Journal of the American Heart Association

ORIGINAL RESEARCH

CHOSEN: A Randomized Controlled Feasibility Trial

Craig J. Smith, BSc (Hons), MD, MCRP; Andrew Brand, PhD; Zoe Hoare, PhD; Eileen Jones, BA (Hons), RN; Catherine Davidson, BSc (Hons), MSc, PhD; Wendy Westoby; Ian Clements; Fiona Sandom, PhD; Clare Gross, DN; Anu Thomas, BSc, MSc, RN; Lucy Talbot, BSc (Hons), MRCSLT; Narayanamoorthi Saravanan, MBBS, MSc; Marian C. Brady, PhD, FRCSLT; Peter Langhorne, PhD, FRCP; Giles I. McCracken, BDS, PhD, RCPSG; Catherine E. Lightbody, BN (Hons), MPhil, PhD, RN; Caroline L. Watkins, BA (Hons), PhD, RN; Paul R. Brocklehurst, BDS, MDPH, PhD, RCS Eng

BACKGROUND: Improving oral health in patients with acutely dysphagic stroke is a plausible approach to prevent pneumonia. We aimed to determine whether a phase 3, definitive trial of oral health care (OHC) treatments, supported by staff education and training, is feasible in stroke unit care.

METHODS: The CHOSEN (Chlorhexidine or Toothpaste, Manual or Powered Brushing to prevent Pneumonia Complicating Stroke) trial was conducted and reported in line with the Consolidated Standards of Reporting Trials 2010 statement extended to feasibility trials. We aimed to recruit 120 participants with acute stroke and dysphagia within 24 hours of admission, from 4 stroke units in the northwest of England, randomized (1:1:1:1) to 1 of 4 OHC treatments: manual toothbrush or powered toothbrush with either nonfoaming toothpaste or chlorhexidine 1% gel. Stroke unit nursing staff received standardized education and training. Feasibility was assessed using a priori criteria.

RESULTS: Between January 2022 and end of January 2023, 626 patients were screened. A total of 101 participants (median age, 73 [interquartile range, 62–80] years; median National Institutes of Health Stroke Scale score, 10 [interquartile range, 5–18]; 44% women) were enrolled (77% of eligible patients approached). Adherence was 91%, with no substantial difference between the OHC treatments, and 88% completed follow-up. There were 19 serious adverse events but no marked differences between allocated OHC treatments. In exploratory secondary analyses, again there were no substantial differences in survival, incident pneumonia, modified Rankin Scale score, or quality of life at 3 months between the OHC treatment allocations.

CONCLUSIONS: OHC treatments incorporating chlorhexidine and powered brushing and supported by standardized staff training appeared feasible and safe in patients with acutely dysphagic stroke. Progression criteria were met for a definitive trial of efficacy and cost effectiveness.

REGISTRATION: URL: https://doi.org/10.1186/ISRCTN52421361; Unique identifier: ISRCTN52421361

Key Words: chlorhexidine ■ oral health care ■ poststroke pneumonia ■ randomized trial ■ stroke, acute

Pneumonia is the most common complication of stroke, occurring most often in the first 7 days after onset. It independently increases the inpatient mortality rate, length of hospital stay, and likelihood of a poor functional outcome in survivors,[1] as well as health care costs and risk of recurrent stroke.[2,3] Treatment of

Correspondence to: Craig J. Smith, BSc (Hons), MD, MCRP, Academic Neurosciences, Clinical Sciences Building, Manchester Centre for Clinical Neurosciences, Salford Royal Hospital, Greater Manchester, M6 8HD, UK. Email: craig.smith-2@manchester.ac.uk

This manuscript was sent to Charalambous C. Charalambous, PhD, Assistant Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.124.040677

For Sources of Funding and Disclosures, see page 11.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Improving oral health in patients with acutely dysphagic stroke is a plausible approach to prevent pneumonia and improve clinical outcomes but is challenging and lacks evidence from randomized trials.
- Our multicenter, randomized feasibility trial showed that oral health care treatments with chlorhexidine or nonfoaming toothpaste and powered or manual brushing, supported by staff training, were safe and well-tolerated, meeting all a priori feasibility criteria.

What Are the Clinical Implications?

- Definitive, large-scale, multicenter, randomized trials of oral health care interventions for patients with dysphagic stroke with appropriate clinical and health economic outcomes are warranted.

Nonstandard Abbreviations and Acronyms

CHOSEN	Chlorhexidine or Toothpaste, Manual or Powered Brushing to Prevent Pneumonia Complicating Stroke
GOHAI	General Oral Health Assessment Index
mRS	modified Rankin Scale
OHC	oral health care
SSNAP	Sentinel Stroke National Audit Program

poststroke pneumonia consumes considerable antibiotics, and there are currently limited preventive strategies. A recent registry study estimated that prevention of pneumonia in severe stroke could reduce the mortality rate by 43%, highlighting the substantial unmet need.[4]

Risk factors for poststroke pneumonia such as increased stroke severity, dysphagia, and advanced age, are well recognized.[5] In acute stroke, poor oral health is linked to the risk of developing poststroke pneumonia resulting from aspiration of oral biofilm, and may also contribute to poor nutrition, dehydration, pain, and decreased quality of life.[6] Poor oral health status and serum immunoglobulin G titers to periodontal pathogens were also associated with worse functional outcome in patients with acute stroke.[7,8] Targeting poor oral health in patients with acute dysphagic stroke is therefore a biologically plausible approach to prevent pneumonia if effective cleaning of the mouth and dentures can be achieved.

People with a stroke have a higher prevalence of poor oral health, including gingivitis, periodontal disease, dental caries, xerostomia, tooth loss, and use of dentures, compared with people without a previous stroke.[9,10] Provision of oral health care (OHC) is a priority for stroke survivors and their carers and for staff, yet it is a neglected aspect of stroke unit care, with a paucity of evidence informing staff training, assessment, and delivery.[11,12]

In self-caring adults, powered brushing and use of chlorhexidine reduces measures of dental plaque and gingivitis, compared with manual brushing with toothpaste.[13,14] OHC interventions using manual or powered brushing can reduce dental plaque within 1 week compared with baseline,[15,16] which is biologically relevant, as the majority of pneumonia occurs within 7 days of stroke onset. The microorganisms associated with poststroke pneumonia overlap with those associated with ventilator-associated pneumonia and hospital-acquired pneumonia.[17] A Cochrane review identified that using chlorhexidine as part of OHC prevented ventilator-associated pneumonia on the intensive care unit, but there were insufficient data to conclude on the role of powered versus manual brushing.[18] It is uncertain how this evidence applies to nonventilated patients in the stroke unit setting, where diverse neurological impairments, complex swallowing problems, high prevalence of oral disease, and requirement for assistance from staff or carers pose unique challenges.

A previous interrupted time series study reported that implementation of an OHC intervention comprising oral antiseptics and suction brushes with staff training significantly reduced the frequency of poststroke pneumonia.[19] However, a Cochrane review of randomized trials of OHC interventions in stroke care found no evidence of improvement in gingival or periodontal disease and no evidence for prevention of pneumonia.[20] This included trials comparing enhanced OHC with standard or conventional care. The review also did not find any evidence for OHC interventions improving patient satisfaction and quality of life. However, the included studies were few in number, small scale, generally of low quality, and focused on the stroke rehabilitation setting rather than patients at higher risk of pneumonia in the acute phase.

