Question 57 evidence tables

Question 57: For nutritionally vulnerable stroke patients, does nutritional support or meal time interventions result in improved outcomes?

NB Any discrepancies between reviewers in evidence quality and comment were discussed at the corresponding evidence review meeting

NG = nasogastric, FIM =functional independence measure, GCS = Glasgow Coma Scale, GNRI = Geriatric Nutritional Risk Index, EN = enteral nutrition, BMI = body mass index, FILS = food intake level scale, SMI = Skeletal muscle mass index, WHOQOL = World Health organization Quality of Life measure, SWAL-QOL = Swallowing quality of life measure, MNA = Mini Nutritional Assessment, MUAC = Mid Upper Arm Circumference, GI = gastrointestinal, UTI = urinary tract infection, SR = systematic review, MA = meta-analysis, RCT = randomised controlled trial, IPDMA = individual patient data meta-analysis, MDT = multidisciplinary team, PICO = patient/population, intervention, comparison and outcomes, OR = odds ratio, CI = confidence interval, QoL = quality of life, ADL = activities of daily living, mRS = modified Rankin Scale, OR = odds ratio, RR = relative risk, aOR = adjusted odds ratio, cOR = crude odds ratio, CI = confidence interval, RoB = risk of bias, I^2 = heterogeneity statistic.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
461	S. T. Robertson et al. (2020). Acute stroke patients not meeting their nutrition requirements: Investigating nutrition within the enriched environment. *Clinical Nutrition,* 39:5 1470-1477	Setting: Stroke unit, regional hospital Queensland, Australia. Design: A sub study of a prospective observational before and after study. Subjects: 60 participants, admitted to acute stroke unit within 24-72hr of stroke onset. 30 subjects experienced standard care. An enriched environment (EE) was then embedded in the ward. Data was then collected from 30 participants experiencing the enriched environment. This gave a total of 232 days of data for standard care, and 152 days for the enriched environment.	Enriched environment. This comprised: communal mealtimes in dining room (breakfast on 3 weekdays, and lunch on all weekdays) – voluntary or scheduled, activity cards placed at bedside to highlight nutrition priorities and empower patients and family, nutrition nurse champions empowered staff through change management strategies.	Nutritional intake (energy and protein), Mon-Sat over admission. Estimated either by visual estimation of intake by dietitian/nutrition assistants (Breakfast + lunch) or review of food charts which had been completed by nursing staff (Evening meal + other) Nutritional intake was expressed as a percentage of requirements.	No statistically significant differences in nutritional intake were seen between those that experienced standard care or the enriched environment. This remained when patients were stratified by NIHSS score - although n = max of 18, and some differences warranted further studies in future. No other outcomes reported e.g. weight/anthropometry/ patient experience/ functional change.	SIGN checklist not applicable. There were differences in patient characteristics between groups – LoS was longer for those receiving standard care. The study was a sub study of a wider study so not adequately powered to detect significant differences in nutritional intake. No blinding. Study does not mention time since stroke or impairments that may affect potential response to the interventions. Factors affecting results: some patients were also receiving enteral nutrition, dysphagia not described, data not stratified according to risk of malnutrition – those at

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
						different risk may have benefited to different extents. Strength of study is that it measured intake over whole admission (not a snapshot).
461	S. T. Robertson et al. (2020). Acute stroke patients not meeting their nutrition requirements: Investigating nutrition within the enriched environment. *Clinical Nutrition,* 39:5 1470-1477	Australian study. Acute Stroke Unit. A prospective observational study (before/after) looking at the differences between energy and protein intake between standard care and the enriched groups. Part of a larger study to determine differences in activity levels at mealtimes. 195 patients were screened. 32 standard care (2 withdrawn) and 30 to the enriched group. Data were collected from patients with a minimum of 2 days stay and a maximum of 25 days stay over six weeks. Aim to study the effect of enriched environment strategies that altered the approach to nutrition care on intake and malnutrition rate in an acute stroke unit.	To determine if embedding environmental enrichment altered nutritional intake and if environmental strategies reduced malnutrition. The Control group receives standard care. The intervention group had meals in an enriched environment for 6 weeks, 6 days a week, 3 breakfasts, and all lunchtime meals. Not explored: patients' preferences for communal dining.	Nutritional intake: body weight using the ratio method. Energy and protein intake. Observation of meals while visual estimations of portions were collated using the hospital ready reckoner. (Fluid balance charts were used for those NG fed). Malnutrition was assessed with a subjective global assessment and body weight.	The intervention of communal mealtimes did not significantly impact nutrition intake overall. Length of stay was longer in the standard care group, but the number of days on enteral feeding was higher P=0.01, indicating a greater dependency in this group. Also, NIHSS and dysphagia were slightly higher for the standard care group. Neither group met daily requirements for energy or protein (70% of nutritional requirements were met). No significant differences between the two groups for energy and protein intake (enteral feeding date was excluded). Mean body weight dropped for both groups from admission to discharge and malnutrition rates increased for both groups, although the absolute difference was not significantly different between the two groups. Logistic regression models showed that the length of stay, protein, or energy intake was independently associated.	**0** Limitations: Samples size was not powered to detect significant differences between groups for nutritional intake—lack of blinding. No formal assessment of inter-rater reliability was conducted for the observers. The use of estimated requirements could have impacted on findings. No qualitative data were collected to understand the patient experience and perceptions of strategies. There is some discussion about the acuity of patients (mild. Moderate, severe) and how these could have affected outcomes. Impacts of physical and cognitive deficit. There were 6 more patients in the standard care group with dysphagia. This could have skewed the results. Confounding factors and exposure levels are not discussed. The patients were only observed over 6 days, with no explanation as to why it was not over 7 days. Another staff was observing at

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
						weekends. The possibility of differences in the assessment was not discussed. There were also significantly more patients with enteral feeding in the standard group (58v20 days), and the length of stay was longer, indicating that the level of complexity and disability might have been higher in the standard carry group. It's not clear if all the patients in the intervention group attended every communal dining experience as it says they were 'encouraged' to go, and it was voluntarily. The communal meals were only 3-weekday breakfasts and all lunch meals Monday to Friday. The dose of intervention is low. The training provided for the intervention staff was not described.
462	K. Sakai et al. (2019). Effects of Nutrition Therapy in Older Stroke Patients Undergoing Rehabilitation: A Systematic Review and Meta-Analysis. *Journal of Nutrition, Health & Aging,* 23:1 21-26	Setting: Country and care setting varied and not always described Design: Systematic review and Meta analysis Subjects: 8 RCTs, 5484 participants – stroke patients, undergoing rehab – all but 1 study in acute phase. Mean age over 65years. 79% had infarct, time since stroke varied. One	Intervention: Nutritional therapy: 3 studies oral nutritional support 2 studies essential amino acids 2 studies early enteral nutrition 1 study individualized nutritional care.	Primary outcome: ADL (eg Barthel index or FIM) Secondary outcomes: All-cause mortality, infections, pneumonia incidence, disability level (mRS), walking ability, fall, stroke recurrence, QoL	No significant effects on ADL scores of nutritional therapy (data from 2 trials n=248, low quality evidence based on risk of bias and trial size) Significant effect of nutritional therapy on infections (data from 3 trials, n= 311, low quality evidence) RR 0.65, CI 0.51-0.84, p<0.001. This was a secondary outcome.	**+** Well conducted systematic review but limitations in quality of small number of varied studies included. Interventions were varied and population characteristics varied and not all described (e.g. nutritional status at baseline) makes interpretation of results limited. Other

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		trial accounted for 73.3% of participants.	Control: nil/sham/standard care			outcome measures may be useful in future.
462	K. Sakai et al. (2019). Effects of Nutrition Therapy in Older Stroke Patients Undergoing Rehabilitation: A Systematic Review and Meta-Analysis. *Journal of Nutrition, Health & Aging,* 23:1 21-26	Systematic Review Meta-analysis exploring the effects of nutrition therapy in older people undergoing stroke rehabilitation. (Tokyo, Japan). Studies with a mean age of 56 were included. 32 potentially relevant studies were retrieved only 8 were included.	Nutrition therapy- lectures, counselling, fortified foods, oral nutrition, supplements, or parenteral/enteral feeding.	Activities of daily living were measured using Barthel and FIM. Secondary outcomes included mortality, infections, pneumonia and disability level, mobility, falls and quality of life.	The meta-analysis for ADL was only conducted on 3 trials (FIM)- this showed no significant effect on ADL. The reason for not including the other studies included low-quality evidence, small samples, and insufficient information. No effect was found in 5 trials regarding mortality and nutritional interventions. Only 3 trials could be analysed for infection complications and nutrition therapy, but a clinically significant effect was found. 3 trials were analysed for severe disability and nutritional therapy, with no significant effect. 0 trials were analysed for walking ability and falls. No effect on stroke recurrence. No analysis on QoL was included as mean values were published. In summary nutritional therapy has a possible link to decreasing infections. However, the review findings should be interpreted with caution as overall the studies included were of moderate to low quality and several had a high risk of bias.	**0** The study used the Cochrane tool for assessing risk. 24 studies were excluded- the reason for exclusion notes but the list of excluded studies was not provided. The GRADE approach was used to assess the quality of the evidence, but the details of this were not included. Potential for overestimating the effects of the intervention. Egger's test could have been used. No funnel plots included. The trials included had a high or unclear risk of bias for each outcome. 4 trials had an increased risk of bias for blinding for patients and personnel and 2 trials had a high risk of blinding bias for outcome assessors.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
50	X. Cheng et al. (2019). Association between enteral nutrition support and neurological outcome in patients with acute intracranial haemorrhage: A retrospective cohort study. *Scientific Reports,* 9:1 16507	Design: Retrospective cohort study Setting: Single centre in China. Subjects: 230 patients admitted to ICU after intracerebral surgery due to ICH.	Study investigated association between amount of enteral nutrition (EN) (caloric intake per kg within first 48hr) and GCS score on discharge from hospital 4 models were developed using different methods to stratify amount of EN. EN as: 1. Continuous variable, 2. ≤25 or >25kcal/kg/48hr, 3. ≤10, 10-25 or >25kcal/kg/48hr, or 4. Quartiles Q1-Q4. Propensity score matching analysis compared patients receiving EN≤25 and EN>25 kcal/kg/48hr (n=69 pairs).	Primary Outcome: GCS on discharge, dichotomized to ≤8 and >8 Secondary Outcomes: Duration of ICU stay, duration of hospital stay and occurrence of hospital acquired pneumonia	Higher EN in first 48hr was associated with favourable GCS on discharge – when analysed as a continuous variable and when stratified. Propensity score matching, to minimize the effect of confounders, completed on two groups: those receiving >25 kcal/kg/48hr compared to those receiving ≤25kcal/kg/48hr. Based on 69 pairs, the proportion of patients with GCS at discharge > 8 was higher in those receiving >25 kcal/kg/48hr (60/69 v 48/69 p = 0.013). Causal relationship could not be inferred due to study design.	**+** Limitations: Sources of bias – performance and detection bias. Confounders not comprehensive. Population is ICU population with one diagnosis (ICH) in single centre in China. Unclear if results applicable to UK/ Ireland stroke patients. Nutrition was quantified for first 48hr (short time and unclear if this is a clinically significant period). Although EN reported as kcal/kg, we do not know how this compares to an individual's requirements.
50	X. Cheng et al. (2019). Association between enteral nutrition support and neurological outcome in patients with acute intracranial haemorrhage: A retrospective cohort study. *Scientific Reports,* 9:1 16507	Dongyang, China. A retrospective study exploring the association between the amount of enteral nutrition caloric intake and Glasgow coma scale (GCS) scores at discharge. Subjects had a diagnosis of Intra-cranial haemorrhage, 230 participants in a single-centre trial over two years. Two groups a) GCS 3-8, 56 participants and b) GCS 9-15, 174	Topic: Enteral nutrition. The study mentions non-stroke patients in the discussion. It's not clear what data was collected from these participants and how this was relevant.	Enteral nutrition and Glasgow coma scale.	For patients with relatively low enteral nutrition (EN) intake, an increased amount of EN intake had associated with favourable GCS scores on discharge. However, only 32.6% of participants had 50% of the target EN goal. So, no conclusions can be drawn as the optimal intake was not	**0** The number of co-morbidities included is small, they do not include cancers or other neurological disease such as dementia. Propensity scores were used to reduce selection bias. Confounding variables are not robustly discussed. The authors discuss that their

