Systematic voiding programme in adults with urinary incontinence following acute stroke: the ICONS-II RCT

Caroline Watkins,[1,2*] Svetlana Tishkovskaya,[1] Chris Brown,[1] Chris Sutton,[3] Yvonne Sylvestre Garcia,[3] Denise Forshaw,[1] Gordon Prescott,[1] Lois Thomas,[2] Christine Roffe,[4] Joanne Booth,[5] Kina Bennett,[6] Brenda Roe,[7] Bruce Hollingsworth,[8] Ceu Mateus,[8] David Britt[9†] and Cliff Panton[10]

[1]Lancashire Clinical Trials Unit, Applied Health Research Hub, University of Central Lancashire, Preston, UK
[2]Faculty of Health and Care, University of Central Lancashire, Preston, UK
[3]Centre for Biostatistics, Division of Population Health, Health Services Research & Primary Care, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, UK
[4]Research Institute for Science and Technology in Medicine, Keele University, Stoke-on-Trent, UK
[5]Research Centre for Health, School of Health and Life Sciences, Department of Nursing and Community Health, Glasgow Caledonian University, Glasgow, UK
[6]Centre for Health Research and Innovation, NIHR Lancashire Clinical Research Facility, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK
[7]Faculty of Health, Social Care and Medicine, Edge Hill University, Ormskirk, UK
[8]Division of Health Research, Lancaster University, Lancaster, UK
[9]Chester, UK
[10]Manchester, UK

*Corresponding author clwatkins@uclan.ac.uk
†In memoriam

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Christine Roffe is chairperson of the TSC for the Imaging cerebral Neuro-inflammation in acute and chronic CerebroVascular Disease: a predictor of outcome and biomarker for guiding treatment (IN-CVD) study, funded by the NIHR Efficacy and Mechanism Evaluation (EME) programme; is a member of the DMC for the CAARBS (RCT of: a Calcium channel or Angiotensin converting enzyme inhibitor or Angiotensin Receptor Blocker regime to reduce blood pressure variability following ischaemic Stroke) feasibility study comparing a calcium-channel blocker versus angiotensin-converting enzyme inhibitors/angiotensin receptor blockers-based regime to target blood pressure variability following transient ischaemic attack and minor ischaemic stroke funded by a British Heart Foundation (BHF; London, UK)/The Stroke Association (TSA; London, UK) programme grant (2016–present); is a member of the DMC for the Penumbral Rescue by Normobaric O = O Administration in Patients With Ischaemic Stroke and Target Mismatch ProFile (PROOF) study, examining high-dose oxygen treatment in patients with large vessel occlusion and acute ischaemic stroke, funded by a European Union Horizon 2020 grant (2016–present); is an independent member of the TSC for the LACunar Intervention (LACI-2) Trial–2, funded by a BHF grant; is an independent member of the TSC for the Paramedic Acute Stroke Treatment Assessment (PASTA) study; is a co-applicant member of the TSC for the Right-2 study of pre-hospital treatment with glyceryl trinitrate patches in acute stroke; is a co-applicant member of the TSC for the Tranexamic acid for hyperacute primary IntraCerebral Haemorrhage (TICH-2) study; is a member of the James Lind Alliance Stroke Research Priority Setting Group (2020–present), UK Biotechnology and Biological Sciences Research Council Future Leaders Funding board (2020–present), TSA Research Awards Panel (2019–present), the UK Swallowing Research Group (2019–present) and the UK Stroke Forum Steering Group (2015–present); was a member of the NIHR HTA General Board (2017–21) and the NIHR Stroke National Specialty Group (2015–18); is chairperson of the NIHR Hyperacute Stroke Research Centre Oversight Group (2015–present); and is the Stroke NIHR National Specialty Group Portfolio Lead for Acute Clinical Studies (2015–present). Chris Sutton is a member of the NIHR HTA Commissioning Funding Committee (January 2020–present) and reports receiving institutional funding from NIHR for his role as co-investigator on several projects [not related to stroke or incontinence research, except for funding for the NIHR Global Health Research Group Improving Stroke Care in India (IMPROVISE) to July 2020], was an independent member of the TSC for the ELECtric Tibial nerve stimulation to Reduce Incontinence in Care homes trial and is an independent member of the Programme Steering Committee for the OPTimising Implementation of Ischaemic Stroke Thrombectomy (OPtimIST) programme grant. Lois Thomas was a Health and Social Care Delivery Research (HSDR)-commissioned panel member (2015–19). Caroline Watkins reports several current and recent NIHR-funded projects; is a member of the NIHR advanced fellowship panel, NIHR PARADISE (Predicting af AfteR cArDIac SurgEry - the PARADISE Score: A Clinical Prediction Rule for Post-operative Atrial Fibrillation in Patients Undergoing Cardiac Surgery) oversight panel, international advisory committee of NIHR Global Health Research Group on Atrial Fibrillation and the TSC/DMC for the NIHR Metoclopramide for Avoiding Pneumonia after Stroke (MAPS-2) study; is chairperson of the TSC/DMC for NIHR COVID-NURSE and the DMC for NIHR HomeHealth; is a co-applicant on the NIHR CLAHRC North West Coast Confirming the Mechanism of Motivational Interviewing Therapy after Stroke (COMMITS) project, NIHR Symptoms, Trajectory, Inequalities and Management: Understanding Long COVID to Address and Transform Existing Integrated Care Pathways (STIMULATE-ICP) grant, NIHR PREPARE programme development grant, NIHR Risk rEduction interVEntion for Raised blood preSsurE (REVERSE)

