Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings
Jawaid et al 2010 Cohort study	Class I for prognostic accuracy	285 subjects with 274 completing. BMI and progression evaluated. Analysis of BMI as an independent indicator of prognosis.	Cohort followed over several years to assess whether baseline BMI or change in BMI over 2 years was associated with "age at onset, rate of disease progression and survival". BMI measurements made by nurses unaware of the study (this is the blinding for this study). Patients divided into 6 BMI categories (underweight to obese class III). Change in BMI over 2 years divided into gain > 1unit, stable, or loss >1 unit.	Survival	274 in analysis. Only 3 in group BMI underweight. 92 were normal and rest were overweight or obese. Survival was not influenced by baseline BMI. P=0.23. Over 2 years BMI >1 unit loss was associated with poorer survival p=0.02 and faster progression p=0.001. Mean survival was 16 months longer for stable weight than weight loss (10 months for weight gain vs weight loss).
Marin 2016 Cohort study	Class I for diagnostic accuracy	322 subjects with 261 completing.	Weight loss analyzed for association with survival	Survival	During follow-up period 226 of 261 patients died, median survival 17.5 months. At diagnosis, 50.6% had WL>5%. WL at diagnosis was associated with worse survival. Risk of death increased by 14% (5-23%) for each 5% loss of weight. No information on benefit of nutritional support.
ProGas Study Group 2015 Prospective non-randomized cohort study.	Class II	330 subjects enrolled with 323 completing.	Multicenter prospective study of subjects with a decision made to insert tube. Insertion method (PEG, RIG or PIG) was decided by treating physicians. Subjects assessed at baseline, 3 months and 12 months.	Primary outcome was 30 d. survival. Secondary outcomes were: procedural complication rate, post gastrostomy survival, nutritional status, QOL, care giver strain.	No difference in survival for the 3 procedures. Analyzing the 30 d. data, there was a 10.7 times higher (95% CI 1.3-87.0; p=0.027) risk of dying if wt. loss >10% from time of diagnosis compared to <10%. They conclude that a 10% threshold for nutritional intervention

					is possibly too high. 5% might be more effective. They note the PIG group had the lowest FVC and did as well as the other 2 groups. The PEG and PIG tubes fared better over time. They suggest PEG if good FVC and PIG if poor, but this is not proven.
Desport 1999 Prospective cohort study	Class I for prognostic accuracy	55 subjects with 55 completing.	Prospective cohort series following nutritional status of patients enrolled in clinic for a mean of 7 +/-4 mths. They divided patients into < or > BMI 18.5 at entry. Malnourished defined as <18.5. PEG status noted.	Survival	55 patients with 29+/-25 months since initial signs at enrollment. 9 were malnourished. No other sig. diff. in baseline characteristics. Multivariate analysis demonstrated risk of death increased in malnourished patients RR 7.4 (95% CI, 1.7 to 32.1; $p < 0.01$). This risk did not change if gastrostomy fed patients were excluded.
Calvo 2017 Cohort study	Class III	2648 patients with ALS followed in 13 centers.	Kaplan-Meier method to determine survival time; Multivariate Cox regression models used to estimate covariate-adjusted risk of death or tracheostomy.	Time to death or tracheostomy	Higher BMI (>24) at diagnosis was an independent prognostic factor for better survival.
Limousin 2010 Retrospective cohort study	Class III	63 patients	Mann-Whitney tests were used to test the association between survival and clinical parameters, including nutritional parameters.	Disease duration defined as months from symptom onset to death or tracheostomy.	13 of 63 patients (21%) had lost >10% wt. at t1. None were BMI<18.5 at t1. At t2 30 (48%) lost >10% and 9 (14%) were BMI<18.5. Disease duration was 17+/-6 month for t1<10% vs. 35+/-26 for >10% p=.002. Early severe weight loss had a worse prognosis.

