National Institute for Health and Care Excellence

Draft for consultation

Stroke rehabilitation in adults (update)

[J] Evidence reviews for the clinical and cost-effectiveness of interventions to support oral hygiene for adults after a stroke

NICE guideline GID-NG10175

Evidence reviews underpinning recommendations 1.10.1 to 1.10.3

April 2023

Draft for Consultation

These evidence reviews were developed by the Guideline Development Team at NICE

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1.1 Review question

In people after stroke, what is the clinical and cost effectiveness of interventions to improve oral hygiene?

1.1.1 Introduction

Dryness of the mouth is very uncomfortable, can be embarrassing, and the presence of secretions and debris in the mouth and pharynx can cause distress and lead to feelings of choking. Poor oral hygiene is associated with an increased risk of respiratory tract infections and therefore is an important risk factor for aspiration pneumonia after a stroke. Additionally, poor oral hygiene can result in a reduced oral intake and contribute to malnutrition and dehydration.

Maintaining good oral hygiene can be difficult for some people after a stroke because of cognitive issues, plus weakness to limbs or face. This review aims to compare the effectiveness of different methods for maintaining good oral hygiene in people after a stroke.

1.1.2 Summary of the protocol

Table 1: PICO characteristics of review question

Population	Inclusion: • Adults (age ≥16 years) who have had a first stroke or recurrent stroke (including people who had a subarachnoid haemorrhage) Exclusion: • Children (age <16 years) • People who have had a transient ischaemic attack

Interventions	• Oral hygiene interventions
	  ○ Frequency of intervention
	  – Once a day
	  – Twice a day
	  – Three times a day
	  – Four times a day or more
	  – Hourly oral care
	
	Oral hygiene interventions could include: Powered toothbrush, chlorhexidine mouth rinse, oral hygiene instruction, education (for the person and staff supporting them), professional tooth cleaning.

Comparisons	• 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
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])
	• Carer utility health-related quality of life (continuous outcomes will be prioritised [validated measures])
	• 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)
	• Dysphagia severity (continuous outcomes will be prioritised)
	• 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)

Study design	• 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: 1. Prospective and retrospective cohort studies 2. Case control studies (if no other evidence identified)

For full details see the review protocol in Appendix A.

1.1.3 Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in Appendix A and the methods document.

Declarations of interest were recorded according to NICE's conflicts of interest policy.

1.1.4 Effectiveness evidence

1.1.4.1 Included studies

Nine randomised controlled trial studies (from thirteen papers) were included in the review;[2, 4, 5, 8-12, 16] these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 3).

These studies reported the following comparisons:

- Oral hygiene intervention (once a day) compared to usual care[2, 4, 10]
- Oral hygiene intervention (twice a day) compared to usual care[5, 8, 11, 12]
- Oral hygiene intervention (three times a day) compared to usual care[16]
- Oral hygiene intervention (four times a day or more) compared to usual care[9]

The following comparisons were not included in the protocol, but were included as the committee agreed they were relevant for their decision making:

- Oral hygiene intervention (twice a day with additional treatment twice a week) compared to oral hygiene intervention (twice a day)[12]
- Oral hygiene intervention (twice a day with additional treatment twice a week) compared to usual care[12]

No relevant clinical studies comparing the following were identified:

- Hourly oral care compared to usual care
- Any oral hygiene intervention compared to placebo/sham procedures
- Any oral hygiene intervention compared to each other (except for oral health interventions [twice a day with additional treatment twice a week] compared to oral health interventions [twice a day])

Studies included people after ischaemic and haemorrhagic strokes (including people after subarachnoid haemorrhage). The severity of the stroke was mostly not reported, but when reported was of moderate severity (or NIHSS 5-14). Some studies included participants with dysphagia at baseline[4, 5, 9] while other studies did not discuss the inclusion of people with dysphagia. Some only included people who were nil-by-mouth at baseline[4, 11], while others included a mixture of people who were and were not nil-by-mouth [5], excluded people who were nil by mouth [12] or did not discuss the inclusion of people who were nil-by-mouth.

The type of intervention varied, with the majority of interventions being a combination of various interventions (including tooth brushing [with or without an electrical toothbrush], tongue brushing, oral swabbing, flossing, mouthwash, education and professional cleaning).

There was limited evidence for most outcomes. Some outcomes were not reported in any of the included studies, including:

- Person/participant and carer generic health-related quality of life
- Stroke outcome (modified Rankin scale)
- Presence of denture-induced stomatitis
- Re-admission
- Stroke-specific Patient-Reported Outcome Measures (including stroke-specific quality of life measures)

See also the study selection flow chart in Appendix C, study evidence tables in Appendix D, forest plots in Appendix E and GRADE tables in Appendix F.

Indirectness

Some evidence was considered as indirect. The reasons for this included:

- Intervention indirectness – in Chen 2019[4] the amount of treatment provided was less frequent than the smallest category provided in the protocol (care was provided three times a week rather than once a day). In this case the study was considered as indirect but included in the oral hygiene intervention (once a day) category.
- Outcome indirectness
  - In Kim 2014[10] length of hospital stay was reported as length of intensive care unit admission only. As the person may have been in hospital for longer than this, the outcome was considered an indirect measure.
  - Some studies reported outcomes in forms that were not prioritised in the protocol. For example:
    - Dysphagia severity – provided as dichotomous data instead of continuous[5]
    - Presence of oral disease (gingivitis) – provided as continuous data instead of dichotomous[10, 12]

These outcomes were included in the analysis but downgraded in the GRADE analysis.

Meta-analysis

In the majority of cases there was insufficient evidence to form meta-analyses for outcomes. Where meta-analysis was possible there was no inconsistency seen.

Kim 2014[10] reported presence of oral disease (oral candidiasis) in two different methods: presence on the tongue and presence in saliva. When compared to other studies reporting the same outcome, it was decided to meta-analyse the outcome measuring presence on the tongue as this was most likely to complement the data from the other study. The outcome reporting presence in saliva was reported separately for completeness.

1.1.4.2 Excluded studies

A Cochrane review, Campbell 2020[3] was identified but was not included in this review. This was excluded as it included oral hygiene assessment as an intervention, while this shall be analysed in a separate review question. Additionally, it did not include the stratifications for the interventions that the committee decided were relevant and included outcomes that the committee did not think were relevant. Instead, the studies included in the Cochrane review were checked for inclusion in this review.

See the excluded studies list in Appendix J.

1.1.5 Summary of studies included in the effectiveness evidence

Table 2: Summary of studies included in the evidence review

Study	Intervention and comparison	Population	Outcomes	Comments
Ab Malik 2018[2] Subsidiary paper: Ab Malik 2018[1]	**Oral hygiene intervention (once a day)** (n=38) "Intense method for plaque control" - daily powered tooth brushing (Oral B(R) Pro-Health DB4010) with a 1%	**People after a first or recurrent stroke** Age: Majority >40 years N = 86 Type of stroke: Haemorrhagic: 9	Mortality at ≤3 months Presence of oral disease – Oral candidiasis at ≤3 months	Setting: Five public hospitals in Malaysia. Sources of funding: No additional information.

Study	Intervention and comparison	Population	Outcomes	Comments
	Chlorhexidine gel. Followed up at 3 months and 6 months. Type of intervention: Combination (powered toothbrush and chlorhexidine toothpaste). **Usual care** (n=48) "Conventional method for plaque control" - daily manual tooth brushing (Oral B(R) - super thin and extra soft bristles) with a standardised commercial toothpaste (Colgate (R) Maximum Cavity Protection). Followed up at 3 months and 6 months. **Concomitant therapy:** No additional information.	Ischaemic: 75 Severity: Not stated/unclear Dysphagia at baseline: Not stated/unclear People who are nil-by-mouth at baseline: Not stated/unclear		
Chen 2019[4]	**Oral hygiene intervention (three times a week*)** (n=33) Oral health care 30 minutes before the swallowing training three times a week for 3 weeks. First, the person's sputum in the oral cavity was assessed. A suction was used to clear the saliva when necessary. Next, an oral cleaning tool (dental floss and/or interdental brush) was used, and the patient's teeth were brushed using the	**People after a first or recurrent stroke** Age: Mixture of people at less than and greater than 65 years N = 66 Type of stroke: Infarction: 35 Haemorrhagic: 31 Severity: Not stated/unclear. Dysphagia at baseline: Presence of dysphagia at baseline. People who are nil-by-mouth at	Requirement of enteral feeding support at ≤3 months Oral health outcome scales at ≤3 months Dysphagia severity at ≤3 months	Setting: Primary care (four rehabilitation units of a medical centre in Taiwan). Sources of funding: This research received no external funding. *This intervention was at less than once per day. In the analysis it is included with the once per day evidence, but downgraded for indirectness.

Study	Intervention and comparison	Population	Outcomes	Comments
	Bass method. Finally, a fluoride toothpaste (fluoride >1000ppm, <0.5cm used to prevent cavities) was used to coat all teeth. Type of intervention: Combination. Mixture of suctioning, oral swabbing, toothbrushing, floss and interdental brushes before swallowing therapy. **Usual care** (n=33) Usual oral care provided in the unit (e.g. tooth brushing or sponge stick cleaning) twice a day (morning and evening) and were provided with an instructional manual to promote eating (including information such as food choice and safe eating tips). **Concomitant therapy:** Usual care was provided to both study arms.	baseline: People who are nil-by-mouth at baseline (presumed due to nasogastric tube insertion at baseline).		
Chipps 2014[5]	**Oral hygiene intervention (twice a day)** (n=29) Provided by a nurse trained by dentist and dental hygienists. Battery-operated toothbrush, Braun Oral B with timer(TM) twice daily, Timed toothbrushing for 30 seconds in each quadrant of the mouth, Crest-Pro-	**People after a first or recurrent stroke** Mean age (SD): 63.1 (14.5) years N = 51 Type of stroke: Not stated/unclear. Severity: Not stated/unclear. Dysphagia at baseline: Presence of	Requirement for enteral feeding support at ≤3 months Oral health outcome scales at ≤3 months Dysphagia severity at ≤3 months	Setting: A free-standing 60-bed acute rehabilitation hospital that is part of a major academic medical center in the Midwest (United States of America). Sources of funding: This project was funded through Sigma Theta Tau International and the Rehabilitation Nurses Foundation.

Study	Intervention and comparison	Population	Outcomes	Comments
	Health(TM) toothpaste, Listerine(TM) 10-15mL once per day, Glide Disposable Floss Picks (TM), Sunstar(TM) Dual Action Tongue Cleaner and Carmex(TM) lip balm. Care provided twice a day. Type of intervention: Combination. Includes electric toothbrush, mouthwash, floss, tongue cleaner, lip balm. **Usual care** (n=22) Provided by a nursing assistant. Toothbrushing with a hospital toothbrush Sage(TM), twice daily using Sage Oral Care Sodium Bicarbonate Mouthpaste (toothpaste), Careline(TM) alcohol free mouthwash once a day (rinse and spit), and lip care with regular Chaplet(TM). **Concomitant therapy:** No additional information	dysphagia at baseline. People who are nil-by-mouth at baseline: Mixed (4 people were at Functional Oral Intake Scale 1-3 at baseline).		This study includes dysphagia severity but reports it as a dichotomous outcome rather than as a continuous outcome. As this was not the prioritised reporting method, this outcome has been downgraded for indirectness.
Dai 2017[8] Subsidiary papers: Dai 2017[6] Dai 2019[7]	**Oral hygiene intervention (twice a day)** (n=47) An advanced oral hygiene care programme - supply of a powered	**People after a first or recurrent stroke** Mean age (SD): 66.6 (10.9) years N = 94 Type of stroke: Ischaemic: 66	Occurrence of pneumonia at ≤3 months	Setting: The Mrs Ng Wah Memorial Day Outpatients Centre, Tung Wah Hospital in Hong Kong SAR. Sources of funding: This study was supported by

Study	Intervention and comparison	Population	Outcomes	Comments
	toothbrush (Oral-B (R) AdvancePower(TM) 400 series), 0.2% chlorhexidine gluconate mouth rinse (Corsodyl (R)), a standardised tooth paste (Colgate (R) Maximum Cavity Protection), and oral hygiene training. Type of intervention: Combination (powered toothbrush, chlorhexidine mouthwash and education). **Usual care** (n=47) Conventional oral hygiene care programme - supply of a manual toothbrush (Oral-B (R) Pro-Health All-In-One), a standardised tooth paste (Colgate Maximum Cavity Protection), and oral hygiene training. **Concomitant therapy:** No additional information.	Haemorrhagic: 28 Severity: Not stated/unclear Dysphagia at baseline: Not stated/unclear People who are nil-by-mouth at baseline: Not stated/unclear.		General Research Fund, Hong Kong (Project number 774012).
Gosney 2006[9]	**Oral hygiene intervention (four times a day)** (n=103) Orobase gel, containing 2% (w/v) colistin, 2% (w/v) polymyxin E and 2% (w/v) amphotericin B, 500mg applied to the mucous membranes of the mouth four times	**People after a first stroke** Median age (range): Intervention: 70.5 (16-96) years Control: 73.3 (45-92) years N = 203 Type of stroke: Not stated/unclear.	Mortality at ≤3 months Occurrence of pneumonia at ≤3 months	Setting: Acute stroke assessment units of three hospitals in the northwest of England. Sources of funding: This project was funded by the Northwest Zonal Research and Development. One investigated was employed as a

Study	Intervention and comparison	Population	Outcomes	Comments
	daily for 2-3 weeks (2 weeks if they had a safe swallow, 3 weeks if they had an unsafe swallow). Type of intervention: Other. **Usual care** (n=100) Placebo gel applied four times daily for 2-3 weeks (2 weeks if they had a safe swallow, 3 weeks if they had an unsafe swallow). **Concomitant therapy:** No additional information.	Severity: Not stated/unclear. Dysphagia at baseline: Mixed (25 in the intervention arm, 33 in the control arm). People who are nil-by-mouth at baseline: Not stated/unclear.		research nurse by the funding body.
Kim 2014[10]	**Oral hygiene intervention (once a day)** (n=45) Oral hygienic management administered by one dentist once every day for an average of 2.2 weeks (range 1-5 weeks) using a toothbrush and interdental brush, tongue cleaner and 0.5% chlorohexidine swabs. Type of intervention: Professional tooth cleaning. **Usual care** (n=45) No specific oral hygiene intervention. **Concomitant therapy:** No additional information.	**People after a first or recurrent stroke** Mean age (SD): 56.8 (14.4) years N = 90 Type of stroke: Infarct: 6 Haemorrhagic: 50 Severity: Not stated/unclear Dysphagia at baseline: Not stated/unclear People who are nil-by-mouth at baseline: Not stated/unclear.	Mortality at ≤3 months Presence of oral disease (oral candidiasis) at ≤3 months Presence of oral disease (gingivitis) at ≤3 months	Setting: People admitted to the intensive care unit of the neurosurgery department of a university hospital (South Korea). Sources of funding: This research was supported by research grants from Yeung-nam University in 2010. This study reports presence of oral candidiasis on the tongue and in saliva. Both were extracted and meta-analysed as appropriate if studies report similar methods of determining the presence of the disease. This study reports gingivitis as a continuous outcome rather than as a

Study	Intervention and comparison	Population	Outcomes	Comments
				dichotomous outcome. As this was not the prioritised reporting method, this outcome has been downgraded for indirectness.
Kuo 2016[11]	**Oral hygiene intervention (twice a day)** (n=50) Home-based oral care training programme including advice on providing oral care twice a day including toothbrushing and tongue brushing. Followed up for two months. Type of intervention: Combination (education programme, tooth brushing, tongue cleaning). **Usual care** (n=50) Routine oral care practices (including oral cleaning with cotton swabs) for two months (after which they complete the home-based oral care training programme. **Concomitant therapy:** No additional information.	**Caregivers of and people after a first or recurrent stroke** Mean age (SD): 53.3 (14.3) years N = 100 Type of stroke: Not stated/unclear Severity: Not stated/unclear Dysphagia at baseline: Not stated/unclear People who are nil-by-mouth at baseline: People who are nil-by-mouth at baseline.	Mortality at ≤3 months	Setting: Home based (Taiwan). Sources of funding: No external sources of funding. This study reports outcomes for the caregivers (but does not report health-related quality of life). Mortality was reported for the people after stroke and so this was included in the report.
Lam 2013[12] Subsidiary papers: Lam 2013[13]	**Oral hygiene intervention (twice a day and additional treatment twice a week)** (n=35) Oral hygiene intervention and chlorhexidine mouthrinse twice	**People after a first or recurrent stroke** Mean age (SD): 69.8 (11.0) years N = 102 Type of stroke: Ischaemic: 68	Occurrence of pneumonia at ≤3 months Presence of oral disease (gingivitis) at ≤3 months	Setting: The rehabilitation unit at Tung Wah Hospital in Hong Kong. Sources of funding: Supported by the Committee of Research and Conference Grants

Study	Intervention and comparison	Population	Outcomes	Comments
	daily (0.2%, 10mL) and assistance with toothbrushing 2 times per week for a 3 week period. Type of therapy: Combination (education, mouthwash, professional cleaning) **Oral hygiene intervention (twice a day)** (n=34) Oral hygiene instruction and chlorhexidine mouthrinse twice daily (0.2%, 10mL) for a 3 week period. Type of therapy: Combination (education, mouthwash) **Usual care** (n=33) Oral hygiene instruction only. **Concomitant therapy:** No additional information.	Haemorrhagic: 13 Severity: Not stated/unclear. Dysphagia at baseline: Not stated/unclear. People who are nil-by-mouth at baseline: People who are not nil-by-mouth at baseline.		of the University of Hong Kong. This study reports an intervention twice a day with an additional treatment twice a week. This group was been kept separate to the intervention delivered twice a day only and provided to the committee for their consideration. This study reports gingivitis as a continuous outcome rather than as a dichotomous outcome. As this was not the prioritised reporting method, this outcome has been downgraded for indirectness.
Yuan 2020[16]	**Oral hygiene intervention (three times a day)** (n=56) Intensified oral hygiene interventions in addition to oral self-care (or instead of routine saline swabbing), all teeth and oral soft tissues (including the gingiva, vestibule, buccal mucosa, floor of the mouth, tongue dorsum, and pharynx oralis), were swabbed with	**People after a first or recurrent stroke** Mean age (SD): 58.7 (13.7) years N = 113 Type of stroke: Ischaemic: 50 Intracerebral haemorrhage: 17 Subarachnoid haemorrhage: 17 Severity: Moderate (or NIHSS 5-14).	Mortality at ≤3 months Occurrence of pneumonia at ≤3 months	Setting: One neurological intensive care unit in a hospital in China. Sources of funding: This work was supported by the Beijing Science and Technology Committee (grant number Z151100004015041) and the Beijing Stomatological Hospital Subject Construction Fund (grant number 16-09-20).

Study	Intervention and comparison	Population	Outcomes	Comments
	0.12% chlorhexidine digluconate mouth wash (5-minute duration, 3 times daily). All interventions were performed by nurses who had been trained by a dental professional prior to the commencement of the study. For a duration of 7 days. Type of therapy: Oral swabbing. **Usual care** (n=57) Routine oral hygiene care. People who could not perform oral care by themselves received oral swabbing with saline (2-minute duration, twice daily). **Concomitant therapy:** All participants received usual care.	Dysphagia at baseline: Not stated/unclear People who are nil-by-mouth at baseline: Not stated/unclear.		

1 See Appendix D for full evidence tables.

1.1.6 Summary of the effectiveness evidence

1.1.6.1 Oral hygiene intervention (once a day) compared to usual care

Table 3: Clinical evidence summary: oral hygiene intervention (once a day) compared to usual care

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with usual care	Risk difference with oral hygiene intervention (once a day)	
Mortality at ≤3 months	142 (2 RCTs) follow up: mean 7 weeks	⊕◯◯◯ Very low [a,b]	RR 0.79 (0.27 to 2.37)	93 per 1,000	**20 fewer per 1,000** (68 fewer to 128 more)	MID (precision) = RR 0.80 – 1.25.
Requirement of enteral feeding support (nasogastric tube removal) at ≤3 months	66 (1 RCT) follow up: 6 weeks	⊕◯◯◯ Very low [b,c,d]	RR 3.50 (0.78 to 15.62)	61 per 1,000	**152 more per 1,000** (13 fewer to 886 more)	MID (precision) = RR 0.80 – 1.25.
Oral health outcome scales (Oral Health Assessment Tool, 0-16, lower values are better, final value) at ≤3 months	66 (1 RCT) follow up: 6 weeks	⊕◯◯◯ Very low [d,e]	-	The mean oral health outcome scales was 5.99	**MD 2.57 lower** (3.54 lower to 1.6 lower)	MID = 1.07 (0.5 x median baseline SD)
Dysphagia severity (Functional Oral Intake Scale, 1-7, higher values are better, final value) at ≤3 months	66 (1 RCT) follow up: 6 weeks	⊕◯◯◯ Very low [b,d,e]	-	The mean dysphagia severity was 3.52	**MD 0.42 higher** (0.62 lower to 1.46 higher)	MID = 0.96 (0.5 x median baseline SD)
Presence of oral disease (oral candidiasis - on tongue) at ≤3 months	142 (2 RCTs) follow up: mean 7 weeks	⊕⊕◯◯ Low [a,b]	RR 0.98 (0.75 to 1.28)	493 per 1,000	**10 fewer per 1,000** (123 fewer to 138 more)	MID (precision) = RR 0.80 – 1.25.

