1 PROJECT IDENTIFIER

1.1 Title of project

A Prospective Multi-Centre Evaluation of Gastrostomy in Patients with Motor Neurone Disease

Short Title: PROGAS

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I confirm that I have read and understood protocol (Version …… Dated ……). I agree to comply with the study protocol, research governance, clinical trial regulations and appropriate reporting requirements.

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2 Scientific Summary

Background

Motor neurone disease (MND) is a neurodegenerative illness which causes progressive paralysis of muscles leading to death usually within 3 years of diagnosis. Dysphagia is a common problem in patients with MND, and causes difficulties in maintaining a safe and adequate oral intake of food and fluids. Gastrostomy feeding tubes are commonly used to support patients with dysphagia. The current practice of gastrostomy feeding is largely based on consensus and expert opinion rather than the outcomes of appropriately designed trials. There is lack of evidence to indicate the optimal timing for gastrostomy or which method of gastrostomy insertion is most appropriate. Additionally high quality evidence regarding survival and quality of life following gastrostomy insertion is lacking.

Aims

i) Identify the current practice with regard to gastrostomy insertion in MND Care Centres within the UK and compare it with the practice in the Sheffield and Leeds MND Care & Research Centres.

ii) Identify the most appropriate method for gastrostomy insertion in patients with MND.

iii) Identify the optimal timing for gastrostomy use in patients with MND.

iv) Compare outcomes between different gastrostomy protocols within and between centres with regard to (a) survival; (b) complications; (c) change in weight; (d) change in quality of life; and (e) carer burden, post gastrostomy.

v) Develop guidelines for gastrostomy use in patients with MND.

Plan of Investigation

Patients will be prospectively recruited into PROGAS when a decision to refer a patient for gastrostomy is made. The recruitment target is 504 patients over 21 months. Questionnaires will be completed collecting disease-related data, details of the procedure and complications. Over the subsequent 12 month period, data will be collected on complications, quality of life, and carer burden. A qualitative study will be conducted at the Leeds and Sheffield sites which will assess the outcomes of gastrostomy from the perspectives of the patients, and their carers; delineate their concerns, problems and needs; and enhance our understanding of the factors that are associated with gastrostomy feeding and impact on the quality of life.

Potential Impact

The project addresses an area of unmet need of key strategic importance which has been identified as a research priority by the Dementias & Neurodegenerative Diseases Research Network. The results of this work will translate into the development of guidelines for gastrostomy insertion use in patients with Motor Neurone Disease locally within the regional MND centres in Sheffield and Leeds. Additionally this work may inform guidelines nationally. The principles will be readily applicable to patients with severe dysphagia symptoms who are eligible for gastrostomy insertion due to other neurological diseases. Once a need for gastrostomy has been established, these guidelines will provide recommendations for optimising benefit and the patient and carer experience of gastrostomy.

3 Lay / Plain English Summary

Motor neurone disease (MND) is a devastating illness which leads to progressive muscle weakness and eventual death, usually within 3 years. Difficulty in swallowing is a common problem in patients with MND. Patients with severe swallowing difficulty experience malnutrition, dehydration, choking and an increased risk of chest infections. Long-term nutritional support of patients with severe swallowing difficulty can be achieved by placing a feeding tube, known as a gastrostomy, directly into the stomach. However, the current practice of gastrostomy feeding is largely based on consensus and expert opinion rather than the outcomes of appropriately designed trials. Currently gastrostomy technique and timing of insertion within the disease course vary throughout the UK. There is a lack of evidence to suggest what the optimal timing for gastrostomy is, or which method is most appropriate. In addition, although gastrostomy is routinely performed, the benefits, such as improved survival and quality of life following gastrostomy, have not been proven.

The main aim of this study is to develop evidence-based guidelines for gastrostomy use in patients with MND.

Patients and carers will be recruited at the participating MND Centres in Sheffield, Leeds and around the UK. Questionnaires will be used to assess the safety, complications and benefits of the differing timings and methods of gastrostomy insertion. Participants recruited at the Leeds and Sheffield MND Centres will take part in an additional interview study, to further explore the perceptions and experiences of patients and carers with regard to the impact of gastrostomy on quality of life.

The results of this work will translate into the development of guidelines, which will optimise the benefit, and the patient and carer experience of gastrostomy. The principles will be readily applicable to patients with severe swallowing problems who are eligible for gastrostomy insertion due to other neurological diseases.

4 Research Aims & Hypotheses

The overall aim is to produce evidence based guidelines which will optimise the standard of care of patients with MND requiring gastrostomy. In order to do this we aim to:

i) Identify the current practice with regard to gastrostomy insertion in MND care centres within the UK and compare it with the practice in the Sheffield and Leeds MND Care & Research Centres.

There are currently no evidence based guidelines for the management of dysphagia in patients with MND [1]. Consequently we hypothesise that practice around the country will vary with regard to indication and method of insertion for gastrostomy for MND patients. We aim to carry out a survey to assess the variation in practice and identify good practice points. The results of the survey will inform the design of the main prospective component of PROGAS.

ii) Identify the most appropriate method for gastrostomy insertion in patients with MND.

The literature is inconclusive with regards to which method of gastrostomy is preferable for patients with MND. We hypothesise that PIG/RIG procedures are safer for patients with MND and will result in reduced one month mortality, in this patient group.

iii) Identify the optimal timing for gastrostomy use in patients with MND.

The American Academy of Neurology Practice Parameter for ALS suggests that gastrostomy insertion should be performed before FVC falls below 50% [2]. However, there are no specific evidence based guidelines on when in the course of MND a gastrostomy should be inserted. We hypothesise that patients undergoing gastrostomy before malnutrition or with early dysphagia symptoms will have an improved survival compared to patients who have gastrostomy insertion when significant malnutrition and dysphagia have occurred.

iv) Identify the effect on quality of life of gastrostomy.

The evidence regarding improvement in quality of life following gastrostomy is inconclusive [1]. We hypothesise that gastrostomy feeding is associated with an improvement in quality of life of the patient. We will also assess the quality of life and views of the carers regarding the gastrostomy.

v) Identify the effect on nutritional status of gastrostomy.

The evidence regarding an improvement in nutritional status is inconclusive [1]. We hypothesise that gastrostomy feeding is associated with an improvement in nutritional status.

vi) Identify the complication rate associated with the various gastrostomy protocols.

We hypothesise that the different gastrostomy techniques are associated with differing complication rates such as post procedure infection, respiratory complications, tube displacement, and tube falling out.

5 Nature of Project

PROGAS has been designed in response to particular uncertainties faced by ourselves as healthcare practitioners, and as a result of the research priorities identified by the Dementias and Neurodegenerative Diseases Research Network (DeNDRoN) Clinical Studies Group for MND and the Motor Neurone Disease Association (MNDA). For PROGAS we have adopted an all-inclusive approach, inviting as many MND care centres in the UK, as possible. Following ethical and research governance approvals, PROGAS will run for 3 years. Participant recruitment will occur for the first 21 months. The follow up period will take 12 months. Finally, a 3-month period at the end of the project will enable analysis of data, dissemination of findings and report writing. A more detailed project timetable is available in section 19 of this protocol.

A mixed methodology approach will be employed:

(a) Quantitative questionnaires will be used to evaluate the UK clinical practice in relation to gastrostomy in patients with MND.

(b) Qualitative interviews will be used to illuminate unexplored issues surrounding the experience of patients, and their informal carers, with regard to gastrostomy and its impact on quality of life.

We have chosen this methodology approach as it enables us to use quantitative questionnaires designed to investigate issues apparent from our pilot work and clinical experience, as well as allowing the opportunity for new, previously unrecognised issues important to the patient and the carer to be identified and explored through qualitative interviews. The quantitative part of the study will form the main study and will be conducted with participants (i.e., patients and their carers) from all participating sites. The qualitative part of the study will form a smaller component and will be conducted only at the MND Care and Research Centres in Sheffield and Leeds, with patients and their informal carers.

6 Background and Rationale

Background

Motor neurone disease (MND) is the third commonest adult onset neurodegenerative disorder with an annual incidence of 2 in 100,000 and prevalence of 5-7 in 100,000 [3]. MND causes progressive weakness and wasting of muscles controlling movement, breathing and swallowing due to a degeneration of the innervating motor neurones. The cause of the motor neurone death is unknown and currently there are no effective treatments to prevent progression which on average leads to death with 2-3 years of diagnosis [3]. Evidence suggests that Riluzole, an anti-glutamate drug, slows progression by approximately 3 months [4] and non-invasive ventilation (NIV) has been demonstrated to prolong average survival by up to 7 months [5]. Specialist multidisciplinary clinics provide disease-management and palliative care services aiming to alleviate symptoms, maximise function, and to improve quality of life by means of reducing psychological distress and maintaining the autonomy of patients as long as possible [6-11].

Dysphagia, difficulty in swallowing, is a common problem in patients with MND [12, 13] and can present relatively early on in the disease course in patients with bulbar onset MND. Dysphagia results from weakness of the tongue, muscles of mastication and swallowing, as well as from loss of co-ordination of the chewing and swallowing actions [14]. Patients with severe dysphagia experience malnutrition and dehydration; continued weight loss; distressing choking and coughing on attempts to swallow; slow, prolonged and effortful

mealtimes which are a burden on the patient and carer; and frequent aspiration which increases the risk of recurring chest infections and pneumonia [12, 13, 15-17]. Malnutrition is associated with shortened survival rates [4, 18, 19]. The management of nutritional status and dysphagia is, consequently, a major aspect of the multi-disciplinary care provided to patients with MND [20]. Dysphagia management in MND aims to provide patients with an adequate calorific intake, in a safe manner, while maintaining their quality of life as much as possible [20]. When patients experience early symptoms of dysphagia simple measures can be employed, such as introducing soft, moist, easy to swallow food and thickened fluids [21, 22], together with teaching patients safe-swallowing techniques (e.g., to concentrate on eating and drinking, to avoid speaking and laughing with food in the mouth, and adopt an ideal head position when eating) [11, 22]. With disease progression, enteral tube feeding becomes necessary and is frequently used as a means of delivering an adequate protein and calorific intake in a safe manner [12, 13, 15-17]; hence, preventing malnutrition and dehydration as well as stabilising body weight [23]. Enteral tube feeding in patients with dysphagia can be delivered either via nasogastric tube (NGT) or gastrostomy insertion. Gastrostomy is favoured over NGT as problems with tubes falling out, migrating tubes causing aspiration, nasal discomfort and poor cosmesis make NGT a poor long term solution [14, 20]. Additionally, survival post gastrostomy was superior in a small retrospective review of gastrostomy versus NGT [24].

