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Effectiveness of interventions for optimising adherence to treatments for the prevention and management of scars: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Treatments used in the management of scarring following wounds of the skin can be complex and time consuming, and patients may experience difficulties adhering to these treatments. Therefore, the aim of this systematic review is to identify the types of interventions that have been used to optimise adherence to treatment for preventing or reducing skin scars in adults and children and to determine the effectiveness of these interventions.

Methods and analysis Databases (PubMed, Embase, the Cumulative Index to Nursing and Allied Health Literature, PsycINFO, Web of Science and OTSeeker) will be searched using the developed search strategy to identify eligible randomised trials. Adults and children using scar treatments to prevent or manage scarring as a result of a dermal wound (which may occur following burn injury, surgery, lacerations, piercings, vaccinations, acne and other conditions affecting the skin) will be included. Any intervention with the potential to effect adherence will be included. Titles and abstracts located through searching will be screened by two independent reviewers. Full text of studies will also be screened to determine eligibility for final inclusion. Two reviewers will assess the quality of included studies using the Cochrane 'risk of bias' tool. Data extraction forms will be developed and two reviewers will extract the data. A third reviewer will be used at each stage to ensure consensus is achieved. Meta-analysis and meta-regression will be completed if appropriate, otherwise a narrative synthesis of results will be undertaken.

Ethics and dissemination No ethical approval is necessary for this systematic review as no patients will be directly involved. Results of this systematic review will be disseminated through journal publications and relevant conference presentations.

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Strengths and limitations of this study

- This review will provide a broad understanding of the types of adherence interventions used in adults and children with scarring and the effectiveness of these interventions.
- Differing interventions, patients and outcomes may mean a meta-analysis is unable to be conducted and that a narrative synthesis of the results will be required.
- A limitation may be that only studies available in English will be included.

INTRODUCTION

The term adherence has been described by WHO as 'the extent to which a person's behaviour—taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider'.[1] It has been suggested that adherence requires clear communication between the patient and healthcare provider to ensure that treatments are accurately followed.[2 3] Healthcare providers rely on patients carrying out health recommendations exactly as directed, to optimise patients' health outcomes and improve health-related quality of life (HRQoL).[4]

Adherence to treatment is an issue of concern across a range of health conditions, however particularly in conditions that require the use of long-term treatment, such as wounds of the skin resulting in scarring.[1] Scars can develop following a dermal wound caused by burns, surgery, lacerations, piercings, vaccinations, acne and other conditions affecting the skin.[5 6] Scars may be grouped into the following subtypes: normotrophic, hypertrophic, atrophic, contracted and pigmented.[7 8] These scar subtypes correspond with the characteristics deemed important by patients with burn scars and treating clinicians (eg, colour, pliability, stretchability, scar height and scar sensitivity).[9] Normotrophic scars are defined as scars not elevated above skin level,[10] while hypertrophic scars are raised and tight, and often present with changes in colour and sensation.[11–13] For the purposes of this systematic review, keloid scars will be classified under hypertrophic scars. Recent literature indicates that keloid scars can be considered part of the hypertrophic continuum, with main clinical differences in the extent and time period of inflammation of the reticular dermis.[6 14] Atrophic scars (such as those frequently seen in patients with acne) appear sunken and depressed, rather than raised[15] and contracted scars are defined as scars which shorten, often occurring across a joint and limiting range of motion.[16] Lastly, pigmented scars may either appear hypopigmented (a lighter colour to the surrounding skin) or hyperpigmented (a darker colour to the surrounding skin) and may have significant cosmetic and psychological implications.[8 17] These scar subtypes can also be classified according to the mechanism of scar development (eg, hypertrophic burn scar, atrophic acne scar).

