# **BMJ Open** Ultrasound measurement of traumatic scar and skin thickness: a scoping review of evidence across the translational pipeline of research-to-practice

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### ABSTRACT

**Objectives** To identify the ultrasound methods used in the literature to measure traumatic scar thickness, and map gaps in the translation of these methods using evidence across the research-to-practice pipeline.

**Design** Scoping review.

**Data sources** Electronic database searches of Ovid MEDLINE, Embase, Cumulative Index of Nursing and Allied Health Literature and Web of Science. Grey literature searches were conducted in Google. Searches were conducted from inception (date last searched 27 May 2022).

**Data extraction** Records using brightness mode (Bmode) ultrasound to measure scar and skin thickness across the research-to-practice pipeline of evidence were included. Data were extracted from included records pertaining to: methods used; reliability and measurement error; clinical, health service, implementation and feasibility outcomes; factors influencing measurement methods; strengths and limitations; and use of measurement guidelines and/ or frameworks.

Results Of the 9309 records identified, 118 were analysed (n=82 articles, n=36 abstracts) encompassing 5213 participants. Reporting of methods used was poor. B-mode, including highfrequency (ie, >20 MHz) ultrasound was the most common type of ultrasound used (n=72 records: 61% of records), and measurement of the combined epidermal and dermal thickness (n=28; 24%) was more commonly measured than the epidermis or dermis alone (n=7, 6%). Reliability of ultrasound measurement was poorly reported (n=14; 12%). The scar characteristics most commonly reported to be measured were epidermal oedema, dermal fibrosis and hair follicle density. Most records analysed (n=115; 97%) pertained to the early stages of the research-to-practice pipeline, as part of research initiatives.

**Conclusions** The lack of evaluation of measurement initiatives in routine clinical practice was identified as an evidence gap. Diverse methods used in the literature identified the need for greater standardisation of ultrasound thickness measurements. Findings have been used to develop nine methodological considerations for practitioners to guide methods and reporting.

### STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Use of the Australian Government Department of Health and Aged Care Medical Research Future Fund research-to-practice pipeline phases to categorise records allowed identification of gaps in the use of ultrasound for clinical practice.
- ⇒ Clinical, health service, implementation and feasibility outcomes related to ultrasound measurement in included records were summarised to determine what is needed to close the research-to-practice gap for ultrasound measurement of scar thickness.
- ⇒ A limitation is that only articles available in English or with an English abstract were considered for inclusion and data extraction, thus findings are likely most relevant to English-speaking countries.

### INTRODUCTION

Traumatic cutaneous injury, caused by sharp object penetration (eg, surgery or vaccination) or burns (including thermal, chemical and friction) may result in the formation of hypertrophic scarring.<sup>1</sup> Hypertrophic scars result from an aberrant cutaneous healing response that leads to the formation of red, raised scars, often accompanied by pruritus and skin tightening, which remain within the boundaries of the initial injury.<sup>2–7</sup> The sequelae of hypertrophic scars can impact on patient's physical and psychosocial quality of life.<sup>89</sup>

A characteristic of hypertrophic scarring that both patients and clinicians have identified as being important, and which has subsequently been used as a way to measure clinical and treatment outcomes, is scar thickness.<sup>9–17</sup> Scar thickness can be measured both subjectively, through clinician assessment and patient-reported outcomes, or objectively, using medical imaging methods.<sup>18 19</sup> The pathological complexity of hypertrophic scars means that they generally extend below the level of the surrounding skin, supporting

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Correspondence to Brandon Meikle; brandon.meikle@uq.net.au the use of medical imaging modalities such as ultrasound for thickness quantification, as these are capable of providing information about subcutaneous structures and processes.<sup>19 20</sup> Scar thickness measurement using ultrasound can be conducted in both clinical and research contexts. Where routine measurements like ultrasound are used to guide clinical decision-making and treatment, this practice is known as measurementbased care.<sup>21</sup>

Ultrasound is a safe, non-invasive and largely costeffective (compared with other imaging modalities) imaging method with measurement utility in both adult and paediatric populations.<sup>22–24</sup> Modern brightness mode (B-mode) ultrasound, particularly high-frequency (ie,  $\geq 20$  MHz) or ultra-high-frequency (30–100 MHz)<sup>25</sup> ultrasonography, allows differentiation between the epidermis and dermis, which permits quantification of skin layerspecific scar characteristics. This differentiation may allow assessors to observe and understand the pathological mechanisms of individual scars and adjust treatment protocols accordingly.<sup>24 26–31</sup> Additionally, B-mode ultrasound is commonly used as the basis for other imaging methods, such as colour Doppler ultrasound or elastography, which can allow quantification of additional scar characteristics, such as their elastic properties.<sup>26–29 32 33</sup>

Despite the clinical advantages of B-mode ultrasound for scar thickness measurement, methods are poorly reported and lack standardisation in the literature. This casts doubt on the validity of clinical decision-making in measurement-based care initiatives (eg, setting depth of ablative fractional carbon dioxide laser penetration) informed by research findings (eg, response to treatment) where ultrasound measurements are used.<sup>34</sup> Lack of standardisation also makes between-study comparison, such as systematic reviews and meta-analyses, difficult,<sup>35</sup> and poor methodological reporting hampers the ability to accurately replicate findings. This scoping review focuses on mapping and identifying gaps in ultrasound methods and evaluation reported in the current literature along the research-to-clinical practice pipeline.<sup>36</sup> Methodological considerations for people performing ultrasound scar thickness measurements, including practitioners (herein termed assessors) using ultrasound in clinical practice, are presented based on the review findings.