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with usual care	Risk difference with oral hygiene intervention (once a day)	
Presence of oral disease (oral candidiasis - in saliva) at ≤3 months	56 (1 RCT) follow up: 2 weeks	⨁◯◯◯ Very low [b,f]	RR 1.02 (0.76 to 1.39)	741 per 1,000	**15 more per 1,000** (178 fewer to 289 more)	MID (precision) = RR 0.80 – 1.25.
Presence of oral disease (gingivitis - gingival index, 0-3, lower values are better, final value) at ≤3 months	56 (1 RCT) follow up: 2 weeks	⨁◯◯◯ Very low [g,h]	-	The mean presence of oral disease was 1.6	**MD 1.13 lower** (1.46 lower to 0.8 lower)	MID = 0.25 (0.5 x median baseline SD)
Length of hospital stay (length of ICU admission, days, lower values are better) at ≤3 months	56 (1 RCT) follow up: 2 weeks	⨁◯◯◯ Very low [b,g,h]	-	The mean length of hospital stay was 18.15 days	**MD 2.46 days lower** (7.21 lower to 2.29 higher)	MID = 4.0 (0.5 x median control group SD)

[a.] Downgraded by 1 increment as the majority of the evidence was at high risk of bias (due to a mixture of bias arising from the randomisation process and bias due to missing outcome data)

[b.] Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

[c.] Downgraded by 1 increment as the majority of the evidence was at high risk of bias (due to bias arising from the randomisation process)

[d.] Downgraded by 1 or 2 increments because of intervention indirectness (as the intervention included was delivered as less than the smallest frequency stated in the protocol)

[e.] Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to a mixture of bias arising from the randomisation process and bias due to deviations from the intended interventions)

[f.] Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process and bias due to missing outcome data)

[g.] Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to a bias arising from the randomisation process, bias due to deviations from the intended interventions and bias due to missing outcome data)

[h.] Downgraded by 1 or 2 increments because of outcome indirectness (continuous scale for an outcome specified to be dichotomous in the protocol)

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1.1.6.2 Oral hygiene intervention (twice a day) compared to usual care

Table 4: Clinical evidence summary: oral hygiene intervention (twice a day) compared to usual care

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with usual care	Risk difference with oral hygiene intervention (twice a day)	
Mortality at ≤3 months	100 (1 RCT) follow up: 2 months	⊕◯◯◯ Very low [a,b]	RR 0.25 (0.03 to 2.16)	80 per 1,000	**60 fewer per 1,000** (78 fewer to 93 more)	MID (precision) = RR 0.80 – 1.25.
Occurrence of pneumonia at ≤3 months	141 (2 RCTs) follow up: mean 8 weeks	⊕⊕◯◯ Low [c,d]	RD 0.00 (-0.04 to 0.04)	0 per 1,000	**0 fewer per 1,000** (40 fewer to 40 more) [e]	MID (precision) = RR 0.80 – 1.25.
Requiring enteral feeding support (FOIS 1-3 at end of trial) at ≤3 months	51 (1 RCT) follow up: 10 days	⊕◯◯◯ Very low [b,f]	RR 0.38 (0.04 to 3.92)	91 per 1,000	**56 fewer per 1,000** (87 fewer to 265 more)	MID (precision) = RR 0.80 – 1.25.
Oral health outcome scales (revised-THROAT, 7-21, lower values are better, final value) at ≤3 months	51 (1 RCT) follow up: 10 days	⊕◯◯◯ Very low [b,f]	-	-	**MD 0.8 lower** (1.68 lower to 0.08 higher)	MID = 1.2 (0.5 x median baseline SD)
Dysphagia severity (progression in FOIS from 4-5 to 6-7 at end of trial) at ≤3 months	51 (1 RCT) follow up: 10 days	⊕◯◯◯ Very low [b,f,g]	RR 1.08 (0.49 to 2.39)	318 per 1,000	**25 more per 1,000** (162 fewer to 442 more)	MID (precision) = RR 0.80 – 1.25.
Presence of oral disease (gingivitis - gingival bleeding index, scale range unclear, lower values are better,	67 (1 RCT) follow up: 3 weeks	⊕◯◯◯ Very low [b,f,g]	-	The mean presence of oral disease was 17.7	**MD 7.7 lower** (24.44 lower to 9.04 higher)	MID = 11.6 (0.5 x median control group SD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with usual care	Risk difference with oral hygiene intervention (twice a day)	
final value) at ≤3 months						

a. Downgraded by 1 increment as the majority of the evidence was at high risk of bias (due to bias arising from the randomisation process)

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 increment as the majority of the evidence was at high risk of bias (due to a mixture of bias arising from the randomisation process and bias due to missing outcome data)

d. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

e. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

f. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process, bias due to deviations from the intended interventions and bias due to missing outcome data)

g. Downgraded by 1 or 2 increments because of outcome indirectness (continuous scale for an outcome specified to be dichotomous in the protocol)

1.1.6.3 Oral hygiene intervention (three times a day) compared to usual care

Table 5: Clinical evidence summary: oral hygiene intervention (three times a day) compared to usual care

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with usual care	Risk difference with oral hygiene intervention (three times a day)	
Mortality at ≤3 months	84 (1 RCT) follow up: 7 days	⨁◯◯◯ Very low [a,b]	RR 0.48 (0.09 to 2.46)	98 per 1,000	**51 fewer per 1,000** (89 fewer to 142 more)	MID (precision) = RR 0.80 – 1.25.
Occurrence of pneumonia at ≤3 months	84 (1 RCT) follow up: 7 days	⨁◯◯◯ Very low [a,b]	RR 0.50 (0.25 to 1.00)	415 per 1,000	**207 fewer per 1,000** (311 fewer to 0 fewer)	MID (precision) = RR 0.80 – 1.25.

a. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process and bias due to missing outcome data)

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.1.6.4 Oral hygiene intervention (four times a day or more) compared to usual care

Table 6: Clinical evidence summary: oral hygiene intervention (four times a day or more) compared to usual care

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with usual care	Risk difference with oral hygiene intervention (four times a day or more)	
Mortality at ≤3 months	203 (1 RCT) follow up: 3 weeks	⊕⊕◯◯ Low [a]	RR 0.79 (0.34 to 1.83)	110 per 1,000	**23 fewer per 1,000** (73 fewer to 91 more)	MID (precision) = RR 0.80 – 1.25.
Occurrence of pneumonia at ≤3 months	203 (1 RCT) follow up: 3 weeks	⊕⊕⊕◯ Moderate [a]	RR 0.14 (0.02 to 1.11)	70 per 1,000	**60 fewer per 1,000** (69 fewer to 8 more)	MID (precision) = RR 0.80 – 1.25.

[a]. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.1.6.4 Oral hygiene intervention (twice a day with additional treatment twice a week) compared to oral hygiene intervention (twice a day)

Table 7: Clinical evidence summary: oral hygiene intervention (twice a day with additional treatment twice a week) compared to oral hygiene intervention (twice a day)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with oral hygiene intervention (twice a day)	Risk difference with oral hygiene intervention (twice a day and additional treatment twice a week)	
Occurrence of pneumonia at ≤3 months	69 (1 RCT) follow up: 3 weeks	⊕◯◯◯ Very low [a,b,c]	RD 0.0 (-0.5 to 0.5)	0 per 1,000	**0 fewer per 1,000** (50 fewer to 50 more) [d]	MID (precision) = RR 0.80 – 1.25.
Presence of oral disease (gingivitis - gingival bleeding index, scale range	69 (1 RCT) follow up: 3 weeks	⊕◯◯◯ Very low [a,e,f]	-	The mean presence of oral disease was 10	**MD 2.4 lower** (10.29 lower to 5.49 higher)	MID = 7.97 (0.5 x median control group SD)

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with oral hygiene intervention (twice a day)	Risk difference with oral hygiene intervention (twice a day and additional treatment twice a week)	
unclear, lower values are better, final value) at ≤3 months						

a. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process and bias due to missing outcome data)

b. Downgraded by 1 increment due to intervention indirectness (due to the intervention being one that is not stated in the protocol but does indicate an increased intensity of oral hygiene intervention)

c. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

d. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

e. Downgraded by 2 increments because of intervention and outcome indirectness (due to the intervention being one that is not stated in the protocol but does indicate an increased intensity of oral hygiene intervention and using a continuous outcome for one specified to be dichotomous in the protocol)

f. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1.1.6.5 Oral hygiene intervention (twice a day with additional treatment twice a week) compared to usual care

Table 8: Clinical evidence summary: oral hygiene intervention (twice a day with additional treatment twice a week) compared to usual care

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with usual care	Risk difference with oral hygiene intervention (twice a day and additional treatment twice a week)	
Occurrence of pneumonia at ≤3 months	68 (1 RCT) follow up: 3 weeks	⊕◯◯◯ Very low [a,b,c]	RD 0.0 (-0.6 to 0.6)	0 per 1,000	**0 fewer per 1,000** (60 fewer to 60 more) [d]	MID (precision) = RR 0.80 – 1.25.

Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects		Comments
				Risk with usual care	Risk difference with oral hygiene intervention (twice a day and additional treatment twice a week)	
Presence of oral disease (gingivitis - gingival bleeding index, scale range unclear, lower values are better, final value) at ≤3 months	68 (1 RCT) follow up: 3 weeks	⨁◯◯◯ Very low [a,e,f]	-	The mean presence of oral disease was 17.7	**MD 10.1 lower** (26.98 lower to 6.78 higher)	MID = 23.2 (0.5 x median control group SD)

a. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process and bias due to missing outcome data)

b. Downgraded by 1 increment because of intervention indirectness (due to the intervention being one that is not stated in the protocol but does indicate an increased intensity of oral hygiene intervention)

c. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

d. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

e. Downgraded by 2 increments because of intervention and outcome indirectness (due to the intervention being one that is not stated in the protocol but does indicate an increased intensity of oral hygiene intervention and using a continuous outcome for one specified to be dichotomous in the protocol)

f. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

1 See Appendix F for full GRADE tables.
2

1.1.7 Economic evidence

1.1.7.1 Included studies

No health economic studies were included.

1.1.7.2 Excluded studies

No relevant health economic studies were excluded due to assessment of limited applicability or methodological limitations.

See also the health economic study selection flow chart in Appendix G

1.1.8 Summary of included economic evidence

No health economic studies were included in this review.

1.1.9 Economic model

New cost-effectiveness analysis was not prioritised in this area.

1.1.10 Unit costs

Oral hygiene interventions may require additional resource use over usual care. In the studies included in the clinical review this varied (see Table 1 for details) and could be due to:

- Different health care professionals undertaking mouth care (for example, a nurse rather than a nursing assistant).
- Increased health care professional time required to undertake mouth care.
- Additional or different consuables (such as electric instead of standard toothbrushes, modified toothbrushes to aid handling, different toothpaste, mouth wash, dental floss, mouth gel and other hygiene related equipment).
- Additional training costs.

Relevant unit costs are provided below to aid consideration of cost effectiveness.

Table 9: Unit costs of health care professionals who may be involved in delivering oral hygiene interventions

Resource	Cost per working hour	Source
Hospital-based staff (cost per working hour)		
Band 4 hospital nurse	£34	PSSRU 2021{, #4635}
Band 5 hospital nurse	£44	
Band 6 hospital nurse	£54	
Band 6 PT/OT/SLT or dietitian	£53	
Band 7 PT/OT	£64	
Dental staff (cost per working hour)		
NHS dentist	£105-£136	PSSRU 2021{, #4635}
Band 6 NHS dental hygienist	~£53[(a)]	
Band 7 NHS dental hygienist	~£64[(a)]	

Abbreviations: OT= occupational therapist; PT= physiotherapist; SLT= speech and language therapist,

Note: Costs per working hour include salary, salary oncosts, overheads (management and other non-care staff costs including administration and estates staff), capital overheads and qualification costs (except for dentist as not available).

(a) Assumed to be similar to other allied healthcare professionals of the same agenda for change band [PT/OT/dietitian/SLT] as not reported by PSSRU.

If an intervention reduces clinical events (such as pneumonia) this may result in cost savings due to treatment costs avoided, reduced length of stay (if already in hospital) or reduced readmission (if discharged).

1.1.11 Evidence statements

Effectiveness/Qualitative

Economic

No relevant economic evaluations were identified.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

The committee included the following outcomes: mortality, person/participant and carer generic health-related quality of life, occurrence of pneumonia, stroke outcome (modified Rankin scale), requirement for enteral feeding support, oral health outcome scales, dysphagia severity, presence of oral disease (including gingivitis, oral candidiasis and denture-induced stomatitis), length of hospital stay, readmission and stroke-specific patient-reported outcome measures (including stroke-specific quality of life measures). All outcomes were considered equally important for decision making and therefore have all been rated as critical. Mortality, occurrence of pneumonia and presence of oral disease were considered important as direct markers of the consequence of poor oral hygiene for people after a stroke. Requirement for enteral feeding support and dysphagia severity was selected as important areas that could be improved by oral hygiene intervention that would have significant benefits for the person. The committee chose to not investigate the rates of dental plaque, as they did not consider this to be critically important for their decision making. The committee chose to investigate these outcomes up to 3 months, as they considered that any improvements would likely be seen before this point and any changes afterwards may be attributable to other factors.

There was limited evidence for most outcomes. Some outcomes were not reported in any of the included studies, including:

- Person/participant and carer generic health-related quality of life
- Stroke outcome (modified Rankin scale)
- Presence of denture-induced stomatitis
- Readmission
- Stroke-specific Patient-Reported Outcome Measures

The committee concluded that while this produced an element of uncertainty, they could still form recommendations based on the information available.

1.1.12.2 The quality of the evidence

Nine randomised controlled trial studies were included in the review. Evidence was available for the following comparisons:

- Oral hygiene intervention (once a day) compared to usual care – 3 studies
- Oral hygiene intervention (twice a day) compared to usual care – 4 studies
- Oral hygiene intervention (three times a day) compared to usual care – 1 study
- Oral hygiene intervention (four times a day) compared to usual care – 1 study

Two additional comparisons, which were not explicitly stated in the protocol, were reported for the committee to consider while making decisions.

- Oral hygiene intervention (twice a day with additional treatment twice a week) compared to oral hygiene intervention (twice a day)
- Oral hygiene intervention (twice a day with additional treatment twice a week) compared to usual care

There were no studies discussing hourly oral care, and different daily frequencies of oral hygiene care were not compared to each other.

The evidence varied from moderate to very low quality, with the majority being of very low quality. Outcomes were commonly downgraded for risk of bias and imprecision. In most cases, it was not possible to conduct a meta-analysis on outcomes as there was limited outcome data reported by the studies. Furthermore, with small sample sizes in the majority of studies, very severe imprecision was seen in most outcomes. Risk of bias was commonly due to bias arising from the randomisation process and bias due to missing outcome data. The quality of some outcomes was further reduced due to indirectness. This included intervention indirectness (where the amount of treatment provided was less than the minimum time category) and outcome indirectness. Where meta-analysis was possible, no inconsistency was seen.

The type of oral hygiene intervention varied between studies. This included interventions where more minimal changes were implemented (such as using an electric toothbrush) and where more substantial changes were made (including professional cleaning). Most commonly, the intervention was a combination of multiple techniques (including tooth brushing [with or without an electrical toothbrush], tongue brushing, oral swabbing, flossing, mouthwash, education and professional cleaning).

The usual care provided varied between studies. This varied from manual toothbrushing with commercial toothpaste, to toothbrushing and sponge stick cleaning, to both of these and mouthwash and lip care. In the case of the trial where an antimicrobial oral gel was used, a placebo oral gel was used in the usual care group. The committee acknowledged this heterogeneity when examining the studies and took this into account when considering the effects of each trial.

The committee concluded that the evidence was of a sufficient quality to make recommendations. They acknowledged the small sample sizes which had an effect on the precision. They noted that 2 of the studies were conducted in stroke units, while others were conducted in neurological intensive care units and rehabilitation wards. Only 1 study was completed in the United Kingdom but the committee agreed that the interventions described could be applied to the NHS and most would be available now, although additional resource would be required for the more intense oral hygiene regimens described.

1.1.12.3 Benefits and harms

1.1.12.3.1 Key uncertainties

The committee noted that there was no evidence for some outcomes, in particular for health-related quality of life. However, the patient and carer representatives were unanimous in emphasising the negative impact of inadequate mouthcare on quality of life, and each had experience of poor practice in this area. They reflected that mouth discomfort would have a significant effect on their ability to participate in other aspects of rehabilitation and would influence their mood throughout the day. It would also affect their ability to taste, and so influence their oral intake adding a further barrier to effective care.

The committee discussed the effect on pneumonia. It is commonly believed that poor mouthcare influences rates of pneumonia. While some comparisons showed evidence of this, in others there was no evidence that rates of pneumonia were affected by oral hygiene

measures. In at least 1 of these studies pneumonia rates were surprisingly low in both arms (no cases), raising questions about the ascertainment methods for pneumonia. Of the 2 other studies showing a reduction in pneumonia rates, 1 was in a population admitted to ICU and so only reflected a subset of the stroke population. People in ICU will have a higher rate of pneumonia than the general stroke population. The other was in acute stroke assessment units and looked at the use of an oral gel 4 times daily in addition to usual care. Overall, the committee agreed that the link between oral health and pneumonia was well accepted, but this review provided only weak evidence that oral health care interventions reduce the incidence.

The committee discussed the effect on mortality. They would have predicted that a reduction in mortality from improved mouth care would be mediated by a reduction in pneumonia, but this is not apparent in some of the studies in this review. This may be because of a failure to report pneumonia consistently, but the committee also reflected that other mechanisms may be relevant, including the effect of good oral hygiene on hydration and nutrition.

There was no evidence investigating oral hygiene interventions completed hourly. The committee noted that this is an important area for people with significant swallowing problems who may require extra support to prevent aspiration. While some studies included participants who were nil-by-mouth who were provided with less frequent interventions, there are people who may require more frequent intervention.

The committee considered whether they could identify the key elements of an oral hygiene care package, but the interventions used were different in each study and it was not possible to do this with confidence. They acknowledged the importance of assessing the individual needs of the person after a stroke. Some people may require more intense care than others, including the use of an electric toothbrush, chlorhexidine mouthwash and suctioning, but this may not be appropriate for all people (for example: people who bite down on their toothbrush may find it harder to use an electric toothbrush, people with sensory differences may find the intensity of some procedures uncomfortable). A person-centred approach should be taken for all interventions and mouth care should be adapted to the needs of the person.

There were no studies comparing different frequencies of oral care to each other, and some evidence of benefit at each of the frequencies described by the studies. The committee decided that providing oral care at least twice a day was important, noting that basic dental advice is that teeth should be cleaned a minimum of 2 times per day.

1.1.12.3.2 Oral hygiene intervention (once a day)

The results showed that, when compared to usual care, there were clinically important benefits from oral hygiene interventions (once a day) for mortality, requirement of enteral feeding support, oral health outcome scales, presence of oral disease (gingivitis only) and length of hospital stay. However, there was no clinically important difference seen in dysphagia severity and presence of oral disease (oral candidiasis only). These outcomes were reported in small studies, with the majority having approximately 30 participants in each study arm. Most outcomes were of very low quality due to risk of bias, imprecision and indirectness.

The committee acknowledged that the interventions included in the evidence for this comparison was unlikely to be the only oral care provided to participants. In 2 cases, the oral hygiene intervention was of high intensity, including professional cleaning in one case, and a combination of suctioning, oral swabbing, toothbrushing, flossing and interdental brushes, being performed 30 minutes prior to swallow training in the other. The latter comparison was downgraded for indirectness as this care was only provided three times a week specifically before swallowing training. They reflected that common guidance is to at least complete tooth brushing with a fluoride-containing toothpaste twice a day and providing care less frequently than this is unlikely to be rigorous enough to maintain oral health. However, more intense care may be required less frequently than this dependent on the needs of the person.

1.1.12.3.3 Oral hygiene intervention (twice a day)

The results showed that, when compared to usual care, there were clinically important benefits from oral hygiene interventions (twice a day) for mortality, requiring enteral feeding support and oral health outcome scales. However, there was no clinically important difference seen in occurrence of pneumonia, dysphagia severity and presence of oral disease (gingivitis). These outcomes were reported in small studies, with the majority having approximately 35 participants in each study arm. Most outcomes were of very low quality, due to risk of bias, imprecision and indirectness.

One study discussed adding an additional intervention three times a week to an intervention twice a day. This showed no clinically important difference to the oral hygiene intervention completed twice a day.

The committee considered this evidence as important for showing the benefit of oral hygiene interventions. They noted that the interventions used were more intense than those regularly offered to people in current practice, including: electric toothbrushing, chlorhexidine mouthwash, flossing, tongue cleaning and lip balm. Each package included education and training for either the person after a stroke, healthcare staff or caregivers to ensure the tools were being used appropriately. While this is more intense than usual care, they also noted that the usual care provided in the studies may be more intense than that currently provided. Expert patient and healthcare staff experience reflected that in some cases oral health care may not be provided twice a day and people may not receive the mouthcare that they require. Given the effect on mortality seen in the evidence, the committee members agreed that regular mouthcare was important to help prevent death as well as a range of additional benefits for quality of life that were not captured in this evidence.

The committee noted that there was an inconsistency in the results for mortality and pneumonia in this comparison. The mortality outcome (including one study) showed a clinically important benefit (leading to 60 fewer deaths per 1000 people), while the occurrence of pneumonia outcome showed no clinically important difference with zero pneumonia events in both study arms. The committee reflected that they would expect the rate of pneumonia to be higher than this in people after stroke (they would expect 20-30% of people after stroke to develop pneumonia). On looking at the evidence, they noted that the Kuo 2016 study, which was included in the mortality outcome, did not report the occurrence of pneumonia. Therefore, it was unclear as to whether these events were linked to pneumonia. The committee discussed that other causes may prevent deaths in people receiving oral hygiene interventions after stroke.

1.1.12.3.4 Oral hygiene intervention (three times a day)

The results showed that, when compared to usual care, there were clinically important benefits from oral hygiene interventions (three times a day) for mortality and occurrence of pneumonia. The outcomes were reported in one study, including approximately 40 participants in each study arm. The outcomes were of very low quality due to risk of bias and imprecision.

There was only 1 study included in the evidence for this comparison. This study looked specifically at oral swabbing with chlorhexidine mouthwash for people in an intensive care unit. The committee noted that a minority of stroke victims are admitted to intensive care and had reservations about the applicability of this study to usual practice.

1.1.12.3.5 Oral hygiene intervention (four times a day)

The results showed that, when compared to usual care, there were clinically important benefits from oral hygiene interventions (4 times a day) for mortality and occurrence of pneumonia. These outcomes were reported in 1 study, including a larger number of

participants (approximately 100 in each study arm). The outcomes ranged from moderate (for occurrence of pneumonia) and low quality (for mortality) due to imprecision.

The committee noted the benefits seen in this one study included in the evidence for this outcome. This study was conducted in England in a group of acute stroke assessment units and was considered directly applicable to NHS practice. They noted that oral gels including antibacterial and antifungal properties may be helpful for people after a stroke to prevent infections. They concluded that this should be assessed based on the needs of the person after a stroke.

1.1.12.3.6 Weighing up the benefits and harms

Weighing up the benefits and the absence of harms from the evidence, and from their committee consensus, it was agreed that oral hygiene should be assessed using standard national or local protocols (such as Mouthcare Matters) to ensure that mouthcare is considered for all people. All people should be encouraged to protect their oral health by brushing their teeth and gums, using an electric or battery-powered toothbrush if needed and using mouthwash and dental gel as needed, at least twice a day. Other measures may be necessary and these can be advised by appropriately trained staff. This may include increased frequency of care (for example: for people at risk of aspiration). Finally, they recommended that people who are suitably trained should deliver or supervise mouth care for people who are not able to do this on their own at this time, acknowledging that not all people may be able to look after their mouth care after a stroke. The committee wanted to emphasise the importance of care being provided at least twice a day, but that more frequent mouthcare may be beneficial and care should be provided as frequently as the person requires.

1.1.12.4 Cost effectiveness and resource use

No relevant health economic analyses were identified for this review; therefore, unit costs were presented to aid committee consideration of cost-effectiveness.

As described above, the studies included in the clinical review varied in terms of the oral hygiene interventions being assessed but would all involve some additional resource use over usual care. It was also noted that usual care comparator in the studies may be more than is current usual NHS practice. Additional costs could relate to different or additional consumables (such as electric toothbrushes or oral gels), the healthcare professionals who delivered the mouth care to patients, the additional staff time required to provide mouth care, and whether training was provided to staff or family members. Four of the 9 studies had a nurse deliver the intervention and the committee noted that mouth care is often delivered by the nursing team in practice, although in some committee members' experience potentially any member of the stroke rehabilitation team could currently be responsible for providing care.

The clinical evidence suggested there may be reductions in oral health problems and pneumonia, and this could potentially result in cost savings due to treatment costs avoided.

The committee discussed that the potential mortality benefit seen in the clinical evidence could result in gains of quality-adjusted life years. The committee also highlighted the potential for quality of life improvements from people simply receiving sufficient oral hygiene treatment. Some members noted that inadequate oral care left stroke patients feeling discomfort, embarrassment and low confidence which can deter them from engaging in therapy. Poor mouth care hinders speech and language therapists from providing treatment to patients as well. These benefits are difficult to formally assess due to the lack of quality of life data from the clinical review.

