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The research reported in this monograph was commissioned by the HTA Programme as project number 99/12/01. The contractual start date was in October 2000. The draft report began editorial review in September 2003 and was accepted for publication in January 2005. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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Abstract

Outcomes of electrically stimulated gracilis neosphincter surgery

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Objectives: To examine patient quality of life (QoL) and long-term costs of electrically stimulated gracilis neosphincter surgery (ESGNS).

Design: Independently conducted prospective case-comparison study of patients at the Royal London Hospital (RLH), plus a cross-sectional study of outcomes of ESGNS performed at three other UK centres.

Participants: Cases were patients who underwent ESGNS at the participating hospitals during a 5-year period from 1977. Comparisons were made with two groups of people with similar bowel disorders who did not undergo ESGNS.

Intervention: ESGNS is a procedure designed to improve bowel function for people living with severe faecal incontinence or stomas. It involves transposition of the gracilis muscle to form a neo-anal sphincter. The transposed muscle is electrically stimulated via an electronic pulse generator implanted beneath the skin of the abdomen.

Main outcome measures: Clinical success and symptomatic outcomes of surgery. Generic, domain and condition specific measures of QoL. Comparative costs to the NHS of ESGNS and conventional alternatives.

Results: At 3 years after surgery approximately three-quarters of patients still had functioning neosphincters. At this stage, bowel-related QoL and continence improved by more than 20% for nearly two-thirds of RLH patients. However, ongoing bowel evacuation difficulties occurred in half of those with good continence outcomes. QoL improvements were maintained in the smaller group of RLH patients who had reached 4 and 5 years of follow-up, although at this stage the proportion with failed neosphincters had increased. The RLH findings were supported by those from the three other UK centres. No significant changes in QoL were observed in the comparison groups during the follow-up period. The mean cost of patient care at RLH, was £23,253. In the other three centres, the estimated mean cost of the intervention per patient was £11,731, reflecting fewer planned operations and repeat admissions. Costs of patient care for those with stomas who did not undergo ESGNS were estimated at £2125 per patient-year and for those who remained with severe faecal incontinence, £442 per patient-year. For patients with prior faecal incontinence, a decision to refer to ESGNS resulted in a cost-effectiveness ratio, estimated over 25 years of follow-up, of between £30,000 and £40,000 per quality-adjusted life-year (QALY) gained, depending on centre. The choice of stoma for these patients resulted in a slightly higher cost than ESGNS. For those with prior stoma, referral to ESGNS resulted in a cost-effectiveness ratio of between £5000 and £15,000 per QALY gained, depending on the centre. Cost-effectiveness ratios of around £30,000 per QALY gained are generally regarded to be reasonably attractive in the UK NHS context.

Conclusions: Although ESGNS is a major procedure associated with a high rate of long-term failure and bowel evacuation difficulty, it could be considered as an option at the extreme end of the treatment spectrum for refractory faecal incontinence. A strategy to refer patients for ESGNS would be regarded as cost-effective for patients already with stoma, whilst on the margin of cost-effectiveness for patients initially being managed conservatively.

Contents

List of abbreviations

ABS	artificial bowel sphincter
ANOVA	analysis of variance
BAC	beliefs, attitudes and characteristics
BNF	British National Formulary
CI	confidence interval
CNS	Clinical Nurse Specialist
EQ-5D	EuroQoL 5 domain
ESGNS	electrically stimulated gracilis neosphincter surgery
FI	faecal incontinence
GIQLI	Gastrointestinal Quality of Life Index
HADS	Hospital Anxiety and Depression Scale
ICER	incremental cost-effectiveness ratio
IPG	implanted pulse generator (also known as a stimulator)
NHP	Nottingham Health Profile
NICE	National Institute for Health and Clinical Excellence
NSCAG	National Specialist Commissioning Advisory Group
PAIS	psychosocial adjustment to illness scale
PY	person-year
QALY	quality-adjusted life-year
QoL	quality of life
RCT	randomised controlled trial
REC	Research Ethics Committee
RLH	Royal London Hospital
SD	standard deviation
SF-36	Short Form with 36 Items
SNS	sacral nerve stimulation
UCOE	Unit for Costs and Outcomes Evaluation
US	ultrasound
VAT	value added tax

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Electrically stimulated gracilis neosphincter surgery (ESGNS) is a complex surgical procedure designed to improve bowel function for people living with faecal incontinence refractory to conventional medical or surgical treatments.

Objectives

The objectives of the study were to test two hypotheses:

1. That ESGNS leads to a better quality of life (QoL) than either continued medical management of refractory anal incontinence or the formation of a permanent stoma.
2. That the long-term costs of ESGNS are less than the costs of alternative management options or are justifiable in terms of improved patient QoL.

Design

Part 1 was a longitudinal and prospective case-comparison study of patients at the Royal London Hospital (RLH). As a result of a recruitment shortfall, Part 2 was added; this was a cross-sectional and retrospective study of outcomes of ESGNS performed at three other UK centres.

Setting

Three NHS Hospital Surgery Departments in England (London, Hull and Newcastle) and one in Scotland (Edinburgh).

Participants

Cases were patients who underwent ESGNS at the participating hospitals during a 5-year period from 1997. Comparisons were made with two groups of people with similar bowel disorders who did not undergo ESGNS.

Intervention

ESGNS involves the transposition of the gracilis muscle from the inner thigh to form a neo-anal sphincter. The transposed muscle is then electrically stimulated via an electronic pulse generator (IPG) implanted beneath the skin of the abdomen. The IPG initiates and maintains conversion of the gracilis muscle from a fast-twitch fatiguable muscle to a slow-twitch non-fatiguable muscle, and results in the formation of a potentially continent neosphincter.

Method

Part 1 (prospective case-comparison study)

Outcomes were determined by comparing measurement on recruitment to the London study with measurement at regular intervals following surgery (for cases) or recruitment to the study (for the comparison groups). The main outcomes described are:

1. clinical success or failure of surgery
2. QoL, bowel- and surgery-related symptoms, anxiety, depression and patients' opinions of surgical outcomes
3. the comparative costs to the NHS of caring for patients who undergo ESGNS or the conventional alternative treatments.

Difficulties in evaluating response to bowel surgery using **generic** QoL measures can be minimised by using **bowel-specific** measures, but such measures, because they are symptom-specific, are difficult to use as a measure of an overall response. Both types of measure were used in this study.

Part 2 (cross-sectional study)

Postal questionnaires and case-note review were used to determine outcomes, as listed above, for patients who had previously undergone ESGNS at Hull, Newcastle and Edinburgh.

Results

Clinical and patient-based outcomes

Based on the findings of this study, a realistic expectation might be that 3 years postoperation, nearly three-quarters of all patients will still have a functioning neosphincter. Approximately two-thirds

will have a satisfactory continence outcome at 3 years of follow-up, although half of them will have ongoing evacuatory difficulties. Bowel-related QoL and continence, when measured between 1 and 3 years postoperation, improve significantly (in excess of 20%) when compared with preoperative status for nearly two-thirds of all the patients who undergo the surgery. The findings indicate that these improvements in QoL and symptoms are maintained in the smaller cohort of patients who have reached 4 and 5 years of follow-up, even though the clinical success rate has fallen somewhat at this length of follow-up. ESGNS was unsuccessful in two-thirds of the small group of patients whose disorders were caused by congenital anomalies.

Addition of cross-sectional data from the three northern centre ESGNS patients confirmed the findings recorded for the RLH patients in the postoperative period. Similar, but not identical, surgical techniques were used in the four centres.

Comparison group patients experienced no significant changes in symptoms, QoL, anxiety or depression over a 2-year follow-up period.

Costs of ESGNS

The mean cost of patient care at RLH during and before the intervention itself was £23,253, 91% of which was for inpatient ward use, theatre use and devices. The estimated cost per patient year was higher for patients with prior stomas than for patients without prior stomas. Costs of patient care for those with stomas who did not undergo ESGNS were estimated at £2125 per patient year and for those who remained with severe faecal incontinence costs were estimated at £442 per patient year.

In the northern centres, the estimated mean cost of the intervention per patient was lower at £11,731. This value is lower than that for RLH, reflecting differences in techniques for performing ESGNS requiring fewer repeat admissions and operations.

Calculating costs for 25 years of follow-up with prior faecal incontinence, it was estimated that the decision to refer to ESGNS at RLH resulted in a cost-effectiveness ratio of about £40,000 per quality-adjusted life-year (QALY) gained. Using inpatient care costs based on the three northern ESGNS centres, this value reduced to around £30,000 per QALY gained. The choice of stoma for these patients resulted in a slightly higher cost than ESGNS.

For patients with prior stoma, referral to ESGNS at RLH resulted in a cost-effectiveness ratio of around £15,000 per QALY gained, reducing to £5000 per QALY gained when inpatient costs were based on the three northern ESGNS centres.

Cost-effectiveness ratios of around £30,000 per QALY gained or less are generally regarded as being reasonably attractive in the UK NHS context.

Conclusions

Limitations

Evaluating a surgical intervention without a randomised controlled trial is difficult enough, but in addition this evaluation faced other limitations in the fulfilment of its objectives, principally relating to insufficient numbers of patients. A separate limitation became evident during the study, when it was observed that outcomes of surgery were unstable for several years in some patients, suggesting that a longer than planned follow-up was important. To deal partially with these difficulties, the study period was extended and limited data from patients from the northern areas were collected. A third limitation, associated with the time period, involved dealing with changes in the management of incontinence and the growing expertise of teams in selecting patients and in performing the surgical procedure. Further limitations apply to the economic analyses, where caution is needed in interpreting cost-effectiveness ratios owing to the small numbers of patients and very small changes observed in the EQ-5D measure on which the QALY calculations are based.

Although these methodological limitations are significant and the conclusions must be interpreted with caution, we believe that, without the option of a randomised controlled trial, we have come as close as is possible to providing robust evidence concerning the outcomes of the procedure.

Implications for healthcare

One view is that this treatment has limited long-term benefit. It may also lead to pain and difficulty with evacuation. Improved continence is of measurable benefit in some patients, but is achieved at considerable cost and the procedure has not achieved the desired outcome in sufficient numbers to justify its continuation.

An alternative view is that there is a place for ESGNS, but it is at the extreme end of the treatment spectrum for refractory faecal

incontinence. It is a complex operation associated with a high incidence of morbidity and a high incidence of failure in the long term (15–30% at 3 years and 30–50% at 5 years after surgery). However, as an option for patients who have considered other conventional treatments and are facing the formation of a permanent stoma or continuing to live with a debilitating, socially disabling disorder, the procedure deserves consideration. It may be the only alternative for patients intolerant of a stoma. Previous studies have indicated a high level of long-term serious complications associated with stomas. Patients should be given a realistic picture of the possible outcomes of ESGNS.

Patients whose disorders are caused by anorectal agenesis (congenital anomalies) pose awkward surgical challenges. The outcomes for this group were poor; two-thirds of procedures failed during the study period.

The study has indicated the value of centres of excellence that can, when needed, perform this procedure with the support of a multidisciplinary and experienced team. Funding for centres treating faecal incontinence needs to include all the elements of treatment for refractory faecal incontinence, including the most conservative. ESGNS should not be performed outside such centres owing to the rarity and complexity of the procedure and the need for specialist support before, during and after surgery. Lifelong specialist follow-up is required.

Recommendations for research

1. Since the start of this study, less invasive procedures such as sacral nerve stimulation (SNS) have developed and these may benefit some patients who might previously have undergone ESGNS. We recommend an independent study of long-term patient-based outcomes of SNS. All four existing UK ESGNS centres are ideally placed to conduct such an assessment.
2. Audit of centres performing artificial bowel sphincter operations within the UK. (The Acticon Neosphincter artificial bowel sphincter consists of an inflatable cuff of silicone elastomer placed around the anal canal and connected to a pressure-regulating balloon in the iliac fossa via a control pump placed in the labium or scrotum. Although this is less invasive than ESGNS, it is still a major procedure and is associated with a high level of complications, morbidity and explantation.) We advise that such centres should provide details of the number of procedures performed, immediate and long-term outcomes and provision for follow-up, prior to a possible National Institute for Health and Clinical Excellence (NICE) interventional procedures review. There is no good-quality evidence regarding safety and efficacy of this procedure; if it is still being performed in the UK, it should also undergo a long-term patient-based outcomes study.
3. Further study of the effects on outcomes of ESGNS of different surgical techniques is warranted, in particular with regard to the formation of a covering stoma in those patients who do not already have a stoma. Interim stoma formation is associated with increased numbers and lengths of hospital stays and it is not clear from our data that the outcomes are better as a result of this additional procedure.
4. In view of the frequency of disordered evacuation and groin and leg pain following ESGNS, research into the reasons and possible treatment for these distressing symptoms is needed.

The above recommendations may be problematic in their implementation. Waiting for available data means that any study is not prospective, not independently organised, is small and does not present either patient perspectives or the long-term outcomes. Funding bodies will have to decide whether to fund future studies such as this one – we believe that they should.

Chapter 1
Introduction

Faecal incontinence, stomas and electrically stimulated gracilis neosphincter surgery

Electrically stimulated gracilis neosphincter surgery (ESGNS) (also known as dynamic graciloplasty or stimulated graciloplasty) is a procedure designed to improve bowel continence for people living with refractory faecal incontinence (FI) or it may be performed as part of a reconstruction procedure to restore bowel continuity and continence to people who are living with stomas. A stoma (colostomy or ileostomy) is an incontinent opening of the bowel brought out on to the front of the abdomen and through which all faecal matter is collected in a bag applied around the stoma.

FI of a severity to warrant this type of surgery most commonly occurs in women as a result of obstetric trauma and in both men and women as a result of anorectal surgery, usually for anal fistulae or haemorrhoids. Childbirth was associated with variable degrees of FI in 4% of women interviewed 10 months after delivery.[1] Other causes in both sexes include anorectal agenesis, trauma, neurogenic causes or ill-defined causes termed 'idiopathic'. People with stomas whose bowel state may be suitable for ESGNS have had stomas formed either as a means of managing faecal (anal) incontinence or as a result of previous surgical treatment for bowel cancer, anorectal agenesis or trauma.

Living with FI can cause devastating physical, mental and social problems.[2–6] First-line treatments for FI include dietary modification, constipating drugs, biofeedback therapy, injection of biomaterials and anal repair operations. A newer technique, sacral nerve stimulation (SNS), which applies low-level electrical stimulation via electrodes through the sacral foramina to the nerves of the sacral plexus, appears to be a promising and non-invasive treatment for a group of patients with intact or mildly disrupted anal sphincters.[7]

Although these treatments are effective for the majority of patients who seek help, there remain a number for whom these have failed or are not appropriate and for whom the remaining alternatives are to continue as they are or to have a permanent stoma. For such people, a stoma may be an acceptable and welcome outcome, but there are many who contemplate the prospect of a permanent stoma with dismay. Likewise, those who already live with stomas may find the stoma an acceptable means of managing their disorder or they may suffer severe physical and mental problems as a consequence of the incontinence and appearance of the stoma.[8–13] Immediate and long-term physical complications resulting from stoma formation are also common; these can be debilitating and may require further surgical intervention; they include difficulties in stoma management due to poor siting, peristomal dermatitis, stomal retraction, stenosis or prolapse and peristomal herniation.[14] Makela and colleagues[15] reported the cumulative risk of complications at 8 years at 50% and Londono-Schimmer and colleagues[16] reported a 58% cumulative risk at 13 years after stoma formation. Both studies also reported a high cumulative risk of peristomal hernia development (25 and 37%, respectively); other studies have reported incidences between 1 and 11%.[17–19] Peristomal herniation poses a difficult problem and results of surgical repair are poor.

A number of studies have compared quality of life (QoL) between people living with stomas and those who have undergone sphincter-saving surgery, usually as a result of treatment for cancer. Sprangers and colleagues[20] concluded that non-stoma patients generally fare better than stoma patients in terms of QoL, although they may suffer from physical impairments such as bowel or sexual dysfunction, and Grumann and colleagues[21] concluded that patients who underwent sphincter-saving surgery had a poorer QoL than those who underwent stoma formation. It is difficult to apply the findings of either of these studies to the patient group who would be appropriate for ESGNS, as these are people who are already living with FI or with a stoma and who, in our study, are unlikely to have recently diagnosed cancer or a generalised bowel disorder, such as inflammatory bowel disease.

Prevalence of faecal incontinence and stomas

There is a paucity of information about the prevalence of end-stage FI. Although not life-threatening, the embarrassment and stigma associated with bowel incontinence mean that many sufferers delay seeking or never seek professional help. A recent UK community-based study of nearly 16,000 adults[22] over 40 years old living in their own homes reported that 0.9% of those aged 40–64 years and 2.3% of those aged ≥65 years had major FI. In those with major FI, there was no significant difference in prevalence between men and women and just over half reported that bowel symptoms had a major impact on their QoL. This study also reported that nearly two-thirds of the group with major incontinence that had a significant impact on QoL wanted help with their symptoms, although respondents were not questioned as to whether they had previously sought help. There are no published studies on the prevalence of end-stage FI, i.e. FI which is refractory to conventional conservative or surgical management. The Academic Department of Surgery at the Royal London Hospital (RLH) sees 30–40 such new referrals each year, of whom approximately three-quarters are women. However, it is likely that there is a high level of unmet need, particularly amongst men.

It is also difficult to be certain how many stomas are formed each year in the UK. Anecdotal evidence suggests that 100–150 individuals a year in the UK have a colostomy formed for anorectal agenesis and that 3000 people per year have a permanent stoma following an abdomino-perineal resection of the rectum or anus for cancer. Approximately 50% of these cancer patients will be cured, but many will have had surgical excision of their ano-rectum, necessitating the formation of a stoma. Increasing use of sphincter-saving surgery for cancer of the rectum and anus, although reducing the numbers of patients with permanent stomas, may result in problems of anal incontinence for up to one-quarter of these patients.

The procedure

The procedure under study (ESGNS) is major and complex and involves the transposition of the gracilis muscle from the inner thigh to form a neo-anal sphincter. The transposed muscle is then electrically stimulated via an electronic pulse generator (IPG) implanted beneath the skin of the abdomen. The IPG initiates and maintains conversion of the gracilis muscle from a fast-twitch fatiguable muscle to a slow-twitch non-fatiguable muscle in order to form a potentially continent neosphincter.[23] In order to achieve the conversion of the muscle fibres, the patient undergoes a period, usually of 2–3 months' duration following graciloplasty, known as 'muscle training', where the level of stimulation is gradually adjusted to a continuous level. The patient is able to relax the muscle, in order to empty the bowel, using a hand-held programmer. The IPG is powered by a battery and needs periodic replacement by means of a simple operation. ESGNS is an end-of-the-road option for patients who cannot tolerate life with a stoma or for whom conventional management of anal incontinence has been unsuccessful.

History of the procedure

The gracilis muscle is a superficial adductor situated in the inner thigh. It is not essential for either normal locomotion or maintenance of normal posture and was first used to form a neo-anal sphincter by Pickrell and colleagues[24] in the 1950s. Since the gracilis is a skeletal muscle, the majority of its fibres are type II fast-twitch fatiguable fibres and are unable to maintain a continuous contraction, unlike the muscles of the normal anal sphincter. During the 1960s, it was discovered that electrical stimulation of the nerve of a type II muscle could transform the fibres to type I, non-fatiguable fibres.[25] Dickson and Nixon performed the first procedure involving electrical stimulation of a transposed gracilis muscle in 1968,[26] although their long-term results were not published. Baeten and colleagues[27] and Williams and colleagues[28] independently further developed these techniques during the mid-1980s with the implantation of neurostimulators (IPGs) which delivered electrical stimulation to the gracilis muscle via the obturator nerve.

The evidence base

Recent multicentre[29–31] studies have confirmed that, for between 50 and 70% of patients, ESGNS can improve or restore continence. A high incidence of major morbidity, including ongoing bowel evacuatory disorders, has been reported. A long-term follow-up study[32] reported a success rate of 72% at a median follow-up time of 5 years (success being defined as continence to solid and liquid stool) and median survival of the IPG battery of 7.8 years. This study also reported chronic evacuation difficulties in 16% of patients. All studies reported to date have been case series

conducted by the clinical teams responsible for the operations and have employed varying criteria for patient selection and varying definitions of successful outcome. With one exception,[33] no studies have included any form of comparison or control group and good-quality evidence regarding the long-term outcomes is lacking. A recent systematic review conducted on behalf of the Australian Safety and Efficacy Register of New Interventional Procedures (ASERNIP)[34] found no high-level evidence regarding safety or efficacy and suggested that ESGNS "appears to be an efficacious alternative to colostomy for restoring continence in around 60% of patients (including those who have congenital disorders of the anorectum)" and concluded that although ESGNS appears to be associated with a higher rate of complications than colostomy, "it is clearly a superior intervention for restoring continence in some patients". The same review recommended that a comparative non-randomised study should be undertaken to evaluate the safety of dynamic graciloplasty in comparison with colostomy.

Little is known about either the cost implications or the effects on QoL of this major reconstructive surgery. Only one study of cost-effectiveness[33] has been conducted and this compared costs of ESGNS with those of a retrospective cohort of colostomy patients – a study which has been criticised for overestimating colostomy pouch costs (see discussion in reference 28). At the time of writing (September 2003), the cost of the basic 'kit' (IPG, epineural electrode and hand-held patient controller) is ~£6800 [value added tax (VAT) included]. Health service resources are always limited and there is a need to ensure rigorous evaluation of the outcomes of surgery in both the near and long terms and to compare these outcomes with those of a suitable comparator group prior to making the procedure more widely available.

The surgical programme

Supra-regional funding was granted to the Academic Department of Surgery at the RLH for a series of up to 110 ESGN operations, starting from April 1997. The Department of Health National Specialist Commissioning Advisory Group (NSCAG) has funded the service costs of these procedures on the condition that an independent assessment of outcomes would be undertaken, with the proviso that separate funding be sought for the outcomes assessment. NSCAG funding was originally agreed for the period April 1997 to March 2000, but was extended for a further 2 years to March 2003, to allow for the recruitment of sufficient patients to permit the completion of the outcomes assessment.

The initial NSCAG funding was granted on the basis that ESGNS would be performed at RLH as part of total anorectal reconstruction procedures for patients whose bowel disorders were due to either cancer or anorectal agenesis, as these were expected to be the predominant groups of people seeking ESGNS. However, it became clear at a very early stage that women with bowel disorders caused by obstetric trauma would form the largest group and that anorectal agenesis and cancer would be uncommon reasons for seeking this surgery; indeed, during the study period, only one patient has undergone ESGNS following abdomino-perineal resection for cancer. The unexpected pattern of referrals led to a revision of the criteria for acceptance of patients into the surgical programme to include patients with intractable FI due to obstetric or other forms of trauma.

The outcomes assessment study

The outcomes assessment study was carried out by the Unit for Costs and Outcomes Evaluation (UCOE) based at Barts and The London, Queen Mary's School of Medicine and Dentistry, and led by Professor Roger Feldman. The outcomes assessment was funded for 3 years to October 2000 by the London NHS Research and Development Programme and for over 2.5 years to July 2003 by the NHS Health Technology Assessment Programme (NCCHTA). The funding extension was sought because of slow recruitment to the ESGNS and comparison groups.

Inclusion of patients from three additional centres in the outcomes assessment study

NSCAG funding for the ESGNS programme at RLH had been intended to provide for ESGNS as part of total anorectal reconstruction surgery at only one centre in England during the outcomes assessment process. During the course of the study, it became apparent that surgeons at two other centres in England (Hull and Newcastle) were already performing ESGNS procedures, although generally not as part of total anorectal reconstruction surgery. The changing criteria for patient selection at RLH and the varying nomenclature used to describe ESGNS seem to

have been unclear to the health authorities which continued to fund the procedure at these centres, where surgeons were unaware of the NSCAG restrictions. Another surgeon in Edinburgh also performs ESGNS, again generally not as part of anorectal reconstruction. Hence, somewhat late in the evaluation process, these three surgeons were approached and agreed to the inclusion of their patients in a limited retrospective study of costs and outcomes.