### **METHODS**

### Protocol publication and review structure

The protocol for this review has been published a priori.<sup>37</sup> This scoping review was conducted and is reported according to the framework by Arksey and O'Malley.<sup>38</sup> The steps outlined in this framework are: (1) identifying the research question; (2) identifying the relevant records; (3) selecting appropriate records; (4) charting extracted data; and (5) collating, summarising and reporting the results.<sup>38</sup>

### Identifying the research question

The primary question of this scoping review was: "What do we know and not know about the measurement of traumatic cutaneous scar thickness using ultrasound?" This question was addressed through exploration of: methods used; reliability and measurement error; clinical, health service, implementation and feasibility outcomes; factors influencing ultrasound imaging and measurement methods; strengths and limitations of measurement methods and use of measurement guidelines and/ or frameworks. While the focus of this review was the measurement of traumatic cutaneous scar thickness with ultrasound, methods used to measure the thickness of unscarred skin were reported where these were used in combination with measurement of scar thickness (eg, as control or comparator measurements).

### Identifying the relevant records

A standardised search strategy was developed and piloted with the assistance of a medical librarian using the concepts 'ultrasound', 'skin', 'thickness' and 'measure', with associated terms and truncations (online supplemental box 1). Ovid MEDLINE, Embase, Cumulative Index of Nursing and Allied Health Literature (CINAHL) and Web of Science electronic databases were searched from conception to identify original studies (date last searched 27 May 2022).

The phrase 'ultrasound scar thickness measurement' was used to conduct additional searches in (1) Google Scholar and (2) Google to identify original studies in grey literature, and studies not identified in database searches. Title and abstract searches in Google Scholar and Google were limited to the first 200 results.<sup>39</sup>

### **Record selection**

Following deduplication, six reviewers screened records using Covidence (Veritas Health Innovation, Melbourne, Australia; available at www.covidence.org) for eligibility according to the inclusion criteria (table 1). Both peerreviewed journal articles and abstracts were included to ensure that all the available and most recent methodological information was obtained.<sup>40</sup> Data collected from peer-reviewed journal articles were considered the primary source of data, with information from abstracts used to confirm or extend the journal data. The inclusion of abstracts will assist future authors to further investigate the information presented as full texts may become available. During both title and abstract and full-text screening, one researcher (BM) screened all records as a single reviewer, while other researchers (MS, TM, TR, BD and ZT) screened records as a second reviewer. Conflicts were resolved through discussion between at least two authors to reach agreement. A third author was used as a tiebreaker where agreement could not be reached.

### **Charting the data**

The data extraction table was developed in Microsoft Excel and piloted by two authors (BM and ZT) through

<ul> <li>Inclusion</li> <li>Exclusion</li> <li>Traumatic scars measured with ultrasound based on brightness mode ultrasound (including high-frequency, ultra-high-frequency and Doppler)</li> <li>Measurements taken of living, human individuals</li> <li>Measurement of traumatic cutaneous scarring arising from penetration of the skin with sharp objects (including surgery or vaccination), or as a result of burns (including thermal, chemical or friction)</li> <li>Articles written in English, or with English abstracts</li> </ul>	Table 1         Inclusion and exclusion criteria for studies included in the scoping review					
<ul> <li>Traumatic scars measured with ultrasound based on brightness mode ultrasound (including high-frequency, ultra-high-frequency and Doppler)</li> <li>Measurements taken of living, human individuals</li> <li>Measurement of traumatic cutaneous scarring arising from penetration of the skin with sharp objects (including surgery or vaccination), or as a result of burns (including thermal, chemical or friction)</li> <li>Articles written in English, or with English abstracts</li> <li>Reviews, discussion papers, opinion pieces</li> <li>Measurement of non-traumatic scars measured along with burn scars, these were included</li> <li>Measurement of skin thickness in non-traumatic conditions (eg, diabetes)</li> <li>Measurement of skin thickness where there is no cutaneous involvement in the trauma (eg, traumatic brain injury)</li> </ul>	Inclusion	Exclusion				
Measurement using A-mode ultrasound	<ul> <li>Traumatic scars measured with ultrasound based on brightness mode ultrasound (including high-frequency, ultra-high-frequency and Doppler)</li> <li>Measurements taken of living, human individuals</li> <li>Measurement of traumatic cutaneous scarring arising from penetration of the skin with sharp objects (including surgery or vaccination), or as a result of burns (including thermal, chemical or friction)</li> <li>Articles written in English, or with English abstracts</li> </ul>	<ul> <li>Reviews, discussion papers, opinion pieces</li> <li>Measurement of non-traumatic scars         <ul> <li>(eg, acne scars). Where non-traumatic scars measured along with burn scars, these were included</li> </ul> </li> <li>Measurement of skin thickness in non-traumatic conditions (eg, diabetes)</li> <li>Measurement of skin thickness where there is no cutaneous involvement in the trauma (eg, traumatic brain injury)</li> <li>Measurement using A-mode ultrasound</li> </ul>				

independent extraction and comparison of data from two records. The table was then modified to include the scar characteristics (eg, fibrosis, oedema) measured, measurer/assessor training, the number of measurements taken and funding sources (online supplemental table 1). Full-text data extraction was completed by four authors (BM, MS, TM and ZT). An additional author (BD) independently extracted data from five randomly selected records, which was compared with data extracted by other authors. Minimal differences between data extracted by the independent author and that by other authors were observed, thus further independent extraction was not performed. As is typical in scoping reviews, the certainty or quality of evidence was not appraised.<sup>38</sup>

The research-to-practice pipeline published by the Australian Government Department of Health and Aged Care Medical Research Future Fund (figure 1) was used to categorise each included record based on their stated aims into one of the four phases.<sup>36</sup> Studies related to phase I of this pipeline, basic research, were only included in this review when data on scar or skin thickness pertained to human participants (table 1). Phase II of this pipeline included randomised controlled trials, while phase III included pragmatic and observational studies conducted outside randomised controlled trials. The final phase of this pipeline (phase IV) indicates initiatives used in routine clinical practice.