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		participants; comparison of outcome data between the two groups.	There were no interventions as this study was exploring data retrospectively.		achieved for half of the participants.	definition of 'high caloric EN intake group' may not have been sufficient and suggest this may have affected the outcomes. In summary, due to the retrospective nature of the study and the low caloric intake (only 32.6% of participants received 50% of the target EN) a causal link cannot be inferred.
458	M. Nii et al. (2016). Nutritional Improvement and Energy Intake Are Associated with Functional Recovery in Patients after Cerebrovascular Disorders. *Journal of Stroke and Cerebrovascular Diseases,* 25:1 57-62	Setting: Convalescent rehab ward in one hospital in Japan Design: Cross sectional retrospective study Subjects: 67 post stroke patients aged 65yr or older who were admitted to rehab ward.	Subjects divided in to 2 groups: One where Geriatric Nutritional Risk Index (GNRI) did not change over admission and one where GNRI increased (i.e improved) over admission	FIM efficiency i.e. change in FIM score divided by length of stay	Patients whose GNRI improved had significantly better improvement in FIM over their admission in the rehab setting: FIM Gain of 17 v 20 (p=0.036), FIM efficiency 0.14 v 0.22 (p=0.02). Multivariate regression analysis showed improvement in GNRI, amount of energy intake and type of ICH were independently associated with increase in FIM efficiency. Study designed to report an association and not causation.	**N/A** SIGN checklist not applicable Limitations: GNRI is not widely used measure of risk of malnutrition in UK, not all relevant confounders accounted for (e.g. length of stay, stroke severity, time since stroke). Concern around selection bias (16% of subjects had missing variables so were excluded). Data from one rehab ward in Japan. Interesting to link a change in nutritional status to functional outcomes.
458	M. Nii et al. (2016). Nutritional Improvement and Energy Intake Are Associated with	Sakurakai Japan. The cross-sectional, retrospective, single-centre study, investigating stroke patients over 65 admitted to	Topic: Nutritional improvement and energy intake.	GNRI- nutritional risk index (Serum albumin concentration and body weight)	The group with improved GNRI levels had lower serum albumin levels. Patients in the improved group had better recovery. An improvement in	**N/A** As the data was retrospective it was not possible to establish a causal link between improved nutritional status and ADL. A

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	Functional Recovery in Patients after Cerebrovascular Disorders. *Journal of Stroke and Cerebrovascular Diseases,* 25:1 57-62	hospital for stroke rehabilitation in two years. 11.65 hours of rehab a week. Patients treated by a specialist nutrition team were included in the study. The participants were split into two groups by their GNRI score. 67 participants (45 male and 22 females) mean age of 78 years were included. The study explores changes in nutritional status, energy intake, and rehabilitation outcomes.	There weren't any interventions as this study was exploring data retrospectively.	Bodyweight is defined by BMI score. The severity of dysphagia FILS (food intake level scale) FIM- functional independence measure. The level of stroke severity was not reported- this is a confounding variable.	nutritional status was associated with improved ADL and the amount of energy intake was associated with a degree of improvement in ADL. Indicating nutritional care could be effective for patients in stroke rehab. However, the content of the rehabilitation was not described, and the content of nutritional care was not described.	small sample size of 67 means that confounding factors could not be adjusted for. No clear definitions of the source population. Not sure who was excluded and why. 16.1% of participants had missing variables and were excluded from the study, therefore possible selection bias. The intensity of rehabilitation was not reported.
465	S. Shimazu et al. (2021). Frequent and personalized nutritional support leads to improved nutritional status, activities of daily living, and dysphagia after stroke. *Nutrition,* 83: 111091	Setting: Japan 225-bed post-acute care hospital which included 135 convalescent rehab beds Design: Prospective cohort study. Single centre. Subjects Post stroke patients newly admitted to wards over a 4-year period (Jan 2016 - Dec 2019). Median inpatient stay = 96days n = 426 Mean age 71.8yrs +/- 3.3 53.1% men, 46.9% women Excluded if had altered consciousness, did not consent or had incomplete data.	Tailored nutritional management implemented by an MDT under the guidance of registered dietitians and a nutritional support team. Each patient was reviewed at least weekly and dietary prescriptions were issued as required. Prescriptions included adjustments to: energy/protein/fluid provision (oral, enteral or parenteral), provision of nutritional supplements, modified meal texture,	Primary outcome measure: -Functional Independence Measure (FIM) motor domain score at discharge. (score range 13-91 points) Other outcome measures: -Skeletal muscle mass index (SMI - measured via bioelectrical impendence analysis) -Length of stay -Presence of dysphagia at discharge	Patients in the high frequency group had significantly greater FIM motor gains (p=0.028) and a significantly longer length of stay (p=0.001) than those in the low frequency group. Nil significant difference between the two groups in terms of frequency of dysphagia (defined as FILS score <7) or nutritional status (including SMI) at discharge.	- Low quality Single centre Significant confounders not discussed: -Compliance with dietary prescriptions -Different health care professional conducting nutritional assessments/providing nutritional counselling -Wider stroke care (medical input, physical therapy) not standardised Significant difference in FIM score and prevalence of dysphagia between groups at baseline

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
			tableware, time of meal delivery and nutrient balancing. Patients categorised depending on how frequently they needed their prescription changing: Low frequency group (n=193) <5 prescriptions/admission High frequency group (n=233) >5 prescriptions/admission Also receiving up to 3hrs/day of individualised rehab to include: physical therapy, ADL training and dysphagia rehabilitation			
465	S. Shimazu et al. (2021). Frequent and personalized nutritional support leads to improved nutritional status, activities of daily living, and dysphagia after stroke. *Nutrition,* 83: 111091	Kumamoto Japan. Exploring the effect (content) and frequency of dietary prescriptions issued for individuals undergoing rehabilitation. Single-centre prospective cohort study. Multivariate analysis to explore dietary prescriptions issued during hospitalisation was	Multidisciplinary nutritional assessments were conducted weekly for the period of admission. A specific tool wasn't used. The reason for this was justified.	Main outcomes of interest: FIM cognitive and motor scores, skeletal muscle strength, length of stay, and presence of dysphagia at discharge. Multiple measures described included: Nutritional status changes in skeletal muscle mass,	A median of 5 dietary prescriptions was issued per participant during the 96 days of hospitalization. A) Diet texture modification B) Oral energy/protein enhancements. 3352 prescriptions were issued to 426 patients (median stay 3 months). Prescriptions	**+** There was a clear definition for the dietary prescription (oral, enteral, or parenteral)- all counted separately. Limitations: single-centre study, limiting generalisation of findings. No mention of sensitivity analysis. Limited details on the content of

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		independently associated with outcomes of interest. 454 participants were screened 426 enrolled. The mean was age 71.8 years, 53.1% male 46.9% female.		physical function, dysphagia status (food intake level scale), and length of stay in hospital. The mIni nutritional assessment (MNA-SF) was completed during a face-to-face interview. Energy and protein intake was calculated by nurses or nutritionists, and the average daily value of intake for one week was considered as the daily intake. Nutrient intake was calculated by dividing each intake by the actual body weight. Co-morbidities and pre-morbidities were calculated using the Charlson comorbidity index and the modified Rankin scale. Analysis of skeletal body mass and handgrip were taken on admission using a Smedley hand dynamometer. Dysphagia status was determined by the Food level intake scale FILS. Skeletal muscle mass was measured 72hours before discharge. Changes in this were recorded by subtracting the measurement from	for internal and parenteral feeding were issued less often. Main findings: Frequency of dietary prescriptions were potentially independently associated with a change in muscle mass, function independence and length of stay, improved nutritional status, and presence of dysphagia on discharge. The frequency of prescriptions issued was not related to nutritional status but the severity of a stroke, paralysis, and dysphagia diagnosis. The most frequent prescription was for texture modification followed by energy and protein fortification. Findings suggest that nutritional support (perceptions) could potentially improve patient outcomes.	rehabilitation, staff skills, and knowledge could be confounding factors. No causal relationship can be found as this is an observational study. The type of prescription was described however the therapeutic support provided and accompanying interventions were not described.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
				admission to the measurement at discharge. 1unit= 20 minutes of rehab. The total number of units was divided by the number of days of hospitalisation. This was used to calculate the rehabilitation therapy dose.		
453	S. C. Lin et al. (2021). Effects of a food preparation program on dietary well-being for stroke patients with dysphagia: A pilot study. *Medicine,* 100:25 e26479	Setting Department of Neurology, Teaching hospital in Taiwan. Design Pilot RCT Single blinded Participants N=22 Outpatients with stroke who were in stable physical conditions and suffered from dysphagia (as defined by an EAT-10 score of >3. EAT-10 is a Chinese self-assessment of dysphagia tool) Ischaemic stroke, n= 21 Haemorrhagic stroke, n =1	Intervention Group N= 11 Food preparation program. Delivered once a week for one hour at a time for 6 consecutive weeks. Caregivers attended alongside patients The program included: 1) Oral motor exercises 2) Recognising food texture and thickener 3) Hands-on food preparation Control Group N=11 Did not receive any nutrition related interventions	Dietary Well-Being (domains: physical, emotional, psychological and social) Tool = Dietary Well-being Questionnaire Health related quality of life (domains: physical, psychological, social, environment) Tool = WHO Quality of Life (brief version) Quality of life related to Swallowing Tool = SWAL-QOL Nutritional status Tool = Mini Nutritional Assessment	Dietary Well-being -Significant increase in mean scores for all 4 domains (p value ranging 0.001-0.024). Success rate difference: *Physical = 0.23 (small effect size) *Emotional = 0.46 (moderate effect size) *Psychological = 0.46 (moderate effect size) *Social = 0.46 (moderate effect size) Health related QOL *Physical – nil significant change *Psychological – significant increase in score, p=0.006, SRD=0.40 (moderate)	**- (SIGN)** Low quality Single blinded (assessors blinded) Very small sample size No consideration of, nor discussion around what could be significant confounding factors given these are outpatients. A few of the assessment tools not used in Western setting e.g. Dietary wellbeing scale, EAT-10, SWAL-QOL