Differing techniques and the evolution of ESGNS and other surgical procedures during the course of the outcomes assessment

Since the outcomes assessment study started in 1997, it is inevitable that surgeons and other members of their clinical teams will have built on experience and moved up the learning curve. Surgeons may have fine-tuned their operating techniques. Teams have expanded and developed, becoming familiar with managing the before- and after-care of their ESGNS patients. Experience is also likely to lead to a refinement of selection procedures for surgery and a more realistic picture of outcomes develops which can be imparted to prospective patients as an aid to their decision-making – in effect both clinicians and patients become more selective.

There are some important differences in procedures and techniques at the four different centres. First, almost all RLH patients who do not have stomas prior to ESGNS will have a covering stoma formed at the time of muscle transposition, whereas this is seldom the case at the other three centres. Second, at RLH the electrode for neural stimulation is almost always fixed directly to the obturator nerve ('epineural' stimulation), whereas surgeons at the other UK centres will generally fix two electrodes intramuscularly close to the nerve branches.

Specific changes in operating technique have occurred in two centres outside London, where harvesting of the gracilis muscle is now carried out endoscopically rather than as an open procedure. In addition, one surgeon uses an anchor lock and another uses a stapling device to attach the gracilis tendon to the bone.

A small group of patients at RLH who suffered symptoms of faecal urgency in association with demonstrable rectal hypersensitivity were offered an additional procedure known as rectal augmentation at the time of ESGNS. Rectal augmentation involves the mobilisation of a segment of small bowel on its vascular pedicle; this is then anastomosed to the anterior surface of the rectum to create an 'augmented' rectum, with the aim of reducing symptoms of urgency.

As noted above, a newer technique, SNS, which applies low-level electrical stimulation via electrodes through the sacral foramina to the nerves of the sacral plexus, appears to be a promising and non-invasive treatment for a group of patients with intact or mildly disrupted anal sphincters.[7] The same IPG is required for SNS as for ESGNS, hence SNS is also a costly procedure. Little is known about either the long-term outcomes of SNS or the extent of its potential application in patients with different anatomical and physiological disorders. However, in the future, SNS may occupy the centre of the treatment spectrum for FI and may even be effective in patients with moderate degrees of sphincter disruption, who might previously have been offered ESGNS.

Chapter 2

Aims and objectives

Aims

The aims of this study were to assess outcomes of ESGNS as perceived by patients and to examine QoL, symptoms, health service costs and societal costs of ESGNS as compared with the conventional alternative treatments.

Objectives

For RLH patients whose ESGNS treatment was started and completed between 1 April 1997 and 31 December 2002

1. To test the hypotheses:
   (a) That electrically stimulated gracilis neosphincter surgery leads to a better QoL than continued medical management of anal incontinence or the formation of a permanent stoma.
   (b) That the long-term costs of patient care following ESGNS are less than the costs of alternative management options, or are justifiable in terms of improved patient QoL.
2. To examine patients' perceptions of the success of ESGNS in alleviating their bowel symptoms.
3. To examine the symptomatic outcomes and clinical 'survival' of the neosphincters together with functioning circuitry.

For patients whose ESGNS treatment at Edinburgh, Hull and Newcastle was started and completed between 1 January 1997 and 30 June 2001

To assess the following post-ESGNS outcomes in order to supplement findings from the RLH prospective study:

(a) clinical 'survival' of the neosphincter together with functioning circuitry
(b) symptoms: continence, evacuation and pain
(c) QoL
(d) patients' opinions regarding the experience and aftermath of undergoing ESGNS
(e) NHS and patient resource use.

(Outcomes assessment at these three centres was performed retrospectively during the period 2002–03. The evidence from these three centres complements evidence gathered during the course of the prospective assessment of outcomes of ESGNS performed at RLH.)

Chapter 3

Patients and methods

Royal London Hospital Prospective Outcomes Assessment Study

This was a prospective case-comparison study to examine outcomes of ESGNS. The primary outcome measures are of QoL, symptoms and patients' opinions of outcomes of surgery. Resource use and costs are also assessed.

When assessing outcomes of health interventions, the study design of choice should ideally be a randomised controlled trial (RCT). However, for ESGNS, it was considered ethically unacceptable to randomise patients to undergo either ESGNS or its alternative surgical treatment, stoma formation, since the two procedures and their end results are very different. The next best alternative to an RCT was to find suitable comparators who were living with either severe FI or permanent stomas. Therefore, findings for the ESGNS group are compared with those of two groups of people who did not undergo surgery. These comparison groups consist of people who were offered ESGNS but who decided not to proceed – the 'not-accepting surgery' group, or they were people with similar bowel disorders who had never been referred for consideration of ESGNS – the 'not-offered surgery' group.

Patients

RLH ESGNS group

All patients who underwent ESGNS at RLH or the London Independent Hospital after 1 April 1997 and whose treatment was complete by 31 December 2002 were asked to participate in the outcomes assessment study. They were either already living with a stoma or they were suffering end-stage FI which was not amenable to other conventional medical or surgical treatment. The presence of rectal or anal sphincter anatomy was not a prerequisite for undergoing surgery. Their bowel disorders were due to anorectal agenesis, previous curative surgery for cancer, obstetric or other forms of trauma, neurogenic causes or ill-defined causes labelled 'idiopathic'. [The original intention of the study was to assess outcomes of ESGNS when performed as part of a total anorectal reconstruction procedure (for patients whose anorectums had been removed or were congenitally absent). It became clear early in the study period that such patients were a small minority of those who would seek ESGNS and the selection criteria for the surgery were widened accordingly to those described above.] All patients included in this outcomes assessment were aged ≥15 years.

Patients were informed about the outcomes assessment study and asked to participate once they had made the decision to proceed with surgery.

Criteria for inclusion in the outcomes assessment study were wider than those which applied to NSCAG funding for the surgical programme. The study aimed to examine outcomes for all ESGNS performed by the RLH surgical team, provided that the patients were able to complete the study outcome measures.

Seven patients who underwent ESGNS were excluded from the outcomes assessment study for the following reasons:

1. Two patients were excluded retrospectively from the QoL study because they were discovered to be unsuitable for ESGNS after the first stage of the procedure. One of these patients was found to possess inadequate remaining bowel for anastomosis and the other had a spinal injury that rendered neural stimulation impossible; both now have permanent end stomas. However, clinical outcomes for these two patients are reported and their resource use has been included in the economic analyses.
2. Three patients who underwent ESGNS were excluded from the QoL and symptom assessment because they spoke little or no English; these exclusions were necessary owing to the paucity of adequately tested translations of QoL and symptom measures. Clinical outcomes for these three patients are reported and resource use for one of them (not privately funded) has been included in the economic analyses.
3. Two patients who underwent total anorectal reconstruction including ESGNS at the time of resection of primary rectal cancer were excluded from the outcomes assessment study

as they did not have stomas or FI prior to surgery and they are not directly comparable with other ESGNS patients.

In addition, the following surgical and NSCAG exclusion criteria apply:

1. Patients with inflammatory bowel disease were excluded from the surgical programme.
2. Patients resident in Wales or Northern Ireland were not eligible for NSCAG-funded ESGNS. However, patients resident in Wales were recruited to the not-offered surgery group of the outcomes assessment study.

Comparison groups

Comparison group patients had similar bowel disorders to the ESGNS group, although they did not undergo ESGNS. They were recruited from two sources:

1. The **'not-offered' surgery** group consists of patients who had never been referred to RLH but who had been referred for specialist surgical advice at other centres for their bowel disorders. These patients had not undergone ESGNS. They were, with two exceptions, identified by their consultant surgeons and were recruited to the study via their GPs. The method of recruitment for this group was laborious and initially involved an attempt to approach all consultant general and colorectal surgeons in England and Wales, enquiring whether they would be willing to help in identifying any patients who had refractory FI or stomas (excluding patients with inflammatory bowel disease) whom they had seen as secondary referrals during the previous 2 years. Multicentre ethical approval was obtained and local trust and ethical committee authorisation was obtained for over 50 areas where surgeons had agreed to help and had suitable patients. Surgeons provided us with the patients' initials, dates of birth and GP contact details. We then wrote to the GPs and asked them to forward information about the study to the patients; patients could contact us by telephone for more information or return a reply slip and written consent form directly to us. Where no response was obtained within 1 month, a reminder letter was sent for forwarding by the GP.

   Also included in this group are two patients who volunteered following an appeal for suitable patients in a magazine published by a patient support group, 'InContact'; both patients were similar in terms of symptoms and bowel history to others in the not-offered surgery group.
2. The **'not-accepting surgery'** group consists of patients who were referred to RLH and were offered ESGNS as a potential means of treating their bowel disorders, but who decided not to proceed with the surgery. These patients were approached regarding the outcomes assessment study by letter once they had made their decision not to proceed with surgery. Reminder letters were sent if no response was received within 1 month.

In order to simplify interpretation and because it is likely that the not-offered surgery group will be more representative of an untreated comparison group, we will treat the not-offered surgery group as the main group for comparison of symptomatic and QoL outcomes.

Table 1 shows the numbers of patients in each of the three study groups.

TABLE 1 *Recruitment to prospective outcomes assessment study at RLH*

	RLH ESGNS group	Not-offered surgery group	Not-accepting surgery group
Number approached who were suitable for inclusion in outcomes assessment study	50	70	68
Number who agreed to participate (%)	49 (98)	45 (64)	42 (62)
Number who returned two or more questionnaires (including at least one in the postoperative period for the ESGNS group) (%)	48 (96)	40 (57)	38 (56)
Additional patients who agreed to participate in outcomes assessment but who were later excluded for the following reasons:			
Did not speak English	3	–	–
Unsuitable for surgery (retrospective exclusion)	2	–	–
Total anorectal reconstruction at time of cancer surgery	2	–	–

Method

This was a prospective case-comparison study which observed symptoms, QoL, patients' opinions of outcomes (ESGNS group only) and resource use. Data were collected by means of self-completion questionnaires and telephone or face-to-face interviews. Patients in the ESGNS group were asked to complete questionnaires prior to surgery and at regular intervals following the completion of surgery until the end of the study period (up to 5 years of follow-up). Patients in the two comparison groups completed questionnaires on recruitment to the study and on three further occasions during a 2-year follow-up period.

Ethical and hospital trust approval

Ethical approval for the study was granted by East London and City Health Authority Research Ethics Committee and London Multi-centre Research Ethics Committee. Permission to approach patients for the not-offered surgery group was granted by 58 local NHS trusts and their respective local research ethics committees.

Sample size calculations for RLH ESGNS and comparison groups

Based on a small pilot study, prior to the start of this study, a power calculation had indicated that at a significance level of 0.05 and with a power of 80%, 70 patients would be required in each group in order to detect a 25% greater improvement for the ESGNS group when compared with the not-offered surgery group. The improvement was based on the Nottingham Health Profile (NHP) social isolation scale at 1 year post-ESGNS or recruitment to the study.

During the course of this study, the NHP social isolation scale was found to have large 'floor' effects (in excess of 40% for the ESGNS group). ['Floor' effects occur when a scale is not sufficiently sensitive to detect small impairments to QoL, hence many patients may start at the best level ('floor') that the scale can demonstrate. Such a scale will be unable to demonstrate improvements for those patients who start at the floor, although it may detect deteriorations.] Early observation of patients and their questionnaire and interview responses had also indicated that 1 year postoperation might be too soon for assessment of final outcomes. In the results section, we indicate the statistical power that our study has to detect the effects that were observed, given the sample size.

The original intention had been to match cases with between one and four patients in the not-offered surgery group on age, gender, presence of stoma and cause of disorder. In the event, slow recruitment to both groups rendered any matching impractical.

Quality of life and symptom questionnaires: RLH ESGNS and comparison groups

The QoL and symptom questionnaires were administered several times. Patients in all three study groups were sent questionnaires at recruitment and 6, 12 and 24 months later (four early patients in the ESGNS group did not receive the preoperation questionnaire). The ESGNS group also received questionnaires at 3, 9 and 18 months and yearly after 24 months up to 5 years of follow-up.

The questionnaires are listed in *Table 2*. Questionnaires were chosen to reflect the domains of QoL and distress which have previously been demonstrated to be affected by living with FI or stomas.[2–6,8–13] The EuroQoL 5 domain (EQ-5D),[35] Nottingham Health Profile (NHP),[36,37] Hospital Anxiety and Depression Scale (HADS)[38] and beliefs, attitudes and characteristics (BAC) questionnaires were tested in a pilot study with an earlier group of ESGNS patients. As described below, condition specific measures (RLH bowel-specific and BAC questionnaires) were developed during the pilot study and at the start of the outcomes assessment study.

The psychosocial adjustment to illness scale (PAIS) was added after the start of the study and is appropriate only for patients who can remember life before their bowel disorder started; hence numbers of responses to this questionnaire are limited.[39]

All the questionnaires, with the exception of the PAIS, were contained in one booklet. All questions were accessible to people with a standard reading age of 12 years. The order of questionnaires within the booklet was as follows:

> EQ-5D, NHP, HADS, RLH condition-specific measure, symptom questionnaire, BAC, costs

The total form took 20–30 minutes to complete and consisted mainly of check boxes and visual analogue scales. The booklet included opportunities for comments.

The following four questionnaires measuring psychosocial factors known to be related to the impact of and recovery from illness were administered once only, on or close to recruitment to the study:

TABLE 2 *Quality of life, symptom and resource use questionnaires*

Questionnaire name	Description	Domains	Population/normative values
EQ-5D (EuroQoL)	Generic QoL Standardised	5 single domains of health status: mobility, self-care, anxiety/depression, pain/discomfort and usual activities. Population-based single index of health status and a self-rated score for health status	Sample of 3395 UK adults[35]
Nottingham Health Profile (NHP)[37]	Generic Measure of distress Standardised	38 single yes/no items give scores in 6 domains: emotional reaction, energy, pain, physical mobility, sleep, social isolation	Sample of 6506 UK adults
Psychosocial adjustment to illness scale (PAIS)[39]	Generic QoL Standardised (Suitable only for patients with recent acquired disorders)	Gives scores on 7 domains of QoL: Healthcare orientation Vocational environment Domestic environment Sexual relationships Extended family relationships Social environment Psychological distress	Normative values for patient groups: cancer, diabetes and hypertension
Hospital Anxiety and Depression Scale (HADS)[38]	Domain specific Standardised	14 items give scores on scales for anxiety and depression	Scales can be categorised into normal, mild, moderate and severe
RLH bowel questionnaire	Disorder specific (suitable for people with stomas or FI) Locally devised and tested	16 items of daily living, gives scores on two scales of impact of the bowel disorder: 'Psychosocial impact' 'Lifestyle impact' Plus single item: 'Effect on sex life' See *Table 3* for items	–
Beliefs, attitudes and characteristics (BAC)	Disorder specific Locally devised and tested	Visual analogue scales for rating expectations of success of surgery (ESGNS group only) and satisfaction with life in general 4 questions on body image and perception of control of body	–
Symptoms	Disorder specific, locally devised, contains questions from the Cleveland Clinic incontinence scale	Questions on frequency and severity of FI and evacuatory difficulties. For ESGNS group questions on use of stimulator, pain and other postoperative symptoms Can be used to generate the Cleveland Clinic incontinence score[44]	–
Resource use	Resource use – patient and community	Questions on patient resource use related to the bowel disorder, also GP and other related resource use, such as stoma care appliances, prescriptions and visits to healthcare professionals	–

- short social support questionnaire (SSQ-6)[40]
- COPE, a generic measure of a person's approaches to dealing with stress[41]
- generalised self-efficacy scale[42]
- recovery locus of control scale[43] (ESGNS group only).

Non-responding patients were sent reminders after 1 month. ESGNS patients also received telephone reminders or personal reminders at hospital in- and outpatient visits.

Semi-structured interviews were conducted wherever possible by telephone or in person with ESGNS patients both preoperation and 1 year after surgery to assess the impact of the bowel disorder on QoL. Some patients operated on towards the end of the outcomes assessment study have not been interviewed in person, but have received postal questionnaires covering similar topics. Wherever possible within study time constraints and patient willingness and availability, similar interviews were conducted on one or two occasions with patients from the not-accepting surgery and not-offered surgery groups.

Main outcome measures

The following main outcome measures were chosen to reflect global changes in health status, changes relating to psychological distress and to the impact on daily living associated with FI or the presence of a stoma, symptoms of incontinence or disordered bowel evacuation and the patients' opinions of success of surgery in solving their bowel disorder:

- EQ-5D weighted index of health status.[35]
- NHP pain scale.[36]
- NHP social isolation scale.[36]
- HADS.[38]
- RLH condition-specific measure – psychosocial impact and lifestyle impact scales.
- Cleveland Clinic FI scale, together with frequency of incontinence to solid or liquid stool.[44] (The Cleveland Clinic Incontinence Score includes questions regarding incontinence to solid and liquid stool, incontinence to flatus, use of pads and ability to perform usual activities. It gives scores of between zero and four according to frequency for each item, 20 being the worst possible score. Scores of ≥ 9 on the Cleveland Clinic scale have previously been shown to be associated with a significantly impaired QoL.)
- assessment of bowel evacuation symptoms. (We have defined evacuatory difficulty as any one or more of the following required to achieve evacuation: straining for more than 20 minutes, use of enemas, rectal irrigation, digitation or suppositories.)
- patients' opinions of success of surgery in solving their bowel disorders.

Secondary outcome measures

The following secondary outcomes measures are included in this report:

- EQ-5D self-rated health status visual analogue scale
- NHP emotional reaction scale
- NHP energy scale
- NHP physical mobility scale
- NHP sleep scale
- RLH bowel-specific questionnaire item 'effect on my sex life'
- Satisfaction with life in general.

Findings from the following measures will be reported in separate papers:

- PAIS[39]
- questions on body image and control of the body from the BAC questionnaire
- short social support questionnaire (SSQ-6)[40]
- COPE, a generic measure of a person's approaches to dealing with stress[41]
- generalised self-efficacy scale[42]
- recovery locus of control scale[43] (ESGNS group only)
- detailed findings from semi-structured interviews.

Development of questionnaires to assess the impact of the bowel disorder

At the start of the study, it was not known whether generic measures such as the EQ-5D and NHP would be sufficiently sensitive to detect changes in QoL which might occur following bowel surgery, hence a condition-specific measure was required. In the absence (at the time of the start of the outcomes assessment study) of an adequately tested incontinence- or stoma-specific QoL measure, the RLH bowel questionnaire was developed.

This condition-specific questionnaire was developed during the early part of the outcomes assessment study – a less than ideal circumstance which did not allow a great deal of time for rigorous pretesting and development. The questionnaire evolved from earlier work carried out during the pilot study, when patients were asked to list the five aspects of their disorder which they hoped would improve following surgery – a 'questioning of objectives' approach. Discussions

were also held with clinical staff and new patients. Initially a 20-item scale was developed and tested for acceptability and relevance on a sample of patients who had previously undergone surgery. The items were intended to reflect the impact of the bowel disorder on daily activities. Some modifications to wording of questions were made and a further five items were added. Interim analyses indicated that the new measure was sensitive to changes following successful and unsuccessful bowel surgery and was able to discriminate between the patient groups at baseline.

In order to identify groups of variables which might form subscales within the new measure, the technique of factor analysis was applied. Factor analysis attempts to identify variables which correlate closely with one another to form groups ('factors'); the variables within each group or factor identified should correlate weakly with variables in other groups. Exploratory factor analysis was carried out on 16 items from questionnaires completed at baseline (n = 111) using principal component analysis with orthogonal rotation. This generated two groups; the higher factor loading determined the grouping for each item [factor loadings indicate the importance of the item to each group (factor) and are equal to the correlations between the factors and the items]. The resulting subscales were named 'lifestyle impact' (10 items) and 'psychosocial impact' (six items) (*Table 3*). The subscales showed strong internal consistency (lifestyle impact, Cronbach's alpha = 0.93; psychosocial impact, Cronbach's alpha = 0.91) and responses correlated strongly with appropriate domains of the standardised measures at baseline and in the follow-up period. Nine items had been excluded from the factor analysis either because responses correlated closely with other items and therefore appeared to measure the same constructs, or because they had generated substantial proportions (10% or more) of missing responses. The item 'effect on my sex life', although excluded from the principal components analysis owing to low response rates, has been retained as a secondary outcome measure.

The BAC questionnaire was developed during the pilot study and includes linear scales for patients to indicate their satisfaction with life in general and, for ESGNS patients, preoperative predictions and postoperative estimates of the success of surgery in solving the bowel problems. It also includes four questions on body image, feeling 'a complete person' and the extent to which people feel in control of their bodies; all are constructs which have previously been found to be important

TABLE 3 *RLH bowel-specific questionnaire: principal component analysis and development of subscales from baseline questionnaire responses (numbers shown are factor loadings)* (n = *111*)[a]

Item No.	Item	Component 1: 'lifestyle impact' (items 1–10, values in bold) (Cronbach's alpha = 0.93)	Component 2: 'psychosocial impact' (items 11–16, values in bold) (Crombach's alpha = 0.91)
1	Going on holiday	**0.79**	0.32
2	Going out socially	**0.77**	0.43
3	Going to work, school or carrying out usual activities	**0.69**	0.47
4	Being incontinent or having accidents when at home	**0.84**	0.18
5	Being incontinent or having accidents when not at home	**0.75**	0.33
6	Time taken managing the bowel condition	**0.85**	0.27
7	Not being able to eat certain foods	**0.41**	0.31
8	Not being able to wear certain clothes	**0.53**	0.32
9	Feeling smelly	**0.62**	0.55
10	Not sleeping well	**0.50**	0.47
11	Feeling anxious or depressed	0.56	**0.65**
12	Others knowing about the bowel condition	0.48	**0.67**
13	Loss of self-confidence	0.49	**0.71**
14	Feeling unattractive	0.40	**0.71**
15	Forming and keeping relationships	0.27	**0.75**
16	Relationships with friends	0.13	**0.87**

[a] Extraction method: principal component analysis. Rotation method: varimax (orthogonal).

to patients with stomas or FI.[10] ESGNS patients' responses to questions on satisfaction with life in general and postoperative estimates of success of surgery correlated closely and significantly at all stages of follow-up with each other and all main outcome measures.

Questions regarding body image, completeness and control correlated closely and significantly with each other. Findings from this part of the questionnaire will be reported in a separate paper.

Resource use: RLH ESGNS patients and comparison groups

Methods of assessment of resource use are described in detail in Chapter 6.

Planned analysis: Royal London Hospital Prospective Outcomes Assessment Study

All data were entered on to a Microsoft Access database and checked. Statistical analyses were carried out using SPSS v.11 software.

Baseline findings

We describe baseline patient characteristics in some detail because the three study groups are not derived from the same patient population and it is important to understand their comparability at the start of the study period.

Clinical success of surgery

Kaplan–Meier 'survival' plots are shown for the RLH ESGNS group over the 5-year study period. 'Survival' or, in other words, 'success', is defined as the absence of a stoma and the presence of functioning stimulator and circuitry at the last time of observation. Patients with stimulators that require replacement only because of battery depletion at the time of the last observation are considered 'successes'. 'Success' is additionally described for the entire group of RLH ESGNS patients including five patients who were excluded from the outcomes assessment study [as described in section 'Patients' (p. 7)]. Further success curves were examined for patients whose disorders were not congenital in origin.

