Question 21 evidence tables

Question 21: How should eating and drinking be managed towards the end of life after a stroke?

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

AD = Advanced directives, GCS = Glasgow Coma Scale, PEG = Percutaneous endoscopic gastrostomy, EDAR = Eating and drinking with acknowledged risk, EN = enteral nutrition, IRF = inpatient rehabilitation facilities, 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, OR = odds ratio, RR = relative risk, aOR = adjusted odds ratio, cOR = crude odds ratio, CI = confidence interval, RoB = risk of bias, I2 = heterogeneity statistic.

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ID						checklist score) and comment
49	A. Alonso et al. (2017). Critical appraisal of advance directives given by patients with fatal acute stroke: an observational cohort study. <i>BMC medical</i> <i>ethics</i> , 18(1): 7	Setting - Germany; Design - Retrospective analysis of medical records of patients with advanced directives (AD) and risk scores; Subjects - 35 patients ischemic stroke or spontaneous intracranial hemorrhage patients who died during hospitalisation from January 2011-December 2014 with AD.	Analysis of the Advanced Directives of patients with fatal stroke, focussing on: (a) availability and type, (b) stated circumstances to which the AD should apply, and (c) stated wishes regarding specfic treatment options.	 Type of AD Applicability to the circumstances at presentation Specifications referring to medical and therapeutic actions (such as diagnostic procedures, nutrition, medication, and initiation of palliative measures). 	35/143 (24.5%) ADs were available 1. Type of AD - 10/35 AD witnessed by notary; 13/35 AD witnessed by other; 12/35 AD not witnessed. 24/25 of the without notarial certified used standard AD forms. 2. Circumstances that the AD should apply were: 21/35 (60%) "terminal condition that will cause death within a relatively short time" or ongoing "dying process"; 17/35 (48.6%) "permanent unconciousness/irreversible coma"; 12/35 (34.3%) "irreversible loss of ability to reason/of power of judgement/of decision making ability"; 11/35 (31.5%) "end stage condition of an incurable/fatal disease, even if dealth is not yet conceivable";	+ Acceptable. Limitations relate to sample size and study design (retrospective chart analysis).
		from January 2011-December 2014 with AD.	apply, and (c) stated wishes regarding specfic treatment options.	nutrition, medication, and initiation of palliative measures).	should apply were: 21/35 (60%) "terminal condition that will cause death within a relatively short time" or ongoing "dying process"; 17/35 (48.6%) "permanent unconciousness/irreversible coma"; 12/35 (34.3%) "irreversible loss of ability to reason/of power of judgement/of decision making ability"; 11/35 (31.5%) "end stage condition of an incurable/fatal disease, even if dealth is not yet conceivable";	

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					10/35 (28.6%) "permanent brain damage"; 9/35 (25.7%) in each "advanced degenerative brian disease with need for artifical nutrition", "failure of vital functions"; 3/35 (8.6%) in each "most severe physical disability/disease", "intolerable pain"; 2/35 (5.7%) "no improvement over 3 weeks after severe stroke" and 1/35 (2.9%) "no will to live". 16/35 (45.7%) were considered to be applicable to severe stroke by the treating physician. 3. Specifications referring to medical and therapeutic actions: Refusing treatments: 22/35 (62.9%) objected to cardiopulmonary resuscitation, 19/35 (54.3%) mechanical ventilation and 26/35 (74.3%) artifical nutrition, 11.4% did not want hydration, 5.7% antibiotics or hemodialysis (2.9%). 33/35, 94.3%directed that treatment for alleviation of pain or discomfort should be provided at all times.	
49	A. Alonso et al. (2017). Critical appraisal of advance directives given by patients with fatal acute stroke: an observational cohort	Observational cohort study hospitalised patients n=35	No intervention - analysed the ADs of patients with fatal stroke	ADs (a) their availability and type, (b) stated circumstances to which the AD should apply, and (c) stated wishes	143 patients died 42 (29.4%) had an AD, but only 35 ADs (24.5%) were available. AD's were in place by 21/35 (60%) as a "terminal condition that	- Unacceptable reject

