Comparing alternating pressure mattresses and high-specification foam mattresses to prevent pressure ulcers in high-risk patients: the PRESSURE 2 RCT

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Declared competing interests of authors: Christopher McCabe has received grant funding from the University of Alberta and Alberta Innovates Health Solutions (Edmonton, AB, Canada). Julia Brown is Deputy Director of the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Clinical Evaluation and Trials Board and has received grant funding for the following studies: the NIHR eRAPID Programme Grants for Applied Research (PGfAR) trial, the NIHR Efficacy and Mechanism Evaluation (EME) GLiSten trial, the NIHR HTA LAVA trial (liver resection surgery versus thermal ablation for colorectal liver metastases), the NIHR EME IntAct (Intraoperative flourescence angiography to prevent Anastomotic leak in rectal cancer surgery), NIHR Research for Patient Benefit LACE (Life After Cancer Epidemiology) trial, the NIHR EME ROLARR (RObotic vs. LAparoscopic Resection for Rectal cancer) trial, the NIHR HTA SaFarI (Sacral nerve stimulation versus the FENIX TM magnetic sphincter augmentation for faecal incontinence: a Randomised Investigation and the NIHR StamINA Programme Development Grant trial. Claire Hulme and E Andrea Nelson have been members of the NIHR HTA Commissioning Board and E Andrea Nelson has received funding for the NIHR HTA CODIFI (Concordance in Diabetic Foot Ulcer Infection) study. Elizabeth McGinnis has received funding for NIHR Health Service and Delivery Research (HSDR) Information Systems, Monitoring and Managing from Ward to Board and the NIHR PGfAR SWHSI (Surgical Wounds Healing by Secondary Intention) trial. Isabelle L Smith and Susanne Coleman have received a NIHR personal fellowship. Benjamin Thorpe has received a NIHR research methods fellowship. Delia Muir has received a Wellcome Trust Engagement Fellowship. Rachael Gilberts has received funding for the NIHR HTA ALPHA (ALitretinoin versus PUVA in severe chronic HAnd eczema) and MIDFUT (Multiple Interventions for Diabetic Foot Ulcer Treatment) trials. Nikki Stubbs has received funding for NIHR PGfAR SWHSI and NIHR HTA AMBER (Abdominal Massage for Bowel Dysfunction Effectiveness Research) trial. Jane Nixon has received funding for NIHR HTA MIDFUT, CODIFI and ALPHA. Sarah Brown has received funding for NIHR HTA ALPHA, MIDFUT, FORVAD (Clinical and cost-effectiveness of posterior cervical FORaminotomy Versus Anterior cervical Discectomy in the treatment of cervical brachialgia: a multicentre, Phase III, randomised controlled trial), the NIHR PGfAR PROMPT (early detection to improve outcome in patients with undiagnosed psoriatic arthritis), ARUK (Arthritis Research UK) SALRISE (SALivary electro-stimulation for the treatment of dry mouth in patients with Sjögren's syndrome: a multicentRe randomISEd sham-controlled double-blind study).

Published September 2019
DOI: 10.3310/hta23520

Scientific summary

The PRESSURE 2 RCT

Health Technology Assessment 2019; Vol. 23: No. 52
DOI: 10.3310/hta23520

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Scientific summary

Background

Pressure ulcers (PUs) are a cross-specialty problem; they are a complication of serious acute or chronic illness in patient populations characterised by high levels of comorbidity and mortality.

Specialist mattresses are used to minimise intensity and duration of pressure on vulnerable skin sites and are classified by their mode of action as 'low technology' (e.g. static) or 'high technology' (e.g. electrically powered).

National/international guidelines recommend low-technology high-specification foam mattresses (HSFMs) as a minimum for high-risk patients to prevent PUs and these are in widespread clinical use. There is clinical uncertainty about the additional benefit of high-technology mattresses because of a lack of high-quality evidence; however, use in the NHS is also widespread.

This study compared the two main mattress types utilised in the NHS: (1) high-technology alternating pressure mattresses (APMs) and (2) low-technology HSFMs.

