Protocol: Interventions for treating urinary incontinence after stroke in adults: a systematic review update, 03/05/23.

ADMINISTRATIVE INFORMATION

Title: Interventions for treating urinary incontinence after stroke in adults: a systematic review update

Registration

Authors: Catherine E Davidson[1], Caroline Watkins[1], Liz Lightbody[1], Andrew Clegg[1], Christine Roffe[2], Jo Booth[3], Cath Harris[1], Selina Johnson[4], Clare Gordon[1]

[1] University of Central Lancashire; [2] University Hospitals of North Midlands NHS Trust; [3] Retired from Glasgow Caledonian University; [4] University of Liverpool

Contact: Miss Catherine Davidson, cdavidson4@uclan.ac.uk

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Please note: purple text is used to highlight differences between the ICONS systematic review (1) and the planned update review.

This protocol has been written in line with the PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol (2).

INTRODUCTION

Rationale

Around 95,000 people per annum survive a stroke in the UK (3). Urinary incontinence (UI) is a major problem and long-term burden post-stroke, affecting between 30-50% of stroke survivors (4). Up to 44% and 38% of stroke survivors remain incontinent at 3 and 12 months respectively. Patients with stroke and UI have worse outcomes in relation to death, disability and increased likelihood of discharge into residential care (4-6). UI is also costly in terms of incontinence product costs and carer burden (7-9).

Policy and guidance highlight the need for effective management of UI and promotion of continence post-stroke. Improving the management of UI post-stroke is highlighted as a priority in Sentinel Stroke National Audit Programme (SSNAP) reports (10, 11). However, there is little evidence of improvement and a lack of consideration of LUTS. Consequently, and demonstrating why this work is

needed, NICE have recommended further research into improved continence care after neurological events (12).

With previous funding from UCLan, we conducted a systematic review exploring methods of assessing UI post-stroke. We found 11 methods, with only one validated for use in stroke (13). Results also showed that patients experience mixed symptoms, with lower urinary tract symptoms (LUTS) (e.g., urgency, frequency) without UI being more common than UI. This suggests that interventions should address both UI, and LUTS without UI. Addressing UI and LUTS early and effectively could impact these outcomes and significantly improve wellbeing for patients and their carers (14). Consensus from our writing group was that while important to identify the type of post-stroke UI, interventions are often beneficial for multiple types of UI and LUTS.

An existing systematic review published in 2019, with searches run in 2017 concluded that there was insufficient evidence to guide continence care for adults post-stroke. We plan to update this review to identify any additional methods that have been used to treat UI or LUTS post-stroke.

Objectives

This review aims to update the existing review: Interventions for treating urinary incontinence after stroke in adults (ICONS) (1). This previous review was published in 2019, with searches run in 2017. The objective is to assess the effects of interventions for treating urinary incontinence after stroke in adults at least one-month post-stroke (see Table 1).

METHODS

Eligibility criteria

PICO

The eligibility criteria are presented in PICO format in Table 1 and elaborated upon below.

Table 1. PICO criteria for the review question.

Population	Intervention	Comparison	Outcome
• Adults (aged 18 years or older) at least one-month post-stroke	• Intervention to promote continence	• Comparison of particular interest: no intervention/ usual care	• Continence

Population

Adults with a diagnosis of stroke (ischaemic and primary intracerebral haemorrhage) (as stated by study authors), including people with incontinence who have had a stroke identified as a subgroup within a larger group for whom relevant data were reported.

- **Stroke:** ischaemic stroke or intracerebral haemorrhage caused by a sudden disruption of blood supply to the brain. The WHO describes stroke as a clinical syndrome typified by "rapidly developing clinical signs of focal or global disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause apart that of vascular origin" (15).
- **Urinary incontinence (UI):** defined as the complaint of any involuntary leakage of urine (16). **Lower urinary tract symptoms (LUTS)** will also be included in the review. These include "*voiding or obstructive symptoms* such as hesitancy, poor and/or intermittent stream, straining, prolonged micturition, feeling of incomplete bladder emptying, dribbling, etc, and *storage or irritative symptoms* such as frequency, urgency, urge incontinence, and nocturia" (17).

Intervention

Current guidelines for the management of UI recommend an assessment to guide management (18). This begins with physical assessment and history taking, including identification of urological problems before the stroke occurred such as bladder outlet obstruction or stress incontinence. The choice of method to promote continence will then depend on the person's history and type of incontinence. Behavioural interventions are recommended as first-line therapy for managing UI (19). These include interventions designed to promote continence, for example bladder training (appropriate for urge incontinence) and pelvic floor muscle training (appropriate for stress incontinence (20)), and toileting assistance programmes such as prompted or timed voiding or habit retraining. These are designed to minimise incontinence episodes and are appropriate for people experiencing problems after stroke, such as memory loss or restriction of movement (21-24).

Other management techniques include specialised professional input interventions (e.g. specialist continence advisors); complementary therapy interventions (e.g. acupuncture; (25)); homeopathy; drug treatments (e.g. anticholinergics; (26)); physical therapies (e.g. electrical stimulation); physical aids (e.g. pessaries) and environmental or lifestyle interventions (e.g. diet and fluid management).