Current practice regarding the next phase of dysphagia management using gastrostomy feeding is largely based on consensus and expert opinion rather than the outcomes of appropriately designed trials. There is currently an ongoing debate in relation to the impact of gastrostomy tube placement on survival for patients with MND. Evidence suggests that there is a benefit in survival for patients with gastrostomy; however, this evidence is weak and inconclusive [1]. In addition, although gastrostomy placement is widely considered to have a beneficial impact on the nutritional outcome for patients with MND, there is little evidence to support this conclusion [1]. The effect of gastrostomy on quality of life for patients with MND remains largely unexplored [1], although consensus exists among neurologists that this intervention improves quality of life and should be offered to patients when indicated [11, 21]. There is recent indirect evidence to suggest quality of life benefits following gastrostomy but this has not been studied as a primary outcome [25]. The American Academy of Neurologists (AAN) and European Federation of Neurological Societies both recommend gastrostomy feeding for MND patients [2, 21]. However, there is currently no common consensus on the timing of gastrostomy [1]. The AAN recommend gastrostomy when either BMI<18.5 kg/m^2, weight loss of at least 10% from pre-morbid weight, or dysphagia graded 6/10 on the ALS severity scale [2].

There are several methods of gastrostomy insertion described in the MND literature; percutaneous endoscopic gastrostomy (PEG) [1, 26-34]; percutaneous radiologic gastrostomy (PRG), also known as radiologically inserted gastrostomy (RIG)[24, 34-38]; and per-oral image-guided gastrostomy (PIG) [29]. Percutaneous endoscopic gastrostomy (PEG) is the most commonly used method for gastrostomy insertion in MND patients [8, 20]. Normally, it is a relatively quick and easy procedure, performed under endoscopic guidance using conscious sedation. However, there are certain limitations and risks for MND patients associated with a PEG insertion. Patients with MND are at risk of aspiration due to bulbar muscle dysfunction, and the risk is further increased during a PEG insertion procedure. This is a result of the sedation and pharyngeal anaesthesia required for the procedure, as well as of the weak anti reflux mechanism [39, 40]. In addition, a “high riding” stomach in MND patients, due to diaphragmatic muscle weakness, can make transillumination of anterior abdominal wall difficult during the procedure, thus increasing the risk of complications [37]. PEG insertion is unsuitable for the patients with moderate to severe respiratory dysfunction (FVC 30-50% of predicted), as the positioning of the patient, laryngospasm, and sedation

required put the patient at high risk of significant respiratory compromise [41-43]. Often such patients will be dependent on non-invasive ventilation (NIV) and it is impractical to perform standard PEG placement with NIV in place.

A pure percutaneous technique, percutaneous radiologic gastrostomy (PRG) also known as radiologically inserted gastrostomy (RIG), has been alternatively used in patients with MND. PRG/RIG is considered a safe intervention with low complication rates [30, 34, 35]. PRG/RIG does not require conscious sedation or endoscope use; instead, it is performed by initial insufflation of air into the stomach, followed by tube insertion under fluoroscopic guidance [30]. A modified per oral technique, per-oral image-guided gastrostomy (PIG), has not been widely used in the management of dysphagia in patients with MND, although it has been used in other disease areas, such as stroke, multiple sclerosis and malignant disorders involving upper gastrointestinal tract [44]. PIG is a hybrid technique, requiring minimal conscious sedation, in which the stomach is punctured under fluoroscopic guidance, following which the oesophagus is catheterised in a retrograde fashion using a guide wire. The gastrostomy tube is then passed over the guidewire, through the mouth, oesophagus and out through the abdominal wall. Evidence suggests that PIG combines the advantages of PEG and PRG/RIG constituting an effective alternative method of gastrostomy with better long-term clinical outcomes in terms of success, re-intervention and complication rate [44].

The AAN guidance recognising the increased risk of a PEG procedure in patients with significant respiratory compromise, suggests that gastrostomy should be performed before the FVC falls below 50% [2]. Alternative methods, such as RPG/RIG and PIG, may offer advantages particularly in patients with significant respiratory compromise. In addition, the application of NIV during gastrostomy procedures [36] and newer sedative agents, such as Remifentanil [45], may also allow a later successful and safe insertion of gastrostomy. There is little evidence in the MND literature to suggest what the optimal timing for gastrostomy is or which of the gastrostomy insertion methods is superior in a given situation [1, 46]. Consequently, multiple gastrostomy techniques and timings of gastrostomy insertions, within the disease course of MND are used throughout the UK. There is a consensus and it is our hypothesis that PRG/RIG and PIG procedures are a safer gastrostomy technique in patients with MND than PEG, particularly if there is any degree of respiratory compromise. One small prospective study [30] reported that there was a significant difference ($p = 0.004$) between survival in PEG patients and survival in RIG patients, but this was in the subgroup of patients with respiratory failure. The median survival after gastrostomy was 140% higher in the RIG group compared to PEG group. There are few studies in the MND literature comparing survival time or one month post procedure mortality of patients with MND following different methods of gastrostomy. Three recent studies [24, 34, 47] reported that there was no significant difference in survival between PEG patients and RIG patients. These studies were retrospective, comprised small numbers and were not adequately powered to detect potentially important clinical differences. Given the lack of comparative studies we have reviewed the literature for mortality data. For MND patients undergoing PEG the 30 day mortality rates range from 4% to 25% [19, 26, 30-32, 47-51]. For MND patients undergoing RIG procedures the 30 day mortality rate ranges from 4% to 9% [30, 35, 47].

MND care in the UK is largely delivered by multi-disciplinary teams, led by a consultant neurologist, within Motor Neurone Disease Association funded MND Care and Research Centres embedded within the NHS. There are currently 17 MND Care and Research Centres. At a recent meeting of the UK MND Care Centre workers and at the Association of British Neurologists MND Special Interest Group (SIG) an agreement recognised the need to develop an evidence based gastrostomy practice. The network of the MNDA MND Care and Research centres along with other MND clinics provides an excellent opportunity to

prospectively evaluate gastrostomy practice within the UK and develop evidence based guidelines for gastrostomy use in MND.

Rationale

The current clinical practice with regard to gastrostomy use in patients with MND has not been evaluated. There is little evidence on the optimal timing and method for gastrostomy insertion in patients with MND. PROGAS is a prospective nation-wide study in the UK that will provide an evidence base to inform dysphagia and nutritional management of patients with MND.

7 Research Plan and Methodology

7.1 Plan of Investigation

A. Centre Pathway Review

We have 15 MND centres committed to participating in PROGAS. A provisional survey of the centres has identified that 360 gastrostomies are performed for MND patients in the UK per year. The first component of PROGAS will be to perform a detailed survey of current practice regarding gastrostomy pathways at each centre. A questionnaire will be completed by the director of each centre capturing data regarding indication for gastrostomy, timing, and type of gastrostomy. This survey will highlight current practice, good practice points and will enable refinement of the data analysis plan of the main phase of the study. The centre director will also identify a "local champion" who will assist in recruiting patients and liaise with the central study co-ordinator who will be based in Sheffield.

B. Prospective evaluation of Gastrostomy

Following ethical and research governance approvals, participants will be recruited into PROGAS from all participating sites over a period of 21 months. All centres will be encouraged to maintain their usual practice and protocols for gastrostomy provision.

i) Patient enrolment

The study will be discussed with patients and carers, when a gastrostomy is being considered by the clinical team as part of their normal standard care. Patients and carers will be asked to consent to the study at the time of referral for gastrostomy. We will aim to recruit 504 patients and carers over 21 months. This figure is based on 80% (i.e., the anticipated patient response rate) of the 630 eligible patients seen according to the provisional survey of centres undertaken.

ii) Pre Gastrostomy Patient Evaluation

Once patients are successfully recruited and consented into PROGAS, the local investigator will complete a Pre Gastrostomy Patient evaluation form. This form is designed to capture routine data already being recorded in clinics, including demographic and functional characteristics, nutritional and respiratory status and gastrostomy-related data.

iii) Peri-Procedure Evaluation

Patients will then undergo the gastrostomy procedure. At the end of the procedure, either the local investigator or a member of the team performing the gastrostomy insertion will complete a Peri-procedure evaluation form. This form will capture the details of the procedure as well as any complications that occur during the procedure.

iv) Follow Up Patient Evaluation

Patients will attend their usual follow up appointments at their centre. Each patient will be followed up over 12 months following gastrostomy. At the visits which coincide nearest with 3 months and 1 year post gastrostomy, follow up evaluation forms will be completed. Data on weight, gastrostomy related complications, ALS-FRS and survival will be collected. At the follow-up visits patients and carers will complete quality of life assessment and carer burden assessments respectively.

v) Quality of life for patients and carers

Aspects related to the quality of life of patients, and their carers, following gastrostomy will be assessed with a combination of qualitative and quantitative tools. The qualitative sub-study at Sheffield and Leeds sites will evaluate the gastrostomy experience from the perspective of the patients and their carers. In addition, at baseline and at the following up visits patients and carers at all participating sites will complete quality of life and carer burden assessments respectively, as outlined in the following section.

All forms will be anonymised by the local champion at each site and will be returned to the Sheffield-based PROGAS co-ordinator.

7.2 Measures, Questionnaires and Interviews

A. Main Study

i) Centre Pathway Review Form (see Appendix 1)

This is an initial questionnaire which will be completed by the centre director at each site. It is designed to assess the current clinical practice of gastrostomy insertion in patients with MND at each centre. It will record data with regard to the number of gastrostomies performed; the type of gastrostomies offered and the preferred circumstances for each different type; as well as the decision-making criteria influencing the timing of gastrostomy.

ii) Pre Gastrostomy Patient Evaluation Form (see Appendix 2)

This evaluation form, which will be completed by the local champion at enrolment, is designed to capture data already being recorded in the neuromuscular clinic as part of routine clinical care. It will record the following data about a recruited patient:

Demographic and functional characteristics: Demographic and functional characteristics of the patients will be recorded including age, gender, date of onset of MND symptoms, date of MND diagnosis, site of onset of MND, severity of bulbar dysfunction, time since first symptom of significant weakness, weight, and height. A functional rating scale for MND/ALS, the Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised (ALSFRS-R) [52] will also be completed *(see Appendix 6)*. These data are available in each patient's medical records.

Measures of respiratory function: Forced vital capacity (FVC); Sniff Nasal Inspiratory Pressure (SNIP); and arterial blood gas or non-invasive measurement of $P_{tc}O_2$ - $P_{tc}CO_2$, will be recorded. These parameters of respiratory function are measured routinely in the neuromuscular clinic as part of routine clinical care.

Indices of disease progression: Weight measurement and the ALSFRS-R score will be recorded for each patient. These parameters of disease progression are also measured routinely in the neuromuscular clinic as part of routinely clinical care.