Changes in outcome measure scores over time

The distributions of scores at 2 and 3 years of follow-up and the distributions of the changes in scores at 2 years (and 3 years for the ESGNS group) of follow-up compared with baseline were examined in each patient group for the main outcome measures.

Statistical significance was accepted at the 5% level. Testing of statistical significance was limited to two occasions in order to reduce the risks of multiple significance testing and was carried out at 2 and 3 years of follow-up for the main and secondary outcome measures (excepting patients' estimates of success of surgery). Tests were carried out at 2 years of follow-up for within-group changes in scores (paired sample *t*-tests/Wilcoxon matched pairs signed rank sum test according to distribution) and the between-group differences in changes in scores [Mann–Whitney *U*-tests, one-way analysis of variance (ANOVA), Student's *t*-tests] to examine differences between the ESGNS group and the not-offered surgery group and between the ESGNS group and the not-accepting surgery group. Two years was chosen for the first testing of final outcomes because the majority of complications or clinical failures occurred during this period, nearly three-quarters of ESGNS patients had comparative scores at this stage and it was the last occasion when patients in either comparison group had completed questionnaires. Further within-group tests (paired *t*-tests, McNemar's test or Wilcoxon signed rank sum tests, according to distribution) were carried out for the main outcome measures for changes in scores within the ESGNS group at 3 years post-operation compared with baseline.

Clinical failure

The above analyses were carried out including all patients who underwent ESGNS. There are some problems with this approach, in that patients whose surgery has failed may be offered the alternative of a stoma and may therefore have an altered QoL as a result of having a stoma rather than because of undergoing ESGNS. Patients whose circuitry has been removed but who have not chosen to have a stoma formed may also feel some benefit from having an unstimulated graciloplasty. Tabulations showing the proportions of patients include columns for those with clinically failed and clinically successful surgery and the proportions who improved or deteriorated by at least 10 and 20% are shown for the main outcome measures at 2 and 3 years. Values of 10 and 20% were chosen as cut-off points for estimating the proportions as there is some evidence that on a 100-point scale, a moderate change as perceived by the patient is indicated by a 10-point change and a large change is indicated by a 20-point change.[45]

Analyses excluding anorectal agenesis patients

The subgroup of patients whose disorders are caused by anorectal agenesis, although small, poses an extremely awkward surgical challenge, in that the extents of their congenital anomalies vary

widely and they are likely to have undergone multiple previous operations in childhood. It is widely believed, and has recently been confirmed, that they are less likely to have a successful clinical outcome than other patients; Rongen and colleagues found a success rate of 52% in patients with congenital disorders compared with an overall success rate of 72% in a study of 200 patients.[32] Therefore, the above analyses for the main outcome measures were compared with similar analyses which excluded patients with anorectal agenesis.

Analyses excluding cancer patients
Contrary to expectations, only one patient whose bowel disorder had resulted from curative cancer treatment chose to proceed with ESGNS surgery during the study period. Since there are more cancer patients in the not-accepting surgery group [$n = 4$ (11%)] and in the not-offered surgery group [$n = 8$ (20%)], the above analyses for the main outcome measures were compared with similar analyses which excluded patients whose disorder was due to cancer.

Interview analyses
Analyses from semi-structured interviews will be reported separately.

Economic analyses
The economic analyses are described in Chapter 6.

Further details of the planned investigation at the time of application for HTA funding are contained in Appendix 2.

Chapter 4

Results: Royal London Hospital Prospective Outcomes Assessment Study

This chapter begins with a summary of outcomes for RLH ESGNS patients and patients from both comparison groups, followed by detailed descriptions of baseline and follow-up findings.

In order to simplify interpretation, we focus only on the RLH ESGNS and not-offered surgery groups in the detailed descriptions of baseline and follow-up findings for symptomatic and QoL outcome measures. Findings for the not-accepting surgery group are included in *Tables 42–50* in Appendix 1.

Summary of ESGNS outcomes at the Royal London Hospital and some comparisons with not-offered surgery and not-accepting surgery patient groups

ESGNS is a major, lengthy and complex procedure with a high level of morbidity and requires a high level of commitment from those who choose to proceed with it. ESGNS patients at RLH undergo several operations resulting in an average of nearly 12 hours of operating time per patient. Inpatient stays are lengthy. The time interval from the start of surgery to the completion of primary treatment is between 2.5 and 16 months. On average patients spent 35 days in hospital during this primary treatment phase. Covering stomas were formed at the time of graciloplasty in 23 of 27 patients who did not already have stomas. Of the total of 248 RLH admissions, for 48 patients over half were due to complications, the majority occurring after the end of primary treatment. The commonest hospitalised complications were related to evacuation difficulties or pain (33) and infective (31) or circuitry problems (23). Following completion of primary treatment, admissions to RLH resulted in an average of 20 inpatient bed days per patient during the study follow-up period.

At 3 years postoperation, three-quarters of RLH ESGNS patients were without stomas and had intact circuitry. At 4 years postoperation, this proportion was 57%.

Nearly two-thirds of RLH ESGNS patients experienced large improvements in the Cleveland Clinic incontinence scale and improved continence to solid and liquid stool at 2 years post-operation.

Evacuatory difficulties were a problem for approximately one-third of all ESGNS patients and were ongoing throughout the follow-up. Nearly half of all patients with satisfactory continence outcomes experienced frequent evacuatory difficulties.

Significantly more ESGNS patients than comparison patients deteriorated by ≥10% on the NHP pain scale at 2 years of follow-up. Although pain did appear to be a problem, particularly in the leg from which the gracilis muscle was harvested, there were similar proportions of patients in both comparison groups who experienced moderate or severe pain or discomfort throughout their 2-year follow-up period.

There were trends towards improvements in the median scores for the main condition-specific QoL outcome measures following ESGNS; these improvements increased over the first postoperative year and began to stabilise after 12 months. The trend was most marked and significant for the condition-specific RLH psychosocial and lifestyle impact scales, where nearly two-thirds of RLH ESGNS patients experienced large improvements at 2 years postoperation. The improvements for the surgery group appeared to be maintained at 3 and 4 years of follow-up, although numbers in the cohort are small by 4 years. The generic QoL measures did not indicate a significant improvement in general health status for the ESGNS group as a whole at 2 years postoperation, although there were wide variations between individuals and nearly half of the group experienced a moderate or large improvement as measured by the EQ-5D index of health status.[35] At 3 years post-operation there was a modest but significant improvement for the group as measured by this generic index.

The measures of psychological distress suggested that the majority of patients in all groups were not clinically anxious or depressed at baseline, although there were improvements in postoperative scores for the ESGNS group compared with the scores of the comparison groups at the same follow-up points. ESGNS patients' self-ratings of psychological distress indicated that they felt less anxious or depressed following surgery. There were also significant improvements for the ESGNS group in self-rated health status, impact of the bowel disorder on sexual activity and patients' satisfaction with life in general at 2 and 3 years post-operation.

The comparison groups (not-offered surgery and not-accepting surgery groups) showed very little change in any measures over the 2-year follow-up period. There were some differences between the ESGNS and comparison groups at baseline for the RLH psychosocial and lifestyle impact scales, with the ESGNS group being significantly more affected by their bowel disorders than those in the comparison groups. There were some indications of small improvements in a number of measures for the not-accepting surgery group at 1 year of follow-up; these improvements were not sustained at 2 years of follow-up and may reflect a transient beneficial effect following referral for specialist assessment.

Reassuringly, with the exception of the NHP pain scale, none of the main or secondary outcome measures indicated that ESGNS patients had worse outcomes than the comparison groups. There were no clear patterns of deterioration or improvement in any of the main measures in those for whom surgery had been clinically unsuccessful.

None of the findings were altered by reanalyses which excluded patients with congenital disorders or cancer. Whether patients had stomas or FI prior to surgery did not materially affect clinical, symptomatic, psychological or QoL outcomes.

Patients' expectations of success of surgery were significantly higher than their actual estimates of success of surgery in solving the bowel problems, when assessed at 2 years of follow-up. However, postoperative estimates of success indicated that half of the patients considered the surgery to have been highly successful (75% or more successful) throughout 4 years of follow-up, with some tail-off at 5 years of follow-up, although at this stage numbers were very small. Three-quarters of patients who were less than 3 years postoperation and 56% of those who were ≥ 3 years postoperation indicated that their bowel conditions were better or much better following surgery. In the early postoperative period none of the RLH patients expressed any regrets about having undergone the procedure.

Detailed results: Royal London Hospital Prospective Outcomes Assessment Study

Part 1: Clinical, symptomatic, psychological and quality of life outcomes

Recruitment to the London ESGNS group

In total, 57 patients underwent and completed ESGNS between April 1997 and December 2002. Fifty-one were treated at the RLH and six were treated at the London Independent Hospital. The total number of ESGNS procedures was 58 as one patient underwent a second ESGNS. All patients included in this report were aged ≥15 years at the time of surgery.

Of the 51 RLH patients, 47 were funded by the NSCAG surgical programme. The remaining four RLH patients were funded by their health authorities.

A total of 214 patients with refractory FI or stomas, who were aged ≥15 years, were assessed at RLH under the NSCAG-funded programme during the same 5.5-year period; 165 of these patients (77%) either had conditions that were not appropriate for ESGNS or they decided that they did not wish to proceed with the surgery.

As described in the section 'Patients' (p. 7), seven patients were excluded from the outcomes assessment study (*Table 1*), although clinical outcomes for five of them are included in *Figure 1* (p. 22), and three of them (NHS patients) are included in the economic analyses.

Of the 50 patients who were suitable to take part in the outcomes assessment, only one did not participate. One other patient who was in the early postoperative period agreed to participate, but has not returned any postoperative questionnaires. The outcomes for the remaining 48 ESGNS patients who have returned at least one postoperative questionnaire will be described in this chapter; of these 48, seven also underwent an additional procedure known as rectal augmentation, described in Chapter 1, which aims to reduce symptoms of urgency in patients with rectal hypersensitivity. The participating ESGNS

TABLE 4 *Questionnaire response rates: RLH ESGNS and not-offered surgery groups*

	Number of patients (% of group)							
	Baseline	**3–5 months**	**6–9 months**	**12 months**	**24 months**	**36 months**	**48 months**	**60 months**
RLH ESGNS group	49	49	47	45	40	31	23	12
Sent questionnaire[a]	45	46	47	45	40	29[b]	21	10
Returned questionnaire	45 (92)[c]	45 (92)	44 (94)	44 (98)	39 (98)	29 (94)	19 (83)	8 (75)
Not-offered surgery group	45	–	45	45	45	–	–	–
Sent questionnaire	45		45	44	40[d]			
Returned questionnaire	41 (91)[c]		39 (87)	36 (80)	32 (71)			

[a] 4 patients underwent ESGNS prior to the start of the outcomes assessment study.
[b] 2 patients dropped out.
[c] Amongst these, the numbers who returned at least one follow-up questionnaire were 44/45 of the ESGNS group and 40/41 of the not-offered surgery group.
[d] 5 previous non-responders not approached.

patients are referred to as the 'RLH ESGNS' group, although they include four patients who underwent surgery at the London Independent Hospital. The same surgical team carried out all operations.

Not-offered surgery group
Seventy patients with refractory FI or stomas, who had never been referred for consideration of ESGNS, were approached by letter through their GPs and agreed to join the not-offered surgery group. Forty-five (64%) agreed to take part in the study. Forty (57% of those approached) have returned questionnaires at baseline and on at least one further occasion. The not-offered surgery group is considered to be the main comparison group.

Not-accepting surgery group
Sixty-eight patients who had been offered ESGNS surgery, but had decided not to proceed with the surgery during the period April 1997 to March 2001, were invited to join the not-accepting surgery group. These 68 patients do not represent the entire group of people who decided not to proceed, since some were still undergoing assessment or were in the process of decision-making at the recruitment cut-off time. Forty-two (62%) agreed to participate and 38 (56%) of them have returned questionnaires at baseline and on at least one further occasion. A number of patients in the not-accepting surgery group underwent alternative treatments during the study period; two had colonic conduits formed to aid regular evacuation of the bowel, four had permanent stomas formed and one underwent formation of an artificial bowel sphincter and closure of colostomy.

Comparative findings for the not-accepting surgery group are contained in *Tables 42–50* in Appendix 1.

Questionnaire response rates
Table 4 summarises the questionnaire response rates in the ESGNS and not-offered surgery groups.

Length of follow-up
The mean length of follow-up for the RLH ESGNS patients was 39 months and ranged between 4 and 71 months. Two-thirds of patients were at least 3 years postoperation at the time of writing this report (September 2003). Both comparison groups were followed for 2 years.

Baseline observations
Demographics
The RLH ESGNS and not-offered surgery groups were similar in terms of gender and the length of time that the patients had lived with their disorders. The not-offered surgery group were older than the RLH ESGNS group ($p = 0.06$). Approximately half of all non-stoma patients in each group had undergone one or more previous operations which were intended to alleviate their incontinence (*Table 5*).

There were significant differences between the ESGNS and the not-offered surgery groups in terms of the causes of the bowel disorders ($p = 0.01$). Obstetric trauma accounted for 50% of the ESGNS group and 30% of the not-offered surgery group. Only one cancer patient chose to proceed with ESGNS, whereas 20% of the not-offered surgery group were cancer patients. Congenital disorders accounted for 13% of the

TABLE 5 *Baseline characteristics RLH ESGNS group and not-offered surgery group*

Characteristic	RLH ESGNS group[a]	Not-offered surgery group[a]	*p*-Value for between-groups difference
Number who have responded on at least one occasion after baseline (%)	48 (96)	40 (89)	–
Age on recruitment (**years**)			
<20	4 (8)	4 (10)	
20–39	14 (29)	8 (20)	
40–64	28 (58)	20 (50)	
65+	2 (4)	8 (20)	
Mean	42	49	0.06[b]
Range	15–71	16–81	
Gender			
Male	12 (25)	10 (25)	0.60[c]
Female	36 (75)	30 (75)	
Cause of disorder			
Congenital	6 (13)	9 (23)	0.01[c]
Cancer	6 (13)	8 (20)	
Obstetric trauma	24 (50)	12 (30)	
Other trauma/neuropathic/idiopathic	17 (35)	10 (25)	
Stoma on recruitment			
Yes	18 (38)	21 (53)	0.12[c]
No	30 (63)	19 (47)	
Number of years with disorder (**median**)			
Congenital disorders	20	20	0.9[d]
Acquired disorders	5	5	0.99[d]
Previous incontinence-related operations (**non-stoma patients**)	$n = 30$	$n = 13$	
Yes	14 (47)	6 (46)	0.62[c]
No	16 (53)	7 (54)	
Not interviewed	–	6	

[a] Number (%) unless indicated otherwise.
[b] Student's *t*-test.
[c] χ^2 test.
[d] Mann–Whitney *U*-test.

ESGNS group compared with 23% of the not-offered surgery group.

Over half of the not-offered surgery group had stomas compared with 38% of the ESGNS group ($\chi^2 = 2$, $p = 0.2$) (*Table 5*).

Removal of the cancer patients renders the groups more comparable by cause of disorder ($\chi^2 = 1.6$, $p = 0.2$).

Baseline symptoms

Continence. Continence symptoms and scores can only be assessed in those patients who did not have stomas on recruitment to the study. The groups were similar in terms of frequency of incontinence to solid or liquid stool. Worryingly, one ESGNS patient reported no episodes of FI prior to surgery, although this patient reported the need to wash the perianal area in order to avoid soiling following defaecation (*Table 6*).

Evacuation. To repeat, we have defined evacuatory difficulty as any one or more of the following required to achieve evacuation: straining for more than 20 minutes, use of enemas, rectal irrigation, digitation or suppositories. Although this question was not asked of earlier patients at baseline, evacuatory difficulties were infrequently reported in those who were asked, in either the ESGNS or not-offered surgery group (*Table 6*).

Pain. There were no significant differences between groups for either the NHP pain scale or the EQ-5D pain or discomfort domain at baseline (*Table 6*).

TABLE 6 *Baseline symptoms: incontinence, evacuation and pain for the RLH ESGNS and not-offered surgery groups*

Symptoms	RLH ESGN group[a]	Not-offered surgery group[a]	*p*-Value for between-groups difference
Frequency of incontinence to solid or liquid stool	*n* = 48	*n* = 40	
Never	1 (2)	0 (0)	0.08[b]
< 1/month	0 (0)	2 (5)	(non-stoma patients
< 1/week	3 (6)	6 (15)	only)
≥ 1/week	6 (13)	5 (13)	
Daily	20 (42)	6 (15)	
Stoma	18 (38)	21 (53)	
Cleveland Clinic incontinence score **(based on respondents without stomas). Scale: 0–20, 20 = worst**	*n* = 27	*n* = 19	
Median score	14	11	
Inter-quartile range	11.5 16	7 14	0.11[c]
Number (%) with score 9+	24 (89)	14 (74)	
Frequency of evacuatory difficulties[d]	*n* = 37	*n* = 39	
Never	14 (38)	10 (26)	0.17[b]
< 1/month	2 (5)	2 (5)	(non-stoma patients
< 1/week	0 (0)	1 (3)	only)
≥ 1/week	0 (0)	2 (5)	
Daily	1 (2)	2 (5)	
Colonic conduit	2 (5)	1 (3)	
Stoma	18 (49)	21 (54)	
NHP pain scale. **Scale: 0–100, 0 = best**	*n* = 44	*n* = 39	
Median score	0	0	0.60[c]
Inter-quartile range	0 23	0 24	
Number (%) at floor (best health)	26 (58)	21 (54)	
Population mean score adjusted for age and gender	*5.7*	*7.4*	
EQ-5D pain/discomfort domain	*n* = 43	*n* = 39	
Number (%) of patients reporting moderate or severe pain or discomfort	31 (72)	25 (64)	0.30[b]
% *of general UK population reporting moderate or severe pain or discomfort*	*33*	*33*	

[a] Number (% of respondents) unless stated otherwise.
[b] χ^2 test.
[c] Mann–Whitney *U*-test.
[d] Question added after start of study.

Baseline quality of life and psychological distress

Generic measures at baseline. The ESGNS and not-offered surgery groups had similar baseline scores for the EQ-5D population-weighted index; both groups had median scores which were substantially poorer than the age- and gender-adjusted UK population mean scores. Approximately one-third of RLH ESGNS and not-offered surgery groups had *z* scores of ≤–2 when compared with the population scores, indicating extremely low (poor) scores. The EQ-5D population-weighted index[35] is based on five domains and the proportions of patients indicating moderate or severe problems in each domain were similar in all groups, with the exception of 'performing usual activities', where 74% of ESGNS group reported moderate or severe problems compared with 59% of the not-offered surgery group (between-groups difference, $p = 0.02$). The responses in all EQ-5D domains from all patient groups indicated more moderate or severe problems than would be expected in the general UK population, and this was most marked in the usual activities and anxiety and depression domains.

The NHP social isolation scale is reported despite its considerable floor effects; 42% of the ESGNS groups and over half of the not-offered surgery group had baseline scores at the best possible level. The population-adjusted mean score is close to the floor (0) value for all groups, indicating that this is a measure of severe distress (*Table 7*).

Psychological distress at baseline. The HADS indicated that the median scores for both groups were within the mild range for anxiety and within the normal range for depression.

Patients' self-ratings of psychological distress as recorded in the EQ-5D domain 'anxiety or depression' indicated that approximately two-thirds of both groups felt that they suffered moderate or severe anxiety or depression, compared with 21% of the general UK population. These findings are in contrast with those of the HADS scales, which give an indication of clinical anxiety or depression (*Table 7*).

Impact of the bowel disorder at baseline. The locally devised measure of impact of the bowel disorder was the only main measure to demonstrate differences between the two groups. The ESGNS group had markedly poorer baseline scores than the not-offered surgery group on both the psychosocial and lifestyle impact scales (*Table 7*).

ESGNS patients' expectations of success of surgery

ESGNS patients were asked (preoperatively) to predict how successful the surgery would be in solving their bowel problems. This question was added after the start of the study and 36 patients were asked to make the prediction. All were optimistic and expectations of success of surgery ranged between 60 and 100% with a median prediction that the surgery would be 80% successful (*Table 7*).

Clinical outcomes

Clinical success

Success was defined as the presence of functioning circuitry and the absence of a stoma at the end of the study period. A Kaplan–Meier 'success' curve shows the cumulative probability of success up to 6 years postoperation. This curve includes all patients who underwent ESGNS at RLH or the London Independent Hospital during the study period, regardless of whether they met the criteria for inclusion in the outcomes assessment study (two patients who underwent total anorectal reconstruction at the time of rectal cancer excision remain excluded) (see *Table 1*). Censored observations reflect the cohort effect and are due to patients reaching the end of the study period with varying periods of follow-up. This is a purely clinical definition of success and makes no reference to patient-based outcome measures (*Figure 1*).

Of the 55 patients who underwent surgery, 20 were considered clinical failures. The cumulative success proportion at 2 years postoperation was 75% [95% confidence interval (CI): 63 to 87%), at 3 years it was 73% (95% CI: 61 to 85%) and at 4 years it was 57% (95% CI: 41 to 73%).

Patients whose disorders are caused by anorectal agenesis (congenital anomalies) pose awkward surgical challenges. The outcomes for this group were poor, with two-thirds of procedures failing during the study period. However, since the group is small, it is not surprising that analyses of clinical success proportions are not materially changed when such patients are excluded.

Clinical failure

The outcomes for 20 patients out of the 55 (32%) who met the surgical inclusion criteria were defined as clinical failures as above. The median time to failure was 21 months; however, clinically defined failures occurred at all times during the

TABLE 7 *Baseline quality of life, anxiety and depression and patients' predictions of success of surgery for the RLH ESGNS and not-offered surgery groups*

Measure	RLH ESGNS[a]	Not-offered surgery group[a]	% general UK population reporting moderate or severe problems	*p*-Value for between-groups difference
EuroQol (EQ-5D) **weighted index of health status. Scale 0–1, 1 = best health (negative scores are possible)**	*n* = 43	*n* = 39	–	
Median	0.69	0.69		0.50[b]
Inter-quartile range	0.59–0.81	0.62–0.85		
Number (%) at floor (best health)	5 (11)	8 (21)		
Population mean score adjusted for age and gender	*0.88*	*0.85*		
Number (%) with *z* scores of ≤ –2 (extreme low) when compared with the population score adjusted for age and gender	15 (34)	12 (30)		0.70[c]

continued

TABLE 7 *Baseline quality of life, anxiety and depression and patients' predictions of success of surgery for the RLH ESGNS and not-offered surgery groups (cont'd)*

Measure	RLH ESGNS[a]	Not-offered surgery group[a]	% general UK population reporting moderate or severe problems	*p*-Value for between-groups difference
EQ-5D categories: **number (%) who report moderate or severe problems**	*n* = 43	*n* = 39	–	
Mobility	16 (37)	17 (43)	19	0.55[c]
Self-care	7 (16)	6 (15)	4	0.91
Anxiety/depression	30 (70)	26 (67)	21	0.77
Pain/discomfort	31 (72)	25 (64)	33	0.44
Usual activities	32 (74)	23 (59)	16	0.14
NHP social isolation scale. **Scale 0–100, 0 = best**	*n* = 44	*n* = 40	–	
Median score	20.2	0		0.58[b]
Inter-quartile range	0–44	0–42		
Number (%) at floor (best health)	19 (42)	22 (55)		
Population mean score adjusted for age and gender	*4.7*	*5.3*		
HADS. Anxiety score. **Scale 0–7 = normal, 8–10 = mild, 11–14 = moderate, 15–21 = severe**	*n* = 44	*n* = 40	–	
Median score	9.0	8.0		0.20[b]
Inter-quartile range	6.8–10.9	4.3–11		
Number (%) at floor (best health)	1 (2)	3 (7)		
HADS anxiety categories, number (%) in each range				
Normal	14 (32)	19 (48)		0.20[c]
Mild	12 (27)	9 (23)		
Moderate	14 (32)	6 (15)		
Severe	4 (9)	6 (15)		
HADS. Depression score	*n* = 44	*n* = 40	–	
Median score	6.8	4		0.21[b]
Inter-quartile range	2.3–10.9	2.3–9.8		
Number (%) at floor (best health)	0	4 (10)		
HADS depression categories, number (%) in each range				
Normal	27 (61)	28 (70)		0.67[c]
Mild	6 (14)	4 (10)		
Moderate	9 (21)	5 (13)		
Severe	2 (5)	3 (8)		
RLH bowel-specific measure. Psychosocial impact **Scale 0–10, 0 = best health**	*n* = 41	*n* = 39	–	
Median score	4.8	3.3		
Inter-quartile range	2.9–7.3	0.3–6.5		0.05[b]
Number (%) at floor (best health)	1 (2)	5 (13)		
Number (%) above overall median (= 4.2)	26 (63)	19 (49)		
RLH bowel-specific measure. Lifestyle impact	*n* = 44	*n* = 39	–	
Median score	7.3	4.1		0.001[b]
Inter-quartile range	5.3–7.9	1.9–6.8		
Number (%) at floor (best health)	0	1 (3)		
Number (%) above overall median (= 5.8)	30 (68)	13 (33)		
Patients' predictions of success of surgery in solving their bowel problems (0–100%)	*n* = 36[d]	–	–	–
Median prediction (%)	80			
Inter-quartile range (%)	78–100			

[a] Number (%) unless indicated otherwise.
[b] Mann–Whitney *U*-test.
[c] χ^2 test.
[d] Question added after start of study.