The committee took the uncertainties in cost effectiveness into consideration when making recommendations. They agreed that the potential health benefits of improved oral hygiene

were likely to justify additional resource use. It was also noted that twice daily mouthcare is the national standard for oral hygiene and should be facilitated as part of the essential requirements of care.

The committee agreed it was difficult to judge whether there was likely to be a substantial resource impact from the recommendations due to a number of uncertainties including a lack of information about what mouth care is currently being provided to stroke patients, difficulties estimating the number of people where additional intervention would be required and uncertainty about what downstream cost savings might be realisable. The committee noted that the number of people who require assistance with mouthcare after stroke was likely to be a fairly large proportion of the stroke population as it will include people who experience a range of issues such as dysphagia, sensory loss, lack of balance, limited upper limb function and those who are nil-by-mouth. The committee agreed that current practice is variable, and patients often report a lack of support for mouth care. However, it was also highlighted that there is an existing NHS initiative (Mouth Care Matters) that aims to improve mouth care in hospitals including for those requiring assistance. There could be a significant resource impact if interventions such as electric toothbrushes were routinely provided for all stroke patients due to their cost, however, the committee recommended that use of such interventions should be based on individual assessment of need and so would not be applicable to the entire stroke population. The committee noted that mouth care training should already be available to healthcare professionals involved in delivering it. Appropriate training to family members or carers may incur additional resource use to the NHS as this is beyond current practice for some areas in the UK. The committee highlighted that training is important to ensure that effective oral hygiene is being offered and to prevent complications.

1.1.12.5 Other factors the committee took into account

The committee acknowledged the importance of empowering the person after stroke to complete mouth care themselves as far as they can, to support their return to independence. Adjustments may be needed to help the person to do this. Where this is not possible, caregivers should work with the person to complete mouth care. The committee noted that a holistic approach is needed for this, as people may be unable to complete oral care for a variety of reasons (for example: memory problems, visual neglect, physical difficulties in using a sink, sensory sensitivities).

The committee noted that a variety of healthcare professionals and other individuals may be involved in providing mouthcare. This included:

- Healthcare assistants
- Nurses
- Family members/carers
- Speech and language therapists
- Physiotherapists
- Occupational therapists
- Doctors
- Dentists and dental hygienists
- Volunteers

They noted that anyone providing help with mouth care should have the appropriate training to complete the task. This is particularly important for people with dysphagia and people who are nil-by-mouth, as extra considerations may need to be taken to ensure mouth care is provided safely.

The effect of poor oral care on the work of professionals was discussed. Speech and language therapists on the committee explained that they would require someone to have had good mouth care before completing swallowing assessments, as if this is not achieved

then it may lead to poorer outcomes. When this is not completed beforehand, they may not be able to do swallowing assessments on that day, which can have an effect on providing holistic rehabilitation care and supporting discharge from hospital care.

The committee noted that currently recording of mouth care in healthcare services is not consistent across the country. Given the potential impact mouth care interventions could have, they would encourage that consistent monitoring is used by services and that this could be an important area for auditing in the future.

Mouth care is considered in other NICE guidance, including NG48: Oral health for adults in care homes. This includes the consideration of assessment of mouth care. The committee took this into consideration when making the recommendation about assessment of oral hygiene. Ultimately they agreed that any national or local protocol that is agreed as acceptable would be relevant to use, as they noted that some are currently used (such as Mouthcare Matters), and that use of these protocols may be useful for ensuring continuity of practice.

The previous version of this guidance from 2013 included the following guidance:

1.7.3 Ensure that effective mouth care is given to people with difficulty swallowing after stroke, in order to decrease the risk of aspiration pneumonia.

The committee considered the new recommendation to contain this information and provide clearer guidance to help support people with difficulty swallowing after stroke.

1.1.13 Recommendations supported by this evidence review

This evidence review supports recommendations 1.10.1 to 1.10.3.

1.1.14 References

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Appendices

Appendix A – Review protocols

Review protocol for the clinical and cost-effectiveness of interventions for oral hygiene

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):

<table>
<tr><td></td><td></td><td colspan="3">• 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</td></tr>
<tr><td rowspan="7">18.</td><td rowspan="7">Type and method of review</td><td>☒</td><td colspan="2">Intervention</td></tr>
<tr><td>☐</td><td colspan="2">Diagnostic</td></tr>
<tr><td>☐</td><td colspan="2">Prognostic</td></tr>
<tr><td>☐</td><td colspan="2">Qualitative</td></tr>
<tr><td>☐</td><td colspan="2">Epidemiologic</td></tr>
<tr><td>☐</td><td colspan="2">Service Delivery</td></tr>
<tr><td>☐</td><td colspan="2">Other (please specify)</td></tr>
<tr><td>19.</td><td>Language</td><td colspan="3">English</td></tr>
<tr><td>20.</td><td>Country</td><td colspan="3">England</td></tr>
<tr><td>21.</td><td>Anticipated or actual start date</td><td colspan="3">24/02/2021</td></tr>
<tr><td>22.</td><td>Anticipated completion date</td><td colspan="3">14/12/2022</td></tr>
<tr><td rowspan="3">23.</td><td rowspan="3">Stage of review at time of this submission</td><td>Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td>Preliminary searches</td><td>☐</td><td>☐</td></tr>
<tr><td>Piloting of the study selection process</td><td>☐</td><td>☐</td></tr>
</table>

		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	

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1 Review protocol for health economic literature review

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below. Databases searched: • Centre for Reviews and Dissemination NHS Economic Evaluations Database (NHS EED) – all years (closed to new records April 2015) • Centre for Reviews and Dissemination Health Technology Assessment database – all years (closed to new records March 2018) • International HTA database (INAHTA) – all years • Medline and Embase – from 2014 (due to NHS EED closure)
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2006 (including those included in the previous guideline), abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[15] Studies published in 2006 or later that were included in the previous guideline will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified. **Inclusion and exclusion criteria** • If a study is rated as both 'Directly applicable' and with 'Minor limitations' then it will be included in the guideline. A health economic evidence table will be completed and it will be included in the health economic evidence profile. • If a study is rated as either 'Not applicable' or with 'Very serious limitations' then it will usually be excluded from the guideline. If it is excluded then a health economic evidence table will not be completed and it will not be included in the health economic evidence profile. • If a study is rated as 'Partially applicable', with 'Potentially serious limitations' or both then there is discretion over whether it should be included. **Where there is discretion** The health economist will make a decision based on the relative applicability and quality of the available evidence for that question, in discussion with the guideline committee if required. The ultimate aim is to include health economic studies that are helpful for decision-making in the context of the guideline and the current NHS setting. If several studies are considered of sufficiently high applicability and

	methodological quality that they could all be included, then the health economist, in discussion with the committee if required, may decide to include only the most applicable studies and to selectively exclude the remaining studies. All studies excluded on the basis of applicability or methodological limitations will be listed with explanation in the excluded health economic studies appendix below. The health economist will be guided by the following hierarchies. *Setting:* • UK NHS (most applicable). • OECD countries with predominantly public health insurance systems (for example, France, Germany, Sweden). • OECD countries with predominantly private health insurance systems (for example, Switzerland). • Studies set in non-OECD countries or in the USA will be excluded before being assessed for applicability and methodological limitations. *Health economic study type:* • Cost–utility analysis (most applicable). • Other type of full economic evaluation (cost–benefit analysis, cost-effectiveness analysis, cost–consequences analysis). • Comparative cost analysis. • Non-comparative cost analyses including cost-of-illness studies will be excluded before being assessed for applicability and methodological limitations. *Year of analysis:* • The more recent the study, the more applicable it will be. • Studies published in 2006 or later (including any such studies included in the previous guideline) but that depend on unit costs and resource data entirely or predominantly from before 2006 will be rated as 'Not applicable'. • Studies published before 2006 (including any such studies included in the previous guideline) will be excluded before being assessed for applicability and methodological limitations. *Quality and relevance of effectiveness data used in the health economic analysis:* • The more closely the clinical effectiveness data used in the health economic analysis match with the outcomes of the studies included in the clinical review the more useful the analysis will be for decision-making in the guideline.

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Appendix B – Literature search strategies

B.1 Clinical search literature search strategy

Searches were constructed using a PICO framework where population (P) terms were combined with Intervention (I) and in some cases Comparison (C) terms. Outcomes (O) are rarely used in search strategies as these concepts may not be indexed or described in the title or abstract and are therefore difficult to retrieve. Search filters were applied to the search where appropriate.

Table 10: Database parameters, filters and limits applied

Database	Dates searched	Search filter used
Medline (OVID)	1946 – 08 January 2023	Randomised controlled trials Systematic review studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
Embase (OVID)	1974 – 08 January 2023	Randomised controlled trials Systematic review studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
The Cochrane Library (Wiley)	Cochrane Reviews to 2023 Issue 1 of 12 CENTRAL to 2023 Issue 1 of 12	Exclusions (clinical trials, conference abstracts)
Epistemonikos (The Epistemonikos Foundation)	Inception – 08 January 2023	Exclusions (Cochrane reviews) English language

Medline (Ovid) search terms

1.	exp Stroke/
2.	Stroke Rehabilitation/
3.	exp Cerebral Hemorrhage/
4.	(stroke or strokes or cva or poststroke* or apoplexy or "cerebrovascular accident").ti,ab.
5.	((cerebro* or brain or brainstem or cerebral*) adj3 (infarct* or accident*)).ti,ab.
6.	"brain attack*".ti,ab.
7.	or/1-6
8.	letter/

9.	editorial/
10.	news/
11.	exp historical article/
12.	Anecdotes as Topic/
13.	comment/
14.	case report/
15.	(letter or comment*).ti.
16.	or/8-15
17.	randomized controlled trial/ or random*.ti,ab.
18.	16 not 17
19.	animals/ not humans/
20.	exp Animals, Laboratory/
21.	exp Animal Experimentation/
22.	exp Models, Animal/
23.	exp Rodentia/
24.	(rat or rats or mouse or mice or rodent*).ti.
25.	or/18-24
26.	7 not 25
27.	limit 26 to English language
28.	Oral health/
29.	exp Oral hygiene/
30.	((dental or oral or buccal cavity or periodontal or interdental) adj3 (device* or care or caring or hygien* or prophylaxis or health* or brush* or clean* or "look* after" or intervention* or treatment*)).ti,ab.
31.	((gum* or mouth or teeth or tooth or denture*) adj3 (care or caring or hygien* or prophylaxis or health* or brush* or clean* or "look* after")).ti,ab.
32.	((dental or oral or buccal cavity or periodontal or interdental or gum* or mouth or teeth or tooth or denture*) adj3 (educ* or inform* or instruct* or deliver* or carer*)).ti,ab.
33.	Chlorhexidine/
34.	(toothbrush* or toothpaste* or tooth paste* or dental floss* or water irrigat* or water pick* or gingival stimulator* or mouth wash* or mouthwash* or mouth rins* or mouthrins* or chlorhexidine or plaque remov*).ti,ab.
35.	((dental or oral or periodontal or gum*) and disease*).ti,ab.
36.	((dental or tooth or teeth) and (caries or decay*)).ti,ab.
37.	(breath adj (bad or smell* or odour or odor)).ti,ab.
38.	(gingivitis or halitosis).ti,ab.
39.	or/28-38
40.	27 and 39
41.	randomized controlled trial.pt.
42.	controlled clinical trial.pt.
43.	randomi#ed.ti,ab.
44.	placebo.ab.
45.	randomly.ti,ab.
46.	Clinical Trials as topic.sh.
47.	trial.ti.
48.	or/41-47

49.	Meta-Analysis/
50.	exp Meta-Analysis as Topic/
51.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
52.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
53.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
54.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
55.	(search* adj4 literature).ab.
56.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
57.	cochrane.jw.
58.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
59.	or/49-58
60.	40 and (48 or 59)

1 **Embase (Ovid) search terms**

1.	exp Cerebrovascular accident/
2.	exp Brain infarction/
3.	Stroke Rehabilitation/
4.	(stroke or strokes or cva or poststroke* or apoplexy or "cerebrovascular accident").ti,ab.
5.	((cerebro* or brain or brainstem or cerebral*) adj3 (infarct* or accident*)).ti,ab.
6.	"brain attack*".ti,ab.
7.	Intracerebral hemorrhage/
8.	or/1-7
9.	letter.pt. or letter/
10.	note.pt.
11.	editorial.pt.
12.	case report/ or case study/
13.	(letter or comment*).ti.
14.	(conference abstract or conference paper).pt.
15.	or/9-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animal/ not human/
19.	nonhuman/
20.	exp Animal Experiment/
21.	exp Experimental Animal/
22.	animal model/
23.	exp Rodent/
24.	(rat or rats or mouse or mice).ti.
25.	or/17-24
26.	8 not 25
27.	limit 26 to English language
28.	Dental health/

29.	exp Mouth hygiene/
30.	((dental or oral or buccal cavity or periodontal or interdental) adj3 (device* or care or caring or hygien* or prophylaxis or health* or brush* or clean* or "look* after" or intervention* or treatment*)).ti,ab.
31.	((gum* or mouth or teeth or tooth or denture*) adj3 (care or caring or hygien* or prophylaxis or health* or brush* or clean* or "look* after")).ti,ab.
32.	((dental or oral or buccal cavity or periodontal or interdental or gum* or mouth or teeth or tooth or denture*) adj3 (educ* or inform* or instruct* or deliver* or carer*)).ti,ab.
33.	Chlorhexidine/
34.	(toothbrush* or toothpaste* or tooth paste* or dental floss* or water irrigat* or water pick* or gingival stimulator* or mouth wash* or mouthwash* or mouth rins* or mouthrins* or chlorhexidine or plaque remov*).ti,ab.
35.	((dental or oral or periodontal or gum*) and disease*).ti,ab.
36.	((dental or tooth or teeth) and (caries or decay*)).ti,ab.
37.	(breath adj (bad or smell* or odour or odor)).ti,ab.
38.	(gingivitis or halitosis).ti,ab.
39.	or/28-38
40.	27 and 39
41.	random*.ti,ab.
42.	factorial*.ti,ab.
43.	(crossover* or cross over*).ti,ab.
44.	((doubl* or singl*) adj blind*).ti,ab.
45.	(assign* or allocat* or volunteer* or placebo*).ti,ab.
46.	crossover procedure/
47.	single blind procedure/
48.	randomized controlled trial/
49.	double blind procedure/
50.	or/41-49
51.	systematic review/
52.	meta-analysis/
53.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
54.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
55.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
56.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
57.	(search* adj4 literature).ab.
58.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
59.	cochrane.jw.
60.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
61.	or/51-60
62.	40 and (50 or 61)

1 **Cochrane Library (Wiley) search terms**

#1.	MeSH descriptor: [Stroke] explode all trees
#2.	MeSH descriptor: [Stroke Rehabilitation] explode all trees

#3.	MeSH descriptor: [Cerebral Hemorrhage] explode all trees
#4.	(stroke or strokes or cva or poststroke* or apoplexy or "cerebrovascular accident"):ti,ab
#5.	((cerebro* or brain or brainstem or cerebral*) near/3 (infarct* or accident*)):ti,ab
#6.	brain attack*:ti,ab
#7.	(or #1-#6)
#8.	conference:pt or (clinicaltrials or trialsearch):so
#9.	#7 not #8
#10.	MeSH descriptor: [Oral Health] explode all trees
#11.	MeSH descriptor: [Oral Hygiene] explode all trees
#12.	((dental or oral or buccal cavity or periodontal or interdental) adj3 (device* or care or caring or hygien* or prophylaxis or health* or brush* or clean* or "look* after" or intervention* or treatment*)):ti,ab
#13.	((gum* or mouth or teeth or tooth or denture*) near/3 (care or caring or hygien* or prophylaxis or health* or brush* or clean* or "look* after")):ti,ab
#14.	((dental or oral or buccal cavity or periodontal or interdental or gum* or mouth or teeth or tooth or denture*) near/3 (educ* or inform* or instruct* or deliver* or carer*)):ti,ab
#15.	MeSH descriptor: [Chlorhexidine] explode all trees
#16.	(toothbrush* or toothpaste* or tooth paste* or dental floss* or water irrigat* or water pick* or gingival stimulator* or mouth wash* or mouthwash* or mouth rins* or mouthrins* or chlorhexidine or plaque remov*):ti,ab
#17.	((dental or oral or periodontal or gum*) and disease*):ti,ab
#18.	((dental or tooth or teeth) and (caries or decay*)):ti,ab
#19.	(breath near/1 (bad or smell* or odour or odor)):ti,ab
#20.	(gingivitis or halitosis):ti,ab
#21.	(or #10-#20)
#22.	#9 and #21

1 **Epistemonikos search terms**

1.	(title:((title:((title:(dental OR oral OR buccal cavity OR periodontal OR interdental) OR abstract:(dental OR oral OR buccal cavity OR periodontal OR interdental)) AND (title:(care OR caring OR hygien* OR prophylaxis OR health* OR brush* OR clean*) OR abstract:(care OR caring OR hygien* OR prophylaxis OR health* OR brush* OR clean*))) OR abstract:((title:(dental OR oral OR buccal cavity OR periodontal OR interdental) OR abstract:(dental OR oral OR buccal cavity OR periodontal OR interdental)) AND (title:(care OR caring OR hygien* OR prophylaxis OR health* OR brush* OR clean*) OR abstract:(care OR caring OR hygien* OR prophylaxis OR health* OR brush* OR clean*)))) AND (title:((stroke OR strokes OR cva OR poststroke* OR apoplexy OR "cerebrovascular accident")) OR abstract:((stroke OR strokes OR cva OR poststroke* OR apoplexy OR "cerebrovascular accident")))) OR abstract:((title:((title:(dental OR oral OR buccal cavity OR periodontal OR interdental) OR abstract:(dental OR oral OR buccal cavity OR periodontal OR interdental)) AND (title:(care OR caring OR hygien* OR prophylaxis OR health* OR brush* OR clean*) OR abstract:(care OR caring OR hygien* OR prophylaxis OR health* OR brush* OR clean*))) OR abstract:((title:(dental OR oral OR buccal cavity OR periodontal OR interdental) OR abstract:(dental OR oral OR buccal cavity OR periodontal OR interdental)) AND (title:(care OR caring OR hygien* OR prophylaxis OR health* OR brush* OR clean*) OR abstract:(care OR caring OR hygien* OR prophylaxis OR health* OR brush* OR clean*)))) AND (title:((stroke OR strokes OR cva OR poststroke* OR apoplexy OR "cerebrovascular accident")) OR abstract:((stroke OR strokes OR cva OR poststroke* OR apoplexy OR "cerebrovascular accident")))))

B.2 Health Economics literature search strategy

Health economic evidence was identified by conducting searches using terms for a broad Stroke Rehabilitation population. The following databases were searched: NHS Economic Evaluation Database (NHS EED - this ceased to be updated after 31st March 2015), Health Technology Assessment database (HTA - this ceased to be updated from 31st March 2018) and The International Network of Agencies for Health Technology Assessment (INAHTA). Searches for recent evidence were run on Medline and Embase from 2014 onwards for health economics, and all years for quality-of-life studies. Additional searches were run in CINAHL and PsycInfo looking for health economic evidence.

Table 2: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 08 January 2023	Health economics studies Quality of life studies Exclusions (animal studies, letters, comments, editorials, case studies/reports,) English language
	Quality of Life 1946 – 08 January 2023	
Embase (OVID)	Health Economics 1 January 2014 – 08 January 2023	Health economics studies Quality of life studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
	Quality of Life 1974 – 08 January 2023	
NHS Economic Evaluation Database (NHS EED) (Centre for Research and Dissemination - CRD)	Inception –31st March 2015	
Health Technology Assessment Database (HTA) (Centre for Research and Dissemination – CRD)	Inception – 31st March 2018	
The International Network of Agencies for Health Technology Assessment (INAHTA)	Inception - 08 January 2023	English language
PsycINFO (OVID)	1 January 2014 – 08 January 2023	Health economics studies Exclusions (animal studies, letters, case reports) Human English language

Database	Dates searched	Search filters and limits applied
Current Nursing and Allied Health Literature - CINAHL (EBSCO)	1 January 2014 – 08 January 2023	Health economics studies Exclusions (Medline records, animal studies, letters, editorials, comments, theses) Human English language

1 **Medline (Ovid) search terms**

1.	exp Stroke/
2.	exp Cerebral Hemorrhage/
3.	(stroke or strokes or cva or poststroke* or apoplexy or "cerebrovascular accident").ti,ab.
4.	((cerebro* or brain or brainstem or cerebral*) adj3 (infarct* or accident*)).ti,ab.
5.	"brain attack*".ti,ab.
6.	or/1-5
7.	letter/
8.	editorial/
9.	news/
10.	exp historical article/
11.	Anecdotes as Topic/
12.	comment/
13.	case report/
14.	(letter or comment*).ti.
15.	or/7-14
16.	randomized controlled trial/ or random*.ti,ab.
17.	15 not 16
18.	animals/ not humans/
19.	exp Animals, Laboratory/
20.	exp Animal Experimentation/
21.	exp Models, Animal/
22.	exp Rodentia/
23.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/17-23
25.	6 not 24
26.	Economics/
27.	Value of life/
28.	exp "Costs and Cost Analysis"/
29.	exp Economics, Hospital/

30.	exp Economics, Medical/
31.	Economics, Nursing/
32.	Economics, Pharmaceutical/
33.	exp "Fees and Charges"/
34.	exp Budgets/
35.	budget*.ti,ab.
36.	cost*.ti.
37.	(economic* or pharmaco?economic*).ti.
38.	(price* or pricing*).ti,ab.
39.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
40.	(financ* or fee or fees).ti,ab.
41.	(value adj2 (money or monetary)).ti,ab.
42.	or/26-41
43.	quality-adjusted life years/
44.	sickness impact profile/
45.	(quality adj2 (wellbeing or well being)).ti,ab.
46.	sickness impact profile.ti,ab.
47.	disability adjusted life.ti,ab.
48.	(qal* or qtime* or qwb* or daly*).ti,ab.
49.	(euroqol* or eq5d* or eq 5*).ti,ab.
50.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
51.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
52.	(hui or hui1 or hui2 or hui3).ti,ab.
53.	(health* year* equivalent* or hye or hyes).ti,ab.
54.	discrete choice*.ti,ab.
55.	rosser.ti,ab.
56.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
57.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
58.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
59.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
60.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
61.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
62.	or/43-61
63.	25 and 42
64.	25 and 62
65.	limit 63 to English language
66.	limit 64 to English language

1 Embase (Ovid) search terms

1.	exp Cerebrovascular accident/

2.	exp Brain infarction/
3.	(stroke or strokes or cva or poststroke* or apoplexy or "cerebrovascular accident").ti,ab.
4.	((cerebro* or brain or brainstem or cerebral*) adj3 (infarct* or accident*)).ti,ab.
5.	"brain attack*".ti,ab.
6.	Intracerebral hemorrhage/
7.	or/1-6
8.	letter.pt. or letter/
9.	note.pt.
10.	editorial.pt.
11.	case report/ or case study/
12.	(letter or comment*).ti.
13.	or/8-12
14.	randomized controlled trial/ or random*.ti,ab.
15.	13 not 14
16.	animal/ not human/
17.	nonhuman/
18.	exp Animal Experiment/
19.	exp Experimental Animal/
20.	animal model/
21.	exp Rodent/
22.	(rat or rats or mouse or mice).ti.
23.	or/15-22
24.	7 not 23
25.	health economics/
26.	exp economic evaluation/
27.	exp health care cost/
28.	exp fee/
29.	budget/
30.	funding/
31.	budget*.ti,ab.
32.	cost*.ti.
33.	(economic* or pharmaco?economic*).ti.
34.	(price* or pricing*).ti,ab.
35.	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
36.	(financ* or fee or fees).ti,ab.
37.	(value adj2 (money or monetary)).ti,ab.
38.	or/25-37
39.	quality adjusted life year/
40.	"quality of life index"/
41.	short form 12/ or short form 20/ or short form 36/ or short form 8/