Side effects of chlorhexidine (eg, hypersensitivity reactions and staining of the teeth and gums) are well recognized. The effects of chlorhexidine on the oral biofilm in people with acute illness are not well understood. Use of powered brushing on a large scale in hospitals is potentially expensive, and the effects of enhanced mechanical disruption of oral biofilm in terms of aspiration risk are not known. It therefore remains unclear whether chlorhexidine and powered brushing are feasible, safe, acceptable, and well tolerated in acutely unwell patients with dysphagic stroke or if they

confer any benefit over and above manual brushes and toothpaste (regarded as standard care). The aim of this study was therefore to determine whether a phase 3, definitive, randomized controlled trial of OHC interventions to prevent poststroke pneumonia, supported by nursing staff education and training, is feasible in UK stroke unit care. Here, we present the findings from the main feasibility trial. The findings from the process evaluation will be reported separately.

METHODS

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Design and Setting

CHOSEN (Chlorhexidine or Toothpaste, Manual or Powered Brushing to Prevent Pneumonia Complicating Stroke) was a randomized, controlled, feasibility trial in hospitalized patients with dysphagic acute stroke, with a theoretically informed embedded process evaluation. Regulatory approvals were obtained from the Integrated Research Application System (ID: 270544), the Health Research Authority and Health and Care Research Wales Research Ethics Committee (21/YH/0014), and the Northern Care Alliance National Health Service Trust. The trial was undertaken in 4 participating stroke services in the northwest of England, each providing assessment and management of hyperacute and acute stroke plus stroke rehabilitation. The sites were selected on the basis of varying service provision, volume of patients admitted, staffing numbers, bed numbers, and incidence of poststroke pneumonia (Table S1). The trial was conducted and reported in line with the Consolidated Standards of Reporting Trials 2010 statement extended to feasibility trials.[21]

Participants

Eligible participants were aged at least 18 years, within 24 hours of admission to the stroke unit with acute ischemic or hemorrhagic stroke, dysphagic (bedside swallow assessment or speech and language therapy assessment), and with at least 1 natural tooth. Patients planned for repatriation to a nonparticipating site, for imminent mechanical ventilation or palliative care, taking antibiotics at the point of screening, or with a known allergy to chlorhexidine were excluded. Potential participants were screened by trained research practitioners, and informed consent was obtained from all participants. Where all other inclusion criteria were met, potential participants with aphasia were given the opportunity to participate in the trial. Aphasia-friendly participant information sheets and consent forms were developed in collaboration with our Patient and Public Involvement partners (and were inclusive of people with aphasia) to facilitate this process. For people with severe (global) aphasia and potential cognitive involvement (or for potential participants who lacked capacity), and where our adapted materials and communicative approaches were insufficient to ensure that the potential participant understood the project, then consent was sought from a personal consultee if available or a professional consultee (a senior clinician independent of the study).

Intervention

Participants were randomized (1:1:1:1) to 1 of 4 OHC treatments: chlorhexidine 1% gel and manual toothbrush treatment, chlorhexidine 1% gel and powered toothbrush treatment, nonfoaming toothpaste and manual toothbrush treatment, or nonfoaming toothpaste and powered toothbrush treatment. The allocated OHC treatment was administered, or self-care was supervised, by stroke unit health care assistants or registered nurses. For each OHC treatment, brushing was for up to 2 minutes (30 seconds for each of the 4 mouth quadrants) twice daily, with the participant in an upright position, with bedside suction at the discretion of the attending staff. To facilitate evaluation of fidelity and tolerability, the allocated OHC treatment was prescribed on the participant's drug chart and ward staff instructed to record whether it was received and, if not, what the reasons were.

As part of the implementation strategy, the drug charts were reviewed every 2 weeks during the first 2 months of the intervention period to evaluate fidelity to the allocated OHC treatment for each patient. If the intervention was not being implemented as per protocol, the need for further training was reviewed. Cleaning of dentures was standardized for all participants regardless of OHC treatment allocation. Dentures were scrubbed with liquid soap at least once daily and soaked in clean water overnight. Participants were encouraged to wear dentures during the day but especially at mealtimes where appropriate.

Participants received the allocated OHC treatment until discharge from inpatient stroke services or until 3 months after enrollment, if remaining an inpatient within the participating stroke service. Discontinuation of allocated OHC treatment was permitted without formally withdrawing from the trial. Crossover of allocated OHC treatment was also permitted at the request of the participant or at the discretion of the local clinical team. In such cases, the participant continued in the trial on an "intention to treat" basis.

OHC education and training was provided for stroke unit nursing staff and health care assistants at the participating sites to support delivery of the trial OHC treatments. The OHC education and training was developed and implemented in a previous single-site study at Salford Royal Hospital.[22] In brief, we modified our existing 1-hour online resource comprising core learning modules, self-assessment questions, and video demonstrations, in collaboration with Mouthcare Matters (http://mouthcarematters.hee.nhs.uk/index.html), a national initiative of OHC education and training including hospitalized adult patients. The OHC education and training included background information on OHC and stroke; an overview of the CHOSEN trial; the role of nursing staff and health care assistants and the role of the "OHC champions" in the trial; the OHC treatments used in the trial and how to implement them. Nursing staff and health care assistants accessed the training and education online using an individual password-protected platform that recorded successful completion. In addition, after commencing the trial, an abridged laminated paper version of the training and education (CHOSEN lite) was available for quick reference on the participating stroke units in response to initial feedback from the sites.

At least three staff from each site (designated OHC champions) also received additional education and training by a dental hygiene therapist (F.S.) to facilitate and cascade hands-on training and competency assessments in their units, thus supporting fidelity to the OHC treatments. Implementation of the education and training at the participating sites was facilitated by the study dental therapist, local Mouthcare Matters teams, research teams, and the stroke unit ward managers.

Randomization and Blinding

Randomization was undertaken using an online encrypted platform delivered by the North Wales Organization for Randomized Trials in Health Clinical Trials Unit, stratified by site, stroke severity (National Institutes of Health Stroke Scale score <13 versus ≥13) and age (<75 versus ≥75 years). Blinding of the participants and research staff (including the trial manager) was not possible; hence, only the trial statistician was blinded to the treatment allocation.

Baseline Data Collection

Baseline clinical and stroke characteristics (age, sex, stroke subtype, National Institutes of Health Stroke Scale score, hyperacute treatment, vascular risk factors, medications, prestroke disability using the modified Rankin Scale [mRS]), interval from admission to randomization, the Holistic and Reliable Oral Assessment Tool,[23] number of natural teeth, denture status, aphasia format oral health–related quality of life using the General Oral Health Assessment Index (GOHAI),[24] and nutrition status were collected.

Outcome Measures and Data Collection

The a priori feasibility outcome measures were as follows:

Recruitment of sites and setup, recruitment of participants (including reasons for nonparticipation), adherence to allocated OHC treatment (including reasons for nondelivery and need for further training), tolerability and safety of the OHC treatments, retention of recruited participants, and appropriateness and collection of the clinical outcome measures.

