

Global Burn Core Outcome Set

Scar Free Foundation partnership project

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Executive summary:

The project detailed below was funded by the Scar Free Foundation (SFF) as partnership funding to the National Institute for Health and Care Research (NIHR) funding for a Doctoral Fellowship for Dr AE Young. Both workstreams enabled work to produce an international Core Outcome Set (COS) for burn care research. The aim of the international COS was to support consistent outcome reporting in trials in burn care, enabling synthesis of evidence from individual trials, to support stronger evidence for clinical decision-making. The SFF funding enabled a set of add-on projects which resulted in a greater impact for the Burn COS. These are detailed below.

SFF-funded research team:

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Table of Contents:

Title page and executive summary	1
Background	3
Sub-projects	4
Exploring what is important during burn recovery: a qualitative study investigating priorities of patients and healthcare professionals over time	4
An exploration of the views of health care professionals from Low-, Middle- and High-Income Countries on the prioritisation of outcomes for a burn care Core Outcome Set demonstrates the need for standards for involvement.....	5
A systematic review of the time taken for scars to mature following acute thermal burn injuries.....	5
Clinical trials in burn care focus on short-term outcomes rather than outcomes of importance to patients: a systematic review.....	6
Dissemination	7
Future Research	8

Background:

Clinical decision-making in burn care is challenging. New technology and surgical care pathways are continually being introduced. Clinical decisions require evidence synthesised from trials. Evidence can only be collated and compared if outcome reporting is consistent and if outcomes are reported that are important to all stakeholders. In burns, this is limited by the use of multiple different outcomes, that may be ill-defined and assessed in different ways and at different times. In a five-year systematic review of clinical outcomes from 147 burn trials, 955 unique outcomes were reported with 166 different definitions of wound healing (Young AE, Davies A, Bland S, Brookes S, Blazeby JM. *Systematic review of clinical outcome reporting in randomised controlled trials of burn care. BMJ open. 2019 Feb 1;9(2):e025135*). Costly research and valuable patient input is being wasted because of this inability to compare outcomes and synthesise evidence.

A Core Outcome Set (COS) is a minimum set of outcomes, agreed by patients and professionals to ensure relevance, that are measured and reported in a standardised way across trials. Researchers can report other outcomes, as long as those that are in the COS are used. A COS will improve trial design, evidence synthesis, technology assessment and effective use of research funding.

The COSB (International Core Outcome Set in burn care) funded by a 4-year NIHR grant, has achieved a burn COS (April 2020). The Core Outcome Set contains both short-term and longer-term outcomes. These are: **death (to include death from any cause, including from the burn), serious complications (to specifically include wound infection, sepsis, venous thrombosis), ability to do daily tasks (to include walking), time to heal (to include burn wound healing, grafted and donor site wound healing), neuropathic pain and itch, patient psychology (to include anxiety and anxiety about the future) and time to return to work or school or previous occupation**). The agreement involved 126 UK patients and 775 multidisciplinary health care professionals from 75 countries, from all continents and across all income statuses (Young A, Davies A, Tsang C, Kirkham J, Potokar T, Gibran N, Tyack Z, Meirte J, Harada T, Dheansa B, Dumville J. *et al Establishment of a core outcome set for burn care research: development and international consensus. BMJ Medicine. 2022 Jul 1;1(1)*). The aim is that researchers include these agreed seven outcomes in all trials of burn care interventions so that studies are comparable and stronger synthesised evidence can be produced to support clinical decision-making.

The core outcomes chosen for this COS, clearly reflect priorities in recovery for both patients, carers and clinicians. This diversity of stakeholder involvement is increasingly common in COS development. Interestingly, stakeholders agreed on outcomes that span both short and long-term recovery. Death, pre-specified acute complications including infection and time to heal, are outcomes to measure the effect of interventions in short-term efficacy RCTs. The other outcomes, (ability to undertake tasks of daily living, neuropathic pain and itch, psychological well-being and time to return to work, school or previous occupation), are patient-important and more likely to be of value when assessing clinical interventions in longer-term pragmatic trials. A remaining question, is whether all the COSB-i core outcomes should be in be used in all trial types? In other words, would it be useful to develop or encourage the use of the short-term outcomes in efficacy trials and the longer-term outcomes in pragmatic trials.

The aim of the Scar Free Foundation (SFF)-funded project was to gain a greater understanding of how important the timing of outcomes are to patients, professionals and international stakeholders.

Sub-projects:

1. Exploring what is important during burn recovery: A qualitative study investigating priorities of patients and healthcare professionals over time.
2. An exploration of the views of health care professionals from Low-, Middle- and High- Income Countries on the prioritisation of outcomes for a burn Core Outcome Set demonstrates the need for standards for involvement.
3. A systematic review of the time taken for scars to mature following acute thermal burn injuries.
4. Clinical trials in burn care focus on short-term outcomes rather than outcomes of importance to patients: a systematic review.

