

Review protocol

# Research priorities for fundamental wound research in Australia: a scoping review protocol

Bui UT, Aitcheson SM, Boxall S, Parker T, Wood F, Murray RZ, Finlayson K and Cowin AJ

**Keywords** wound healing, scar, skin, Australian wound research, literature review**For referencing** Bui et al. Research priorities for fundamental wound research in Australia: a scoping review protocol. *Wound Practice and Research* 2021; 29(4):230-233.**DOI** <https://doi.org/10.33235/wpr.29.4.230-233>

Submitted 16 July 2021, Accepted 1 October 2021

## Abstract

**Background** While many aspects of the wound repair process are understood, there is still limited understanding about why chronic wounds develop, how we predict,

diagnose and improve healing outcomes, and why some wounds heal with scarring. Identifying current gaps in knowledge, as well as areas of strengths, will inform recommendations for future research-based themes and influence the targeting of resources.

Ut T Bui RN, PhD<sup>1,2†</sup>

Savannah M Aitcheson BBiomedSc<sup>3†</sup>

Sharon Boxall MN<sup>4</sup>

Tony Parker PhD<sup>3</sup>

Fiona Wood FRCS, FRACS, AM<sup>5</sup>

Rachael Z Murray PhD<sup>3</sup>

Kathleen Finlayson RN, PhD<sup>1,2</sup>

Allison J Cowin PhD<sup>6</sup>

Email [allison.cowin@unisa.edu.au](mailto:allison.cowin@unisa.edu.au)

<sup>1</sup>School of Nursing, Centre for Healthcare Transformation, Queensland University of Technology, Brisbane, QLD, Australia

<sup>2</sup>Brisbane Diamantina Health Partners, Brisbane, QLD, Australia

<sup>3</sup>School of Biomedical Science, Faculty of Health Queensland University of Technology, Brisbane, QLD, Australia

<sup>4</sup>School of Nursing, Midwifery and Paramedicine Curtin University, Bentley, WA, Australia

<sup>5</sup>Burn Injury Research Unit, University of Western Australia, Crawley, WA, Australia

<sup>6</sup>Future Industries Institute, University of South Australia, Adelaide, SA, Australia

\* Corresponding author

† These authors contributed equally

**Aims** This scoping review aims to (i) map current knowledge and research activities into wound healing in Australia and (ii) understand strengths and identifying research gaps in science-focused wound research in Australia.

**Methods** Guided by the PRISMA-ScR framework, this scoping review will include original laboratory-based science studies on wounds conducted in Australia. Records will be searched in PubMed, CINAHL and Embase from January 2010 to March 2021. All screened titles and abstracts will be independently assessed by two reviewers using Rayyan<sup>®</sup>. A third reviewer will solve any conflicts that arise. This will be followed by full text screening and in-depth analysis after resolution of conflicts.

**Results and dissemination** Following data extraction from the final included articles, results will be grouped according to area of research and synthesised in a narrative review. Findings will be published in a peer-reviewed journal.

## Introduction

While normal wound healing is a common, well-regulated process, not all wounds heal in a timely manner and some can become chronic, persisting for months, even years<sup>1</sup>. Impaired wound healing can lead to delayed wound healing, complications and chronic wounds<sup>2</sup>. These delayed healing wounds are reported with high prevalence and recurrent rates which create a significant socioeconomic burden<sup>3</sup>. Each year in Australia wound care costs approximately US\$2.85 billion, equivalent to A\$3.8 billion<sup>4</sup>, putting considerable strain on the healthcare system<sup>5</sup>. Impaired wound healing can reduce quality of life through factors such as loss of mobility,

isolation, anxiety and depression depending on the type and extent of the wound<sup>6</sup>.

The broad purpose of laboratory-based wound studies is to obtain a scientific understanding of the mechanistic processes that underpin normal and abnormal wound healing<sup>7</sup>. For wounds to heal they must proceed through a series of overlapping phases to restore skin integrity and function<sup>8,9</sup>. This repair process is complex and driven by numerous cells present in the wound, as well as cells that are recruited to the wound during the inflammatory process, and by the extracellular matrix (ECM)<sup>9</sup>. Cell signalling pathways and factors secreted by these cells orchestrate wound closure through their modulation of processes such as coagulation, migration, proliferation, inflammation and remodelling of the ECM<sup>9</sup>. These must all come together at the appropriate times, otherwise the repair process is impaired and, in some cases, halted. Factors such as infection and underlying comorbidities can also abrogate the repair processes, leading to the formation of chronic wounds<sup>9,10</sup>. Wounds often heal with a scar which can result in impaired functionality of the skin<sup>9,11</sup>.