One arm of the study must include an intervention designed to promote urinary continence. We will include trials evaluating any of the following:

- behavioural interventions, for example prompted or scheduled voiding, bladder training, habit retraining (i.e., identification of voiding pattern and development of an individualised toileting schedule), PFMT or other behavioural management programmes;
- specialised professional input interventions, for example provision of information or education, assessment schedules,
- generic multidisciplinary rehabilitation programmes, continence advisors, home-support programmes or CNPs;
- complementary therapy interventions, for example homeopathy, acupuncture (traditional manual acupuncture or electroacupuncture);
- pharmacotherapy interventions, for example anticholinergics, adrenergics, hormonal treatment;
- physical therapy interventions, for example electrical stimulation, biofeedback;
- physical aids, for example pessaries, other appliances; and
- environmental or lifestyle interventions, for example voiding position, diet, and fluid management.

Trials will be excluded that relate solely to surgical or physical interventions for pre-existing continence problems that were not associated with stroke (e.g., transurethral resection of the prostate) unless it was a cointervention in a wider trial testing an included method of continence promotion. We will exclude trials relating to urological diagnosis, or to the management of incontinence or retention of urine in the acute phase of stroke (defined as up to one-month post-stroke). We will also exclude trials if continence was not measured either by reporting participant symptoms or by a physical measure (e.g., a pad test).

Comparison

Acceptable control interventions are usual care, no treatment, placebo, or attention control (clinical attention in the form of an intervention inducing an expectation of therapeutic benefit; (27)).

Outcome

See outcomes and prioritization.

Study design

Randomised and quasi-randomised trials evaluating the effects of interventions designed to promote continence in people who have had a stroke will be included. Quasi-random methods

include allocation by the person's date of birth, by the day of the week or month of the year, by a person's medical record number or allocating every alternate person.

Setting

Studies in both hospital and community settings, involving any country, will be included.

Report characteristics

Articles must have been published in peer reviewed journals since 2017, which is when the searches were run for the review being updated (1).

Information sources

In the original ICONS review (1), relevant trials were identified through searching the Cochrane Stroke Group and Cochrane Incontinence Group Specialised Registers of controlled trials. We are no longer able to access these Registers. As an alternative we have developed a search strategy combining the Cochrane search strategies which were used to compile the Stroke (28) and Incontinence Specialised Registers (29) and will use this to search the following databases:

- Ovid MEDLINE(R) ALL
- Ovid Embase
- CINAHL Ultimate (EBSCOhost)
- PsycINFO (EBSCOhost)

  Cochrane CENTRAL
- Clinicaltrials.gov
- WHO ICTRP

Search dates were from 2017 to March 2023. Searches will not be re-run prior to final analysis due to the short timeline of the project.

We will attempt to obtain missing data, as well as data collected but not reported, by contacting trialists. We will contact study authors of trials which include a subgroup of people with stroke to obtain stroke subgroup data. If no response is received from study authors after one contact, we will make a second request to obtain the required data.

We will search the reference lists of all relevant reviews and trial reports to identify further relevant studies.

Search strategy

Appendix 1 shows the search strategy used across the databases. We imposed no language or other restrictions on any of the searches.

We excluded animal studies.

Study records:

Data management

All records will be imported into Rayyan QCRI® software (30) which facilitates collaboration among investigators during the screening process. Extracted data will be managed in Microsoft Word or Microsoft Excel.

Selection process

Two review authors will screen titles and abstracts for potentially eligible studies. Any disagreements regarding the inclusion or exclusion of individual studies will be resolved by discussion or, if necessary, by consulting a third review author. Selection processes will be recorded in line with the PRISMA guidelines (31).

Data collection process

Two authors will perform data extraction. A piloted data collection form (in the format of a Microsoft Word or Excel spreadsheet) will be used. The data collected will include information on study design, study population, interventions, outcomes measurement and results. We will resolve any discrepancies in data extraction either by discussion between the two authors or with involvement of a third review author. We will contact authors of identified articles where there were missing or unclear data in order to inform study selection decisions. There will be no masking of the source and authorship of the trial reports.

Data items

Table 2 shows the variables for which data will be sought.

Table 2. Variables for which data will be sought based on PICO.

Population	Intervention	Comparison	Outcome

• Type, location & severity of stroke (e.g., NIHSS) • Urinary symptoms (e.g., frequency, urgency, nocturia) • Disability (e.g., mRs, Barthel Index)	• Intervention (e.g., type, duration)	• No intervention, usual care, placebo	• Continence after treatment • Number of incontinent episodes • Perception of improvement or cure • Participant satisfaction • Health status and quality of life • Functional ability • Adverse events

Outcomes and prioritization

Main outcomes

Primary outcomes (urinary incontinence)

Continence, measured by the following:

- Number of participants continent after treatment
- Number of incontinent episodes (indicated by bladder charts, total and mean number of episodes)
- Perception of improvement or cure (as reported by participant or carer)
- Adverse events