Marin 2011 Retrospective cohort study	Class III for prognostic significance	92 patients, with 74 reaching endpoint by study end between 1997 and 2007.	Cox model to analyze association between nutritional variables and death	Survival	74 of the 92 had died by end of study. Multivariate analysis showed a HR 1.31 (95% CI 1.08 to 1.60) p=0.006 decrease in survival for 5% decrease in weight from usual weight at time of diagnosis. BMI drop 1 unit from usual BMI HR 1.23 (95% CI 1.07 to 1.41) p= 0.003. Over follow-up period drop of 5% from usual HR 1.34 (1.18 to 1.51) p <0.0001 and BMI drop by 1 HR 1.24 (1.13 to 1.36) p <0.0001 .
Fasano 2017 Prospective cohort study	Class III	545 patients in registry, with 152 undergoing PEG analyzed.	Multivariate Cox regression model to calculate covariate risk of death or tracheostomy	Tracheostomy free survival	Loss of BMI from time of diagnosis to PEG insertion was associated with poorer survival (HR 1.05, 95% CI 1.02–1.09; p=0.003), suggesting tube insertion should be before weight loss.
Dorst 2015 Prospective cohort study	Class IV	Multicenter observational study of 89 patients.	Each center decided on criteria for PEG insertion. Non-parametric tests (Mann-Whitney and Kruskal-Wallis) were used to compare independent samples.	Survival	Follow-up mean 4.49 ± 4.74 months (max. 18 months) No difference in survival post-PEG between FVC>50% and FVC<50% group. Survival difference between Caloric intake >1500 kcal/d vs < 1500 kcal/d for those who survive beyond 12 months p=0.042. Survival better post PEG for those who had lost <5kg before PEG.
Nunes 2016	Class IV	37 patients	Multivariate analysis using ordinal least squares regression model. Low BMI	Survival	High initial BMI associated with better

Retrospective case series			defined as <18.5 kg/m2 if <65 years or < 22kg/m2 for ≥ 65.		survival (R2 = 0.39; p = 0.004).
McDonnell 2017 Causal inference study	Class III	481 patients. Data previously collected in a ceftriaxone trial.	Secondary analysis of data on effect on G-tube insertion. Effect on survival used structural nested accelerated failure time model. Marginal structural models assessed QOL.	Survival and QOL (ALSSQOL inventory)	They calculated a 46% decrease survival time from G tube placement and no effect on QOL. The data cannot be used to conclude there is a negative effect from G tube, but suggests the need for an RCT.
Lopez-Gomez 2018 Cohort study	Class III	27 protocol patients (retrospective) and 16 control (prospective)	Protocol patients had nutrition referral at diagnose and control standard treatment. Multivariate analysis to assess risk of developing severe malnutrition.	Subjective Global Assessment of nutritional status.	Nutritional referral at diagnosis was independent protective factor for severe malnutrition (odds ratio, 0.20; 95% confidence interval, 0.03–0.73; *P* = 0.02).
Kasarskis 2014 Prospective cohort study	Class I	80 ALS patients were followed over 48 weeks.	Total daily energy expenditure (TDEE) was determined over 10d every 16 wks. using doubly labeled water. Formula developed using resting metabolic rate and 6 items (sum of 1,4,6,7,8,10) from the ALSFRS-R to estimate TDEE	TDEE estimate compared to actual. Various models were evaluated for correlation with the measured TDEE.	TDEE estimate was +/- 500 kcal/d of actual TDEE across different stages of the disease. The authors conclude the TDEE calculator can be used to determine if a G tube is needed to supplement nutrition (as opposed to weight loss or dysphagia)
Lee 2017 Cohort study	Class I for diagnostic accuracy	370 patients	TDEE was calculated for ALS patients at different stages of disease	Spearman correlation coefficient compared clinical stages of ALS with TDEE	TDEE decreased as patients progressed and actual energy intake was lower than TDEE in all stages, most marked when 3 regions of the body are affected. The TDEE calculation can be used to assess nutritional requirement of patients.
Higo 2004 Cohort study	Class III	50 patients	50 patients had 72 videofluoroscopy (VF) examinations. Subgroups	Change in VF findings and change in ALS severity scale	ALSSS swallowing score and bulbar symptom duration