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					*Social – nil significant change *Environment – significant increase in score, p=0.005, but with small effect size, SRD = 0.27 Swallowing QOL Nil significant difference Nutritional status Nil significant difference	
453	S. C. Lin et al. (2021). Effects of a food preparation program on dietary well-being for stroke patients with dysphagia: A pilot study. *Medicine,* 100:25 e26479	Taiwan, China. To investigate the effects of a food preparation programme on dietary well-being for stroke patients with dysphagia. Participants were outpatients at a large teaching hospital. There were two groups, a treatment group, and a non-treatment group. The treatment group received a nutrition programme once a week for one hour every week for six weeks. 162 patients were screened. 140 excluded. 22 included. 11 in each group.	Food preparation programme. 3-4 patients. Includes conducting oral exercises, recognising food textures and thickener, and hands-on food preparation. Specific topics included each week, education on healthy eating, maintaining a healthy diet, and how to prepare ingredients. A full explanation of programme topics in the paper.	Dietary well-being scale WHOQOL World Health organization Quality of Life measure, Swallowing quality of life measure SWAL-QOL and Mini Nutritional Assessment MNA. Conducted by a dietician, blinded to participants' group allocation. EAT-10 Screening tool for detection of dysphagia (self-administered). Good explanation of all outcome measures.	Participants with dysphagia showed some positive effects on perceived dietary intake. The treatment group showed some improvements in health-related quality of life and quality of life associated with swallowing. There was a large effect size on the Dietary Well-being Scale for psychological, emotional and social categories suggesting that the programme support influences wellbeing. The programme also had a significant difference in the environment domain of the WHOQOL-BREF. No difference in the physical and social domains. A recommendation is that food preparation training is included for patients with swallowing difficulties.	**+/-** This paper is interesting as there are very few studies reported on eating programs such as this. This study doesn't mention the physical abilities of the participants, so we don't know how much assistance they required. This could have affected the study outcomes. We don't know if they had help and if there was homework to complete in between each session in addition to the sessions with the dietician. More detail about the program for each group is required. There was not enough information about the program content. No guidance was used to report the study e.g., CONSORT guidelines, and this affected the quality of detail provided, there were some gaps in reporting. The

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
						intervention could not be replicated in this paper. There was no detail about the randomization process. Statistical methods were used to compare outcomes however there was no intention to treat analysis. Confidence intervals were not reported. No harm was reported. Some limitations were highlighted by the authors. The findings could not be generalisable as there was too little detail about the design of the study.
463	I. Setyopranoto et al. (2021). The Effects of Local Food-Based Enteral Nutrition to Improve Nutritional Status of Post-Stroke Patients. *Journal of Neurosciences in Rural Practice,* 12:1 204-209	Setting: Indonesia Design: Pre- and post-test study design, no control. Experimental research Participants: Post stroke patients who had been discharged from the hospital for at least 6 months. Exclusion criteria: Diabetes mellitus, chronic renal failure, allergic to any fish product. n = 22 (started with 24, 2 excluded as consumption of nutritional supplement was <75%) Further categorised into "dependent" post stroke patients	Oral nutrition supplement made from locally sourced ingredients. Nutritional profile: 160.55kcal, 8g protein, 4/6g fat, 22g carbohydrate, 3.8g total fibre, 12.8ppm antioxidant activity, 0.03 QE/gram flavonoid, and 0.08mg phenol per serving. Given twice a day for 3 consecutive weeks in addition to patients' daily meals. Drop out defined: consumption of the	Parameters measured before and after the 3 week period. Clinical parameters: - BMI - Mid Upper Arm Circumference (MUAC) - Body fat percentage Laboratory parameters: Blood levels of: - albumin - urea - creatinine - haemoglobin - fasting blood glucose - total cholesterol - sodium - potassium	When dependency is defined by BI <90 Dependent patients: - Nil significant difference in any parameter Independent patients: - Significant increase in body weight (p=0.014), and BMI (0.013) - Significant increase in creatinine (p= 0.033) and decrease in sodium (p=0.04) When dependency is defined by NIHSS >3 Dependent patients: - Significant increase in total cholesterol (p value 0.03)	**(SIGN -)** - Daily dietary consumptions not recorded and not controlled for - Activity levels not accounted for - Short follow up period - Small sample size - Very limited data on comorbidities - Limited data on baseline characteristics - Nil information on weight/volume/presentation of supplement

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		and “independent” post stroke patients. Dependent post stroke patients defined as NIHSS >3 or Barthel index (BI) <90.	supplement was <75% in total over 3 weeks.		Independent patients: - MUAC significantly declined from 30.21cm to 29.36cm. (p=0.029)	
463	I. Setyopranoto et al. (2021). The Effects of Local Food-Based Enteral Nutrition to Improve Nutritional Status of Post-Stroke Patients. *Journal of Neurosciences in Rural Practice,* 12:1 204-209	Yogyakarta, Indonesia. Pre and post-test study. Exploration of nutritional status before and after enteral nutrition supplementation. 22 post-stroke patients completed the study from 24 (2 excluded for less than 75% consumption). Members of the Indonesia stroke society. Discharged from a hospital for at least 6 months post-stroke.	The supplement was administered twice a day for three weeks in addition to usual meals. A routine follow-up was provided weekly to ensure compliance and assess any adverse events. Counselling was provided as needed. Compliance was assessed at 75% for the three weeks.	Body mass index, mid-upper arm circumferences, body fat percentage. Blood albumin levels, blood urea levels, blood creatinine leave, blood haemoglobin level, fasting glucose leave, total cholesterol, sodium, and potassium.	Significant reduced mid-upper arm circumstance and increased body mass index for dependent stroke patients after the enteral nutritional supplementation. In the dependent post-stroke patients, the cholesterol level increased significantly after enteral nutritional supplementation as did the body mass index. Dependent patients showed almost no change in nutritional indices both from clinical and lavatory parameters. In contrast, the most independent participants showed an increase in body weight, BMI, blood creatinine leaves and well as arm circumference, and blood sodium level. This result was discussed as contradictory. Arm circumference and BMI in both groups were still in the overweight range and there were no statistically significant results Local food-based enteral nutritional supplementation for three consecutive weeks	The exclusion of participants with multiple morbidities may limit generalisability. The content of the daily meals was unrecorded; therefore, the results of this study cannot be taken seriously as we have no idea what other meals have been taken. The physical exercise of participants was also not recorded, and this could be a significant confounding variable.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					post-stroke may improve nutritional status.	
457	T. Mori & K. Yoshioka (2020). Quick and effective improvement of leucine enriched dietary supplement on malnutrition in acute stroke patients receiving enteral tube feeding. *BMC Emergency Medicine,* 20:1 56	Retrospective observational study including 29 malnourished Japanese stroke patients admitted over the year 2016-2017. Enterally fed from day 2 of admission for >7days Excluded patients able to take oral diet. BMI on admission 19.8-21.8 Age 80.5-82 years	Participants who had transthyretin TTR level less than 15mg/dl included and were commenced on enteral feed on day 2 of admission and received from day 5 twice a day leucine enriched branched-chain amino acids supplement (LEBD) or standard branched-chain amino acids supplement (SBD). Both groups exclusively enterally fed, with varying enteral feed forumlas n=15 LEBD n= 14 SBD	transthyretin (TTR) Albumin (alb) C-reactive protein (CRP) Serum creatinine on admission, 5th and 7th day Glasgow Coma Scale Clinical Outcome No of days in hospital	Significant differences found in Creatinine on day 5: LEBD 0.74 v SBD 0.63 significant difference TTR day 7: LEBD 15.7 v SBD 10.7 no significant differences found elsewhere	**(SIGN -)** Characteristics of participants at baseline may impact on the outcomes with the variable medical history, BMI ranged from 13.0-25.8 – unclear how reliable the marker of malnutrition is. Unclear how calculated target calorie intake as this seems quite low therefore unclear if aim was to meet nutritional requirements. Variety of enteral feeds used in study, other components in the feed used could have affected the outcomes eg the lipids and not clear its content in all the feeds used. Study population not representative of UK population.
457	T. Mori & K. Yoshioka (2020). Quick and effective improvement of leucine enriched dietary supplement on malnutrition in acute stroke patients receiving enteral tube feeding. *BMC*	Retrospective cohort study. Japanese acute hospital n=29 subjects, all enterally fed, differing acute stroke diagnoses (ischemic and haemorrhagic) of differing sizes. Age 80.5-82yo, 60-64% female. Considered malnourished based on serum blood markers (TTR, Alb, CRP)	Subjects were given, from day 5 onward, twice daily; Leucine enriched BCAA (LEBD) or standard BCAA supplement (SBD). Both groups exclusively enterally fed, with varying enteral feed forumlas	Transthyretin (TTR) Albumin (alb) C-reactive protein (CRP) Secondary outcomes: Glasgow Coma Score (GCS), clinical outcome, Length of stay (LOS), serum Creatinine (Cre) on	No differences detected for TTR on 5th day. Significant difference ($p<0.05$) for TTR between groups, LEBD (15.7 (10.2-20.2) v SAB (10.7 (8.3-1.2). No statistical differences detected for CRP, Alb	**SIGN -** Unacceptable. It is not felt study designed to control for bias or confounders. Further concerns: Small sample size Nil consideration of pre-admission nutritional status, nil malnutrition screening

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	Emergency Medicine, 20:1 56		LEBD n=15 100ml/200kcal/8g protein (1.44g Leu) SBD n=14 125ml/200kcal/7.5g protein (0.72g Leu)	admission - 5th and 7th day	Not serum Alb decreaded for both groups: LEBD (3.5, 3.6, 2.6 on D1, D5, D7 respectively), and SEB (3.3, 2.6, 2.5 on D1, D5, D7 respectively). CRP increased in both groups also: LEBD (1.02, 5.243, 4.774 on D1, D5 and D7 respectively) and SEB (0.673, 4077, 2.459 on Day 1, Day 5 and Say 7 respectively)	performed or any consideration of pre admission weight loss. Different enteral feeds used for each participant, with varying leucine content, with nil effort to correct for this – renders results unreliable Unclear if adding branched-chain amino acid supplements to enteral feeding is typical practice in Japan. Author did not consider nutritional requirements met in each group. Nil other factors considered that may confound TTR change – infection, chronic or acute other illnesses/comorbidities.
468	Y. Yoshimura et al. (2019). Effects of a leucine-enriched amino acid supplement on muscle mass, muscle strength, and physical function in post-stroke patients with sarcopenia: A randomized controlled trial. *Nutrition,* 58: 01-Jun	8 week, 2-parallel group, single centre, RCT, open label, blinded outcome assessment study of older Japanese patients who were post-stroke patients in a rehab hospital with sarcopenia. Conducted between September 2014-April 2017. Included patients over 65years, medically stable able to stand with/without an aid. Diagnosis of sarcopenia determined via bioelectrical impedance analysis and hand grip strength. Participants were receiving	Intervention was leucine-enriched amino acids containing jelly-type supplement, control group did not receive the supplement. Supplement=3g of leucine 40% enriched essential amino acid, no lipids in supplement. From day one the supplement was administered once daily 30 minutes	Physical function score (performance of ADL) using functional independence measure (FIM). Skeletal muscle index and hand grip strength Nutritional status (serum albumin, calf-circumference, BMI) - Used Mini-Nutritional Assessment Short form (MNA-SF). Dietary assessments conducted by dietitians who were	No differences found between groups for cognitive levels, nutritional status (MNA-SF score), albumin. Significant difference in FIM-M (increased significantly in both groups) with greater increase in intervention group (p=0.045). Significant improvement in Handgrip strength in the intervention group p=0.002	**+** Single centre study with small sample size. Exclusion criteria has meant that excluded a large proportion of stroke patients with selection bias. Intervention group had more haemorrhagic strokes which can have significant negative impact on individuals outcomes therefore can impact the results. Study conducted in Japanese population therefore may not