Days 7 to 10 from randomization: The Holistic and Reliable Oral Assessment Tool, aphasia format GOHAI, swallow and nutrition status, incident pneumonia (antibiotic initiation, and clinician-diagnosed pneumonia episodes), number of antibiotic doses, serious adverse events (SAEs) and adverse events.

Weekly to discharge from inpatient stroke services: swallow and nutrition status, incident pneumonia, SAEs, and adverse events.

Discharge from inpatient stroke services: number and percentage of total prescribed doses of allocation OHC, tolerability (reasons for participant noncompliance), GOHAI, quality of life (aphasia format EuroQoL-5D-5L), mRS, length of stay, discharge destination, incident pneumonia, number of antibiotic doses, adverse events, and SAEs.

Three months from randomization: survival, mRS, postdischarge mouth care.

Feasibility outcome measures were assessed on a Stop/Review/Go basis (Table 1). Assessment and interpretation of these outcomes also incorporated qualitative information from the parallel process evaluation, which included exploring the acceptability of the intervention to participants and their carers, attitudes of staff to the OHC treatments and training, and the facilitators/barriers to delivery, to provide an overall feasibility framework (reported separately).

Sample Size

We proposed a sample size of 120 participants for the main feasibility trial. From preceding national registry (Sentinel Stroke National Audit Program [SSNAP]) data, 45% of patients were dysphagic on the basis of admission bedside swallow assessment and post-stroke pneumonia occurred in 16% of these within the first week of admission, and the median length of stay for patients with dysphagia was 13 days compared with 5 days in those without dysphagia. We anticipated that 60% of the participants would complete the required period of intervention. A sample of 120 participating patients would achieve a 95% CI of 51% to 69% around our expected value of 60% completion,

Table 1. A Priori Feasibility and Progression Criteria

Feasibility criterion	Go	Review	Stop
Recruitment and setup of sites within time allocated	≥3 sites	2 sites	1 site
Implementation of staff education and training within time allocated	≥3 sites	2 sites	1 site
Recruitment of participating patients (of total sample size), %	≥85	42–84	<42
Retention of achieved consented participants, %	≥60	40–59	<40
Adherence to allocated oral health care treatment, %	≥90	70–89	<70
Collection of each outcomes data at a time point,* %	≥80	65–79	<65

*This criterion would reflect the potential outcomes for exclusion at full trial stage rather than nonprogression.

providing acceptable precision to inform progression to a phase 3 trial. Using SSNAP data to inform recruitment feasibility, in 2018, 9946 patients with confirmed acute stroke were admitted to stroke units in the northwest of England. Allowing for an estimated 20% of patients with stroke having no natural teeth, we estimated that 4 sites collectively recruiting 2 to 3 patients/wk would achieve the recruitment target in 12 months.

Statistical Analysis

The primary analysis centered on the feasibility outcomes defined earlier. The focus of results for clinical outcomes was based on estimates of treatment effects rather than statistical significance and, as such, no hypothesis testing was undertaken. Differences between the main factors are presented as mean differences or odds ratios with associated 95% CIs. The proportion of participants unable to receive the allocated OHC treatments on ≥1 occasions were summarized using descriptive statistics to identify potential barriers to implementation. One author (C.J.S.) had full access to all the data in the study and takes responsibility for its integrity and the data analysis.

RESULTS

Site Setup, Screening, and Recruitment

Setup and delivery of the trial was affected by the first Omicron COVID-19 wave, which led to delayed admissions to the stroke unit, staff sickness, and redeployment. Starting in September 2021, all 4 sites were successfully set up with sufficient numbers of staff trained within a 4-month period. Between January 2022 and end of January 2023, 626 patients were screened across the 4 sites (Figure 1). Of those screened, 148 (23%) were eligible. Reasons for ineligibility (potentially >1) included out of time window or research team nonavailability (n=257), receiving antibiotics on admission (n=77), deemed too unwell or palliative (n=60), edentulous (n=36), no available consultee for consent (n=43), active COVID-19 (n=8), and other (n=12). Of the 132 eligible patients approached, 101 (77%) were enrolled. Characteristics of the participating patients are shown in Table 2. The median age was 73 [interquartile range [IQR], 62–80] years, 44% were women, and median National Institutes of Health Stroke Scale score on admission was 10 (IQR, 5–18). Median interval from stroke onset (or time last seen

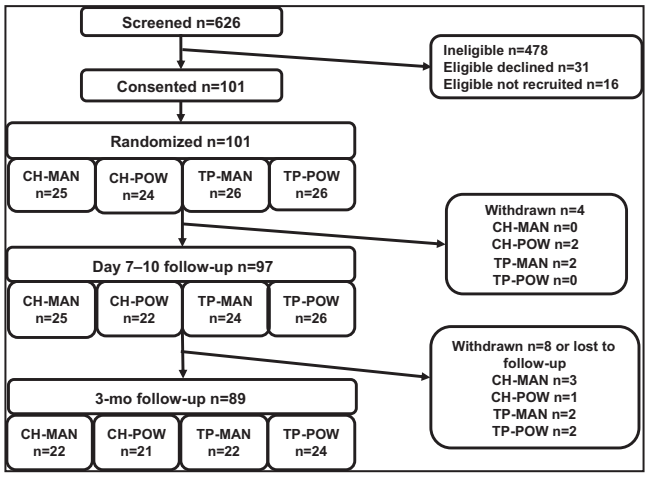

Figure 1. Study Consolidated Standards of Reporting Trials flow diagram.
CH-MAN indicates chlorhexidine with manual brushing; CH-POW, chlorhexidine with powered brushing; TP-MAN, nonfoaming toothpaste with manual brushing; and TP-POW, nonfoaming toothpaste with powered brushing.