Where clinical (eg, treatment satisfaction, scar symptoms), health service (eg, efficiency, safety, effectiveness, equity, patient-centredness and timeliness) and implementation (eg, acceptability, adoption, appropriateness, fidelity, cost, penetration and sustainability) outcomes were addressed, they were reported and defined according to Proctor *et al.*<sup>41</sup> For example, in the context of this scoping review, acceptability is defined as the level to which ultrasound is palatable among stakeholders (eg, assessors), appropriateness is the perceived fit of ultrasound within regular clinical practice and fidelity is the degree to which ultrasound is used in the way it was initially described.<sup>41</sup> Measurement instrumentspecific feasibility outcomes defined by Prinsen *et al*<sup>42</sup> are reported in the current review. These outcomes included ease of administration, standardisation, completion time, instrument cost and availability and ease of score calculation.<sup>42</sup> Reliability and measurement error were defined according to COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) tools.43 44 Measurements with an intraclass correlation coefficient (ICC) of 0.7 or greater were considered reliable.<sup>44</sup> Measurement error was assessed by comparing the reported SEM with the reported smallest detectable change (SDC). Where the reported measurement error was smaller than the reported smallest detectable change, it was interpreted as indicating real change or variance can be detected, and that change or variance is not a result of error.44

### Patient and public involvement

There was no patient and/or public involvement in the design, conduct, reporting or dissemination of information in this scoping review.

#### RESULTS

Electronic database searches identified 9309 records. After removal of 3703 duplicate records, the titles and abstracts of 5606 records were screened for relevance according to the inclusion criteria (table 1). Following full-text screening, 104 records proceeded to data extraction. Searches in Google and Google Scholar identified an



Figure 1 Research to clinical practice pipeline.

Iable 2         Summary of characteristics of records included in this review <sup>*</sup>						
Characteristic	Category	Number of records (translational pipeline phase II)†	Number of records (translational pipeline phase III)†	Number of records (translational pipeline phase IV)†		
Journal articles						
Funding source	Commercial	2	1	1		
	Non-commercial	23	13	0		
	Commercial and non-commercial	2	1	1		
	No funding	6	3	0		
	Not reported	16	12	0		
Population type	Adult	27	16	0		
	Paediatric	6	4	0		
	Paediatric and adult	13	7	2		
	Not reported	3	3	0		
Scar aetiology	Burn	22	18	1		
	Surgical‡	5	2	0		
	Mixed	10	3	0		
	Not specified	12	7	0		
Abstracts						
Funding source	Commercial	0	0	0		
	Non-commercial	3	1	0		
	Commercial and non-commercial	0	0	0		
	No funding	0	0	0		
	Not reported	17	14	1		
Population type	Adult	1	2	0		
	Paediatric	0	3	0		
	Paediatric and adult	4	1	0		
	Not reported	15	9	1		
Scar aetiology	Burn	12	10	1		
	Surgical‡	1	2	0		
	Mixed	2	1	0		
	Not specified	5	2	0		

Paediatric: measurement of patients under the age of 18 years; adult: measurement of patients aged 18 years or older; burn: scars caused by thermal, chemical or friction injury; surgical: scars caused by surgical procedures (including biopsies); mixed: scars of included record were of mixed origin (eg, burn and acne).

\*A breakdown of each characteristic per record is presented in online supplemental table 2.

†Stage in the research to clinical practice translational pipeline, as defined by the Australian Government Department of Health and Aged Care.<sup>36</sup>

‡Type of surgery defined in online supplemental table 2.

additional 14 records, providing a total of 118 records for data extraction. Search and screening results are presented according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram (online supplemental figure 1).<sup>45</sup>

### **Record characteristics**

Of the 118 records included in this review, 82 were journal articles (69%) and 36 were abstracts (31%) (table 2), representing a total of 5213 participants (range 1–438; mode 20 participants per record). Adults aged 18 years and older were the most highly represented age group reported in articles

(n=43 articles; 52% of articles),  $^{17262946-85}$  while most abstracts did not report the age group measured (n=25 abstracts; 69% of abstracts).  $^{86-110}$  The most common scar type measured was burn scars in both journal articles (n=43 articles; 52% of articles),  $^{1722-24274757-59616264-6771-75818284111-130}$  and abstracts (n=23 abstracts; 64% of abstracts)  $^{283086-8891-949698102-106131-135}$  (table 2). Most identified articles used ultrasound measurement of scar thickness as part of research initiatives, and were categorised as either phase II (n=50 articles; 61% of articles)  $^{17}$   $^{22263146-4951-566163-656769-7174-767881838411112114115117124-127129}$   $^{130136-145}$  or phase III (n=30 articles; 37% of articles).  $^{2324272950}$ 

pertained to phase I.

57-60 62 66 68 72 73 77 79 80 82 85 116 118 120-123 128 146-149 on the researchto-practice pipeline.<sup>36</sup> Phase II was also the most common phase represented by abstracts (n=21; 58% of abstracts), 86 88 91 93 95 97 99-104 106-108 131-134 150 151 followed by phase III (n=15 abstracts; 42% of abstracts).<sup>28</sup> 30 87 89 90 94 96 98 105 109 110 135 152-154 Phase IV was addressed by two articles (2% of articles)<sup>113</sup> 119 and one abstract (2% of abstracts),<sup>92</sup> which used ultrasound to measure treatment response to an intervention already used in routine clinical practice, including compression garments<sup>113</sup> 119 and CO<sub>2</sub> fractional laser.<sup>92</sup> No records

Methods used to measure traumatic cutaneous scar thickness B-mode, including high-frequency B-mode ultrasound (ie,  $\geq$ 20 MHz) was the most commonly reported ultrasound type in the included articles (n=56; 68% of articles), <sup>17</sup>22-24 26 29 31 46-49 53 54 56 57 59 60 64 65 67 69-78 80-82 84 85 111 112 114 116-118 120 122 123 126-130 138 139 141 142 144-146 149 while most abstracts did not report the type of ultrasound used (n=22; 61% of abstracts)<sup>86 87 92-98 101 103 105 106 108 131-134 150-153</sup> (table 3). Specialised B-mode ultrasound devices, including the tissue ultrasound palpation system (TUPS; a B-mode ultrasound transducer in-series with a load cell to allow measured compression of the skin),<sup>68 99 100 124</sup> and colour Doppler ultrasound,<sup>52 149</sup> were used in six records (table 3).