Gastrostomy-related data: The pre-procedure evaluation form will also record data for each patient with regard to gastrostomy indication; type of gastrostomy preferred and preference reasons; potential benefits of gastrostomy; and, patient's influence on the timing of gastrostomy.

iii) Peri-procedure Patient Evaluation Form (see Appendix 3)

This form will be completed at the end of the gastrostomy procedure, either by the local champion or the member of the team performing the gastrostomy insertion. The form is designed to capture the details of the procedure with regard to staffing; gastrostomy equipment; drugs given; patient monitoring and respiratory support; as well as, any complications that occur during the procedure.

iv) 3-month Follow Up Patient Evaluation Form (see Appendix 4)

This form is designed to capture data with regard to gastrostomy complications occurred prior to patient's hospital discharge and those occurred after the hospital discharge up to the 3-month patient evaluation. Weight and ALSFRS-R for each patient will also be recorded. This form will be completed by the local champion after a patient's usual follow up visit which coincides nearest with 3 months post gastrostomy.

v) *12-month Follow Up Patient Evaluation Form (see Appendix 5)*

This form is designed to capture data with regard to gastrostomy complications occurred in the period of time between the 3-month patient evaluation and the 12-month patient evaluation. Weight and ALSFRS-R for each patient will also be recorded. This form will be completed by the local champion after a patient's usual follow up visit which coincides nearest with 12 months post gastrostomy.

vi) McGill Quality of Life Questionnaire (MQOL) (see Appendix 7)

This is a well-established questionnaire, designed in the context of palliative care, to identify the health-related quality of life of patients with a terminal illness. It balances physical and non-physical aspects of quality of life, and includes both positive and negative influences on quality of life [53]. This questionnaire will be completed by patients at baseline and at 3 months post gastrostomy.

vii) Modified Caregiver Strain Index (MCSI) (see Appendix 8)

This is a well-established questionnaire, designed to identify the strain levels among informal carers of patients with long-term illness. It will be used in this study to assess the quality of life of the main carer of the patient and the impact that the treatment is having on the carer [54]. It will be completed by carers at baseline and at 3 months post gastrostomy.

viii) Gastrostomy-specific questionnaire (Gastro-Qu) (see Appendix 9)

This is a questionnaire designed to relate the outcomes of gastrostomy insertion to health-related quality of life of patients. It is used to identify the complications and difficulties of gastrostomy as well as its interference with family and social life, from the point of view of patients [55]. It will be completed by patients at 3 months post gastrostomy.

B. Qualitative Interview Study

The qualitative component of PROGAS at Sheffield and Leeds involves the conduct of semi-structured interviews with patients, and their informal cares (10 patients and 10 carers per site), in relation to their experience of gastrostomy insertion and its impact on their quality of life. The advantage of including a qualitative component into PROGAS is that it compensates for any preconceived assumptions inherent in the structured questionnaires, and provides interviewees with the opportunity to talk about what is important to them setting their views in context [56]. This component will assess the outcomes of gastrostomy from the perspective of the patients and carers; delineate their concerns, problems and needs; give an insight of how these needs could be addressed to improve care; and enhance our understanding of the factors that are associated with gastrostomy feeding and impact

on the quality of life. Each patient and each carer will take part in one interview at 3 months following gastrostomy.

i) Interviews with patients

Interviews will be semi-structured and conducted in a location of the participant's choosing after establishing informed consent. The interviews will be recorded. These recordings will be anonymised before being transcribed. All the interviews will be semi structured and therefore the exact details of interview cannot be predicted. Broad themes will be used to offer structure to the interview. These broad themes will be discussed with the Sheffield Motor Disorders Research Advisory Group (SMND-RAG) to enable the public, carers and patients to input in deciding these. Evidence from previous qualitative work on the impact of gastrostomy on quality of life of patients with severe dysphagia due to other underlying conditions, e.g., oral and oropharyngeal cancer, CNS tumours and injuries, multiple sclerosis, dementia, Parkinson's disease, digestive disorders [55, 57-62], will be taken into account when discussing the interview schedule for PROGAS. Once the broad themes have been identified two pilot interviews will carried out to test the structure. Although yet to be discussed at the SMND-RAG, the broad themes may involve the following issues related to gastrostomy: feeding regimens; quality of life; alleviation of problems present prior to gastrostomy; support from healthcare professionals; difficulties encountered; feed administration/delivery; impact of feeding on daily, social and family life; impact on relationships. Each theme will be introduced with an open ended question, e.g., "Do you experience any difficulties that arise directly from gastrostomy feeding and how do they impact on your daily life?" Further follow on questions depending on the initial discussion would explore both issues important to the patient regarding this theme and also issues identified by the SMND-RAG.

We will be sensitive to the preferences of the participants about whether patients and carers will be interviewed together (conjoint) or will be interviewed separately or a combination of both. Interviewers will be sensitive to the emotional and physical state of the participants and if they become upset or tired, the interview will stop. After every interview, individual or conjoint debriefing sessions will take place to talk about the situations or feelings that may have triggered their emotions. In the final phase of the illness, patients may be too tired and unwell to participate. We will be sensitive to the patient's wishes with regard to participation and will re-establish consent. If the patient would like to participate, but is physically unable, in agreement with all parties, we will invite the carer to be a proxy and review the responses with the patient so they remain involved [63].

ii) Interviews with the informal carers of patients

Similarly, interviews with the informal carers of MND patients with a gastrostomy will be conducted in a location of the participant's choosing after establishing informed consent. The interviews will be recorded and these recordings will be anonymised before being transcribed. The interviews will follow a similar semi-structured design and the broad themes will be decided as described above. We will stop interviews if carers become distressed and facilitate appropriate counselling.

7.3 Participant Involvement in PROGAS

Patients will undergo routine clinical assessments, related to the gastrostomy procedure, before and during the actual operation. Following gastrostomy, patients will undergo routine assessments at their usual visits to the neuromuscular clinic at each participating site. PROGAS-only related assessments include completion of the MQOL and Gastro-Qu, and participation in a qualitative interview (for patients at Sheffield and Leeds sites only). The following table (Table 1) shows a detailed grid of all the patient assessments undertaken during PROGAS.

Carers involvement in PROGAS requires no other assessments than completion of the MCSI (at baseline and 3 months post gastrostomy) and participation in a qualitative interview (for caresrs at Sheffield and Leeds sites only).

	Sheffield and Leeds MND Centres				Other participating MND Centres			
PROGAS	Pre Gastrostomy	Peri Procedure	3 months Follow up	12 months Follow up	Pre Gastrostomy	Peri Procedure	3 months Follow up	12 months Follow up
Weight	✓	-	✓	✓	✓	-	✓	✓
Height	✓	-	-	-	✓	-	-	-
FVC%	✓	-	-	-	✓	-	-	-
SNIP	✓	-	-	-	✓	-	-	-
pO_2	✓	-	-	-	✓	-	-	-
pCO_2	✓	-	-	-	✓	-	-	-
O_2 Sats	✓	-	-	-	✓	-	-	-
Heart rate	-	✓	-	-	-	✓	-	-
Respiratory rate	-	✓	-	-	-	✓	-	-
Blood pressure	-	✓	-	-	-	✓	-	-
CO_2	-	✓	-	-	-	✓	-	-
ALSFRS-R	✓	-	✓	✓	✓	-	✓	✓
MQOL	✓	-	✓	-	✓	-	✓	-
Gastro-Qu	-	-	✓	-	-	-	✓	-
Interview	-	-	✓	-	-	-	-	-

Table 1: Grid of patient assessments undertaken during PROGAS

7.4 Participants and Recruitment

Inclusion & Exclusion Criteria

Patients, and their carers, will be recruited locally at the participating centres. Patients with MND will be eligible when a decision has been made to refer the patient for a gastrostomy, regardless of indication.

Patient Inclusion Criteria:

i) A diagnosis of definite, probable, laboratory supported or possible MND, as defined by the revised El-Escorial criteria

ii) A decision has been taken to refer the patient for a gastrostomy

Patient Exclusion Criteria:

i) Contradiction to gastrostomy

ii) Patient declines gastrostomy

Carer Inclusion Criteria:

i) Being the main carer of an MND patient who has been referred for a gastrostomy placement.

Carer Exclusion Criteria:

i) Patient declines to participate in an interview (only for the qualitative component of PROGAS)

Participant Recruitment

Patients and their carers will be recruited at each of the participating sites. A typical site (Sheffield Care and Research Centre for Motor Neurone Disorders), serving a population of approximately 2.2million undertakes approximately 16 gastrostomies per year for patients with MND. With the inclusion of 18 sites, and anticipating an 80% participant response rate, we estimate that we will recruit at least 504 patients over a 21-month recruitment period.

Patients and carers will be informed of the study after a decision to refer for a gastrostomy has been made by a member of the research team. Patients and carers who are not interested will not be contacted again for this study. A patient information sheet, explaining the details of the study, will be given to interested patients meeting all the inclusion criteria and none of the exclusion criteria and a carer information sheet will be given to interested carers. They will be asked to contact the local researcher if they would like to participate in the study. One follow up call will be made by a member of the research team, to initially interested patients and carers who do not contact the local researcher, approximately two weeks following the invitation. Patients and carers who respond negatively to the follow up call will not be contacted again for this study. Patients and carers who contact the local researcher and those who respond positively to the follow up call will be asked to provide their consent for participation in the study.

Once consented and successfully recruited into the study the participants will be further informed verbally about the next stages of PROGAS by the local researcher and undergo the gastrostomy procedure as scheduled. Data will be collected, by a member of the research team, before and following the gastrostomy procedure with the completion of the pre-procedure and the peri-procedure gastrostomy patient evaluation forms, respectively. Following hospital discharge, the participants will continue their standard visits (approximately every 2-3 months) to the neuromuscular clinic as part of routine clinical care.

For this study data will also be collected, by a member of the research team, 3 months and 1 year following gastrostomy.

During their participation into PROGAS, patients will be asked to complete a health-related quality of life questionnaire (MQOL) twice (at baseline and approximately at 3 months following gastrostomy), and a gastrostomy-specfic questionnaire once (approximately at 3 months following gastrostomy). Participating carers will be asked to complete a quality of life questionnaire (MCSI) twice (at baseline and approximately 3 months following gastrostomy). Both patients and carers will be given freepost/pre-paid envelopes to return the questionnaires to the study's central co-ordinator.

The recruitment process of patients and carers for the qualitative component of PROGAS at Sheffield and Leeds MND Care and Research Centres will be similar to the process described above. Once consented and recruited, participants will be contacted by the local researcher by telephone (approximately 3 months following the gastrostomy procedure) to arrange with each one a date and time for a face-to-face interview at a place of each participant's choice. For this part of PROGAS, we will aim to recruit 10 patients and 10 carers. Quantitative data will be collected as described for the other sites. A detailed visual representation of the recruitment process is shown in the following chart (Chart 1).