Sub-project detail:

1. Exploring what is important during burn recovery: a qualitative study investigating priorities of patients and healthcare professionals over time

This project involved interviews with 53 UK patients, carers and health care professionals on the importance of different outcomes during recovery from burn injury. This has taken more than 50 hours interviewing time, as well as interview transcription, data analysis, data synthesis and theme extraction.

Research permissions: A favourable opinion for the project was granted by the South West - Frenchay Research Ethics Committee, reference 17/SW/0025. Written informed consent of each participant was taken before conducting the interviews. Participants were encouraged to read the study information sheet sent to them prior to the interview and were informed about their rights as participants, that the conversation would remain confidential, and that the transcript would be anonymised.

Objectives: This qualitative study aimed to investigate what is most important to patients and healthcare professionals during recovery from a burn injury.

Design: Semi-structured interviews were conducted. Interviews were audio recorded, transcribed and analysed thematically.

Setting, participants: A total of 53 patients and healthcare professionals were recruited from four NHS burn services across England and Wales across England and Wales. Patient participants (n=32) included adults, adolescents and parents of paediatric patients, with a variety of burn injuries in terms of severity and cause of burn injury. Healthcare professionals (n=21) were NHS staff members involved in burn care and included clinicians with a range of experience and roles (e.g. nurses, surgeons, occupational therapists, physiotherapist, administration).

Results: A total of ten themes relating to priorities during recovery from a burn injury were identified for patients and professionals. Of those, six were identified for both stakeholder groups ('pain', 'psychological wellbeing', 'healing', 'scarring', 'function' and 'infection'); three were unique to professionals ('patient knowledge, understanding & support', 'sense of control', 'survival') and one was unique to patients ('uncertainty'). Results highlighted that importance of these priorities changes over time (e.g. 'survival' was a concern for clinicians in the short term, but not in the medium to long

term). Likewise, it was revealed that priorities differed between patients and professionals (e.g. 'pain' was a concern in the short term for professionals but important to patients throughout their recovery). A total of seven themes overlapped with outcomes commonly assessed in burn research, whereas three themes could not be mapped to reported outcomes ('uncertainty', 'patient knowledge, understanding & support', 'sense of control').

Conclusion: Professionals' and patients' priorities (important outcomes) change over time after injury and differ between stakeholder groups. Burn care research should take into account the time-sensitivity of routinely measured outcomes to accurately reflect complexity of burn recovery.

Output: the completed manuscript has been submitted to BMJ Open. It has been accepted subject to revisions (in progress August 2022).

2. An exploration of the views of health care professionals from Low-, Middle- and High- Income Countries on the prioritisation of outcomes for a burn care Core Outcome Set demonstrates the need for standards for involvement.

A secondary analysis of data from the Burn Core Outcome Set (COSB-i) was undertaken.

Objectives: To compare the views of participants from different income-status countries on outcome selection for a burn care Core Outcome Set (COS).

Study Design and Setting: A retrospective analysis of data collected during a two round Delphi survey to prioritise the most important outcomes in burn care research.

Results: There was considerable agreement between participants from low- and middle-income countries (LMICs) and high-income countries (HICs) across outcomes. The groups agreed on 91% of 88 outcomes in round 1 and 92% of 100 outcomes in round 2. In cases of discordance, the consensus of participants from LMICs was to include the outcome and for participants from HICs to exclude. There was also considerable agreement between the groups for the top-ten ranking outcomes.

Discordance in outcome prioritisation gives an insight into the different values clinicians from LMICs place on outcomes compared to those from HICs. Limitations of the study were that outcome rankings from international patients were not available. Healthcare professionals from LMICs were not involved in the final consensus meeting due to funding and timing issues.

Conclusion: COS developers should consider the need for a COS to be global at protocol stage. Global COS should include equal representation from both LMICs and HICs at all stages of development.

Output: Publication: Davies PA, Davies AK, Kirkham JJ, Young AE. Secondary analysis of data from a core outcome set for burns demonstrated the need for involvement of lower income countries. Published in the *Journal of clinical epidemiology*. 2022 Apr 1;144:56-71.

3. A systematic review of the time taken for scars to mature following acute thermal burn injuries.

Background: Thermal burns are common and often result in scarring. In children, these are usually due to hot drinks or hot surfaces. There is a paucity of literature describing the time taken for scars to mature following burns injuries. Accurate information on time to scar maturation would be useful to determine the optimal length of follow up for trials investigating the effects of interventions in scarring. It would also ensure that the optimum time for scar management strategies to start.