Patients with scars may experience heavy burden from living with daily scar symptoms and also being required to manage ongoing, complex scar treatments. The burden of scars, such as hypertrophic and atrophic scarring, includes reduced quality of life[18–20] and itch and pain.[18 21] Scars may also impact a patient's ability to carry out usual activities of daily living, with contracted scars causing physical limitations.[22 23] Having an altered appearance or cosmetic disfigurement from scarring may hinder an individual's psychological functioning leading to an increased risk of depression and post-traumatic stress disorder.[17 19]

To prevent and reduce the impact of scarring on activities of daily living, physical appearance, psychological well-being and HRQoL, patients may require both acute medical treatment and longer term rehabilitation.[24 25] Treatment regimens used to manage scarring may be complex and time consuming for patients and their families to follow, which may influence whether treatment is carried out as recommended by the health professional.[26] A range of non-invasive treatment modalities including moisturisers, silicone products (such as topical silicone gels, silicone gel sheeting), pressure garments, splints, exercises and medications may be used to manage scar symptoms.[11] Minimally invasive treatments may also be used to manage these scars, with preliminary evidence suggesting that medical needling (also known as percutaneous collagen induction) and laser may be effective for managing hypertrophic and atrophic scars.[15]

As discussed, patients with scarring, or those at risk of developing scarring, may be required to adhere to complex treatment regimens for months or years after the wound has occurred. Healthcare providers expect patients to follow treatments exactly; however, little is known about how often patients actually adhere to their treatment regimens and what strategies or interventions may improve their adherence. Adherence rates are unclear in both adults and children with scarring, with a variety of adherence measures limiting the comparability of findings. From studies that have examined adherence rates, 41%–81.3% of adults treated with pressure garments for hypertrophic scarring post burns were found to be adherent.[27–29] A systematic review of adherence to both oral and topical acne treatment also found adherence rates varied from as little as 7%–98%.[30] However, it has been purported that adherence rates in clinical studies may be higher than in usual practice given the potential for participants to over-report their adherence and due to the increased number of follow-up appointments conducted in clinical studies.[30]

It is essential that interventions for improving adherence are considered, to reduce the impact of scars and scar treatments on the individual patient and improve HRQoL. A diverse range of adherence interventions have been discussed in the literature, with interventions mostly focused on optimising medication adherence in patients with HIV/AIDS, psychiatric disorders, chronic obstructive pulmonary disease, cardiovascular disease, hypertension and diabetes.[31] Nieuwlaat *et al*[31] highlighted the difficulties in comparing adherence interventions due to inconsistencies in adherence measures and clinical outcomes. Across patients using treatments to prevent or manage scarring, limited research has examined interventions for optimising adherence. This presents a dilemma for clinicians working with this population group, as there is little guidance on how to better support patients' adherence to scar treatments.

To further understand adherence and adherence interventions, it is important to understand the factors that contribute to patients' non-adherence to scar treatments. A literature review by Szabo *et al*[32] that focused on adherence to burn care described a range of potential factors related to treatment adherence in patients with burns. Factors discussed as relating to non-adherence to pressure garments included the unpleasant experience of wearing pressure garments (such as irritation and physical restrictions) and a dislike of the colour or fit of garments. Alternatively, having adequate social support, anticipating good outcomes, using problem solving or coping strategies and believing in the treatment were described as aiding adherence to garments.[32] However, the relationship between adherence and these factors has not been quantitatively examined.

Interventions based on theoretical frameworks have generally been found to be more effective than those not based on theoretical frameworks.[33 34] Therefore, frameworks are useful to consider when reporting on the effectiveness of adherence interventions. A variety of theoretical frameworks or models have been discussed in relation to adherence; however, consensus is lacking in regards to the most critical theoretical domains. The Theoretical Domains Framework (TDF), which has been informed by behavioural change theories, includes the overarching components of 'capability', 'motivation' and 'opportunity'. The TDF has been identified as useful to classify barriers and facilitators of adherence and may assist in the development and testing of intervention strategies.[35 36] This systematic review will use the TDF to classify the psychosocial variables targeted by the interventions (eg, barriers and facilitators to adherence), and to interpret the findings, and will report on the theoretical domains used to develop interventions.

