ID	Field	Content
0.	PROSPERO registration number	CRD42021245827
1.	Review title	In people after stroke, what is the clinical and cost effectiveness of interventions to improve oral hygiene?
2.	Review question	In people after stroke, what is the clinical and cost effectiveness of interventions to improve oral hygiene?
3.	Objective	To determine the clinical and cost-effectiveness of interventions to support oral hygiene for people after a stroke who require extra support with oral hygiene.
4.	Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE Searches will be restricted by: • English language studies • Human studies Other searches: • Inclusion lists of systematic reviews The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
5.	Condition or domain being studied	Adults and young people (16 or older) after a stroke

6.	Population	Inclusion: • Adults (age ≥16 years) who have had a first stroke or recurrent stroke Exclusion: • Children (age <16 years) • People who have had a transient ischaemic attack
7.	Intervention	• Oral hygiene interventions o Frequency of intervention – Once a day – Twice a day – Three times a day – Four times a day or more – Hourly oral care
8.	Comparator	• Compared to each other (for example: oral hygiene once a day compared to oral hygiene three times a day) • Placebo/sham procedures (as defined by the study) • Usual care
9.	Types of study to be included	• Systematic reviews of RCTs • Parallel RCTs • Cluster randomised crossover trials (unit of randomisation = stroke unit) including stepped wedge trial designs If insufficient RCT evidence is available, non-randomised studies will be considered, including: 3. Prospective and retrospective cohort studies 4. Case control studies (if no other evidence identified) Published NMAs and IPDs will be considered for inclusion.
10.	Other exclusion criteria	• Non-English language studies • Crossover RCTs (unit of randomisation = participant) Conference abstracts will be excluded as it is expected there will be sufficient full text published studies available.
11.	Context	People with problems with oral hygiene after a stroke. This is likely to discuss people after acute stroke in particular.
12.	Primary outcomes (critical outcomes)	All outcomes are considered equally important for decision making and therefore have all been rated as critical:

		All outcomes are to be assessed at ≤3 months (90 days). If outcomes are reported after this time period they may be included but downgraded for outcome indirectness. If multiple outcomes are reported before this time period then the latest time period that is ≤3 months will be extracted and used in the analysis.
		• Mortality (dichotomous outcomes)
		• Person/participant generic health-related quality of life (continuous outcomes will be prioritised [validated measures])
		  ○ EQ-5D
		  ○ SF-6D
		  ○ SF-36
		  ○ SF-12
		  ○ Other measures (AQOL, HUI, 15D, QWB)
		• Carer utility health-related quality of life (continuous outcomes will be prioritised [validated measures])
		  ○ EQ-5D
		  ○ SF-6D
		  ○ SF-36
		  ○ SF-12
		  ○ Other utility measures (AQOL, HUI, 15D, QWB)
		• Occurrence of pneumonia (dichotomous outcomes)
		• Stroke outcome – modified Rankin scale (continuous outcomes will be prioritised)
		• Requirement for enteral feeding support (dichotomous outcomes)
		• Oral health outcome scales (continuous outcomes will be prioritised)
		  ○ Oral Health Impact Profile-14 (OHIP-14)
		  ○ General Oral Health Assessment Index (GOHAI)
		  ○ Oral Health Transitional Scale (OHTS)
		• Dysphagia severity (continuous outcomes will be prioritised)
		  ○ Functional intake scale (FOIS)
		• Presence of oral disease (dichotomous outcomes)
		  ○ Gingivitis
		  ○ Oral candidiasis
		  ○ Denture-induced stomatitis
		• Length of hospital stay (continuous outcomes will be prioritised)
		• Re-admission (dichotomous outcomes)
		• Stroke-specific Patient-Reported Outcome Measures (continuous outcomes will be prioritised)