Aim: This systematic review aimed to determine the length of time taken for scars to mature following acute thermal burn injuries in adults and children.

Methods: Medline and Excerpta Medica Database (EMBASE) were searched from inception to 17th May 2021. To be included, studies had to recruit a cohort of patients with an acute thermal burn and follow them up for a minimum of six months, measuring scar quality at a minimum of two timepoints and using a validated tool. The quality of the included studies was assessed using criteria derived from checklists for case series adapted to be specific to the clinical topic. A narrative synthesis was conducted.

Results: 23 studies met the inclusion criteria. Two studies followed up participants until scar maturation. Average time to scar maturation ranged from 8 to 12.4 months with a median of nine months. 21 studies compared scar quality at two time points. The conclusions obtained from these studies were heterogeneous.

Discussion: The findings of the review were limited by the quality of the evidence identified. Sample sizes were often small with high numbers of participants lost to follow up. Few studies followed participants beyond 12 months. A greater understanding of the time taken for scars to mature would allow clinicians to improve patient outcomes through appropriate targeting of interventions and increase research efficiency by optimising the length of follow-up in studies. A large prospective cohort study is recommended to provide better insight into scar maturation over time.

Conclusions This review indicates that a high quality longitudinal prospective study of burn scar maturation is needed.

Output: the manuscript has been submitted to the journal *Burns* July 2022. Awaiting response.

4. Clinical trials in burn care focus on short-term outcomes rather than outcomes of importance to patients: a systematic review.

Background: This systematic review was undertaken to explore the timings of outcome assessment in burn care trials and examine whether short-term outcomes are used by researchers as proxies to claim longer term patient benefit.

Study design and setting: Eligible burn care randomised trial (RCT), pilot and RCT protocols were included using Ovid MEDLINE, EMBASE, Web of Science and the Cochrane Library from January 2017 to March 2019. Timings of the last reported outcome assessment were recorded for individual outcomes and whole studies and categorised as < 6/12 or > 6/12 after injury. Reported associations between short and longer term outcomes were examined including the use of the word surrogate.

Results: Of 103 studies reporting 1,021 individual outcomes, 706(69%) were last assessed at < 6 months after burn injury, 179(18%) at > 6 months and 136(13.3%) did not clearly state the time of assessment. Of whole studies, 74(72%) reported the last outcome assessment at < 6 months after injury. Of studies reporting outcomes at < 6 months, 19(26%) made narrative associations with longer-term patient impact. No validated surrogate outcomes were used.

Discussion: Short-term outcomes are likely more commonly used in burn care RCTs, as they are easier to measure, and trials are shorter and cheaper. If longer-term trials are too difficult or costly, burn care research needs to validate surrogate outcomes, by establishing the relationship between short-term outcomes and the longer-term patient important outcomes.

Conclusion: Trials of burn care most commonly report short-term outcomes with most not extending beyond six months after injury. It is unclear if these translate are considered of importance to patients and are of patient benefit in the longer term.

Output: Manuscript complete and awaiting submission.

Dissemination of the Burn Core Outcome Set and future research

Dissemination:

1. The COSB protocol was published in the BMJ Open: *Young A, Brookes S, Rumsey N, Blazeby J. Agreement on what to measure in randomised controlled trials in burn care: study protocol for the development of a core outcome set. BMJ open. 2017 Jun 1;7(6):e017267.*
2. The burn Core Outcome Set has been published in BMJ Medicine *Young A, Davies A, Tsang C, Kirkham J, Potokar T, Gibran N, Tyack Z, Meirte J, Harada T, Dheansa B, Dumville J. Establishment of a core outcome set for burn care research: development and international consensus. BMJ Medicine. 2022 Jul 1;1(1).*
 - a. This was published with an associated editorial and opinion piece.
3. The burn Core Outcome Set, designed to ensure consistent outcome reporting across trials, is to be used in an randomised controlled trial in the Netherlands – Radboud MC University.
4. COSB-I will also be used in a new paediatric burn registry in Queensland.
5. This year (2022), the UK national burns community, through the burn operational delivery networks, is planning to deliver a new set of national burn care standards and outcomes. The Core Outcome Set (minimum set of most important outcomes to be reported in burn care trials) will be explored as the basis for outcome reporting for this report.

Future research:

1. There is agreement with NHS England to use the Core Outcomes in the UK burn registry (iBID: <https://www.ibidb.org/>). Each of the seven outcomes are either already recorded through iBID or are in process of being reported through iBID (2022-23)
2. International registry project using the COSB-i. This project is on-going. Team members include Michael Peck, Yvonne Singer, Emily Bebbington, Joanna Miles and Amber Young. The first part of this project is to assess the similarities and differences between variables (demographics, process, outcomes etc) across national burn databases globally (n=13).