42.	sickness impact profile/
43.	(quality adj2 (wellbeing or well being)).ti,ab.
44.	sickness impact profile.ti,ab.
45.	disability adjusted life.ti,ab.
46.	(qal* or qtime* or qwb* or daly*).ti,ab.
47.	(euroqol* or eq5d* or eq 5*).ti,ab.
48.	(qol* or hql* or hqol* or h qol* or hrqol* or hr qol*).ti,ab.
49.	(health utility* or utility score* or disutilit* or utility value*).ti,ab.
50.	(hui or hui1 or hui2 or hui3).ti,ab.
51.	(health* year* equivalent* or hye or hyes).ti,ab.
52.	discrete choice*.ti,ab.
53.	rosser.ti,ab.
54.	(willingness to pay or time tradeoff or time trade off or tto or standard gamble*).ti,ab.
55.	(sf36* or sf 36* or short form 36* or shortform 36* or shortform36*).ti,ab.
56.	(sf20 or sf 20 or short form 20 or shortform 20 or shortform20).ti,ab.
57.	(sf12* or sf 12* or short form 12* or shortform 12* or shortform12*).ti,ab.
58.	(sf8* or sf 8* or short form 8* or shortform 8* or shortform8*).ti,ab.
59.	(sf6* or sf 6* or short form 6* or shortform 6* or shortform6*).ti,ab.
60.	or/39-59
61.	limit 24 to English language
62.	38 and 61
63.	60 and 61

1 **NHS EED and HTA (CRD) search terms**

#1.	MeSH DESCRIPTOR Stroke EXPLODE ALL TREES
#2.	MeSH DESCRIPTOR Cerebral Hemorrhage EXPLODE ALL TREES
#3.	(stroke* or cva or poststroke* or apoplexy or "cerebrovascular accident")
#4.	(((cerebro* or brain or brainstem or cerebral*) adj3 (infarct* or accident*)))
#5.	("brain attack*")
#6.	#1 OR #2 OR #3 OR #4 OR #5

2 **INAHTA search terms**

1.	(brain attack*) OR (((cerebro* or brain or brainstem or cerebral*) and (infarct* or accident*))) OR ((stroke or strokes or cva or poststroke* or apoplexy or "cerebrovascular accident")) OR ("Cerebral Hemorrhage"[mhe]) OR ("Stroke"[mhe])

3 **CINAHL search terms**

1.	MH "Economics+"
2.	MH "Financial Management+"
3.	MH "Financial Support+"
4.	MH "Financing, Organized+"
5.	MH "Business+"
6.	S2 OR S3 or S4 OR S5
7.	S1 not S6
8.	MH "Health Resource Allocation"

9.	MH "Health Resource Utilization"
10.	S8 OR S9
11.	S7 OR S10
12.	(cost or costs or economic* or pharmacoeconomic* or price* or pricing*) OR AB (cost or costs or economic* or pharmacoeconomic* or price* or pricing*)
13.	S11 OR S12
14.	PT editorial
15.	PT letter
16.	PT commentary
17.	S14 or S15 or S16
18.	S13 NOT S17
19.	MH "Animal Studies"
20.	(ZT "doctoral dissertation") or (ZT "masters thesis")
21.	S18 NOT (S19 OR S20)
22.	PY 2014-
23.	S21 AND S22
24.	MW Stroke or MH Cerebral Hemorrhage
25.	stroke* or cva or poststroke* or apoplexy or "cerebrovascular accident"
26.	(cerebro* OR brain OR brainstem OR cerebral*) AND (infarct* OR accident*)
27.	"brain attack*"
28.	S24 OR S25 OR S26 OR S27
29.	S23 AND S28

1 **PsycINFO search terms**

1.	exp Stroke/
2.	exp Cerebral hemorrhage/
3.	(stroke or strokes or cva or poststroke* or apoplexy or "cerebrovascular accident").ti,ab.
4.	((cerebro* or brain or brainstem or cerebral*) adj3 (infarct* or accident*)).ti,ab.
5.	"brain attack*".ti,ab.
6.	Cerebrovascular accidents/
7.	exp Brain damage/
8.	(brain adj2 injur*).ti.
9.	or/1-8
10.	Letter/
11.	Case report/
12.	exp Rodents/
13.	or/10-12
14.	9 not 13
15.	limit 14 to (human and english language)
16.	First posting.ps.
17.	15 and 16
18.	15 or 17

19	"costs and cost analysis"/
20.	"Cost Containment"/
21.	(economic adj2 evaluation$).ti,ab.
22.	(economic adj2 analy$).ti,ab.
23.	(economic adj2 (study or studies)).ti,ab.
24.	(cost adj2 evaluation$).ti,ab.
25.	(cost adj2 analy$).ti,ab.
26.	(cost adj2 (study or studies)).ti,ab.
27.	(cost adj2 effective$).ti,ab.
28.	(cost adj2 benefit$).ti,ab.
29.	(cost adj2 utili$).ti,ab.
30.	(cost adj2 minimi$).ti,ab.
31.	(cost adj2 consequence$).ti,ab.
32.	(cost adj2 comparison$).ti,ab.
33.	(cost adj2 identificat$).ti,ab.
34.	(pharmacoeconomic$ or pharmaco-economic$).ti,ab.
35.	or/19-34
36.	(0003-4819 or 0003-9926 or 0959-8146 or 0098-7484 or 0140-6736 or 0028-4793 or 1469-493X).is.
37.	35 not 36
38.	18 and 37

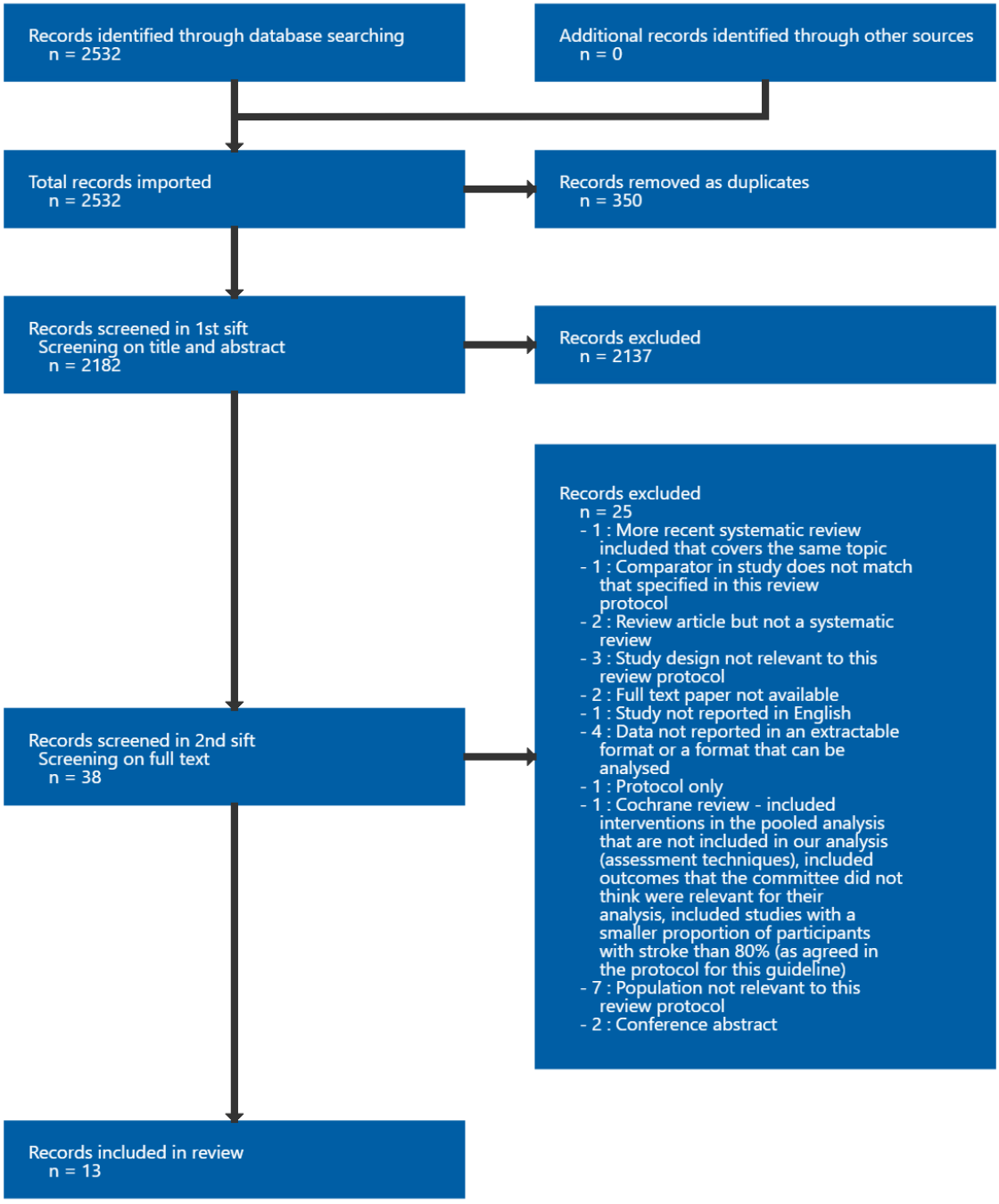
1

2

3

Appendix C – Effectiveness evidence study selection

Figure 1: Flow chart of clinical study selection for the review of oral hygiene interventions for people after a first or recurrent stroke



Appendix D – Effectiveness evidence

Ab Malik, 2018

Bibliographic Reference	Ab Malik, N.; Abdul Razak, F.; Mohamad Yatim, S.; Lam, O. L. T.; Jin, L.; Li, L. S. W.; McGrath, C.; Oral Health Interventions Using Chlorhexidine-Effects on the Prevalence of Oral Opportunistic Pathogens in Stroke Survivors: A Randomized Clinical Trial; The Journal of Evidencebased Dental Practice; 2018; vol. 18 (no. 2); 99-109

Study details

Secondary publication of another included study- see primary study for details	Ab Malik, N.; Mohamad Yatim, S.; Abdul Razak, F.; Lam, O. L. T.; Jin, L.; Li, L. S. W.; McGrath, C.; A multi-centre randomised clinical trial of oral hygiene interventions following stroke-A 6-month trial; Journal of Oral Rehabilitation; 2018; vol. 45 (no. 2); 132-139

Ab Malik, 2018

Bibliographic Reference	Ab Malik, N.; Mohamad Yatim, S.; Abdul Razak, F.; Lam, O. L. T.; Jin, L.; Li, L. S. W.; McGrath, C.; A multi-centre randomised clinical trial of oral hygiene interventions following stroke-A 6-month trial; Journal of Oral Rehabilitation; 2018; vol. 45 (no. 2); 132-139

1 **Study details**

Secondary publication of another included study- see primary study for details	No additional information.
Other publications associated with this study included in review	Ab Malik, N.; Abdul Razak, F.; Mohamad Yatim, S.; Lam, O. L. T.; Jin, L.; Li, L. S. W.; McGrath, C.; Oral Health Interventions Using Chlorhexidine-Effects on the Prevalence of Oral Opportunistic Pathogens in Stroke Survivors: A Randomized Clinical Trial; The Journal of Evidencebased Dental Practice; 2018; vol. 18 (no. 2); 99-109
Trial name / registration number	National Medical Research Register (Ministry of Health; Malaysia): NMRR-13-1664-17247(IIR).
Study type	Randomised controlled trial (RCT)
Study location	Malaysia.
Study setting	Five public hospitals in Malayasia.
Study dates	June 2015 to August 2016.
Sources of funding	No additional information.
Inclusion criteria	Hospitalised stroke patients managed by a stroke rehabilitation team with a Modified Barthel Index score of less than 70; cognizant to follow instructions; deemed medically stable by attending physician
Exclusion criteria	Receiving antibiotics or antimicrobial agents; edentulous
Recruitment / selection of participants	No additional information.
Intervention(s)	Oral hygiene intervention (once a day) N=38 "Intense method for plaque control" - daily powered tooth brushing (Oral B(R) Pro-Health DB4010) with a 1% Chlorhexidine gel.

Comparator	Usual care N=48 "Conventional method for plaque control" - daily manual tooth brushing (Oral B(R) - super thin and extra soft bristles) with a standardised commercial toothpaste (Colgate (R) Maximum Cavity Protection)
Number of participants	86
Duration of follow-up	6 months (reports outcomes at 3 months and 6 months, in this review we will accept outcomes reported at 3 months for inclusion in our analysis).
Additional comments	No additional information.
Subgroup 1: Severity (as stated by category or as measured by NIHSS scale)	Not stated/unclear
Subgroup 2: Type of stroke (using the Bamford scale)	Not stated/unclear
Subgroup 3: Dysphagia at baseline	Not stated/unclear
Subgroup 4: Type of intervention	Combinations of the above
Subgroup 5: People who are nil-by-mouth at baseline	Not stated/unclear
Subgroup analysis - further details	Type of stroke: Reported haemorrhagic and ischaemic (majority ischaemic). Type of intervention: Powered toothbrush and chlorhexidine toothpaste.

Study arms

Oral hygiene intervention (once a day) (N = 38)

"Intense method for plaque control" - daily powered tooth brushing (Oral B(R) Pro-Health DB4010) with a 1% Chlorhexidine gel.

Usual care (N = 48)

"Conventional method for plaque control" - daily manual tooth brushing (Oral B(R) - super thin and extra soft bristles) with a standardised commercial toothpaste (Colgate (R) Maximum Cavity Protection)

Characteristics

Arm-level characteristics

Characteristic	Oral hygiene intervention (once a day) (N = 38)	Usual care (N = 48)
% Female Sample size	n = 14 ; % = 36.8	n = 20 ; % = 41.7
20-39 years Sample size	n = 6 ; % = 15.8	n = 7 ; % = 14.6
<40 years Sample size	n = 32 ; % = 84.2	n = 41 ; % = 85.4
Malay ethnicity Sample size	n = 27 ; % = 71.1	n = 35 ; % = 72.9

Characteristic	Oral hygiene intervention (once a day) (N = 38)	Usual care (N = 48)
Less than or equal to 1 comorbidity Sample size	n = 19 ; % = 50	n = 22 ; % = 45.8
Greater than 2 comorbidities Sample size	n = 19 ; % = 50	n = 26 ; % = 54.2
Severity Nominal	NR	NR
Haemorrhagic stroke Sample size	n = 3	n = 6 ; % = 12.5
Ischaemic stroke Sample size	n = 33 ; % = 86.8	n = 42 ; % = 87.5
Dysphagia at baseline Nominal	NR	NR
People who are nil-by-mouth at baseline Nominal	NR	NR
Left side Sample size	n = 21 ; % = 55.3	n = 30 ; % = 62.5
Right side Sample size	n = 17 ; % = 44.7	n = 18 ; % = 37.5

Characteristic	Oral hygiene intervention (once a day) (N = 38)	Usual care (N = 48)
No/mild cognitive impairment Sample size	n = 23 ; % = 60.5	n = 30 ; % = 62.5
Severe cognitive impairment Sample size	n = 15 ; % = 39.5	n = 18 ; % = 37.5
Total/severe dependence Sample size	n = 28 ; % = 73.7	n = 33 ; % = 68.8
Moderate/mild/minimal dependence Sample size	n = 10 ; % = 26.3	n = 15 ; % = 31.3
First stroke Sample size	n = 33 ; % = 86.8	n = 42 ; % = 87.5
Recurrent stroke Sample size	n = 5 ; % = 13.2	n = 6 ; % = 12.5

Outcomes

Study timepoints

- Baseline
- 3 month (Reports data at 6 months but as this is the closest time to 3 months this time period will be reported here.)

Oral hygiene interventions (once a day) compared to usual care at ≤3 months

Outcome	Oral hygiene intervention (once a day), Baseline, N = 38	Oral hygiene intervention (once a day), 3 month, N = 38	Usual care, Baseline, N = 48	Usual care, 3 month, N = 48
Mortality Nominal	NA	3	NA	4
Presence of oral disease (Oral candidiasis) Nominal	NA	12	NA	13

Mortality - Polarity - Lower values are better

Presence of oral disease (Oral candidiasis) - Polarity - Lower values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Oralhygieneinterventions(onceaday)comparedtousualcareat≤3months-Mortality-Nominal-Oral hygiene intervention (once a day)-Usual care-t3

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns
Overall bias and Directness	Overall Directness	Directly applicable

Oralhygieneinterventions(onceaday)comparedtousualcareat≤3months-Presenceoforaldisease(Oralcandidiasis)-Nominal-Oral hygiene intervention (once a day)-Usual care-t3

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns
Overall bias and Directness	Overall Directness	Directly applicable

Chen, 2019

Bibliographic Reference	Chen, H. J.; Chen, J. L.; Chen, C. Y.; Lee, M.; Chang, W. H.; Huang, T. T.; Effect of an Oral Health Programme on Oral Health, Oral Intake, and Nutrition in Patients with Stroke and Dysphagia in Taiwan: A Randomised Controlled Trial; International Journal of Environmental Research & Public Health [Electronic Resource]; 2019; vol. 16 (no. 12); 24

Study details

Secondary publication of another included study- see primary study for details	No additional information.
Other publications associated with this study included in review	No additional information.
Trial name / registration number	Clinicaltrials.gov ID: NCT03219346
Study type	Randomised controlled trial (RCT)

Study location	Taiwan.
Study setting	Primary care - four rehabilitation units of a medical centre in Taiwan.
Study dates	Not stated/unclear.
Sources of funding	This research received no external funding.
Inclusion criteria	People following a first-time stroke in four rehabilitation units in northern Taiwan, who received swallowing treatment. The people also had to be able to communicate in Chinese (Mandarin or Taiwanese), comply with the instructions and be willing to participate in this study. People had nasogastric tubes inserted at baseline.
Exclusion criteria	History of dysphagia because of oral cancer or head and neck cancer; having already received more than 6 months of swallowing treatment.
Recruitment / selection of participants	No additional information.
Intervention(s)	Oral care group (3 times a week) N=33 Provided the usual oral care and manual provided to the control group, and received oral health care 30 minutes before the swallowing training three times a week for 3 weeks. The primary author instructed the caregiver on how to perform the oral health procedure until the caregiver was confident in performing the procedure independently, taking 10-15 minutes each time. Before providing oral health care, the caregiver had to prepare the necessary oral health tools (such as water, toothbrush, dental floss, and interdental brush) and suction equipment (including saliva pipette) and help the patient sit in an upright position. First, the person's sputum in the oral cavity was assessed. A suction was used to clear the saliva when necessary. Next, an oral cleaning tool (dental floss and/or interdental brush) was used, and the patient's teeth were brushed using the Bass method. Finally, a fluoride toothpaste (fluoride >1000ppm, <0.5cm used to prevent cavities) was used to coat all teeth. This intervention will be considered as indirect evidence (as it is not once a day up to hourly oral care as specified in the protocol) Concomitant therapy: Usual care was provided to both study arms.
Comparator	Usual care N=33

	Usual oral care provided in the unit (e.g. tooth brushing or sponge stick cleaning) twice a day (morning and evening) and were provided with an instructional manual to promote eating (including information such as food choice and safe eating tips). Concomitant therapy: Usual care was provided to both study arms.
Number of participants	66
Duration of follow-up	6 weeks
Additional comments	No additional comments
Subgroup 1: Severity (as stated by category or as measured by NIHSS scale)	Not stated/unclear
Subgroup 2: Type of stroke (using the Bamford scale)	Not stated/unclear
Subgroup 3: Dysphagia at baseline	Presence of dysphagia at baseline
Subgroup 4: Type of intervention	Combinations of the above
Subgroup 5: People who are nil-by-mouth at baseline	People who are nil-by-mouth at baseline

Subgroup analysis - further details	Type of stroke: Separate by infarction (35) and haemorrhagic (31). Type of intervention: Mixture of suctioning, oral swabbing, toothbrushing, floss and interdental brushes before swallowing therapy. People who are nil-by-mouth at baseline: Presumed nil-by-mouth due to nasogastric tube insertion at baseline.

Study arms

Oral care group (3 times a week) (N = 33)

Provided the usual oral care and manual provided to the control group, and received oral health care 30 minutes before the swallowing training three times a week for 3 weeks. The primary author instructed the caregiver on how to perform the oral health procedure until the caregiver was confident in performing the procedure independently, taking 10-15 minutes each time. Before providing oral health care, the caregiver had to prepare the necessary oral health tools (such as water, toothbrush, dental floss, and interdental brush) and suction equipment (including saliva pipette) and help the patient sit in an upright position. First, the person's sputum in the oral cavity was assessed. A suction was used to clear the saliva when necessary. Next, an oral cleaning tool (dental floss and/or interdental brush) was used, and the patient's teeth were brushed using the Bass method. Finally, a fluoride toothpaste (fluoride >1000ppm, <0.5cm used to prevent cavities) was used to coat all teeth. This intervention will be considered as indirect evidence (as it is not once a day up to hourly oral care as specified in the protocol)

Usual care (N = 33)

Usual oral care provided in the unit (e.g. tooth brushing or sponge stick cleaning) twice a day (morning and evening) and were provided with an instructional manual to promote eating (including information such as food choice and safe eating tips).