			divided according to swallowing subscale and duration of bulbar symptoms.		significantly correlated (r=0.409, n=72, P=0.0004). In the group with normal eating habits, 52.4% showed some abnormality on VF. Aspiration risk was present even in those with normal eating habits and no bulbar symptoms.
Lo Re 2007 Case series	Class IV	23 patients	Patients had VF. Patients divided into ALSSS scale groups.	Correlation of ALSSS groups with VF.	23 subjects. 1 could not complete test. There were no nothing by mouth (NBM) subjects. In NEH (normal eating habit) subjects 66.7% had abnormal VF. VF detected swallowing dysfunction in 19/23 subjects. They conclude that VF is more sensitive than self-reported symptoms in detecting swallowing dysfunction in ALS patients.
Paris 2012 Cohort series	Class II for diagnostic accuracy	20 patients	Comparison of videoflouroscopy and Volume-Viscosity Swallow Test (V-VST). Patients divided into 2 groups (normal and abnormal VF). Compared to results of V-VST. Sensitivity and specificity of V-VST calculated with Chi2.	Impaired swallowing	15 patients had abnormal VF. 15 had abnormal V-VST. Sensitivity of V-VST 93%, specificity 80% p=0.007. They conclude V-VST is a good evaluation of swallowing dysfunction in ALS. Does not require radiation exposure.
D'Ottaviano 2013 Case series	Class IV	12 patients	Case series evaluating swallowing with FEES in a clinic over a year.	Impaired swallowing	Though 72% of patients had swallowing symptoms, 100% had abnormal studies.
Plowman 2016 Cohort study	Class II for diagnostic accuracy	70 patients	EAT-10 questionnaire compared to VF evaluation for swallowing safety. VF rated by	Impaired swallowing	EAT-10 scores rose significantly between each step from safe

			blinded observers. Diagnostic accuracy of EAT-10 determined by analyzing a receiver operating characteristic curve.		swallowers to penetrators to aspirators. EAT-10 cutoff scores for the different degrees of swallowing impairment were established, with sensitivity ranging from 85.7% to 88% and specificity from 56.7% to 71.9%.
Albert 2001 Prospective cohort series	Class IV	121 patients with 101 completing	Patients included in the Project on Death in America. ALS cohort followed for 2 to 4 years. Interviews included attitudes about PEG. Multivariate proportional hazards model to include sociodemographic and disease factors.	PEG placement	36% had PEG. 9.3% of patients had PEG, if initial interviews stated they did not want a future PEG. For those that said they were "leaning toward" or "absolutely wanted" a future PEG, 57.1% received PEGs ($p<0.01$)
Kasarskis 1999 Retrospective analysis	Class III	172 patients (136 BDNF and CNTF patients and 36 placebo patients)	Retrospective analysis of data from 2 RCTs (BDNF & CNTF). They analyzed patient characteristics at time of PEG and survival.	Survival post-PEG	Median FVC at 39.1% (CNTF) and 52.5% (BDNF) at time of PEG. 13 (9.6%) died within 30 days of PEG and all had FVC <50% at time of PEG. Conclusion was that PEG may not be safe with FVC<50%.
Katzberg 2011 Cochrane review meta-analysis	Meta-analysis	Multiple non-randomized studies	Effect of gastrostomy on ALS. No data analysis, as no randomized trials. Reported data on non-randomized series.	Primary outcome was survival. Secondary outcomes: objective nutritional measurement, QOL and safety	No randomized or quasi-randomized studies. They report on non-randomized studies. For survival: 3 prospective trials. 2 reported survival advantage for PEG and one did not. There were 8 retrospective trials. 2 showed a positive survival advantage with PEG and 6 did not. For nutritional outcome: 2 controlled studies show an improvement in