The type of scar and skin thickness measurement (ie, thickness of the dermis, epidermis or combined epidermal and dermal measurement) was reported in 39 records (33%) (table 3). Where reported, combined measurement of epidermal and dermal thickness was the most common method used in articles (n=32; 76% of articles reporting skin measurement type).<sup>17 22-24 27 29 50 53 56-58 60 64-66 70 72-77 80-82 114 116 118 122 126 127 130 139 146 148 Separate</sup>

epidermal and/or dermal thickness measurements were reported in seven journal articles (17% of articles reporting skin thickness measurement type).<sup>264748525371118</sup> Of these records, two authors provided a rationale for this decision: each skin layer provided different information on the scar;<sup>26</sup> or responded differently to treatment.<sup>6771</sup> Most abstracts did not report the type of skin measurement used (n=30; 83% of abstracts).<sup>283091-101103-110131-134150-154</sup>

Three articles  $(4\% \text{ of articles})^{47 \text{ 110 111}}$  and one abstract  $(3\% \text{ of abstracts})^{28}$  directly reported that fibrosis was the scar characteristic targeted by the measurement. One of these records also quantified hair follicle density to assess the difference between scared and unscarred skin.<sup>47</sup> An additional 25 articles  $(30\% \text{ of articles})^{17 \text{ 46 52 53}}$  56 63–65 67 70 79 80 83 84 112 120 123 125–127 140 142 145 148 149 155 and 1 abstract  $(3\% \text{ of abstracts})^{110}$  made indirect reference (ie, within the introduction or discussion) to the measurement of fibrosis. Ten journal articles (12%) made indirect reference to the measurement of both oedema and fibrosis, <sup>31 54 55 71 74 76–78 138 144</sup> and one record made indirect reference to the measurement of oedema.<sup>59</sup>

Additional objective and/or subjective measurement methods were employed alongside ultrasound measurement in 72 articles (88% of articles)  $^{17\ 22\ 24\ 26\ 29\ 31\ 46-53\ 55-57}$ 

 Table 3
 Summary of measurement methods used in included record\*

Characteristic	Parameters	Number of records		
Journal articles				
Ultrasound	B-mode	24		
type	Mid-range	2		
	High-frequency	29		
	Other	4		
	Not reported	22		
Measurement	Epidermal	0		
parameters	Dermal	4		
	Epidermal and dermal	2		
	Combined epidermal and dermal	32		
	Other	3		
	Not reported	40		
Scar	Fibrosis	27		
characteristic	Oedema	1		
measured	Fibrosis and oedema	10		
	Other	1		
	Not reported	42		
Abstracts				
Ultrasound	B-mode	3		
type	Mid-range	0		
	High-frequency	9		
	Other	3		
	Not reported	21		
Measurement	Epidermal	0		
parameters	Dermal	1		
	Epidermal and dermal	4		
	Combined epidermal and dermal	1		
	Other	1		
	Not reported	29		
Scar	Fibrosis	2		
characteristic	Oedema	0		
measureu	Fibrosis and oedema	0		
	Other	0		
	Not reported	34		

B-mode ultrasound (<20 MHz); high-frequency: high-frequency B-mode ultrasound (>20 MHz); other: fields are expanded with additional detail in online supplemental table 3. \*A full summary of each included record is available in online supplemental table 3.

B-mode, brightness mode.

 $^{60-70}$  72-81 83-85 111-122 124-130 136-142 144 145 147-149 and 31 abstracts (86% of abstracts)<sup>86</sup> 88 89 91-95 97-110 131-134 150 151 153 154 (online supplemental table 4). All three phase IV studies

investigating routine clinical practice used additional measurements.<sup>92 113 119</sup> The additional objective measurements used in included records were elastography (elasticity), cutometric assessment (pliability) and Doppler ultrasound (vascularity). The additional subjective measurements were conducted using clinician-based rating scales (eg, Vancouver Scar Scale (VSS) or modified VSS) or patient-reported outcome measures (PROMs). The VSS was used in 35 articles (43% of articles)<sup>17 31 46 47 49</sup> 50 52 55 57 61-64 66-70 73 85 111 112 114 116 118 121 124 128 130 136-138 140-142 and 11 abstracts (31% of abstracts).<sup>88919298-100107134150151153</sup> PROMs were used in 27 articles (33% of articles) and 11 abstracts (31% of abstracts).<sup>46 53 56 57 60 72-75 85 91 94 97</sup> 101-106 111 112 114 115 117 118 120 122 129 131-133 138 140 141 148 150 151

<sup>153</sup> <sup>154</sup> Of the records that reported using PROMs, the most commonly used was the patient report of the Patient and Observer Scar Assessment Scale (POSAS), used in 17 articles (63% of articles reporting use of PROMs)  $^{17\,22\,46\,50\,53\,61\,62\,64\,76\,77\,79\,114\,121\,125-127\,147}$  and 8 abstracts (73% of abstracts reporting use of PROMs)<sup>9193102104106132153</sup> (online supplemental table 4). In most cases, additional measurement methods were used to supplement ultrasound thickness measurements as research outcomes. In some records (n=16; 14% of records), however, ultrasound was compared with histology, POSAS, dermoscopy, VSS and modified VSS, clinical assessment, modified Seattle Scar Scale, high-definition optical coherence tomography, three-dimensional (3D) camera, immunohistochemistry and immunohistomorphom-etry.<sup>17</sup> <sup>24</sup> <sup>26</sup> <sup>29</sup> <sup>31</sup> <sup>50</sup> <sup>51</sup> <sup>64</sup> <sup>73</sup> <sup>77</sup> <sup>86</sup> <sup>95</sup> <sup>110</sup> <sup>120</sup> <sup>124</sup> <sup>149</sup> Where the effectiveness of ultrasound was judged against other methods, it was only found to be inadequate against histology.<sup>26 86</sup>