1 **Characteristics**

2 ***Arm-level characteristics***

Characteristic	Oral care group (3 times a week) (N = 33)	Usual care (N = 33)
% Female Sample size	n = 14 ; % = 42.4	n = 9 ; % = 27.3
Greater than or equal to 65 years Sample size	n = 18 ; % = 54.5	n = 18 ; % = 54.5
Less than 65 years Sample size	n = 15 ; % = 45.5	n = 15 ; % = 45.5
Comorbidities Nominal	NR	NR
Severity Nominal	NR	NR
Infarction Sample size	n = 18 ; % = 54.5	n = 17 ; % = 51.5
Haemorrhagic Sample size	n = 15 ; % = 45.5	n = 16 ; % = 48.5
Dysphagia at baseline Nominal	33	33

Characteristic	Oral care group (3 times a week) (N = 33)	Usual care (N = 33)
People who are nil-by-mouth at baseline Nominal	33	33
Mild No of events	n = 12 ; % = 36.4	n = 12 ; % = 36.4
Moderate No of events	n = 14 ; % = 42.4	n = 14 ; % = 42.4
Severe No of events	n = 7 ; % = 21.2	n = 7 ; % = 21.2
Right Sample size	n = 20 ; % = 60.6	n = 14 ; % = 42.4
Left Sample size	n = 12 ; % = 36.4	n = 16 ; % = 48.5
Time interval from stroke onset to date of the oral health programme (Months) Range	0.5 to 2	0.5 to 2
Time interval from stroke onset to date of the oral health programme (Months) Mean (SD)	0.5 (NR)	0.5 (NR)

1

Outcomes

Study timepoints

- Baseline
- 6 week (Shall be included in the ≤3 months period)

Oral hygiene intervention (less than once per day) compared to usual care at ≤3 months - Continuous outcomes

Outcome	Oral care group (3 times a week), Baseline, N = 33	Oral care group (3 times a week), 6 week, N = 33	Usual care, Baseline, N = 33	Usual care, 6 week, N = 33
Oral health outcome scales (Oral Health Assessment Tool) Scale range: 0-16 Mean (SD)	5.64 (2.54)	3.42 (1.89)	5.24 (1.77)	5.99 (2.14)
Dysphagia severity (Functional Oral Intake Scale) Scale range: 1-7 Mean (SD)	3.15 (2.06)	3.94 (2.38)	3.15 (1.79)	3.52 (1.92)

Oral health outcome scales (Oral Health Assessment Tool) - Polarity - Lower values are better

Dysphagia severity (Functional Oral Intake Scale) - Polarity - Higher values are better

Oral hygiene intervention (less than once per day) compared to usual care at ≤3 months - Dichotomous outcomes

Outcome	Oral care group (3 times a week), Baseline, N = 33	Oral care group (3 times a week), 6 week, N = 33	Usual care, Baseline, N = 33	Usual care, 6 week, N = 33
Requirement of enteral feeding support (nasogastric tube removal)	NA	7	NA	2

Outcome	Oral care group (3 times a week), Baseline, N = 33	Oral care group (3 times a week), 6 week, N = 33	Usual care, Baseline, N = 33	Usual care, 6 week, N = 33
Nominal				

Requirement of enteral feeding support (nasogastric tube removal) - Polarity - Higher values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Oralhygieneintervention(lessthanonceperday)comparedtousualcareat≤3months-Continuousoutcomes-Oralhealthoutcomescales(OralHealthAssessmentTool)-MeanSD-Oral care group (3 times a week)-Usual care-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Partially applicable *(Downgraded for intervention indirectness as it is provided at less than the smallest frequency stated by the committee in the protocol)*

Oralhygieneintervention(lessthanonceperday)comparedtousualcareat≤3months-Continuousoutcomes-Dysphagiaseverity(FunctionalOralIntakeScale)-MeanSD-Oral care group (3 times a week)-Usual care-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High

Section	Question	Answer
Overall bias and Directness	Overall Directness	Partially applicable *(Downgraded for intervention indirectness as it is provided at less than the smallest frequency stated by the committee in the protocol)*

Oralhygieneintervention(lessthanonceperday)comparedtousualcareat≤3months-Dichotomousoutcomes-Requirementofenteralfeedingsupport(nasogastrictuberemoval)-Nominal-Oral care group (3 times a week)-Usual care-t6

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns
Overall bias and Directness	Overall Directness	Partially applicable *(Downgraded for intervention indirectness as it is provided at less than the smallest frequency stated by the committee in the protocol)*

Chipps, 2014

Bibliographic Reference	Chipps, E.; Gatens, C.; Genter, L.; Musto, M.; Dubis-Bohn, A.; Gliemmo, M.; Dudley, K.; Holloman, C.; Hoet, A. E.; Landers, T.; Pilot study of an oral care protocol on poststroke survivors; Rehabilitation Nursing Journal; 2014; vol. 39 (no. 6); 294-304

Study details

Secondary publication of another included study- see primary study for details	No additional information.

Other publications associated with this study included in review	No additional information.
Trial name / registration number	No additional information.
Study type	Randomised controlled trial (RCT)
Study location	United States of America.
Study setting	A free-standing 60-bed acute rehabilitation hospital that is part of a major academic medical center in the Midwest.
Study dates	No additional information.
Sources of funding	This project was funded through Sigma Theta Tau International and the Rehabilitation Nurses Foundation.
Inclusion criteria	Age 18 years or older, able to communicate in English and able to give informed consent; primary diagnosis of a stroke within 30 days of admission to the rehabilitation unit; admitted directly from an acute care facility; oral or phayngeal dysphagia identified by a bedside swallow exam by a Speech-Language Pathologist (SLPs), Modified Barium Swallow, or Fiberoptic Endoscopic Evaluation of Swallowing.
Exclusion criteria	Current comorbid diagnosis of pneumonia; known infection of the oral cavity and/or receiving therapy for infection of the oral cavity; documented history of a haematological disorder; medically restricted fluid intake; allergy to Listerine(TM) or other study products; currently wearing dentures; pregnant or nursing mothers; a history of MRSA infection or colonization.
Recruitment / selection of participants	No additional information.
Intervention(s)	Enhanced oral care (twice a day) N=29 Care provided by a registered nurse trained by dentist and dental hygienist in use of equipment and approach with periodic monitoring and feedback on oral care technique. Care included: battery-operated toothbrush, Braun Oral B with timer(TM) twice daily, Timed toothbrushing for 30 seconds in each quadrant of the mouth, Crest-Pro-Health(TM) toothpaste, Listerine(TM) 10-15mL once per day, Glide Disposable Floss Picks (TM), Sunstar(TM) Dual Action Tongue Cleaner and Carmex(TM) lip balm. Care provided twice a day.

Comparator	Usual care N=22 Care provided by a nursing assistant once/twice daily or as clinically appropriate. Toothbrushing with a hospital toothbrush Sage(TM), twice daily using Sage Oral Care Sodium Bicarbonate Mouthpaste (toothpaste), Careline(TM) alcohol free mouthwash once a day (rinse and spit), and lip care with regular Chaplet(TM).
Number of participants	51
Duration of follow-up	10 days
Additional comments	No additional information.
Subgroup 1: Severity (as stated by category or as measured by NIHSS scale)	Not stated/unclear
Subgroup 2: Type of stroke (using the Bamford scale)	Not stated/unclear
Subgroup 3: Dysphagia at baseline	Presence of dysphagia at baseline
Subgroup 4: Type of intervention	Combinations of the above
Subgroup 5: People who are nil-by-mouth at baseline	Mixed
Subgroup analysis - further details	Subgroup 5: people who are nil-by-mouth at baseline - 4 participants were at Functional Oral Intake Scale 1-3.

1

Study arms

Enhanced oral care (twice a day) (N = 29)

Care provided by a registered nurse trained by dentist and dental hygienist in use of equipment and approach with periodic monitoring and feedback on oral care technique. Care included: battery-operated toothbrush, Braun Oral B with timer(TM) twice daily, Timed toothbrushing for 30 seconds in each quadrant of the mouth, Crest-Pro-Health(TM) toothpaste, Listerine(TM) 10-15mL once per day, Glide Disposable Floss Picks (TM), Sunstar(TM) Dual Action Tongue Cleaner and Carmex(TM) lip balm. Care provided twice a day.

Usual care (N = 22)

Care provided by a nursing assistant once/twice daily or as clinically appropriate. Toothbrushing with a hospital toothbrush Sage(TM), twice daily using Sage Oral Care Sodium Bicarbonate Mouthpaste (toothpaste), Careline(TM) alcohol free mouthwash once a day (rinse and spit), and lip care with regular Chaplet(TM).

Characteristics

Arm-level characteristics

Characteristic	Enhanced oral care (twice a day) (N = 29)	Usual care (N = 22)
% Female Sample size	n = NR ; % = 47.8	n = NR ; % = 34.5
Mean age (SD) Mean (SD)	62.54 (13.5)	63.74 (15.6)
Caucasian Sample size	n = NR ; % = 77.8	n = NR ; % = 65.2

Characteristic	Enhanced oral care (twice a day) (N = 29)	Usual care (N = 22)
African American Sample size	n = NR ; % = 22.2	n = NR ; % = 30.4
Asian American Sample size	n = NR ; % = 0	n = NR ; % = 4.3
Comorbidities Nominal	NR	NR
Severity Nominal	NR	NR
Type of stroke Nominal	NR	NR
Dysphagia at baseline Nominal	NA	NA
People who are nil-by-mouth at baseline Nominal	2	2

Outcomes

Study timepoints

- Baseline
- 10 day (End of intervention)

1

2 ***Oral hygiene intervention (twice a day) compared to usual care at ≤3 months - continuous outcomes***

Outcome	Enhanced oral care (twice a day), Baseline, N = 29	Enhanced oral care (twice a day), 10 day, N = 29	Usual care, Baseline, N = 22	Usual care, 10 day, N = 22
Oral health outcome scales (revised-THROAT) Scale range: 7-21. Final value. P value reported is for the difference between the two when adjusted for interaction of time and group. Mean (p value)	NA (NA)	10.1 (0.08)	NA (NA)	10.9 (NA)
Oral health outcome scales (revised-THROAT) Scale range: 7-21. Final value. P value reported is for the difference between the two when adjusted for interaction of time and group. Mean (SD)	10.8 (2.6)	NA (NA)	12.2 (2.1)	NA (NA)

3 Oral health outcome scales (revised-THROAT) - Polarity - Lower values are better

4 ***Oral hygiene intervention (twice a day) compared to usual care at ≤3 months - dichotomous outcomes***

Outcome	Enhanced oral care (twice a day), Baseline, N = 29	Enhanced oral care (twice a day), 10 day, N = 29	Usual care, Baseline, N = 22	Usual care, 10 day, N = 22
Requirement for enteral feeding support Taken as people still requiring enteral feeding support at the end of the trial, indicated by FOIS score of 1-3. Nominal	2	1	2	2

Outcome	Enhanced oral care (twice a day), Baseline, N = 29	Enhanced oral care (twice a day), 10 day, N = 29	Usual care, Baseline, N = 22	Usual care, 10 day, N = 22
Dysphagia severity (progression in Function Intake Oral scale from 4-5 to 6-7) Dichotomous version of a continuous outcome. Will be downgraded for indirectness as this is not the preferred reporting method. Nominal	NR	10	NR	7

Requirement for enteral feeding support - Polarity - Lower values are better

Dysphagia severity (progression in Function Intake Oral scale from 4-5 to 6-7) - Polarity - Higher values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Oralhygieneintervention(twiceaday)comparedtousualcareat≤3months-continuousoutcomes-Oralhealthoutcomescales(revised-THROAT)-MeanPValue-Enhanced oral care (twice a day)-Usual care-t10

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable

Oralhygieneintervention(twiceaday)comparedtousualcareat≤3months-dichotomousoutcomes-Requirementforenteralfeedingsupport-Nominal-Enhanced oral care (twice a day)-Usual care-t10

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable

Oralhygieneintervention(twiceaday)comparedtousualcareat≤3months-dichotomousoutcomes-DysphagiaseverityprogressioninFunctionIntakeOralscalefrom4-5to6-7)-Nominal-Enhanced oral care (twice a day)-Usual care-t10

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Partially applicable *(Downgraded as the outcome is a dichotomous outcome while we prioritised continuous reporting)*

Dai, 2017

Bibliographic Reference	Dai, R.; Lam, O. L. T.; Lo, E. C. M.; Li, L. S. W.; McGrath, C.; Corrigendum to "A randomized clinical trial of oral hygiene care programmes during stroke rehabilitation" [J. Dent. 61 (2017) 48-54]; Journal of Dentistry; 2017; vol. 64; e1

Study details

Secondary publication of	Dai, R.; Lam, O. L. T.; Lo, E. C. M.; Li, L. S. W.; McGrath, C.; A randomized clinical trial of oral hygiene care programmes during stroke rehabilitation; Journal of Dentistry; 2017; vol. 61; 48-54

another included study- see primary study for details	
Other publications associated with this study included in review	No additional information

Dai, 2017

Bibliographic Reference	Dai, R.; Lam, O. L. T.; Lo, E. C. M.; Li, L. S. W.; McGrath, C.; A randomized clinical trial of oral hygiene care programmes during stroke rehabilitation; Journal of Dentistry; 2017; vol. 61; 48-54

Study details

Secondary publication of another included study- see primary study for details	No additional information.
Other publications associated with this study included in review	Dai, R.; Lam, O. L. T.; Lo, E. C. M.; Li, L. S. W.; McGrath, C.; Effect of oral hygiene programmes on oral opportunistic pathogens during stroke rehabilitation; Oral Diseases; 2019; vol. 25 (no. 2); 617-633 Dai, R.; Lam, O. L. T.; Lo, E. C. M.; Li, L. S. W.; McGrath, C.; Corrigendum to "A randomized clinical trial of oral hygiene care programmes during stroke rehabilitation" [J. Dent. 61 (2017) 48-54]; Journal of Dentistry; 2017; vol. 64; e1
Trial name / registration number	Hong Kong Clinical Trial Register: 003900. Clinicaltrials.gov: NCT03003871

Study type	Randomised controlled trial (RCT)
Study location	Hong Kong
Study setting	The Mrs Ng Wah Memorial Day Outpatients Centre, Tung Wah Hospital in Hong Kong SAR.
Study dates	No additional information.
Sources of funding	This study was supported by General Research Fund, Hong Kong (Project number 774012).
Inclusion criteria	Being admitted to the outpatient rehabilitation programme within six months; having moderate to severe functional disability - Barthel Index scores of <70; being able to follow a one-step command (as an assessment of communication)
Exclusion criteria	Being edentulous; more than mild cognitive impairment - Mini Mental State Examination ≤18; indwelling naso-gastric feeding tubes
Recruitment / selection of participants	People who were discharged from the hospital and had sustained functional impairments were referred to this centre for further rehabilitation involving a multidisciplinary team.
Intervention(s)	Oral hygiene intervention (twice a day) N=47 An advanced oral hygiene care programme - supply of a powered toothbrush (Oral-B (R) AdvancePower(TM) 400 series), 0.2% chlorhexidine gluconate mouth rinse (Corsodyl (R)), a standardised tooth paste (Colgate (R) Maximum Cavity Protection), and oral hygiene training.
Comparator	Usual care N=47 Conventional oral hygiene care programme - supply of a manual toothbrush (Oral-B (R) Pro-Health All-In-One), a standardised tooth paste (Colgate Maximum Cavity Protection), and oral hygiene training.
Number of participants	94
Duration of follow-up	3 months of treatment, additional 3 months of follow up (6 months in total). Only data from the 3 months follow up will be included in our analysis.
Additional comments	No additional information.
Subgroup 1: Severity (as stated	Not stated/unclear

by category or as measured by NIHSS scale)	
Subgroup 2: Type of stroke (using the Bamford scale)	Not stated/unclear
Subgroup 3: Dysphagia at baseline	Not stated/unclear
Subgroup 4: Type of intervention	Combinations of the above
Subgroup 5: People who are nil-by-mouth at baseline	Not stated/unclear
Subgroup analysis - further details	Type of stroke: States that 70.2% had an ischaemic stroke and 29.8% had a haemorrhagic stroke. Type of intervention: Mouthwash and powered toothbrush.

Study arms

Oral hygiene intervention (twice a day) (N = 47)

An advanced oral hygiene care programme - supply of a powered toothbrush (Oral-B (R) AdvancePower(TM) 400 series), 0.2% chlorhexidine gluconate mouth rinse (Corsodyl (R)), a standardised tooth paste (Colgate (R) Maximum Cavity Protection), and oral hygiene training.

Usual care (N = 47)

Conventional oral hygiene care programme - supply of a manual toothbrush (Oral-B (R) Pro-Health All-In-One), a standardised tooth paste (Colgate Maximum Cavity Protection), and oral hygiene training.

Characteristics

Study-level characteristics

Characteristic	Study (N = 94)
Ethnicity Nominal	NR
Comorbidities Nominal	NR
Severity Nominal	NR
Dysphagia at baseline Nominal	NR
People who are nil-by-mouth at baseline Nominal	NR

Arm-level characteristics

Characteristic	Oral hygiene intervention (twice a day) (N = 47)	Usual care (N = 47)
% Female Sample size	n = 18 ; % = 38.3	n = 19 ; % = 40.4
Mean age (SD) Mean (SD)	66.3 (11.2)	66.9 (10.6)
Ischaemic No of events	n = 31 ; % = 66	n = 35 ; % = 74.5
Haemorrhagic No of events	n = 16 ; % = 34	n = 12 ; % = 25.5

Outcomes

Study timepoints

- Baseline
- 3 month

Oral hygiene intervention (twice a day) compared to usual care at ≤3 months - dichotomous outcomes

Outcome	Oral hygiene intervention (twice a day), Baseline, N = 47	Oral hygiene intervention (twice a day), 3 month, N = 44	Usual care, Baseline, N = 47	Usual care, 3 month, N = 30
Occurrence of pneumonia Nominal	NA	0	NA	0

Occurrence of pneumonia - Polarity - Lower values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Oralhygieneintervention(twiceaday)comparedtousualcareat≤3months-dichotomousoutcomes-Occurrenceofpneumonia-Nominal-Oral hygiene intervention (twice a day)-Usual care-t3

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns
Overall bias and Directness	Overall Directness	Directly applicable

Dai, 2019

Bibliographic Reference	Dai, R.; Lam, O. L. T.; Lo, E. C. M.; Li, L. S. W.; McGrath, C.; Effect of oral hygiene programmes on oral opportunistic pathogens during stroke rehabilitation; Oral Diseases; 2019; vol. 25 (no. 2); 617-633

Study details

Secondary publication of another included study- see primary study for details	Dai, R.; Lam, O. L. T.; Lo, E. C. M.; Li, L. S. W.; McGrath, C.; A randomized clinical trial of oral hygiene care programmes during stroke rehabilitation; Journal of Dentistry; 2017; vol. 61; 48-54
Other publications associated with this study included in review	No additional information.
Trial name / registration number	Clinicaltrials.gov: NCT03003871
Study setting	

Gosney, 2006

Bibliographic Reference	Gosney, M.; Martin, M. V.; Wright, A. E.; The role of selective decontamination of the digestive tract in acute stroke; Age Ageing; 2006; vol. 35 (no. 1); 42-7

Study details

Secondary publication of another included	No additional information.

study- see primary study for details	
Other publications associated with this study included in review	No additional information.
Trial name / registration number	No additional information.
Study type	Randomised controlled trial (RCT)
Study location	England.
Study setting	Acute stroke assessment units of three hospitals in the northwest of England.
Study dates	January 2001 and 2003.
Sources of funding	This project was funded by the Northwest Zonal Research and Development. One investigated was employed as a research nurse by the funding body.
Inclusion criteria	People within 24 hours of admission to hospital following a first acute stroke.
Exclusion criteria	People receiving antibiotic or steroid medication, including inhaled steroids, or having had ha previous stroke.
Recruitment / selection of participants	No additional information.
Intervention(s)	Oral hygiene intervention (four times a day) N=103 Orobase gel, containing 2% (w/v) colistin, 2% (w/v) polymyxin E and 2% (w/v) amphotericin B, 500mg applied to the mucous membranes of the mouth four times daily for 2-3 weeks (2 weeks if they had a safe swallow, 3 weeks if they had an unsafe swallow).
Comparator	Placebo N=100 Placebo gel applied four times daily for 2-3 weeks (2 weeks if they had a safe swallow, 3 weeks if they had an unsafe swallow).

Number of participants	203.
Duration of follow-up	3 months in total.
Additional comments	No additional information.
Subgroup 1: Severity (as stated by category or as measured by NIHSS scale)	Not stated/unclear
Subgroup 2: Type of stroke (using the Bamford scale)	Not stated/unclear
Subgroup 3: Dysphagia at baseline	Mixed
Subgroup 4: Type of intervention	Other Antimicrobial oral gel
Subgroup 5: People who are nil-by-mouth at baseline	Not stated/unclear
Subgroup analysis - further details	No additional information.

1

Study arms

Oral hygiene intervention (four times a day) (N = 103)

Orobase gel, containing 2% (w/v) colistin, 2% (w/v) polymyxin E and 2% (w/v) amphotericin B, 500mg applied to the mucous membranes of the mouth four times daily for 2-3 weeks (2 weeks if they had a safe swallow, 3 weeks if they had an unsafe swallow).

Placebo (Usual care) (N = 100)

Placebo gel applied four times daily for 2-3 weeks (2 weeks if they had a safe swallow, 3 weeks if they had an unsafe swallow). For this analysis this will be treated as usual care.

Characteristics

Arm-level characteristics

Characteristic	Oral hygiene intervention (four times a day) (N = 103)	Placebo (Usual care) (N = 100)
% Female Nominal	49	48
Mean age (SD) Range	16 to 96	45 to 92
Mean age (SD) Median (IQR)	70.5 (NR to NR)	73.3 (NR to NR)
Ethnicity Nominal	NR	NR

Characteristic	Oral hygiene intervention (four times a day) (N = 103)	Placebo (Usual care) (N = 100)
Comorbidities Nominal	NR	NR
Severity Nominal	NR	NR
Type of stroke Nominal	NR	NR
Dysphagia at baseline Nominal	25	33
People who are nil-by-mouth at baseline Nominal	NR	NR

Outcomes

Study timepoints

- Baseline
- 3 week (During inpatient stay. Additional information about mortality was reported at 3 months, but this was not reported by group so it was unable to extract this information.)

Oral hygiene intervention (four times a day) compared to usual care at ≤3 months - dichotomous outcomes

Outcome	Oral hygiene intervention (four times a day), Baseline, N = 103	Oral hygiene intervention (four times a day), 3 week, N = 103	Placebo (Usual care), Baseline, N = 100	Placebo (Usual care), 3 week, N = 100
Mortality Nominal	NR	9	NR	11
Occurence of pneumonia Nominal	NR	1	NR	7

Mortality - Polarity - Lower values are better

Occurence of pneumonia - Polarity - Lower values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Oralhygieneintervention(fourtimesaday)comparedtousualcareat≤3months-dichotomousoutcomes-Mortality-Nominal-Oral hygiene intervention (four times a day)-Placebo-t3

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Oralhygieneintervention(fourtimesaday)comparedtousualcareat≤3months-dichotomousoutcomes-Occurenceofpneumonia-Nominal-Oral hygiene intervention (four times a day)-Placebo-t3

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Low
Overall bias and Directness	Overall Directness	Directly applicable

Kim, 2014

Bibliographic Reference	Kim, E. K.; Jang, S. H.; Choi, Y. H.; Lee, K. S.; Kim, Y. J.; Kim, S. H.; Lee, H. K.; Effect of an oral hygienic care program for stroke patients in the intensive care unit; Yonsei Medical Journal; 2014; vol. 55 (no. 1); 240-6

Study details

Secondary publication of another included study- see primary study for details	No additional information.
Other publications associated with this study included in review	No additional information.
Trial name / registration number	No additional information.
Study type	Randomised controlled trial (RCT)

Study location	South Korea (Daegu)
Study setting	People admitted to the intensive care unit of the neurosurgery department of a university hospital.
Study dates	No additional information.
Sources of funding	This research was supported by research grants from Yeung-nam University in 2010.
Inclusion criteria	First-ever stroke; had six or more teeth.
Exclusion criteria	Sign of infection with any contagious pathogen.
Recruitment / selection of participants	No additional information.
Intervention(s)	Oral hygiene intervention (once per day) N=45 Oral hygienic management administered by one dentist once every day for an average of 2.2 weeks (range 1-5 weeks). For people without consciousness, a mouth gag for dental care was used to keep the mouth open. A children's toothbrush and an interdental toothbrush were used for removal of plaque on the teeth, while a tongue cleaner was used to get rid of plaque on the tongue. Then, gauze soaked with 0.5% chlorohexidine was used to clean oral mucosa and tooth surfaces and to remove foreign bodies inside the mouth.
Comparator	Usual care N=45 No specific oral hygiene intervention.
Number of participants	90
Duration of follow-up	For the duration of their ICU stay (mean 2.2 weeks, range 1-5 weeks). Will consider the mean follow up time for analysis.
Additional comments	No additional information.
Subgroup 1: Severity (as stated by category or as	Not stated/unclear

measured by NIHSS scale)	
Subgroup 2: Type of stroke (using the Bamford scale)	Not stated/unclear
Subgroup 3: Dysphagia at baseline	Not stated/unclear
Subgroup 4: Type of intervention	Professional tooth cleaning
Subgroup 5: People who are nil-by-mouth at baseline	Not stated/unclear
Subgroup analysis - further details	Type of stroke: Reported infarction (6) compared to haemorrhage (50).