					nutritional markers with PEG. For QOL:2 controlled studies. Neither showed improved QOL. For safety and timing: 2 uncontrolled studies show PEG can be done with low FVC. Method of tube PEG vs RIG: 4 case control studies. Uncertain conclusions due to poor methodology. Overall, similar results.
Boitano 2001 Case series	Class IV	5 patients with FVC < 50%	PEG inserted with NIV support in patients with poor respiratory function.	PEG safety	All patients had successful PEG. FVC ranged from 21 to 44%. All discharged the next day without complications.
Gregory 2002 Cohort series	Class IV	33 patients with FVC < 50%	Evaluation of patients referred for PEG who had FVC<50%. NIV was used during procedure.	PEG success and patient survival	No major morbidity. Survival ranged from 29 to 600 days. 4 failed PEG placements.
Czell 2013 Retrospective cohort study	Class III	26 patients referred for PEG	Patients divided into group of FVC >50% and FVC <50%. 5 patients didn't have an FVC, but judged clinically normal and were included in FVC>50% group. All patients had periprocedural NIV. They analyzed complications and survival descriptively or with 2-tailed unpaired *t* test	Survival and procedure complications	Procedural complications - FVC>50% 4; <50% 0, no statistic calculated.; 1 month survival FVC >50% 91%, FVC <50% 100%, no statistic calculated.; long term survival FVC <50% mean 12+/- 9 month vs FVC >50% 14 +/- 12 month p= .62
Kak 2017 Retrospective case series	Class III	162 patients with 102 completing	Series was divided into patients with and without G tube insertion and in each group, those with FVC>50% and those with FVC between 30% and 50%. Subgroups compared using Cox Hazard Ratio model.	Survival	There were no procedure related deaths. G-tube placement did not have significant survival benefit.

Sancho 2010 Prospective Cohort study	Class IV	30 patients	Study of patients requiring PEG with FVC <50% or using home NIV. They assessed safety of procedure with NIV and mechanically assisted cough (MAC) support.	Procedure safety	FVC was 35.9±18.0%. 27/30 had successful PEG insertion using NIV support. They reported no deaths or major complications.
Strijbos 2017 Retrospective case Series	Class IV	48 patients with 45 completing	Safety of PEG with sedation All PEG insertions were done using conscious sedation.	Procedure safety	FVC ranged from 24-116%. (<50% in 8.8%) No 30 day mortality. Complications generally mild. They conclude that sedation is safe, including in patients with poor respiratory function.
Sarfaty 2013 Retrospective cohort study	Class III	30 patients	Cohort of patients undergoing PEG divided into FVC ≤ 30% and FVC > 30%. No differences in outcome and safety. They emphasize that 80% of patients just had local anesthesia. Groups compared by Cox stepwise proportional hazards model.	Survival.	20 FVC>30%; 10 FVC≤ 30%. No other differences in baseline characteristics. 1 death in each group within 30 days. 1, 3 and 6 month survival no different in the 2 groups.
Chio 2004 Retrospective cohort study	Class III	50 patients	Patients with FVC <50% undergoing PRG from 2000 to 2002 compared to patients prior to 2000 with FVC<50% who underwent PEG (25 in each group). Cox stepwise proportional hazards model for multivariate analysis.	Safety and survival.	No significance data on safety. No other major or minor complications. PEG unsuccessful in 8% vs PRG 0%. Survival post procedure PRG 204±15 d vs 85±12 d, p=0.004. Multivariate analysis of survival demonstrated higher risk of death in PEG OR 1.58 (95% CI 1.12 to 2.01; p=0.03).
Desport 2005 Prospective cohort study	Class III	50 patients	Patients undergoing PEG or RIG between 1996 and 2002. RIG suggested if Slow VC<50% or PEG refused by patient. Quantitative variables compared by Mann-Whitney test. Multivariate analysis performed by Cox model.	Procedure complications and survival.	30 PEG and 20 RIG. Videoflouroscopy risk of aspiration 65% RIG, 19.2% PEG p=0.002. SVC 51.6±25.0 RIG, 67.4±26.7 PEG p=0.03. No other significant differences between groups. Pain 39.4%