Objectives

Primary objective

The primary objective was to compare the time taken to develop a new PU of category ≥ 2 in patients using an APM with those using a HSFM by 30-day final follow-up.

Secondary objectives

- To compare the time taken to develop a new PU of category ≥ 3, to develop a new PU of category ≥ 1 and to heal all pre-existing category 2 PUs, and to compare incidences of mattress changes and safety.
- To determine the impact of APM and HSFM on health-related quality of life (HRQoL) and incremental cost-effectiveness from health and social care sectors' perspectives.

Secondary substudy objectives

- To assess the responsiveness of the Pressure Ulcer Quality of Life – Prevention (PU-QoL-P) instrument.
- To determine the extent of under-/over-reporting of PUs of category ≥ 2 and the feasibility of photographs for blinded PU outcome assessment.

Methods

Trial design

Multicentre, Phase III, open, prospective, planned as a double-triangular group sequential, parallel-group, randomised controlled trial (RCT), with two planned interim analyses.

Participants

Adult inpatients with evidence of acute illness at a high risk of PU development, managed on electric profiling beds, with an expected length of stay of ≥ 5 days.

Interventions

Alternating pressure mattress or HSFM, with a treatment phase of 60 days maximum.

End points

Primary end point

The time taken to develop a new PU of category ≥ 2 from randomisation, during (maximum) 60-day treatment phase to 30-day final post-treatment follow-up.

Randomisation

Patients were randomised (1 : 1 allocation ratio) to receive APM or HSFM using minimisation with factors such as centre, PU status, setting and consent type.

Analysis

Fine and Gray models were fitted to primary and secondary end points on the intention-to-treat (ITT) population, with adjustment for minimisation factors and covariates, such as presence of pain and conditions affecting peripheral circulation. A likelihood ratio test was used to assess the effect of the mattress group.

Exploratory moderator analyses were conducted, and mediator and safety data were summarised.

For the primary cost-effectiveness analysis, total cost and quality-adjusted life-years (QALYs) over the full final 30-day follow-up and incremental cost-effectiveness ratios (ICERs) are reported for each group.

Data collection

Baseline

Demographic, skin status, risk factors, PU prevention interventions and researcher-administered HRQoL questionnaires [i.e. Short Form questionnaire-12 items (SF-12), Pressure Ulcer Quality of Life – Utility Index (PU-QoL-UI) and EuroQol-5 Dimensions, five-level version (EQ-5D-5L)].

Treatment phase (maximum 60 days)

During treatment, clinical follow-up assessments were undertaken twice weekly up to day 30 and weekly from day 31 to day 60. These included skin assessment (with photography when applicable), mattress compliance, safety and PU prevention interventions.

Health-care resource utilisation and HRQoL questionnaires were initially completed weekly but were reduced to weeks 1 and 3 to limit patient burden.

Final 30-day post-treatment follow-up

A follow-up visit 30 days from the end of the treatment phase comprised skin assessment (with photography when applicable), safety, HRQoL questionnaires and health resource utilisation.

Sample size

The original calculation expected a maximum of 588 events, corresponding to 2954 participants, to have 90% power to detect a 5% difference in the incidence of PUs of category ≥ 2 between the APM and HSFM arms, assuming an incidence of 18% on APM and 23% on HSFM [hazard ratio (HR) 0.759], two-sided 5% significance level and 6% loss to follow-up.

Owing to slower recruitment than anticipated and the request for a recruitment extension, the funder requested an unplanned interim analysis that was conducted and reviewed by the DMEC. A no-cost recruitment extension was approved and the final sample size was 2030 participants.

Trial results

Screening and recruitment

A total of 15,277 patients were screened and 2030 randomisations took place between August 2013 and 30 November 2016 from 39 NHS trusts/health boards (42 centres, comprising 25 teaching hospitals, 13 general hospitals and 9 community hospitals).