Methods used to relocate the scar for repeated measurements were reported in 34 records (29%) (online supplemental table 3). The most common relocation method was tracing the outline or boundaries of the scar on a transparent or translucent sheet (n=14 articles; 35% of articles reporting scar relocation),  $^{23\,49\,65\,74\,81\,115\,116\,120\,124\,125\,153}$  occasionally including prominent or bony landmarks close to the scar.  $^{23\,24\,72\,73\,123}$  Photographs (n=10 articles; 25% of articles reporting relocation and n=1 abstract) and linear measurements from defined points or anatomical landmarks on or around the scar (n=4 articles; 10% of articles reporting relocation) were also used for scar relocation. The 'worst' or 'thickest' part of the scar, as determined by patients or assessors, was chosen as the measurement site in 14 journal articles (35% of journal articles reporting relocation)  $^{23\,31\,52\,54\,57\,61\,62\,67\,126\,127\,138\,141\,148\,155}$  and 1 abstract.<sup>105</sup>

Measurement of unscarred skin, either contralateral or adjacent to the scar, was performed in 32 articles (39% of articles)  $^{17\,22-24\,27\,29\,46-48\,50\,51\,53\,56-60\,64\,72\,73\,80\,81\,85\,114\,118\,120-122\,128}$   $^{145\,146\,148}$  and 7 abstracts (19% of abstracts).  $^{28\,94\,95\,150\,151\,153\,154}$ 

These measurements were primarily used as controls or comparators to scar measurements (n=27, 69% of records reporting unscarred skin measurement).<sup>17</sup> <sup>22</sup> <sup>23</sup> <sup>28</sup> <sup>29</sup> <sup>47</sup> <sup>48</sup> <sup>51</sup> <sup>53</sup> <sup>56–60</sup> <sup>64</sup> <sup>67</sup> <sup>73</sup> <sup>80</sup> <sup>85</sup> <sup>95</sup> <sup>118</sup> <sup>120</sup> <sup>122</sup> <sup>128</sup> <sup>146</sup> <sup>148</sup> <sup>153</sup> <sup>154</sup> Additionally, four records (10% of records reporting unscarred skin

measurement) evaluating treatment efficacy measured both unaffected skin thickness and the thickness of a 'control' or untreated scar.<sup>46 74 94 114</sup> All instances where additional ultrasound measurements were taken of unscarred skin or untreated scars were reported as part of research initiatives aligning with phases II and III of the research-to-practice pipeline (figure 1).<sup>36</sup>

### **Reliability and measurement error**

Reliability was calculated for both scarred and unscarred skin in 13 articles (16% of articles) and 2 abstracts (5% of abstracts), and was generally considered acceptable (online supplemental table 5). This included inter-rater reliability (n=5; 4% of articles), 54 64 73 120 137 intra-rater reliability (n=3; 4% of journal articles)<sup>22 23 65</sup> and both inter-rater and intra-rater reliability (n=7; 6%; including two abstracts).<sup>17 24 57 82 87 105 124</sup> The ICC was the most commonly reported reliability statistic (n=10; 8% of records, including one abstract),<sup>17</sup> <sup>24</sup> <sup>57</sup> <sup>64</sup> <sup>65</sup> <sup>73</sup> <sup>82</sup> <sup>87</sup> <sup>120</sup> <sup>124</sup> where it was reported for both scar and unscarred skin measurements in four articles (5% of articles).<sup>17245773</sup> The reported combined thickness (ie, epidermal and dermal) ICCs for inter-rater reliability of scarred skin ranged from 0.82 to 0.985, while the inter-rater ICC for the measurement of unscarred skin ranged from 0.33 to 0.98, with one of the four records reporting an ICC below the threshold value of 0.7 (ICC=0.33)<sup>24</sup> and one record simply reported that the inter-rater ICC for scarred skin was 'acceptable to high'.<sup>64</sup> The reported intra-rater reliability for combined thickness measurements of scarred skin ranged from 0.89 to 0.983, and for unscarred skin ranged from 0.61 to 0.982, with one record reporting an ICC below the threshold of 0.7 (ICC=0.61).<sup>24</sup> One record reported both the inter-rater and intra-rater ICCs for individual epidermal (inter-rater ICC=0.297; intra-rater ICC=0.809) and dermal (inter-rater ICC=0.991; intrarater ICC=0.991) scar thickness measurement.<sup>87</sup> Four articles (5% of articles) reporting reliability used Pearson's R, an undisclosed method, or description (eg, high), as detailed in online supplemental table 2.<sup>22 54 105 137</sup>

Measurement error for inter-rater and intra-rater reliability of combined, epidermal or dermal thickness was reported in four articles (5% of articles) and one abstract using SEM. The inter-rater SEM for the combined epidermal and dermal thickness of scarred skin ranged from 0.11 to 0.5 mm, and the intra-rater SEMs ranged from 0.18 to 0.52 mm. Individual records reported SEM values for unscarred skin, and separate epidermal and dermal measurements, available in online supplemental table 5.<sup>17 23 24 82 87</sup> Only one record reported calculation of the SDC. In that record, the inter-rater and intra-rater SDC was calculated for both scarred and unscarred skin. The scarred skin SDCs were 1.4 mm (inter-rater) and 0.6 mm (intra-rater), and unscarred skin SDCs were 0.8 mm (inter-rater) and 0.5 mm (intra-rater).<sup>24</sup> The reported SEMs were all close to or below the largest SDC value reported. This finding may indicate that ultrasound can detect true variance in scar thickness above measurement error for traumatic scar and skin thickness.

Of the records that reported reliability and measurement error, measurements were taken by practitioners with varying clinical expertise and roles within the treating team. These included therapists, nurses, and doctors, sometimes under the supervision of trained radiologists. One record reported that 3 assessors received 3 hours of training, and conducted 10 assessments using the study protocol before the study began.<sup>57</sup>

## Clinical, health service, implementation and feasibility outcomes

No record specifically investigated clinical, health service, implementation or feasibility outcomes of ultrasound as a measurement-based care initiative. Ultrasound was used to assess the clinical outcomes of scar treatment initiatives in all included records. Clinical, health service, implementation and feasibility outcomes related to ultrasound measurement were, however, reported in 53 journal articles<sup>17</sup> <sup>22–24</sup> <sup>26</sup> <sup>27</sup> <sup>31</sup> <sup>46–48</sup> <sup>50</sup> <sup>51</sup> <sup>54</sup> <sup>56–61</sup> <sup>63–66</sup> <sup>69–75</sup> <sup>77</sup> <sup>80</sup> <sup>82</sup> <sup>113–116</sup> <sup>119</sup> <sup>120</sup> <sup>122–124</sup> <sup>128</sup> <sup>129</sup> <sup>138</sup> <sup>142–144</sup> <sup>148</sup> <sup>149</sup> <sup>155</sup> and <sup>14</sup> abstracts<sup>28 86 87 89 90 95 96 102 105 107 109 110 152 153</sup> that focused on scar treatments.