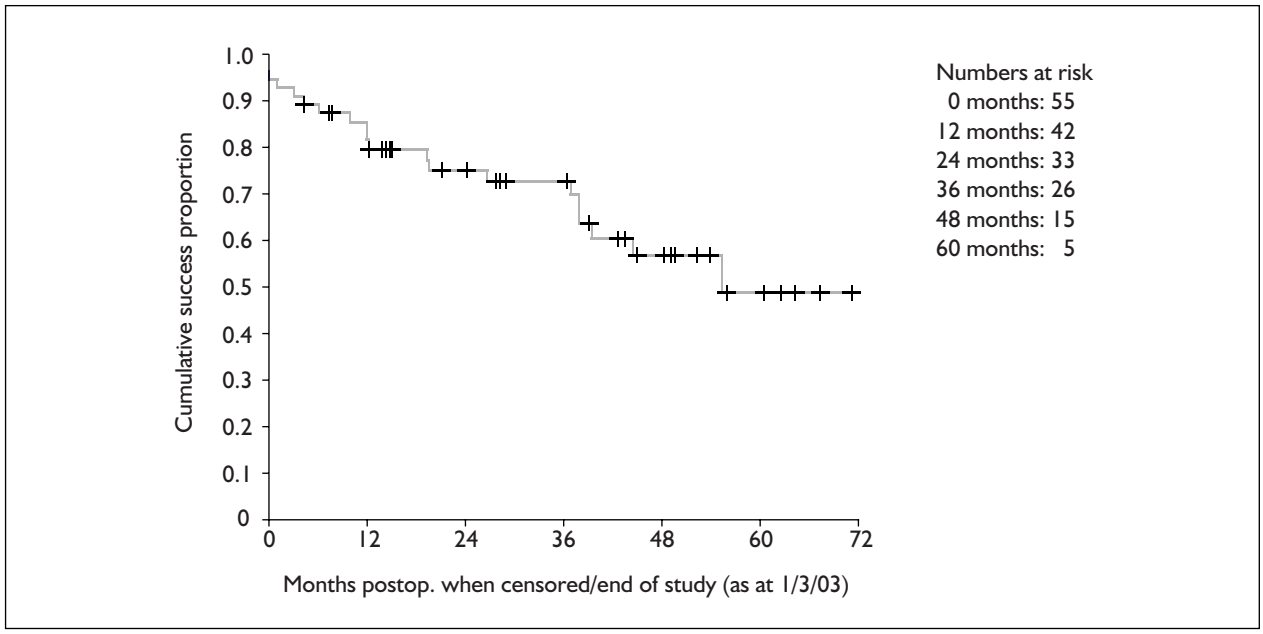

FIGURE 1 *Kaplan–Meier plot for all RLH ESGNS patients at 1 March 2003 (*n *= 55, failures = 20). 'Success' curve (functioning neosphincter, no stoma). Line, survival function; +, censored.*

follow-up period. It should be noted, however, that the times allocated to 'failure' represent the time of operation to remove circuitry or to form a stoma and may be later than the time when the patient first recognised that the operation had failed. The term clinical failure does not necessarily imply that the operation was not 'technically' successful.

Events leading to clinical failure were usually multiple and included evacuation difficulty in nearly half of the failed cases. Other causes included perianal pain, sepsis, circuitry problems and ongoing faecal soiling.

Clinical failure occurred in nine (41%) of those who had stomas prior to ESGNS and in 11 (33%) of the non-stoma cases. Fourteen patients, whose ESGNS surgery resulted in clinical failure, went on to have permanent end-stoma formation (*Table 8*).

Clinical failure occurred in 67% of patients with congenital disorders, in 35% of those with disorders caused by obstetric trauma and in 26% of those with other causes of their disorders.

Symptomatic outcomes

Continence

There was little change in frequency of incontinence to solid or liquid stool for the not-offered surgery group over the 2-year follow-up period. However, there was a significant improvement for the ESGNS group. This improvement was maintained in those who have reached 3 years postoperation (*Table 9*). Assessment of the RLH patient group from 6 months to 4 years of follow-up reveals that at all follow-up points, between 59 and 65% are either never incontinent to solid or liquid stool or they are incontinent less than once per week (*Table 10*). Nearly half of the patients remain incontinent to flatus several times daily and one-quarter are incontinent to flatus several times per week.

For those without stomas prior to ESGNS or on recruitment, the Cleveland Clinic incontinence score shows large (>20%) and significant improvements for the ESGNS group at 2 and 3 years post-operation, whereas no significant changes were seen in either comparison group at 2 years of follow-up. Some 58% of the ESGNS patients without stomas at 24 months postoperation have scores of ≥9; this compares with 77% of the not-offered surgery group at the same follow-up stage.

ESGNS patients who had stomas preoperation were no different from those who did not in terms of continence to solid or liquid stool or the Cleveland Clinic scores at any follow-up point between 6 months and 4 years postoperation.

Evacuation

Approximately one-third of ESGNS patients suffered with evacuatory difficulties either daily or at least once per week at all stages following surgery. A small number of patients had colonic

TABLE 8 *RLH ESGNS clinical failures: events leading to failure by time of failure*[a]

Time of failure (months post-op)	Number (total = 20)	Pre-ESGN state	Cause/pre-ESGN surgery	Event leading to failure	Outcome
0–3	1	FI	Obstetric trauma	Evacuation difficulty	Stoma
	1	FI	Obstetric trauma	Perianal sepsis, failure of advancement flap repair	Stoma
	1	Stoma	Congenital	Insufficient bowel remaining for anastomosis	Stoma
	1	Stoma	Other trauma	Spinal injury rendered neural stimulation impossible	Stoma
	1	Stoma	Congenital	Severe anal pain and evacuation difficulty	Stoma
4–5	1	FI	Obstetric trauma	Severe anal pain and evacuation difficulty	Stoma
	1	FI	Obstetric trauma	Repeated circuitry problems, evacuation difficulty	ACE procedure, removal of circuitry
6–11	1	FI	Obstetric trauma	Uncertain (non-participant in evaluation, stoma formed at other hospital)	Stoma
	1	Stoma	Congenital	Evacuation and irrigation difficulty (antegrade continence enema) and soiling	Stoma
	1	Stoma	Obstetric trauma	Severe anal pain, evacuation difficulty	Removal of circuitry
	1	FI	Congenital	Soiling	Removal of circuitry
12–23	1	FI	Obstetric trauma	Repeated episodes of subacute obstruction, severe evacuation difficulty, urgency and soiling	Stoma
	1	FI	Obstetric trauma	Initial ESGN had circuitry problems, second leg ESGN unsuccessful – pain and evacuatory difficulty	Stoma
24–35	1	Stoma	Other trauma	Sepsis in circuitry	Removal of circuitry
36–47	1	FI	Congenital	Soiling	Stoma
	1	Stoma	Congenital	Soiling, excoriation of perineum	Stoma
	1	FI	Obstetric trauma	Severe evacuation difficulties and leaking	Stoma
	1	Stoma	Other trauma	Abdominal trauma caused lead fracture, previous good outcome. Sepsis occurred in replacement circuitry	Removal of circuitry
	1	FI	Other trauma	Pain and evacuatory difficulty	Removal of circuitry
48–59	1	Stoma	Obstetric trauma	Soiling following post-ESGNS trauma, had previously had good outcome	Stoma

[a] 'Failure' is stoma or removal of circuitry at end of study period.

TABLE 9 *Frequency of incontinence to solid or liquid stool: RLH ESGNS and not-offered surgery groups*

	RLH ESGNS group[a]				Not-offered surgery group[a]	
	Preop.	**24 months postop.**	**Preop.**	**36 months postop.**	**Baseline**	**24 months post-recruitment**
Total number of respondents	37	37	27	27	35	35
number of respondents (% of total)						
Never/<once per week	2 (5)	23 (62)	1 (4)	17 (63)	8 (23)	7 (20)
Several times per week	5 (14)	7 (19)	4 (15)	6 (22)	3 (9)	3 (9)
Daily/stoma	30 (81)	7 (19)[b]	22 (81)	4 (15)[b]	24 (69)	25 (71)[c]

[a] McNemar's test for within-group changes.
[b] $p < 0.0001$ (RLH ESGNS group).
[c] $p = 1.0$ (not-offered surgery group).

TABLE 10 *Frequency of incontinence to solid or liquid stool, preoperation to 4 years postoperation: RLH ESGNS group (cross-sectional data)*

	Preop.	**6–9 months postop.**	**12 months postop.**	**24 months postop.**	**36 months postop.**	**48 months postop.**
Number of respondents (% of total)	48 (100)	46 (94)	43 (96)	37 (93)	27 (87)	22* (96)
Number (% of respondents)						
Never/<1/week	4 (8)	25 (54)	27 (65)	23 (62)	17 (63)	13 (59)
>1/week	6 (13)	9 (20)	9 (21)	7 (19)	6 (22)	1 (5)
Daily/stoma	38 (79)	12 (26)	6 (14)	7 (19)	4 (15)	8[a] (36)

[a] Includes 3 non-responders known to have stomas at this stage.

TABLE 11 *Frequency of evacuatory difficulties: RLH ESGNS group (cross-sectional data)*[a]

Frequency of evacuatory difficulty	**6–9 months postop.**	**12 months postop.**	**24 months postop.**	**36 months postop.**	**48 months postop.**
Number of respondents (% of total)	39 (87)	39 (87)	36 (90)	27 (87)	21* (91)
Number (% of respondents)					
Never/<once per week	14 (36)	17 (43)	15 (41)	12 (45)	7 (33)
Several times per week	5 (13)	6 (15)	2 (6)	2 (7)	1 (5)
Daily	8 (21)	6 (15)	11 (31)	7 (26)	5 (24)
Colonic conduit	5 (13)	5 (13)	4 (11)	3 (11)	2 (10)
Stoma	7 (18)	5 (13)	4 (11)	3 (11)	6[b] (29)

[a] Evacuatory difficulty is defined as any one or more of the following required to achieve evacuation: straining for more than 20 minutes, use of enemas, rectal irrigation, digitation or suppositories.
[b] Includes 3 non-responders known to have stomas at this stage.

conduits formed to enable evacuation to occur by means of irrigation through a channel from the abdominal wall into the colon (*Table 11*).

In those patients who had a 'satisfactory' continence outcome (never incontinent or incontinent less than once per week) at 2 years postoperation, the result was marred by at least weekly evacuatory difficulties in 48% and daily problems in 30%; a similar effect was seen at 3 years of follow-up.

At 2 years of follow-up, the proportion of not-offered surgery patients with daily or weekly evacuatory problems remained small.

Pain or discomfort
When grouped into quintiles, there is very little difference between NHP pain scores for the ESGNS and not-offered surgery groups at 2 years of follow-up, with ~20% of patients in all three groups scoring in the range 50–100 (100 = worst score). At 3 years postoperation the upper quintile for the ESGNS group represented scores ranging from 49 to 70. There were no significant between-group differences on comparing changes in scores for the NHP pain scale at 2 years from baseline.

At 2 years of follow-up, the EQ-5D pain/discomfort categories demonstrated almost identical changes for all patient groups; overall 15% worsened, 15% improved and the remainder stayed the same.

When the ESGNS patients were asked directly about pain associated with the bowel disorder or the surgery at 2 years postoperation, two-thirds said that they had experienced pain during the previous month with intensity during the previous week ranging between 1 and 10 with an average of 5 (10 = worst). The commonest sites of pain were the leg from which the gracilis muscle had been harvested and in the groin/anus. At 3 years postoperation, 56% had experienced pain during the previous month; the intensity ranged between 1 and 8 with an average of 4.5 and the commonest sites remained the leg and groin/anus. This question was not asked of comparison group patients.

For many ESGNS patients, pain was associated with the effect of the stimulator being switched on. When patients were asked about their use of the stimulator at 2 years postoperation, six (15%) had been removed (one owing to pain), six (15%) were not using the stimulators at all (one owing to pain, three because it was not needed and two for temporary technical reasons) and 13 (33%) either switched it off at night, or during the day for varying periods, or both, in order to alleviate pain.

Changes in quality of life and psychological distress over time
Although the baseline and follow-up scores for the main outcome measures are not normally distributed, the paired within-person differences between baseline and 2 and 3 years of follow-up closely approximate to the normal for each patient group for most main measures. Hence scores are shown as medians, and differences between scores at baseline and later follow-up points are shown as means (95% CIs). Parametric and non-parametric statistical methods are chosen according to data distributions.

Generic measures
There was a small, non-significant improvement in the EQ-5D weighted index of health status, on comparing the preoperative score with 2 years of follow-up for the RLH ESGNS group (mean improvement, 7%; 95% CI: –3 to +18%); this improvement was not significantly different from changes in scores for either comparison group (*Table 12* and *Table 47* in Appendix 1). The age- and gender-adjusted UK normative value for all three patient groups was 0.86; at baseline, the median score for the ESGNS group was 0.69 and at 2 years of follow-up it was 0.76.

At 3 years postoperation the ESGNS group showed a moderate mean improvement in EQ-5D score of 11% (95% CI: 2 to 20%) (*Table 12*).

At 2 years of follow-up, 31% of the ESGNS group had improved in the usual activities domain of the EQ-5D compared with 6% of the not-offered surgery groups. At 3 years, 46% of the ESGNS group had improved in this domain and 46% reported any problem at this stage. There were no significant within-group changes in mobility or self-care at 2 years (all groups) and at 3 years (ESGNS group only). Pain and anxiety and depression domains are reported in the sections below on symptomatic outcomes and psychological distress.

The NHP social isolation scale also showed a non-significant improvement for the ESGNS group at 2 years postoperation, although there was no significant difference between groups in change in scores at this stage. A small and significant improvement was seen for the ESGNS group at 3 years postoperation (*Table 12*).

Changes at 12 months of follow-up closely resemble those seen at 24 months of follow-up in both study groups.

Changes in psychological distress
At 2 years of follow-up, a small improvement in the HADS anxiety score was seen for the ESGNS group. A small, non-significant deterioration occurred in the not-offered surgery group and the between-group difference in change in scores was significant ($p = 0.03$). A significant within-group improvement of 11% was seen for the ESGNS group at 3 years postoperation (*Table 12*). Prior to surgery, 37% of the ESGNS group were within the normal range for anxiety; this proportion increased to 63% at 2 years postoperation and to 71% at 3 years postoperation; the main shift being of patients who were mildly anxious prior to

TABLE 12 *Percentage changes in main outcome measures at 12, 24 and 36 months of follow-up: RLH ESGNS and not-offered surgery groups*

Measure	Mean changes compared with baseline (95% CI)[a]					Between-group differences in change in score at 24 months: *p*-values (Student's *t*-test)
	RLH ESGNS group			Not-offered surgery group		
	12 months *n* = 37–40	24 months *n* = 30–35	36 months[b] *n* = 23–24	12 months *n* = 34–36	24 months *n* = 28–32	
Cleveland Clinic incontinence score	*n* = 23 +5 (+2 to +7)	*n* = 17 +24 (+11 to +37)	*n* = 13 +25 (+16 to +35)	*n* = 13 –1 (–3 to +1)	*n* = 13 –8 (–19 to +3)	0.001
EQ-5D weighted index of health status	+4 (–5 to +13)	+7 (–3 to +18)	+11 (+2 to +20)	–1 (–8 to +5)	+7 (–3 to +16)	0.92
NHP pain scale	–8 (–18 to +7)	–0.3 (–0.6 to 0)	0 [–13 to 0][c]	–6 (–13 to +2)	0 (–0.2 to +0.2)	0.21[d]
NHP social isolation	+12 (+3 to +20)	+10.2 (+0.4 to +21)	+6 [0 to +22][c]	0 (0 to +23)	+2 (–4 to +9)	0.07[d]
HADS anxiety	+8 (–1 to +16)	+9 (+0.1 to +17)	+11 (+2 to +19)	–2 (–6 to +2)	–3 (–9 to +3)	0.03
HADS depression	+7 (–1 to +16)	+6.0 (–3 to +15)	+18 (+10 to +26)	–5 (–1 to –8)	–4 (–8 to +1)	0.05
RLH psychosocial scale	+28 (+19 to +38)	+26 (+16 to +36)	+34 (+24 to +44)	+0.2 (–6 to +7)	+0.1 (–8 to +8)	<0.0001
RLH lifestyle scale	+36 (+26 to +46)	+31 (+19 to +43)	+40 (+28 to +52)	–4 (–10 to +2)	–3 (–11 to +5)	<0.0001

[a] Positive changes = improvements in scores.
[b] RLH ESGNS group only (not-offered surgery group followed for 24 months only).
[c] Medians and 95% CIs of the medians are shown for the NHP pain and social isolation scale at 36 months of follow-up owing to non-normality of distributions.
[d] Mann–Whitney *U*-test.

TABLE 13 *HADS anxiety and depression categories: RLH ESGNS and not-offered surgery groups*

	RLH ESGNS group				Not-offered surgery group	
	Preop.	**24 months postop.**	**Preop.**	**36 months postop.[a]**	**Baseline**	**24 months post-recruitment**
Number of respondents (% of total)	35	35	24	24	32	32
HADS anxiety ranges[b]						
Normal	13 (37)	22 (63)	9 (38)	17 (71)	17 (53)	16 (50)
Mild	10 (29)	3 (9)	8 (33)	3 (13)	7 (22)	7 (22)
Moderate	10 (29)	8 (23)	6 (25)	3 (13)	5 (16)	5 (16)
Severe	2 (6)	2 (6)	1 (4)	1 (4)	3 (9)	4 (13)
HADS depression ranges[b]						
Normal	22 (63)	23 (66)	17 (71)	21 (88)	24 (75)	23 (72)
Mild	5 (14)	7 (20)	3 (13)	3 (13)	4 (13)	4 (13)
Moderate	6 (17)	3 (9)	3 (13)	0	2 (6)	4 (13)
Severe	2 (6)	2 (6)	1 (4)	0	2 (6)	1 (3)

[a] RLH ESGNS group only (not-offered surgery group followed for 24 months only).
[b] Number (%)

surgery, there were no perceptible trends for change within the not-offered surgery group at 2 years of follow-up (*Table 13*).

The HADS depression score showed a small, non-significant mean improvement for the ESGNS group and the between-group difference in change in scores was significant at 2 years of follow-up ($p = 0.05$). A significant improvement in scores of 18% was seen at 3 years postoperation for the ESGNS group (*Table 12*). At baseline, approximately two-thirds of patients in both ESGNS and not-offered surgery groups were within the normal range for depression; at 2 years postoperation there was a small improvement for the ESGNS group and a small deterioration for the not-offered surgery group. At 3 years postoperation, 88% of ESGNS patients were within the normal range and the remainder were mildly depressed (*Table 13*). This finding was continued at 4 years postoperation, although the cohort with completed measures at all follow-up points is much smaller (results not shown, $n = 15$).

Changes at 12 months of follow-up closely resemble those seen at 24 months in both the ESGNS and not-offered surgery groups.

There were significant within-group changes for the ESGNS group at 2 years postoperation for the EQ-5D anxiety and depression domain ($p = 0.002$) and at 3 years postoperation ($p = 0.003$). There were no significant within-group changes for the not-offered surgery group at 2 years of follow-up. Nearly three-quarters of ESGNS patients classified themselves as being moderately or severely anxious or depressed prior to surgery, compared with 41% at 2 years postoperation and 38% at 3 years postoperation (results not shown).

Changes in impact of the bowel disorder

At 1, 2 and 3 years of follow-up, large (>20%) and significant improvements are seen within the ESGNS group in the RLH psychosocial impact and lifestyle impact scales (*Table 12*). The not-offered surgery group did not change significantly on either scale at 1 and 2 years of follow-up. The between-group differences in change in scores at 2 years are highly significant.

The improvements in scores for the ESGNS group appear to be maintained at 4 years postoperation, although numbers with completed measures at all follow-up points to 4 years are small (results not shown, $n = 13$).

Changes in secondary outcome measures

Table 45 in Appendix 1 shows median scores for the secondary outcomes measures at 2 years of follow-up, with the exceptions of the PAIS scales, for which the numbers of completed questionnaires are very small. Median values and 95% CIs of the medians are shown for changes in scores on these scales because of their generally skewed distributions. The EQ-5D visual analogue scale ('thermometer') for self-rating of health state has improved by a median of 11% in the ESGNS groups and not at all in the not-offered surgery group (between-group comparison of change in score, $p = 0.06$). A similar change is seen for the

TABLE 14 *Percentage of patients with ≥ 10% improvement at 2 years of follow-up: main outcome measures*

Measure	RLH ESGNS clinical 'successes'	RLH ESGNS clinical 'failures'	All RLH ESGNS patients	Not-offered surgery group	*p*-Value[a]
Cleveland Clinic incontinence score[b]					
Number of patients	15	2	17	13	0.001
% with 10–19% improvement	13	0	12	8	
% with ≥ 20% improvement	67	50	65	8	
EQ-5D					
Number of patients	28	7	35	29	0.30
% with 10–19% improvement	14	14	14	14	
% with ≥ 20% improvement	36	14	31	14	
NHP pain					
Number of patients	27	7	34	30	0.92
% with 10–19% improvement	11	0	9	7	
% with ≥ 20% improvement	7	14	9	10	
NHP social isolation					
Number of patients	28	7	35	30	0.11
% with 10–19% improvement	7	0	9	3	
% with ≥ 20% improvement	39	14	34	13	
HADS anxiety					
Number of patients	28	7	35	32	0.002
% with 10–19% improvement	11	14	9	6	
% with ≥ 20% improvement	32	14	34	3	
HADS depression					
Number of patients	28	7	35	32	0.02
% with 10–19% improvement	25	14	23	3	
% with ≥ 20% improvement	18	0	14	9	
RLH psychosocial impact scale					
Number of patients	23	7	30	31	0.003
% with 10–19% improvement	13	29	17	10	
% with ≥ 20% improvement	61	43	57	19	
RLH lifestyle impact scale					
Number of patients	26	7	33	31	<0.0001
% with 10–19% improvement	15	0	12	10	
% with ≥ 20% improvement	65	57	64	19	

[a] χ^2 test comparing those who improved by ≥ 10% in the total ESGNS group and in the not-offered surgery group.
[b] Only applies to patients who did not have stomas at either baseline or 2 years of follow-up.