					RIG, 10.0% PEG p=0.003. Mechanical obstruction or tube migration 9.1% RIG, 35.0% PEG p=0.003. Survival no different between groups p=0.28.
Rio 2010 Retrospective case series	Class III	159 patients	Consecutive cases (1999 to 2006) of ALS who had PEG, RIG or NG tubes placed for feeding. PEG chosen if FVC >60%, RIG group had poor respiratory function. NG when end stage or refused other procedure. Multivariate analysis through Cox regression.	Survival	PEG 21 patients; RIG 121; NG 17. Survival no different between PEG and RIG p=0.902, but significantly shorter for NG p=.034. Groups were not similar.
Shaw 2006 Retrospective case series	Class III	98 patients	Compared survival of ALS patients requiring enteral nutrition. Groups utilizing PEG, RIG or NG. Baseline characteristics of groups very different. PEG with normal respiratory function, RIG with abnormal respiratory function, and NG if patients medically unsuitable or declined PEG and RIG. Survival plotted on Kaplan-Meier curves. Multivariate analysis through Cox regression.	Survival	72 RIG, 18 PEG, 8 NG. Median survival: RIG 6.31 months (95% CI 4.58–8.04 months); PEG 7.13 months (95% CI 4.81–9.45 months); NG 0.95 months (95% CI 0.00–2.77 months). PEG and RIG survival not different p=0.50. NG survival reduced versus PEG and RIF p<0.03.
Park 2009 Prospective case series	Class IV	25 patients	All patients with low FVC <50%, using BiPAP. They performed RIG without sedation, but using BiPAP.	Safety and feasibility of PRG	Mean FVC 33.3 ± 17.8%. 100% success rate of tube insertion. No major complications.
Park 2010 Retrospective case series	Class IV	36 patients	Retrospective review of 36 consecutive patients with very low FVC undergoing PRG.	Safety and Feasibility of PRG	Mean FVC 17.7% ± 10.5%. 100% success rate. No major complications. 9/36 were receiving mechanical ventilation via trach. 21/36 used BiPAP (7 during procedure).

Shaw 2004 Retrospective case series	Class IV	25 patients	RIG chosen when respiratory function abnormal or failed PEG insertion. NIV in patients with more marked respiratory dysfunction. No sedation given.	Tube insertion success and complications.	100% success rate. 7/25 had periprocedural NIV. No tube related deaths or major complications.
Bach 2010 Retrospective case series	Class IV	62 patients with neuromuscular disease (44 with ALS)	Open gastrostomy with sedation performed on NMD patients dependent on NIV. FVC<40% in all. NIV was used during the procedure.	Descriptive data	All patients had successful open gastrostomy. None needed general anesthesia.
Kawa 2012 Retrospective cohort study	Class III	60 patients	Nurse administered propofol sedation (NAPS) ± NIV versus standard opiod/benzodiazepam sedation ± NIV. Data analysed χ^2 or Fisher's exact test	Insertion success and desaturations	31 traditional sedation; 29 NAPS. FVC significantly lower in NAPS group (p=.004). More patients used NIV with NAPS (p<0.001). 2 in each group failed first attempt. pO2 desaturation (<90%) occurred in 7 standard sedation and 1 NAPS patient (p=.05). No difference in desaturations with or without NIV.
Cui 2018 Meta-analysis of studies reporting survival data after PEG	Meta-analysis	10 studies. 996 patients.	They selected 10 studies that provided survival data after PEG. Mixture of retrospective and prospective studies. The control groups were RIG, NG, PRG or other. Odds ratios with random-effects model used.	Survival	No difference between survival after PEG and control at 30 days, 10 months and 30 months. There was a higher survival at 20 months (OR = 1.97; 95% CI 1.21–3.21; P = 0.007). Due to the variable design and control groups, this may not be a clinically significant finding.
Strijbos 2018 Meta-analysis of studies comparing PEG and PRG. 5	Meta-analysis	6 of 16 studies analyzed were on ALS (529 patients)	Subgroup analysis performed on ALS patients. Pooled risk difference for PEG and PRG were calculated.	Survival, complications	There was no difference in procedure related complications, 30-day mortality, or tube related complications