Study arms

Oral hygiene intervention (once per day) (N = 45)

Oral hygienic management administered by one dentist once every day for an average of 2.2 weeks (range 1-5 weeks). For people without consciousness, a mouth gag for dental care was used to keep the mouth open. A children's toothbrush and an interdental toothbrush were used for removal of plaque on the teeth, while a tongue cleaner was used to get rid of plaque on the tongue. Then, gauze soaked with 0.5% chlorohexidine was used to clean oral mucosa and tooth surfaces and to remove foreign bodies inside the mouth.

Usual care (N = 45)

No specific oral hygiene intervention.

1

2 **Characteristics**

3 ***Arm-level characteristics***

Characteristic	Oral hygiene intervention (once per day) (N = 45)	Usual care (N = 45)
% Female Sample size	n = 16 ; % = 55.2	n = 13 ; % = 48.1
Mean age (SD) Mean (SD)	57.38 (14.22)	56.15 (14.55)
Ethnicity Nominal	NR	NR
Comorbidities Nominal	NR	NR
Severity Nominal	NR	NR
Infarct Sample size	n = 3 ; % = 10.3	n = 3 ; % = 11.1
Haemorrhagic Sample size	n = 26 ; % = 89.7	n = 24 ; % = 88.9
Dysphagia at baseline Nominal	NR	NR

Characteristic	Oral hygiene intervention (once per day) (N = 45)	Usual care (N = 45)
People who are nil-by-mouth at baseline Nominal	NR	NR

Outcomes

Study timepoints

- Baseline
- 2 week (Will be included as ≤3 months)

Oral hygiene intervention (once per week) compared to usual care at ≤3 months - dichotomous outcomes

Outcome	Oral hygiene intervention (once per day), Baseline, N = 45	Oral hygiene intervention (once per day), 2 week, N = 29	Usual care, Baseline, N = 45	Usual care, 2 week, N = 27
Presence of oral disease (oral candidiasis) - tongue Including anyone with candida >grade 1. Intervention: Grade 1 = 6, grade 2 = 3, grade 3 = 14. Control: Grade 1 = 6, grade 2 = 9, grade 3 = 9. Nominal	NR	23	NR	24
Presence of oral disease (oral candidiasis) - saliva Including anyone with candida >grade 1. Intervention: Grade 1 = 6, grade 2 = 6, grade 3 = 10. Control: Grade 1 = 6, grade 2 = 7, grade 3 = 7. Nominal	NR	22	NR	20

Outcome	Oral hygiene intervention (once per day), Baseline, N = 45	Oral hygiene intervention (once per day), 2 week, N = 29	Usual care, Baseline, N = 45	Usual care, 2 week, N = 27
Mortality Reported in study as 'expiration' Nominal	NR	2	NR	3

1 Presence of oral disease (oral candidiasis) - tongue - Polarity - Lower values are better

2 Presence of oral disease (oral candidiasis) - saliva - Polarity - Lower values are better

3 Mortality - Polarity - Lower values are better

4 ***Oral hygiene intervention (once per week) compared to usual care at ≤3 months - continuous outcomes***

Outcome	Oral hygiene intervention (once per day), Baseline, N = 45	Oral hygiene intervention (once per day), 2 week, N = 29	Usual care, Baseline, N = 45	Usual care, 2 week, N = 27
Presence of oral disease (gingivitis - gingival index) Continuous outcome. Will be downgraded due to indirectness. Scale range: 0-3. Mean (SD)	1.54 (0.47)	0.47 (0.64)	1.3 (0.53)	1.6 (0.61)
Length of hospital stay (length of ICU admission) (days) Downgrade for indirectness as only reporting ICU admission length Mean (SD)	NA (NA)	15.69 (10.02)	NA (NA)	18.15 (8.07)

Presence of oral disease (gingivitis - gingival index) - Polarity - Lower values are better

Length of hospital stay (length of ICU admission) - Polarity - Lower values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Oralhygieneintervention(onceperweek)comparedtousualcareat≤3months-dichotomousoutcomes-Presenceoforaldisease(oralcandidiasis)-tongue-Nominal-Oral hygiene intervention (once per day)-Usual care-t2

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable

Oralhygieneintervention(onceperweek)comparedtousualcareat≤3months-dichotomousoutcomes-Presenceoforaldisease(oralcandidiasis)-saliva-Nominal-Oral hygiene intervention (once per day)-Usual care-t2

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable

Oralhygieneintervention(onceperweek)comparedtousualcareat≤3months-dichotomousoutcomes-Mortality-Nominal-Oral hygiene intervention (once per day)-Usual care-t2

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable

Oralhygieneintervention(onceperweek)comparedtousualcareat≤3months-continuousoutcomes-Presenceoforaldisease(gingivitis-gingivalindex)-MeanSD-Oral hygiene intervention (once per day)-Usual care-t2

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Partially applicable *(Downgraded due to outcome indirectness (continuous scale for an outcome prespecified to be dichotomous in the protocol))*

Oralhygieneintervention(onceperweek)comparedtousualcareat≤3months-continuousoutcomes-Lengthofhospitalstay(lengthofICUadmission)-MeanSD-Oral hygiene intervention (once per day)-Usual care-t2

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Partially applicable *(Downgraded due to outcome indirectness (length of ITU stay rather than length of hospital admission))*

Kuo, 2016

Bibliographic Reference	Kuo, Y. W.; Yen, M.; Fetzer, S.; Chiang, L. C.; Shyu, Y. I.; Lee, T. H.; Ma, H. I.; A home-based training programme improves family caregivers' oral care practices with stroke survivors: a randomized controlled trial; International Journal of Dental Hygiene; 2016; vol. 14 (no. 2); 82-91

Study details

Secondary publication of another included study- see primary study for details	No additional information.
Other publications associated with this study included in review	No additional information.
Trial name / registration number	No additional information.
Study type	Randomised controlled trial (RCT)
Study location	Taiwan
Study setting	Home based.
Study dates	September 2012 and February 2013.
Sources of funding	There was no external funding for this study.
Inclusion criteria	The family caregivers if their family member had experienced a stroke (ICD 9 430-438); had a Barthel index score of less than 60 and were unable to intake orally. Each family caregiver was actively caring for their stroke survivor for at least 8 hours per day and was able to communicate in Mandarin or Taiwanese.

Exclusion criteria	If their stroke survivor had a confirmed diagnosis of pulmonary infection or a diagnosis of oral or tongue pathology. The family caregivers who were unable to open their stroke survivor's mouth were also not eligible for this study; this is because stroke survivors with unstable conditions will increase intervention risk.
Recruitment / selection of participants	People contacted through nursing directors of three hospital-based home healthcare institutions.
Intervention(s)	Oral hygiene intervention (twice a day) N=50 Home-based oral care training programme. Guided by the PRECEDE-PRO-CEED model for planning, implementation and evaluation of the programme. The programme included an oral care overview (a 20-min oral care health and disease verbal presentation based on an oral care educational pamphlet), discussion of basic oral care procedures and the risks, face-to-face education at the family caregiver's home, provision of oral care products that included a dual action tongue cleaner (Sunstar American, Inc.) and a finger toothbrush, teaching strategies for the family caregivers that included assessment, method, skill, frequency and time of oral care, demonstrations, return demonstrations and a reminder mechanism with daily record sheets for oral care and follow-up phone calls. In this training programme, the family caregivers' feelings about providing oral care were taken seriously, because most family caregivers often feel unprepared to provide care, have inadequate knowledge to deliver proper care and receive little guidance from the healthcare providers. Elements of care: Oral care overview: An educational pamphlet related to oral care was provided to the family caregivers of the intervention group. Discussion of basic oral care procedures and risks: Based on the oral care educational pamphlet provided to the family caregivers of the intervention group, a 20-min verbal presentation was followed by a discussion of basic oral care procedures and risks. Providing oral care products: Two kinds of oral care products: Intervention group were provided with two kinds of oral care products: a dual action tongue cleaner and a finger toothbrush.

	Teaching content: Emphasize the importance of home-based oral care. Assist the family caregivers in planning and assessment the oral care of stroke survivors. Provide guidance for appropriate cleaning techniques of dentures, natural teeth and tongue. Teaching strategies: The health care programme emphasizes the need for well trained and skilled caregivers who have the knowledge, attitude and self-efficacy in stroke survivors. An ideal teaching of oral care would have several strategies that are listed below: 1) twice (after breakfast and before sleep) a day; 2) two minutes per time; 3) learning brushing sequence (from teeth to tongue); 4) learning tongue cleaning (distinguishing six regions, from left-middle-right of the anterior tongue to left-middle-right of the posterior tongue); 5) learning how to use the equipment (tongue cleaner and finger toothbrush); 6) checking the dental cavities; 7) confirming the method of toothbrush; 8) using the technique of Bass brushing and oral mucosa cleaning. Demonstration: The provider demonstrated the method of toothbrushing and tongue cleaning to family caregivers. Return demonstrations: The provider return demonstrations of these techniques. Reminder mechanism for oral care: Provide the daily record sheet for oral care. Follow-up: Telephone follow-up at one month to reinforce oral care practices. Family caregivers' feelings about providing oral care were investigated and discussed during a 20-min conversation with the provider. Assess oral care behaviour: Assessed by a trained research assistant with a nursing background. The Behaviour of Oral Care questionnaire was used based on the provider intervention protocol.
Comparator	Usual care N=50 People were encouraged to maintain their routine oral care practices (included oral cleaning with cotton swabs) during the two months of the intervention period. After the two months of the intervention period, this group also received the home-based oral care training programme.
Number of participants	100. The participants were the family caregivers with stroke survivors. However, the study reports the mortality for the stroke survivors separately. The characteristics table will show the characteristics of the family caregivers.
Duration of follow-up	2 months

Additional comments	No additional information.
Subgroup 1: Severity (as stated by category or as measured by NIHSS scale)	Not stated/unclear
Subgroup 2: Type of stroke (using the Bamford scale)	Not stated/unclear
Subgroup 3: Dysphagia at baseline	Not stated/unclear
Subgroup 4: Type of intervention	Combinations of the above
Subgroup 5: People who are nil-by-mouth at baseline	People who are nil-by-mouth at baseline
Subgroup analysis - further details	Type of intervention: Education programme, tongue cleaner, tooth brushing.

Study arms

Oral hygiene intervention (twice a day) (N = 50)

Home-based oral care training programme. Guided by the PRECEDE-PRO-CEED model for planning, implementation and evaluation of the programme. The programme included an oral care overview (a 20-min oral care health and disease verbal presentation based on an oral care educational pamphlet), discussion of basic oral care procedures and the risks, face-to-face education at the family caregiver's home, provision of oral care products that included a dual action tongue cleaner (Sunstar American, Inc.) and a finger toothbrush, teaching strategies for the family caregivers that included assessment, method, skill, frequency and time of oral care,

demonstrations, return demonstrations and a reminder mechanism with daily record sheets for oral care and follow-up phone calls. In this training programme, the family caregivers' feelings about providing oral care were taken seriously, because most family caregivers often feel unprepared to provide care, have inadequate knowledge to deliver proper care and receive little guidance from the healthcare providers.

Usual care (N = 50)

People were encouraged to maintain their routine oral care practices (included oral cleaning with cotton swabs) during the two months of the intervention period. After the two months of the intervention period, this group also received the home-based oral care training programme.

Characteristics

Arm-level characteristics

Characteristic	Oral hygiene intervention (twice a day) (N = 50)	Usual care (N = 50)
% Female Sample size	n = 32 ; % = NA	n = 27 ; % = NA
Mean age (SD) Mean (SD)	52.71 (11.29)	53.91 (16.74)
Ethnicity Nominal	NR	NR
Comorbidities Nominal	NR	NR

Characteristic	Oral hygiene intervention (twice a day) (N = 50)	Usual care (N = 50)
Severity Nominal	NR	NR
Type of stroke Nominal	NR	NR
Dysphagia at baseline Nominal	NR	NR
People who are nil-by-mouth at baseline Nominal	NA	NA

Baseline characteristics reported in the study has a different number of participants (oral hygiene intervention = 48, usual care = 46).

Outcomes

Study timepoints

- Baseline
- 2 month

Oral hygiene intervention (twice a day) compared to usual care at ≤3 months

Outcome	Oral hygiene intervention (twice a day), Baseline, N = 50	Oral hygiene intervention (twice a day), 2 month, N = 50	Usual care, Baseline, N = 50	Usual care, 2 month, N = 50
Mortality Oral hygiene intervention: 1 death within the first month. Control: 4 deaths within the two months. Nominal	NA	1	NA	4

Mortality - Polarity - Lower values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Oralhygieneintervention(twiceaday)comparedtousualcareat≤3months-Mortality-Nominal-Oral hygiene intervention (twice a day)-Usual care-t2

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	Some concerns
Overall bias and Directness	Overall Directness	Directly applicable

Lam, 2013

Bibliographic Reference	Lam, O. L.; McMillan, A. S.; Samaranayake, L. P.; Li, L. S.; McGrath, C.; Effect of oral hygiene interventions on opportunistic pathogens in patients after stroke; American Journal of Infection Control; 2013; vol. 41 (no. 2); 149-54

Study details

Secondary publication of another included study- see primary study for details	Lam, O. L.; McMillan, A. S.; Samaranayake, L. P.; Li, L. S.; McGrath, C.; Randomized clinical trial of oral health promotion interventions among patients following stroke; Archives of Physical Medicine & Rehabilitation; 2013; vol. 94 (no. 3); 435-43

Lam, 2013

Bibliographic Reference	Lam, O. L.; McMillan, A. S.; Samaranayake, L. P.; Li, L. S.; McGrath, C.; Randomized clinical trial of oral health promotion interventions among patients following stroke; Archives of Physical Medicine & Rehabilitation; 2013; vol. 94 (no. 3); 435-43

Study details

Secondary publication of another included study- see primary study for details	Not applicable.
Other publications associated with this study included in review	Lam, O. L.; McMillan, A. S.; Samaranayake, L. P.; Li, L. S.; McGrath, C.; Effect of oral hygiene interventions on opportunistic pathogens in patients after stroke; American Journal of Infection Control; 2013; vol. 41 (no. 2); 149-54

Trial name / registration number	Hong Kong Clinical Trial Register No: HKCTR-1159. United States National Institutes of Health Clinical Trial Registry Number: NCT01265043.
Study type	Randomised controlled trial (RCT)
Study location	Hong Kong.
Study setting	The rehabilitation unit at Tung Wah Hospital in Hong Kong.
Study dates	July 2008 to January 2011.
Sources of funding	Supported by the Committee of Research and Conference Grants of the University of Hong Kong.
Inclusion criteria	People with stroke, Barthel Index <70, aged 50 years and older, admission to the rehabilitation unit up to 7 days previously.
Exclusion criteria	Edentulous; presented with communication difficulties (unable to follow a 1-step command) or severe cognitive impairment (Mini-Mental State Examination score ≤9); had an indwelling nasogastric feeding tube.
Recruitment / selection of participants	No additional information.
Intervention(s)	Oral hygiene instruction (twice a day and additional treatment twice a week) N=35 Oral hygiene intervention and chlorhexidine mouthrinse twice daily (0.2%, 10mL) and assistance with toothbrushing 2 times per week for a 3 week period Oral hygiene intervention (twice a day) N=34 Oral hygiene instruction and chlorhexidine mouthrinse twice daily (0.2%, 10mL) for a 3 week period
Comparator	Usual care N=33 Oral hygiene instruction only.
Number of participants	102

Duration of follow-up	3 weeks
Additional comments	No additional information.
Subgroup 1: Severity (as stated by category or as measured by NIHSS scale)	Not stated/unclear
Subgroup 2: Type of stroke (using the Bamford scale)	Not stated/unclear
Subgroup 3: Dysphagia at baseline	Not stated/unclear
Subgroup 4: Type of intervention	Combinations of the above
Subgroup 5: People who are nil-by-mouth at baseline	People who are not nil-by-mouth at baseline
Subgroup analysis - further details	Subgroup 5: People who are nil-by-mouth at baseline: Presumed that people are not nil-by-mouth as they exclude people who had an indwelling nasogastric tube.

Study arms

Oral hygiene instruction (twice a day and additional treatment twice a week) (N = 35)

Oral hygiene intervention and chlorhexidine mouthrinse twice daily (0.2%, 10mL) and assistance with toothbrushing 2 times per week for a 3 week period

Oral hygiene intervention (twice a day) (N = 34)

Oral hygiene instruction and chlorhexidine mouthrinse twice daily (0.2%, 10mL) for a 3 week period

Usual care (N = 33)

Oral hygiene instruction only.

Characteristics

Arm-level characteristics

Characteristic	Oral hygiene instruction (twice a day and additional treatment twice a week) (N = 35)	Oral hygiene intervention (twice a day) (N = 34)	Usual care (N = 33)
% Female Sample size	n = 11 ; % = 36.7	n = 10 ; % = 38.5	n = 9 ; % = 36
Mean age (SD) (years) Mean (SD)	71 (11.7)	69.4 (9.6)	68.9 (11.4)
Ethnicity Nominal	NR	NR	NR
Comorbidities Nominal	NR	NR	NR
Severity	NR	NR	NR

Characteristic	Oral hygiene instruction (twice a day and additional treatment twice a week) (N = 35)	Oral hygiene intervention (twice a day) (N = 34)	Usual care (N = 33)
Nominal			
Ischaemic Nominal	27	22	19
Haemorrhagic Nominal	3	4	6
Dysphagia at baseline Nominal	NR	NR	NR
People who are nil-by-mouth at baseline Nominal	NR	NR	NR

Outcomes

Study timepoints

- Baseline
- 3 week

Oral hygiene intervention (twice daily with additional treatment twice a week) compared to oral hygiene intervention (twice daily) compared to usual care - dichotomous outcome

Outcome	Oral hygiene instruction (twice a day and additional treatment twice a week), Baseline, N = 35	Oral hygiene instruction (twice a day and additional treatment twice a week), 3 week, N = 35	Oral hygiene intervention (twice a day), Baseline, N = 34	Oral hygiene intervention (twice a day), 3 week, N = 34	Usual care, Baseline, N = 33	Usual care, 3 week, N = 33
Occurence of pneumonia Nominal	NA	0	NA	0	NA	0

Occurence of pneumonia - Polarity - Lower values are better

Oral hygiene intervention (twice daily with additional treatment twice a week) compared to oral hygiene intervention (twice daily) compared to usual care - continuous outcome

Outcome	Oral hygiene instruction (twice a day and additional treatment twice a week), Baseline, N = 35	Oral hygiene instruction (twice a day and additional treatment twice a week), 3 week, N = 30	Oral hygiene intervention (twice a day), Baseline, N = 34	Oral hygiene intervention (twice a day), 3 week, N = 26	Usual care, Baseline, N = 33	Usual care, 3 week, N = 25
Presence of oral disease (gingival bleeding index) Scale range unclear (half mouth design with each tooth being examined at 6 sites but actual scale not clear). Final value. Mean (p value)	16.7 (NA)	7.6 (0.003)	18.8 (NA)	10 (0.002)	16.7 (NA)	17.7 (0.9)

Presence of oral disease (gingival bleeding index) - Polarity - Lower values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Oralhygieneintervention(twicedailywithadditionaltreatmenttwiceaweek)comparedtooralhygieneintervention(twicedaily)comparedtousual care-dichotomousoutcome-Occurenceofpneumonia-Nominal-Oral hygiene instruction (twice a day and additional treatment twice a week)-Oral hygiene intervention (twice a day)-Usual care-t3

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Partially applicable *(Intervention indirectness - reports an intervention that was not specified in the protocol but does represent an increased intensity of oral hygiene intervention so was included)*

Oralhygieneintervention(twicedailywithadditionaltreatmenttwiceaweek)comparedtooralhygieneintervention(twicedaily)comparedtousual care-continuousoutcome-Presenceoforaldisease(gingivalbleedingindex)-MeanPValue-Oral hygiene instruction (twice a day and additional treatment twice a week)-Oral hygiene intervention (twice a day)-Usual care-t3

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Indirectly applicable *(Downgraded due to outcome being a continuous outcome when dichotomous outcomes were prioritised and Intervention indirectness - reports an intervention that was not specified in the protocol but does represent an increased intensity of oral hygiene intervention so was included)*

Yuan, 2020

Bibliographic Reference	Yuan, D.; Zhang, J.; Wang, X.; Chen, S.; Wang, Y.; Intensified Oral Hygiene Care in Stroke-Associated Pneumonia: A Pilot Single-Blind Randomized Controlled Trial; Inquiry; 2020; vol. 57; 46958020968777

Study details

Secondary publication of another included study- see primary study for details	No additional information.
Other publications associated with this study included in review	No additional information.
Trial name / registration number	Chinese Clinical Trial Registry: ChiCTR-IPR-17013403.
Study type	Randomised controlled trial (RCT)
Study location	China.
Study setting	One neurological intensive care unit in a hospital in China.
Study dates	June 2017 to September 2018.
Sources of funding	This work was supported by the Beijing Science and Technology Committee (grant number Z151100004015041) and the Beijing Stomatological Hospital Subject Construction Fund (grant number 16-09-20).
Inclusion criteria	A clinical diagnosis of acute stroke; admission within 24 hours after stroke onset; age 18 years or older.
Exclusion criteria	Diagnosed with pneumonia or showed clinical signs of infection on admission; required mechanical ventilation; were prescribed antibiotics or immunosuppressive agents within the preceding 2 months; were unable to receive oral care within 12 hours of admission; had an allergy to chlorhexidine; were pregnant.

Recruitment / selection of participants	No additional information.
Intervention(s)	Intensified oral hygiene interventions (3 times a day) N=56 Routine oral hygiene care for a duration of 7 days. Cognitively intact participants with adequate manual dexterity and unimpaired mouth opening capacity were asked to perform oral care by themselves, with or without the help of a nursing assistant. Those participants with adequate manual dexterity and unimpaired mouth opening capacity were asked to perform oral care by themselves, with or without the help of a nursing assistant. Those participants lacking the ability to perform oral care, including all participants in the intensive care unit, received oral swabbing with saline (2-minute duration, twice daily). Intensified oral hygiene interventions in addition to oral self-care (or instead of routine saline swabbing), all teeth and oral soft tissues (including the gingiva, vestibule, buccal mucosa, floor of the mouth, tongue dorsum, and pharynx oralis), were swabbed with 0.12% chlorhexidine digluconate mouth wash (5-minute duration, 3 times daily). All interventions were performed by nurses who had been trained by a dental professional prior to the commencement of the study.
Comparator	Usual care N=57 Routine oral hygiene care for a duration of 7 days. Cognitively intact participants with adequate manual dexterity and unimpaired mouth opening capacity were asked to perform oral care by themselves, with or without the help of a nursing assistant. Those participants with adequate manual dexterity and unimpaired mouth opening capacity were asked to perform oral care by themselves, with or without the help of a nursing assistant. Those participants lacking the ability to perform oral care, including all participants in the intensive care unit, received oral swabbing with saline (2-minute duration, twice daily).
Number of participants	113
Duration of follow-up	7 days
Additional comments	No additional information
Subgroup 1: Severity (as stated by category or as	Moderate (or NIHSS 5-14)

measured by NIHSS scale)	
Subgroup 2: Type of stroke (using the Bamford scale)	Not stated/unclear
Subgroup 3: Dysphagia at baseline	Not stated/unclear
Subgroup 4: Type of intervention	Oral swabbing for secretions
Subgroup 5: People who are nil-by-mouth at baseline	Not stated/unclear
Subgroup analysis - further details	Severity: Given median and interquartile range values. People were between mild and severe, with the majority being of moderate severity. Type of stroke: Discusses ischaemic, intracerebral haemorrhage and subarachnoid haemorrhage (majority ischaemic).