NHP emotional reaction scale, where the difference in change in score between the ESGNS and not-offered surgery group is significant ($p = 0.03$). A 20% improvement in the RLH 'effect on my sex life' item is seen in the ESGNS group. A marked improvement (43%) occurred for the ESGNS group in the patients' ratings of satisfaction with life in general and this is significantly greater than that seen in the not-offered surgery group. Other secondary outcome measures have median values of zero for change in score over the 2-year period for all groups.

At 3 years postoperation, the RLH ESGNS group demonstrated large and significant improvements in the EQ-5D self-rated VAS score, the NHP emotional reaction scale, the RLH 'impact on sex life' item and patients' ratings of satisfaction with life in general. There was a moderate improvement in the NHP sleep scale and no significant changes in the NHP physical mobility and energy scales (*Table 48*, Appendix 1).

Proportions of patients who improve or deteriorate over 2–3 years of follow-up

The above analyses included all the selected ESGNS patients regardless of clinical outcomes. Since failure of ESGNS may result in either stoma formation or removal of circuitry whilst leaving a transposed gracilis muscle in place and may have

TABLE 15 *Percentage of patients with ≥ 10% deterioration at 2 years of follow-up: main outcome measures*

Measure	RLH ESGNS clinical 'successes'	RLH ESGNS clinical 'failures'	All RLH ESGNS patients	Not-offered surgery group	*p*-Value[a]
Cleveland Clinic incontinence score[b]					
Number of patients	15	2	17	13	0.04
% with 10–19% deterioration	7	0	6	23	
% with ≥ 20% deterioration	0	50	6	23	
EQ-5D					
Number of patients	28	7	35	29	0.51
% with 10–19% deterioration	0	0	0	10	
% with ≥ 20% deterioration	14	43	20	10	
NHP pain					
Number of patients	27	7	34	30	0.03
% with 10–19% deterioration	4	0	3	0	
% with ≥ 20% deterioration	33	29	32	10	
NHP social isolation					
Number of patients	28	7	35	30	0.67
% with 10–19% deterioration	0	14	3	3	
% with ≥ 20% deterioration	11	29	14	10	
HADS anxiety					
Number of patients	28	7	35	32	0.83
% with 10–19% deterioration	4	0	3	9	
% with ≥ 20% deterioration	7	29	11	9	
HADS depression					
Number of patients	28	7	35	32	0.41
% with 10–19% deterioration	14	14	14	3	
% with ≥ 20% deterioration	4	14	6	9	
RLH psychosocial impact scale					
Number of patients	23	7	30	31	0.08
% with 10–19% deterioration	4	0	3	7	
% with ≥ 20% deterioration	0	14	3	16	
RLH lifestyle impact scale					
Number of patients	26	7	33	31	0.03
% with 10–19% deterioration	0	14	3	16	
% with ≥ 20% deterioration	12	0	9	19	

[a] χ^2 test comparing those who deteriorated by ≥ 10% in the total ESGNS group compared with the not-offered surgery group.
[b] Only applies to patients who did not have stomas at either baseline or 2 years of follow-up.

an advantageous or deleterious effect on QoL when compared with the preoperative situation, the proportions of patients improving or deteriorating were tabulated against clinical success or failure within the ESGNS group for the main outcome measures at 2 years of follow-up and compared with the two comparison groups (*Tables 14* and *15*) The clinical failures group is small ($n = 8$ at 2 years postoperation) and includes two patients who dropped out of the study after 2 years of follow-up and two patients with no preoperative measures. In general, the effect of separately reporting the clinical successes is to increase slightly the proportions who report a 10–20% improvement, although it is difficult to see any clear pattern in outcomes for the failures group and they are as likely to improve, sometimes substantially, as to deteriorate.

Generally, the ESGNS group were more likely to improve by ≥10% on all the main outcome scales at 2 years of follow-up, although the between-group difference was not significant for the EQ-5D, NHP pain and NHP social isolation scales. With the exceptions of the NHP pain and the RLH lifestyle impact scales, there were no differences between the ESGNS group and the not-offered surgery group in the proportions who deteriorated by ≥10% at 2 years of follow-up. Significantly more ESGNS patients deteriorated on the NHP pain

TABLE 16 *Power of study to detect 10, 20 and 30% differences between the RLH ESGNS group and the not-offered surgery group in changes in scores at 2 years of follow-up*

Measure	Effective total sample size (RLH ESGNS and not-offered surgery groups) at 2 years of follow-up	Power of study to detect between-group difference in changes in scores at 2 years of follow-up at 5% significance (%)		
		10% between-group difference	20% between-group difference	30% between-group difference
Cleveland Clinic incontinence scale	30	17	52	80
EQ-5D index of health status	64	30	80	98
HADS depression scale	67	58	95	99
RLH psychosocial impact scale	61	25	67	94
RLH lifestyle impact scale	64	30	82	99

scale and significantly fewer ESGNS patients deteriorated on the RLH lifestyle impact scale at the same follow-up point (*Tables 14* and *15*).

Outcomes for patients with preoperative stomas versus non-stoma patients
For the main outcome measures at 2 years of follow-up, there were no significant differences between changes in scores of patients who had stomas on recruitment and those who had FI on recruitment in any patient group.

Analyses excluding atresia patients
Exclusion of patients whose disorders were congenital in origin did not substantially alter any of the within-group changes in scores or the between-group differences at 2 years for the main measures. The within-ESGNS group changes at 3 years remained after exclusion of atresia patients.

These repeat analyses were restricted to the main outcome measures and did not include the Cleveland Clinic incontinence score, where the group size was already small owing to the exclusion of stoma patients.

Analyses excluding cancer patients
Exclusion of cancer patients did not substantially alter any of the within-group changes in scores or the between-group differences at 2 years. The within-ESGNS group change at 3 years remained after exclusion of cancer patients.

As above, these repeat analyses were restricted to the main outcome measures and did not include the Cleveland Clinic incontinence score.

Study power
Five main outcome measures were chosen to estimate the power of the study to detect 10, 20 and 30% differences between the RLH ESGNS group and the not-offered surgery group changes in scores when comparing baseline with 2 years of follow-up. The powers achieved for each of these measures at 5% significance are shown in *Table 16*.

On comparing *Tables 12* and *16*, it is clear that the study is underpowered to detect small differences (≤10%) between the groups at 2 years of follow-up, but that the power is adequate to detect between-group differences in of >20%, such as those seen in the Cleveland Clinic incontinence scale and the RLH psychosocial and lifestyle impact scales, making it unlikely that these differences are due to chance.

The study power to detect changes within the ESGNS group when comparing 3 years of follow-up with baseline is shown in *Table 17*. Again, the study is underpowered to detect small changes but adequately powered to detect larger changes such as those seen in the Cleveland Clinic, HADS depression and RLH psychosocial and lifestyle impact scales.

Patients' opinions of outcomes
Preoperative predictions of success of surgery in solving the bowel problems were high (median score: 80% successful). During the first four postoperative years, median estimates of success were between 73 and 83%; those patients who had reached 5 years had a median score of 57% (n = 10 at 5 years). At 5 years, half of the 10 responding patients estimated success of surgery at ≤26% and the remaining half estimated success at between 87 and 99%. There were some significant differences between preoperative predictions of success and postoperative estimates of success at 24 months of follow-up, where the postoperative median scores were 18% lower than

TABLE 17 *Power of study to detect 10 and 20% difference within the RLH ESGNS group when comparing scores at 3 years of follow-up with baseline*

Measure	RLH ESGNS group with baseline and 3-year follow-up data (number)	Power of study to detect within-group change in score at 3 years of follow-up (%)	
		10% within-group difference	20% within-group difference
Cleveland Clinic incontinence scale	13	50	95
EQ-5D index of health status	24	60	90
HADS depression scale	24	70	90
RLH psychosocial impact scale	21	50	90
RLH lifestyle impact scale	23	42	90

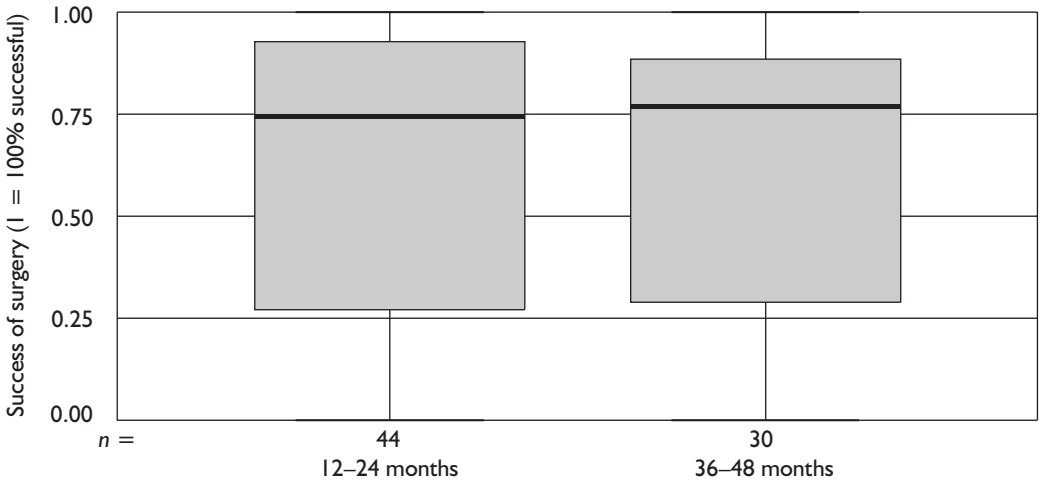

FIGURE 2 *RLH ESGNS patients' estimates of success of surgery, 12–23 months and 36–47 months postoperation. Box and whisker plots (boxes represent data between the 25th and 75th percentiles; medians are shown by the bold horizontal lines).*

the preoperative median ($p = 0.007$). The within-group differences were not significant when comparing 12–24 months with 36–48 months of follow-up ($p = 0.24$). The range of estimates of success at all follow-up stages was wide (0–100%) (*Figure 2*).

When asked at 1 year postoperation whether they had any regrets about having undergone the surgery, all of the 34 patients who were asked said that they had no regrets. Many, including some for whom surgery had not been successful, commented that they felt privileged to be given this opportunity and that if they had not taken it they would always have wondered whether the operation would have worked for them. Of the 22 patients who were asked at 1 year postoperation whether they would go through the procedure again, armed with their current knowledge of what was entailed, all except two (9%) said that they would. The two who would not go through the procedure again would have preferred to have a stoma formed rather than go through such major surgery. Most patients would be prepared to advise a friend with a similar bowel problem to explore the possibility of undergoing ESGNS.

Patients were also asked on one or two occasions to categorise the change in their bowel disorder since before surgery on a five-point scale between much worse and much better. Of the 45 patients who responded to this question during the first 3 years of follow-up, 73% said that their bowel condition was better or much better; of the 25 asked after 3 years of follow-up, 56% said that their bowel condition was better or much better. (This question was not asked at a uniform follow-up stage in the later stages of the study, as it was an additional question added at the time of the northern centres' study.)

Part 2: Royal London Hospital admissions, surgical procedures and inpatient resource use

The patient group

Data reported in Part 2 relate to the 48 RLH patients who are included in the cost analyses (Chapter 6). The group differs from the outcomes assessment group with the substitution of four private patients by four patients who were not included in the outcomes assessment, but who nevertheless underwent graciloplasty at RLH during the study period. These four patients comprise two who underwent graciloplasty, but whose bowel disorders were found to render them unsuitable for completion of ESGNS surgery, one patient who did not complete any postoperative questionnaires (this patient had agreed to participate in the study and to allow review of casenotes) and one patient who was excluded from the outcomes assessment owing to language difficulty. This group consists of the 47 NSCAG-funded patients, together with one patient who was funded by her health authority. With the exception of one patient who declined to participate in this study in any way and two patients who underwent ESGNS at the time of rectal cancer excision, this group represents all patients who underwent and completed NHS-funded ESGNS during the study period at RLH.

Hospital admissions and lengths of stay

There were 248 admissions to hospital for 48 patients with average follow-up of 39 months per patient. Of these admissions, nine were for preoperative investigations, 137 took place during the primary treatment (average 3.0 per patient) and 102 took place following the end of primary treatment (average 2.1 per patient).

Twenty-seven admissions were due to complications during the primary treatment phase, and all 102 admissions following the primary treatment phase were due to complications.

Complications which required readmission were mainly due to evacuation difficulties or pain (33 admissions), sepsis (31 admissions) and technical or circuitry related problems (23 admissions) (*Table 18*).

The average total length of inpatient stay was 55 days per patient, 35 days during the primary treatment phase and 20 days following the end of primary treatment. The average length of stay for graciloplasty and insertion of stimulator was 19 days and the average length of stay for stoma closure at the end of the primary treatment phase was 12 days.

The average length of the primary treatment phase, that is, the time from admission for graciloplasty to completion of the 'muscle training' programme and closure of stoma, was 5.4 months and ranged from 2.5 to 16.4 months.

Operations

A total of 234 operations (average 4.9 operations per patient) were performed, which occupied 631 theatre hours and 1342 surgeon hours. On average, each patient spent 11.9 hours in the operating theatre. The average length of the graciloplasty procedure was 5.7 hours (this average is based on all theatre visits which included graciloplasty; some of these visits also included stoma formation, insertion of stimulator and other procedures, such as rectal augmentation).

TABLE 18 *Admissions to hospital before, during and after ESGNS, based on 48 RLH patients included in cost analyses: number of admissions (mean per patient)*

Reason for admission	Pre-ESGNS	Primary treatment phase	Post-primary treatment	Total number of admissions
Pre-ESGN investigation	9 (0.19)	–	–	9 (0.15)
Planned ESGN procedure		112 (2.4)	–	112 (2.3)
Evacuation/pain investigation		7 (0.15)	26 (0.54)	33 (0.69)
Infective complication		6 (0.13)	25 (0.52)	31 (0.65)
Technical/circuitry problem		8 (0.17)	15 (0.31)	23 (0.48)
Bowel obstruction (acute/subacute)		–	11 (0.23)	11 (0.23)
Formation of permanent stoma		1 (0.02)	9 (0.19)	10 (0.21)
Leaking/soiling		–	4 (0.08)	4 (0.08)
Other complications relating to ESGNS		2 (0.04)	7 (0.15)	9 (0.19)
Other		1 (0.02)	5 (0.13)	6 (0.13)
Total	9 (0.19)	137 (2.85)	102 (2.1)	248 (5.2)

Covering stomas were formed at the time of graciloplasty in 23 of 27 (85%) patients who did not already have stomas. Colonic conduits were formed in five patients to permit irrigation of the bowel through a conduit on the abdominal wall; two patients had already undergone similar procedures prior to ESGNS. Seven patients also underwent rectal augmentation, a procedure described in Chapter 1.

Survival of stimulators and use of electrodes

Fifty-two stimulators were implanted in the 48 patients; only one stimulator required replacement owing to battery depletion during the study period and the median stimulator survival is in excess of 6 years.

Fifty-eight epineural and four intramuscular electrodes were used. Epineural electrodes were the first choice in all primary graciloplasty procedures at RLH.

Chapter 5

Retrospective study of outcomes: Edinburgh, Hull, Newcastle and RLH

This chapter begins with a summary of ESGNS outcomes for the three northern UK centres and the combined UK centres (including RLH), followed by detailed descriptions of methods and findings for the three Northern UK centres.

Summary of ESGNS outcomes for northern UK centres and RLH

Although there was no significant between-centre difference in the proportions of patients for whom surgery had been clinically unsuccessful, there was a significant difference between the 'success' curves in favour of the combined northern UK centres; this may be explained in part by timing artefacts. The proportion of patients with pre ESGNS stomas is significantly higher for RLH patients and this may indicate a more complex case mix, although it is not possible to confirm this owing to the wide variety of disorders and prior treatments experienced by these patients. The addition of data from the northern centres' patients increases the cumulative 'success' proportion for the combined UK groups. At 4 years postoperation, 65% of all UK ESGNS patients are likely to be without stomas and with intact circuitry.

There are no preoperative data from the northern centres and it is therefore important to give the greatest weight to those measures which 'stand alone' at the two follow-up points: symptomatic outcomes and patients' opinions of outcomes.

Symptoms of incontinence and pain are remarkably similar when comparing the northern centres with RLH patients at all stages of follow-up.

Patients' estimates of success of surgery were slightly lower at the northern centres compared with those from RLH, although the between-centre difference was not significant. More northern centres' patients expressed regret at having undergone surgery and slightly fewer felt that their bowel conditions had improved. However, this is most likely to be due to patients being questioned at different stages of follow-up, with the northern centre patients generally being asked the questions at ≥ 2 years of follow-up compared with 1 year for the RLH patients.

With regard to symptomatic, psychological and QoL measures of outcome, the findings from the northern centres' cross-sectional study support and reinforce those of the prospective study conducted at RLH as summarised in the previous chapter. With the exception of the HADS depression score, there were no significant differences at 12–24 months postoperation or at 36–48 months postoperation between the RLH patients and those from the combined northern centres, although there was tendency for the northern centres' patients to have somewhat poorer scores than the RLH patients. This difference may be explained by the age differences between centres – the northern centres' patients were, on average, 6 years older.

There were substantial differences in lengths of hospital stay on comparing the RLH patients with those from the combined northern centres. The RLH patients had significantly longer inpatient stays and underwent more surgical procedures. The difference may in part be explained by the fact that the majority of RLH patients have covering stomas formed at the time of graciloplasty. These patients need a further operation and inpatient stay to close the stomas and readapt to bowel continuity. Some RLH patients have also undergone additional procedures such as rectal augmentation. Another factor which may influence length of stay is that the majority of RLH patients live long distances from the hospital and it is often 'safer' to keep the patients in hospital for slightly longer in order to avoid complications occurring when they have returned home, rather than adopting a 'wait and see' approach which is possible when patients live nearby.

Detailed methods and findings of retrospective cross-sectional study of outcomes of ESGNS performed in Edinburgh, Hull and Newcastle (compared and combined with findings from RLH)

Objectives of study at Edinburgh, Hull and Newcastle

The objectives were to assess the following post-ESGNS outcomes in order to supplement findings from the RLH prospective study:

1. clinical 'survival' of the neosphincter together with functioning circuitry
2. symptoms: continence, evacuation and pain
3. QoL
4. patients' opinions regarding the experience and aftermath of undergoing ESGNS
5. NHS and patient resource use.

Patients and methods: Edinburgh, Hull and Newcastle

Patients

Patients were those whose ESGNS treatment at Edinburgh, Hull and Newcastle was started and completed between 1 January 1997 and 30 June 2001 and who were at least 6 months postoperation at the time of first assessment. This time period was chosen to correspond with the period of study at RLH.

Methods

Local ethical committee and hospital trust approvals were granted. Outcomes of ESGNS for patients from these three centres were assessed during 2002 by means of postal questionnaires regarding postoperative QoL, views on the success of the surgery in solving their bowel problems and costs incurred by them in living with their bowel disorder and undergoing treatment for it. Postal questionnaires covering QoL, symptoms and resource use were sent on two occasions ~6 months apart. An additional questionnaire concerning the patients' experiences of undergoing ESGNS and its aftermath was sent following return of the first QoL measures. Reminders were sent to non-responders after 1 month. Questionnaire information was supplemented, whenever possible, by means of semi-structured interviews conducted by telephone. Information regarding preoperative treatments, resource use and costs of medical treatment were gathered from hospital, departmental or patient records.

Quality of life and symptom questionnaires: Edinburgh, Hull and Newcastle patients

Postal questionnaires contained the same measures of QoL, symptoms and resource use as administered to the RLH ESGNS group (see Chapter 3), with the exception of the PAIS scale, which was omitted.

Part 2, which was sent between administrations of the above measures, was developed and tested with the help of a group of RLH ESGNS patients and covered the following topics:

- How well or otherwise were expectations met?
- Any regrets?
- If the clock could be turned back, would you go through the procedure again?
- What has been the best thing about the overall experience?
- What has been the worst thing about the overall experience?
- Comparison of bowel disorder now with preoperation (five-point scale: much worse–much better).
- What has improved or deteriorated with regard to the bowel disorder and with regard to health in general?
- Effect on family and friends of bowel disorder and the treatment for it.
- Any other comments.

Analyses: retrospective analysis of ESGNS patients from Edinburgh, Hull and Newcastle in combination with and comparison with findings from RLH

Assessment of outcomes for patients from Edinburgh, Hull and Newcastle took place during 2002, when patients were at varying postoperative stages.

Clinical success is reported separately for the combined northern UK centre patients who agreed to participate in the outcomes assessment study and all patients who underwent ESGNS at RLH. Log-rank tests were conducted to assess for differences in success curves between RLH and the combined northern UK centres.

The main QoL, psychological distress, and symptom outcome findings are shown for RLH and for the combined three northern centres, generally by means of average scores at 12–24 months and 36–48 months, in order to maximise the numbers available at each stage. In addition, summary UK findings (combining all four centres) are given for clinical success, continence, main QoL measures and patients' estimates of success of surgery.

Of the 53 patients from the northern centres who agreed to participate in the study, 48 returned at least one questionnaire; hence the numbers available for analysis are smaller than those shown in the success curves. The EQ-5D tariff score and NHP scales are compared with population normative values adjusted for age and gender. Because of the lack of preoperative data, it is not possible to examine changes in scores following ESGNS for the three northern centres. However, incontinence frequency and scores and patients' estimates of success of surgery are less likely to be dependent on preoperative health status than the QoL findings. Differences between RLH ESGNS patients and those from the combined northern centres were tested for statistical significance at 12–24 months and at 36–48 months for the main outcome measures. Numbers of patients at each of the northern centres at each follow-up point were too small for further tests of statistical significance.

Limited findings from Part 2 of the questionnaires are included in this report; the remainder of the findings from Part 2 will be reported separately.

Results from the three northern centres are not shown in any way which could identify participating surgeons or patients. Centres are referred to as the combined northern centres or as centres B, C and D.

Recruitment to study

Fifty-three patients out of a total of 58 (91%) from the northern centres agreed to participate in the study and 48 (83%) have returned questionnaires on at least one occasion. Proportions of patients who returned at least one questionnaire ranged between 72 and 92% at the three centres. Resource use findings for the northern centres are based on 45 patients whose case notes were available for review at the time of visits to the three centres. Clinical success is based on all patients who underwent ESGNS at RLH, with the exception of two patients who underwent the surgery at the time of rectal cancer excision ($n = 55$) and all patients who agreed to participate in this study at the northern centres ($n = 53$). As reported in Chapter 4, 48 patients out of a total of 50 (96%) suitable patients at RLH agreed to participate in this study and returned at least one postoperative questionnaire.

Length of follow-up

The mean length of postoperative follow-up for Edinburgh, Hull and Newcastle patients was 45 months (range 18–73 months), which compares with a mean follow-up time of 39 months (range 4–71 months) for the RLH ESGNS group. Approximately two-thirds of patients from all centres were at least 3 years postoperation at the time of writing this report (September 2003).

Results

Baseline observations

Patients from the four ESGNS centres were similar in terms of gender and cause of disorder. Northern centres' patients were significantly older than those in the RLH group; in particular, centre B patients were on average 10 years older than those from RLH. The combined northern centre patients' average age was 48 years compared with 42 years for the RLH patients.

There were significant differences in the proportions of patients with pre-ESGNS stomas between the centres, RLH patients being significantly more likely to have preoperative stomas than either centre B or D. However, non-stoma patients from centres C and D were more likely to have undergone previous sphincter repair surgery than patients from RLH (*Table 19*).