To date, no systematic reviews have examined the effectiveness of interventions promoting adherence in patients using treatments to prevent or manage scars. This highlights the need to better understand what interventions or intervention components may be most effective in promoting adherence to treatment for these patients. This systematic review will provide researchers and clinicians with information regarding the interventions delivered and the effectiveness of those interventions. Future research directions will also be identified.

METHODS AND ANALYSIS

The Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols checklist was used in the development of this systematic review protocol.[37]

Patient and public involvement

No patients or public were directly involved in the development of this systematic review protocol. However, a qualitative study of patient experiences of burns scars was used to inform the design of this systematic review protocol.[38]

Research objective

This systematic review aims to identify the types of adherence interventions that have been studied, to report the theoretical frameworks used to develop these interventions and to determine the effectiveness of adherence interventions in adults and children with, or at risk of developing scarring. The population, intervention, comparison, outcome, study design (PICOS) framework was used to develop an appropriate search strategy for database searching.

Inclusion and exclusion criteria

Population

Adults and children using treatments to prevent or manage normotrophic, hypertrophic, atrophic, contracted or pigmented scars following skin wounds (such as burn injury, surgery, lacerations, piercings, vaccinations or acne) will be included (or a combination of these scar types).

Interventions

Studies examining interventions with the potential to improve adherence to treatment will be considered. Intervention components may include education (disseminated via written information sheets, educational websites, videos, phone or tablet applications, emails), reminders (eg, via text messages or emails), additional face-to-face appointments, counselling, patient accountability (eg, via the use of written contracts or treatment plans), simplifying treatment schedules and communication via information communication technology. Interventions may be delivered face to face, over the phone, using text messages or via any information communication technology (such as email or internet-based platforms). They may be individual or group-based and may be individually tailored to each patient. They may require materials and/or training, and be run by any health professional (eg, doctor, nurse, occupational therapist, physiotherapist, psychologist). Interventions may be delivered in patient's homes, community centres, hospitals or a variety of settings. The time period of the intervention, the number and duration of sessions/intervention components and intervention fidelity will also be reported. Theoretical frameworks or models used to inform the development of the intervention will be described.

Comparison

Interventions will be compared with 'standard practice' which may involve the use of routine verbal or written education, or with a different dose of the intervention or with a different intervention.

Outcomes

Adherence will be the primary outcome. Adherence may be measured subjectively via patient self-report (eg, keeping a diary or calendar, rating adherence with the use of a survey) or objectively (eg, though the use of an electronic monitoring system). Studies that do not specifically measure adherence will be excluded. Secondary outcomes will include HRQoL, adverse effects and barriers and facilitators of adherence, when reported in studies that include adherence as an outcome. Changes in scar severity will also be reported as a secondary outcome, where possible, using physical characteristics or sensory symptoms of scars including height or thickness, pigmentation, tightness or presence of a contracted scar, and itch, pain or neuropathic-like sensations.[18] The TDF will be used to classify the psychosocial variables targeted by the interventions, if stated (eg, barriers and facilitators of adherence).

Study design

Only randomised trials will be eligible for inclusion. These randomised trials may have a qualitative component.

Database searching

The following databases will be searched using the developed PICOS framework: PubMed, Embase, CINAHL, PsycINFO, Web of Science and OTSeeker. No dates will be excluded. Studies will be excluded if the full text is not available in English. When English abstracts are found for non-English studies, the authors will be contacted to determine if an English full-text version of their work exists. Based on initial scoping searches, it is anticipated that only a small percentage (<8%) of studies may be excluded due to language. Refer to online supplementary file 1 for an example database search strategy. The search strategy was initially developed by the authors with input from a medical librarian with systematic review experience, who will conduct the search. The search strategy has been piloted to ensure that eligible studies identified through other means, such as handsearching, are captured. The search will be rerun prior to publication of the systematic review so that the search is up to date.