The clinical outcome of patient satisfaction related to ultrasound measurement was only reported in one journal article. While patient satisfaction was not directly measured in that record, a proxy measure of satisfaction was reported by the authors stating that no paediatric patient or their caregiver refused ultrasound measurement once the purpose was explained.<sup>24</sup>

Timeliness was the only reported health service outcome, reported as the time required to take ultrasound measurements. Where reported in three journal articles, this was short, taking between 1 and 5 minutes.<sup>24 27 122</sup>

The most common implementation outcomes reported in the identified records were fidelity, acceptability and appropriateness. Fidelity to the measurement method was reported through the use of experienced or trained assessors (n=6 journal articles; n=1 abstract),<sup>24 57 58 87 142 144 148</sup> and/or using the same assessor/s for all measurement sessions (n=5 journal articles; 6% of included journal articles).<sup>24</sup> <sup>61</sup> <sup>138</sup> <sup>144</sup> <sup>148</sup> Differences between intended and actual measurement methods were not discussed. The training and/or experience of the assessors was discussed in 24 records (23 journal articles and 1 abstract),<sup>17</sup> <sup>23</sup> <sup>24</sup> <sup>27</sup> <sup>51</sup> <sup>56-59</sup> <sup>63-66</sup> <sup>71</sup> <sup>73</sup> <sup>115</sup> <sup>116</sup> <sup>120</sup> <sup>123</sup> <sup>124</sup> <sup>138</sup> <sup>144</sup> <sup>149</sup> <sup>153</sup> where measurements were either taken by a clinician (n=13; 54% of records reporting training),  $^{172324585964-6771120124141}$ members of the research team (n=6;25% of records reporting training)<sup>57</sup> <sup>63</sup> <sup>73</sup> <sup>115</sup> <sup>123</sup> <sup>144</sup> or by specialist sonographers and/or radiologists (n=5, including 1 abstract; 21% of records reporting training).<sup>56 116 138 149 153</sup> Only one record reported on fidelity in the context of routine clinical practice. In this instance, ultrasound was conducted in the Department of Radiology, however the role or training of the staff was not reported.<sup>119</sup>

The acceptability and appropriateness of the ultrasound methods used in individual records were generally based on author's opinion and outlined in the discussion. Acceptability was reported in 26 records (23 journal articles and 3 abstracts),<sup>17</sup> <sup>22–24</sup> <sup>26–28</sup> <sup>31</sup> <sup>57</sup> <sup>64</sup> <sup>70</sup> <sup>74</sup> <sup>75</sup> <sup>77</sup> <sup>80</sup> <sup>82</sup> <sup>86</sup> <sup>96</sup> <sup>116</sup> <sup>119</sup> <sup>120</sup> <sup>122</sup> <sup>124</sup> <sup>143</sup> <sup>149</sup> <sup>155</sup> including for paediatric popu-

lations, where one record reported potential difficulty in measuring this population,<sup>22</sup> contrasting that which reported that measurement was acceptable to both children and their caregivers.<sup>24</sup> One record reported acceptability where the intervention being analysed by ultrasound was already part of routine clinical practice. In this instance, the authors referenced additional publications which stated that ultrasound had an accuracy of 0.5 mm, which was judged by the authors to be sufficient for assessment of scar thickness.<sup>24 27 119 122</sup> Potential difficulty was identified in the measurement of open wounds,<sup>24</sup> and traditionally hard-to-reach areas (such as the axillae or groin).<sup>22</sup>

The appropriateness of the ultrasound methods was reported in 35 journal articles  $(43\% \text{ of included journal articles})^{22}$  24 26 27 31 46–48 50 54 57 60 61 64–66 69 72–75 77 80 82 113 114 116 119 120 122 124 128 148 149 155 and 11 abstracts (31% of included abstracts), <sup>86</sup> 87 89 90 95 102 105 107 109 110 152 where it was generally addressed in the discussion. Of these records, two (4% of records reporting appropriateness) determined that ultrasound was not appropriate for scar measurement. The first stated that it was too inaccurate and complex<sup>86</sup>; and the second, which reported on initiatives within routine clinical practice, determined that the minimum resolution of the Diasonography ultrasonic scanner (Nuclear Enterprises, Edinburgh, UK) precluded its use in scars thinner than 3 mm.<sup>113</sup>

The feasibility of ultrasound was reported in 12 journal articles (15% of included journal articles).  $^{22\ 24\ 26\ 46\ 57\ 70\ 80\ 119\ 120\ 124\ 129}$  Five records considered ultrasound not feasible for scar measurements. The rationale presented included high-frequency 20 MHz ultrasound having an inadequate penetration depth<sup>26 57</sup>; and ultrasound measurement and training of investigators requiring too much time (as reported in one record in phase IV of the research-topractice pipeline).<sup>22 119 120</sup> Another factor identified as precluding feasibility was the inability to consistently relocate the measurement site.<sup>24</sup> Conversely, one record reported ultrasound to be feasible in combination with VSS measurement,<sup>70</sup> and another stated that ultrasound was able to distinguish between subcutaneous fat and muscle, which was interpreted by the authors of that record to mean that skin thickness measurements were accurate.<sup>129</sup> The majority (n=11; 92%) of the records reporting feasibility were research initiatives in phase II or phase III of the research to practice pipeline. One record examined feasibility in the context of routine clinical practice (ie, phase IV; figure 1),<sup>119</sup> where it was determined that ultrasound was not suitable for use in their 12-year longitudinal study due to changes in staff, equipment and software

over such a long time period, which introduced additional variables to the measurement process that were impossible to control.<sup>119</sup>