Understanding how wounds heal has helped to inform clinical practice guidelines and has contributed to the development of new antibiotics, dressings and technologies<sup>12,13</sup>. However, non-healing wounds still exist and there are still limited therapeutic approaches available that stimulate the repair process so it is important that continued investigations take place. In addition, the implementation of extensive new techniques in wound care have often been supported by inconsistent and sometimes limited evidence, resulting in additional and/or increased costs without the certainty of improved outcomes<sup>7</sup>.

Development of new therapies and diagnostics requires an improvement in our knowledge of how wounds heal and what prevents them from healing, which is limited compared to some fields, such as cancer, where the targeting of resources has led to a greater understanding of the processes involved<sup>14</sup>. This greater understanding has driven many of the major advancements in cancer therapeutics<sup>7</sup>. More recently we have seen how the intense focusing of research questions and resources to laboratory-based scientific studies have helped develop vaccines and improve patient outcomes in response to the COVID-19 pandemic<sup>15</sup>.

To facilitate similar advances in wound care there is a need to understand current research capacity, map research activity, and identify gaps in knowledge. A greater understanding of the healing process, why scars form and how the repair process becomes dysregulated will help focus resources to emerging areas. Increased understanding of wound pathologies will translate into the development of new therapeutics, advanced dressings, diagnostic devices and technologies that can be used to improve healing and consequently the lives of those affected by wounds<sup>16,17</sup>.

## Rationale

In May 2018 the Australian Health Minister announced that wound management would be “the first priority of the new health system’s translation program under the Medical Research Future Fund (MRFF)”. In 2019 the Australian Health Research Alliance (AHRA) conducted a high-level review of the current wound practice environment and met with key stakeholders where AHRA identified urgent action is needed to address current wound care challenges. One of these challenges is the current lack of awareness of the breadth and quality of fundamental laboratory-based wound research that has been and is being conducted in Australia over the past 10 years. It is, therefore, important to gain a better understanding of the Australian scientific wound research landscape to identify its strengths as well as potential gaps to help inform recommendations for future research-based themes and inform funding-related decision-making.

## Aims and objectives

The aim of the scoping review is to undertake a review of the literature to:

- Map current knowledge and laboratory-based research activities into wound healing in Australia.
- Determine the areas of strength and identify gaps that exist in fundamental wound research in Australia.

The objectives are to:

- Identify and describe the current gaps in knowledge as well as areas of strengths in Australian wound laboratory research through a systematic approach using scoping review methodology.
- Group data, extracted from the final included articles, according to area of research and synthesise a narrative review that can be used to promote collaborations and inform the targeting of future resources.

## Methods

This scoping review will use the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) framework<sup>18</sup>. This will be used to guide the review process, classify fundamental scientific wound research areas, and collate the available evidence found in the literature. The PRISMA-ScR framework uses a checklist of 20 essential reporting items and two optional items to include when completing a scoping review that allows a greater understanding of the terminology, core concepts and key items to report in a scoping review (Table 1)<sup>18</sup>.

## Protocol and registration

The scoping review protocol has been prospectively registered in the Open Science Framework (<https://osf.io/bzs38>). Scoping review registration doi:10.17605/OSF.IO/ATX4J.

### Eligibility criteria

As this project aims to scope the breadth of wound research Australia, the decision was made to review all laboratory-based wound research conducted in Australia. The scope of this review is therefore restricted to the Australian context with search limits restricted to Australian-based research. Extending the search to include international research is beyond the scope of this review.

### Inclusion criteria

- Published from January 2010 to March 2021.
- Published in English and conducted in Australia.
- Document types: articles that include original laboratory-based studies focussed on wound healing.

### Exclusion criteria

- Individual studies not meeting the inclusion criteria.
- Case studies, case series, case reports, clinical studies.
- Conference abstracts and conference proceedings.
- Other types of documents that are not listed in the inclusion criteria such as: opinions, editorial statements, call for papers and reviews (including systematic reviews).

### Information sources

The academic databases used to search for literature will be PubMed, CINAHL and Embase.

### Search strategy

The search strategy will consist of three main parts and follow the methodology described in Arksey et al.<sup>19</sup>. The electronic databases PubMed, CINAHL and Embase will be searched for literature published between January 2010 to March 2021. It is acknowledged that the above period is a limitation in this scoping review; however, it is appropriate for understanding the current state of laboratory-based research in Australia and ensures this review covers contemporary findings in the areas of interest. The effect of wounds on patient wellbeing/social impact/mental health/nursing will not be included.

