce this burden. These devices have shown feasibility in measuring plantar foot temperature, and in the case of the foot mat has shown assessments to be predictive of foot ulceration, but the effectiveness and long-term usability of these devices in the prevention of foot ulceration is not known, limiting implementation. An important finding in observational studies investigating the value of thermal asymmetry between the left and right foot is the number of false positives.<sup>35,37</sup> The RCTs on infrared thermography provide limited information on false alarms and protocol compliance. A high false positive rate may demotivate patients to use these tools and may increase health-cost burden due to unnecessary visits to a healthcare professional. Furthermore, specific patient groups at high risk may not benefit, for example, because of presence of amputation, limiting the measurement of left-to-right asymmetry. Finally, apart from local cost calculations of foot complications,<sup>83</sup> no data have been published on the cost-effectiveness of dermal thermography. Well-designed trials are currently underway to investigate cost-effectiveness and usability.<sup>81,84</sup>

Regarding liquid-crystal thermography, only three small clinical studies were found on the prediction of ulceration<sup>38,39</sup> and diagnosis of foot complications.<sup>40</sup> While liquid-crystal thermography is easy to use and gives temperature patterns of the entire foot, interpretation of the data can be difficult, and since the year 2000, no studies have been published on the use of liquid-crystal thermography in the diabetic foot, suggesting a limited applicability.

## 4.2 | Hyperspectral imaging

Hyperspectral imaging was mostly investigated for assessing and monitoring diabetic foot ulcers in a clinical setting.<sup>41-47,49-51</sup> Most of these studies included a small number of patients,<sup>41,44-47,49</sup> poorly defined foot ulcers at baseline,<sup>42,45,48,49,51</sup> and report no or limited clinical treatment/follow-up strategies.<sup>41-43,46-48,50,51</sup> A healing index based on hyperspectral data was proposed to predict the occurrence of diabetic foot ulcers' however, this healing index was retrospectively determined and poorly defined.<sup>41,42</sup> Weingarten et al described an easier method to predict ulcer healing, but in a small subgroup analysis.<sup>43</sup> Additionally, contradicting outcomes from hyperspectral imaging studies have been reported. Previous studies from Nouvong et al and Khaothiar et al showed that oxygenation levels at baseline were higher in ulcers that healed compared to non-healing ulcers, while the most recent study from Jeffcoate et al showed that healed ulcers had a significantly lower baseline oxygenation level compared to non-healing ulcers.<sup>41,42,51</sup> Jeffcoate et al postulate, with limited supporting evidence, that microvascular disease can reduce oxygen delivery to extravascular tissues because of thickening of the basement membrane, so that intravascular hemoglobin rises.<sup>51</sup> Secondly, according to the authors, microvascular shunting caused by vasomotor neuropathy might reduce oxygen delivery to extravascular tissue and raise oxyhemoglobin at microvascular level.<sup>51</sup> These conflicting results show that the use of hyperspectral imaging as diagnostic and monitoring tool in diabetic foot disease is still in its infancy and both basic science and clinical effectiveness studies are needed. Furthermore, hyperspectral imaging is currently an experimental and expensive technique, only studied in the clinical setting; effective applications for the home environment are far from being developed.

## 4.3 | Photographic imaging

For digitally measuring ulcer area,<sup>52-57</sup> photographic imaging is a feasible and applicable tool. Four studies on the measurement of foot ulcer area included a large number of diabetic foot ulcers (20-56 cases) to draw relevant conclusions from Refs. 52-55

Two photographic imaging devices, the one used by Hazenberg et al,<sup>61</sup> and the TeleDiaFos system,<sup>63,64</sup> show to be feasible for use in the home environment. The feasibility analysis with the TeleDiaFoS system was done in a small group of relatively young patients and patient characteristics were not reported.<sup>63,64</sup> The feasibility analysis on the photographic foot imaging device used by Hazenberg et al included a larger patient sample, but the 4 month follow-up was too short for a sufficient number of foot complications to develop and, therefore, to study feasibility in a robust way.<sup>61</sup> A limitation of both systems is that only the plantar foot surface can be assessed.

While two studies suggest that with photographic foot imaging diabetic foot ulcers can be reliably assessed,<sup>59,60</sup> the diagnosis of abundant callus proves to be moderately reliable and the studies were too small to reliably assess other important signs such as blisters, fissures, and erythema. The same research group showed that the combination

of photographic imaging and infrared thermography improves accuracy over a single modality alone in the diagnosis of diabetic foot infection.<sup>62</sup> This is the first time that home-monitoring approaches for the early diagnosis of foot infection have been presented.

More recently, Van Netten et al concluded that there was a low interobserver and moderate intraobserver reliability in the diagnosis of a variety of diabetic foot problems based on mobile phone images.<sup>58</sup> Overall, these findings suggest that digital (mobile phone) images have applicability in some areas of assessment of pre-signs of ulceration, but are limited in use in others. Future research should show the validity and reliability of photographic foot imaging in assessing blisters, fissures, and erythema and should investigate the effectiveness of this tool.