Of the 15,277 patients screened, 877 (5.7%) were not assessed for eligibility, and, of the remaining 14,400 patients, 9323 (64.7%) were ineligible, with reasons including not being at a high risk of PU development ($n = 2180$; 23.4%), expected length of stay of < 5 days ($n = 1640$; 17.6%), patient ($n = 938$; 10.1%) or staff ($n = 1116$; 12.0%) unwilling to change mattress and patient too unwell to change mattress ($n = 709$; 7.6%). Of 5077 eligible patients, 2068 (40.7%) consented and 2030 (40.0%) were randomised.

Of 2030 randomisations, 1017 (50.1%) were allocated to APM and 1013 (49.9%) were allocated to HSFM. One patient was inadvertently randomised twice and so data from the second randomisation were excluded. The ITT population includes a total of 2029 participants, and 81.5% of patients in each group received their mattress within 48 hours. Withdrawals APM 6.1% ($n = 62$) vs. HSFM 5.6% ($n = 57$)] and deaths [APM 8.1% ($n = 82$) vs. HSFM 8.3% ($n = 84$)] were balanced across arms.

Primary outcome

The primary outcome was the development of a new PU of category ≥ 2 to 30-day final follow-up.

Of the 2029 participants, 160 (7.9%) developed a new PU of category ≥ 2 [APM 6.9% ($n = 70$) vs. HSFM 8.9% ($n = 90$), absolute difference 2%]. There was insufficient evidence of a difference between mattress groups in time to PU development [Fine and Gray model HR 0.76, 95% confidence interval (CI) 0.56 to 1.04; exact p-value of 0.0890]. The median time to development for the APM group was 18 days (range 2–86 days) and for the HSFM group and was 12 days (range 2–94 days) for the APM group; a total of 213 new PUs of category ≥ 2 were observed in 160 patients [APM, $n = 89$ (1.3 per patient), vs. HSFM, $n = 124$ (1.4 per patient)].

Baseline skin status was statistically significantly associated with category ≥ 2 PU development (Wald p-value = 0.0057) including category 1 PUs (HR 1.83, 95% CI 1.17 to 2.87) and category 2 PU (HR 1.83, 95% CI 1.09 to 3.09).

Sensitivity analysis: time to development of a new pressure ulcer of category ≥ 2 during the treatment phase

Of the 2029 participants, 132 (6.5%) developed a new PU of category ≥ 2 between randomisation and the end-of-treatment phase with a difference of 2.6% between mattress groups [APM 5.2% ($n = 53$) vs. HSFM 7.8% ($n = 79$); absolute difference 2.6%]. There was a statistically significant difference in the treatment-phase time-to-event sensitivity analysis (Fine and Gray model HR 0.66, 95% CI 0.46 to 0.93; exact p-value = 0.0176).

Secondary end points

Time to development of a pressure ulcer of category ≥ 1 to the 30-day final follow-up

Of the 2029 participants, 350 (17.2%) developed a new PU of category ≥ 1 [APM 15.7% ($n = 160$) vs. HSFM 18.8% ($n = 190$), absolute difference 3.1%]. There was no evidence of a difference between mattress groups in time to PU development (Fine and Gray model HR 0.83, 95% CI 0.67 to 1.02; exact p-value = 0.0733).

Development of a pressure ulcer of category ≥ 3 to the 30-day final follow-up

Of the 2029 participants, 32 (1.6%) developed a new PU of category ≥ 3 [APM 1.4% ($n = 14$) vs. HSFM 1.8% ($n = 18$); absolute difference 0.4%]. There was insufficient evidence of a difference between mattress groups in time to PU development (Fine and Gray model HR 0.81, 95% CI 0.40 to 1.62; exact p-value = 0.5530). The number of category 3 PUs was comparable by trial arm (APM, $n = 19$ vs. HSFM, $n = 21$).

Healing of pre-existing pressure ulcers to 30-day final follow-up

Of the 2029 participants, 145 had a pre-existing PU of category 2, of which 89 (61.4%) healed [APM 62.9% (n = 44/70) vs. HSFM 60.0% (n = 45/75); absolute difference 2.9%]. There was insufficient evidence of a difference in time to healing (Fine and Gray model HR 1.12 95% CI 0.74 to 1.68; exact p-value = 0.6122).