It was difficult to ascertain lengths of time with the bowel disorder for many patients from the northern centres and this variable is not shown in *Table 19*. Details are shown for patients from these centres who had returned at least one questionnaire. Because of the cross-sectional and retrospective nature of the study at the northern centres, no baseline observations of symptoms or QoL were available for these centres.

Clinical outcomes

There were 12 failures (23%) out of 53 patients who underwent ESGNS at the three northern centres. This compares with 20 out of 55 patients at RLH (36%), although this difference did not reach statistical significance ($\chi^2 = 2.6$, $p = 0.11$). The aggregated cumulative success proportions for all four UK centres at 2, 3 and 4 years postoperation were 84% (95% CI: 76 to 92%), 79% (95% CI: 74 to 84%) and 65% (95% CI: 55 to 75%), respectively. The log-rank test showed a significant difference for success proportions when comparing RLH with the combined northern centres ($p = 0.03$) (*Figure 3*). *Table 20* indicates the cumulative success proportion and numbers of RLH and northern centre patients at risk at each period of follow-up.

Exclusion of patients with congenital disorders did not affect the survival curves significantly. Of the total 13 patients with congenital bowel disorders, seven failures occurred during the study period

TABLE 19 *Baseline characteristics, all ESGNS centres (B, C, D = northern centres)*[a]

Characteristic	RLH ESGNS	B ESGNS	C ESGNS	D ESGNS	Total ESGNS	*p*-Value for differences between RLH and combined centres B, C and D
Total who underwent ESGNS and were suitable for inclusion in outcomes assessment study	50				108	
Number (%) who returned at least one postop. questionnaire (percentages only shown for centres B, C, D)	48 (96)	(81)	(72)	(92)	96 (89)	
Age at time of first operation (years)						
<20	4 (8)	(23)	0	0	5 (5)	
20–39	14 (29)	(69)	(31)	(32)	28 (29)	
40–64	28 (58)	(7)	(54)	(68)	59 (61)	
65+	2 (4)	0	(15)	0	5 (5)	
Mean	42	52	48	47	45	
Range	15–71	35–71	28–67	30–64	15–71	0.03[b]
Gender:						
Male	12 (25)	0	(31)	(9)	18 (19)	
Female	36 (75)	(100)	(69)	(91)	79 (81)	0.11[c]
Cause of disorder:						
Congenital	6 (13)	(8)	(15)	(5)	10 (10)	
Cancer	1 (2)	0	0	0	1 (2)	
Obstetric trauma	24 (50)	(62)	(54)	(68)	54 (56)	
Other	17 (35)	(31)	(31)	(27)	31 (31)	0.9[c]
Preoperature stoma						
Yes	18 (38)	0	(23)	(9)	25 (26)	
No	30 (63)	(100)	(77)	(91)	72 (74)	0.009[c]
Previous incontinence-related operations (non-stoma patients)	$n = 30$				$n = 72$	
Yes	14 (47)	(46)	(60)	(64)	40 (56)	
No	16 (53)	(46)	(30)	(32)	27 (38)	
Case notes not reviewed	–	(8)	(10)	(5)	5 (7)	0.05[c]

[a] Number (% of respondents) unless otherwise stated
[b] *t*-test.
[c] χ^2 test.

TABLE 20 *Cumulative success proportions: RLH and northern UK centres' ESGNS patients*

Period (months)	RLH		Northern UK centres	
	Number at risk at start of period	Success proportion (95% CI)	Number at risk at start of period	Success proportion (95% CI)
0	55	0.96 (0.91 to 1.00)	53	1.00
12	42	0.81 (0.71 to 0.91)	52	0.98 (0.94 to 1.00)
24	33	0.75 (0.63 to 0.87)	47	0.92 (0.84 to 1.00)
36	26	0.73 (0.61 to 0.85)	30	0.85 (0.75 to 0.95)
48	15	0.57 (0.41 to 0.73)	17	0.72 (0.57 to 0.87)
60	5	0.49 (0.29 to 0.69)	7	0.72 (0.57 to 0.87)

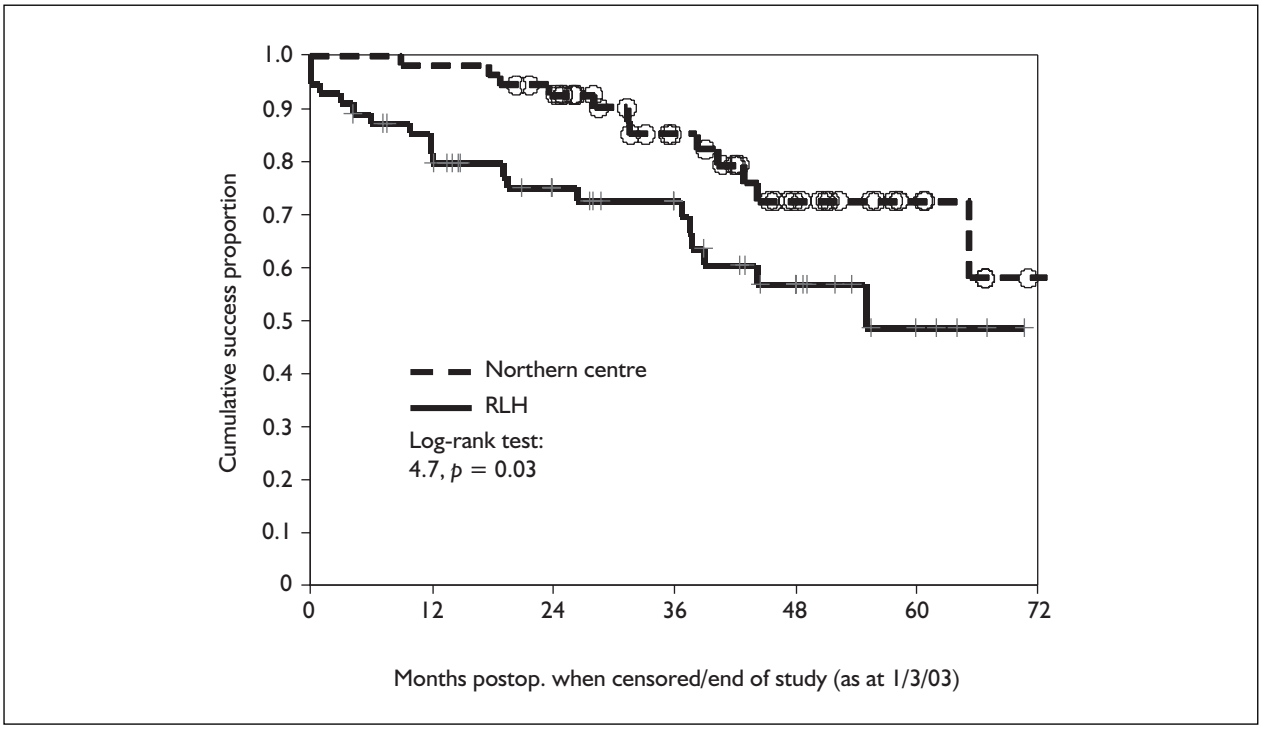

FIGURE 3 *Kaplan–Meier 'success' curves (functioning neosphincter, no stoma) at 1 March 2003: RLH (n = 55) and northern centres ESGNS (n = 53)*

and the cumulative success proportion at 4 years postoperation was 29% (95% CI: 0 to 59%).

Events leading to clinical failure were similar for patients at all centres. RLH patients were more likely to have permanent stomas formed following unsuccessful surgery; this finding is likely to reflect the significantly higher proportion of RLH patients who had stomas pre-ESGNS (*Table 21*).

Symptomatic outcomes

Continence

There were no significant differences between the RLH ESGNS group and the combined northern UK centres ($p = 0.27$ at 3 years and $p = 0.37$ at 4 years postoperation) (*Table 22*). At 2, 3 and 4 years of follow-up, 62, 60 and 55% of patients from the combined four UK centres were either never incontinent to solid or liquid stool or they were incontinent less than once per week. The remaining patients had more frequent incontinence or they had stomas. On average, just over half of patients from all four centres were incontinent to flatus several times each day at 2, 3 and 4 years of follow-up.

The Cleveland Clinic incontinence scale has scores ranging from 0 to 20, where 0 is the best score indicating complete continence. The median scores for the four UK centres combined were 9 at 12–24 months and 10 at 36–48 months postoperation. There were no significant

TABLE 21 *Summary characteristics of clinical 'failures':[a] RLH and combined northern UK centre ESGNS patients*

Characteristic	RLH[b]	Northern UK centres[b]
Total clinical failures	20	12
Pre-ESGNS stoma	9 (45)	3 (25)
Final stoma (% of all ESGNS procedures)	14 (25)	7 (13)
Cause of disorder		
Congenital	6 (30)	2 (17)
Obstetric trauma	10 (50)	6 (50)
Other	4 (20)	4 (33)
Events leading to failure		
Sepsis – perineal or circuitry	3 (15)	3 (25)
Soiling	5 (25)	3 (25)
Soiling and evacuation difficulty	2 (10)	–
Pain and soiling	–	1 (8)
Pain and evacuation difficulty	5 (25)	2 (17)
Unsuitable for surgery	2 (10)	–
Evacuation difficulty	1 (5)	1 (8)
Circuitry problems and evacuation difficulty	1 (5)	1 (8)
Uncertain [non-participant, stoma formed at other hospital (1), notes not reviewed (1)]	1 (5)	1 (8)

[a] 'Failure' = stoma or removal of circuitry at end of study period.
[b] Number (% of clinical failures) unless stated otherwise.
[c] Does not include 5 non-participants.

TABLE 22 *RLH and northern UK centres: frequency of incontinence to solid or liquid stool (cross-sectional data)*

	RLH			Combined northern UK centres		
	24 months postop.	36 months postop.	48 months postop.	24 months postop.	36 months postop.	48 months postop.
Number of respondents (%)	37	43	22	13	16	16
Never/<1/week	31 (62)	26 (60)	21 (55)	8 (62)	9 (56)	8 (50)
>1/week	9 (18)	9 (21)	4 (11)	2 (15)	3 (19)	3 (19)
Daily/stoma	10 (20)	8 (18)	13 (34)	3 (23)	4 (25)	5 (31)

differences between the RLH ESGNS group and the combined northern centres at either follow-up point (p = 0.66 and 0.74, respectively) (*Table 23*).

Evacuation

Frequencies of evacuatory difficulty for RLH and the combined northern UK centres are shown in *Table 23*. The results for the combined northern UK centres at 2, 3 and 4 years post-ESGNS are similar to the results for the RLH ESGNS group, with approximately one-third of all patients experiencing daily or weekly evacuatory difficulties at each stage. Half of those from the aggregated group with a satisfactory continence outcome (never or less than once per week incontinent to solid or liquid stool) had frequent evacuatory difficulties.

Pain

There were no significant differences on the NHP pain scale between RLH and the combined northern UK centres at 12–24 months postoperation (p = 0.39) or at 36–48 months postoperation (p = 0.15) (*Table 24*). The scale ranges between 0 and 100, with 0 indicating the best level. The all UK centres' combined median score was 11 at 12–24 months of follow-up (age and gender adjusted population norm = 6) and 14 at 36–48 months of follow-up (adjusted population norm = 7).

At 3 years postoperation, 27 out of 42 ESGNS patients (64%) at all centres had experienced pain during the previous month which they considered was associated with their bowel disorder or its

TABLE 23 *RLH and northern UK centres: frequency of evacuatory difficulties 2–4 years postoperation (cross-sectional data)*

	RLH			Combined northern UK centres		
	24 months postop.	36 months postop.	48 months postop.	24 months postop.	36 months postop.	48 months postop.
Number of respondents (%)	36	27	21	13	16	18
Never	15 (41)	12 (45)	7 (33)	9 (69)	9 (56)	9 (50)
Several times per week	2 (6)	2 (7)	1 (5)	1 (8)	2 (13)	3 (17)
Daily	11 (31)	7 (26)	5 (24)	3 (23)	3 (19)	3 (17)
Colonic conduit	4 (11)	3 (11)	2 (10)	0	0	1 (6)
Stoma	4 (11)	3 (11)	6 (29)	0	2 (13)	2 (11)

treatment. The most frequently mentioned sites were the leg (36%), groin/anus (36%) and the abdomen or back (19%). When asked to score the intensity of the worst pain experienced during the previous week, the average score was 4.7 on a scale between 0 and 10, where 10 was the worst possible pain.

Quality of life scores at 1–4 years post-ESGNS

Generic measures

Table 24 shows the EQ-5D weighted index of health status at 12–24 months and 36–48 months postoperation for the RLH and northern UK centres' ESGNS patients. There were no significant differences between RLH and the combined northern centres at either follow-up point, although the RLH median scores were better than the combined northern UK centres at both follow-up points (Mann–Whitney *U*-test, p = 0.16 and 0.07, respectively). However, it should be remembered that the northern UK centres' patients were on average 6 years older than those from RLH, which may account for their slightly poorer scores. Scores for all ESGNS patient groups remain well below (worse than) the adjusted UK population norms at each stage.

There were no significant differences on the NHP social isolation scale between RLH and the combined northern UK centres at either follow-up point (p = 0.74 and 0.66, respectively). The median NHP social isolation score at both 12–24 and 36–48 months postoperation for the aggregated patient group from all four UK centres was zero (0 = best score) (*Table 24*).

Psychological distress

There were no significant differences between RLH and the combined northern UK centres at either follow-up point on the HADS anxiety scale or at 12–24 months of follow-up on the HADS depression scale. However, the northern centres' patients had slightly worse HADS depression scale scores at 36–48 months (p = 0.007), although the median scores for all centres were within the normal range at this follow-up point (*Table 24*) Again, any differences may be accounted for by the age difference between the RLH and northern centre patients.

Impact of the bowel disorder

The RLH psychosocial and lifestyle impact median scores were similarly low for RLH and northern centres' patients at both 12–24 and 36–48 months of follow-up (*Table 24*).

Patients' estimates of success of surgery in solving their bowel problems

The northern UK patients' median estimates of success of surgery were 67% at 12–24 months and 60% at 36–48 months. The median estimates at the same follow-up points for the RLH ESGNS group alone were 75 and 77%; these between-centre differences were not significant at either follow-up point (p = 1.0 and 0.64, respectively) (*Table 24*).

The northern centres' patients were asked whether they had any regrets about having decided to proceed with surgery. They were also asked whether, if they could turn the clock back, they would go through the procedure again with the knowledge of what is entailed. Of the 44 patients who responded to these questions, 31 (70%) said they had no regrets and 28 (64%) said that they would go through the procedure again. It should be noted that these questions were asked at varying follow-up periods and always in excess of 12 months postoperation, owing to the cross-sectional nature of the study, hence comparison cannot be made with the responses of the RLH patients to these questions.

At the latest time of questioning, of the 32 patients (all centres) who were <3 years postoperation,

TABLE 24 *Median scores for the main outcome measures: RLH and northern UK centres*

Measure	12–24 months postoperation			36–48 months postoperation		
	Number of patients	Median score	*p*-Value, RLH vs northern centres	Number of patients	Median score	*p*-Value, RLH vs northern centres
Cleveland Clinic incontinence score (scale 0–10, 0 = best)						
RLH	40	9	0.68	26	11	0.74
Northern centres	13	10		28	10	
Combined UK centres	53	9		54	10	
EQ-5D (scale 0–1, 1 = best)						
RLH	45	0.78	0.16	28	0.79	0.07
Northern centres	14	0.69		31	0.69	
Combined UK centres	59	0.73		59	0.76	
NHP pain (scale 0–100, 0 = best)						
RLH	43	4	0.39	28	9	0.15
Northern centres	14	18		30	21	
Combined UK centres	57	11		58	14	
NHP social isolation scale (scale 0–100, 0 = best)						
RLH	43	0	0.74	28	0	0.66
Northern centres	14	0		30	0	
Combined UK centres	57	0		58	0	
HADS anxiety (scale 0–21, 0 = best)						
RLH	44	6	0.12	28	4	0.32
Northern centres	14	9		31	6	
Combined UK centres	58	8		59	6	
HADS depression (scale 0–21, 0 = best)						
RLH	44	5	0.43	28	1	0.007
Northern centres	14	6		31	5	
Combined all centres	58	5		59	3	
RLH psychosocial impact (scale 0–10, 0 = best)						
RLH	44	1	0.19	27	1	0.34
Northern centres	14	4		31	2	
Combined UK centres	58	1			1	
RLH lifestyle impact (scale 0–10, 0 = best)						
RLH	44	1	0.14	27	2	0.13
Northern centres	14	4		31	3	
Combined UK centres	58	3		58	2	
Patients' estimates of success of surgery in solving their bowel problems (0–100%)						
RLH	44	75%	1.0	30	77%	0.64
Northern centres	14	67%		31	60%	
Combined UK centres	58	72%		61	63%	

TABLE 25 *Admissions to hospital during and after ESGNS, based on 48 RLH and 45 northern centres' patients included in economic analyses: number of admissions (mean per patient)*

Reason for admission	RLH ESGNS (n = 48)			Northern UK centres ESGNS (n = 45)		
	Primary treatment phase	Post-primary treatment	Total number of admissions	Primary treatment phase	Post-primary treatment	Total number of admissions
Planned ESGN procedure	112 (2.3)	–	112 (2.3)	54 (1.2)	–	54 (1.2)
Infective complication	6 (0.13)	25 (0.52)	31 (0.65)	13 (0.29)	15 (0.33)	28 (0.62)
Evacuation/pain investigation	7 (0.15)	26 (0.54)	33 (0.69)	2 (0.04)	15 (0.33)	17 (0.38)
Technical/circuitry problem	8 (0.17)	15 (0.31)	23 (0.48)	2 (0.04)	13 (0.29)	15 (0.33)
Bowel obstruction (acute/subacute)	–	11 (0.23)	11 (0.23)	0	0	0
Formation of temporary/permanent stoma	1 (0.02)	9 (0.19)	10 (0.21)	0	5 (0.11)	5 (0.11)
Leaking/soiling	–	4 (0.08)	4 (0.08)	0	1 (0.02)	1 (0.02)
Other complications relating to ESGNS	2 (0.04)	7 (0.15)	9 (0.19)	3 (0.07)	10 (0.22)	13 (0.29)
Other	1 (0.02)	5 (0.10)	6 (0.13)	6 (0.13)	4 (0.08)	10 (0.22)
Total	137 (2.9)	102 (2.1)	239 (5.0)	80 (1.8)	63 (1.4)	143 (3.2)

60% said that their bowel condition was better or much better compared with before the surgery. Of the 64 patients who were ≥3 years postoperation, 49% said that their bowel condition was better or much better. There was no significant difference between RLH and the combined northern centres for those who were ≥3 years postoperation ($\chi^2 = 2.8$, $p = 0.4$). No significance testing was carried out in the groups who were <3 years postoperation owing to small numbers.

Hospital admissions, surgical procedures and inpatient resource use

Hospital admissions and lengths of stay

For the 45 patients from the northern UK centres whose case notes were reviewed, there were 143 admissions to hospital during the study period (total 176 person years); on average this amounts to 3.2 admissions per patient. Eighty admissions occurred during the primary treatment period. The total number of bed days was 862, of which 639 were occupied during the primary treatment phase (average: 14 days per patient during primary treatment and 5 days after the end of primary treatment). Lengths of stay were substantially shorter at the northern centres than RLH (RLH average: 35 days per patient during primary treatment and 20 days after the end of primary treatment). Part of these differences during the primary treatment phase can be explained by the routine practice of forming covering stomas at RLH in addition to the small number of patients who underwent rectal augmentation in addition to ESGNS at RLH. A total of 127 admissions to RLH (2.7 per patient) and 85 admissions to northern centres (2.0 per patient) were due to complications. Admission rates for infective complications were almost identical when comparing centres (*Table 25*).

Operations

A total of 120 operations were carried out on the 45 patients whose case notes were reviewed from the combined northern centres; this amounts to an average of 2.7 procedures per patient and compares with an average of 4.9 procedures per patient at RLH. Northern centre procedures occupied 204 theatre hours and 360 surgeon hours; on average each patient spent 4.5 hours in the operating theatre during the study period and the average length of the graciloplasty operation was 2.8 hours (*Table 26*).

Only one patient in the northern centres group had a covering stoma formed at the time of graciloplasty [38 (84%) did not have stomas prior to ESGNS]. One patient had a colonic conduit formed prior to ESGNS and one had one formed following ESGNS.

RLH patients underwent approximately twice as many surgical procedures and were in the

TABLE 26 *Hospital stays, operations and devices implanted: RLH and combined northern centres*[a]

	RLH ESGNS group	**Combined northern centres ESGNS group**
Number of patients	48	45
Person years in study	165	176
Mean number of admissions per patient (mean number per person year)	5.2 (1.5)	3.2 (0.8)
Mean total bed days per patient (mean number per person year)	55 (16)	19 (4.8)
Mean number of operations per patient (mean number per person year)	4.9 (1.4)	2.7 (0.7)
Mean number of theatre hours per patient (mean number per person year)	11.9 (3.8)	4.5 (1.1)
Number (%) with pre-ESGNS stomas	21 (44)	7 (15.6)
Number (% of those without pre-ESGNS stomas) of covering stomas formed	23 (85)	1 (2)
Number of stimulators implanted (mean number per patient)	52 (1.1)	53 (1.2)
Number of epineural electrodes implanted (mean number per patient)[b]	58 (1.2)	0
Number of intramuscular electrodes implanted (mean number per patient)	4 (0.1)	96 (2.1)

[a] Patient groups represented in this table do not correspond exactly with the patient groups included in the outcomes assessment.
[b] For epineural stimulation one lead/electrode is required per patient. For intramuscular stimulation two leads/electrodes are required per patient.

operating theatre for 2.5 times longer than the northern centre patients. As noted previously, the routine practice of forming covering stomas at RLH and the additional procedures performed on some patients accounts for some of the additional operating time.

Survival of stimulators and use of electrodes

There was no significant difference between RLH and the northern centres' rate of stimulator replacement. Median stimulator life is >6 years at all centres.

Chapter 6

Cost analysis of ESGNS

Method

Overview of analytical approach

The economic evaluation consists of a cost description, a comparative cost analysis and a cost-effectiveness analysis.

Cost description (ESGNS)

The cost of patient management associated with undertaking the ESGNS procedure has been calculated based on resource utilisation reported by patients attending the Colorectal Development Unit at RLH. Costs of work-up of patients referred to the unit, including those not proceeding to surgery, have been included, as these would not have been incurred if the ESGNS surgery had not been available. Hospital resource use (ward use, theatre use, outpatient visits) has been obtained from a review of patients' hospital records, and other resource use (community health services, prescribed medications, prescribed appliances, use of hospital resources elsewhere) from repeated interviews of ESGNS patients. Costs were calculated by multiplying resource use by unit costs, which were obtained from the RLH finance department (inpatient care, theatre use and outpatient care) and from standard sources (Personal Social Services Research Unit, BNF) for other resource use.

The ESGNS intervention itself was defined as the time from the date of the first scheduled (surgical) admission to date of discharge of the last scheduled admission in the case of surgical success and the date of discharge of the (surgical) revision to alternative management of FI (stoma care, medical management, artificial bowel) in the case of patients who did not achieve a functioning neosphincter.

Costs have been calculated for the intervention itself (including work-up before the start date) and subsequent to the intervention. They have also been calculated by year from the start of the intervention. As patient experience is censored at different durations of follow-up, costs of patient management subsequent to the intervention have been calculated per person-year (PY) of reported experience.

As a supplementary analysis, the cost of patient management (inpatient care only) of patients initiated on ESGNS surgery at three other centres have been estimated from a less detailed review of their medical records. The resulting values have been used to derive alternative costings for use in cost-effectiveness analysis.