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		adequate nutrition as per dietitian (calculated using Harris-Benedict equation). Excluded: unconsciousness, advanced dementia, delirium, BMI greater than 25kg/m2, swallowing difficulties, inability to rise from chair with/without aid, inability to communicate/consent to study, co-morbidities such as kidney, liver or heart failure.	after sit to stand exercises n = 21 intervention n = 23 in control	blinded to the study groups	Significant improvement in SMI in the intervention group p=0.041	be applicable to a UK population.
468	Y. Yoshimura et al. (2019). Effects of a leucine-enriched amino acid supplement on muscle mass, muscle strength, and physical function in post-stroke patients with sarcopenia: A randomized controlled trial. *Nutrition,* 58: 01-Jun	RCT, 8 weeks, 2 parallel groups, single centre, control, open label, blinded outcome assessment Japanese rehabilitation hospital. Subjects (n=54). Convalescent rehabilitation, medically stable, able to stand with or without aid. Sarcopenic, based on cut off value for older asians, skeletal muscle index of <7kg/m2 (men) or <5.7kg/m2 (women) - measured using BIA. Patients currently receiving 'appropriate nutrition' - energy intake according to dietitian Exclusions: unconsciousness, advanced dementia, delirium, implanted pacemaker, obesity or overweight, GFR <30ml, swallowing difficulties, inability	Intervention: 8 week post stroke rehabilitation programme (PT, OT, SLT - standard protocols - <3hrs day, individual to each patient. Both groups also sit to stand exercise, with aids as necessary, starting at 2 sets of 10 reps, incrementally increased with functional gains, max 2 x 120 reps. Nutritional management - meeting energy requirements (using Harris-Benedict equation adjusted for	Blinded medical staff assessed outcomes. Primary outcome: Physical function score (performance of ADL), using functional independence measure (FIM) - low score = poorer ADL performance. Secondary outcomes: Skeletal muscle index (SMI) - in 'properly hydrated patients' Handgrip strength in non-dominant hand Other outcomes: Nutritional status (using mini nutritional assessment short form), serum albumin level, calf circumference and BMI. Dietary assessments completed by dietitians. All food from hospital, nil	Results: Nil differences detected between groups for cognitive levels, nutritional status (MNA-SF score), albumin. FIM-M increased significantly in both groups, with greater increase in intervention group (25 - 62 in intervention group v 26-53 in control (p=0.045) Handgrip strength significant increased in both groups, with significantly greater increase in intervention group (12.1 to 21.1kg increase v 13.2 to 16.3kg increase respectively) SMI increased significantly in intervention group but not control group over time (0.50kg/m2 increase in medican, 95% CI, 0.01-2.11)	**+** Pulse v bolus protein intake? Higher MPS threshold in older people Exclusion criteria means that results cannot be applied to a large proportion of stroke survivors e.g dysphagia/dysphasia/aphasia. Excluding overweight/obese patients results in ingoring any applicable data from sacropenic obese patients. No reason given for the patients who refused to continue the study Slightly higher female representation 3 more haemorrhages in control group Intervention group median kcal/kg intake was 3.2kcal

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		to rise from chair with or without aid, inability to communicate or understand purpose of study, any contraindication for high protein diet (e.g, renal, liver or heart failure).	height, weight, age, sex, physical activity and stress factor level). Intervention group: Leucine-enriched amino acids jelly supplement (3g leucine, 40% enriched amino acids), 9.7g carbohydrate, 30kcal/100g.Given 30 minutes post end of sit to stand session. n=21 in intervention, n=23 in control.	additional food from family or patient.		higher, which although maybe not statistically significant could feasibly result in 200kcal/day more in intervention group (based on 60kg person), which could be significant over 8 week period - confounder? Small sample size, single centre, selection bias Placebo trial may have been more efficacious
454	X. Liu et al. (2021). Effect of probiotics on the nutritional status of severe stroke patients with nasal feeding that receive enteral nutrition: A protocol for systematic review and meta-analysis of randomized controlled trials. *Medicine,* 100:17 e25657	Systematic review and meta-analysis conducted in China. Aim was to investigate the effect the effect of the pro-biotics on nutrition status and clinical efficacy in severe stroke patients with nasal feeding. PRISMA guidelines were used for the review. Databases searched for studies conducted from 1974 to 2021. 24 RCTs included from 2013 to 2021 with a total of 2003 participants. 57% male, mostly between 60-80 years of age, participants where treatment ranged from 14-60 days	Enteral nutrition with added probiotic (n=1007) v standard enteral nutrition (n=996)	-GCS -Infection rate -Rate of intestinal flora dyspiosis -Gastrointestinal complication - time to reach target nutrition -MUAC -Prealbumin content	GCS, n=8 trials, probiotics in EN, significant improvement in GCS p<.00001 Infection rate n=6 trials, studied effect of probiotics on infection rate (OR = 0.25, 95% CI, 0.15-0.43, p<.00001). Intestinal floral dysbiosis n-4 trials, lower incidence of intenstinal flora dysbiosis in probiotics group (OR = 0.24, 95% CI, 0.12-0.48, p<.0001) GI complications n-12 trials, pooled analysis - probiotics decreased GI	**+** Although criteria was met on the whole, there is a lack of detail provided related to specific studies included in the paper, limited information on the type of stroke, prognosis, feed used. Difference in study period from 14 days to 60 days which will also impact how quickly changes such as MUAC would show. Pre-albumin not a good indicator nutritional status. No indication of nutritional status of participants at start of the studies.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		Inclusion criteria RCT, GCS>9, treatment time 14-60 days.			complications (OR =0.25, 95% CI, 0.16-0.37, p<.00001) Time to reach target nutrition n-4 studies, probiotics plus EN associated with shorter time to reach target nutrition p<.00001 MUAC n=3, probiotics, no differences detected between groups Prealbumin content n=8 trials, probiotics associated with improvement on prealbumin content (MD=25.83, 95% CI, CI: 13.68 - 37.99, p<.0001)	All studies conducted in China not representative of a UK population.
454	X. Liu et al. (2021). Effect of probiotics on the nutritional status of severe stroke patients with nasal feeding that receive enteral nutrition: A protocol for systematic review and meta-analysis of randomized controlled trials. *Medicine,* 100:17 e25657	SR and MA, from authors based in China Aim: Investigate the effect of probiotics on nutritional status and clinical efficacy in severe stroke patients with nasal feeding. Clinical prognosis of severe stroke patients with nasal feeding RCTs that applied probiotics in patients with severe stroke (n=24 studies), n=2003 participants. 57% male, 60-80y.o, treatment course 14-60 days,	Enteral nutrition with added probiotic (n=1007) v standard enteral nutrition (n=996)	Varying time scales, between 14-60 days: -Glasgow coma score -Infection events -Rate of intestinal floral dysbiosis, -GI complications, -time to reach target nutrition -prealbumin	GCS, n=8 trials, probiotics in EN, significant improvement in GCS p<.00001, MD=1.03, 95% CI, 0.78-1.27 Infection rate n=6 trials, studied effect of probiotics on infection rate (OR = 0.25, 95% CI, 0.15-0.43, p<.00001). Intestinal floral dysbiosis n-4 trials, lower incidence of intestinal flora dysbiosis in probiotics group (OR = 0.24, 95% CI, 0.12-0.48, p<.0001)	**+** Majority of criteria met, some flaws with associated risk of bias – heterogeneity present in n=4 outcomes, reason for study being 'popular topic in China' Other concerns/comments: Infection events not specified, severity, source GI complications not specified (e.g. diarrhoea, vomiting, reflux, bloating, constipation)

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					GI complications n-12 trials, pooled analysis - probiotics decreased GI complications (OR =0.25, 95% CI, 0.16-0.37, p<.00001) Time to reach target nutrition n-4 studies, probiotics plus EN associated with shorter time to reach target nutrition (MD=-1.80, 95% CI: -2.42 to 1.18, p<.00001). Significant heterogeneity, i2 =95%) MUAC: n=3, probiotics, no differences detected between groups Prealbumin content: n=8 trials, probiotics associated with improvement on prealbumin content (MD=25.83, 95% CI, CI: 13.68 - 37.99, p<.0001). Significant heterogeneity.	No information on how each study measured intestinal floral dysbiosis Heterogeneity present in 4 outcomes Nil comments on type of enteral nutrition used (e.g. fibre, fibre-free, osmolality, whole protein vs peptide) – could all confound time to target nutrition and GI function Minimal mention of type of probiotics used. In discussion authors suggested study only completed as is 'hot topic in China'. All patients of Chinese origin, may not be generalisation to western population. Nil reports of nutritional status other than prealbumin, which is a poor measure of nutritional status. Other factors of nutritional status not included, weight, functional strength, malnutrition screening tools. Nil further information on severity of stroke or functional status When each outcome evaluated, sample sizes are

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
						much smaller than authors imply
470	D.-Y. Zhong et al. (2021). The Effect of Probiotics in Stroke Treatment. *Evidence-based complementary and alternative medicine : eCAM,* 2021: 4877311	Systematic Review/Meta-analysis conducted in China. Searches from database inception to 2020. 1816 Participants from 21 RCTs and 2 CCTs.	Curative effect of probiotics combined with enteral nutrition and life support treatment versus enteral nutrition and life support treatment.	-NIHSS -Hospitalisation time -average bedrest duration time to reach target nutrient solution -Haemoglobin, Albumin, total protein, pre-albumin, TNF, CRP, procalcitonin & Interleukin before and after treatment -adverse indicators: vomiting, oesophageal reflux, abdominal distension, constipation, diarrhoea, gastric retention -infection: lung, GI & UTI	NIHSS - no differences detected; although only 2 studies had evaluated this. LOS - probiotic group average 8.94 day less stay (95% CI, p<0.000001) Bedrest periods probiotic group average 10.34 days less (95% CI, p<0.00001) 'Nutritional status' Hb (MD 8.36, p<0.00001) in favour of probiotic group Alb (MD 2.91 p<0.00001) in favour of probiotic group TP (MD 4.90, p<0.00001) in favour of probiotic group prealbumin (MD 15.50 p<0.00001) in favour of probiotic group Inflammation, only 2-3 studies evaluated this: CRP - nil differences detected procalcitonin - nil differences detected TNF-a (reduction of MD -3.22, p<0.0001) in probiotic group)) IL-6 (reduction of MD 16.40, p <0.0001) in probiotic group)) IL-10 (reduction of MD -6.63, p=0.03) in probiotic group Adverse reactions:	+ All studies not randomly assigned, not all mention concealment methods or blinding methods. Data missing in some studies: age, duration of treatment. Lack of detail included with reference to the pro-biotic used, query if participants used probiotic before, nutritional status before as well as after the intervention. GI symptoms not monitored before, length of time tube fed prior to commencing probiotic. Chinese publications only which may not be representative on the UK population