Additional outcomes

Secondary outcomes (LUTS)

- Urinary symptoms, including frequency, urgency, nocturia
- Physical measures (e.g., pad tests of quantified leakage, postvoid retention of urine, void volume, urodynamic measures)
- Health status and quality of life (impact of incontinence e.g., Incontinence Impact Questionnaire (IIQ), 36-Item Short Form Health Survey Questionnaire (SF-36), Bristol Female Urinary Symptoms Questionnaire, knowledge, quality of life)
- Functional ability (activities of daily living e.g., Barthel Index)

- Participant satisfaction

Risk of bias in individual studies

Two authors will assess the risk of bias using Cochrane's 'Risk of bias' tool (32) and a second author will check agreement. The tool covers the domains of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other bias. We will classify each domain as either low risk, high risk or unclear risk of bias.

Sensitivity analysis

Where data allows, we will explore the effects of including studies assessed as having a high risk of bias using sensitivity analyses. Up to three review authors will assess and document the quality of evidence for the prespecified outcomes outlined in the main and additional outcomes, based on the GRADE approach (33). We will downgrade the evidence from high-quality by one level for serious (or by two levels for very serious) study limitations:

- risk of bias due to flawed design or conduct of studies (random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, and incomplete outcome data). We reassessed all studies from the original review (34) using the updated 'Risk of bias' tool (32);
- imprecision (e.g., when CIs for treatment elect were wide);
- inconsistency (e.g., when point estimates varied widely, the IU was large);
- indirectness (e.g., variations in participants, interventions, comparisons and outcomes); and
- publication bias (may be explored with the use of funnel plots and classed as not suspected, suspected, strongly suspected or very strongly suspected).

We will report the risk of bias assessments and sensitivity analyses with the results.

Data synthesis

Studies will be synthesised through narrative reviews with tabulation of results of included studies. Where possible, treatment effects for all comparisons and outcomes will be synthesized through meta-analyses, with the approach taken dependant on the outcome assessed and the data available (35). Dichotomous data (e.g., number continent or incontinent; occurrence of urinary symptoms; participant satisfaction) will be presented as risk ratios with 95% confidence intervals (CI). Continuous data will be synthesised as weighted mean differences (MD) when outcomes are

assessed on the same scale, or standardised weighted mean difference (SMD) when different scales are used to measure the same underlying construct, with 95% CI. Where the outcomes represent time-to-event data (e.g., overall survival, time to continence), the (log) hazard ratio with 95% CI will be used as the summary measure. Heterogeneity will be assessed through visual inspection of forest plots and the calculation of the Chi^2 and I^2 statistics. Causes of heterogeneity will be assessed where sufficient data is available, including factors such as participant characteristics (e.g., age, sex), stroke location and type, stroke severity, communication and/or cognitive impairment, care setting, and intervention (type, duration, dose, time since stroke). Where appropriate, these will be investigated further through sub-group analyses and through meta-regression. Sensitivity analyses will explore possible causes of methodological heterogeneity, where sufficient data are available. This would include assessing the effects of studies that may be affected by factors such as risk of bias associated with allocation concealment, high loss to follow-up or lack of blinding in assessment of outcomes. Where data are missing, particularly measures of variation (e.g., standard deviation), we will contact study authors or impute values. It is likely that the analysis will focus on direct comparisons of intervention effects through pairwise meta-analyses. Where evidence allows, we will consider conducting network meta-analysis through both direct and indirect evidence within connected networks of trials. Pairwise meta-analyses of direct comparisons will be conducted using STATA v17 (36) or Comprehensive Meta-analysis v4 (37), while NMAs will be estimated using the WinBUGS software (version 1.4.3) (38).

Unit of analysis issues

For cross-over trials where there are no carry-over or period effects, we will analyse the data using a paired samples mean and SE test. We will analyse multi-arm trials comparing two interventions arms with one control group using methods described by Higgins 2011 (section 16.5.4) (32). To prevent inappropriate double-counting of individuals, we will analyse each treatment arm separately against the common control group but divide the sample size of the common comparator group proportionately across each intervention comparison.

'Summary of findings' tables

We will use GRADE to interpret findings and to create 'Summary of findings' tables for the main comparison (intervention versus no intervention/usual care) using the outcomes below for behavioural interventions, specialised professional input, complementary therapy and physical therapy:

- number of participants continent after treatment;
- number of incontinent episodes in 24 hours;

- perception of improvement or cure;
- health status and quality of life;
- functional ability; and
- adverse events.

We have chosen outcomes for the 'Summary of findings' tables based on the primary outcomes, outcomes of clinical importance, and outcomes of most importance to patients.

Analysis of subgroups or subsets

Possible causes of heterogeneity will be examined through sub-groups defined a priori (e.g., urological diagnosis, time from stroke onset to recruitment).

Meta-bias(es)

We will search clinical trial registers to assist in reducing publication bias. We will also investigate selective outcome reporting though the comparison of the methods section of papers with the results reported.

Confidence in cumulative evidence

The strength of the body of evidence will be assessed using GRADE (see 'Summary of findings' tables).

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