Table 2. Baseline Characteristics at Study Enrollment by Treatment Allocation

	CH-MAN	CH-POW	TP-MAN	TP-POW	Overall
Age* (y)	71 (61–83)	74 (63.5–83)	69.5 (61.3–79.8)	74 (69.3–78.8)	73 (62–80)
Female sex	11 (44%)	12 (50%)	8 (31%)	13 (50%)	44 (44%)
Stroke subtype					
Ischemic stroke	24 (96%)	19 (79%)	19 (73%)	18 (69%)	80 (79%)
ICH	1 (4%)	5 (21%)	7 (27%)	8 (31%)	21 (21%)
NIHSS score*	9 (6–17)	11.5 (7.3–19)	10.5 (4.3–17.8)	9 (6–18)	10 (5–18)
Number of natural teeth*	17 (11–24)	15.5 (11.5–20)	18 (16–20)	18 (9–24)	18 (11.5–20)
Dentures	8 (32%)	3 (12%)	10 (38%)	7 (27%)	28 (28%)
THROAT score*	3 (1–6)	3 (2–5.5)	2 (1.25–4.5)	3 (2–6)	3 (2–5.3)
GOHAI score*	30.5 (28.5–34.3)	31 (28–34)	32 (29.3–33.8)	26.3 (23.3–29.3)	31 (29–34)
BMI (kg/m^2)*	23.6 (22.3–28.4)	28.3 (23.6–31.7)	27.2 (23.7–31.9)	26.3 (23.3–29.3)	26.4 (22.6–31.1)
Pre-stroke mRS					
0	13 (52%)	9 (38%)	12 (46%)	11 (42%)	45 (45%)
1	5 (20%)	5 (21%)	5 (19%)	6 (23%)	21 (21%)
2	0 (0%)	0 (0%)	1 (4%)	5 (19%)	6 (6%)
3	5 (20%)	5 (21%)	4 (15%)	3 (12%)	17 (17%)
4	2 (8%)	4 (17%)	2 (8%)	1 (4%)	9 (9%)
5	0 (0%)	0 (0%)	2 (8%)	0 (0%)	2 (2%)
Previous stroke					
Yes	4 (16%)	6 (25%)	8 (31%)	4 (15%)	22 (22%)
No	21 (84%)	18 (75%)	18 (69%)	22 (85%)	79 (78%)
Hypertension					
Yes	13 (52%)	13 (54%)	16 (62%)	18 (69%)	60 (59%)
No	12 (48%)	11 (46%)	10 (38%)	8 (31%)	41 (41%)
Atrial fibrillation					
Yes	6 (24%)	3 (12%)	7 (27%)	4 (15%)	20 (20%)
No	19 (76%)	21 (88%)	19 (73%)	22 (85%)	81 (80%)
Coronary artery disease					
Yes	2 (8%)	2 (8%)	2 (8%)	1 (4%)	7 (7%)
No	23 (92%)	22 (92%)	24 (92%)	25 (96%)	94 (93%)
Diabetes					
Yes	7 (28%)	7 (29%)	9 (35%)	5 (19%)	28 (28%)
No	18 (72%)	17 (71%)	17 (65%)	21 (81%)	73 (72%)
Dyslipidemia					
Yes	4 (16%)	6 (25%)	2 (8%)	6 (23%)	18 (18%)
No	21 (84%)	18 (75%)	24 (92%)	20 (77%)	83 (82%)
PVD					
Yes	0 (0%)	1 (4%)	1 (4%)	3 (12%)	5 (5%)
No	25 (100%)	23 (96%)	25 (96%)	23 (88%)	96 (95%)
Chronic lung disease					
Yes	3 (12%)	2 (8%)	1 (4%)	4 (15%)	10 (10%)
No	22 (88%)	22 (92%)	25 (96%)	22 (85%)	91 (90%)
Smoking status					
Current smoker	8 (32%)	5 (21%)	5 (19%)	2 (8%)	20 (20%)
Ex-smoker	4 (16%)	5 (21%)	6 (23%)	4 (15%)	19 (19%)
Never smoker	13 (52%)	14 (58%)	15 (58%)	20 (77%)	62 (61%)

(*Continued*)

Table 2. Continued

	CH-MAN	CH-POW	TP-MAN	TP-POW	Overall
Antiplatelet therapy					
Yes	17 (68%)	13 (54%)	13 (50%)	12 (46%)	55 (54%)
No	8 (32%)	11 (46%)	13 (50%)	14 (54%)	46 (46%)
Anticoagulants					
Yes	1 (4%)	1 (4%)	7 (27%)	5 (19%)	14 (14%)
No	24 (96%)	23 (96%)	19 (73%)	21 (81%)	87 (86%)
Thrombolysis					
Yes	4 (16%)	5 (21%)	4 (15%)	4 (15%)	17 (17%)
No	21 (84%)	19 (79%)	22 (85%)	22 (85%)	84 (83%)

BMI indicates body mass index; CH-MAN, chlorhexidine with manual brushing; CH-POW, chlorhexidine with powered brushing; GOHAI, General Oral Health Assessment Index; ICH, intracerebral hemorrhage; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PVD, peripheral vascular disease; THROAT, The Holistic and Reliable Oral Assessment Tool; TP-MAN, non-foaming toothpaste with manual brushing; and TP-POW, non-foaming toothpaste with powered brushing.

*Median (interquartile range).

well) to randomization was 23.4 (IQR, 19–26.4) hours and from admission to the stroke unit to randomization was 20.5 (IQR, 15.6–23.2) hours. Overall median length of stay in hospital stroke services was 16.5 (IQR, 5–41.5) days, with 81% discharged home and 19% discharged to a care home.

Adherence

Overall adherence to the allocated OHC treatment was 91%, with no substantial difference between allocations (chlorhexidine 1% gel and manual toothbrush treatment, 94%; chlorhexidine 1% gel and powered toothbrush treatment, 84%; nonfoaming toothpaste and manual toothbrush treatment, 87%; nonfoaming toothpaste and powered toothbrush treatment, 80%). By visit, adherence was 85% at 7 to 10 days, 92% weekly to 3 months, and 92% at discharge. The most frequent reason recorded for nonadherence at all time points was “patient declined” (62%). Other reasons included “patient off ward” (7%), “patient asleep” (1%), “too unwell” (2%), “clinical team requested omission” (2%), “equipment not available” (9%), and “other–unclassified” (17%). A small number of participants chose to switch to an alternative OHC regimen from that originally allocated. This occurred in only 5% of the total number of prescriptions and did not differ markedly between treatment allocations.

Safety

There were 19 SAEs in 16 participating patients, comprising pneumonia/sepsis (n=5), other infection or sepsis (n=4), venous thromboembolism (n=2), seizure (n=1), massive intracranial hemorrhage (n=1), hydrocephalus (n=1), recurrent severe stroke (n=1), other deterioration with palliative care (n=2), cardiac arrest (n=1), and syncope (n=1). No SAEs were deemed attributable to the allocated OHC treatments. There were no allergic reactions or instances of tooth staining associated with chlorhexidine. There were no substantial differences in numbers of SAEs between treatment allocations (chlorhexidine 1% gel and manual toothbrush treatment, n=3; chlorhexidine 1% gel and powered toothbrush treatment, n=7; nonfoaming toothpaste and manual toothbrush treatment, n=3; nonfoaming toothpaste and powered toothbrush treatment, n=6) or between the participating sites.

Retention of Participants

Eleven randomized participants withdrew or were withdrawn from the trial, and 1 was lost to follow-up, with 89 completing 3-month follow-up (Figure 1). Of the 11 withdrawals, 3 were by the supervising medical team and the remaining 8 by the participants (or their consultee) with no specific reason given. There was no marked difference in withdrawals between allocation groups (chlorhexidine 1% gel and manual toothbrush treatment, n=2; chlorhexidine 1% gel and powered toothbrush treatment, n=3; nonfoaming toothpaste and manual toothbrush treatment, n=4; nonfoaming toothpaste and powered toothbrush treatment, n=2).