Study arms

Intensified oral hygiene interventions (3 times a day) (N = 56)

Routine oral hygiene care for a duration of 7 days. Cognitively intact participants with adequate manual dexterity and unimpaired mouth opening capacity were asked to perform oral care by themselves, with or without the help of a nursing assistant. Those participants with adequate manual dexterity and unimpaired mouth opening capacity were asked to perform oral care by themselves, with or without the help of a nursing assistant. Those participants lacking the ability to perform oral care, including all participants in the intensive care unit, received oral swabbing with saline (2-minute duration, twice daily). Intensified oral hygiene interventions in addition to oral self-care (or instead of routine saline swabbing), all teeth and oral soft tissues (including the gingiva, vestibule, buccal mucosa,

floor of the mouth, tongue dorsum, and pharynx oralis), were swabbed with 0.12% chlorhexidine digluconate mouth wash (5-minute duration, 3 times daily). All interventions were performed by nurses who had been trained by a dental professional prior to the commencement of the study.

Usual care (N = 57)

Routine oral hygiene care for a duration of 7 days. Cognitively intact participants with adequate manual dexterity and unimpaired mouth opening capacity were asked to perform oral care by themselves, with or without the help of a nursing assistant. Those participants with adequate manual dexterity and unimpaired mouth opening capacity were asked to perform oral care by themselves, with or without the help of a nursing assistant. Those participants lacking the ability to perform oral care, including all participants in the intensive care unit, received oral swabbing with saline (2-minute duration, twice daily).

Characteristics

Arm-level characteristics

Characteristic	Intensified oral hygiene interventions (3 times a day) (N = 56)	Usual care (N = 57)
% Female Baseline characteristics only reported in 43 in the intervention group, and 41 in the control group. Sample size	n = 19 ; % = 44.2	n = 14 ; % = 34.1
Mean age (SD) Mean (SD)	57.1 (13.4)	60.3 (13.7)
Ethnicity Nominal	NR	NR

Characteristic	Intensified oral hygiene interventions (3 times a day) (N = 56)	Usual care (N = 57)
Comorbidities Nominal	NR	NR
Severity Median (IQR)	9 (1 to 18)	10 (1.5 to 17)
Ischaemic Nominal	25	25
Intracerebral haemorrhage Nominal	8	9
Subarachnoid haemorrhage Nominal	10	7
Dysphagia at baseline Nominal	NR	NR
People who are nil-by-mouth at baseline Nominal	NR	NR
Stroke more than once Baseline characteristics only reported in 43 in the intervention group, and 41 in the control group. Nominal	7	11

1

Outcomes

Study timepoints

- Baseline
- 7 day (This group will be included in the ≤3 months.)

Oral hygiene intervention (3 times a day) compared to usual care - dichotomous outcomes

Outcome	Intensified oral hygiene interventions (3 times a day), Baseline, N = 56	Intensified oral hygiene interventions (3 times a day), 7 day, N = 43	Usual care, Baseline, N = 57	Usual care, 7 day, N = 41
Mortality Nominal	NR	2	NR	4
Occurence of pneumonia Intervention: 5 Staphylococcus aureus, 3 Klebsiella pneumoniae, 1 Candida albicans. Control: 5 Staphylococcus aureus, 6 Klebsiella pneumoniae, 4 Acinetobacter baumannii, 1 Candida albicans, 1 Psuedomonas aeruginosa. Nominal	NR	9	NR	17

Mortality - Polarity - Lower values are better

Occurence of pneumonia - Polarity - Lower values are better

Critical appraisal - Cochrane Risk of Bias tool (RoB 2.0) Normal RCT

Oralhygieneintervention(3timesaday)comparedtousualcare-dichotomousoutcomes-Mortality-Nominal-Intensified oral hygiene interventions (3 times a day)-Usual care-t7

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable

Oralhygieneintervention(3timesaday)comparedtousualcare-dichotomousoutcomes-Occurenceofpneumonia-Nominal-Intensified oral hygiene interventions (3 times a day)-Usual care-t7

Section	Question	Answer
Overall bias and Directness	Risk of bias judgement	High
Overall bias and Directness	Overall Directness	Directly applicable

Appendix E – Forest plots

E.1 Oral hygiene intervention (once a day) compared to usual care

Figure 2: Mortality at ≤3 months

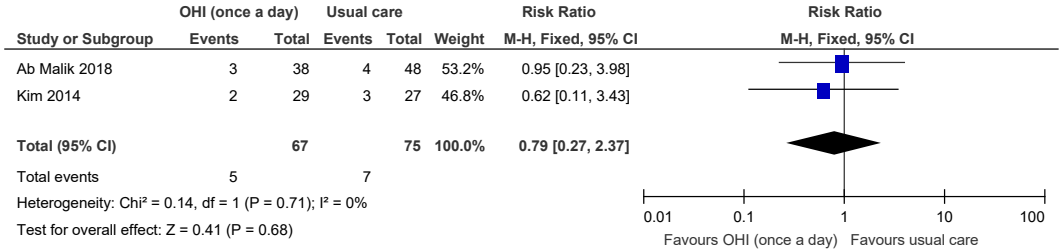


Figure 3: Requirement of enteral feeding support (nasogastric tube removal) at ≤3 months

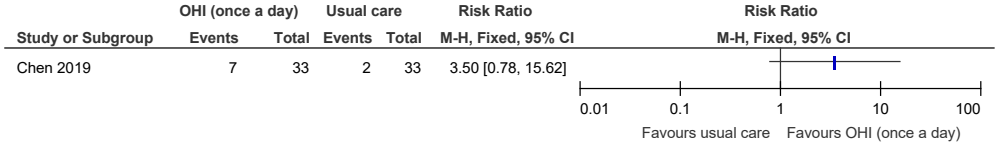
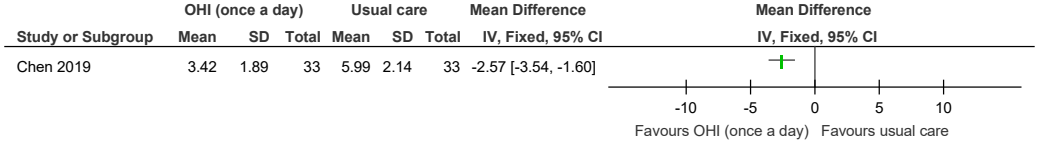


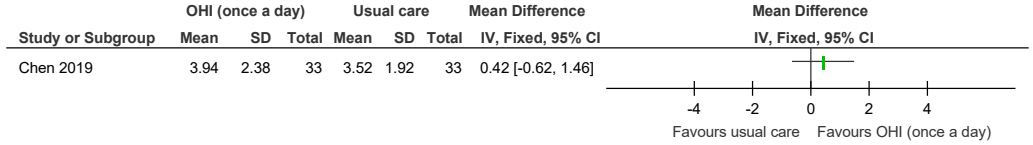
Figure 4: Oral health outcome scales (Oral Health Assessment Tool, 0-16, lower values are better, final value) at ≤3 months



Notes: Oral health intervention (once a day): 5.64 (2.54). Usual care: 5.24 (1.77).

1

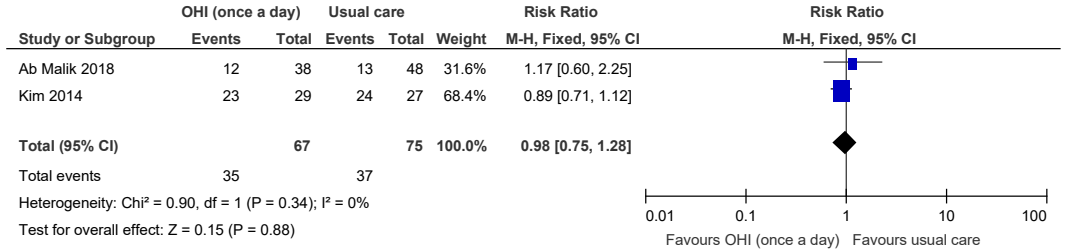
Figure 5: Dysphagia severity (Functional Oral Intake Scale, 1-7, higher values are better, final value) at ≤3 months



Notes: Oral health intervention (once a day): 3.15 (2.06). Usual care: 3.15 (1.79).

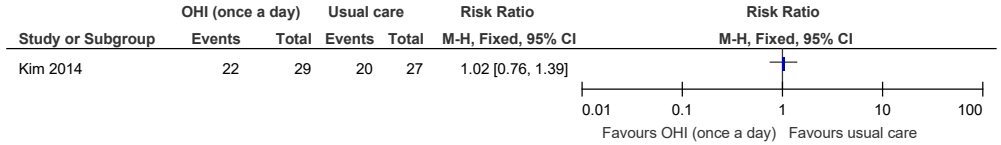
2

Figure 6: Presence of oral disease (oral candidiasis - on tongue) at ≤3 months



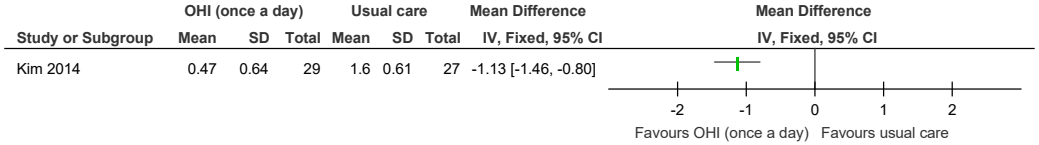
3

Figure 7: Presence of oral disease (oral candidiasis - in saliva) at ≤3 months



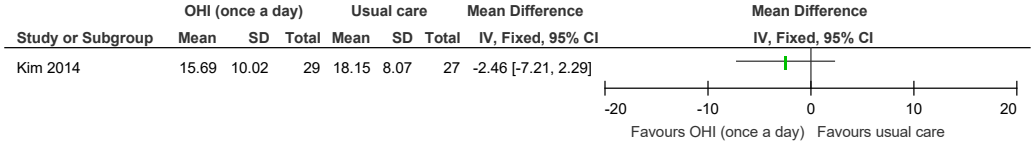
4

Figure 8: Presence of oral disease (gingivitis - gingival index, 0-3, lower values are better, final value) at ≤3 months



Notes: Baseline oral hygiene intervention (once a day): 1.54 (0.47). Baseline usual care: 1.3 (0.53).

Figure 9: Length of hospital stay (length of ICU admission, days, lower values are better) at ≤3 months



E.2 Oral hygiene intervention (twice a day) compared to usual care

Figure 10: Mortality at ≤3 months

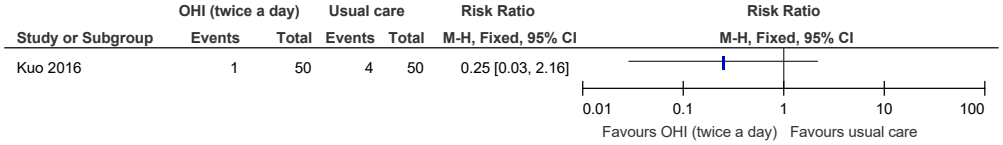
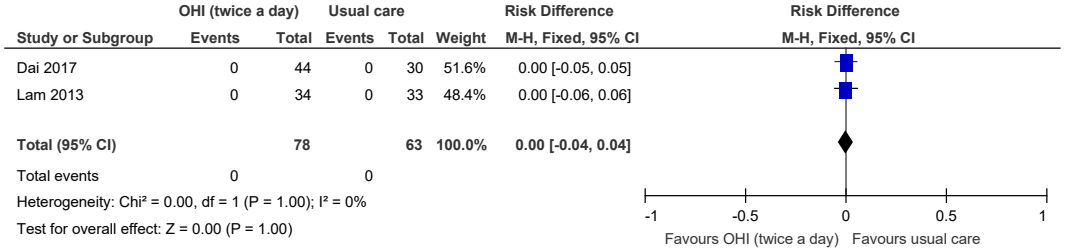
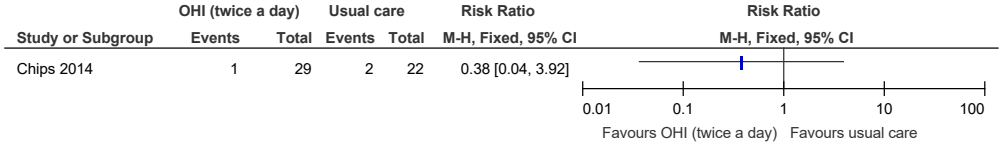


Figure 11: Occurrence of pneumonia at ≤3 months



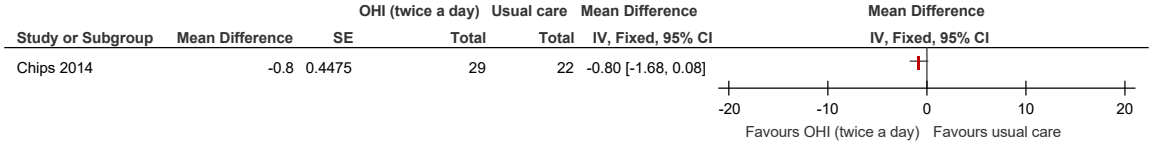
1

Figure 12: Requiring enteral feeding support (FOIS 1-3 at end of trial) at ≤3 months



2

Figure 13: Oral health outcome scales (revised-THROAT, 7-21, lower values are better, final value) at ≤3 months



Notes: Baseline oral health intervention (twice a day): 10.8 (2.6). Baseline usual care: 12.2 (2.1).

3

Figure 14: Dysphagia severity (progression in FOIS from 4-5 to 6-7 at end of trial) at ≤3 months

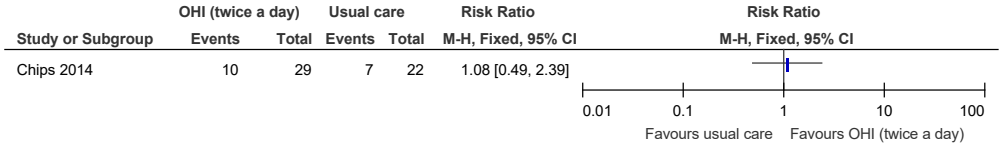
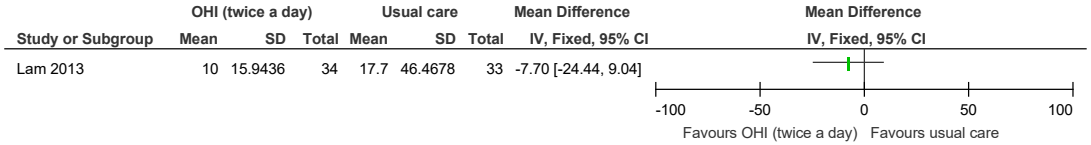


Figure 15: Presence of oral disease (gingivitis - gingival bleeding index, scale range unclear, lower values are better, final value) at ≤3 months



Notes: Baseline oral health intervention (twice a day). 18.8. Baseline usual care: 16.7.

E.3 Oral hygiene intervention (three times a day) compared to usual care

Figure 16: Mortality at ≤3 months

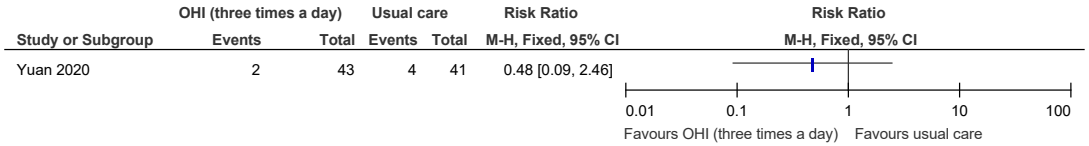
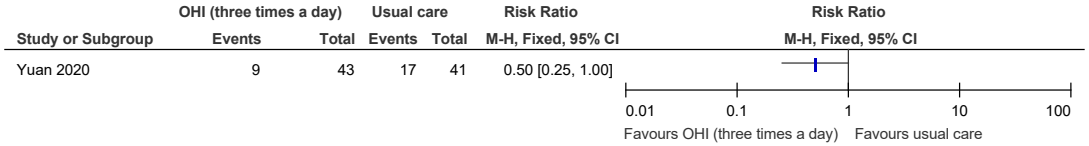


Figure 17: Occurrence of pneumonia at ≤3 months



E.4 Oral hygiene intervention (four times a day or more) compared to usual care

Figure 18: Mortality at ≤3 months

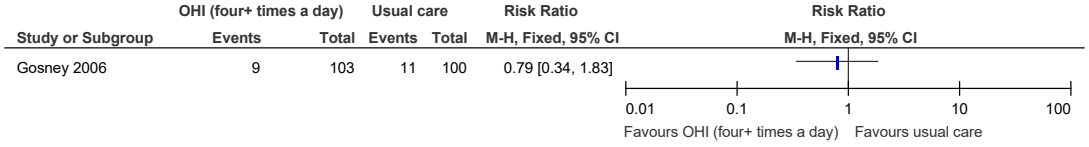
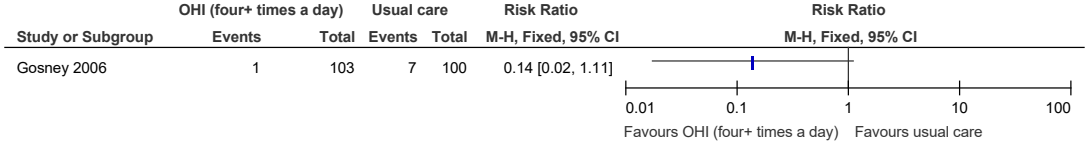


Figure 19: Occurrence of pneumonia at ≤3 months



E.5 Oral hygiene intervention (twice a day with additional treatment twice a week) compared to oral hygiene intervention (twice a day)

Figure 20: Occurrence of pneumonia at ≤3 months

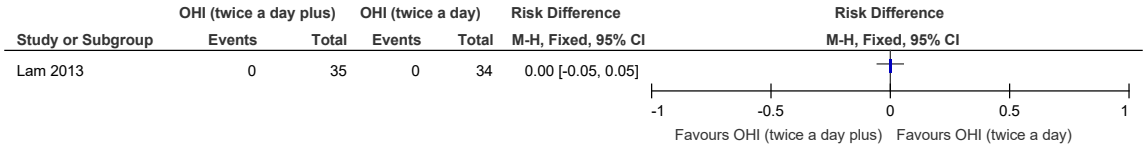
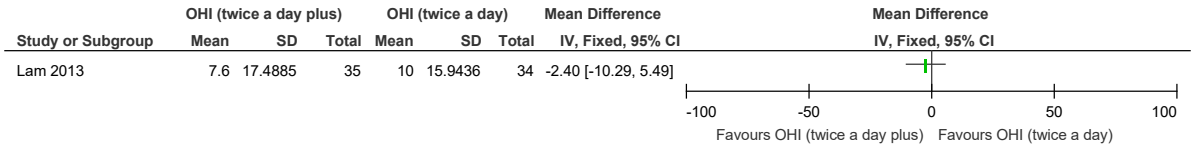


Figure 21: Presence of oral disease (gingivitis - gingival bleeding index, scale range unclear, lower values are better, final value) at ≤3 months



Notes: Baseline oral health intervention (twice a day with additional treatment twice a week): 16.7. Baseline oral health intervention (twice a day). 18.8.

E.6 Oral hygiene intervention (twice a day with additional treatment twice a week) compared to usual care

Figure 22: Occurrence of pneumonia at ≤3 months

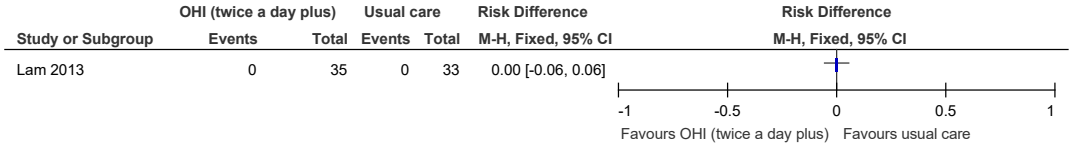
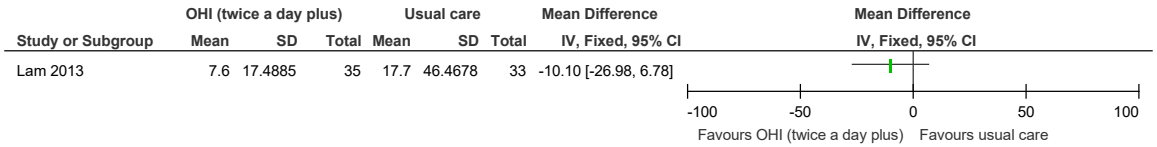


Figure 23: Presence of oral disease (gingivitis - gingival bleeding index, scale range unclear, lower values are better, final value) at ≤3 months



Notes: Baseline oral health intervention (twice a day with additional treatment twice a week): 16.7. Baseline usual care: 16.7.