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	study. BMC medical ethics, 18(1): 7			regarding specific treatment options	will cause death within a relatively short time" or an ongoing "dying process." Only 16/35 ADs (45.7%) described circumstances that could have been considered applicable by the treating physicians. Majority objected to CPR (22/35, 62.9%), mechanical ventilation (19/35, 54.3%), and artificial nutrition (26/35, 74.3%), while almost all (33/35, 94.3%) directed that treatment for pain/discomfort should be provided at all times even if it could hasten death.	
50	X. Cheng et al. (2019). Association between enteral nutrition support and neurological outcome in patients with acute intracranial haemorrhage: A retrospective cohort study. <i>Scientific</i> <i>Reports</i> , 9:1 16507	Single Chinese Centre. Retrospective cohort study of 230 ICH ICU patients. Assessed the association between Enteral feeding (calorie intake in first 48 hours) and outcome (discharge GCS). Four different statitical models analysed, each treating the intervention (EN) as either a continuous variable or split into 2, 3 or 4 categories. Second propensity score matching analysis comapring patients receiving EN<25 and EN>25 kcl/kg/48hr (n=69 pairs).	Calorific intake assessed for association with outcome. No specific intervention as such.	Discharge GCS dichotomised at 8 (3-8 versus 9-12). GCS above 12 was excluded	In all models, higher EN intake was associated with a better discharge GCS. Propensity score matched groups (including for severity (APCHEII score and baseline GCS) showed a higher proportion of patients with GCS>8 in the high EN intake group (60/69 vs 48/69, p=0.013)	Outcome measure not approprite for our question. Multiple areas of bias. Retrosepctive analysis, no causal conclusions can be drawn. Major confounder not including ICH volume or baseline BP. Only ICU patients in single chinese centre.
50	X. Cheng et al. (2019). Association between enteral nutrition	China, Intensive Care Unit, Retrospective Cohort study, Patients with acute intracranial	Calories delivered within the first 48	Primary outcome GCS at discharge, Secondary Outcomes - duration of	An increase in the amount of enteral nutrition calories intake delivered in th first 48	+

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	support and neurological outcome in patients with acute intracranial haemorrhage: A retrospective cohort study. <i>Scientific</i> <i>Reports,</i> 9:1 16507	haemorrhage post intracerebral surgery n=230	hours (<=25 and >25kcal/kg/48H)	ICU and hospital stay, and occurrence of hospital acquired pneumonia.	hours was significantly associated with favourable GCS score at d/c. ≤25kcal/kg/48 GCS >8 at d/c 69.5% vs >25kcal/kg/48 GCS > 8 at d/c 86.9%. No significant increase in incidence of acquired pneumonia between the two groups.	Acceptable quality . I did not feel there was clear evidence to change practice because of the retrospective study design which the authors acknowledged - a randomized trial would be needed to validate
51	K. Meisel et al. (2017). Survival, Functional Status, and Eating Ability After Percutaneous Endoscopic Gastrostomy Tube Placement for Acute Stroke. Journal of the American Geriatrics Society, 65:8 1848- 1852	Retrospective cohort study (n=174) of community based older adults who have had a stroke and PEG placed and had already been recruited to Health and Recruitment Study (HRS) in America between 1992-2012	PEG placement following hospitalisation for stroke	Functional Status, Mobility, Eating ability, Place of residence for survivors and Mortality within 2 years of the stroke		- The study did not compare mortality or other outcome measures of the Stroke Patients who had a PEG vs stroke patient who did not have a PEG.
51	K. Meisel et al. (2017). Survival, Functional Status, and Eating Ability After Percutaneous Endoscopic Gastrostomy Tube Placement for Acute Stroke. Journal of the American Geriatrics Society, 65:8 1848- 1852	Retrospective cohort study of nationally representative community-based sample who had a PEG (N = 174, mean age 79, 51% female, 29% African American).	Long-term survival PEG placement	Long-term survival and functional and eating ability. Groups were compared according to age and pre-stroke functional disability	Mortality 66%. Fifteen participants survived and regained independent ADL (9%). Of those who survived to follow-up 33 (56%) could not eat independently, and 31 (53%) required assistance to walk, 85 and older was associated withworse outcomes (10% vs 29% at 2 years, P < .001), but baseline ADL disability was not.	- Unacceptable reject

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52	N. Soar et al. (2021). Approaches to Eating and Drinking with Acknowledged Risk: A Systematic Review. <i>Dysphagia</i> , 36:1 54-66	All care settings (hospital/community), A systematic review, Adults with oropharyngeal dysphasia, 8 articles met the inclusion criteria out of 984 articles and conference abstracts identified.	Comparison of EDAR protocol with a control group.	Primary outcome- improved patient care following implementation of an EDAR protocol as indicated by changes in documentation processes, days nil by mouth, length of hospital admission, staff/patient/carer feedback. Secondary aim - to identify important factors and success of EDAR protocols via reports of views/experiences of staff, patients, families and carers related to EDAR.	8 papers articles all published in peer reviewed journals were reviewed. All reported on comparison of key quality markers before and after introduction of an EDAR protocol. Evidence is limited regarding EDAR protocols. However there is growing support for a coordinated approach for managing EDAR - positive outcomes were reported when there is a protocol in place.	++ High quality, good study design that appeared well conducted. Although evidence base found within this study was small, it did demonstrate some evidence directly related to management of EDAC in Stroke and relevant to the question. It is noted s that there was a lack of current research to explore the impact EDAR protocols on patient experience and quality of life.
53	L. Sutcliffe et al. (2020). Percutaneous Endoscopic Gastrostomy and Mortality After Stroke in England From 2007 to 2018: A Retrospective Cohort Study. <i>Stroke</i> , 51:12 3658-3663	Setting - England; Design - A retrospective cohort study using NHS Episode Statistics of finished stroke admission episodes in England with and without PEG insertion and OFS mortality records at 3,6 and 12 months (April 2007-March 2018). Linear regression was used to describe time trends in PEG procedures and mortality and logistical regression (Odds Ratios) were used to examine demographic characteristics (age, sex, ethnicity, and ICD 10 code) and PEG insertion; Subjects - Patients with stroke (n=923236 stroke admissions)	Number of cases with and without PEG procedure and mortality cases at 3, 6 and 12 months	1. Population level trends over time in PEG procedures 2. Key demographic associations with PEG insertion 3. Mortality after PEG insertion at 3, 6, and 12 months	923,236 patients with stroke underwent 17,532 PEG procedures (mean rate 1.9%) 1. Population level trends in PEG procedures - An average reduction of -27 procedures/per year ([95% CI, -56 to 1.4];P=0.06) despite annual increases in stroke admission volume. 2. Key demographics associated with PEG - Relative to age < 60 years, PEG insertion had a +ive association with patients aged 60-79 years (OR, 1.97 [95% CI, 1.86-2.09]) and 80 + years (OR, 2.73 [95% CI, 2.58-2.90]). There was a +ive association with female relative to male	+ Acceptable. A well designed study using NHS Hospital Episode Statistics healthcare data and ONS mortality data to statistically analyse population trends over time in PEG procedures, key demographic associations with PEG insertions and mortality after PEG insertion.