Exploratory Clinical Outcome Measures

Feasibility of collecting the exploratory secondary outcome measures is shown in Table 3. Collection of the mRS was ≥80% at all visits, although collection of The Holistic and Reliable Oral Assessment Tool and GOHAI was <80% at the discharge visit. Collection of EuroQoL-5D-5L was in the review range (Table 1) at both the discharge and 3-month visits. In these exploratory analyses, there were no marked differences in mRS distribution by allocation for discharge and 3 months (Figure 2, Table 4), occurrence of pneumonia by days 7 to 10 and discharge by allocation (Figure 3, Table 4), or survival between any of the 4 allocated

Table 3. Collection of the Secondary Outcome Measures by Visit

	Baseline, %	7–10 d, %	Discharge, %	3 mo, % inpatient	3 mo following discharge, %	Overall, %
mRS	99	N/A	92	100	88	95
THROAT	99	83	76	N/A	N/A	86
GOHAI	96	81	79	N/A	N/A	85
EuroQoL-5D-5L	N/A	N/A	75	75	N/A	75
EuroQoL-5D-5L-VAS	N/A	N/A	71	75	N/A	73

GOHAI indicates General Oral Health Assessment Index; mRS, modified Rankin Scale; N/A, not applicable; and THROAT, The Holistic and Reliable Oral Assessment Tool.

OHC treatment groups (Figure 4, Table 4). Distribution of The Holistic and Reliable Oral Assessment Tool, GOHAI, and aphasia format EuroQoL-5D-5L scores did not substantially differ by OHC treatment allocation (Table 4 and Figures S1–S3).

DISCUSSION

OHC is a neglected area of stroke unit care, with 1 study suggesting that at least 40% of patients had no documented oral care.[25] We evaluated the feasibility of OHC treatments supported by standardized staff training in patients with stroke at increased risk of developing poststroke pneumonia. The OHC treatments appeared well tolerated, and there were no safety concerns. Overall, our quantitative feasibility criteria were met when considering the impact of COVID-19 on trial delivery, justifying completion of the trial and supporting progression to a definitive efficacy trial with health economic evaluation.

We selected patients at relatively high risk of developing poststroke pneumonia, with all enrolled participants having oropharyngeal dysphagia and at least moderate-severity stroke. However, the observed frequency of pneumonia at days 7 to 10 (2.1%) was lower than might be expected from randomized trials of preventive antibiotics in patients with dysphagia (11%)[26] or from real-world UK registry data (8.6%) available in SSNAP for the duration of our trial. This was despite using clinician-diagnosed pneumonia, which may overestimate frequency compared with adjudicated algorithm-based diagnosis.[26] However, as we did not include a usual-care OHC arm, we were unable to directly compare with the frequency of poststroke pneumonia in participants receiving usual care. As usual care is heterogeneous between stroke units, in terms of both staff education and training and provision of equipment,[25,27] a usual-care arm is an important consideration for design of a future phase 3 trial, which would necessitate a cluster-randomized design.

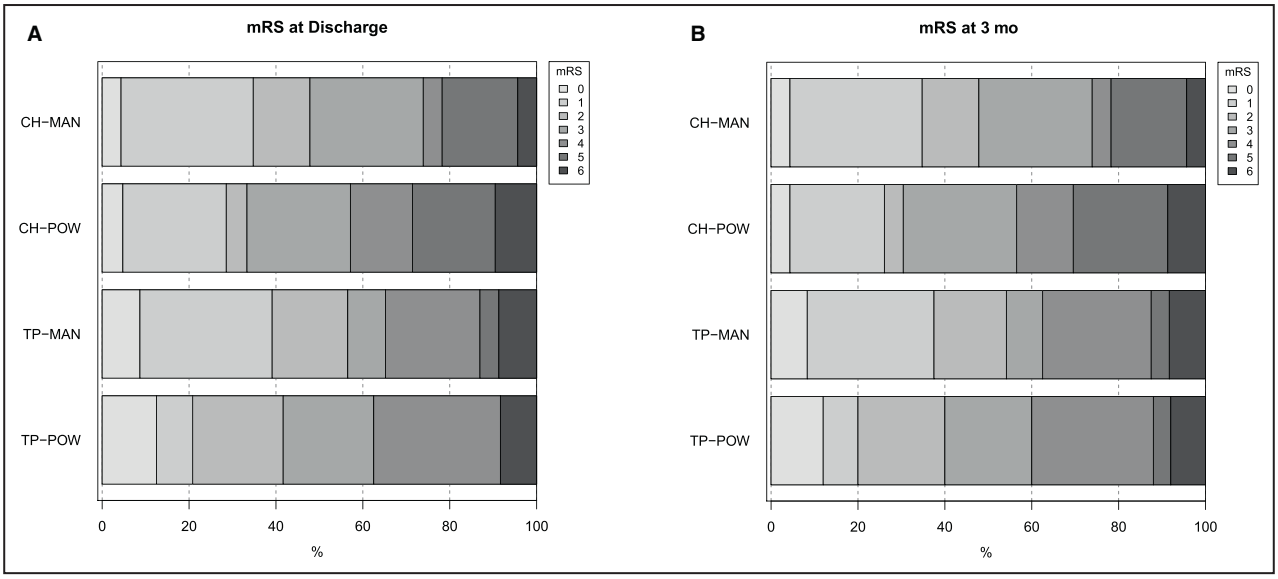

Figure 2. Stacked bar chart showing distribution of mRS scores by treatment allocation at (A) discharge, and (B) 3 months.
CH-MAN indicates chlorhexidine with manual brushing; CH-POW, chlorhexidine with powered brushing; mRS, modified Rankin Scale; TP-MAN, nonfoaming toothpaste with manual brushing; and TP-POW, nonfoaming toothpaste with powered brushing.

Table 4. Effect Sizes and CIs for the Exploratory Outcome Measures

	Effect size			
	Estimate*	CH-MAN	CH-POW	TP-POW
Pneumonia before visit 2 (0 to 1)	Odds ratio	1.30	0	0
	95% CI	(0.05 to 40.5)	NA	NA
Pneumonia before visit 3 (0 to 1)	Odds ratio	3.33	2.83	0
	95% CI	(0.35 to 46.64)	(0.23 to 44.14)	N/A
Pneumonia before visit 4 (0 to 1)	Odds ratio	4.14	2.03	0.71
	95% CI	(0.50 to 50.30)	(0.16 to 28.31)	(0.05 to 8.96)
Survival at 3 mo (0 to 1)	Odds ratio	0.84	0.37	3.37
	95% CI	(0.12 to 5.75)	(0.05 to 8.96)	(0.33 to 77.59)
EuroQoL-5D-5L index at visit 4 or	Mean difference	0.06	−0.09	0.01
visit 4a (−0.224 to 1)	95% CI	(−0.10 to 0.21)	(−0.25 to 0.06)	(−0.14 to 0.17)
EuroQoL-5D-5L VAS at visit 4 or	Mean Difference	−7.47	−13.91	1.53
visit 4a (0 to 100)	95% CI	(−22.16 to 7.23)	(−28.94 to 1.11)	(−13.17 to 16.23)
mRS at 3 mo (0 to 6)	Odds ratio	1.43	2.44	2.01
	95% CI	(0.48 to 4.23)	(0.78 to 7.68)	(0.66 to 6.09)
mRS at discharge (0 to 6)	Odds ratio	1.49	2.05	2.20
	95% CI	(0.50 to 4.46)	(0.63 to 6.60)	(0.71 to 6.78)
GOHAI visit 2 (12 to 36)	Mean difference	−1.30	−0.77	−0.91
	95% CI	(−2.83 to 0.24)	(−2.33 to 0.79)	(−2.46 to 0.65)
GOHAI visit 4 (12 to 36)	Mean difference	−1.11	−0.81	−1.25
	95% CI	(−2.62 to 0.39)	(−2.35 to 0.73)	(−2.81 to 0.30)
THROAT Visit 2 (0 to 24)	Mean difference	−0.18	−0.25	−0.89
	95% CI	(−1.24 to 0.87)	(−1.32 to 0.81)	(−1.98 to 0.20)
THROAT visit 4 (0 to 24)	Mean difference	0.00	0.41	−0.62
	95% CI	(−1.02 to 1.01)	(−0.62 to 1.45)	(−1.69–0.45)