In step one the search will be limited to PubMed, CINAHL and Embase databases with the key search terms as described below. Step two will be conducting the screening of titles, abstracts and full-texts against the selection criteria and step three will involve the critical analysis, data synthesis and reporting of findings in a narrative context.

Key search terms include:

1. (wound\* OR healing OR skin OR derm\* OR cutaneous OR epiderm\* OR injur\*) AND
2. (biol\* OR micro\* OR matri\* OR cell\* OR epithelial\* OR remodel\* OR inflammation OR scar OR bacteria OR pathogen OR scaffold OR graft OR nanoparticle OR cytokine OR nerve OR collagen OR neutrophils OR macrophages OR "hyperbaric oxygen" OR "growth

factor" OR exosomes OR proliferation OR migration OR fibro\* OR keratinocyte OR endothelial OR "hair follicle" OR infection OR "tumor necrosis factor" OR "tumour necrosis factor")

3. NOT (respiratory OR pulmonary OR gastr\* OR renal OR kidney OR hepat\* OR lung OR pancreas\* OR bowel OR colon\* OR liver OR tumours OR spinal OR bone OR brain OR eye OR retinal OR neoplasm\* OR melanoma OR surg\* OR tympanic OR periost\* OR intestin\* OR trial OR survey OR self-healing OR veterinary OR malignant)

Limiters: published date 20100101 – 20210331, affiliation includes Australia, English.

### Selection of sources of evidence

Results from searches will be imported into EndNote X9 for management and uploaded to Rayyan® for review based on the inclusion and exclusion criteria following the scoping review process (Figure 1). After excluding duplicates, two levels of screening will be used to identify articles to be included based on selection criteria: (i) title and abstract screening and (ii) full text screening (Figure 1). For both the screening of titles and abstracts and of full text for eligibility, records will be independently screened and selected by two researchers for each screening steps (UB and SA in the screening of titles and abstracts, SA and TP in the screening of full text). Any conflicts in each of these steps will be resolved by a third researcher, AC and UB respectively. Full texts from the included articles will be used for data extraction.

### Data charting process

Data charting forms will be created in Microsoft Excel™

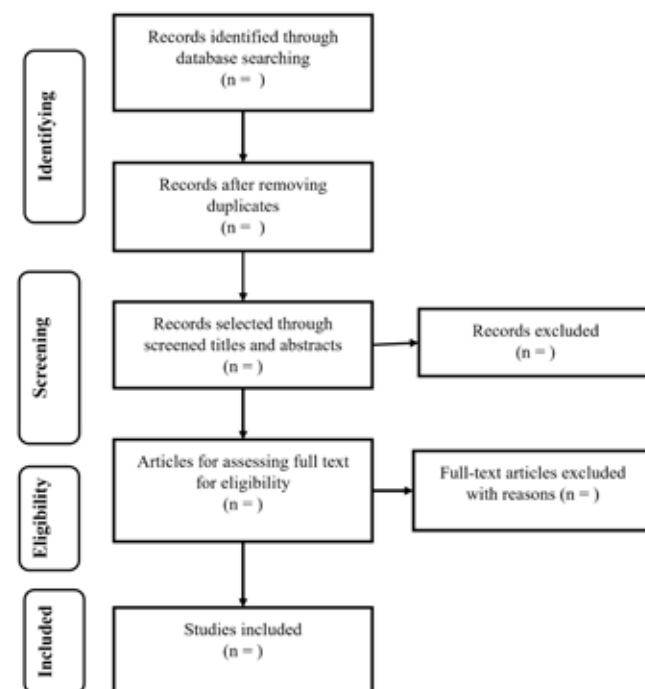


Figure 1. Flow diagram for the scoping review process

and will be piloted initially by one researcher (SA) on a small number of included studies for group review and discussion. Once group agreement has been reached, the full data will then be extracted independently by one researcher (SA) and cross-checked against the original articles by a second researcher (UB) to ensure the data extracted from the studies will be relevant to the research questions.

#### Data extraction items

The data extracted will include descriptive items and focus areas of research items:

- Study characteristics, country of the first and last author of the published paper.
- Research design based on in vivo and/or in vitro laboratory studies; these could be human and/or animal studies.
- Samples investigated may include wound exudate, wound tissue, blood plasma and serum, blister fluid, immune cells, stem cells, skin cells, bacteria, microbiome, skin grafts.
- Studies may focus on inflammation, scarring, wound infection, regeneration, biomaterials, omics, biomarker, basic cell biology, metabolism, 3D printing of cells.
- Application may include sensors, diagnostics, dressings, therapeutics, technology, skin replacement, generation of new knowledge.