		○ Stroke-Specific Quality of Life (SS-QOL) ○ Stroke Impact Scale (SIS) ○ Stroke-specific Sickness Impact Profile (SA-SIP30) ○ Satisfaction with International Classification of Functioning, Disability and Health – Stroke (SATIS-Stroke) ○ Neuro-QOL ○ PROMIS-10 If not mentioned above, other validated scores will be considered and discussed with the committee to deliberate on their inclusion.
14.	Data extraction (selection and coding)	EndNote will be used for reference management, sifting, citations and bibliographies. All references identified by the searches and from other sources will be screened for inclusion. All references identified by the searches and from other sources will be uploaded into EPPI reviewer and de-duplicated. 10% of the abstracts will be reviewed by two reviewers, with any disagreements resolved by discussion or, if necessary, a third independent reviewer. The full text of potentially eligible studies will be retrieved and will be assessed in line with the criteria outlined above. A standardised form will be used to extract data from studies (see Developing NICE guidelines: the manual section 6.4). 10% of all evidence reviews are quality assured by a senior research fellow. This includes checking: • papers were included /excluded appropriately • a sample of the data extractions • correct methods are used to synthesise data • a sample of the risk of bias assessments Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary. Study investigators may be contacted for missing data where time and resources allow.
15.	Risk of bias (quality) assessment	Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual.

		• Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) • Randomised Controlled Trial: Cochrane RoB (2.0) • Non randomised study, including cohort studies: Cochrane ROBINS-I
16.	Strategy for data synthesis	• Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences. Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects. • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ • Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. • WinBUGS will be used for network meta-analysis, if possible given the data identified.
17.	Analysis of sub-groups	Subgroups that will be investigated if heterogeneity is present: Severity (as stated by category or as measured by NIHSS scale): • Mild (or NIHSS 1-5) • Moderate (or NIHSS 5-14) • Severe (or NIHSS 15-24) • Very severe (or NIHSS >25) Type of stroke (using the Bamford scale):

		• Total anterior circulation stroke (TACS) • Partial anterior circulation stroke (PACS) • Lacunar stroke (LACS) • Posterior circulation stroke (POCS) Dysphagia at baseline: • Presence of dysphagia at baseline • Absence of dysphagia at baseline • Mixed Type of intervention: • Tooth brushing • Oral swabbing for secretions • Electronic/powered tooth brushing • Mouthwash • Oral hygiene instruction (for people after a stroke and those supporting them) • Suctioning devices for secretions • Professional tooth cleaning • Combinations of the above People who are nil-by-mouth at baseline: • People who are nil-by-mouth at baseline • People who are not nil-by-mouth at baseline		
18.	Type and method of review	☒	Intervention		
		☐	Diagnostic		
		☐	Prognostic		
		☐	Qualitative		
		☐	Epidemiologic		
		☐	Service Delivery		
		☐	Other (please specify)		
19.	Language	English			
20.	Country	England			
21.	Anticipated or actual start date	24/02/2021			
22.	Anticipated completion date	14/12/2022			
23.	Stage of review at time of this submission	Review stage		Started	Completed
		Preliminary searches		☐	☐
		Piloting of the study selection process		☐	☐

		Formal screening of search results against eligibility criteria	☐	☐
		Data extraction	☐	☐
		Risk of bias (quality) assessment	☐	☐
		Data analysis	☐	☐
24.	Named contact	5a. Named contact National Guideline Centre 5b Named contact e-mail StrokeRehabUpdate@nice.nhs.uk 5e Organisational affiliation of the review National Institute for Health and Care Excellence (NICE) and National Guideline Centre		
25.	Review team members	From the National Guideline Centre: Bernard Higgins (Guideline lead) George Wood (Senior systematic reviewer) Madelaine Zucker (Systematic reviewer) Kate Lovibond (Health economics lead) Claire Sloan (Health economist) Joseph Runicles (Information specialist) Nancy Pursey (Senior project manager)		
26.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.		
27.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.		
28.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the		

		review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ng10175	
29.	Other registration details	N/A	
30.	Reference/URL for published protocol	N/A	
31.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.	
32.	Keywords	Adults; Chlorhexidine; Intervention; Mouthwash; Oral hygiene; Rehabilitation; Stroke	
33.	Details of existing review of same topic by same authors	N/A	
34.	Current review status	☐	Ongoing
		☐	Completed but not published
		☒	Completed and published
		☐	Completed, published and being updated
		☐	Discontinued
35.	Additional information	N/A	
36.	Details of final publication	www.nice.org.uk	