Visit 2, 7–10 d after randomization follow-up; visit 3, weekly follow-ups for 3 mo; visit 4, discharge; visit 4a, inpatient at 3 mo. CH-MAN indicates chlorhexidine with manual brushing; CH-POW, chlorhexidine with powered brushing; GOHAI, General Oral Health Assessment Index; mRS, modified Rankin Scale; THROAT, The Holistic and Reliable Oral Assessment Tool; TP-POW, nonfoaming toothpaste with powered brushing; and VAS, visual analog scale.

*The reference level group for the effect sizes estimate is nonfoaming toothpaste with manual brushing (TP-MAN), since it is considered to be the group that is closest to usual care.

We adapted an existing OHC training and education resource,[22] which was developed by a multidisciplinary team comprising nursing, dental, and medical professionals. The training was designed to be completed online with a minimal face-to-face component to facilitate implementation within nursing practice. Following feedback after initial implementation of the online education and training resource, we introduced an abridged, laminated version of the resource (CHOSEN lite). This was easily available on the stroke units and increased uptake and completion, particularly when considering the challenges posed by the COVID-19 pandemic. Further details of the implementation process will be reported elsewhere with the process evaluation.

We collected a number of secondary outcome measures, in line with recommendations for complex interventions.[28] Data collection at discharge was less feasible than the other time points, which may be due to discharges occurring out of hours or with limited warning. The EuroQoL-5D-5L was collected less frequently than other secondary outcome measures (eg, mRS). This will be explored further in the parallel process evaluation but as a key component of health economics analyses may require further piloting before a phase 3 trial.

We observed no notable differences in any of the secondary outcome measures between the allocated OHC treatments. While these were exploratory secondary analyses and should be interpreted with caution, this has potential implications for a future trial design that aims to compare efficacy between the 4 OHC treatments. Our results do not support dropping any of the 4 allocations on the basis of adherence, fidelity, or safety and will be informed further by the results of the parallel process evaluation in terms of tolerability and acceptability to both participating patients and stroke unit staff.

Strengths and Limitations

Our study has several limitations. We randomized participants to initiate their allocated OHC treatment within 24 hours of admission to the stroke unit, which for some

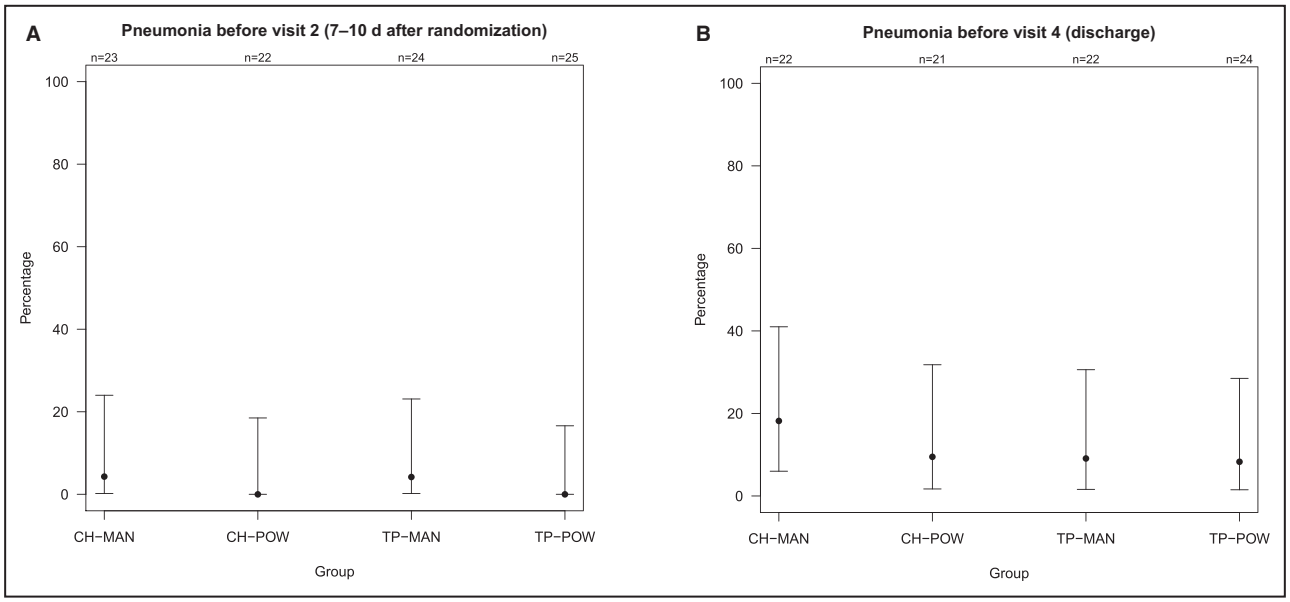

Figure 3. Occurrence of pneumonia by treatment allocation by (A) 7–10 days post-randomization, and at (B) discharge from hospital.
Data are percentage with 95% CI. CH-MAN indicates chlorhexidine with manual brushing; CH-POW, chlorhexidine with powered brushing; TP-MAN, nonfoaming toothpaste with manual brushing; and TP-POW, nonfoaming toothpaste with powered brushing.