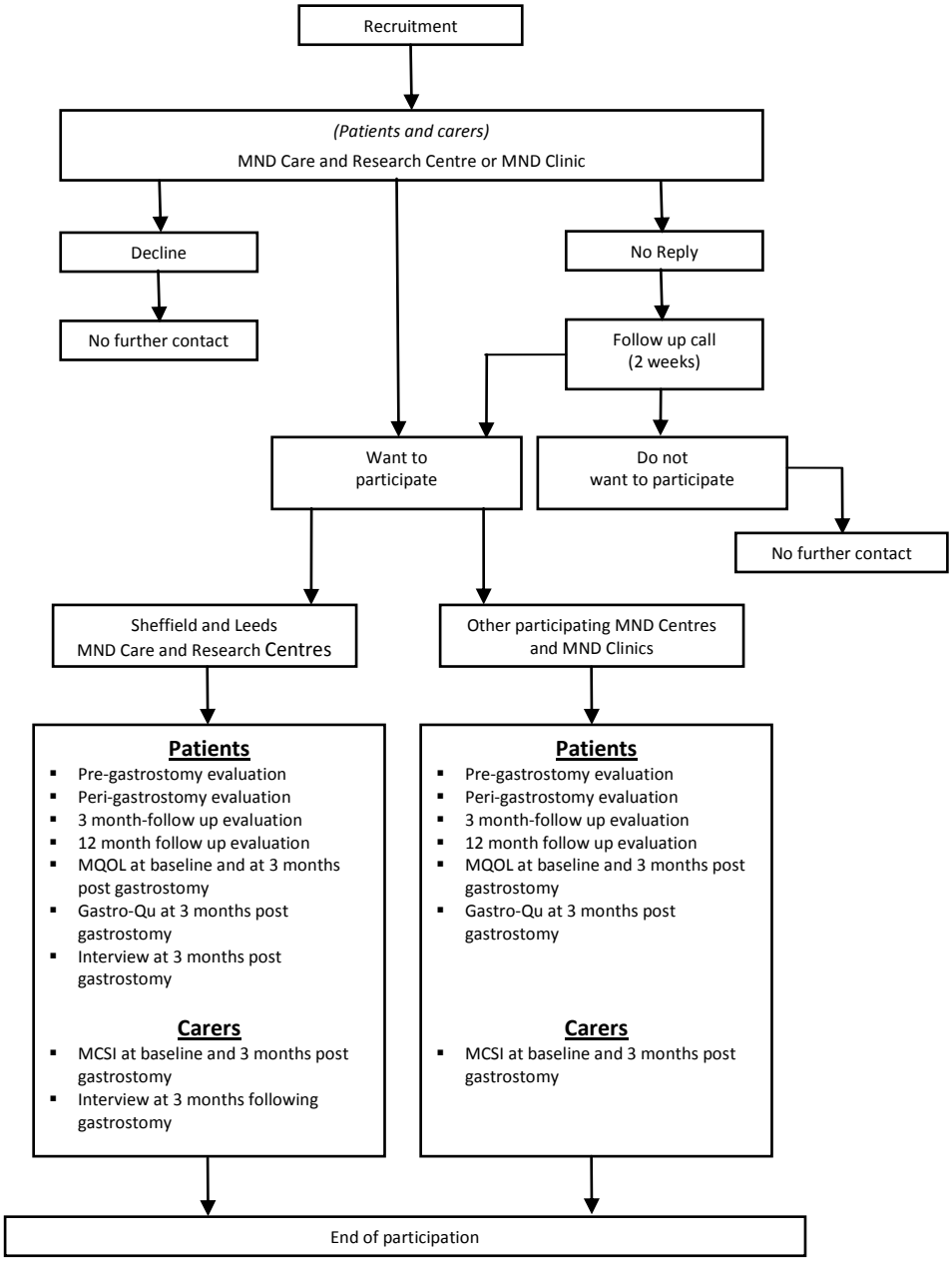

Chart 1: Participant recruitment flow chart

7.5 Study Outcomes

Primary:

i) Difference in the mortality rate in the first month following gastrostomy in PEG and PIG/RIG patients.

Secondary:

i) Difference in the complication rate (classified in groups according to seriousness and time of occurrence) following gastrostomy in PEG and PIG/RIG patients.

ii) Median survival time from (a) placement of feeding tube, (b) symptom onset, and (c) time of diagnosis of the disease in PEG and PIG/RIG patients.

iii) Nutritional status changes (weight and BMI) following gastrostomy in PEG and PIG/RIG patients.

iv) Self-perceived quality of life changes (measured by MQOL, gastrostomy questionnaire and qualitative interviews) following gastrostomy in PEG and PIG/RIG patients.

v) Change in carer quality of life as measured by MCSI and qualitative interviews.

Analysis will also include looking into how factors, such as (a) respiratory status, (b) site of symptoms onset, and (c) stage of disease, influence safety and survival following gastrostomy in PEG and PIG/RIG patients.

7.6 Statistical Power Analysis

There are few studies in the MND literature comparing survival time or one month post procedure mortality of patients with MND following different methods of gastrostomy. Three recent studies [24, 34, 47] reported that there was no significant difference in survival between PEG patients and RIG patients. These studies were retrospective, contained small numbers and were not adequately powered to detect potentially important clinical differences. One small prospective study [30] reported that there was a significant difference ($p = 0.004$) between survival in PEG patients and survival in RIG patients but this was in the subgroup of patients with respiratory failure. The median survival after gastrostomy was 140% higher in the RIG group compared to PEG group. Given the lack of comparative studies we have reviewed the literature for mortality data. For MND patients undergoing PEG the 30 day mortality rates range from 4% to 25% [19, 26, 30-32, 47-51]. For MND patients undergoing RIG procedures the 30 day mortality rate ranges from 4% to 9% [30, 35, 47].

Based on the review of the literature we hypothesise that a difference in one month mortality between PEG and PIG/RIG of between 0 % and 21% may exist. We aim to power PROGAS to detect a conservative, but clinically important, 30 day mortality rate difference of 8%. Power analysis calculations indicated that a minimum sample of 442 patients would be required to attain sufficient statistical power. For PROGAS, anticipating an 80% participant response rate over a 21-month recruitment period, we estimate that we will recruit 504 patients. This sample size will provide statistical power of 80% at a 5% level of statistical significance to detect a difference of 8% in mortality at one month, using a continuity corrected Chi-square (χ^2) test.

We aim to identify the most appropriate method of gastrostomy in terms of safety and patient experience. The study is designed to be easily carried out in a routine clinical setting and to assess in a pragmatic way current practice throughout the UK. It is clear that multiple variables at different sites may impact on the outcomes. However the key variables including MND disease course, nutritional and respiratory status, are being recorded and we will

interrogate the data for the effect of these parameters on the primary and secondary outcome measures. Patient and clinician choices will inevitably impact on the timing of gastrostomy but at most centres these will not have a major effect on the type of gastrostomy procedure undertaken. An initial evaluation of the participating centres has demonstrated that most centres perform either only PIG/RIG procedures or only PEG procedures, which will reduce the variability which could potentially be introduced by physicians selecting particular procedures.

The power analysis calculation and the plan for subsequent statistical analysis were facilitated by experienced statisticians at the Research and Development department of the Sheffield Teaching Hospitals NHS Foundation Trust and the Yorkshire and Humber NIHR Research Design Service.

7.7 Data Analysis

Quantitative data analysis

All quantitative data will be managed and analysed using SPSS for Windows version 14.0 (SPSS Inc., 1998). Exploratory data analysis will be initially carried out to establish the distribution of all continuous and categorical variables. Descriptive statistics (means, standard deviations, percentages) will be used to describe the characteristics of the participating centres, the participants and all the main variables of the study. Non-parametric tests (Spearman rank correlation tests and Mann Whitney U tests) will be performed for non-normally distributed continuous variables. Cronbach's alpha (α) coefficients will be determined for the measures that will be used in the study (i.e., MQOL, MCSI, gastrostomy questionnaire) in order to establish their internal consistency.

Continuity corrected Chi-square (χ^2) tests will be performed to determine the difference in the first-month mortality rate and the complication rate following gastrostomy in PEG and PIG/RIG patients. The same tests will be also performed to determine the self-perceived quality of life changes following gastrostomy in PEG and PIG/RIG patients as well as to determine the changes in carer quality of life. Kaplan-Meier survival curves will be used to determine the median survival time from placement of feeding tube, symptom onset and time of diagnosis of the disease in PEG and PIG/RIG patients. Independent samples t-tests will be used to determine the nutritional status changes following gastrostomy in PEG and PIG/RIG patients. Predictors of survival (e.g., respiratory status, site of symptom onset, stage of disease) following gastrostomy will be determined using logistic regression analysis and Cox proportional hazards regressions analysis.

Qualitative data analysis

All the interviews with patients and/or their informal carers will be tape recorded and subsequently transcribed verbatim in full. The data will be analysed according to the Framework approach for qualitative data analysis [64], with the aid of FrameWork (NatCen Ltd., 2009), a dedicated software package developed by the Qualitative Research Unit of the National Centre for Social Research. Framework analysis, which is increasingly becoming accepted in the context of exploratory qualitative health research [65] has the advantage of being grounded or generative as it is based in, and driven by, the original accounts of the participants. Moreover, it constitutes a dynamic, systematic and comprehensive mode of qualitative data analysis as it is open to change during the analysis process and it allows methodical handling and full review of the collected data. In addition, it enables easy retrieval of the original textual material and comparisons between, and associations within, cases to be made. Finally, Framework analysis is accessible to others, due to the well documented analytical process that involves, allowing other researchers to review the whole process and its results [64].

8 Participant Coding and Data Handling

8.1 Participant coding

At enrolment, each participant will be assigned a unique alphanumeric code, by a member of the research team at each participating site. This code will have the following form:

NN L LL NN (N= a numeral from 0-9, L= a capital letter from A-Z)

- The first two numerals will indicate the participating centre. Each centre will be assigned by the PROGAS co-ordinator a two digit number from 01 to 18, in the order by which centres are listed in section 8 of this protocol.
- The first letter will indicate whether the participant is a patient or a carer, i.e., P for patients and C for carers.
- The following two letters will be the initials of the name and the surname of the participant.
- The last two numbers will indicate the participant's number, based on the order of enrolment (e.g. 01 for the first participant, 02 for the second, 03 for the third, and so on). Patients and carers will be matched, by assigning them the same participant number.

For example, if a patient (with initials AA), and his/her carer (with initials BB), were the first participants to be enrolled at the Sheffield site (centre code 01) they would be assigned the codes **01 P AA 01** and **01 C BB 01**, respectively.

The local research team at each site will maintain a secured file, in a locked drawer, in a locked site office, containing a local recruitment log with all the coding and participant details. These details will be strictly kept within the site and will be only accessible by the local research team, and not to anyone else within or outside the site.