Grey literature searching

Clinical trial registries (ClinicalTrials.gov and WHO—International Clinical Trials Registry Platform), dissertation and theses databases, the OpenGrey database and the general internet will be searched. Hand searching of reference lists will be conducted and key researchers in the field contacted.

Screening and data management

EndNote X9 and Covidence, an online systematic review platform, will be used to combine and manage search results. The titles and abstracts of all located studies will be screened by two independent reviewers, based on the inclusion/exclusion criteria. The full text of studies that meet the inclusion criteria will then be assessed by independent reviewers. A third reviewer during screening and full-text review will be used to achieve consensus. A table of studies excluded at the full-text review will be provided, with reasons for exclusion.

Data extraction

Data extraction forms will be developed by one author and piloted by two authors. Two authors will independently extract data that will include participant characteristics, interventions, comparison groups, outcomes and funding sources. Accuracy between reviewers will be reported and discussion conducted until consensus is reached. If consensus cannot be achieved, a third independent reviewer will be used. Authors of the included papers will be contacted if additional data are required.

Assessing risk of bias

The Cochrane's 'risk of bias' tool will be used to assess the methodological quality of included randomised trials.[39] In addition to the items included in the Cochrane 'risk of bias' tool (random sequence generation, allocation concealment, selective reporting, other bias sources, blinding of participants and personnel, blinding of outcome assessment and incomplete outcome data), other sources of bias that will be evaluated include outcome measure validation, study design, differences in sociodemographics of the groups at baseline, intervention fidelity and funding bias. At the outcome level, the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system may be used to compare the quality of evidence for adherence as an outcome across the studies, providing homogeneity is sufficient. GRADE considers the elements of quality, consistency, directness and effect size.

Synthesis of results

A summary of the types of interventions included and the theoretical frameworks underlying the design and testing of interventions will be reported. Meta-analyses will be conducted if there is sufficient similarity between studies in study design, participant characteristics (eg, age of participants), interventions (including comparators) and time after injury. Meta-analysis will provide information on whether there is an intervention effect, the size of the effect and whether the effect is seen across studies.[40] It will enable both the statistical and clinical significance of intervention characteristics to be determined, which can then be used by clinicians and researchers to inform the development and testing of future adherence interventions based on the characteristics deemed significant. This information will assist in determining the clinical significance of the identified adherence interventions, and has the potential to inform sample size estimates in future studies. Within studies, mean differences with 95% CIs for continuous outcomes and risk ratios with 95% CIs for dichotomous outcomes will be calculated between groups and across study time points. χ^2 and I_2 statistics will be calculated to identify the inconsistency across studies that can be considered due to heterogeneity, instead of chance. It is expected that a random effects approach will be used to pool treatment effects across studies, provided population groups (eg, hypertrophic burn scar, atrophic acne scar), interventions (eg, educational interventions, psychological interventions) and outcomes are sufficiently homogenous. Publication bias will be examined using funnel plots where at least 10 studies are able to be included in a meta-analysis. Sensitivity analyses will be conducted excluding studies that have a high or unclear risk of bias, where available. Subgroup analyses will be conducted where possible to examine scar type and cause (eg, hypertrophic burn scar, atrophic acne scar, etc), scar treatment used (eg, pressure garment, moisturiser), dose of scar treatment used (eg, applying once a day vs multiple times each day), type of adherence intervention provided (eg, educational vs psychological interventions), whether or not the intervention was based on a theoretical framework and participant age (eg, child, adult). In addition, a random-effect meta-regression analysis will be conducted, if possible, to determine the association between the type and dose of the intervention (eg, number of sessions, duration of the intervention and length of sessions) and use of a theoretical framework, with the intervention effect for adherence outcomes. Narrative synthesis of results will be conducted if meta-analysis is not possible, to provide descriptions of the intervention types and effect sizes in individual studies. RevMan V.5.3 and Stata 15 will be used for statistical analyses.