Research for Patient Benefit (RfPB) project grant, NIHR Global Health Research Group Stroke In Sierra Leone (SISLE); has two NIHR-funded doctoral fellowships; is chief investigator of the NIHR Global Health Research Group IMPROVISE and IMPROVIng Stroke care in India – Advancing The INSTRUCT Operations and Network (IMPROVISATION); was a deputy director of NIHR CLAHRC North West Coast; and is currently implementation lead of NIHR Applied Research Collaboration North West Coast.

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Scientific summary

The ICONS-II RCT

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Scientific summary

Parts of this summary have been adapted with permission from the trial protocol [Thomas L, Roffe C, Booth J, Bennett K, Watkins C, Roe B, *et al. ICONS II: Identifying Continence OptioNs after Stroke. Protocol*. Version 2.1. 2019. URL: https://www.fundingawards.nihr.ac.uk/award/16/111/31 (accessed 26 May 2022)].

Parts of this summary have also been adapted with permission from the statistical analysis plan [Tishkovskaya S, Sutton C, France A. *ICONS II: Identifying Continence OptioNs after Stroke. Statistical Analysis Plan (SAP)*. Version 1.0. 2019. URL: https://www.fundingawards.nihr.ac.uk/award/16/111/31 (accessed 26 May 2022)].

Background

Urinary incontinence (UI) affects around half of stroke survivors in the acute phase, and it often presents as a new problem after stroke or, if pre-existing, worsens significantly, adding to the disability and helplessness caused by neurological deficits. Stroke patients with UI have considerably worse outcomes than those who do not have UI, as there are clear associations between UI after stroke and death, disability and an increased likelihood of being discharged into residential care. The trial aimed to evaluate the clinical effectiveness and cost-effectiveness of a systematic voiding programme (SVP) for UI after stroke, which was developed to address incontinence early and effectively.

Objectives

The Identifying Continence OptioNs after Stroke (ICONS)-II trial aimed to evaluate the clinical effectiveness and cost-effectiveness of a SVP for UI after stroke in secondary care.

The study comprised a randomised controlled trial with an internal pilot. The purpose of the internal pilot was to assess the feasibility of participant recruitment and the success of strategies for minimising contamination in the usual-care group.

The primary objective of the randomised controlled trial was to determine if a SVP affects the severity of UI compared with usual care at 3 months post randomisation. The secondary objectives were to:

- determine if a SVP affects the number of urinary tract infections (UTIs), the number of days an indwelling urinary catheter (IUC) is in situ, urinary symptoms, quality of life, functional independence, falls and mortality, compared with usual care
- determine if the SVP is cost-effective in terms of quality-adjusted life-years gained compared with usual care at 6 months post randomisation
- assess fidelity to the intervention and to usual care in a process evaluation.

Design

This was a pragmatic, multicentre, individual-patient-randomised (1 : 1), parallel-group trial with an internal pilot. The trial design was informed by the ICONS-I feasibility trial in which the SVP was developed for UI management.