## Factors influencing ultrasound images and measurement methods

The only factor that was reported to influence the imaging and measurement methods was the measurement of scars with open wounds. This was reported in one record, which determined that ultrasound and ultrasound gel was unsuitable in this instance. The authors of that record suggested the use of a flexible transparent plastic wrap, which is placed over the measurement area prior to measurement with ultrasound.<sup>24</sup>

### Reported strengths and limitations of the measurement methods

The safety, practicality, objectivity, versatility, reliability and non-invasive nature of ultrasound were all reported as strengths of the measurement method. <sup>22</sup> <sup>27–29</sup> <sup>47</sup> <sup>50</sup> <sup>57</sup> <sup>61</sup> <sup>64</sup> <sup>77</sup> <sup>78</sup> <sup>80</sup> <sup>82</sup> <sup>87</sup> <sup>89</sup> <sup>95</sup> <sup>96</sup> <sup>105</sup> <sup>107</sup> <sup>109</sup> <sup>119</sup> <sup>123</sup> <sup>124</sup> <sup>129</sup> <sup>139</sup> <sup>148</sup> When compared with other subjective (eg, VSS) or clinical (eg, 3D camera) measurement methods, ultrasound was viewed as the superior measurement method of scar and skin thickness, due to its improved accuracy, greater sensitivity to change and objectivity. <sup>24</sup> <sup>64</sup> <sup>73</sup> <sup>116</sup> <sup>120</sup> The ability of ultrasound to differentiate between scarred and unscarred skin was also highlighted (n=4; 3%), <sup>47</sup> <sup>60</sup> <sup>72</sup> <sup>122</sup> as was the versatility of ultrasound in its ability to measure a variety of anatomical areas and be used with child participants (ie, <18 years) (n=2; 2%). <sup>22</sup> <sup>149</sup>

The poor correlation between ultrasound and histological thickness measurements,<sup>86</sup> and the established inverse relationship between ultrasound penetration depth and the resolution of superficial structures were identified as limitations of ultrasound in the measurement of scar thickness.<sup>26 27 77 80 89 113 149</sup> This may be an evidence gap worth exploring in more depth. One record, reporting on a longitudinal study that was conducted over 12 years, reported that the continuous development of ultrasound software and hardware over that time limited the usefulness of ultrasound.<sup>119</sup> Despite being reported elsewhere as acceptable (ie, between 1 and  $5 \min^{24} \frac{1}{27} \frac{122}{122}$ ), one record reported that the time-consuming nature of measurement and the requirement for assessors to be trained in the operation of, and techniques required for, ultrasonography was a limitation of the method.<sup>120</sup> Methodologically, concerns were raised around the pressure caused by application of the ultrasound transducer to the skin, and how that may influence thickness measurement.<sup>61 62 123 124</sup> The size of the transducer head relative to the size of scars was also considered a potential limitation, as multiple measurements are required for quantification of larger scars.<sup>57</sup> Finally, it was recognised that there may be a difference between changes to the scar that can be measured by ultrasound, and what is felt and/or experienced by the patient.<sup>75 80 126 127</sup> It was suggested that changes that are detectable by ultrasound may be smaller than those able

to be detected by patients. In patients with burn scars, a minimum change in scar thickness of between 1 and 6mm measured by ultrasound, has been reported to be required before a patient may report noticing any difference to their scar thickness.<sup>24 75</sup> While further research is required to allow generalisation of these findings to other scar aetiologies, this indicates that a holistic approach to scar thickness using the patient's opinion as well as objective measurement through ultrasound may be beneficial.

## Guidelines or frameworks used to guide the measurement methods

No records reported using any guidelines or frameworks to inform their measurement methods. One record used suggestions from The American Wound Healing Society to support the measurement of contralateral, unscarred skin thickness on the same individual as a control or comparator.<sup>75</sup>

### Methodological considerations

Based on the ultrasound methods and outcomes identified in this review, a list of methodological considerations have been compiled (online supplemental table 6). These are intended to guide the decision-making and methodological reporting of researchers and/or clinicians undertaking scar or skin thickness ultrasound measurement.

### DISCUSSION

This review mapped the methods used in the published literature to measure traumatic scar thickness using ultrasound across the research-to-practice translational pipeline. No record reported their methods with sufficient detail to allow them to be independently replicated. Overall, there was a lack of consistent rationale underpinning which skin layers (ie, epidermis, dermis and combined) were measured, and little consideration was given to the training and experience required by assessors. The included records mainly aligned with the second and third phases of the research-to-practice pipeline (figure 1), with only three records (two articles and one abstract) reporting the use of ultrasound in routine clinical practice (phase IV).<sup>92113119</sup> The paucity of records aligning with phase IV studies (use in clinical practice) suggests a translational gap from research to regular clinical practice. There are two likely explanations for this: (1) that ultrasound is most commonly used as an outcome measure for research initiatives and is not regularly used to evaluate care once treatments are implemented into routine clinical practice or (2) that use of ultrasound in routine clinical practice is not reported or evaluated, as routine clinical practice is rarely published.

Searching of grey literature was conducted in an attempt to identify clinical practice documents, however none were located. Surveys of health service departments may be the best method of identifying ultrasound methods used in regular clinical practice as part of future research. While some records reported using additional subjective and objective measurement methods in addition to ultrasound, none used these methods to determine the criterion validity of the ultrasound for scar thickness measurement. This is another evidence gap that should be addressed.