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					Nil differences detected for vomiting or stress ulcers. For probiotic group, reduction in rate of: oesophageal reflux (RR=0.43, (95% CI 0.25-0.58) p=0.002) Bloating (RR = 0.39, 95% CI, 0.26-0.58, p<0.00001) Constipation (RR =0.31, 95% CI, 0.19-0.60, p<0.0001) Diarrhoea (RR=0.22, 95% CI, 0.14-0.34, p<0.00001) Gastric retention (RR=0.34, 95% CI, 0.19-0.60, P=0.0002) GI bleeding (RR=0.39, 95%, 0.28-0.54, p<0.00001) Complication rate: Less complications reported in probiotic group for: Lung infection (RR=0.44, (95% CI, 0.27-0.72, p<0.001) GI infection (RR=0.40, 95% CI, 0.23-0.68, p=0.0008) UTI (RR = 0.27, 95% CI, 0.15-0.49, p<0.0001) Poor prognostic indicators: Reduction in incidence of the following in probiotic group: Fatality rate (RR = 0.45, 95% CI 0.22-0.93, p=0.03) Intestinal flora imbalance rate (RR = 0.32, 95% CI, 0.21-0.48, p<0.0001)	

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
470	D.-Y. Zhong et al. (2021). The Effect of Probiotics in Stroke Treatment. *Evidence-based complementary and alternative medicine : eCAM,* 2021: 4877311	SR/MA based - Chinese authors RCT and CCT up until November 2020 n=23 articles with n=1816 patients; 21 RCTs and 2 CCTs Stroke patients (ischemic and haemorrhagic, without other diseases) Age varying from 52-71 years +/- standard deviations presented	Evaluate 'curative' effect of probiotics combined with EN in stroke EN and probiotic group, varying probiotic and EN formulas used across studies included EN without probiotic (varying EN formulas used)	Measured at 'beginning and end of treatment'. Treatment lengths varied across studies. NIHSS Length of stay Bedrest periods Time to reach target nutrient solution 'Nutritional status': Hb, alb, TP, prealbumin Inflammation: CRP, procalcitonin TNF-a, IL-6, IL-10 reflux, bloating, constipation, diarrhoea, gastric retention, gastric bleeding Infection: lung, GI, UTI Fatality Intenstinal flora imbalance	NIHSS - nil differences detected; although only 2 studies had evaluated this LOS - probiotic group avergage 8.94 day less stay (95% CI, p<0.000001) Bedrest periods probiotic group average 10.34 days less (95% CI, p<0.00001) 'Nutritional status' Hb (MD 8.36, p<0.00001) in favour of probiotic group Alb (MD 2.91 p<0.00001) in favour of probiotic group TP (MD 4.90, p<0.00001) in favour of probiotic group prealbumin (MD 15.50 p<0.00001) in favour of probiotic group Inflammation, not only 2-3 studies evaluated this: CRP - nil differences detected procalcitonin - nil differences detected TNF-a (reduction of MD -3.22, p<0.0001) in probiotic group)) IL-6 (reduction of MD 16.40, p <0.0001) in probiotic group)) IL-10 (reduction of MD -6.63, p=0.03) in probiotic group Adverse reactions: Nil differences detected for vomiting or stress ulcers.	+ Majority of checklist criteria met. Other comments Number of participants in each group not calculated as a total number, some included studies not presenting total patient numbers. Nil consideration to gender split in presentation of results. Different probiotic and enteral formulas used across studies included - can affect GI function/side effects. Different treatment lengths. Nil nutritional status information considered other than blood markers. Nil consideration of dysphagia Nil consideration of oral intake vs artificial feeding. Issues with methodological quality of included studies as identified by authors - 7 studies with incomplete data, only 50% of studies mentioned randomisation methods. Nil studies discussed blinding or concealment methods. Adverse reactions though significiant only ~1/4-1/3 less prevalent. Vomiting, stress

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					For probiotic group, reduction in rate of: oesophageal reflux (RR=0.43, (95% CI 0.25-0.58) p=0.002) Bloating (RR = 0.39, 95% CI, 0.26-0.58, p<0.00001) Constipation (RR =0.31, 95% CI, 0.19-0.60, p<0.0001) Diarrhoea (RR=0.22, 95% CI, 0.14-0.34, p<0.00001) Gastric retention (RR=0.34, 95% CI, 0.19-0.60, P=0.0002) GI bleeding (RR=0.39, 95%, 0.28-0.54, p<0.00001) Complication rate: Less complications reported in probiotic group for: Lung infection (RR=0.44, (95% CI, 0.27-0.72, p<0.001) GI infection (RR=0.40, 95% CI, 0.23-0.68, p=0.0008) UTI (RR = 0.27, 95% CI, 0.15-0.49, p<0.0001) Poor prognostic indicators: Reduction in incidence of the following in probiotic group: Fatality rate (RR = 0.45, 95% CI 0.22-0.93, p=0.03) Intestinal flora imbalance rate (RR = 0.32, 95% CI, 0.21-0.48, p<0.0001)	ulcers, gastric retention only evaluated in a 2-3 studies. Maximum studies assessing each outcome is 14, therefore total subject number much less than reported.
466	C. Wu et al. (2021). Intermittent tube feeding for stroke patients with	Setting China Design	Intermittent tube feeding Defined as:	Rate of dysphagia function improvement (8 studies)	Intermittent tube feeding could: 1) Significantly increase the rate of dysphagia function	**SIGN -** Low quality

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	dysphagia: a meta-analysis and systematic review. *Annals of palliative medicine,* 10:7 7406-7415	Meta-analysis and systematic review. (Only RCTs included in search). Time period: establishment of the library to Feb 15, 2021 Subjects 11 RCTs included, all from China n=762 stroke patients with dysphagia 6 RCTs used intermittent oral to gastric tube feeding, 5 RCTs used intermittent oral to oesophageal tube feeding	"feeding tube inserted into the stomach or oesophagus through the mouth or nose when the patient needs to eat, and the feeding tube is pulled out immediately after eating" Swallowing dysfunction confirmed by tools such as the drinking water test Control Continuous nasogastric tube feeding	Serum albumin level (6 studies) Incidence of aspiration pneumonia (5 studies)	improvement (OR = 5.22, 95% CI: 3.38-8.07, P<0.001, I2 = 27%) 2) Significantly increase serum albumin level (MD=3.07, 95% CI:1.65-4.49, P<0.001, I2 = 85%) 3) Significantly reduce the incidence of aspiration pneumonia (OR = 0.28, 95% CI: 0.15-0.53, P<0.001, I2 = 0%) Pooled data showed intermittent tube feeding could: 1) Significantly increase serum haemoglobin level (MD=1.55, 95% CI: 1.19 – 1.95, P=0.008) 2) Significantly increase prealbumin level (MD=1.79, 95% CI: 1.46-2.12, P<0.001) 3) Reduce incidence of aspiration (OR = 0.27, 95% CI :0.08-0.93, P=0.042). No significant difference in triceps skinfold thickness or arm muscle circumference.	Search terms clearly defined. 7 electronic sources searched Nil mention of grey literature. Only RCTs included in search criteria. Excluded non-Chinese and English reports Excluded studies not listed All RCTs are from China 2 investigators independently extracted data. Differences resolved by a third party Very limited data from the original studies RCTs included – 4 studies did not report on randomisation method, no studies reported on allocation or personnel blinding.
466	C. Wu et al. (2021). Intermittent tube feeding for stroke	Setting: China Design:	Comparison between intervention arm (intermittent tube	Primary outcome: 1) The rate of dysphagia functional improvement	Systematic review: 11/116 identified studies included,	**SIGN -** Low Quality

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	patients with dysphagia: a meta-analysis and systematic review. *Annals of palliative medicine,* 10:7 7406-7415	Meta-analysis and systematic review Subjects: Stroke patients with dysphasia requiring intermittent tube feeding.	feeding versus the control arm (oral feeding exclusively or constant tube feeding)	2) serum albumin level 3)incidence of aspiration pneumonia Other outcomes: triceps skinfold thickness and arm muscle circumference.	published between 2008 and 2020. Primary outcome: 8/11 studies report a significant increase in rate of dysphagia improvement in the intervention arm (p<0.001) 6/11 studies reported significant increase in serum albumin levels in the intervention arm (p<0.001) 5/11 studies revealed that intermittent tube feeding could significantly reduce the incidence of aspiration pneumonia (p<0.001) No significant difference in the triceps skinfold thickness and arm muscle circumference.	All Chinese studies used so ability to generalise to UK is questionable. The sample size in all 11 studies used were small. The duration of each study varied significantly Research methodology in some of the studies used was questionable.
471	W. Zhu et al. (2020). Intermittent versus continuous tube feeding in patients with hemorrhagic stroke: a randomized controlled clinical trial. *European Journal of Clinical Nutrition,* 74:10 1420-1427	Setting: Neurosurgery ward, within a medical and teaching centre in west China. Design: Prospective, parallel, single-blind RCT Participants: N = 78 82 randomised – 4 excluded post randomisation.	7 days enteral nutrition via 15Fr nasogastric tube using 0.9kcal/ml feed once vital signs stable and metabolic disorder corrected. Aiming for 25-30kcal/kg. Intermittent Tube Feeding (ITF) group - (n = 40)	Primary outcome: Incidence of diarrhoea Secondary outcomes: Vomiting Abdominal distension Constipation Gastric retention Gastrointestinal bleeding Caloric intake	Diarrhoea incidence significantly lower in CTF group than in ITF group (7.9 vs 37.5%, p=0.002). Total intolerance rate significantly lower in the CTF group (63.2 vs 85.0%, p=0.027). No significant difference between the groups for total calorie intake	**SIGN -** Low quality Single centre Small sample size Described as single blind but unclear how the participants/legal guardians of the participants would have been unaware of group allocation.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		Patients consecutively admitted to neurosurgery ward between January 2018 – January 2019. GCS 5.6 (ITF group) and 5.9 (CTF group) at baseline Inclusion criteria: 1) Diagnosis of first ever haemorrhagic stroke by CT/MRI, 2) had a GCS <12, 3) aged 18years+, 4) volunteered to participate Exclusion criteria: 1) history of gastrorrhagia or gastralgia, 2) contraindications of the selected enteral nutrition suspension; 3) liver or kidney diseases; 4) under mechanical ventilation	- Nutrition provided 4 times/day via electric feeding pump. - Variable speeds depending on volume required. - Feed time 30-60mins. - Continuous Tube Feeding (CTF) group - (n=38) - Nutrition at up to 100ml/hr over 24hrs If gastric residual volume (GRV) was over 200ml, feeding volume was halved for the next 6 hours. If GRV continued to be over 200ml for a further 12hrs despite decrease in feed volume, feed was held for 12hr and restarted at 50% of goal volume. Enteral nutrition was stopped if: Vomiting Diarrhoea for 3 days Gastrointestinal bleeding		Significant group x time interaction effect for mean caloric intake between the two groups (p<0.001, two-way ANOVA).	Use of medications that may affect stools not accounted for or mentioned e.g., opioids, antibiotics, laxatives. Baseline stool frequency/type not mentioned. Very short period analysed (7 days) Limited information on type of feed used, average rate of feed in each group. No information on number of patients whose feed was reduced due to GRVs of 200ml or more.
471	W. Zhu et al. (2020). Intermittent versus continuous tube	Setting: China, single centre	Group 1: Enteral nutrition administered by intermittent	Primary: incidence of diarrhoea	Incidence of diarrhoea was significantly lower in the continuous feed group than	**+** Acceptable