Sample size

The severity of UI was measured using the International Consultation on Incontinence Questionnaire – Urinary Incontinence – Short Form (ICIQ-UI-SF). The sample size calculations were based on the 3-month ICIQ-UI-SF total scores and required 818 participants to provide $\geq$ 90% power to detect a 1.89-point between-group difference using an independent-samples *t*-test (5% significance level), assuming that $\leq$ 25% of the true effect would be lost to contamination. It was based on a minimal clinically important difference of 2.52 and a common standard deviation (SD) of 8.32, estimated from the ICONS-I feasibility trial data. The ICONS-II trial planned to randomise 1024 participants to allow for 20% attrition.

Participants and setting

Study participants were men and women with acute stroke and UI, including those with cognitive impairment. The inclusion criteria were:

- adults with acute stroke
- UI, defined as 'involuntary loss of urine' within 72 hours of admission to the stroke unit, or presence of an IUC at the time of consent
- patient was conscious within 14 days of admission to the stroke unit.

The exclusion criteria were:

- long-term IUC pre stroke
- subdural or subarachnoid haemorrhage.

We planned to recruit 1024 participants from 18 NHS stroke services. However, because of problems with recruitment and retention, and COVID-19-associated difficulties, the trial was stopped when 157 participants had been recruited. A total of 17 NHS stroke services with stroke units had opened to recruitment by the time of trial closure.

Randomisation

Participants were randomised (in a 1 : 1 ratio) in blocks of random length, stratified by baseline continence category [catheterised, slight (ICIQ-UI-SF score of 0–5), moderate (ICIQ-UI-SF score of 6–12) or severe/very severe (ICIQ-UI-SF score of 13–21)] and by site, to one of two trial groups: (1) the intervention group (who received a SVP) ($n = 79$); or (2) the usual-care group ($n = 78$).

Intervention

The SVP comprised assessment, behavioural interventions (bladder training or prompted voiding) and review. Assessment included evaluation of the need for an IUC, a protocol for catheter removal (if clinically justifiable), a 3-day bladder diary to assess the pattern of UI and an evidence-based continence assessment to classify the type of UI. Patients who were not catheterised, were cognitively able and had some control of their bladder were allocated bladder training; those with cognitive impairment or with no control over their bladder were allocated prompted voiding.

Bladder training aimed to help patients regain bladder control and continence. It comprised:

- focused education for patients and carers on lower urinary tract dysfunction and the theory and practice of bladder training
- individualised voiding regimens to restore regular, normal voiding patterns by progressively lengthening the time between voids
- urge suppression techniques
- a patient-held voiding diary, a cognitive intervention designed to promote self-awareness of voiding habits.

Prompted voiding aimed to improve bladder control and minimise urinary infection episodes using verbal prompts and positive reinforcement from stroke service staff. It comprised:

- approaching participants according to their individualised regimen (e.g. every 2 hours during waking hours)
- asking the participant if they were currently dry or wet
- prompting them to use the toilet
- offering sensitive feedback for correct reporting of dryness/wetness and successful toileting.

In both routes, progress was to be reviewed weekly by clinical staff, with adjustment to the voiding regime or change from prompted voiding to bladder training if the patient's cognitive ability or bladder control improved, or from bladder training to prompted voiding if either or both cognitive ability and bladder control deteriorated.

The intervention was to start within 24 hours of recruitment and to continue until the patient had been discharged from the stroke unit.

Main outcome measures

The primary outcome was severity of UI at 3 months post randomisation, measured using the ICIQ-UI-SF total score. Participants who were catheterised were given a maximum score of 21. Secondary outcomes were measured at 3 and 6 months from randomisation/baseline, and some were also measured at discharge from the stroke unit. They included severity of UI at discharge and 6 months from randomisation, urinary symptoms, number of UTIs, number of days with an IUC in situ, functional independence, quality of life, falls, mortality and costs.

Blinding of health-care staff and patients was not possible. Data co-ordinators at Lancashire Clinical Trials Unit were also not blinded, as they were handling data from the process evaluation in addition to baseline and outcome data. The trial statistician remained blinded until the effectiveness analysis was complete. The process evaluation/internal pilot analysis was performed by an unblinded statistician.