CONCLUSION

This systematic review will consider the effectiveness of interventions that optimise adherence to treatments that aim to prevent or manage scarring following wounds of the skin. By conducting a systematic review that encompasses all scar types and mechanisms, the breadth of information will be increased. Researchers and clinicians will be provided with valuable insights into the types of interventions that may be useful to optimise adherence and the effectiveness of these interventions. This information will then be used to inform the future development of specific interventions aimed at promoting adherence to treatment for people with a range of scar types. These interventions have the potential to improve adherence outcomes and to optimise identified priorities for these patients and to subsequently improve their HRQoL.

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Competing interests None declared.

Patient consent for publication Not required.

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REFERENCES

1. Sabaté E. *Adherence to long-term therapies: evidence for action*. Geneva: World Health Organization, 2003.
2. Greenley RN, Kunz JH, Walter J, *et al*. Practical strategies for enhancing adherence to treatment regimen in inflammatory bowel disease. *Inflamm Bowel Dis* 2013;19:1534–45.
3. Middleton KR, Anton SD, Perri MG. Long-term adherence to health behavior change. *Am J Lifestyle Med* 2013;7:395–404.
4. Pickett K, Frampton G, Loveman E. Education to improve quality of life of people with chronic inflammatory skin conditions: a systematic review of the evidence. *Br J Dermatol* 2016;174:1228–41.
5. Verhaegen PD, van Zuijlen PP, Pennings NM, *et al*. Differences in collagen architecture between keloid, hypertrophic scar, normotrophic scar, and normal skin: An objective histopathological analysis. *Wound Repair Regen* 2009;17:649–56.
6. Ogawa R. Keloid and hypertrophic scars are the result of chronic inflammation in the reticular dermis. *Int J Mol Sci* 2017;18:606.
7. Gangemi EN, Gregori D, Berchialla P, *et al*. Epidemiology and risk factors for pathologic scarring after burn wounds. *Arch Facial Plast Surg* 2008;10:93–102.
8. Chadwick S, Heath R, Shah M. Abnormal pigmentation within cutaneous scars: A complication of wound healing. *Indian J Plast Surg* 2012;45:403–11.
9. Simons M, Lim PCC, Kimble RM, *et al*. Towards a clinical and empirical definition of burn scarring: A template analysis using qualitative data. *Burns* 2018;44:1811–9.
10. van der Veer WM, Niessen FB, Ferreira JA, *et al*. Time course of the angiogenic response during normotrophic and hypertrophic scar formation in humans. *Wound Repair Regen* 2011;19:292–301.
11. Friedstat JS, Hultman CS. Hypertrophic burn scar management: what does the evidence show? A systematic review of randomized controlled trials. *Ann Plast Surg* 2014;72:S198–S201.
12. Ladak A, Tredget EE. Pathophysiology and management of the burn scar. *Clin Plast Surg* 2009;36:661–74.
13. Gauglitz GG, Korting HC, Pavicic T, *et al*. Hypertrophic scarring and keloids: pathomechanisms and current and emerging treatment strategies. *Mol Med* 2011;17:1–25.
14. Huang C, Akaishi S, Hyakusoku H, *et al*. Are keloid and hypertrophic scar different forms of the same disorder? A fibroproliferative skin disorder hypothesis based on keloid findings. *Int Wound J* 2014;11:517–22.
15. Chambers A. Unified approach to the treatment of hypertrophic and atrophic scars. *The American Journal of Cosmetic Surgery* 2016;33:176–83.
16. Kwan PO, Tredget EE. Biological principles of scar and contracture. *Hand Clin* 2017;33:277–92.