Cost analysis and cost-effectiveness analysis

The patient management decision of interest, to be represented in an economic evaluation, is whether to refer a patient with severe FI (who is unhappy with his/her present situation) and potentially suitable for ESGNS surgery to assessment for ESGNS surgery. The referred patient may be currently managed medically or may already have a functioning stoma. In the first of these cases the choice is between referral to ESGNS, stoma formation and continued medical management, and in the latter of these cases the effective choice is between referral to ESGNS or continued stoma care. The further option (conversion from stoma to medical management) has not been considered, although some patients with prior stoma and ESGNS failure did indeed revert to medical management.

The cost of alternative patient management strategies has been estimated by undertaking a record review and questionnaire-based interviews of two sets of 'comparison group' patients. The first of these are patients considered for ESGNS surgery at the RLH, but who do not proceed ('not-accepting surgery group') either owing to not being suitable for surgery or owing to patient choice. The second group were patients with severe FI being managed at other centres, but not referred for ESGNS. These 'not-offered surgery' patients were identified by contacting surgeons from other hospitals as described in the section 'Method' (p. 9).

In order to undertake cost analysis and cost-effectiveness analysis, it is necessary to project patient experience over a period beyond that directly measured in the study. Average costs per PY of experience reported for ESGNS and comparison group patients have accordingly been projected (and discounted) using a conventional spreadsheet economic model.

Effectiveness has been measured as surgical success and as quality-adjusted life-years (QALYs) calculated from repeated administrations of the EQ-5D instrument to ESGNS (RLH) and comparison group patients. Rates of ESGNS failure and QALYs have been estimated by year from the start of the intervention and the average rate reported for later years (≥3 years after the start of the intervention) has been projected forward for use in the economic model. (A QALY can be defined as a year of life adjusted for its quality or its value. A year in perfect health is considered equal to 1.0 QALY. The value of a year in ill health would be discounted. For example, a year bedridden might have a value equal to 0.5 QALY. It is a measurement index derived from a modification of standard life-table procedures and designed to take account of both the quality and the duration of survival. This index can be used in assessing the outcome of healthcare procedures or services.)

The result of the economic analysis is an incremental cost-effectiveness ratio (ICER), in which the extra cost of one strategy option rather than another is related to the extra health benefits (measured as QALYs) that accrue. This provides a metric that is in principle comparable to ICERs for other interventions and nominal threshold values (an analysis of UK NICE guidance has suggested that ICERs of less than about £30,000/QALY gained represent good 'value' investment of healthcare resources).

The robustness of the calculated ICER can be tested in sensitivity analysis by altering node input parameters through reasonable ranges and examining the impact on the resulting ICER value. However, it is not advisable to place too much reliance on the ICER as a single decision criterion, especially where there is some doubt that the impact of this particular intervention on patient experience is adequately captured by the EQ-5D instrument and also without a more comprehensive understanding of the uncertainty surrounding the calculated ratios, which was beyond the scope of the current analysis.

Cost perspective

The primary perspective reported in this analysis is that of the NHS. Further analyses may be undertaken to integrate personal costs and forgone productivity ('indirect costs') into a broader societal perspective. Utility valuations are based on population values applied to EQ-5D health states reported by patients and not on patients' own valuations of their health states.

Hospital inpatient resource use (ESGNS service)

This has been recorded from a review of patient records at RLH. Resource use has been separated into ward use, physiological and other diagnostic tests, theatre use, devices and outpatient visits.

Community resource use (and use of other hospital services)

Information about community resource use was ascertained by means of patient questionnaires. Patients were asked to recall the previous 4 weeks for GP visits, prescription medicines and appliances. For hospital inpatient and outpatient resource use, they were asked to recall the period since the last interview (or previous 12 months for the first interview).

Other resource use

Resource use and costs for comparator patients were collected from patient questionnaires administered over a 2-year period. Up to four questionnaires were administered to each patient at baseline and 6, 12 and 24 months. Information was recorded for inpatient and outpatient use (excluding assessment for ESGNS at RLH), use of community health services, prescribed medications, prescribed appliances and stoma appliances. In addition, information on patient travel, personal over-the-counter costs (medications, incontinence aids, etc.), use of home help and time off work/usual activities was recorded but is not included in the current analysis.

The method of calculating average costs per PY was identical with that used for the same cost categories (non-RLH outpatient and inpatient care, community health services) for ESGNS patients.

Information was provided on outpatient visits and inpatient admissions over the preceding 12-month period at baseline interview and since the previous questionnaire at subsequent interviews. The maximum duration of patient experience recorded was therefore 36 months. Information on the use of community health services, prescribed medications, prescribed appliances and stoma appliances was provided for the preceding 4 weeks only. For these categories of resource use, the rate of resource use reported by patients at each interview was applied to the entire period since the previous interview (or the previous 12 months if at baseline). Resource use was not projected into the future, so those patients with incomplete follow-up provided information for a limited

duration of patient experience (<36 months). For each patient and each cost category, an estimated aggregate cost was calculated and related to a corresponding estimated number of patient months of experience to provide an estimated cost per PY of experience. Costs and PYs were aggregated for each defined patient group to provide and average for each group.

Personal costs and social care costs (patient travel, over-the-counter supplies, home help) and indirect costs (forgone productivity due to inability to work or undertake usual activities) have not been included in the present analysis, as they are outside the chosen cost perspective

Unit costs

Table 27 presents unit costs for RLH used in the cost analysis. The main source of the unit costs is the RLH service, but other conventional services were consulted where appropriate. Bed day unit costs included an allowance for medical and clinical nurse specialist staff time spent on ward-related activities; this allowance was calculated following consultation with the various members of the clinical team.

Health outcomes

Health outcomes for use in cost-effectiveness analysis are reported as surgical success (functioning neosphincter) or QALYs.

Surgical success was assessed at the end of the intervention itself and a failure was recorded at this time if the patient failed to be discharged with a functioning neosphincter. Thereafter, patients who had a functioning neosphincter at the end of the intervention but who subsequently reverted to medical management or stoma care (whether or not the neosphincter was technically functioning adequately) were recorded as late failures, the time of failure being the time of the operation to form a stoma or to remove circuitry.

For patients in the ESGNS group and for comparator patients, QALYs have been estimated from repeated administration of the EQ-5D instrument at baseline and at each patient interview. For ESGNS patients this amounted to up to three measurements during the intervention itself and up to 10 measurements after the intervention. Each EQ-5D health state was associated with a utility score based on a UK population survey.[35] For each patient and for each year from the start of the intervention a QALY has been calculated as the area of the (utility versus time) polygon between the start and end of each year. Year-end utility values were calculated by linear interpolation between previous and subsequent interview-based values. For each patient the last recorded value was carried forward to the end of the year (after intervention) in which the value was recorded, to permit estimation of the QALY for that patient for that year after intervention.

Five patients (recruited early to the study) did not have baseline EQ-5D values. These patients have been included in the QALY calculations for years 2 and years 3–5, but not year 1. Alternative QALY calculations have been made entirely excluding these patients.

Model-based analysis

Figures 4 and *5* describe the model-based approach to estimating the long-term costs and health outcomes for different options for patients eligible for ESGNS. The model has been constructed using conventional spreadsheet software (Microsoft Excel 98).

Model structure: strategies and decisions

Two decisions may be represented by the model, depending on whether patients have prior stoma or not. If this is the case, patients may be referred for ESGNS assessment or may continue with stoma care. If patients are being managed conservatively they may be referred for ESGNS, have a stoma formed or continue with medical management. The choice for patients initially with stoma is to continue with stoma or to be assessed for ESGNS (and proceed with the operation if suitable).

The model is designed to estimate the costs and consequences of each option relevant to each decision, so that a comparison (incremental values) can be made between the costs and health outcomes associated with each option. This is achieved by

- defining pathways associated with each option
- identifying probabilities for each pathway
- identifying costs and health outcomes associated with each pathway
- combining (weighting) costs and outcomes across pathways using the relevant probabilities into a summary (expected) value for each strategy
- undertaking incremental analysis.

The patient management decision starts with a referral to the ESGNS service. This will result in an assessment of the patient for suitability for

TABLE 27 *Unit costs: anorectal reconstruction surgery*

Resource use item	Value (£)	Source	Comments
Main items			
Hospital bed-day	237.00	Barts and the London NHS Trust, 2003	£135 +35% overheads (Rachel Ward). Includes hotel costs and usual hospital drugs, cefuroxime and metronidazole (intravenous antibiotics), but not test, etc. Includes CNS and medical staff time calculated at £55/bed-day
Theatre hour	400.00	Barts and the London NHS Trust, July 2003	Includes overheads, drugs, disposables and staff except surgeons, CNS
Outpatient attendance	122.00	Barts and the London NHS Trust, 2003 (specific to colorectal outpatient department)	Includes doctor, clinic nurse, other staff and overheads, but not CNS – estimated 1 hour for first appointment, 20 minutes for all others
Staff time			
Consultant hour	42.90	Barts and the London NHS Trust, 2003	Does not include overheads
Registrar hour	21.90	Barts and the London NHS Trust, 2003	Does not include overheads
Nurse specialist hour	19.90	Barts and the London NHS Trust, 2003	Does not include overheads
Other hospital resource use			
TPN day	108.70	Barts and the London NHS Trust, 2000	Not included in bed-day costs. Adjusted for inflation
Cross-match	8.70	Barts and the London NHS Trust, 2000	Adjusted for inflation
Units blood transfused	86.96	Barts and the London NHS Trust, 2000	Adjusted for inflation
Physiology			
ARP (manometry, EMG/ electrosensitivity)	350.00	Barts and the London NHS Trust GI Physiology Unit, 2003	Include overheads
24-hour ambulatory manometry	300.00	Barts and the London NHS Trust GI Physiology Unit, 2003	Include overheads
Defecation proctogram	250.00	Barts and the London NHS Trust GI Physiology Unit, 2003	Include overheads
Colonic transit scintigraphy	505.00	Barts and the London NHS Trust GI Physiology Unit, 2003	Include overheads
Endo anal US alone	200.00	Barts and the London NHS Trust GI Physiology Unit, 2003	Include overheads
Pathology tests			
Haematology (band 1)	10.87	Barts & the London NHS Trust private patient prices, 2000–01	Adjusted to 2003 for inflation
Chemistry (band 1)	9.78	Barts & the London NHS Trust private patient prices, 2000–01	Adjusted to 2003 for inflation
Microbiology (band 1)	7.34	Barts & the London NHS Trust private patient prices, 2000–01	Adjusted to 2003 for inflation
Microbiology (band 2)	19.57	Barts & the London NHS Trust private patient prices, 2000–01	Adjusted to 2003 for inflation
Diagnostic Tests			
Plain X-ray	40.22	Barts and the London NHS Trust private prices, 2000–01	Average cost for plain X-rays of chest/abdomen. Adjusted to 2003 for inflation
Contrast X-ray	234.79	Barts and the London NHS Trust private prices, 2000–01	Water-Soluble contrast enema/ pouchogram. Adjusted to 2003 for inflation

continued

TABLE 27 *Unit costs: anorectal reconstruction surgery (cont'd)*

Resource use item	Value (£)	Source	Comments
US (not endo-anal US)	77.18	Barts and the London NHS Trust private prices, 2000–01	One area. Adjusted to 2003 for inflation
ECG	32.61	Barts and the London NHS Trust private prices, 2000–01	Adjusted to 2003 for inflation
Devices and implantable equipment			
Simulator kit	4700.00	Medtronic, 2003	Current list price, including VAT, Includes stimulator, 1 epineural lead, 1 programmer
Intramuscular lead (per lead)	940.00	Medtronic, 2003	Current list price, including VAT
Programmer	346.63	Medtronic, 2003	Current list price, including VAT. NB: 6 programmers replaced during study
Epineural lead	770.80	Medtronic, 2003	Current price, including VAT
Extension kit	734.38	Medtronic, 2003	Current price, including VAT
Inpatient drugs			
Imipenem 500 mg	12.00	BNF, 2003	
Tazocin 500 mg	15.00	BNF, 2003	
Vancomycin 500 mg	6.67	BNF, 2003	
Productivity loss			
Person-day	165.94	OECD, 2001 (GDP per economically active person)	£935,627 m/(27,442 m EA people × 230 days/year). Adjusted for inflation at 2.3%

ARP, anorectal physiology; CNS, Clinical Nurse Specialist; EA, economically active; ECG, electrocardiogram; EMG, electromyography; TPN, total parenteral nutrition; US, ultrasound.

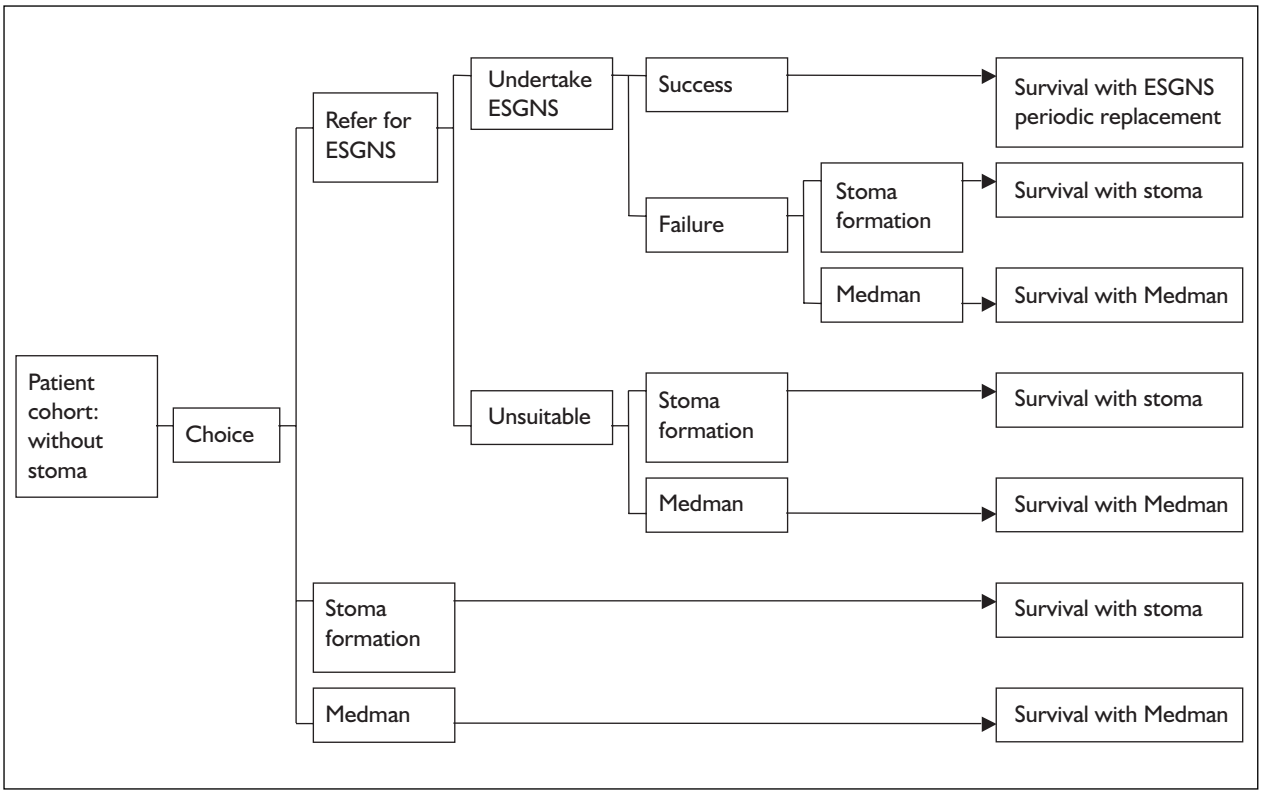

FIGURE 4 *Overview of model-based approach: patients with no prior stoma. Medman = medical management.*

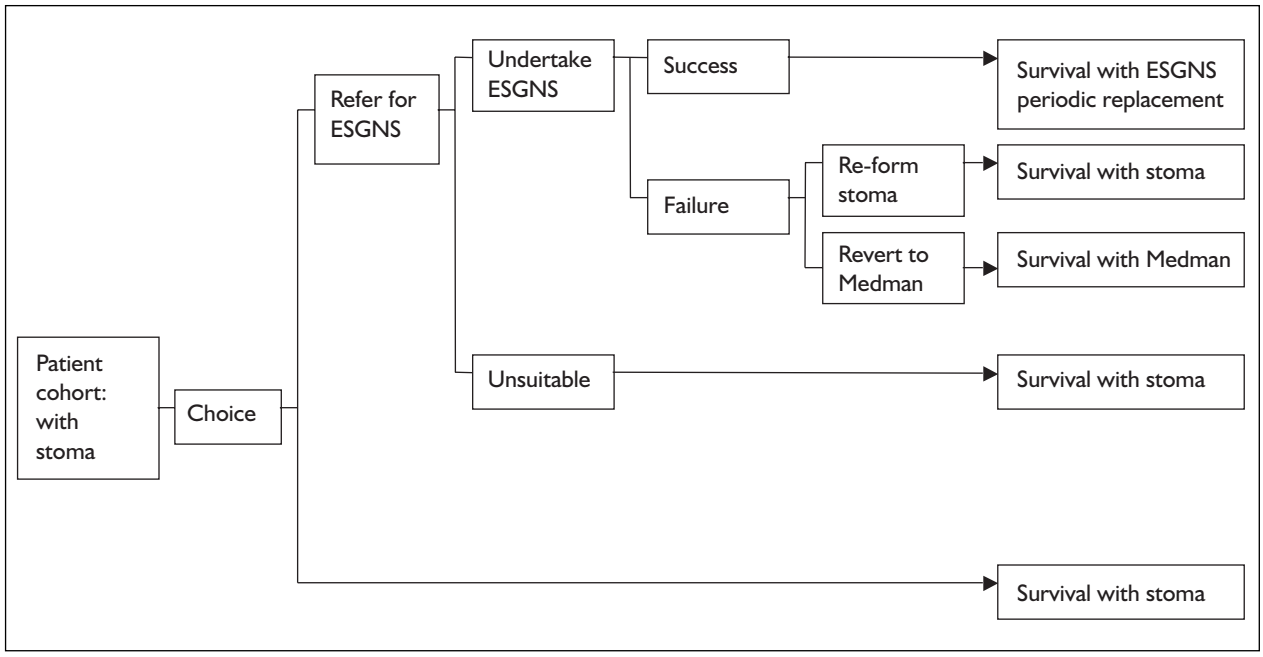

FIGURE 5 *Overview of model-based approach: patients with prior stoma*

surgery, which will generate costs of physiological investigation and assessment. A proportion of patients will be considered unsuitable or will not wish to proceed for other reasons at this stage. If currently managed medically they may now consider stoma formation.

For patients proceeding to ESGNS formation, the operation may or may not be successful, where 'success' is defined as having an adequately functioning neosphincter at the conclusion of the primary treatment. Again, unsuccessful patients will return to medical management or have a new permanent stoma formed (if previously without stoma) or will return to stoma care (if previously with stoma). ESGNS will generate costs of inpatient and outpatient care associated with a sequence of operations and follow-up visits at the ESGNS service itself, in addition to some patient care costs at other facilities and for community services.

Successful ESGNS patients area likely to experience the need for replacement of implantable devices at a certain rate. Some may experience late complications associated with, for example, infection.

Subsequent to the intervention itself (ESGNS, stoma formation or no intervention), all patients will generate costs of continuing care. These are represented in the model of annual costs of patient remaining in the relevant health state (functioning ESGNS, with stoma, without stoma). From an NHS perspective, these costs include stoma supplies and incontinence pads, prescriptions, some inpatient and outpatient care and community health services. In addition, there may be substantial personal costs (and possibly costs to social services) associated with continence-related supplies, laundry and other items.

A proportion of patients managed medically (who were referred for assessment for ESGNS, but did not proceed or were unsuccessful) are likely to convert to stoma care over subsequent years.

Following the initial intervention, all patients will be subject to mortality, assumed to be at the general population rate. Many will, of course, develop other morbidities over time, requiring the use of health services. These costs are not included in the model-based analysis.

Time horizon and discounting

The model projects the experience over a given duration from the intervention. Guidelines for the economic evaluation of health technologies suggest projecting experience over expected lifetime. This provides results that are more likely (in principle) to be comparable with those from other economic evaluations, but it involves making a number of increasingly tenuous assumptions about future costs and event rates. In the base case, a time horizon of 25 years has been used, but a shorter time horizon (5 years) has also been considered.

TABLE 28 *RLH ESGNS patient experience*[a]

	All patients (*n* = 48)	Stoma at baseline (*n* = 21)	No stoma at baseline (*n* = 27)
Total person-days	67576	36461	31295
During intervention	7482	3922	3560
Subsequent to intervention	60094	32539	27735
Mean person-days	1407.8	1490.2	1343.7
During intervention	155.9	169.5	145.3
Subsequent to intervention	1252.0	1320.7	1198.5
Person-days by year after initiation			
Year 1	17512	7665	9847
Year 2	15767	7188	8579
Year 3	13318	6032	7286
Year 4	10693	5028	5665
Year 5	6823	3457	3366
Year 6	3417	1920	1497
Year 7	46	5	41

[a] Patient selection differs slightly from clinical study.

In accordance with current guidance, future health outcomes and costs are discounted to the present at rates of 1.5 and 6% p.a., respectively.

Model inputs

These are probability values, costs and utilities, most of which have been derived from the data collected for ESGNS and comparison patients during the course of this study. Base-case input parameters and their derivations are shown later in *Tables 37* and *38*.

Sensitivity analysis, uncertainty

The impact on the economic result (ICER) of altering model input parameters has been examined in conventional sensitivity analysis. This includes varying long-term costs and utility values using alternative values from the cost description, and also varying (assumed) rates of ESGNS failure, replacement and so on.

A fully probabilistic analysis may be undertaken by specifying distributions for key model inputs for which there is uncertainty and repeatedly running the model with different sampled values for these inputs. However, this was beyond the scope of the present analysis. Presentation of the results using a net benefits framework may also be undertaken, but this requires a conversion of health outcomes to costs (or vice versa) using the shadow price of the health outcome (threshold cost per QALY gained), which may not be warranted in the present context.

Summary of modelling assumptions

Assumptions underpinning the economic model are as follows:

- Patients with initial stoma care will continue with stoma care if ineligible for the ESGNS operation; however, they may revert to medical management if they are ESGNS surgical failures.
- Patients with initial medical management may convert to stomata any time. The rate of conversion to stoma (in those remaining stoma-free) declines with time.
- Mortality of patients is the same as for the general population and is not influenced by the type of management of FI. In particular, surgical mortality is not included in the model (no surgical deaths recorded).
- The costs calculated for the comparison group(s) are a fair representation of the costs that would be incurred by ESGNS patients if this procedure had not been available.
- Patients' health outcomes can be represented using QALYS derived from EQ-5D measurements.
- In the absence of ESGNS, patients would continue to experience their baseline QoL.
- QoL after the period of observation (5 years) remains constant.
- Devices (stimulator, etc.) are replaced at a constant annual rate.
- After the first few years (observed), the rate of late failure of ESGNS (i.e. patients having

TABLE 29 *Rates of failure after RLH ESGNS*

	Year		
	1	2	3+
All patients			
Events	4	7	6
PYs (free of ESGNS failure)	48.06	35.67	58.47
Event rate per PY	0.087	0.196	0.101
Event rate per PY			
Prior stoma	0.101	0.125	0.143
No prior stoma	0.078	0.255	0.063

stimulator removed and converting to other methods of managing FI) is constant.