8.2 Handling of data

Data will be handled, computerised and stored in accordance with the Data Protection Act, 1998. All evaluation forms (i.e., pre-gastrostomy, peri-procedure, 3-month follow up, 12-month follow up, ALSFRS-R) and the self-administered questionnaires (i.e., MQOL, Gastro-Qu, MCSI) will be anonymous, bearing only the unique alphanumeric code of each participant.

The evaluation forms will be completed at appropriate times adhering to the study design, by a member of the local research team at each site. These forms will be regarded as source data for PROGAS and will be kept locally in a secure file, in a locked drawer, in a locked office. The central collection of all forms from all sites to the central PROGAS site (i.e., the Sheffield MND Care and Research Centre) will be facilitated by the PROGAS central co-ordinator with the use of a mail paper-based system. To minimise the risk of lost mail, and subsequent loss of valuable data, the PROGAS co-ordinator will only receive photocopies of the coded source data, by post. This will additionally enable the PROGAS co-ordinator to cross-check the centrally kept data with the source data kept at all other participating sites. The self-administered questionnaires will be either given to the participants during their visit to each site or sent out to them by post, by the local researcher at each site. Together with the questionnaires, participants will be given free post envelopes bearing the address of the central Sheffield site, so that the questionnaires will be returned directly to the PROGAS co-ordinator.

The pre-gastrostomy evaluation form, will also act as the study's registration form. It will be the first form to be completed after enrolment, by a member of the local research team at each site, bearing the participant's unique alphanumeric code. A copy of this form will be sent to the PROGAS co-ordinator, as described above, to register the participant into the study.

All coded data received by the PROGAS co-ordinator in Sheffield, will be entered into an electronic data capture system relating to this study, which will be housed on a University of Sheffield secured computer system. Following data entry, all the received evaluation forms and questionnaires will be archived by centre and will be securely stored in a locked drawer, in a locked office at the Sheffield site. All interview data will be anonymised by the PROGAS co-ordinator, who will be conducting the interviews, using the same coding system used by the clinical and questionnaire data prior to transcription. Coding details will be kept on a recruitment log held on a secure file on a secured University of Sheffield computer in a locked office.

At the end of the study, essential documentation will be archived in accordance with sponsor and local requirements. The retention of study data will be the responsibility of the Chief Investigator. Each participant will be requested to consent to responsible individuals of the local research teams to have access to the relevant sections of their medical notes and data collected during the study where it is relevant to them participating in the research. As the medical notes are being used as source data for the study it is required that all medical notes off patients that are involved in research are retained for 15 years. All consent forms, completed questionnaires and interview transcripts will be held in a secure file which will be archived securely for 15 years following the end of the study.

Participant medical notes will be stored at the participating site that they attended for the study as per the hospital policy.

9 Research Setting

PROGAS is a multi-centre study that will take place in each of the MND Centres and Clinics, listed below. Central co-ordination of the study will be undertaken in Sheffield.

Sheffield MND Care and Research Centre, Royal Hallamshire Hospital (Sheffield Teaching Hospitals NHS Foundation Trust), Principal Investigator: *Dr Christopher McDermott*

Barts and The London MND Centre, (Barts and The London NHS Trust), Principal Investigators: *Dr Aleksandar Radunovic*

Belfast MND Clinic, Royal Victoria Hospital (Belfast Health and Social Care Trust), Principal Investigator: *Dr Colette Donaghy*

Birmingham MND Centre, Queen Elizabeth Hospital (Birmingham NHS Foundation Trust), Principal Investigator: *Professor Karen Morisson*

Basildon Hospital, Basildon University Hospital (Basildon and Thurrock University Hospitals NHS Foundation Trust), Principal Investigators: *Dr Andrea Malaspina*

King's College MND Centre, King's College Hospital (King's College Hospital NHS Foundation Trust), Principal Investigator: *Professor Ammar Al-Chalabi*

Leeds MND Centre, Leeds General Infirmary (Leeds teaching Hospitals NHS Trust), Principal Investigator: *Dr Michael Johnson*

Liverpool MND Centre, The Walton Centre (The Walton Centre NHS Foundation Trust), Principal Investigator: *Professor Carolyn Young*

Greater Manchester (Salford) MND Centre, Hope Hospital (Salford Royal NHS Foundation Trust), Principal Investigator: *Dr John Ealing*

Newcastle MND Centre, Newcastle General Hospital (The Newcastle upon Tyne Hospitals NHS Foundation Trust), Principal Investigator: *Dr Tim Williams*

Norfolk and Norwich MND Clinic, Norfolk and Norwich University Hospital (Norfolk and Norwich University Hospitals NHS Foundation Trust), Principal Investigator: *Dr David Dick*

Nottingham MND Care and Research Centre, Queen's Medical Centre University Hospital (Nottingham University Hopsitals NHS Trust), Principal Investigator: Mrs Carol Gent

Oxford MND Centre, John Radcliffe Hospital (Oxford Radcliffe Hopsitals NHS Trust), Principal Investigator: *Dr Kevin Talbot*

Plymouth/Peninsula MND Centre, (Plymouth Hospitals NHS Trust), Principal Investigator: *Professor Oliver Hannemann*

Preston MND Centre, Royal Preston Hospital (Lancashire Teaching Hospitals NHS Foundation Trust), Principal Investigator: *Professor Douglas Mitchell*

Royal Free Hospital MND Centre (Royal Free Hampstead NHS Trust), Principal Investigator: *Dr Richard Orrell*

Southampton/Wessex MND Centre, Wessex Neurological Centre, Southampton General Hospital (Southampton University Hospitals NHS Trust), Principal Investigator: *Dr Ashwin Pinto*

West Suffolk MND Clinic, West Suffolk Hospital (West Suffolk Hospital NHS trust), Principal Investigator: *Dr Francesca Crawley*

10 Project Management

The lead research team is a collaboration of individuals within Yorkshire who have a track record of performing research with MND patients, and in successfully involving the public in research development. The team will ensure that the research is clinically relevant and is of high quality. Members of this team have been successful in translating research discoveries into benefits for patients.

The project management team will consist of:

Dr McDermott (CM), *Principal Investigator and Project Manager*

Professor Shaw (PS), *Co-Investigator*

Dr Michael Johnson, *Co-Investigator*

Dr Wendy Baird, *Co-Investigator*

The project manager will be responsible for the day to day supervision of the PROGAS co-ordinator who will be based at the Sheffield MND Care and Research Centre. The Project management team will meet quarterly and more frequently if the project manager feels it necessary. Weekly project management meetings will be held, attended by CM, PS and the PROGAS co-ordinator.

The SMND-RAG (a group set up to faciliate public involvement in research consisting patients, relatives of patients and lay public members) will meet 3 times a year to discuss this study. The project management team will update the SMND-RAG on study progress. Members of SMND-RAG will advise on methodological issues, ethical issues, consent and information sheets, analysis and dissemination of results.

Financial management will be overseen by the Research Department within the Sheffield Teaching Hospitals Foundation Trust in collaboration with the University of Sheffield.

11 Expertise

Dr McDermott (CM) will act as the chief investigator and has experience of managing clinical research projects in this patient group.

Professor Shaw (PS) and Dr Michael Johnson (MJ) are the directors of the MND centres in Sheffield and Leeds and have extensive experience of managing patients with MND and successfully recruiting to research projects in this area. They will facilitate recruitment of patients and sit on the project management team.

Dr Wendy Baird (WB), Director of the NIHR RDS for Yorkshire and the Humber, has extensive experience in qualitative health research and will supervise the qualitative component of PROGAS.

Dr Mark McAlindon (MM) is the Clinical Lead for the Sheffield Teaching Hospitals PEG Care Pathway Group, Nutrition Support Team and Nutrition Steering Group. He designed and set up the PEG database, trained the PEG nurse specialist and Home Enteral Feed dieticians, and inserts PEGs.

Dr Fred Lee (FL) is an experienced Consultant Radiologist with a specialist interest in performing image-guided gastrostomies.

Dr Stephen Webber (SW) is an experienced Consultant Anaesthetist, member of the clinical team performing gastrostomies in Royal Hallamshire Hospital.

Dr Theocharis Stavroulakis (TS) has a background in nursing and health promotion and is experienced in research study designs combining both qualitative and quantitative methods.

He will facilitate the process of gaining a favourable ethical opinion from the Sheffield NHS Ethics Committee; co-ordinate governance approval at each site; conduct the qualitative component of PROGAS at the Sheffield and Leeds MND Care and Research Centre; and co-ordinate data collection from the participating MND centres by liaising with the local researchers at all sites.

12 Ethical Issues

Being introduced to the notion of gastrostomy is a particularly emotional time for many patients and carers, and this is recognised by the research team. As a team of experts in MND and gastrostomy, the co-investigators are experienced in introducing patients to gastrostomy.

Participation in the study is entirely voluntary. Participants will be given a comprehensive information sheet, and will have the study explained to them by a member of the research team, as well as having the chance to ask any questions, prior to making a decision about participating. Fully informed consent will be obtained prior to participation, from both the patient and the carer. It will be emphasised to the participants that they have a right to withdraw at anytime from the study without giving a reason, and this will not affect their future medical / nursing care. 'Process' consent will be used throughout the study to re-affirm the patient's willingness to continue to participate. In the event that a patient looses the ability to give consent they will be withdrawn from the study, but any data relating to them collected to that point will continue to be used in the study as explained in the participant information sheet.

Although there is potential for the participants to become upset during the qualitative interview process, we feel that this is an important part of the study which will allow us to better understand their experience during this difficult time, and subsequently work to improve the care currently provided. Interviewers will be sensitive to the emotional and physical state of the participants and if the participants become too upset or tired then the interview will be stopped. After each interview a debriefing session will be offered in order that participants have the opportunity to discuss any situations or feelings that may have triggered an emotional response. In the final phase of the illness it is possible that patients may be too tired or unwell to participate, and the research team will remain sensitive to the patient's wishes with regard to participation.

All participant data will be anonymised, to maintain confidentiality, prior to being entered into a data capture system, and subsequent analysis. All recordings of interviews will have any identifying information removed from file names before being sent to a professional transcription agency with strict guidelines regarding confidentiality. All personal details, including demographic details and information relating their condition will be only accessible to members of the research team. All participant details relating to the study will be stored in a maintained site file in a locked cabinet within a locked room. All electronic files will be password protected and stored on password protected, university maintained information technology systems. All clinical details will be recorded in the medical notes of the participants as standard. Data will be stored in secure archives within the university for 15 years after the study has officially been closed.

13 Patient and Public Involvement

This study has arisen from the research priorities identified by both the Dementias and Neurodegenerative Diseases Research Network (DeNDRoN) Clinical Studies Group for MND and the MND Association. Both these groups have public representation shaping their research priorities.