#### 4.4 | Audio/video/online communication

Audio, video, and online communication as telemedicine support tool has received quite some recent attention in the scientific literature. Two well-designed RCTs show that this form of telemedicine is feasible and as effective as regular outpatient clinic visits in ulcer management.<sup>70,73</sup> The significant higher mortality rate found by Rasmussen et al in the telemedicine group could not be explained by the authors.<sup>70</sup>

Both above-mentioned research groups study groups investigated qualitative aspects of telemedicine in five studies and identified key factors for successful implementation of audio, video, and/or online communication as telemedicine support tool.<sup>72,74-77</sup> Sufficient training of home-care nurses to increase their competence level, followed by continuity of care is essential for both nurses and patients. This is also shown by a prematurely terminated RCT in France, in which a lack of specialized nurses and a lack of confidence by healthcare providers in the telemedicine system used, resulted in a termination of inclusion of patients.<sup>85</sup> Interestingly, the number of outpatient clinic visits did not decrease in the RCT from Rasmussen et al.<sup>72</sup> This was confirmed in the RCT from Smith-Strøm where the total number of outpatient clinical consultations remained equal for the intervention and the control group.<sup>73</sup> Subgroup analysis showed that the number of consultations decreased if patients lived further away from the clinic (>25 km) and if there was more experience with telemedicine consultations.<sup>73</sup> Taking these key factors into account in future trials and in clinical practice may improve potential for remote ulcer care.

Cost-effectiveness based on the data of the RCT from Rasmussen et al showed to be similar between the telemedicine and usual care group.<sup>71</sup> The trial was, however, not powered to detect differences in costs, and cost-analysis was based on only the first 6 months of follow-up. Future studies should further explore the cost-effectiveness of this approach.

#### 4.5 | Cost aspects

All telehealth and telemedicine approaches discussed in this review require investment in equipment, setup, training, and personnel,

and therefore, the benefit for the patient will have to be evaluated in association with the costs involved. Cost-effectiveness is a key aspect that will influence acceptance and implementation in diabetic foot care. Some monitoring tools such as infrared thermometers are low in cost, while other modalities such as hyperspectral imaging are currently still expensive. However, because prevention of a single foot ulcer or an amputation can save the healthcare system between €5000 and €17 000, telehealth and telemedicine tools have good potential to be cost-effective if they lead to a significant reduction in risk of foot ulceration, expedited healing of ulcers, or less outpatient clinic visits.

#### 4.6 | Clinical implications and future perspectives

If feasibility, effectiveness, and cost-savings are demonstrated, successful implementation of telehealth and telemedicine approaches can improve patient mobility, autonomy, and health-related quality of life, in particular for those patients living alone or in rural areas, who have cognitive, visual, or physical impairments, or lack knowledge about the disease. This empowers patients and encourages them to take responsibility in the management of their diabetic foot disease.<sup>86</sup>

The development of such a user-friendly, effective approach is not without challenges. Both patients' and healthcare professionals' adherence play an important role in effectiveness, and implementation is dependent on whether tools are reimbursed by the healthcare system. The continuous and fast technological development increases the risk that devices of which efficacy has been proven become outdated for practical use. Nevertheless, these technological developments also provide great potential for the design of easy to use tools that integrate several of the studied modalities for the prevention and management of diabetic foot disease. A small and easy to use, if needed carry-on, device that can measure local foot temperature and takes photographs of the foot and automatically processes data through intelligent algorithms and feeds back data to the patient when action is needed is probably not far from development. Such tools, when proven feasible and cost-effective, can have great impact in the care of patients with diabetic foot disease.

#### 4.7 | Limitations

We obtained articles from a single database (MEDLINE/PubMed) and did not include other databases. We do think we covered the important medical scientific literature on the topic of interest. Additionally, this systematic review includes only studies on people with diabetes and therefore lacks data on the use of telehealth and telemedicine approaches in other patient populations (with or without foot ulcers) that may be informative. Tcherro et al conducted a systematic review and meta-analysis on telemedicine approaches and also included other than diabetes patients with (risk for) foot ulcers.<sup>87</sup> We believe though that diabetic foot disease is a unique entity with its own characteristic



aspects, physically and psychologically, that require a specific focus on this topic of interest.

## 5 | CONCLUSION

This systematic review shows that the application of telehealth and telemedicine approaches for the management of diabetic foot disease is still in its infancy, and technical limitations and implementation issues apply. However, several approaches have shown to be effective or feasible in assessing, monitoring, preventing or treating diabetic foot disease, and additionally require confirmation in studies in order to have more widespread use in diabetic foot care, in particular for patients living in remote areas. Other approaches require further development towards a feasible and effective solution and proof thereof in well-designed studies. Successful implementation of these telehealth and telemedicine approaches can substantially reduce patient and healthcare burden of diabetic foot disease.

## CONFLICT OF INTERESTS

The authors declare that they have no conflict interests.

## AUTHORS' CONTRIBUTION

CH, JvB, FM, SB conceived and designed the study. CH and SB designed the search string. CH, WadS and SB performed the literature search, assessed the literature, extracted data, and drew conclusions. CH and WadS wrote the manuscript. JvB, FM and SB critically reviewed and edited the manuscript. All authors have read and approved the final manuscript.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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