Moderator analysis

This exploratory analysis suggests that the impact of altered and category 1 skin status, complete immobility, nutritional deficits and the vulnerability afforded by lack of capacity may be modifiable as risk factors through use of the APMs, although the mattress interactions were non-significant.

Health economic analysis

The within-trial and long-term analysis showed APM to be cost-effective compared with HSFM, despite the negligible difference in QALYs (equating to around half a quality-adjusted life-day in both the within-trial and lifetime model analyses). This is because the cost-effectiveness results are driven by the costs difference. It could be posited that the small differences between QALYs could, in part, be down to a lack of sensitivity of the EQ-5D-5L; however, analyses using data collected using the PUQoL-UI (a preference-based measure developed to assess the impact of PUs on HRQoL) produced similar results to the primary analyses. The results of the PSA confirm the results of the deterministic analysis: despite the small difference in QALYs, as in 99% Monte Carlo iterations, use of APM is a cost-saving strategy.

Safety data

No safety concerns were indicated for either mattress. There were no related and unexpected serious adverse events and only three mattress-related events, which were not serious. The proportion of deaths (APM 8.1% vs. HSFM 8.3%), re-admission rates (APM 8.1% vs. HSFM 6.1%) and fall rates (APM 14.9% vs. HSFM 15.7%) were similar in both trial arms. Of all reported falls (n = 486), most occurred after the treatment phase (62.3%) and 5.6% resulted in serious injury, but none was classified as mattress related.

Photographic substudy

Methods

Optional patient consent was obtained for photography of all PUs of category ≥ 2 at first observation by the clinical research nurse/practitioner (CRN/P) and a 10% random sample of patients who had a clinical skin assessment and two photographs taken by an independent clinical assessor.

A strict protocol was used and all photographs were classified by the blinded central expert review panel comprising three clinicians, who rated confidence in their assessment on a 1 to 10 scale.

Sample size

This study was to determine the feasibility and reliability of photography against the 'gold-standard' expert nurse clinical assessment in the assessment of PUs of category ≥ 2. There was no formal sample size calculation; however, it was estimated that a maximum of 1653 photographs would be received.

Results

Owing to the low event rate and reduced sample size, a total of 390 photographs of category ≥ 2 PUs were expected and 248 were received. A total of 264 patients were selected for assessment by the independent clinical assessor (a maximum of 528 photographs) and 284 (53.8%) photographs were returned from 137 (51.9%) patients.

Blinded expert central photographic review versus clinical research nurse/registered health-care professional clinical assessment

Overall agreement was 83.5% (207/248; 95% CI 78.9% to 88.1%); agreement was 88.3% (91/103; 95% CI 82.1% to 94.5%) for the APM arm and 80.0% (116/145; 95% CI 73.5% to 86.5%) for the HSFM arm. Therefore, in both arms, fewer PUs in photographs were classified as a category ≥ 2 PU when compared with the CRN/P clinical assessment.

Blinded expert central photographic review versus independent clinical assessment

Overall agreement was 91.5% (260/284); this was 90.5% (114/126) agreement for the APM arm and 92.4% (146/158) for the HSFM arm.

All photographs: blinded expert central photographic review versus all clinical assessments

Combining all 248 category ≥ 2 PUs and 284 (10% random sample) photographs, the overall agreement was 87.8% (467/532) between the blinded expert central photograph review and clinical assessment with a corresponding kappa statistic of 0.82 and prevalence- and bias-adjusted kappa (PABAK) of 0.82, both indicating 'very good agreement' between photographic assessment and expert clinical assessment.

Compliance

A total of 1711 (84.3%) participants in the ITT population consented to photography [APM 84.6% ($n = 860$) vs. HSFM 84.0% ($n = 851$)]. No patients reported photography as a barrier to trial participation.

Acceptability

There were 170 occasions when photographs of category ≥ 2 PUs were not attempted; the main reason related to consent.