To facilitate service user involvement in motor system disorders research in Sheffield we have established the Sheffield Motor Disorders Research Advisory Group (SMND-RAG). SMND RAG have reviewed and shaped this proposal. The membership of this group includes patients and carers who have experience of motor system disorders including MND. The researchers of this study will collaborate with members of the public through SMND-RAG.

User involvement will be essential in managing the study and disseminating the research findings. One member of the SMND-RAG is a chair of a local branch of the MNDA which hold regular local meetings for patients and carers. This SMND-RAG member will inform the local branch about the study, ensuring the local users are informed and are given a chance to feedback their priorities for this research and other research. We will acknowledge the involvement of the SMND-RAG on all publications and other outputs.

Members of the SMND-RAG were given the opportunity to review early drafts in relation to all aspects of PROGAS, provided their feedback, and contributed in shaping this version of PROGAS protocol.

14 Dissemination

Dissemination of the research findings will have several aims:

i) Inform health care practitioner's about the optimal use of gastrostomy

This will be done locally through regional meetings with MND care groups, local workshops and meetings organised through the local MNDA branches. On a national level the research will be submitted for publication in high impact medical journals and be presented at national and international meetings including the annual International ALS/MND Symposium and the Association of British Neurologists meeting.

ii) Inform members of the public

Public involvement through the SMND-RAG will occur throughout this study. Members of the SMND-RAG are actively involved members of the local branches of the MND Association and as such provide informal support to individuals and their families with MND. These members of SMND-RAG will enable high awareness of the research findings within the affected public.

15 Taking the Work Forward

PROGAS addresses an area of unmet need of key strategic importance which has been identified as a research priority by DeNDRoN and MNDA. It also contributes to a larger programme of MND research coordinated by Professor Shaw and Dr McDermott at the Sheffield Care and Research Centre for Motor Neurone Disorders.

Patient and carer benefit

It is anticipated that the findings from this study will be used as a platform from which to develop ongoing research with the aim to further illuminate issues in relation to gastrostomy and its impact on the quality of life of patients, and their carers. The results of this work will translate into the development of guidelines for gastrostomy insertion use in patients with

Motor Neurone Disease, which will optimise the benefit and the patient and carer experience of gastrostomy. It is anticipated that these guidelines will inform local, within the regional MND centres in Sheffield and Leeds, and possibly national clinical practice.

Delivery across the NHS

The principles will be readily applicable to patients with severe dysphagia symptoms who are eligible for gastrostomy insertion due to other neurological diseases. Once a need for gastrostomy has been established, these guidelines will provide recommendations for optimising benefit and the patient and carer experience of gastrostomy. The pathway may be implemented across the NHS, which will improve care and help patients and carers make informed choices about their care. Although MND is the initial focus for the development of this pathway, the principles will be readily applicable to patients receiving gastrostomy due to any cause of respiratory muscle weakness and assist optimisation of palliative care needs in other chronic neurological diseases.

16 Intellectual Property

Intellectual property generated by University of Sheffield researchers is managed by the University of Sheffield Research Office.

17 Costing Schedule

The major costs of this project come from the appointment of the research staff for 36 months. We will appoint a first class post-doctoral researcher, with experience in qualitative and quantitative methods in social and health care research, who will be able to exclusively carry out PROGAS over the proposed timetable. Further costs are to cover: (i) a dedicated computer and software for the project; (ii) interviewing equipment; (iii) interview transcription services; (iv) questionnaire production and postage; (v) stationary and printing; (vi) travel expenses for researchers, participants and lay public involved through SMND-RAG; (vii) and, dissemination costs to allow travel to local and national meetings and the organisation of workshops.

18 Funding Arrangements

Funding for a part of PROGAS has been secured from the Sheffield Teaching Hospitals NHS Foundation Trust (12 months) and the Motor Neurone Disease Association (3 months). Funding from the NIHR Research for Patient Benefit programme has been sought for the remainder of the project (awaiting decision in November 2010). The STH NHS foundation trust component funding has commenced and is funding Mr Theo Stavroulakis, an experienced mixed methods researcher who has recruited the UK sites, applied for RfPB funding, and written this application. He will continue to attempt to secure the ethical and governance approvals with a view to beginning recruitment in the second half of 2010.

19 Project Timetable (Gannt Chart)

	2010											
	Jan	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**
RfPB application submission												
Ethical approval												
Research governance approval												
Successful award of RfPB grant												
Participant recruitment phase												
	2011											
	Jan	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**
Participant recruitment phase												
Project management meeting 1												
Project management meeting 2												
Project management meeting 3												
SMND-RAG meeting 1												
SMND-RAG meeting 2												
SMND-RAG meeting 3												
	2012											
	Jan	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**
Participant recruitment phase												
Follow up phase												
Interview data analysis												
Interview data reporting												
Project management meeting 4												
Project management meeting 5												
Project management meeting 6												
Project management meeting 7												
SMND-RAG meeting 4												
SMND-RAG meeting 5												
SMND-RAG meeting 6												

	2013											
	Jan	**Feb**	**Mar**	**Apr**	**May**	**Jun**	**Jul**	**Aug**	**Sep**	**Oct**	**Nov**	**Dec**
Follow up phase												
Interview data reporting												
Final data analysis												
Reporting and dissemination												
End of project												
Project management meeting 8												
Project management meeting 9												
Project management meeting 10												
SMND-RAG meeting 6												
SMND-RAG meeting 7												

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21 Principal Investigator Curriculum Vitae

Dr Christopher J McDermott

CURRENT POST

Clinical Senior Lecturer
Honorary Consultant in Neurology
Department of Neuroscience
University of Sheffield

EDUCATION AND PROFESSIONAL QUALIFICATIONS

Institution & Location	*Degree*	*Year*	*Field of study*
University of Leeds	MBChB	1994	Medicine
UK Royal College of Physicians	MRCP	1997	
University of Sheffield	PhD	2004	Neurogenetics and cell biology

PREVIOUS AND OTHER APPOINTMENTS

08/94- House Surgeon, Dewsbury District Hospital, Dewsbury, West Yorks
02/95- House Physician, Hull Royal Infirmary, Hull
08/95- Senior House Officer, Leeds Medical Rotation, Leeds General Infirmary, Leeds
05/98- Specialist Registrar in Neurology, Leeds General Infirmary, Leeds
11/98- Clinical Research Fellow in Neurology, Royal Victoria Infirmary, Newcastle upon Tyne
07/00- Wellcome Training Research Fellow in Neurology, University of Sheffield
02/02- Specialist Registrar in Neurology, Royal Hallamshire Hospital, Sheffield

HONOURS AND AWARDS

Undergraduate: 1992 Honours in Pathology and Pharmacology
Postgraduate: 2000 Award of Wellcome Clinical Training Fellowship

OTHER PROFESSIONAL ACTIVITIES

Member of DeNDRoN MND Clinical Studies Group
Member of NICE NIV Guideline Development Group
Member of Royal College of Physicians Neurology Speciality Advisory Committee
South Yorkshire Neurology Training Programme Director/Chair Specialty Training Committee

RESEARCH INTERESTS

Symptomatic management in Motor Neurone Disease; Management of Respiratory failure in Motor neurone Disease; Epidemiology of motor neurone disease; Models of neurodegeneration; Genetic aspects of neurodegeneration; Hereditary spastic paraparesis – genotype-phenotype correlations and investigation of the effects of relevant mutations in experimental models of disease.

CURRENT AND RECENT RESEARCH GRANTS

The Motor Neurone Association (£168,068) Evaluation of the impact of a cough assist mechanical in-exsufflator (MI-E) device on morbidity, quality of life and survival in patients with motor neurone disease (MND) using non-invasive ventilation (NIV). Joint 2008-2011

The Motor Neurone Disease Association (£150,000) Programme funding for The Sheffield Care and Research Centre for Motor Neurone Disorders 2007-2011.

MRC/Motor Neurone Disease Association (£239,000) Physical exercise as a risk factor for MND. 2009-2011

NIHR – Research for Patient Benefit (£201,896) Non-Invasive ventilation (NIV) in Motor Neurone Disease (MND): Establishing current use, identifying obstacles and developing pathways for optimising care. 2009-2011.

RECENT PUBLICATIONS

G Chavada , A El-Nayal, F Lee, SJ Webber, M McAlindon, PJ Shaw, **CJ McDermott**. Evaluation of two different methods for per-oral gastrostomy tube placement in patients with motor neurone disease (MND): PIG versus PEG procedures. ALS 2010:In press.

Christopher Hewitt, MBChB; Janine Kirby, PhD; J. Robin Highley, DPhil; Judith A. Hartley; Rachael Hibberd, DipHE; Hannah C. Hollinger, MA; Tim L. Williams, PhD;Paul G. Ince, MD; **Christopher J. McDermott**, PhD; Pamela J. Shaw, MD. Novel FUS/TLS Mutations and Pathology in Familial and Sporadic Amyotrophic Lateral Sclerosis. Arch Neurol 2010;67:455-461.

C Douglass, R Kandler, PJ Shaw and **CJ McDermott**. An evaluation of neurophysiological criteria used in the diagnosis of Motor Neurone Disease. J Neurol Neurosurg Neuropsych 2010; In Press.

J Kirby, E Goodall W Smith, J R Highley, R Masanzu, JA Hartley, R Hibberd, HC Hollinger, SB Wharton, K Morrison, PG Ince, **CJ McDermott** and PJ Shaw. Broad clinical phenotypes associated with TAR-DNA binding protein (TARDBP) mutations in amyotrophic lateral sclerosis. Neurology 2009; In press.

Randomised controlled trial of methotrexate for chronic inflammatory demyelinating polyradiculoneuropathy (RMC trial): a pilot, multicentre study. RMC Trial Group. Lancet Neurol 2009;8:158-64.

C Hewamadduma, **C McDermott**, J Kirby, A Grierson, M Panayi, A Dalton, Y Rajabally, P Shaw. New pedigrees and novel mutation expand the phenotype of REEP1-associated hereditary spastic paraplegia (HSP). Neurogenetics 2009;10:105-8.

PR Kasher, KJ De Vos, SB Wharton, C Manser, EJ Bennett, M Bingley, JD Wood, R Milner, **CJ McDermott**, CC Miller, PJ Shaw, AJ Grierson. Direct evidence for axonal transport defects in a novel mouse model of mutant spastin-induced hereditary spastic paraplegia (HSP) and human HSP patients. J Neurochem 2009;110:34-44.

CA Harwood, **CJ McDermott**, PJ Shaw. Physical activity as an exogenous risk factor in motor neuron disease (MND): A review of the evidence. Amyotroph Lateral Sclerosis 2009;10:191-204.