Results

The internal pilot did not meet the target for participant recruitment. A number of barriers to recruitment were encountered. There were delays in the identification and appointment of the study champions, who were required at each site before recruitment could start. Staff were concerned that patients might see differences in care. Potentially eligible patients were not always approached because of concerns about their suitability, particularly those classified as palliative. There was a high rate of staff vacancies in some sites, limiting engagement with the trial and increasing the complexity of staff rotation required to ensure that both intervention-trained staff and usual-care staff were available.

After a review, recruitment was extended until 31 March 2020 to allow a separate assessment of the viability of recruitment to be conducted over a 3-month period in seven established sites. In total, 17 sites participated in the trial, with 14 activated and recruiting and three in the set-up stage. Two sites were closed in December 2020 because of difficulties in identifying suitable participants and being able to deliver the intervention in a systematic way owing to staff shortages. The other five established sites continued to recruit, as did the other sites that opened later. However, the trial was paused in March 2020 because of the COVID-19 pandemic, at which point 157 participants had been randomised. In the end, 12 sites contributed to recruitment.

A contamination analysis was first conducted in late spring of 2020. At that stage of recruitment, analysis concluded that the level of contamination of the usual-care group with the key components of the SVP intervention was much lower than the conservative 25% on which the original sample size had been based. Analysis suggested that any impact of contamination of the usual-care group on the treatment effect was unlikely to be > 10%. Nevertheless, had the trial been restarted, recruiting the required number of participants was deemed infeasible within a reasonable time frame and the remaining budget and in the light of the ongoing COVID-19 situation.

The trial had major issues with attrition, with 45% of 3-month (primary outcome) and 6-month ICIQ-UI-SF total scores missing. There were difficulties with delivering the intervention because of individual patient randomisation, and there were difficulties with recruiting sites. It was also noted that the length of hospital stay in the ICONS-II trial was much shorter than that in the ICONS-I feasibility trial. The overall median length of stay (interquartile range) in the stroke unit was 27 (16–45) days in the ICONS-II trial and 47 (30–68) days in the ICONS-I feasibility trial. It became apparent that a purely hospital-based intervention would not provide a sufficient amount of the SVP to the patient to be effective in managing incontinence.

These factors led to the decision not to restart the ICONS-II trial, resulting in its early termination.

The analysis for the main trial was then conducted on the small sample recruited during the trial, with 157 participants recruited out of the target 1024 (15%); therefore, the results are underpowered and should be interpreted with caution.

With regard to the primary outcome, the severity of urinary incontinence (ICIQ-UI-SF score), presented as a mean (SD), was 8.1 (7.4) for those allocated to the intervention group and 9.1 (7.8) for those allocated to the usual-care group. The difference in means of ICIQ-UI-SF total scores at 3 months between the groups, adjusted for baseline, was −1.35 [95% confidence interval (CI) −4.42 to 1.72].

With regard to secondary outcomes, at 6 months, the usual-care group had a lower ICIQ-UI-SF score than the intervention group, although the difference was small [mean (SD) 7.9 (7.4) compared with 8.5 (7.8) for the usual-care group and the intervention group, respectively]. In addition, the intervention group had lower estimated odds of a catheter being present at discharge than the usual-care group (odds ratio 0.6, 95% CI 0.3 to 1.1).

As insufficient data were collected, the cost-effectiveness analysis was very limited.

Limitations

The trial was unable to recruit a sufficient number of participants and had a very high attrition rate, which resulted in seriously underpowered and potentially biased results. It was not possible to measure the influence of the COVID-19 pandemic on the trial. This introduces a further limitation to the analysis and interpretation of the results.

Conclusions

The trial had major issues with site and participant recruitment and retention, and difficulties delivering the intervention. These factors were aggravated by the ongoing COVID-19 situation and the decision was taken to stop the trial early. There was very low power to draw conclusions about the clinical effectiveness of the ICONS-II trial SVP. Because of the small sample size, the results of this study should not be used to inform changes in clinical practice in the promotion of continence, but they may inform reduction in catheter use. The study findings suggest that, when designing a future trial, the intervention needs to be reviewed. The cause of incontinence should probably be diagnosed in hospital, and the intervention should probably be started in hospital and continue to be delivered in the community.

Future work

Further studies to assess the effectiveness of a similar intervention are required, in particular to investigate components of the intervention related to catheterisation. A future study should consider an intervention probably starting in the hospital but mainly delivered in the community. The feasibility of this approach requires further exploration.

Trial registration

This trial is registered as ISRCTN14005026.

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