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	feeding in patients with hemorrhagic stroke: a randomized controlled clinical trial. *European Journal of Clinical Nutrition,* 74:10 1420-1427	Design: prospective, single blind, RCT Subjects: Patients with haemorrhagic stroke with GCS <13 admitted to hospital in China	tube feeding n=40 Group 2 Enteral nutrition administered by continuous tube feeding n= 38	Secondary: Incidence of other feed intolerance-vomiting, abdominal distension, constipation, gastric retention, and GI bleeding	the intermittent one (p=0.002). The total intolerance rate of enteral nutrition in the continuous group was significantly lower than the intermittent group (p=0.027). There were no significant differences in the incidence of secondary outcome measures.	But- single centre with small sample size. Only haemorrhagic strokes Included Intervention used may not be comparable for use in UK
455	J. J. Lopez-Gomez et al. (2019). Influence of hyperglycemia associated with enteral nutrition on mortality in patients with stroke. *Nutrients,* 11:5 996	Setting: University Hospital in Spain. Design: Retrospective longitudinal observational study Participants -n=115 - Non-diabetic patients admitted with a diagnostic of ischaemic or haemorrhagic stroke. - Received exclusive enteral nutrition via NG or gastrostomy. - Started enteral nutrition within 72hrs of admission - Over 18yrs old Mean age 76 (62.5-83)years 54.8% men 76.5% ischemic stroke, 23.5% haemorrhagic Data collected over 3 years between January 2014 to December 2016	Blood plasma glucose measured before the start of enteral nutrition and one week after it had been started. Hyperglycaemia defined as >126mg/dL before enteral nutrition and/or a value >150mg/dL after enteral nutrition Insulin treatment was prescribed as per protocol: - sliding scale for capillary glycaemia >150mg/dL - Basal insulin at 0.2IU.kg weight/day given in 2 doses at 9am and 9pm in all patients with capillary	Mortality Recovery of the oral route Length of stay 3 study groups Hyper EN - n= 22 (19.1%) -Did not have hyperglycaemia before but suffered after enteral nutrition was commenced HyperEST (Stress hyperglycaemia) - n = 38 (33%) -Had hyperglycaemia before the start of enteral nutrition NoHyper - n = 55 (47.8%) -Did not have hyperglycaemia either before or after the	19% patients suffered hyperglycaemia associated with enteral nutrition Patients who suffered from hyperglycaemia relating to enteral nutrition were older (p=0.03). Mortality 19.1% patients (n=22) died 45.5% of patients who died were in HyperEN group, 15.8% HyperEST and 10.9% NoHyper Patients in HyperEN group were more likely to die (OR 6.83, IC 1.76-26.47, p<0.01) Recovery of Oral Feeding 27.3% patients of recovered oral feeding were in HyperEN group, 42.1% in HyperEST group and 61.8% in NoHyper group.	**+** Acceptable Retrospective design Infection rates not recorded and could have affect likelihood of hyperglycaemia and mortality Baseline comparison did not include other comorbidities

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
			glycaemia above 150mg/dL	beginning of enteral nutrition	Patients in HyperEN group were less likely to recover oral feeding (OR 4.21, IC 1.20-14.79, p=0.02) Patients in HyperEST group also had a higher probability of not recovering orally (OR2.68 (1.06-6.72), p = 0.04). Length of stay Nil significant difference between groups.	
455	J. J. Lopez-Gomez et al. (2019). Influence of hyperglycemia associated with enteral nutrition on mortality in patients with stroke. *Nutrients,* 11:5 996	Setting: Spain Design: Retrospective longitudinal observational study. Subjects: Non-diabetic patients with stroke requiring enteral nutrition support in first 48 hours after stroke n=115	Administration of enteral nutrition in stroke patients in the first 48 hours after stroke and for 1 week after. Evaluation of the frequency/cause of hyperglycaemia associated with enteral nutrition. HyperEN n= 22 HyperEST n= 38 NoHyper n=55	Development of hyperglycaemia (or not) and perceived cause, after 1 week of enteral nutrition LOS, mortality and recovery of the oral route	Development of hyperglycaemia associated with enteral nutrition (those who did not have it before the feed started) was an independent risk factor for mortality and recovery of the oral route.	**SIGN -** Low quality Retrospective – possibility of selection bias. Limited to one area of Spain Use of unique enteral feed formula limiting ability to generalise to other types of enteral feeds. Greater number of patients with haemorrhage included than what would be expected in a normal stroke population. Large number of milder strokes (MRS 0-1) n= 80/115

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
						Cohort number in flow chart does not match the rest of the paper.
459	H. Onodera et al. (2021). Effect of enteral nutrition on in-hospital infection and hospital expense in stroke patients: A retrospective assessment. *Neurologia Medico-Chirurgica,* 61:4 268-274	Setting: Japan. Acute hospital. Design: Retrospective cohort study using data derived from medical records and inpatient claims Single centre Participants: n = 45 Haemorrhagic stroke patients who were admitted and received enteral nutrition via nasogastric tube within 3 days of hospitalisation between April 2017 and March 2019. Exclusion criteria: could not start enteral nutrition e.g. due to serious comorbidities	Split into 2 groups: 1.0 group - N = 24 - Standard 1.0kcal.ml polymeric formula - Received 600kcal, 30g protein by day 4, 1200kcal, 60g protein/day at day 7 1.5+α group - n = 21 - 3 days of 1.5 kcal/ml high protein, whey peptide-digested liquid diet (3 days) - Followed by 3 days of 1.5kcal/ml highly fermentable dietary fibre-containing liquid diet (3 days). - Received 900kcal, 57g protein by day 4, 1800kcal, 68g protein/day by day 7 Provision of enteral nutrition is gradually increased over 7 days so long as patients do not suffer from diarrhoea,	Change in BMI Duration of antibiotics use Infection rates Medical cost Length of hospital stay	Reduction in BMI over a 4-week period was significantly smaller in the 1.5+α group than in the 1.0 group (p= 0.007). *Note only 16 out of 21 patients in the 1.5+α group had data for BMI change Mean number of days prescribed antibiotics, incidence of nosocomial infections, days of therapy all lower in the 1.5+α group but not statistically significant.	**SIGN -** Low quality Retrospective design Single centre study Small sample size Nil information re: total duration of NG feed +/- level of oral intake Nil detail regarding method for classification into groups. Refers to "Driving Surf Protocol" but nil detail on group allocation provided in this paper. Nil information on if or how process measures were managed to acknowledge risk of detection bias Nil information on how quickly patients progressed through the protocol due to incidence of adverse symptoms Very limited discussion on confounding – only addressed by means of comparing patients' characteristics. Nil

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
			constipation for 3 consecutive days, vomiting, 100ml+ gastric remnants.			information on other treatments/therapies/functional status/dysphagia.
459	H. Onodera et al. (2021). Effect of enteral nutrition on in-hospital infection and hospital expense in stroke patients: A retrospective assessment. *Neurologia Medico-Chirurgica,* 61:4 268-274	Setting: Japan. Single centre. Design: Retrospective Cohort study Subjects: 45 patients with haemorrhagic stroke receiving early enteral nutrition.	Group 1: Standard polymeric formula (n=24) Group 2: high-protein formula (n=21).	Changes in BMI Duration of antibiotic use Incidence of postoperative infection Medical costs	Reduction in antibiotic use, more days of therapy given and less BMI reduction in group 1. Longer length of stay in group 2 Reduction in infections in group 2 compared to other Japanese hospitals.	**SIGN -** Low quality Patients with serious co-morbidities not included Small sample size Retrospective Single centre- selection bias Japanese study- surgical management of haemorrhage in stroke patients in the UK differs. Ability to generalise to UK is questionable.
464	L. Sheng et al. (2020). From best evidence to best practice: enteral nutrition from continuous nasal feeding in stroke patients. *International Journal of General Medicine,* 13: 927-936	Setting: Neurology department, Hospital in China Design: Pre and post implementation audit Baseline data collected over 3 months: Aug 13 – Nov 19 2018 Post intervention data collected over 2 months: December 11, 2018, to Feb 18, 2019. Subjects:	Literature search from establishment of the database to October 2018. 6 articles included (3 systematic reviews, 3 clinical guidelines) 6 standard audit criteria were developed around best practise with "nasal" feeding. These	- Nurses compliance with the 6 standard audit criteria -Incidence of gastrointestinal complications -Incidence of aspiration and aspiration pneumonia -Workload of nurses on nasal feeding (time)	-Nurses' compliance rate increased to 100% for all 6 audit standards (no p values provided) -GI complications significantly improved: Vomiting (p= 0.023), diarrhoea (p=0.042), constipation (p=0.035), gastric retention (0.042). - nil significant difference in rate of aspiration pneumonia	**SIGN -** Low quality Single centre Small sample size Single blind – significant risk of bias as nursing staff on the ward acted as observers (on rotation) and were fully aware

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		Ischaemic stroke patients with dysphagia over 18years of age who received enteral nutrition within 48hrs of admission for at least 7 days. N = 68 Control group n = 38 Observation group n = 30	were based on the included evidence (only B-level and above evidence was included). Interventions: 1) Evidence based nursing training and assessment for nurses 2) Standardised nasal feeding process was developed 3) Training and assessment that focused on continuous feeding (as this was an area staff had less experience/training in than intermittent feeding)	-Length of hospitalisation (days)	-Times spent on nasal feeding decreased from 23.71 =/- 3.22min to 7.73 +/- 1.14mins ($p<0.05$). Length of hospitilisation decreased but was not statistically significant.	of the study design and purpose. Comprehensive literature search 2 people extracted data and consensus was agreed Excluded studies not referenced Relevant characteristics of the included studies were not provided
464	L. Sheng et al. (2020). From best evidence to best practice: enteral nutrition from continuous nasal feeding in stroke patients. *International Journal of General Medicine,* 13: 927-936	Setting: China, single centre Design: Audit and field observation Subjects: Registered nurses n= 12 Stroke patients requiring nasal feeding (before application of evidence) n= 38 Stroke patients requiring nasal feeding (after the application of evidence) n= 30	Analysis and introduction of best evidence Training on the evidence available Development of standardised nasal feeding process Training on the nasal feeding process	The effect of evidence-based practice on stroke patient's GI function and complications, aspiration pneumonia, nurse's daily workload involving nasal feeding and length of stay	After the application of evidence, significant reductions in GI complications occurred ($p<0.05$), and nurses workload reduced ($p=<0.05$) The incidence of aspiration pneumonia was lower but not statistically significant.	**SIGN -** Low quality Small sample single centre. Observational study Poor design, difficult to follow. Would struggle to adopt this approach in the UK