CA Hewamadduma, J Kirby, C Kershaw, J Martindale, A Dalton, **CJ McDermott**, PJ Shaw. HSP60 is a rare cause of hereditary spastic paraparesis, but may act as a genetic modifier. Neurology 2008;70:1717-8.

CJ McDermott and PJ Shaw The clinical diagnosis and management of MND. BMJ 2008;336:658-62

Centre Pathway Review

1. Centre: _____

2. Centre Director: _____

3. Number of new diagnosis of MND per year at site: _____

4. Number of gastrostomies in past 12 months: _____

5. There are multiple options for the insertion of a gastrostomy tube. Please indicate which methods are available at your centre and describe in which circumstances you would select this method. A definition sheet is enclosed. If the procedure differs at your centre please indicate how.

Insertion Method	Availability Yes/No	Circumstances Preferred
PEG		
PRG/RIG		
PIG		
Surgical		
Other		

6. We would like to capture information regarding the decision making process with regard to indication for gastrostomy PEG. Gastrostomy should be offered: ***(please, tick Yes or No for each of the options provided)***

	Yes	No
• At time of diagnosis regardless of bulbar involvement	☐	☐
• A short interval after diagnosis (e.g. next clinic visit) regardless of bulbar involvement	☐	☐
• When early signs of bulbar dysfunction	☐	☐
• When BMI is less than 18.5 kg/m^2	☐	☐
• When weight loss of more than 10% from pre-morbid weight	☐	☐
• Dysphagia graded 6/10 on the ALS severity scale	☐	☐
• When patient has prolonged and difficult meals	☐	☐
• When patient has unsafe swallow	☐	☐
• When patient has recurrent chest infection	☐	☐

Please, detail other criteria in relation to when gastrostomy should be offered: (please, use the space provided)

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Contact Details for Local PEG Champion

Name …….. Position ……..

Address **…….** E-mail ……..

……. Telephone Number

……. **……**

Definitions

The terminology can be confusing regarding gastrostomy. To ensure we are all using the same terminology for a procedure, the definitions we would like to use for this prospective study are below. A short description of a standard protocol for each procedure is given. Please use the space provided to indicate substantial deviations from these protocols at your centre.

Percutaneous Endoscopic Gastrostomy (PEG)

PEG is performed under endoscopic guidance using conscious sedation. The endoscope is passed into the stomach, and after an upper gastrointestinal tract endoscopy is performed, the stomach is filled up with air and the appropriate puncture site is located. An approximately 6-mm incision is made with the patient under local anaesthesia, and after the puncture a cannula is advanced into the stomach. Under endoscopic control, a guide wire is inserted through the cannula and grasped with the biopsy forceps, and is drawn out together with the endoscope. The proximal end of the wire is attached to the PEG tube's fixation loop and pulled into the stomach on the distal end of the wire. Then the tube is pulled through the abdominal wall until the silicone disk abuts the inner gastric wall. The correct position of the tube is once again checked endoscopically and the tube flushed with 0.9% sodium chloride and tested for possible leaks.

Variation at your centre (please, use the space provided)

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Radiologically Inserted Gastrostomy (RIG) or Percutaneous Radiologic Gastrostomy (PRG)

During RIG/PRG a nasogastric tube is introduced to inflate the stomach with approximately 500 mL of air. After administration of local anaesthesia, the lower part of the body of the stomach is punctured under fluoroscopic guidance. A guide wire is then introduced, and the tract is enlarged with a series of dilators before the gastrojejunostomy catheter is inserted. A contrast medium is injected to identify the catheter in its correct position and to test the tube for possible leakage. To prevent inadvertent falling out of the catheter, a suture is tied completely around it and a dressing is applied to the site in a routine manner.

Variation at your centre (please, use the space provided)

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Per oral Image guided Gastrostomy (PIG)
PIG is a hybrid technique in which the stomach is punctured under fluoroscopic guidance, following which the oesophagus is catheterised in a retrograde fashion using a guide wire. A gastrostomy tube is then passed over the guide wire at the mouth end, down the oesophagus and out through the abdominal wall. Conscious sedation is used, usually with a combination of midazolam with either pethidine or fentanyl.

Variation at your centre (please, use the space below)

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Please add any other comments that you may have with regard to this study in the space provided.

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Please return to:
Dr Chris McDermott, Academic Neurology Unit, University of Sheffield,
Room N125, Royal Hallamshire Hospital, Glossop Rd, Sheffield, S10 2JF

Pre Gastrostomy Patient Evaluation

Coded participant number: _____

Date of evaluation: _____

Date referred for gastrostomy: _____

Age: _____ **Gender:** (please tick) Female ☐ Male ☐

Date of onset of MND symptoms (weakness): _____

Date of MND diagnosis: _____

Date of first contact by MND Centre: _____

MND site of onset: *(please tick)* Limb ☐ Bulbar ☐

Weight (Kg) _____ Height (m) _____

Weight at diagnosis or earliest previous recorded weight since MND diagnosis:

Weight (Kg) _____ Date _____

Most recent respiratory assessment: *(please, as complete as possible)*

FVC % _____ SNIP _____

Most recent gases (arterial or transcutaneous): Date recorded _____

pO2 _____ pCO2 _____ O2 sats _____

Indication for gastrostomy: *(please, tick any that apply)*

Marked weight loss ☐
Unsafe swallow ☐
Recurrent aspiration ☐
Prolonged and difficult meals ☐
Other _____

What do you think the benefits of gastrostomy will be for this patient? *(please, tick Yes or No for each of the options provided)*

	Yes	No
Prolong survival	☐	☐
Stabilise nutrition and hydration	☐	☐
Reduce risk of choking	☐	☐
Reduce risk of chest infection	☐	☐
Reduce risk/prevent aspiration	☐	☐
Ease the difficulties of feeding (e.g. anxiety)	☐	☐
Alternative route for medication	☐	☐
Improve quality of life	☐	☐
Reduce carer burden	☐	☐

Other _____

Preferred Gastrostomy procedure for this patient: *(please tick)*

PEG ☐ PIG ☐ RIG ☐ Surgical ☐

Other _____

Why was this method selected for this patient? *(please, use the space provided)*

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Has the patient's perception of gastrostomy influenced the timing or any other aspect of dysphagia management? *(please tick)*

Yes ☐ No ☐

- If yes, please detail how in the space provided:

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<u>Important Note</u>

Please issue the MQOL questionnaire to the patient and the MCSI to the carer. These must be completed by the participants before the gastrostomy placement.

Peri-Procedure Patient Evaluation

Coded participant number: _____

Date of hospital admittance: _____

Clinic: _____

Date of Procedure: _____

Type of Gastrostomy : _____

Staffing: *(please, tick if present)*

Anaesthetist ☐ Anaesthetic assistant ☐ Radiologist ☐

Radiographer ☐ Endoscopist ☐ Nurse ☐

Other _____

Patient pre procedure: O_2 sats _____ pCO_2 _____

Drugs given for gastrostomy:

	Name	**Amount**	**Indication**
1			
2			
3			
4			
5			

Monitoring: *(please, tick those performed through procedure and record most abnormal value)*

Heart rate ☐ _____ BP ☐ _____ Respiratory Rate ☐ _____

O_2 Sats ☐ _____ CO_2 ☐ _____

Respiratory support: ***(please tick)***

Does patient use NIV routinely? Yes ☐ No ☐

Was NIV used during the gastrostomy? Yes ☐ No ☐

Was supplementary oxygen given? Yes ☐ No ☐

Gastrostomy equipment:

Tube product number/type _____

Tube size _____

Tube manufacturer _____

Complications:

Duration of procedure _____

Was this a difficult gastrostomy? *(please, tick)* Yes ☐ No ☐

Indicate complications: *(please, tick any that apply)*

Desaturation ☐	Respiratory arrest ☐	Laryngeal spasm ☐
Patient distress ☐	Failure to complete ☐	Haemorrhage ☐

Please, detail other complications or notable issues relating to this gastrostomy procedure *(please, use the space provided)*:

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3 Month Follow Up Patient Evaluation

Coded participant number: _____

Date of evaluation: _____

Date of discharge after gastrostomy: _____

Weight (Kg): _____

Complications following Gastrostomy: *(please, tick any that apply for complications that have occurred since gastrostomy insertion)*

	Prior to Discharge	After Discharge
Tube blockage	☐	☐
Tube displacement	☐	☐
Tube leakage	☐	☐
Infection	☐	☐
Granulation tissue	☐	☐
Pain	☐	☐
Gastric haemorrhage	☐	☐
Perforation	☐	☐
Peritonitis	☐	☐
Pneumonia	☐	☐
Increased anxiety	☐	☐
Nausea	☐	☐
Diarrhoea	☐	☐
Constipation	☐	☐
Fatigue	☐	☐

Please, state how these complications were managed: ***(please, use the space provided)***

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Repeat gastrostomy required: (please, tick) Yes ☐ No ☐

If yes,

- Reason _____
- Method used for 2nd procedure _____

Bedside tube replacement required: (please, tick) Yes ☐ No ☐

If yes,

- Reason _____

If patient dead:

- Date of Death _____
- Cause of Death _____
- Was cause of death directly related to Gastrostomy procedure? *(please tick)*

  Yes ☐ No ☐ Uncertain ☐
- If available record the value and date of the last post procedure weight:

Weight (Kg) _____ Date recorded _____

Please detail other complications or notable issues relating to this gastrostomy procedure:
(please, use the space provided)

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<u>Important Note</u>

Please issue the MQOL and Gastro-Qu questionnaires to the patient and the MCSI to the carer. These must be completed by the participants approximately at 3 months following gastrostomy.