Confidence in photographic assessment

All reviewers tended to be more confident when they assessed a photograph as healthy, altered compared with photographs they assessed as category ≥ 2 PU. There was a small number of photographs for which no assessment could be made.

Pressure Ulcer Quality of Life – Prevention evaluation

Methods

An existing patient-reported outcome instrument of HRQoL, the Pressure Ulcer Quality of Life (PU-QoL), was modified for use in patients at risk of PU development. A subset of patients who completed both the modified Pressure Ulcer Quality of Life – Prevention (PU-QoL-P) and the SF-12 instruments at baseline and at 30 days final follow-up were eligible for psychometric analysis.

Results

The analysis sample consisted of 617 patients. The PU-QoL-P instrument, consisting of nine PU-specific outcomes (three symptom scales and six function scales), meets established criteria for reliability, construct validity and responsiveness. Internal consistency reliability was high, with Cronbach's alpha of > 0.795 (range 0.795–0.970) for all scales. The factor analysis mostly supported the six-function scale structure. Scaling assumptions were satisfied; all item-total correlations were > 0.30. Convergent validity was confirmed by significant correlations between hypothesised scales as expected. Mean scale scores from baseline to 30-day final follow-up were statistically significant for all scales apart from the daily-activities scale (effect sizes ranged from moderate to high), suggesting that PU-QoL-P scales are responsive to change. Worse symptoms and functioning was observed in patients who had a category 1 or 2 PU than in patients with intact skin.

Implications for practice

- Alternating pressure mattresses confer a small treatment phase benefit in acutely ill inpatients who are bedfast/chairfast and/or have a category 1 PU, which is diminished over time.
- Patient compliance with APMs, the low PU incidence rate and the small group differences indicate the need for improved indicators for targeting the use of APMs.
- Individualised decision-making should take into account skin status, patient preferences (movement ability and rehabilitation needs) and the presence of factors that may be potentially modifiable through APM allocation including being completely immobile, having nutritional deficits, lacking capacity and/or having altered skin/category 1 PU.
- Patients with existing category 1 and 2 PUs are most at risk of subsequent PUs of category ≥ 2 and require targeted secondary prevention.
- Improved communication is required before ward transfers to improve the continuity of PU prevention care.
- Improvements are required to ensure continuity in PU prevention post discharge.

Implications for research

- Objective measurement instruments of key risk factors are required to better inform risk stratification and preventative interventions in practice.
- Further analysis is required to explore the relationship between mental capacity, levels of independent movement and repositioning, nutritional status and PU development.
- Further research is required to explore 'what works for whom and in what circumstances' to better inform mattress provision for high-risk patients.
- The health economic analysis was limited by missing data; however, the difference in quality-of-life outcomes between the trial arms was negligible and the difference in cost was small, suggesting no need for further research.
- Central blinded expert photographic review is a reliable method for assessing PU outcomes in research. A robust method needs to be developed to enable repeated photographic assessments that minimises patient burden while enabling sensitivity analyses.
- Clinical end points should be considered for PU research during the treatment phase because skin changes can occur very quickly and may be influenced by factors such as discharge plans.
- Skin site-level data collected in PU research should be detailed in order to understand how skin changes over time. Further methodological work is required to be able to utilise these data fully in the analysis of trial outcomes.
- The PU-QoL-P is suitable for use to capture patient-reported functioning (core domains of HRQoL) and PU-area pain in patients at risk of PU development, and for quantifying the benefits of associated preventative interventions from the patient's perspective; thus far, there is a lack of HRQoL-specific instruments for patients at risk of PU development. The PU-QoL-P can be used in research with adults at risk of PU development in all UK health-care settings.

Trial registration

This trial is registered as ISRCTN01151335.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.819

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the Clarivate Analytics Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

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This report

The research reported in this issue of the journal was funded by the HTA programme as project number 11/36/33. The contractual start date was in March 2013. The draft report began editorial review in December 2017 and was accepted for publication in July 2018. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health and Social Care.

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