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
			Re-audit after the application of evidence.			
469	X. Zeng et al. (2020). Nutrition program selection in acute ischemic stroke patients with GI hemorrhage. *Asia Pacific journal of clinical nutrition,* 29:1 55-60	Setting: Tertiary hospital in China Design: Retrospective cohort study Subjects: Ischaemic stroke patients with GI haemorrhage January 2014 – December 2018 n = 62 (39 males, 23 females)	Group 1 – moderate feeding - n = 30 - Enteral provision only Group 2 – trophic feeding + PN - n = 32 - 16-25% of daily target calories given enterally with the remaining energy intake administered by parenteral nutrition. Each group received 25kcal/day. Nutrition provision gradually increased over 3-5 days to meet approximately 70% daily energy target in 3-5 days. Nutritional therapy was performed for 7-10 days. Enteral nutrition was started 24-48hrs after the haemorrhage had stopped and no signs	Primary outcome measures: Caloric intake Mortality GCS score at discharge Glasgow Outcome Score (GOS) 3 months after discharge Secondary outcome measures: Recurrent GI haemorrhage HAP	Nil significant difference in calorie provision between groups Overall mortality significantly lower in the moderate feeding group (p=0.03) Higher GCS scores at discharge in the moderate feeding group (p=0.001) GOC score 3 months post discharge significantly higher in moderate feeding group (p=0.03) Nil significant difference between groups for recurrent GI haemorrhage or HAP.	**SIGN -** Low quality Retrospective design Small sample size Limitations in method to diagnose GI bleeding. Limited information on baseline characteristics. No information regarding method of group allocation or whether the assessors were blinded. Nil information on if or how process measures were managed to acknowledge risk of detection bias Limited attempt nor discussion to account for confounding factors

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
			of re-haemorrhage were observed. PN started 24hrs post haemorrhage.			
469	X. Zeng et al. (2020). Nutrition program selection in acute ischemic stroke patients with GI hemorrhage. *Asia Pacific journal of clinical nutrition,* 29:1 55-60	Setting: China, single centre Design: Retrospective cohort study Subjects: 62 patients with ischaemic stroke and GI haemorrhage	Group 1: moderate feeding allotment (>70% of optimal caloric uptake) n=30 Group 2: Trophic feeding with supplemental parental nutrition (total caloric uptake above 70%) n=32	Primary: Mortality, GCS at discharge and GOS score at 3 months. Secondary: Recurring GI bleed, hospital acquired pneumonia.	Overall mortality in moderate feeding group was significantly lower ($p<0.05$) than in the trophic feeding group. Higher GCS on discharge in the moderate feeding group than in the trophic group ($p<0.05$) GOS score at 3 months after discharge was higher in the moderate feeding group than in the trophic group ($p<0.05$). No difference observed in secondary outcomes of recurring GI blee and HAP.	**SIGN -** Low quality Retrospective design, single site. Small sample size Stroke severity at baseline not mentioned (only GCS). Unclear what impact this and other variables would have had on mortality and other outcomes. 114 subjects available only 62 selected (reasons for exclusion not discussed) Accuracy of GI haemorrhage diagnosis questionable.
452	X. Chen et al. (2021). Effect of early enteral nutrition combined with probiotics in patients with stroke: a meta-analysis of randomized controlled trials. *European journal of clinical nutrition,* :	China, severe acute stroke patients – criteria from Cerebrovascular Disease conference – diagnosed with CT or MRI. <3 day onset, GCS <9, 'normal GI function'. Exclusions: previous GI and metabolic disease, malignant tumour, severe heart, liver, kidney failure, malnutrition	'Early' EN combined with probiotics, of varying type (n=1111) v standard (non-specified EN) (n=1105) Feed started within 12-48 hours.	Incidence of GI complications, incidence of infections, EN target time, LOS, DAO, d-lactic acid, dysbacteriosis rate, Alb, pre-Alb, total protein, Hb, IGA, IGG, IGM – measured 14 days after treatment.	Sample size of studies ranged from 56-140. 20 studies reported labatory and clinical indicators, 3 – lab indicators only. Results presented in forest plot format. Results tended to favour EEN/probiotic group.	**SIGN -** Low quality. No information presented e.g age/gender. 'Normal GI function' not well defined. Measures of nutritional status limited to biochemistry – evidence for these markers is poor, nil

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		Meta analysis. 26 RCTs, n=2216 patients.			Abdomen distention 29 v 88 diarrhea 21 v 96 Vomiting 10 v 21 Gastric retention 9 v 30 Constipation 20 v 77 Reflux 17 v 35 Digestive tract haemorrhage 20 v 62 Stress ulcer 6 v 9 Pulmonary infection 59 v 168 UTI – 14 v 59 GI infection – 10 v 29 Less target feed time with EEN/pro v EN (-2.18 (95% CI) Less LOS (-8.70, 95% CI) in EEN/pro group Generally higher alb (pre-alb, hb and total protein in EEN/pro group. No overall average given for each.	functional markers or anthropometry. Could have presented descriptive outcome data in table form rather than just forest plots Variable formulation of 'standard EN, e.g fibre v non fibre, whole protein v peptide'. Different probiotics used across studies. 1 study outcome – unsure of participant blinding – subjective nature of GI complication/severity not investigated. Variance in time to commence feed – no information on pre admission nutritional status Query over applicability to western population – diet differences. Outcome measures measured 14 days after treatment – long time – can affect nutritional status. EN target time less in probiotic group – likely to affect GI function. Significant heterogeneity in LOS outcome. Data presented as incidences does not take into account incidences per each participant Nil information on oral trials – when considering pulmonary infection.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
						Results presented don't include specific measured parameter e.g albumin unit of measurement). Forest plots switched direction halfway through making results confusing.
452	X. Chen et al. (2021). Effect of early enteral nutrition combined with probiotics in patients with stroke: a meta-analysis of randomized controlled trials. *European journal of clinical nutrition,* :	Meta-analysis using studies written in Chinese/English. 26 RCTs included with a total of 2216 participants. Studies conducted between 2014-2020. Age ranges nor sex of participants clear. Inclusion criteria was severe stroke diagnosed with CT and MRI, Less than 3 day onset, GCS less than or equal to 9, normal gastrointestinal function. Exclusion criteria was previous history of GI and metabolic disease, malignant tumour and severe heart, liver and kidney failure.	EN versus early enteral nutrition with probiotic - all studies lasted up to 14 days.	Incidence GI complications, incidence of infections, EN target time, length of hospital stay, indications of nutritional status e.g. pre-albumin, total protein	Abdomen distention significantly less with probiotic p<0.00001 (29v88) diarrhoea significantly less with probiotic p<0.00001 (21 v 96) Vomiting (10 v 21) Gastric retention significantly less with probiotic p<0.0006 (9 v 30) Constipation significantly less with probiotic p<0.00001 (20 v 77) Reflux significantly less with probiotic p<0.05 (17 v 35) Digestive tract haemorrhage significantly less with probiotic p<0.00001	**SIGN -** Search conducted overall avoiding bias. No information of the specifics on the stroke, swallowing ability if managing oral diet. ? age of participants and how assessed for nutritional status. The type of enteral feed used and if any oral diet taken by the participants. Other factors which could have affected outcomes not discussed e.g. medications and other factors like dysphagia and aspiration risk, mobility. Appears that all participants were Chinese therefore not reflective of a UK population

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
					(20 v 62) Stress ulcer (6 v 9) Pulmonary infection significantly less with probiotic p<0.00001 (59 v 168) UTI significantly less with probiotic p<0.00001 (14 v 59) GI infection significantly less with probiotic p<0.03 (10 v 29) Less target feed time with EEN/pro v EN (-2.18 (95% CI) Less LOS (-8.70, 95% CI) in EEN/pro group Nutritional markers were higher in the probiotic group	
456	A. Mizuma et al. (2021). Effect of early enteral nutrition on critical care outcomes in patients with acute ischemic stroke. *The Journal of international medical research,*	Japan, acute Tokyo hospital. Cohort study, Patients admitted between 2009-2014 n=499 participants (307m, 192f), 73+/-13 years. Patients admitted within a week of MRI confirmed ischemic stroke. Exclusions: NIHSS <4 or >22. Severe consciousness	Late enteral feeding (>48hrs) (n = 263) v early enteral feeding (<48 hours) (n=236) Enteral feeding defined as both oral and tube feeding	Incidence of SAP within 14 days; length of ICU or hospital stay	EEN group v LEN group: SAP (8.5v28.1%; statistically significant p<0.01) Length of hospitalisation stay (22 v 35 days, statistically significant p <0.01) Length of ICU stay (4 v 6 days, significant (p	**SIGN -** Does not specify amount or type of nutrition for either group, oral or tube feeding. NIHSS score (7v12, p<0.001), Disturbance of consciousness (1.7v8.4%, p<0.01),

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
	49:11 3.0006052111e+15	disturbance (eyes closed), aspiration pneumonia on admission occurring <72 hours prior to commencement of EN				hemiparesis, (194 v 240, p <0.01), dysarthria (116 v 221, p<0.001), worsening of consciousness level (11 v 36, p=<0.01) and symptomatic haemorrhage (2 v 17, p =<0.01); in EEN v LEN groups. All the above are confounding factors that may indicate a poorlier patient population therefore likely more succeptible to infection, poorer nutritional status, higher complications and therefore increased length of stay. Again, no mention of nutritional status, any anthropometry, kcal/pro target v kcal/pro delivered, functional measures, risk of malnutrition scores – could all impact risk of SAP and increased hospital stay.
456	A. Mizuma et al. (2021). Effect of early enteral nutrition on critical care outcomes in patients with acute ischemic stroke. *The Journal of international medical research,* 49:11 3.0006052111e+15	Retrospective observational study with 1511 consecutive patients with acute (ischaemic stroke) ischaemic stroke admitted to a Japanese hospital between 2009 and 2014. Inclusion criteria: admitted a week after ischaemic stroke diagnosed with MRI. Exclusion criteria: severe stroke (NIHSS) Score >22, severe consciousness disturbance, mild stroke (NIHSS) <4, comorbidity of	Early enteral nutrition versus late enteral nutrition (less than 28 hours start versus starting enteral nutrition after 28 hours).	Length of hospitalisation and ICU stay, incidence of pneumonia.	EEN group v LEN group: SAP (8.5v28.1%; statistically significant p<0.01) Length of hospitalisation stay (22 v 35 days, statistically significant p <0.01) Length of ICU stay (4 v 6 days, significant P<0.01	**SIGN -** Detail missing with regards to the nutrition provided, if patients exclusively enterally fed, medications, dysphagia, nutritional status, other acute factors which could affect outcomes, mobility etc.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		aspiration pneumonia on admission, discharge within a week.				
460	J. Peng et al. (2021). Influence of Early Enteral Nutrition on Clinical Outcomes in Neurocritical Care Patients With Intracerebral Hemorrhage. *Frontiers in Neurology,* 12: 665791	Atraumatic ICH patients admitted to neuro ICU between 2012 – 2015 n=166 patients obtained from single centre UKER-ICH registry Exclusion criteria <72hrs in NICU and/or treatment withhold Following propensity score: EEN group (n=47) nEEN group (n=67)	2 groups: Early enteral nutrition (EEN) group, feeding commenced within 48 hours of acute ICH Non early enteral nutrition (nEEN) group, nil enteral feeding commenced within 48 hours of acute event	12 months and 3 months, mRS (0-3), mortality at 3 and 12 months absolute and relative perihaemorrhagic edema, Infection and GI complications (constipation/diarrhoea)	No differences detected for modified rankin scores at 3 or 12 months. No differences detected between day 12 and 15 imaging assessing perihemmorhage oedema. (PHE) Significant differences in maximum absolute PHE during hospital stay in EEN compared to nEEN patients (26.7 (6.5-39.5ml) v 34.8 (8.5 - 58.4ml), p = 0.021). No differences detected for GI or infectious complications	**SIGN -** Unacceptable. Many confounders still not controlled for, as below. Retrospective cohort generally weak evidence. No clear evidence between exposure and outcome. Nil information on route of feeding, stomach/intestine No significant different in total calories provided, at 2-week mark, only first two days. Nil information between these two points. Significant difference in 48-hour initial nutrition provision, EN v NEN (161.4 v 0kcal, p=<0.001). Disparity in Enteral calories and total calories in EEN group despite nil additional PN calories, unclear how this is explained. Nil reports of any PO intake/consideration Which nutritional requirements equation was used – may have effected requirements v nutrition delivery.