12 Month Follow Up Patient Evaluation

Coded participant number: _____

Date of evaluation: _____

Weight (Kg): _____

Complications following Gastrostomy: *(please, tick any that apply for complications that have occurred since the 3 month follow up visit)*

Tube blockage	☐	Tube displacement	☐	Tube leakage	☐
Infection	☐	Granulation tissue	☐	Pain	☐
Gastric haemorrhage	☐	Perforation	☐	Peritonitis	☐
Pneumonia	☐	Increased anxiety	☐	Nausea	☐
Diarrhoea	☐	Constipation	☐	Fatigue	☐

Please, state how these complications were managed: *(please, use the space provided)*

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Repeat gastrostomy required: (please, tick) Yes ☐ No ☐

If yes,

- Reason _____
- Method used for 2nd procedure _____

Bedside tube replacement required: (please, tick) Yes ☐ No ☐

If yes,

- Reason _____

If patient dead:

- Date of Death _____
- Cause of Death _____
- Was cause of death directly related to Gastrostomy procedure? *(please, tick)*

  Yes ☐ No ☐ Uncertain ☐

- If available record the value and date of the last post procedure weight:

  Weight (Kg) _____ Date recorded _____

Please detail other complications or notable issues relating to this gastrostomy procedure:
(please, use the space provided)

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The ALS Functional Rating Scale – Revised (ALSFRS-R)

Patient Coded Number: _____ Centre: _____ Date: _____

Speech

4	*Normal speech processes*
3	*Detectable speech disturbances*
2	*Intelligible with repeating*
1	*Speech combined with non-vocal communication*
0	*Loss of useful speech*

Salivation

4	*Normal*
3	*Slight but definite excess of saliva in mouth; may have night time drooling*
2	*Moderately excessive saliva; may have minimal drooling*
1	*Marked excess of saliva with some drooling*
0	*Marked drooling; requires constant tissue or handkerchief*

Swallowing

4	*Normal eating habits*
3	*Early eating problems – occasional choking*
2	*Dietary consistency changes*
1	*Needs supplemental tube feeding*
0	*NPO (exclusively parenteral or enteral feeding*

Handwriting

4	*Normal*
3	*Slow or sloppy; all words are legible*
2	*Not all words are legible*
1	*Able to grip pen but unable to write*
0	*Unable to grip pen*

Cutting Food and Handling Utensils *(for patients WITHOUT gastrostomy)*

4	*Normal*
3	*Somewhat slow and clumsy, but no help needed*
2	*Can cut most foods, although clumsy and slow; some help needed*
1	*Food must be cut by someone, but can still feed slowly*
0	*Needs to be fed*

Cutting Food and Handling Utensils *(for patients WITH gastrostomy)*

4	*Normal*
3	*Clumsy but able to perform all manipulations independently*
2	*Some help needed with closures and fasteners*
1	*Provides minimal assistance to caregiver*
0	*Unable to perform any aspect of task*

Dressing and Hygiene

4	*Normal function*
3	*Independent and complete self-care with effort of decreased efficiency*
2	*Intermittent assistance or substitute methods*
1	*Needs attendant for self-care*
0	*Total dependence*

Turning in Bed and Adjusting Bed Clothes

4	*Normal*
3	*Somewhat slow and clumsy, but no help needed*
2	*Can turn alone or adjust sheets, but with great difficulty*
1	*Can initiate, but not turn or adjust sheets alone*
0	*Helpless*

Walking

4	*Normal*
3	*Early ambulation difficulties*
2	*Walks with assistance*
1	*Non-ambulatory functional movement*
0	*No purposeful leg movement*

Climbing Stairs

4	*Normal*
3	*Slow*
2	*Mild unsteadiness or fatigue*
1	*Needs assistance*
0	*Cannot do*

Dyspnoea (shortness of breath)

4	*None*
3	*Occurs when walking*
2	*Occurs with one or more of the following: eating, bathing, dressing (ADL)*
1	*Occurs at rest, difficulty breathing when either sitting or lying*
0	*Significant difficulty, considering using mechanical respiratory support*

Orthopnea (breathless lying down)

4	*None*
3	*Some difficulty sleeping at night due to shortness of breath, does not routinely use more than two pillows*
2	*Needs extra pillows in order to sleep (more than two)*
1	*Can only sleep sitting up*
0	*Unable to sleep*

Respiratory Insufficiency

4	*None*
3	*Intermittent use of BiPAP*
2	*Continuous use of BiPAP during the night*
1	*Continuous use of BiPAP during night and day*
0	*Invasive mechanical ventilation by intubation or tracheostomy*

TOTAL SCORE OUT OF 48 ☐

McGill Quality of Life Questionnaire

Directions

The questions in this questionnaire begin with a statement followed by two opposite answers. Numbers extend from one extreme answer to its opposite. For each item, please circle the number between 0 and 10 which is most true for you. There are no right or wrong answers.

EXAMPLE:

I am hungry:

not at all 0 1 2 3 4 5 6 7 8 9 10 **extremely**

- If you are not even a little bit hungry, you would circle 0
- If you are a little hungry, you might circle a 1, 2 or 3
- If you are feeling moderately hungry, you might circle a 4,5 or 6
- If you are very hungry, you might circle a 7,8 or 9
- If you are extremely hungry, you would circle 10

BEGIN HERE:

IT IS VERY IMPORTANT THAT YOU ANSWER ALL QUESTIONS FOR HOW YOU HAVE BEEN FEELING JUST IN THE PAST TWO (2) DAYS

PART A

Considering all parts of my life-physical, emotional, social, spiritual, and financial – over the past two (2) days the quality of my life has been:

very bad 0 1 2 3 4 5 6 7 8 9 10 **excellent**

Please, continue on the next page…

PART B: Physical symptoms or Physical Problems

(1) For the questions in Part B, please list the **PHYSICAL SYMPTOMS** or **PROBLEMS** which have been the biggest problem for you over the past two (2) days (some examples are: pain, tiredness, weakness, nausea, vomiting, constipation, diarrhoea, trouble sleeping, shortness of breath, lack of appetite, sweating, immobility. Feel free to refer to others if necessary)

(2) Circle the number which best shows how big a problem each one has been for you **OVER THE PAST TWO (2) DAYS**

(3) If, over the past two (2) days, you had **NO** physical symptoms or problems, or only one or two, answer for each of the ones you have had and write "none" for the extra questions in Part B, then continue with Part C.

1. Over the past two (2) days,
   one troublesome symptom has been:_____
   (please, write symptom)

no problem 0 1 2 3 4 5 6 7 8 9 10 **tremendous problem**

2. Over the past two (2) days,
   one troublesome symptom has been:_____
   (please, write symptom)

no problem 0 1 2 3 4 5 6 7 8 9 10 **tremendous problem**

3. Over the past two (2) days,
   one troublesome symptom has been:_____
   (please, write symptom)

no problem 0 1 2 3 4 5 6 7 8 9 10 **tremendous problem**

4. Over the past two (2) days I have felt:

physically terrible 0 1 2 3 4 5 6 7 8 9 10 **physically well**

Please, continue on the next page…

Part C

Please choose the number which best describes your feelings and thoughts **OVER THE PAST TWO (2) DAYS**

5. Over the past two (2) days, I have been depressed:

not at all 0 1 2 3 4 5 6 7 8 9 10 **extremely**

6. Over the past two (2) days, I have been nervous or worried:

not at all 0 1 2 3 4 5 6 7 8 9 10 **extremely**

7. Over the past two (2) days, how much of the time did you feel sad?

never 0 1 2 3 4 5 6 7 8 9 10 **always**

8. Over the past two (2) days, when I thought of the future, I was:

not afraid 0 1 2 3 4 5 6 7 8 9 10 **terrified**

9. Over the past two (2) days, my life has been:

utterly meaningless and without purpose 0 1 2 3 4 5 6 7 8 9 10 **very purposeful and meaningful**

10. Over the past two (2) days, when I thought about my whole life, I felt that in achieving life goals I have:

made no progress whatsoever 0 1 2 3 4 5 6 7 8 9 10 **progressed to complete fulfilment**

11. Over the past two (2) days, when I thought about my life, I felt that my life to this point has been:

completely worthless 0 1 2 3 4 5 6 7 8 9 10 **very worthwhile**

Please continue on the next page…

12. Over the past two (2) days, I have felt that I have:

no control over my life	0	1	2	3	4	5	6	7	8	9	10	**complete control over my life**

13. Over the past two (2) days, I felt good about myself as a person

completely disagree	0	1	2	3	4	5	6	7	8	9	10	**completely agree**

14. To me, the past two (2) days were:

a burden	0	1	2	3	4	5	6	7	8	9	10	**a gift**

15. Over the past two (20 days, the world has been:

an impersonal unfeeling place	0	1	2	3	4	5	6	7	8	9	10	**caring and responsive to my needs**

16. Over the past two (2) days, I have felt supported:

not at all	0	1	2	3	4	5	6	7	8	9	10	**completely**

PART D

Please, list or describe the things which had the greatest effect on your quality of life in the past two (2) days. Please, tell us whether each thing you list made your quality of life better or worse during this time. If you need more space, please continue on the back of this page.

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Modified Caregiver Strain Index

Directions: *Here is a list of things that other caregivers have found to be difficult. Please, put a check mark in the columns that apply to you. We have included some examples that are common caregiver experiences to help you think about each item. Your situation may be slightly different, but the item could still apply.*

	YES, regularly	***YES, sometimes***	***NO***
My sleep is disturbed *(For example: the person I care for is in and out of bed or wanders around at night)*	☐	☐	☐
Caregiving is inconvenient *(For example: helping takes so much time or it's a long drive over to help)*	☐	☐	☐
Caregiving is a physical strain *(For example: lifting in and out of a chair, effort or concentration is required)*	☐	☐	☐
Caregiving is confining (For example: helping restricts free time or I cannot go visiting)	☐	☐	☐
There have been family adjustments *(For example: helping has disrupted my routine; there has been no privacy)*	☐	☐	☐
There have been changes in personal plans *(For example: I had to turn down a job; I could not go on holiday)*	☐	☐	☐
There have been other demands on my time *(For example: other family members need me)*	☐	☐	☐
There have been emotional adjustments *(For example: severe arguments about caregiving)*	☐	☐	☐
Some behaviour is upsetting *(For example: incontinence; the person cared for has trouble remembering things; or the person I care for accuses people of taking things)*	☐	☐	☐
It is upsetting to find the person I care for has changed so much from his/her former self *(For example: he/she is a different person than he/she used to be)*	☐	☐	☐
There have been work adjustments *(For example: I have to take time off for caregiving duties)*	☐	☐	☐
Caregiving is a financial strain	☐	☐	☐
I feel completely overwhelmed *(For example: I worry about the person I care for; I have concerns about how I will manage)*	☐	☐	☐

Gastrostomy Questionnaire

Directions: *Here is a list of experiences that other people with gastrostomy have reported. For each of the following items, please circle the number between 1 and 4 which is closest to your experience.*

In the last 3 Months how much of a problem was the feeding tube to you:

	Not at All	A Little	Quite a bit	Very much
Pain/discomfort	1	2	3	4
Leakage	1	2	3	4
Dirtying of your clothes from leakage	1	2	3	4
Redness/irritation	1	2	3	4
Blockage	1	2	3	4
Bleeding	1	2	3	4
Infection	1	2	3	4
Tube splitting	1	2	3	4
Falling out	1	2	3	4
Keeping the tube site clean	1	2	3	4
Appearance	1	2	3	4
Types of clothes worn	1	2	3	4
Difficulties using the feeding tube	1	2	3	4
Interference with family life	1	2	3	4
Interference with intimate relationships	1	2	3	4
Interference with social activities	1	2	3	4
Interference with hobbies or leisure time	1	2	3	4
How much has the feeding tube affected your overall quality of life?	1	2	3	4
How much do you think about your feeding tube?	1	2	3	4
Do you wish your feeding tube could be removed?	1	2	3	4