Appendix F – GRADE tables

F.1 Oral hygiene intervention (once a day) compared to usual care

Table 11: Clinical evidence profile: oral hygiene intervention (once a day) compared to usual care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	oral hygiene intervention (once a day)	usual care	Relative (95% CI)	Absolute (95% CI)		
Mortality at ≤3 months (follow-up: mean 7 weeks)												
2	randomised trials	serious[a]	not serious	not serious	very serious[b]	none	5/67 (7.5%)	7/75 (9.3%)	**RR 0.79** (0.27 to 2.37)	**20 fewer per 1,000** (from 68 fewer to 128 more)	⨁◯◯◯ Very low	CRITICAL
Requirement of enteral feeding support (nasogastric tube removal) at ≤3 months (follow-up: 6 weeks; assessed with: nasogastric tube removal)												
1	randomised trials	serious[c]	not serious	serious[d]	very serious[b]	none	7/33 (21.2%)	2/33 (6.1%)	**RR 3.50** (0.78 to 15.62)	**152 more per 1,000** (from 13 fewer to 886 more)	⨁◯◯◯ Very low	CRITICAL
Oral health outcome scales (Oral Health Assessment Tool, 0-16, lower values are better, final value) at ≤3 months (follow-up: 6 weeks; assessed with: Oral Health Assessment Tool; Scale from: 0 to 16)												
1	randomised trials	very serious[e]	not serious	serious[d]	not serious	none	33	33	-	MD **2.57 lower** (3.54 lower to 1.6 lower)	⨁◯◯◯ Very low	CRITICAL
Dysphagia severity (Functional Oral Intake Scale, 1-7, higher values are better, final value) at ≤3 months (follow-up: 6 weeks; assessed with: Functional Oral Intake Scale; Scale from: 1 to 7)												
1	randomised trials	very serious[e]	not serious	serious[d]	serious[b]	none	33	33	-	MD **0.42 higher** (0.62 lower to 1.46 higher)	⨁◯◯◯ Very low	CRITICAL
Presence of oral disease (oral candidiasis - on tongue) at ≤3 months (follow-up: mean 7 weeks)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	oral hygiene intervention (once a day)	usual care	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	serious[a]	not serious	not serious	very serious[b]	none	35/67 (52.2%)	37/75 (49.3%)	**RR 0.98** (0.75 to 1.28)	**10 fewer per 1,000** (from 123 fewer to 138 more)	⨁◯◯◯ Very low	CRITICAL
Presence of oral disease (oral candidiasis - in saliva) at ≤3 months (follow-up: 2 weeks)												
1	randomised trials	very serious[f]	not serious	not serious	very serious[b]	none	22/29 (75.9%)	20/27 (74.1%)	**RR 1.02** (0.76 to 1.39)	**15 more per 1,000** (from 178 fewer to 289 more)	⨁◯◯◯ Very low	CRITICAL
Presence of oral disease (gingivitis - gingival index, 0-3, lower values are better, final value) at ≤3 months (follow-up: 2 weeks; assessed with: gingival index; Scale from: 0 to 3)												
1	randomised trials	very serious[g]	not serious	serious[h]	not serious	none	29	27	-	MD **1.13 lower** (1.46 lower to 0.8 lower)	⨁◯◯◯ Very low	CRITICAL
Length of hospital stay (length of ICU admission, days, lower values are better) at ≤3 months (follow-up: 2 weeks; assessed with: length of ICU admission)												
1	randomised trials	very serious[g]	not serious	serious[h]	serious[b]	none	29	27	-	MD **2.46 days fewer** (7.21 fewer to 2.29 more)	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. Downgraded by 1 increment as the majority of the evidence was at high risk of bias (due to a mixture of bias arising from the randomisation process and bias due to missing outcome data)

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 increment as the majority of the evidence was at high risk of bias (due to bias arising from the randomisation process)

d. Downgraded by 1 or 2 increments because of intervention indirectness (as the intervention included was delivered as less than the smallest frequency stated in the protocol)

e. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to a mixture of bias arising from the randomisation process and bias due to deviations from the intended interventions)

f. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process and bias due to missing outcome data)

g. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to a bias arising from the randomisation process, bias due to deviations from the intended interventions and bias due to missing outcome data)

h. Downgraded by 1 or 2 increments because of outcome indirectness (continuous scale for an outcome specified to be dichotomous in the protocol)

F.2 Oral hygiene intervention (twice a day) compared to usual care

Table 12: Clinical evidence profile: oral hygiene intervention (twice a day) compared to usual care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	oral hygiene intervention (twice a day)	usual care	Relative (95% CI)	Absolute (95% CI)		
Mortality at ≤3 months (follow-up: 2 months)												
1	randomised trials	serious[a]	not serious	not serious	very serious[b]	none	1/50 (2.0%)	4/50 (8.0%)	**RR 0.25** (0.03 to 2.16)	**60 fewer per 1,000** (from 78 fewer to 93 more)	⨁◯◯◯ Very low	CRITICAL
Occurrence of pneumonia at ≤3 months (follow-up: mean 8 weeks)												
2	randomised trials	serious[c]	not serious	not serious	serious[d]	none	0/78 (0.0%)	0/63 (0.0%)	**RD 0.00** (-0.04 to 0.04)	**0 fewer per 1,000** (from 40 fewer to 40 more)[e]	⨁⨁◯◯ Low	CRITICAL
Requiring enteral feeding support (FOIS 1-3 at end of trial) at ≤3 months (follow-up: 10 days; assessed with: FOIS 1-3 at end of trial)												
1	randomised trials	very serious[f]	not serious	not serious	very serious[b]	none	1/29 (3.4%)	2/22 (9.1%)	**RR 0.38** (0.04 to 3.92)	**56 fewer per 1,000** (from 87 fewer to 265 more)	⨁◯◯◯ Very low	CRITICAL
Oral health outcome scales (revised-THROAT, 7-21, lower values are better, final value) at ≤3 months (follow-up: 10 days; assessed with: revised-THROAT; Scale from: 7 to 21)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	oral hygiene intervention (twice a day)	usual care	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	very serious[f]	not serious	not serious	serious[b]	none	29	22	-	MD **0.8 lower** (1.68 lower to 0.08 higher)	⨁◯◯◯ Very low	CRITICAL
Dysphagia severity (progression in FOIS from 4-5 to 6-7 at end of trial) at ≤3 months (follow-up: 10 days; assessed with: progression in FOIS from 4-5 to 6-7 at end of trial)												
1	randomised trials	very serious[f]	not serious	serious[g]	very serious[b]	none	10/29 (34.5%)	7/22 (31.8%)	**RR 1.08** (0.49 to 2.39)	**25 more per 1,000** (from 162 fewer to 442 more)	⨁◯◯◯ Very low	CRITICAL
Presence of oral disease (gingivitis - gingival bleeding index, scale range unclear, lower values are better, final value) at ≤3 months (follow-up: 3 weeks; assessed with: gingival bleeding index)												
1	randomised trials	very serious[f]	not serious	serious[g]	serious[b]	none	34	33	-	MD **7.7 lower** (24.44 lower to 9.04 higher)	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. Downgraded by 1 increment as the majority of the evidence was at high risk of bias (due to bias arising from the randomisation process)

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

c. Downgraded by 1 increment as the majority of the evidence was at high risk of bias (due to a mixture of bias arising from the randomisation process and bias due to missing outcome data)

d. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

e. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

f. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process, bias due to deviations from the intended interventions and bias due to missing outcome data)

g. Downgraded by 1 or 2 increments because of outcome indirectness (continuous scale for an outcome specified to be dichotomous in the protocol)

F.3 Oral hygiene intervention (three times a day) compared to usual care

Table 13: Clinical evidence profile: oral hygiene intervention (three times a day) compared to usual care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	oral hygiene intervention (three times a day	usual care	Relative (95% CI)	Absolute (95% CI)		
Mortality at ≤3 months (follow-up: 7 days)												
1	randomised trials	very serious[a]	not serious	not serious	very serious[b]	none	2/43 (4.7%)	4/41 (9.8%)	**RR 0.48** (0.09 to 2.46)	**51 fewer per 1,000** (from 89 fewer to 142 more)	⨁◯◯◯ Very low	CRITICAL
Occurence of pneumonia at ≤3 months (follow-up: 7 days)												
1	randomised trials	very serious[a]	not serious	not serious	serious[b]	none	9/43 (20.9%)	17/41 (41.5%)	**RR 0.50** (0.25 to 1.00)	**207 fewer per 1,000** (from 311 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval; **RR:** risk ratio

Explanations

a. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process and bias due to missing outcome data)

b. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

F.4 Oral hygiene intervention (four times a day or more) compared to usual care

Table 14: Clinical evidence profile: oral hygiene intervention (four times a day or more) compared to usual care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	oral hygiene intervention (four times a day or more)	usual care	Relative (95% CI)	Absolute (95% CI)		
Mortality at ≤3 months (follow-up: 3 weeks)												
1	randomised trials	not serious	not serious	not serious	very serious[a]	none	9/103 (8.7%)	11/100 (11.0%)	**RR 0.79** (0.34 to 1.83)	**23 fewer per 1,000** (from 73 fewer to 91 more)	⨁⨁◯◯ Low	CRITICAL
Occurrence of pneumonia at ≤3 months (follow-up: 3 weeks)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	1/103 (1.0%)	7/100 (7.0%)	**RR 0.14** (0.02 to 1.11)	**60 fewer per 1,000** (from 69 fewer to 8 more)	⨁⨁⨁◯ Moderate	CRITICAL

CI: confidence interval; **RR:** risk ratio

Explanations

a. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

F.5 Oral hygiene intervention (twice a day with additional treatment twice a week) compared to oral hygiene intervention (twice a day)

Table 15: Clinical evidence profile: oral hygiene intervention (twice a day with additional treatment twice a week) compared to oral hygiene intervention (twice a day)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	oral hygiene intervention (twice a day and additional treatment twice a week)	oral hygiene intervention (twice a day)	Relative (95% CI)	Absolute (95% CI)		
Occurrence of pneumonia at ≤3 months (follow-up: 3 weeks)												
1	randomised trials	very serious[a]	not serious	serious[b]	serious[c]	none	0/35 (0.0%)	0/34 (0.0%) [d]	**RD 0.0** (-0.5 to 0.5)	**0 fewer per 1,000** (from 50 fewer to 50 more)[d]	⨁◯◯◯ Very low	CRITICAL
Presence of oral disease (gingivitis - gingival bleeding index, scale range unclear, lower values are better, final value) at ≤3 months (follow-up: 3 weeks; assessed with: gingival bleeding index)												
1	randomised trials	very serious[a]	not serious	very serious[e]	serious[f]	none	35	34	-	MD **2.4 lower** (10.29 lower to 5.49 higher)	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process and bias due to missing outcome data)

b. Downgraded by 1 increment due to intervention indirectness (due to the intervention being one that is not stated in the protocol but does indicate an increased intensity of oral hygiene intervention)

c. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

d. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

e. Downgraded by 2 increments because of intervention and outcome indirectness (due to the intervention being one that is not stated in the protocol but does indicate an increased intensity of oral hygiene intervention and using a continuous outcome for one specified to be dichotomous in the protocol)

f. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

F.6 Oral hygiene intervention (twice a day with additional treatment twice a week) compared to usual care

Table 16: Clinical evidence profile: oral hygiene intervention (twice a day with additional treatment twice a week) compared to usual care

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	oral hygiene intervention (twice a day and additional treatment twice a week)	usual care	Relative (95% CI)	Absolute (95% CI)		
Occurrence of pneumonia at ≤3 months (follow-up: 3 weeks)												
1	randomised trials	very serious[a]	not serious	serious[b]	serious[c]	none	0/35 (0.0%)	0/33 (0.0%) [d]	**RD 0.0** (-0.6 to 0.6)	**0 fewer per 1,000** (from 60 fewer to 60 more)[d]	⨁◯◯◯ Very low	CRITICAL
Presence of oral disease (gingivitis - gingival bleeding index, scale range unclear, lower values are better, final value) at ≤3 months (follow-up: 3 weeks; assessed with: gingival bleeding index)												
1	randomised trials	very serious[a]	not serious	very serious[e]	serious[f]	none	35	33	-	MD **10.1 lower** (26.98 lower to 6.78 higher)	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Downgraded by 2 increments as the majority of the evidence was at very high risk of bias (due to bias arising from the randomisation process and bias due to missing outcome data)

b. Downgraded by 1 increment because of intervention indirectness (due to the intervention being one that is not stated in the protocol but does indicate an increased intensity of oral hygiene intervention)

c. Downgraded by 1 to 2 increments for imprecision due to zero events and small sample size

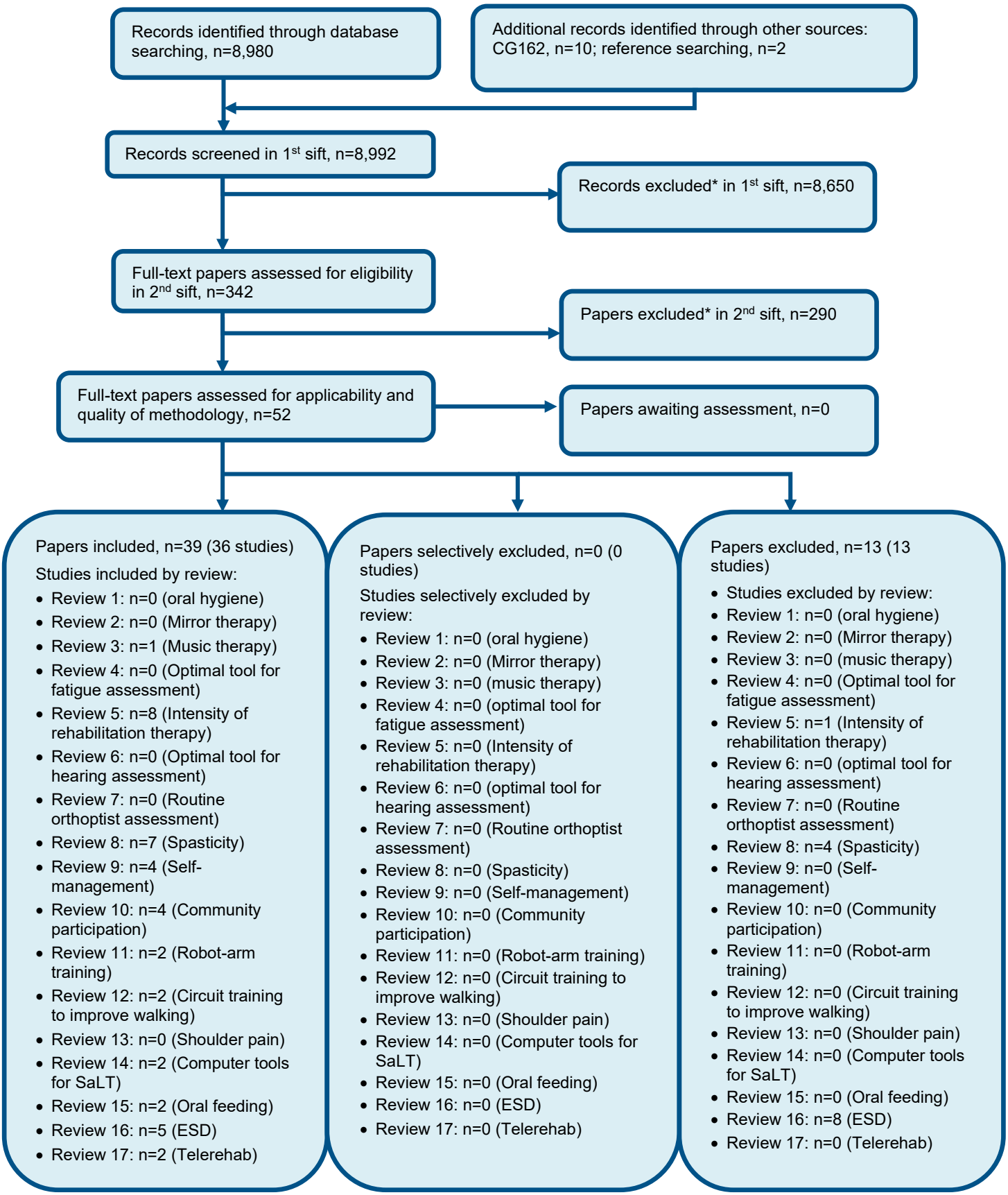
d. Absolute effect calculated by risk difference due to zero events in at least one arm of one study

e. Downgraded by 2 increments because of intervention and outcome indirectness (due to the intervention being one that is not stated in the protocol but does indicate an increased intensity of oral hygiene intervention and using a continuous outcome for one specified to be dichotomous in the protocol)

f. Downgraded by 1 increment if the confidence interval crossed one MID or by 2 increments if the confidence interval crossed both MIDs

Appendix G – Economic evidence study selection

Figure 24: Flow chart of health economic study selection for the guideline



* Non-relevant population, intervention, comparison, design or setting; non-English language

Appendix H – Economic evidence tables

No health economic studies were included in this review.

Appendix I – Health economic model

New cost-effectiveness analysis was not prioritised in this area.

Appendix J – Excluded studies

Clinical studies

Table 17: Studies excluded from the clinical review

Study	Code [Reason]
'Ö, Ä, ö2, Lakhyung, Kim et al. (2011) Effect of Saengmaeg-san Extract on Xerostomia in Stroke Patients : A Double-Blind Randomized Controlled Study. The Journal of Internal Korean Medicine 32: 542-549	- Study not reported in English
Ab Malik, N., Mohamad Yatim, S., Lam, O. L. et al. (2017) Effectiveness of a Web-Based Health Education Program to Promote Oral Hygiene Care Among Stroke Survivors: Randomized Controlled Trial. Journal of Medical Internet Research 19(3): e87	- Population not relevant to this review protocol *Investigating effects purely on the healthcare professionals, not the stroke survivors*
Brady, M. C., Stott, D. J., Norrie, J. et al. (2011) Developing and evaluating the implementation of a complex intervention: using mixed methods to inform the design of a randomised controlled trial of an oral healthcare intervention after stroke. Trials [Electronic Resource] 12: 168	- Study design not relevant to this review protocol *Non-comparative study*
Brady, M. C., Stott, D. J., Weir, C. J. et al. (2020) A pragmatic, multi-centered, stepped wedge, cluster randomized controlled trial pilot of the clinical and cost effectiveness of a complex Stroke Oral healthCare intervention pLan Evaluation II (SOCLE II) compared with usual oral healthcare in stroke wards. International Journal of Stroke 15(3): 318-323	- Population not relevant to this review protocol *Is conducted on a stroke ward but not with stroke patients only. The overall diagnosis rate was 74.8%. Therefore, >20% didn't have a stroke.*
Brady, M. C., Stott, D., Weir, C. J. et al. (2015) Clinical and cost effectiveness of enhanced oral healthcare in stroke care settings (SOCLE II): a pilot, stepped wedge, cluster randomized, controlled trial protocol. International Journal of Stroke 10(6): 979-84	- Population not relevant to this review protocol *Protocol for a different study that was excluded as it was conducted on a stroke ward but not with stroke patients only. The overall diagnosis rate was 74.8%. Therefore, >20% didn't have a stroke.*
Brady, M., Furlanetto, D., Hunter, R. V. et al. (2006) Staff-led interventions for improving oral hygiene in patients following stroke. Cochrane Database of Systematic Reviews: cd003864	- More recent systematic review included that covers the same topic
Campbell, P., Bain, B., Furlanetto, D. L. C. et al. (2020) Interventions for improving oral health in people after stroke. Cochrane Database of Systematic Reviews	- Cochrane review - included interventions in the pooled analysis that are not included in our analysis (assessment techniques), included outcomes that the committee did not think were

Study	Code [Reason]
	relevant for their analysis, included studies with a smaller proportion of participants with stroke than 80% (as agreed in the protocol for this guideline) *References checked*
Dai, R., Lam, O. L. T., Lo, E. C. M. et al. (2017) Oral health-related quality of life in patients with stroke: a randomized clinical trial of oral hygiene care during outpatient rehabilitation. Scientific Reports 7(1): 7632	- Data not reported in an extractable format or a format that can be analysed
Dai, R., Lam, O. L., Lo, E. C. et al. (2015) A systematic review and meta-analysis of clinical, microbiological, and behavioural aspects of oral health among patients with stroke. Journal of Dentistry 43(2): 171-80	- Comparator in study does not match that specified in this review protocol *Compares people who had a stroke with people who did not looking at their oral health care behaviours and status*
Edwards, M. (2008) Staff training improved oral hygiene in patients following stroke. Evidence-Based Dentistry 9(3): 73	- Study design not relevant to this review protocol *Commentary on a systematic review*
Fields, L. B. (2008) Oral care intervention to reduce incidence of ventilator-associated pneumonia in the neurologic intensive care unit. Journal of Neuroscience Nursing 40(5): 291-8	- Study design not relevant to this review protocol *Started as a randomised control trial, but then finished early due to positive response. They did not report results in a way that we could extract.*
Frenkel, H.; Harvey, I.; Needs, K. (2002) Oral health care education and its effect on caregivers' knowledge and attitudes: a randomised controlled trial. Community Dent Oral Epidemiol 30(2): 91-100	- Population not relevant to this review protocol *<80% of participants had a stroke.*
Frenkel, H.; Harvey, I.; Newcombe, R. G. (2001) Improving oral health in institutionalised elderly people by educating caregivers: a randomised controlled trial. Community Dent Oral Epidemiol 29(4): 289-97	- Population not relevant to this review protocol
Juthani-Mehta, M., Van Ness, P. H., McGloin, J. et al. (2015) A cluster-randomized controlled trial of a multicomponent intervention protocol for pneumonia prevention among nursing home elders. Clin Infect Dis 60(6): 849-57	- Population not relevant to this review protocol
Kelly, T. (2010) Review of the evidence to support oral hygiene in stroke patients. Nursing Standard 24(37): 35-8	- Review article but not a systematic review

Study	Code [Reason]
Kim, E. K., Park, E. Y., Sa Gong, J. W. et al. (2017) Lasting effect of an oral hygiene care program for patients with stroke during in-hospital rehabilitation: a randomized single-center clinical trial. Disability & Rehabilitation 39(22): 2324-2329	- Data not reported in an extractable format or a format that can be analysed *Discusses number of people who had systemic infection and recurrence of stroke together, while if reported separately may be able to use systemic infection to discuss pneumonia.*
Kobayashi, K., Ryu, M., Izumi, S. et al. (2017) Effect of oral cleaning using mouthwash and a mouth moisturizing gel on bacterial number and moisture level of the tongue surface of older adults requiring nursing care. Geriatr Gerontol Int 17(1): 116-121	- Data not reported in an extractable format or a format that can be analysed
Kuo, Y. W., Yen, M., Fetzer, S. et al. (2015) Effect of family caregiver oral care training on stroke survivor oral and respiratory health in Taiwan: a randomised controlled trial. Community Dental Health 32(3): 137-42	- Data not reported in an extractable format or a format that can be analysed
Lam, O. L. T. and McGrath, C. P. J. (2010) A clinical trial on the effect of chlorhexidine mouth rinse and assisted tooth brushing on the health condition and quality of life of elderly stroke patients.	- Full text paper not available *Trial registry record*
Lyons, M., Smith, C., Boaden, E. et al. (2018) Oral care after stroke: Where are we now?. European Stroke Journal 3(4): 347-354	- Review article but not a systematic review *Narrative review, references checked*
McMillan, A. S. (2006) A randomized clinical trial on the effect of chlorhexidine mouth rinse and assisted tooth brushing on the health condition and quality of life of elderly stroke patients.	- Full text paper not available *Trial registry record*
Poohkam, J., Meemak, J., Sukhanthaman, M. et al. (2021) The effectiveness of an aspiration pneumonia prevention program in acute ischemic stroke patients. Stroke 52(suppl1)	- Conference abstract
Seguin, P., Laviolle, B., Dahyot-Fizelier, C. et al. (2014) Effect of oropharyngeal povidone-iodine preventive oral care on ventilator-associated pneumonia in severely brain-injured or cerebral hemorrhage patients: a multicenter, randomized controlled trial. Critical Care Medicine 42(1): 1-8	- Population not relevant to this review protocol
Smith, C., Lightbody, C., Sandom, F. et al. (2022) CHLORHEXIDINE OR TOOTHPASTE, MANUAL OR POWERED BRUSHING TO PREVENT PNEUMONIA COMPLICATING	- Conference abstract

Study	Code [Reason]
STROKE (CHOSEN): A 2X2 FACTORIAL RANDOMISED CONTROLLED FEASIBILITY TRIAL. European Stroke Journal 7(1suppl): 150-151	
Wu, J., Dai, Y., Lo, E. C. M. et al. (2020) Using metagenomic analysis to assess the effectiveness of oral health promotion interventions in reducing risk for pneumonia among patients with stroke in acute phase: study protocol for a randomized controlled trial. Trials [Electronic Resource] 21(1): 634	- Protocol only

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2006 or later and not from non-OECD country or USA) but that were excluded following appraisal of applicability and methodological quality are listed below. See the health economic protocol for more details.

Table 18: Studies excluded from the health economic review

Reference	Reason for exclusion
None	

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