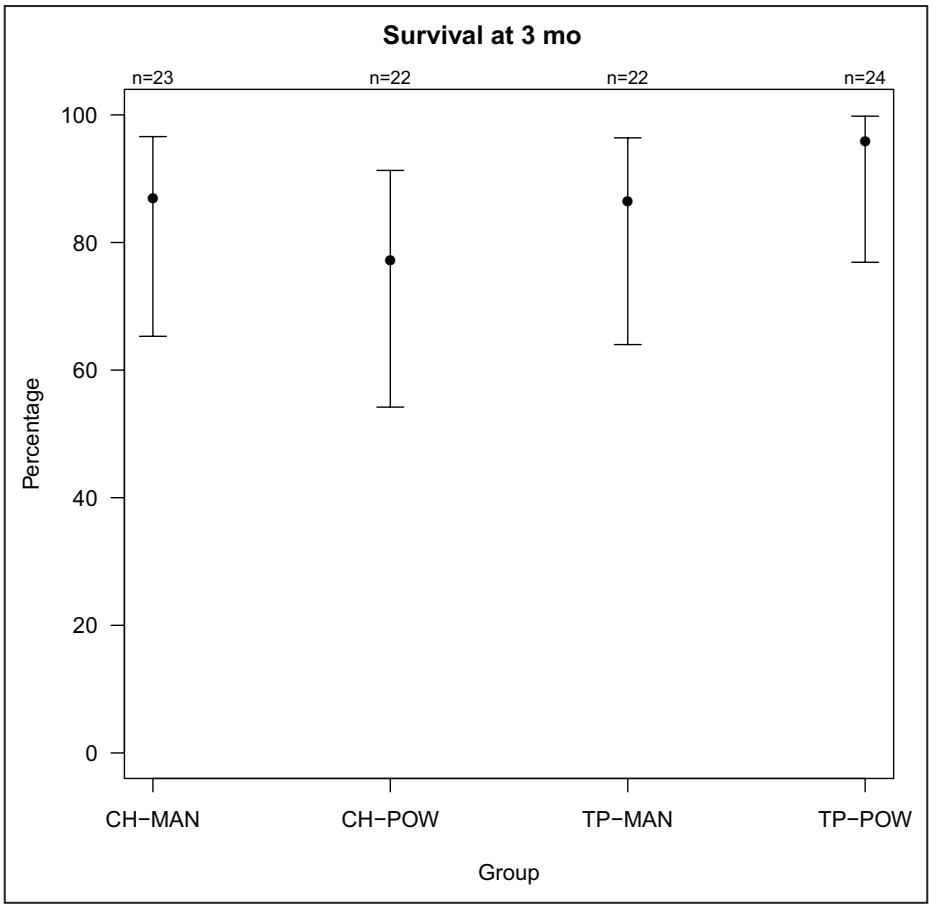

Figure 4. Survival at 3 months by treatment allocation.
Data are percentage with 95% CI. CH-MAN indicates chlorhexidine with manual brushing; CH-POW, chlorhexidine with powered brushing; TP-MAN, nonfoaming toothpaste with manual brushing; and TP-POW, nonfoaming toothpaste with powered brushing.

patients may have been >24 hours after the onset of stroke symptoms. As the majority of poststroke pneumonia manifests clinically (and treatment is initiated) within the first 72 hours,[29] our enrollment window may have been too long to optimally facilitate prevention of pneumonia. Future studies should consider aiming to initiate OHC as early as possible after stroke onset, shifting the focus more into the hyperacute phase, which could be aligned with early swallow screening. The trial was conducted in a single region of the United Kingdom, which is likely to be representative of UK stroke unit care but may not be generalizable more widely to other health care settings or models of stroke unit care. Finally, we did not include completely edentulous patients, which was primarily because the OHC treatments were brushing based. We acknowledge that edentulous patients (with or without dentures) may still have poor oral health status and be at risk of pneumonia and should be considered in future trials of OHC.

CONCLUSIONS

Randomized OHC treatments incorporating chlorhexidine and powered brushing, supported by standardized staff training, were feasible in patients with acutely dysphagic stroke. When accounting for the impact of COVID-19 on the trial delivery, the quantitative progression criteria were met for a definitive efficacy trial with health economic evaluation. Data from the parallel process evaluation will inform future trial design.

ARTICLE INFORMATION

Received December 16, 2024; accepted July 1, 2025.

Affiliations

Division of Cardiovascular Sciences, University of Manchester, Manchester, UK (C.J.S., E.J.); Manchester Centre for Clinical Neurosciences, Geoffrey Jefferson Brain Research Centre, Salford Royal Hospital (C.J.S.), Salford, UK; North Wales Organisation for Randomised Trials in Health (NWORTH) Clinical Trials Unit, Bangor University, Bangor, UK (A.B., Z.H.); School of Nursing and Midwifery, University of Central Lancashire, Preston, UK (C.D., C.E.L., C.L.W.); Stroke Patient and Public Involvement Group, Geoffrey Jefferson Brain Research Centre, Salford Royal Hospital (W.W., I.C.), Salford, UK; All Wales Faculty for Dental Professionals, Bangor, UK (F.S.); Oral and Maxillofacial Surgery, Salford Royal Hospital (C.G.), Salford, UK; Stroke Unit, Department of Clinical Neurosciences, Royal Preston Hospital, Preston, UK (A.T.); Department of Speech and Language Therapy, Whiston Hospital, Liverpool, UK (L.T.); Hyperacute Stroke Unit, Fairfield General Hospital, Northern Care Alliance NHS Trust, Bury, UK (N.S.); Research Centre for Health, Glasgow Caledonian University, Glasgow, UK (M.C.B.); School of Cardiovascular and Metabolic Health, University of Glasgow, Glasgow, UK (P.L.); School of Dental Sciences, Newcastle University, Newcastle, UK (G.I.M.); and Primary Care Division, Public Health Wales, UK (P.R.B.).

Acknowledgments

The authors are grateful to all of the participating patients, staff, and research delivery teams. The authors also acknowledge Mouth Care Matters for their support with the staff education and training and gratefully acknowledge Oral B, who provided the powered brushes for the trial. The authors are grateful to the Independent Trial Steering Committee (Professor Thompson Robinson, University of Leicester, Chair; Dr Jonathan Hewitt, Cardiff University; Dr Thomas Lamont, University of Dundee; Professor Zoe Marshman, University of Sheffield) and Independent Data Monitoring Committee (Professor Sue Pavitt, University of Leeds, Chair; Professor William Whiteley, University of Edinburgh; Dr Girvan Burnside, University of Liverpool).

Sources of Funding

This project was funded by the National Institute for Health and Care Research under its Research for Patient Benefit Programme (Grant Reference Number: NIHR200739) and supported by the National Institute for Health and Care Research Manchester Biomedical Research Centre (NIHR203308). The views expressed are those of the authors and not necessarily those of the National Institute for Health and Care Research or the Department of Health and Social Care.

Disclosures

Oral B provided the powered brushes for the trial but had no other involvement in the trial design, conduct, analyses, or manuscript preparation.