17. Van Loey NEE, Van Son MJM. Psychopathology and psychological problems in patients with burn scars. *Am J Clin Dermatol* 2003;4:245–72.
18. Tyack Z, Ziviani J, Kimble R, *et al*. Measuring the impact of burn scarring on health-related quality of life: development and preliminary content validation of the Brisbane Burn Scar Impact Profile (BBSIP) for children and adults. *Burns* 2015;41:1405–19.
19. Chuah SY, Goh CL. The impact of post-acne scars on the quality of life among young adults in Singapore. *J Cutan Aesthet Surg* 2015;8:153–8.
20. Hayashi N, Miyachi Y, Kawashima M. Prevalence of scars and "mini-scars", and their impact on quality of life in Japanese patients with acne. *J Dermatol* 2015;42:690–6.
21. Bijlard E, Kouwenberg CA, Timman R, *et al*. Burden of keloid disease: a cross-sectional health-related quality of life assessment. *Acta Derm Venereol* 2017;97:225–9.
22. Oosterwijk AM, Mouton LJ, Schouten H, *et al*. Prevalence of scar contractures after burn: a systematic review. *Burns* 2017;43:41–9.
23. Leblebici B, Adam M, Bağiş S, *et al*. Quality of life after burn injury: the impact of joint contracture. *J Burn Care Res* 2006;27:864–8.
24. Tredget EE, Shupp JW, Schneider JC. Scar management following burn injury. *J Burn Care Res* 2017;38:146–7.
25. Dodd H, Fletchall S, Starnes C, *et al*. Current concepts burn rehabilitation, part II: long-term recovery. *Clin Plast Surg* 2017;44:713–28.
26. Heckman BW, Mathew AR, Carpenter MJ. Treatment burden and treatment fatigue as barriers to health. *Curr Opin Psychol* 2015;5:31–6.
27. Brown CA. A comparison of the outcomes of two clinical audits of burn pressure garment satisfaction and compliance in Saudi Arabia. *Burns* 2001;27:342–8.
28. Johnson J, Greenspan B, Gorga D, *et al*. Compliance with pressure garment use in burn rehabilitation. *J Burn Care Rehabil* 1994;15:180–8.
29. Rosser P. Adherence to pressure garment therapy of post traumatic burn injury. *J Burn Care Rehabil* 2000;21:S178.
30. Snyder S, Crandell I, Davis SA, *et al*. Medical adherence to acne therapy: a systematic review. *Am J Clin Dermatol* 2014;15:87–94.
31. Nieuwlaat R, Wilczynski N, Navarro T, *et al*. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev* 2014:CD000011.
32. Szabo MM, Urich MA, Duncan CL, *et al*. Patient adherence to burn care: a systematic review of the literature. *Burns* 2016;42:484–91.
33. Conn VS, Enriquez M, Ruppar TM, *et al*. Meta-analyses of theory use in medication adherence intervention research. *Am J Health Behav* 2016;40:155–71.
34. Michie S, Johnston M, Abraham C, *et al*. Making psychological theory useful for implementing evidence based practice: a consensus approach. *Qual Saf Health Care* 2005;14:26–33.
35. Cox NS, Oliveira CC, Lahham A, *et al*. Pulmonary rehabilitation referral and participation are commonly influenced by environment, knowledge, and beliefs about consequences: a systematic review using the Theoretical Domains Framework. *J Physiother* 2017;63:84–93.
36. McGrady ME, Ryan JL, Brown GA, *et al*. Topical review: theoretical frameworks in pediatric adherence-promotion interventions: research findings and methodological implications. *J Pediatr Psychol* 2015;40:721–6.
37. Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
38. Simons M, Price N, Kimble R, *et al*. Patient experiences of burn scars in adults and children and development of a health-related quality of life conceptual model: a qualitative study. *Burns* 2016;42:620–32.
39. Higgins JP, Altman DG, Gøtzsche PC, *et al*. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
40. Deeks JJ, Higgins JP, Altman DG. *Cochrane handbook for systematic reviews of interventions version 5.1.0 (updated March 2011)*: The Cochrane Collaboration, 2011.