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					sex (OR, 1.10 [95% CI, 1.08- 1.14]), whereas PEG insertion was less likely for patients of White ethnicity (OR, 0.88 [95% CI, 0.83-0.93]) and for hemorrhagic compared to ischemic stroke (OR, 0.94 [95% CI, 0.90-0.98]). 3. Mortality after PEG insertion - Mortality reduced following PEG insertion: -28 deaths/year ([95% CI, -35 to -20]; P<0.001) at 3 months, -33 deaths/year ([95% CI, -46 to -20]; P<0.01) at 6 months and -30 deaths/year ([95% CI, -48 to -13]; P<0.01) at 12 months. With all years combined PEG insertion was weakly associated with reduced mortality at 3 months (OR, 0.94 [95% CI, 0.90-0.97]), but signficantly higher mortality at 6 months (OR, 1.69 [95% CI, 1.64-1.75]) and 12 months (OR, 2.14 [95% CI, 2.08-2.20]).	
53	L. Sutcliffe et al. (2020). Percutaneous Endoscopic Gastrostomy and Mortality After Stroke in England From 2007 to 2018: A Retrospective Cohort Study. <i>Stroke</i> , 51:12 3658-3663	United Kingdom, all admissions setting not specified, Retrospective Cohort Study, All patients admitted with stroke related International Classification of Disease codes n=923,236	PEG placement	Mortality at 3, 6 and 12 months	Reduction in PEG placement and deaths in relational to general mortality - average reduction of -27 procedures/year despite an average increase in stroke admissions 1804/year. Although mortality at 6 and 12 months post stroke remains significantly worse for patients with PEG	+ Acceptable quality. Retrospective study so not high quality evidence but the data is reliable but not all confounding issues can be accounted for

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54	J. Wilmskoetter et al. (2018). Impact of Gastrostomy Feeding Tube Placement on the 1-Year Trajectory of Care in Patients After Stroke. <i>Nutrition in</i> <i>Clinical Practice</i> , 33:4 553-566	Retrospective cohort study. US database of 8911 comercially insured stroke patients (the Truven Health MarketScan Research Database 2010-2012). Included both AIS and ICH, excluded prior stroke and dysphagia. Analyses adjusted for demographics and stroke severity	Comparing two groups, with and without PEG tube placement.	admission and re- admission at 1, 3, 6 and 12 months	1.7% had PEG tube placement (n=148). Pateints with PEG were more likely to have had ICH, longer LoS, more co- morbidities, higher stroke severity; was an independent predictor of discharge to long- term care and re-admission.	Strengthened by adjusted analyses. Limited by drop outs (e.g. at 12 months postdischarge, 39.19% of all patients with a PEG tube placement and 65.42% of all patients without a PEG tube placement were still enrolled). Not a randomised study but statistical control with confounders. SIgnificant loss of follow up provides a major bias.
54	J. Wilmskoetter et al. (2018). Impact of Gastrostomy Feeding Tube Placement on the 1-Year Trajectory of Care in Patients After Stroke. <i>Nutrition in</i> <i>Clinical Practice</i> , 33:4 553-566	Retrospective analysis of commercially insured Stroke patients in America, diagnosed in 2011 (8911 patients in study)	PEG Placement during acute inpatient hospital stay (n=148)	Admission to inpatient rehabilitation facilities (IRF), hospital readmissions as well as Skilled nursing facility, outpatient and home visit encounters	Larger % of patients with PEG discharged to IRF from acute care compared to those without a PEG. Also increased encounters (Skilled Nursing Facility, outpatient appts and home visits) for PEG patients. However there was no statistical difference between numbers of patients readmitted within 30 days and the Length of stay between the 2 groups	- Large proportion of patients lost to follow up (60% in intervention group) and the % of patients receiving PEG placement in this study following stroke is much lower than previous studies.