Supplemental Material

Table S1
Figures S1–S3

REFERENCES

1. Lobo Chaves MA, Gittins M, Bray BD, Vail A, Smith CJ. Do stroke care processes modify clinical outcomes in patients with stroke-associated pneumonia? A registry cohort study in England and Wales. *Cerebrovasc Dis*. 2023;52:21–27. doi: 10.1159/000524917
2. Ali AN, Howe J, Majid A, Redgrave J, Pownall S, Abdelhafiz AH. The economic cost of stroke-associated pneumonia in a UK setting. *Top Stroke Rehabil*. 2018;25:214–223. doi: 10.1080/10749357.2017.1398482
3. Xu J, Yalkun G, Wang M, Wang A, Wangqin R, Zhang X, Chen Z, Mo J, Meng X, Li H, et al. Impact of infection on the risk of recurrent stroke among patients with acute ischemic stroke. *Stroke*. 2020;51:2395–2403. doi: 10.1161/STROKEAHA.120.029898
4. Gittins M, Lobo Chaves M, Vail A, Smith CJ. Does stroke-associated pneumonia play an important role on risk of in-hospital mortality associated with severe stroke? A four-way decomposition analysis of a national cohort of stroke patients. *Int J Stroke*. 2023;18:1092–1101. doi: 10.1177/17474930231177881
5. Kishore A, Vail A, Bray BD, Chamorro A, Di Napoli M, Kalra L, Langhorne P, Montaner J, Roffe C, Rudd AG, et al. Clinical risk scores for predicting stroke-associated pneumonia: a systematic review. *Eur Stroke J*. 2016;1:76–84. doi: 10.1177/2396987316651759
6. Lyons M, Smith C, Boaden E, Brady MC, Brocklehurst P, Dickinson H, Hamdy S, Higham S, Langhorne P, Lightbody C, et al. Oral care after stroke: where are we now? *Eur Stroke J*. 2018;3:347–354. doi: 10.1177/2396987318775206
7. Aoki S, Hosomi N, Nishi H, Nakamori M, Nezu T, Shiga Y, Kinoshita N, Ueno H, Ishikawa E, Imamura E, et al. Serum IgG titers to periodontal pathogens predict 3-month outcome in ischemic stroke patients. *PLoS One*. 2020;15:e0237185. doi: 10.1371/journal.pone.0237185
8. Leao TS, Tomasi G, Ibrahim MS, Conzatti L, Marrone LP, Reynolds MA, Gomes MS. Tooth loss is associated with atherosclerosis and a poorer functional outcome among stroke patients. *Clin Oral Investig*. 2020;24:4541–4548. doi: 10.1007/s00784-020-03319-z
9. Dai R, Lam OL, Lo EC, Li LS, Wen Y, McGrath C. A systematic review and meta-analysis of clinical, microbiological, and behavioural aspects of oral health among patients with stroke. *J Dent*. 2015;43:171–180. doi: 10.1016/j.jdent.2014.06.005
10. Zeng LN, Rao WW, Luo SH, Zhang QE, Hall BJ, Ungvari GS, Chen LG, Xiang YT. Oral health in patients with stroke: a meta-analysis of comparative studies. *Top Stroke Rehabil*. 2019;27:75–80. doi: 10.1080/10749357.2019.1656413
11. Horne M, McCracken G, Walls A, Tyrrell PJ, Smith CJ. Organisation, practice and experiences of mouth hygiene in stroke unit care: a mixed-methods study. *J Clin Nurs*. 2015;24:728–738. doi: 10.1111/jocn.12665
12. Hammond L, Conroy T, Murray J. Exploring oral care practices, barriers, and facilitators in an inpatient stroke unit: a thematic analysis. *Disabil Rehabil*. 2023;45:796–804. doi: 10.1080/09638288.2022.2040616
13. Yaacob M, Worthington HV, Deacon SA, Deery C, Walmsley AD, Robinson PG, Glenny AM. Powered versus manual toothbrushing for

oral health. *Cochrane Database Syst Rev*. 2014;2014:CD002281. doi: 10.1002/14651858.CD002281.pub3
14. James P, Worthington HV, Parnell C, Harding M, Lamont T, Cheung A, Whelton H, Riley P. Chlorhexidine mouthrinse as an adjunctive treatment for gingival health. *Cochrane Database Syst Rev*. 2017;3(3):CD008676. doi: 10.1002/14651858.CD008676.pub2
15. Stoltze K, Bay L. Comparison of a manual and a new electric toothbrush for controlling plaque and gingivitis. *J Clin Periodontol*. 1994;21:86–90. doi: 10.1111/j.1600-051x.1994.tb00284.x
16. Nightingale KJ, Chinta SK, Agarwal P, Nemelivsky M, Frisina AC, Cao Z, Norman RG, Fisch GS, Corby P. Toothbrush efficacy for plaque removal. *Int J Dent Hyg*. 2014;12:251–256. doi: 10.1111/idh.12081
17. Kishore AK, Vail A, Jeans AR, Chamorro A, Di Napoli M, Kalra L, Langhorne P, Roffe C, Westendorp W, Nederkorn PJ, et al. Microbiological etiologies of pneumonia complicating stroke: a systematic review. *Stroke*. 2018;49:1602–1609. doi: 10.1161/STROKEAHA.117.020250
18. Zhao T, Wu X, Zhang Q, Chunjie L, Worthington HV, Hua F. Oral hygiene care for critically ill patients to prevent ventilator associated pneumonia. *Cochrane Database Syst Rev*. 2020;12:CD008367. doi: 10.1002/14651858.CD008367.pub4
19. Wagner C, Marchina S, Deveau JA, Frayne C, Sulmonte K, Kumar S. Risk of stroke-associated pneumonia and oral hygiene. *Cerebrovasc Dis*. 2016;41:35–39. doi: 10.1159/000440733
20. Campbell P, Bain B, Furlanetto DL, Brady MC. Interventions for improving oral health in people after stroke. *Cochrane Database Syst Rev*. 2020;12:CD003864. doi: 10.1002/14651858.CD003864.pub3
21. Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, Lancaster GA. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ (Clinical Rresearch Eed)*. 2016;355:i5239. doi: 10.1136/bmj.i5239
22. Smith CJ, Horne M, McCracken G, Young D, Clements I, Hulme S, Ardron C, Hamdy S, Vail A, Walls A, et al. Development and feasibility testing of an oral hygiene intervention for stroke unit care. *Gerodontology*. 2017;34:110–120. doi: 10.1111/ger.12232
23. Dickinson H, Watkins C, Leathley M. The development of the THROAT: the holistic and reliable oral assessment tool. *Clin Eff Nurs*. 2001;5:104–110. doi: 10.1054/cein.2001.0221
24. Atchison KA, Dolan TA. Development of the geriatric Oral health assessment index. *J Dent Educ*. 1990;54:680–687. doi: 10.1002/j.0022-0337.1990.54.11.tb02481.x
25. Klaic M, Seng E, McGrath R. Factors that influence oral hygiene care with hospitalised stroke patients: a mixed methods study. *Disabil Rehabil*. 2022;44:7926–7935. doi: 10.1080/09638288.2021.2003450
26. Kalra L, Irshad S, Hodsoll J, Simpson M, Gulliford M, Smithard D, Patel A, Rebello-Mesa I. Prophylactic antibiotics after acute stroke for reducing pneumonia in patients with dysphagia (STROKE-INF): a prospective, cluster-randomised, open-label, masked endpoint, controlled clinical trial. *Lancet*. 2015;386:18351844. doi: 10.1016/S0140-6736(15)00126-9
27. Bangee M, Martinez-Garduno CM, Brady MC, Cadilhac DA, Dale S, Hurley MA, McInnes E, Middleton S, Patel T, Watkins CL, et al. Oral care practices in stroke: findings from the UK and Australia. *BMC Nurs*. 2021;20:169. doi: 10.1186/s12912-021-00642-y
28. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, Boyd KA, Craig N, French DP, McIntosh E, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *BMJ (Clinical Rresearch Eed)*. 2021;374:n2061. doi: 10.1136/bmj.n2061
29. de Jonge JC de van Beek D Lyden P Brady MC Bath PM van der Worp HB Temporal profile of pneumonia after stroke *Stroke* 2022 53 53 60 DOI: 10.1161/STROKEAHA.120.032787