retrospective and 1 prospective.					
Allen 2013 Retrospective cohort study	Class III	100 patients	Review of PEG vs RIG placement at a single institution. Intervention decided by treating physician and largely was PEG before 2010 and RIG after 2011. Groups compared with χ^2 or Fisher's exact tests and Wilicoxon rank-sum tests.	Safety and success rates.	57 PEG attempts and 51 RIG attempts (100 patients). Failed PEG 15.7%; RIG 1.9% p=0.02. Length of stay (mean ± SD) PEG 3.1±2.2; RIG 4.0±2.1 p=0.02; Day 0 pain (0-10) PEG 5.1±2.8; RIG 6.2±2.6 p=0.03 [Day 1 pain ns]; Complications with aspiration included PEG 10.5% RIG 0% p=0.02. Life threatening complications higher in PEG 7.0% vs 1.9%, but ns. One month and 6-month survival not different.
Thornton 2002 Retrospective cohort study	Class III	36 patients	Study of patients referred for tubes between July 1997 and March 2001. Criteria for choice of PEG or PRG changed over the period of the study. All PEG 1997 to 1999. From 1999 to 2001 PRG if bulbar symptoms, >10% weight loss or FVC 40-60%. Log-rank test for equality of survivor functions among groups.	Insertion success and survival	PEG 11/20 53% success; PRG 25/25 100% success. No statistic on significance reported. Survival after tube not different in groups.
Blondet 2010 Retrospective cohort study	Class III	40 patients	ALS patients having PEG or PRG from 1999 to 2005 at a single center. Univariate analysis with Fisher and Mann-Whitney tests. Survival study used Cox regression model.	Complications, insertion success, survival	43 attempts (21 PEG, 22 PRG). Success rate not different in 2 groups (PEG 85.7%, PRG 100%). Successful and well tolerated placement was higher in PRG 81.8% vs 57.1%, but ns p=0.1; also pain higher in PRG 81.8% vs 52.4%, but ns p=0.05. One month death the same PRG 9.1%, PEG 9.5%.

Chavada 2010 Retrospective case series	Class III	35 patients	ALS patients in single center between 2004 and 2008 having a PEG or per-oral image guided gastrostomy (PIG) (hybrid technique fo PEG and RIG). PIG chosen when the FVC was <50% and SLP assessment suggested high risk of aspiration.	Complications and survival	19 patients had PIG, 16 had PEG. Similar characteristics, except PIG patients had a non-significant lower FVC and 26% used NIV vs 0%. Success rate PIG 95%, PEG 80% (no statistic done). No statistical difference in complications (very few), 1 month survival or overall survival.
Sato 2017 Case control study	Class IV	45 patients	Comparison of conventional normal diameter esophagogastroduodenoscopy (C-EGD) versus ultrathin endoscopy (UTE) on safety, including need for sedation. Group differences determined by Mann-Whitney U tests and Fisher's exact test.	Safety	PEG placement between 2003 and 2013. C-EGD before Sept 2008 and UTE after. Sedation given with C-EGD in 14 patients, and not with 17 C-EGD patients or with 14 UTE patients (3 groups). No deaths or major complications. Minor complications of aspiration pneumonia were seen on 17.6% of unsedated C-EGD; apnea/hypoventilation in 21.4% of sedated C-EGD. None seen in UTE. Statistics not reported on these measures. Elevated BP was 7.1% UTE, 23.5% unsedated C-EGD and 14.2% sedated C-EGD. (ns)
Verschueren 2009 Prospective cohort study	Class III	65 patients (30 prospective and 35 retrospective controls)	Prospective evaluation of ALS patients referred for nutritional assistance. Parenteral nutrition (PN) used if tube feeding impossible or refused. Retrospective control group of patients undergoing PEG, divided into group with	Complications and survival	30 patients in PN group. 5 died shortly after insertion. Data reported on 25. 4 infectious complications (cause of death in 1 and possibly 2). Weight gain or stabilization in

			respiratory insufficiency and group without insufficiency. ANOVA (F-test) assessed differences with groups and Spearman test to evaluate significance of correlations.		92% of 25. Survival not different between PN and PEG with respiratory insufficiency (p=0.92).
Abdelnour-Mallet 2011 Retrospective case series	Class IV	73 patients	Review of patients not eligible for PEG treated with home parenteral nutrition (HPN). Complication rates compared using χ^2 or Fisher's exact tests.	Safety	Mean survival 2.8 ± 1.12 months. 3.11 central venous catheter complications per 1000 catheter days (mainly infections 1.34/1000 catheter days. 16 patients with septicemia, 8 died due to sepsis.