### Collating, summarising and reporting results

A narrative synthesis of results will be produced describing the extracted data based on the areas of focus around laboratory-based research in the Australian context, types of and outcomes from the research. Study characteristics will be recorded, and qualitative data will be extracted and evaluated; quantitative data will be summarised and a table of findings generated. These results will be used to identify what the current literature says about fundamental wound healing science as well as identify the key areas where there is a lack of understanding of wound healing processes. It is anticipated the findings will help to provide recommendations for future research directions based on themes identified as well as inform the targeting of resources to areas that will have the best opportunity to improve wound management procedures.

### Conflict of interest

The authors declare no conflicts of interest.

### Contributors

Author contributions as per the International Committee of Medical Journal Editors (ICMJE) recommendations<sup>20</sup>.

### Funding

This scoping review is supported by the Australian Government's Medical Research Future Fund (MRFF) Rapid

Applied Research Translation program grant awarded to Brisbane Diamantina Health Partners. The funder had no role in the design, conduct or publication of the review.

### Ethics and dissemination

This scoping review does not require ethics approval as information will be obtained from publicly available databases. Findings will be disseminated through a peer-reviewed journal and conference presentation and other appropriate media platforms.

### References

1. Sen CK, Gordillo GM, Roy S, Kirsner R, Lambert L, Hunt TK, et al. Human skin wounds: a major and snowballing threat to public health and the economy. *Wound Repair Regen* 2009;17:763–71.
2. Armstrong DG, Meyr AJ. Risk factors for impaired wound healing and wound complications. *UpToDate* 2021.
3. Olsson M, Järbrink K, Divakar U, Bajpai R, Upton Z, Schmidtchen A, et al. The humanistic and economic burden of chronic wounds: a systematic review. *Wound Repair Regen* 2019;27:114–25.
4. Graves N, Zheng H. Modelling the direct health care costs of chronic wounds in Australia. *Wound Pract Res* 2014;22:20–33.
5. McCosker L, Tulleners R, Cheng Q, Rohmer S, Pacella T, Graves N, et al. Chronic wounds in Australia: a systematic review of key epidemiological and clinical parameters. *Int Wound J* 2019;16:84–95.
6. Ousey K, Edward K-L. Exploring resilience when living with a wound – an integrative literature review. *Healthcare* 2014;2:346–55.
7. Bolton LL, Baine WB. Using science to advance wound care practice: lessons from the literature. *Ostomy Wound Manag* 2012;58:16–31.
8. Rohl J, Zaharia A, Rudolph M, Murray RZ. The role of inflammation in cutaneous repair. *Wound Pract Res* 2015;23:8–15.
9. Murray RZ, West ZE, McGuinness W. The multifactorial formation of chronic wounds. Cambridge Publishing; 2018.
10. Cowin A, Waters J. The science of wound healing. In: Swanson T, Asimus M, McGuinness B, editors. *Wound management for the advanced practitioner*. Lane Cove, NSW: IP Communications; 2014.
11. Bayat A, McGrouther DA, Ferguson MWJ. Skin scarring. *BMJ* 2003;326:88–92.
12. Ahangar P, Woodward M, Cowin A. Advanced wound therapies. *Wound Pract Res* 2018;26:58–68.
13. Murray RZ, West ZE, Cowin AJ, Farrugia BL. Development and use of biomaterials as wound healing therapies. *Burns Trauma* 2019;7:2.
14. Muller PAJ, Vousden KH. p53 mutations in cancer. *Nat Cell Biol* 2013;15:2–8.
15. Messersmith J, Stoddart-Osumah C, Lennon M, Wirtz D. Emergency seed funding for COVID-19 research: lessons from Johns Hopkins University. *J Clin Invest* 2021;131.
16. Rodrigues M, Kosaric N, Bonham CA, Gurtner GC. Wound healing: a cellular perspective. *Physiol Rev* 2019;99:665–706.
17. Oliveira A, Simões S, Ascenso A, Reis CP. Therapeutic advances in wound healing. *J Dermatol Treat* 2020;1–21.
18. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;169:467–73.
19. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
20. International Committee of Medical Journal Editors (ICMJE). Up-dated ICMJE recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals. ICMJE; 2019.

Supplementary data can be found by logging into the electronic version of the WPR Journal via the Wounds Australia website members' area ([woundsaustralia.com.au](http://woundsaustralia.com.au)).