While efforts have been made to standardise ultrasound measurement procedures elsewhere in dermatology (including tumours, cancers, vascular anomalies and systemic sclerosis<sup>34 35</sup>), this same effort has not yet extended to the measurement of traumatic scarring. Methodological standardisation has the potential to increase confidence in the use of ultrasound as the basis of measurement-based care initiatives for clinical decision-making, allowing patient care and scar treatments to be tailored towards individual needs.<sup>62 147 156</sup> Standardising the core methodological components of ultrasound measurement of scar thickness, or at the very least, creating a standardised framework for methodological decision-making, may support implementation of ultrasound measurement into routine clinical practice, supported by strategies to overcome barriers to implementation at local sites.<sup>157</sup>

This review identified novel insights into the identification of the composition of cutaneous scars using ultrasound, and highlighted the apparent lack of consistent understanding of, or rationale behind, what scar thickness characteristics were being measured. Fibrosis is generally understood to be the primary cause of scar thickness through the deposition of excessive extracellular matrix proteins such as collagen.<sup>158</sup><sup>159</sup> This has been confirmed through histological analysis, which has shown the presence of excess collagen and other extracellular matrix proteins in the dermis of hypertrophic scars.<sup>160 161</sup> An additional method for assessing the effects of scarring on the dermis, as identified by one record in this review,<sup>4</sup> is through quantification of the presence and density of hair follicles. This quantification may serve as a method of differentiation between scarred and physiological skin, and may also serve as a measure of skin function.<sup>47</sup> What is less understood, and perhaps largely overlooked, is the function of the epidermis in scar thickness. In the one record identified in this review that directly reports the measurement of the epidermis, the authors noted that the measurement quantified the presence of oedema.<sup>55</sup> This was further supported by two records that noted that the epidermis and dermis responded differently to treatment,<sup>67 71</sup> indicating that there is likely a difference in the composition of the scar between these skin layers. Cutaneous oedema has been observed using highfrequency ultrasound in other pathologies, including atopic dermatitis and skin ageing, where it is characterised by the presence of a subepidermal low echogenic band, a hyperechoic band at the dermoepidermal junction.<sup>162</sup> Understanding the interplay between epidermal oedema, dermal fibrosis and the presence and density of hair follicles may result in an increased understanding of the mechanisms and treatment responses of cutaneous scarring. With better understanding, more targeted scar

treatments that inform a greater understanding of scar responsivity may arise.

Another important, but potential limiting factor for the use of ultrasound to measure scar thickness raised in this review is the training and/or experience required of assessors, and the ramifications this likely has on the reliability of measurements and interpretation.<sup>163</sup> This review identified 24 records where assessor experience was discussed, however none made any recommendations on the optimal training and/or experience. Identifying the training requirements of assessors may prove an important step towards more widespread implementation of reliable ultrasound scar thickness measurement in research trials and as the basis for measurementbased care in routine clinical practice.<sup>164</sup> A panel of dermatological and ultrasound experts has previously recommended that a physician with a minimum of 300 examinations per year should hold responsibility for ultrasound measurements.<sup>34</sup> It has also been suggested that training existing members of clinical teams and standardising measurement method/s may be the most effective way to achieve minimum reliability standards under clinical conditions. This could allow measurement to be reliably conducted within an outpatient clinic setting by a number of healthcare providers, assisting workflow by negating the requirement for patients to wait for an experienced radiographer.<sup>24164</sup> In the current review, reliability estimates were generally acceptable but were tested under research conditions. The diverse experience and expertise of assessors, where reported for the reliability estimates, means that the acceptable reliability results should be generalisable to most clinical teams, as therapists, doctors and nurses were all included. The cumulative sample size of all reliability studies also supports this generalisation; however, each team should perform their own reliability estimates before conducting ultrasound thickness measurements.

### **Study limitations**

Only articles available in English or with an English abstract were considered for inclusion and data extraction, which may have resulted in the omission of eligible information. Data extraction was completed on the English abstracts of two non-English articles that were available electronically, however the non-English articles themselves were not available to the authors, and thus could not be analysed. Based on the number of records included in this review, however, it is unlikely that this would have impacted the review findings. It is acknowledged that methods reported in included abstracts may not be fully reproducible, due to their brevity. Thus, findings were reported separately to articles. An additional limitation was that authors of included records were not contacted to provide clarification or further information, as this was not feasible given the number of results identified. It should also be acknowledged that the included records were not designed to align with the specific

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aims of this review, which likely explains some of the lack of reporting on outcomes of interest in our review, particularly clinical, health service and implementation outcomes. Furthermore, as this review relied on published information (including grey literature), routine practices employed within organisations may not have been considered and unpublished industry sponsored reports may not have been identified.

It is also important to consider the limitations of ultrasound itself for the holistic quantification of cutaneous scarring. Ultrasound transducers are generally small, meaning that it is difficult to assess the entirety of a scar, necessitating multiple measurements.<sup>165</sup> Additionally, thickness is often not the only scar parameter of clinical or research interest. It has therefore been recommended that multimodal measurement techniques are employed, which include both subjective and objective measurements.<sup>166 167</sup> However, use of these methods may be challenging in routine clinical practice, due to the length of time and training required. Thus, feasibility and implementation outcomes are of importance in evaluating measurement-based care initiatives involving ultrasound alone or multimodal measurement tools in scar care practice-a field in its infancy based on this review.

### **Future directions**

It is intended that the results of this review will be used to inform the creation of a Delphi consensus study, leading to the formation of a guideline for the measurement of traumatic scar thickness using ultrasound. This guideline can then be used by researchers and clinicians to standardise the measurement of scars. In preparation for this study, we have provided a list of methodological considerations for assessors or practitioners when planning to conduct scar thickness measurements with ultrasound (online supplemental table 6). Future research could also investigate aspects that were beyond the scope of this review including factors influencing the implementation of ultrasoundbased care initiatives, strategies to support implementation and how research-based initiatives could be applied in practice. Further studies are needed that compare SDCs with SEMs to interpret reliability estimates to confirm our interpretation that ultrasound may have the ability to detect true change or variance in scar thickness above measurement error, which was based on the SDC reported by a single study. Our interpretation is supported by mostly acceptable reliability estimates of ultrasound thickness for other cutaneous conditions.<sup>168</sup> Additional investigations should also be conducted to determine the criterion validity of ultrasound as a measure for scar thickness.

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12

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6