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
						Imbalance in relevant clinical characteristics therefore propensity score used (balanced, parallel, nearest-neighbour approach) using diabetes, graeb score, mechanical ventilation, and GCS on admission. Not matched numbers in each group. Imbalance in baseline characteristics for each group - NIHSS higher (22 v 14, p=0.002) and GCS lower (7 v 12, p<0.001) in EEN group DM status (23v29, P<0.018) and hepatological dysfunction (3 v 12), not statistically significant, p=0.558). Mechanical ventilation required more, as a percentage, than NEN (92.2% v 63.4%, p=<0.001) - likely lower kcal requirements in ventilated patients Nil mention of nutritional status/screening tool scores/anthropometrical markers This study only demonstrates an association between EEN and absolute PHE volume during hospital stay. Starting nutritional intake in EEN group is negligible, far less than

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
						would usually target feed in practice. Nearly impossible to prove that early EEN is solely responsible for PHE volume.
460	J. Peng et al. (2021). Influence of Early Enteral Nutrition on Clinical Outcomes in Neurocritical Care Patients With Intracerebral Hemorrhage. *Frontiers in Neurology,* 12: 665791	Retrospective cohort study with patients admitted over 4 years 2012-2015 to neurological ICU with ICH. n=166	Early enteral nutrition started within 48 hours of admission versus those without EEN.	Modified Rankin scale at at 12 month and 3 monthds. Mortality at 12 months PHE evolution Infectious complications Gastrointestinal adverse events	No significant differences were found between the two groups. Only in the absolute perihemorrhagic oedema	**SIGN -** Lack of detail in the study. The baseline patients admitted at would impact the outcomes for example a significantly higher NIHSS score for the EEN group at baseline, query over nutritional status, refeeding risk at baseline, mobility, dysphagia etc. Population not representative of the UK Population
467	G. Xiaorong et al. (2018). Effect of Early Enteral Nutrition Support on Nitrogen Balance and Nihss Score in Elderly Patients with Acute Cerebral Stroke and Dysphagia. *Pteridines,* 29:1 91-96	Retrospective cohort study. Acute Hospital in China Patients diagnosed with acute brain stroke (ABS). >70years old, stroke confirmed by CT or MRI, stroke onset time <72hrs, dysphagia diagnses by standardized swallowing assessment (n= 68)	NG fed patients (NG inserted <72hrs post stroke) Control group (n=31) – regular liquid diet (rice soup, milk, fish soup) of unspecified amounts 54.8% male, 58.1% ischemic stroke, 41.9% haemorrhagic stroke, NIHSS score 14.9 +/- 3.3 Intervention group (n=37) – enteral formula (20g protein, 60g maltose, 60g fructo-oligosaccharide,	Nitrogen balance (nitrogen intake g/day) - 24hr urine urea nitrogen +4) Serum albumin NIHSS scores Complications -aspiration pneumonia -pulmonary infection -diarrhoea -abdominal distension -alimentary tract hemorrhage	Nitrogen balance in experimental group significantly higher ($p<0.05$): Experimental group: 1, 2, 3 and 4 weeks after EN - -4.3 +/- 1.3, -3.4 +/- 1.1, -2.6 +/- 1.2 and -2.0 +/- 1.1g/day, respectively Control group: 1,2,3,4 weeks after hospitilisation:-8.5+/- 3.1, -7.0 +/- 2.4, -6.2 +/- 1.5 and -5.7+/- 1.1g/day, respectively Serum Albumin: Significantly higher for intervention group at 2, 3 and 4 weeks; 34.2 +/- 2.1 v 28.6	**0** Reject: -Can't be sure two groups studied are comparible. No information on baseline nutritional status. Nil recognition that knowledge of exposure status could have influence outcome, nil method of assessment of exposure. Main potential confounders are not identified and taken into account within analysis. Nil confidence intervals provided. -Nitrogen balance outcome poorly presented. Figure 1 published doesn't match reference in text

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
			60g starch, refined corn oil 20g, various trace elements. Possibly per 500ml, author not specified). 500ml 6 x day gradually increased to 1500ml, amount unspecified 59.5% male, 62.2% ischemic stroke, 37.8% haemorrhagic stroke, NIHSS 15.3 +/-n 3.2		+/- 1.9, 35.1+/-1.9 v 27.7+/-2.1 and 36.2+/-1.7 v 28.4+/-1.8, respectively NIHSS score: 4 weeks post commencing EN; 7.3 +/- 2.3 and 7.4 +/- 2.4 for intervention and control group respectively. Deemed significantly different (p<0.05) Complications: Nil differences detected between groups for pulmonary infection, UTI or haemorrhage of digestive tract Regurgitation significantly higher in control group (7v2, p<0.05) Diarrhoea significant higher in control group (11v3, p<0.05) Ventosity significantly higher in control group 15v5 (p<0.05)	-Incidence of haemorrhagic strokes higher than widely reported prevalence of 20% ?selection bias -Retrospective cohort study limitations -Informed consent from all individuals - implies all patients had capacity -Nil nutritional information on a conventional liquid diet -Enteral feeding protocol poorly defined, quite confusing - 500ml 6x day for first few days (not specific), gradually increased to 1500ml/day?
467	G. Xiaorong et al. (2018). Effect of Early Enteral Nutrition Support on Nitrogen Balance and Nihss Score in Elderly Patients with Acute Cerebral Stroke and Dysphagia. *Pteridines,* 29:1 91-96	68 patients diagnosed with and admitted to a Chinese hospital with an acute brain stroke were retrospectively analysed. Inclusion criteria: >70years old Diagnosis of stroke confirmed with CT or MRI scan <72 hours onset of stroke Dysphagia diagnosis with standardised swallow assessment.	37 patients were given early enteral nutrition within 72 hours of stroke diagnosis (500ml enteral nutrition for the first few days then increased to 1500ml per day). 31 patients the control group fed with conventional liquid	Nitrogen balance calculated after receiving EENS for 1-4 weeks Serum albumin NIHSS score on admission and after 4 weeks of treatment Complications like aspiration pneumonia, pulmonary infection, diarrhoea, abdominal distension and alimentary tract haemorrhage	Nitrogen balance and serum albumin in intervention group significantly higher than control group p<0.05 NIHSS score significantly lower in intervention group p<0.05	**SIGN -** Small sample used in this study which is not representative of the UK population. Liquid diets are not used in the same way in UK hospital trusts. A lot of detail missing in the baseline characteristics (medical conditions, nutritional status, severity of stroke, severity of swallow disability

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
			diet (homemade rice soup, milk and fish soup) Query if all subjects fed nasogatrically			etc.) which could have affected the outcome of this study. Haemorrhagic strokes were included in this data set and the outcomes from this strokes ore often very different from ischaemic strokes. Nutritional intake not clear e.g. type of feed and query if 300ml x 6 daily = 3litres of feed. Any additional fluid flushes/IV fluids given.
354	K. Ikezawa et al. (2021). Effect of early nutritional initiation on post-cerebral infarction discharge destination: A propensity-matched analysis using machine learning. *Nutrition & dietetics: the journal of the Dietitians Association of Australia,* :	Japanese patients following acute cerebral infarct. Retrospective observational study Patients obtained from Diagnosis Procedure Combination anonymised database in Japan, patients between 2016 and 2019. Total 7082 patients: Age 80-81 +/-11 years Male/female n=1637-1697/ n=1844-1904. Body weight 53kg +/- 12.8kg Barthel index 8.5-9.1 +/= 23.8-24.9 Modified rankin scale = 1.9-1.93 +/- 1.90 Exclusion criteria: <20y.o LOS <3 days or death	Early nutrition initiation (<72 hours post cerebral infarction), oral or enteral(n=3541) v control group (nil early nutrition) (n=3541)). Machine learning using propensity score matching and extreme gradient boosting.	Discharge destination: Home or 'other facilities' e.g. rehabilitation wards and nursing homes	Early nutrition group 812 patients discharged home Control group: 504 patient discharged home Significant dependence between early nutrition and home discharge ($p<0.05$) and odds ratio of 1.79 (95% CI, 1.59-2.03) Prediction of discharge destination evaluated using area under the receiver operating characteristic (ROC) curve. 100 explanatory variables resulting in 0.848 (95% CI, 0.842-0.854) AUC.	**SIGN -** Unacceptable Subjects not comparable in all respects other than the factor under investigation Main confounders are not taken into account in the design It is not felt that there is clear evidence of an association Between exposure and outcome Results are not directly applicable to the patient group targeted in the guideline Other comments: Discharge practices likely to vary from Japan to UK - not applicable to generalise results from this to UK practice. Many reasons other than nutrition

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		Hospitilisation for 2nd or subsequent time Onset of disease after 8 days or asymptomatic Missing height or weight or weight and height outside bounds of 100-250cm and 10-200kg. Lack of description of post discharge outcomes Missing barthel index Insufficient data on comorbidites Lack of information on nutrition within first 3 days				initiation that could effect discharge destination, patient choice, social status, family/nearest available relative, variance in discharge practices/social care across Japan Characteristics of patient not including nutritional status or BMI. Nil consideration of severity of stroke. Nutrition provision likely to vary massively across patient population. Nature of propensity matching means patients used only represent 10.6% of whole database.
354	K. Ikezawa et al. (2021). Effect of early nutritional initiation on post-cerebral infarction discharge destination: A propensity-matched analysis using machine learning. *Nutrition & dietetics: the journal of the Dietitians Association of Australia,* :	Data was collected from - Diagnosis Procedure Combination anonymised database in Japan. Using data from hospitalised patients between 2016-2019 who were admitted following an ischaemic infarct. Before propensity matching n= 4159 control group n = 37318 intervention group After propensity matching n = 3541 in both groups exclusion criteria : <20 years of age	oral or enteral nutrition during first 3 days of hospital admission versus control group who did not receive nutrition in the first three days of admission	Place of discharge home, rehabilitation centre or nursing home	significant difference in the number of patients discharged home p<0.05 22.9% early nutrition group versus 14.2% control group	**SIGN -** Number of factors affect discharge destination e.g. swallowing ability and reliance on long term enteral feeding, severity of stroke, dementia etc. Propensity matching can cause bias although it does aim to balance out the confounding variables and the differences in the baseline characteristics. Unclear if the subjects were meeting their full nutritional requirements at day three and

Ref ID	Source	Setting, design and subjects	Intervention	Outcomes	Results	Evidence quality (SIGN checklist score) and comment
		<3 days hospital stay or d/c due to death 2nd hospitalisation onset >8days or asymptomatic incomplete data on height/weight lack of detail regarding discharge missing Barthel scores insufficient detail on comorbidities lack of information on nutrition treatment for the first 3 days after admission				if the control group were receiving any fluids e.g. via IV route as this can also impact on outcomes. What treatment was provided to participants across the different centres e.g. were they all thrombolysed on admission as this impacts outcomes too. Study sample not representative of UK population