Results

Forty-eight ESGNS patients have been included in the analysis. Private patients have been excluded. Of these, 21 (44%) had a prior stoma. Thirteen (27%) patients were male, 18 (38%) aged under 40 years and 10 (21%) aged ≥55 years. In eight (17%) patients, FI was caused by congenital anomalies, 23 (48%) obstetric trauma, 13 (27%) other trauma and four were due to other cases. Twenty-one (44%) patients had suffered the condition for ≥10 years. Thirty-one (65%) patients had a functioning ESGNS at the end of the study, 12 (25%) reverted to stoma and five (10%) reverted to medical management.

The group included in the cost analysis are slightly different from those included in the outcomes assessment. The difference occurs with the substitution of four private patients by four patients who were not included in the outcomes assessment, but who nevertheless underwent graciloplasty at RLH during the study period and have been described previously.

Health outcomes

Clinical (surgical) success

Seventeen patients were reported to experience surgical failure. Eight of these had stomas prior to ESGNS surgery. Four failures occurred in the first year after the initiation of ESGNS, seven in the second year and six in subsequent years. *Table 29* reports estimated time (PYs) free of failure and calculated hazards of failure by time from start of intervention: 0.09/PY in year 1, 0.20/PY in year 2 and 0.10/PY in years 3+.

Of those experiencing surgical failure, nine were previously being managed medically for FI. Of these, seven (78%) are now receiving stoma care and two are being managed medically. Of eight surgical failures with prior stoma, five (63%) returned to stoma care and three to medical management.

In 45 ESGNS patients from other centres (3.91 PY of experience, 3.20 PY after intervention free of failure), 11 clinical failures were reported. This is equivalent to a hazard rate of 0.08 failures/PY.

Quality-adjusted life-years

In total, 44 RLH ESGNS patients provided QALY information, and for 32 of these QALYs could be calculated for at least 3 years of observation. Results are summarised in *Table 30*.

The mean utility value corresponding to EQ-5D reported at baseline was 0.633 [standard deviation (SD) 0.260]. Patients with prior stoma had a higher value (mean 0.604) than patients being managed medically at baseline (0.653). The median value was 0.690 (inter-quartile range 0.595 to 0.790). Five patients reported values <0.500 at baseline, with one patient reporting a negative value.

Reported utility values dipped to <0.600 during the intervention and immediately afterwards, but thereafter returned to between 0.640 and 0.700. Higher values were reported at beyond 4 years after the intervention, but for relatively few patients (who were entered early into this study).

Aggregate QALYs were 0.596 (SD 0.243) for year 1, 0.674 (SD 0.282) for year 2 and 0.730 (SD 0.280) for the aggregated reported patient experience over years 3–5. Over years 3–5, five patients (two with surgical failure) reported average QALYs <0.500, with two (one with surgical failure) reporting negative values. Excluding patients for whom baseline utility scores were missing results in slightly lower QALY values, the average for years 3–5 now being 0.701.

TABLE 30 *EQ-5D utility valuations and QALYs (RLH ESGNS and comparator groups)*

	ESGNS patients: overall			ESGNS: status at start		Comparison group: overall
	Patients	Mean value	Excluding patients missing baseline	Stoma	No stoma	
Mean utility valuations by timing[a]						
Baseline	39	0.633	0.633	0.604	0.653	0.682
6 weeks	44	0.533	0.511	0.572	0.507	N/A
6 months	44	0.641	0.613	0.692	0.606	0.667
12 months	41	0.677	0.643	0.679	0.676	0.688
24 months	36	0.699	0.671	0.751	0.658	0.681
36 months[b]	31	0.687	0.670	0.710	0.670	N/A
48 months[b]	16	0.770	0.741	0.699	0.826	N/A
60 months[b]	7	0.894	0.893	0.857	0.923	N/A
Mean QALYs[c]						
Year 1	39	0.596	0.596	0.597	0.596	0.673
Year 2	36	0.674	0.643	0.695	0.657	0.684
Year 3	32	0.693	0.661	0.751	0.653	N/A
Year 4	16	0.760	0.755	0.755	0.763	N/A
Year 5	7	0.834	0.789	0.717	0.922	N/A
Average years 3–5[d]	55PYs	0.730	0.701	0.748	0.718	N/A

N/A, not applicable.
[a] In the case of ESGNS patient this refers to time after completion of intervention.
[b] Data for year 3 not collected for comparison group patients.
[c] In the case of ESGNS patients calculated from start of intervention.
[d] Value per PY.

TABLE 31 *Costs of patients assessed for ESGNS but not proceeding to ESGNS (RLH)*

	ESGNS	No ESGNS	Total
Patients assessed by service	51	165	216
Patients not proceeding to ESGNS	**Units**	**Unit cost (£)**	**Cost (£)**
CNS consultation (counselling) hour	137	19	2,603
Outpatient clinic attendance	225	122	27,450
Physiology assessment: ARP	80	350	28,000
Physiology assessment: Endo-anal US	80	200	16,000
Physiology assessment: defecating proctogram	40	250	10,000
Total			**84,053**
Cost per patient not proceeding to ESGNS (£)			509
Additional cost per patient proceeding to ESGNS (£)			1,648

Table 30 also provides information on QALYs for patients with prior stoma or no stoma, and by surgical success or failure. Although starting from a lower baseline, the patients with prior stoma were reported to have higher QALYs than the remaining patients (average for years 3–5, 0.748 versus 0.718). Conversely, patients reporting surgical success had a higher baseline but generally lower values than surgical failures (average for years 3–5, 0.710 versus 0.757).

Finally, QALYs were calculated for 77 comparison group patients. The mean utility value at baseline was 0.682. QALYs calculated for these patients were 0.673 (SD 0.307) for year 1 and 0.684 (SD 0.296) for year 2.

Resource use and costs

Patients not proceeding to surgery

The costs of assessment of those not initiated on ESGNS surgery need to be included in the cost of the intervention, as these costs would not be incurred if the intervention were not available. These costs are estimated in *Table 31*, based on information provided by the Colorectal Development Unit at RLH.

An estimated £84,000 was spent on assessing 165 patients who did not proceed to ESGNS. This corresponded to 51 patients who proceeded to ESGNS [the rate of proceeding to surgery is therefore 23.6% (51/216)]. These costs are £509 per patient not proceeding to ESGNS, equivalent to £1648 per ESGNS patient.

ESGNS patients

Forty-eight patients were included in the cost analysis, with mean follow-up from initiation of ESGNS of 3.4 years. Twenty-one patients had a stoma at baseline.

Hospital resource use (totals and mean values per patient) for these patients is reported in *Table 32*. On average, patients experienced 5.2 admissions, 2.6 during intervention and 2.5 after intervention. The mean length of stay per admission (bottom panel of table) was higher for admissions during intervention (13.1 versus 9.0 days), resulting in 34.4 of the average 54.9 bed-days per patient being during the intervention and 19.5 after the intervention. On average, patients experienced 4.9 operations (2.9 during intervention) and 16.7 outpatient visits and in total 52 stimulators were implanted. There were no clear differences between patients with or without stoma at baseline.

Costs are summarised in *Table 33*. Overall, the average cost per patient included in the study was £33,574, of which the majority (83%) was for inpatient care, theatre use and implantable devices. The mean cost of patient care during the intervention itself was £22,089, 91% of which was for inpatient ward use, theatre use and devices. In addition, on average £1164 was incurred before the intervention start date (admission for first operation), giving a total for 'before and during' the intervention of £23,253. The estimated cost per PY was £3011 for the remainder of year 1 (after the end of the intervention itself; 72% of this cost is for readmissions), £3649 during year 2 and £1864 during subsequent years. The estimated cost per patient year was higher for patients with prior stomas than for patients without prior stomas.

A full analysis of the variation of costs has not yet been undertaken. However, in these patients the average cost of inpatient ward and theatre use (including devices) before and during the intervention was £20,414 (SD £3910), with a median value of £19,713 and an inter-quartile

TABLE 32 *ESGNS patients: use of hospital services (RLH)*[a]

	Numbers			Mean values		
	All patients (*n* = 48)	**Stoma at baseline (*n* = 21)**	**No stoma at baseline (*n* = 27)**	**All patients**	**Stoma at baseline**	**No stoma at baseline**
Admissions	248	108	140	5.2	5.1	5.2
Before primary intervention	9	7	2	0.2	0.3	0.1
During primary intervention	137	66	71	2.9	3.4	2.6
After primary intervention	102	35	67	2.1	1.7	2.5
Bed-days	2640	1105	1535	55.0	52.6	56.9
Before primary intervention	36	31	5	0.8	1.5	0.2
During primary intervention	1668	739	929	34.8	35.2	34.4
After primary intervention	936	335	601	19.5	16.0	22.3
Operations	234	114	120	4.9	5.4	4.4
Before primary intervention	5	5	0	0.1	0.2	0.0
During primary intervention	153	75	78	3.2	3.6	2.9
After primary intervention	76	34	42	1.6	1.6	1.6
Outpatient visits	785	334	451	16.4	15.9	16.7
Before primary intervention	85	34	51	1.8	1.6	1.9
During primary intervention	240	99	141	5.0	4.7	5.2
After primary intervention	460	201	259	9.6	9.6	9.6
Devices						
Stimulator	52	22	30	1.1	1.1	1.1
Epineural electrode	58	26	32	1.2	1.2	1.2
Intramuscular electrode	4	2	2	0.1	0.1	0.1
Mean length of stay (days)						
Overall				10.6	10.2	11.0
Before primary intervention				4.0	4.4	2.5
During primary intervention				12.2	11.2	13.1
After primary intervention				9.2	9.6	9.0

[a] Patient selection differs slightly from clinical study.

range of £17,016 to £22,784. The highest cost (£36,881) was incurred for a patient with a surgical failure, who experienced three admissions and 97 bed-days during the intervention. For the majority of the patient group there was little variation in hospital costs.

Two operations were reported for ESGNS patients where the stimulator was replaced (with or without lead replacement), subsequent to the end of the initial intervention. The mean cost of these operations (including device cost) was £6561. Two further replacement operations were undertaken for patients with complications, costing on average in excess of £10,000.

Other ESGNS sites

Table 34 provides summary information for three other sites in which the ESGNS operation has been performed.

Information was obtained for 45 patients over a mean follow-up period of 3.9 years. These patients experienced 82 admissions (657 bed-days: mean length of stay 8.0 days per admission, 14.6 bed-days per patient) and 62 operations during the intervention itself. A further 61 admissions and 215 bed-days were reported subsequent to the intervention. The estimated mean cost of the intervention per patient (based somewhat crudely on a cost per surgery bed-day of £368 and device costs as for ESGNS patients) was £11,731. Mean costs per patient year of follow-up were £972 for year 2 and £795 for subsequent years after the start of the intervention.

These values are lower than those for RLH, reflecting a different technique for performing ESGNS, requiring fewer repeat admissions and operations.

TABLE 33 *Mean costs per ESGNS patient, by category of cost, time period and prior status (RLH)*

Category of cost	Total	Timing related to intervention			Year after start of intervention		
		Before	During	After	Year 1 (including before ESGNS)	Year 2	Year 3+
Costs by category of cost							
RLH: inpatient ward use (£)	15,053	257	9,548	5,249	11,981	1,735	1,337
RLH: theatre use (including staff, devices) (£)	12,771	42	10,569	2,161	11,042	672	1,056
RLH: outpatient (£)	2,844	692	761	1,391	1,958	472	415
Other: inpatient and outpatient (£)	2,039	174	941	924	281	245	507
Other: community staff (£)	866	0	271	595	181	158	327
Total (£)	**33,574**	**1,164**	**22,089**	**10,320**	**25,443**	**3,282**	**3,643**
PYs			0.43	3.43	1.00	0.90	1.96
Mean cost per PY (£)				3,011	25,472	3,649	1,864
Mean costs by prior status							
Cost/PY: stoma before (£)				3,618	26,105	4,509	1,991
Cost/PY: no stoma before (£)				2,295	24,727	2,623	1,694

TABLE 34 *Resource use and costs: other ESGNS sites (Edinburgh, Hull, Newcastle)*

	Patients	Patient-days	Admissions	Bed-days	Operations	Stimulators	Total cost (£)	Average cost per patient (£)	Average cost per PY (£)
During Intervention	45	6,035	82	657	62	43	527,874	11,731	Not relevant
After Intervention	45	58,300	61	215	42	9	127,408	2,831	798
Year 1	45	16,425	92	685	69	44	544,022	12,089	12,098
Year 2	45	16,096	20	70	9	3	42,824	Not relevant	972
Years 3+	(38)	31,439	31	117	26	5	68,436	Not relevant	795

These values were used to derive alternative model cost inputs by adding to these inpatient (including theatre) costs estimated for other sites the estimated costs of outpatient care, 'other inpatient and outpatent care' and community health services reported for RLH patients. Resulting values are £14,570 (ESGNS intervention), £175 (remainder of year 1, after intervention), £1945 (year 2) and £1435 (years 3+).

Comparison groups

Summary results for comparison groups are presented in *Table 35* (resource use) and *Table 36* (mean costs per PY).

Forty-two patients medically managed for FI and 32 with stoma were included. Of these, 28 (FI) and 11 (stoma) had been assessed for ESGNS surgery but did not proceed to surgery and 19 (FI) and 21 (stoma) were managed at other centres and not considered for ESGNS surgery. A total of 223 questionnaires were administered to these patients (average 2.8 per patient).

Patients with FI managed medically

Of the 28 FI patients who had been considered for ESGNS, five underwent colostomy and converted to stoma care over the course of 2 years. This corresponds to 440 patient-months (36.7 years) of recall (without stoma), at an annual rate of conversion of 13.6% per (stoma-free) PY. None of the 19 FI patients not considered for ESGNS converted to stoma over the study period.

Patients being medically managed for FI reported 81 outpatient visits and 18 hospital admissions (164 bed-days) over the recall period. This corresponded to an estimated £670 per PY. However 12 admissions (126 days) were associated with stoma formation and management. When patients with such admissions were excluded, the estimated cost of patient management (inpatient and outpatient only) became £215 per PY. Mean costs per PY for other cost categories were £98 (community health staff), £33 (prescribed medications) and £94 (prescribed appliances/incontinence aids, etc.). The total estimated cost per PY was £1029 if patients with stoma-related admissions are included and £442 when these patients were excluded. The cost of inpatient and outpatient care appeared to be slightly higher in the period prior to baseline than during study follow-up.

Five patients initially managed medically for FI but converting to stoma during the course of follow-up were reported to have experienced five admissions and 90 inpatient days for stoma formation (plus a further three admissions and 30 days for stoma-related complications). This corresponds to £6624 per patient. One patient experienced 45 inpatient days. NHS reference costs (2002) report the mean cost for HRG F31 (large intestine: complex procedures) as £4951 (length of stay: 15 days).

Patients with initial stoma

Patients with initial stoma reported 38 outpatient visits (12 before baseline and 26 during follow-up) and 15 admissions (eight before baseline and seven during follow-up), resulting in 141 bed-days (116 before baseline and 25 during follow-up). When estimating the ongoing costs of management of patients with stoma, it is somewhat misleading to include the inpatient costs prior to baseline, as these include 62 days (three admissions) occurring for a single patient with severe bowel obstruction, two colostomy formations and two admissions related to ileostomy and subsequent complications. For this reason, totals **excluding** reported inpatient and outpatient care before baseline are used in this analysis.

One patient with stoma considered for ESGNS had an artificial bowel sphincter (ABS) implanted during the course of follow-up.

The mean cost per PY for inpatient and outpatient care for these patients was £238. Mean costs per PY for other cost categories were £88 (community health staff), £19 (prescribed medications) and £1781 (stoma appliances). The total estimated cost per patient year was £2125. This rose to £2663 if pre-baseline inpatient and outpatient resource use was included.

Model-based analysis

Base-case results

Base-case model input parameters are shown in *Table 37* (probabilities) and *Table 38* (costs, utilities). Mortality rates are given in *Table 39*.

Table 40 presents base-case results. For patients initially managed medically, the strategy 'refer for ESGNS assessment' resulted in an estimated lifetime (25-year) discounted cost of £33,720 per patient, compared with £34,043 for immediate conversion to stoma care and £20,309 for continued medical management. The incremental cost compared with continued medical

TABLE 35 *Resource use: comparison group patients, by patient group*

Patient group	Patients	12 months before baseline			Subsequent to baseline		
		Outpatient visits	Inpatient stays	Inpatient days	Outpatient visits	Inpatient stays	Inpatient days
FI at start							
All FI patients	47	45	7	34	36	11	130
Not-accepting ESGNS group	28	28	7	34	18	10	124
Not-offered ESGNS group	19	17	0	0	18	1	6
FI (without subsequent stoma)	42	38	3	28	28	3	10
Stoma at start							
All stoma patients	32	12	8	116	26	7	25
Not-accepting ESGNS group	11	6	3	62	5	3	14
Not-offered ESGNS group	21	6	5	54	21	4	11

TABLE 36 *Mean costs per patient year: comparison group patients, by patient group and category of cost*

Patient group	Patients	Inpatient/outpatient		GP/Nurse visits (£)	Prescription medications (£)	Prescription appliances (£)	Stoma appliances (£)	Total	
		Before baseline and during follow-up (£)	During follow-up only (£)					Including inpatient/ outpatient before baseline (£)	Excluding inpatient/ outpatient before baseline (£)
FI at start									
All FI patients	47	670	824	147	43	92	77	1183	1029
Not-accepting ESGNS group	28	980	1,279	182	45	25	122	1652	1353
Not-offered ESGNS group	19	130	142	86	40	217	0	485	473
FI (without subsequent stoma)	42	215	105	98	33	94	0	331	442
Stoma at start									
All stoma patients	32	776	238	88	19	0	1781	2663	2125
Not-accepting ESGNS group	11	1255	384	45	21	0	1756	3077	2207
Not-offered ESGNS group	21	545	172	109	17	0	1794	2465	2092

TABLE 37 *ESGNS model input parameters: probabilities*

Parameter	Value (%)	Source	Comment
% of referred patients eligible for ESGNS	23.6	Colorectal Development Unit (RLH)	51/216 patients assessed for ESGNS
% of ESGNS failures, initially medical management converted to stoma	78	ESGNS analysis (RLH patients)	7/9 failures with no prior stoma
% of ESGNS failures, initially stoma, returning to stoma	63	ESGNS analysis (RLH patients)	5/8 failures with prior stoma
Annual rate of failure after ESGNS		ESGNS analysis (RLH patients)	
Year 1 (immediate)	8.7		Alternative: 8% (other sites)
Year 2	19.6		Alternative: 8% (other sites)
Years 3–5	10.1		Alternative: 8% (other sites)
Years 6+	5	Assumption	Alternatives: 10.1%, 8%, 0%
Annual rate of replacement of stimulator	14	Assumption	Based on 100% replacement required every 7 years: assume constant rate
Annual rate of conversion from medical management to stoma			
Years 1–2	13.6	Comparator group 'not-accepting surgery' patients (5/28 in first 2 years)	Calculated per PY of follow-up, data are for 2 years
Years 3–4	10	Assumption	Assume rate will decline
Years 5+	5	Assumption	
Patient survival (annual mortality rate)	See *Table 40*	ONS mortality tables	Increase by age, assume same as general population. Median age at start for ESGNS patients is 46 years

ONS, Office of National Statistics.

TABLE 38 *ESGNS model input parameters: costs and utilities*

Parameter	Value	Source	Comment
Costs			
Primary Intervention (ESGNS), including preparation (£)	23,253	ESGNS analysis (RLH patients)	Include 'before' costs; alternative value £14,570 from other ESGNS centres
Diagnostic work-up for patients not proceeding to ESGNS surgery (£)	509	Colorectal Development Unit analysis	
Replacement of stimulator (admission, device) (£)	6,561	ESGNS analysis (RLH patients)	Mean of 2 operations
Stoma formation (inpatient admission) (£)	6,624	Comparator patients analysis	Mean of 5 operations; alternative value (NHSRC HRG F31) £4,951
Cost of patient management (per PY)			
ESGNS patients: year 1 (after intervention) (£)	2,348	ESGNS analysis (RLH patients)	Excluding intervention costs, alternative value £175 from other ESGNS centres
ESGNS patients: year 2 (£)	3,649	ESGNS analysis (RLH patients)	Alternative value £1,945 from other ESGNS centres
ESGNS patients: years 3–5 (£)	1,864	ESGNS analysis (RLH patients)	Alternative value £1,435 from other ESGNS centres
ESGNS patients: long-term (£)	1,512	Assumption	ESGNS patients without clinical failure; alternative value £1,435 from other ESGNS centres
Annual cost of patient management: stoma care (£)	2,125	Analysis: comparator patients	'Before' inpatient/outpatient experience excluded
Annual cost of patient management: medical management (£)	442	Analysis: comparator patients	Excluding costs of stoma formation, stoma care
Utilities			
ESGNS patients: year 1	0.596	EQ-5D utility assessment	Alternative value 0.593 (patients with baseline value)
ESGNS patients: year 2	0.674	EQ-5D utility assessment	Alternative value 0.643 (patients with baseline value)
ESGNS patients: years 3–5	0.730	EQ-5D utility assessment	Alternative value 0.701 (patients with baseline value)
ESGNS patients: long-term	0.710	Assumption	ESGNS patients without clinical failure: alternative value 0.701 (patients with baseline value)
Survival with stoma	0.633	EQ-5D utility assessment	Baseline for ESGNS patients
Survival with medical management	0.633	EQ-5D utility assessment	Baseline for ESGNS patients

management was £13,412, for an estimated (discounted) QALY gain of 0.336, at a cost per QALY gained of £39,927.

For patients initially with a stoma, the discounted costs were £32,601 (ESGNS) and £27,419 (continued stoma care), with an incremental cost of £5182 and cost per QALY gained of £15,428.

When alternative costs of inpatient care for ESGNS patients (based on the analysis of other centres) were used in combination with outpatient and community healthcare costs reported by the RLH patients, the incremental costs were smaller. For patients initially managed medically the incremental cost of ESGNS was £9901 and for those with stoma initially they were £1672. Corresponding ICER, were £29,476 and £4,977 per QALY gained (*Table 40*).

TABLE 39 *England and Wales mortality rates (per 1000 persons, per year, all cause)*

Age group (years)	Males	Females	Both
0–4	1.6	1.2	1.4
5–9	0.2	0.1	0.1
10–14	0.2	0.1	0.2
15–19	0.6	0.3	0.4
20–24	0.9	0.3	0.6
25–29	0.9	0.4	0.6
30–34	1.0	0.5	0.8
35–39	1.3	0.8	1.1
40–44	2.0	1.3	1.7
45–49	3.1	2.1	2.6
50–54	5.3	3.5	4.4
55–59	9.0	5.5	7.3
60–64	15.8	9.2	12.4
65–69	27.5	15.9	21.4
70–74	45.9	26.9	35.3
75–79	72.3	43.1	54.8
80–84	115.4	74.0	88.4
85–89	172.0	121.7	135.8
90+	273.4	214.3	225.6
Total	10.8	11.2	11.0

Sensitivity analysis

Results of univariate sensitivity analysis are reported in *Table 41*.

Using a 5-year rather than a 25-year time horizon results in considerably worse cost-effectiveness values. This is because much of the extra cost is incurred in the first few years, but many of the projected QALY gains from patients having a functioning ESGNS occur after 5 years.

Using undiscounted values has a relatively small impact on the overall result, interestingly in different directions for the two comparisons representing the choices for patients initially managed medically or initially using stoma care. Using the slightly lower utility average values

TABLE 40 *Model-based results: base case*

	Strategy values		Incremental values[a]	
Strategy	**Cost (£)**	**QALY**	**Cost (£)**	**QALY (£)**
Patients managed medically at outset				
Refer to ESGNS (RLH)	33,721	12.796	13,412	39,927
Convert to stoma	34,043	12.460	13,734	Not defined
Remain with medical management	20,309	12.460		
Patients managed with stoma at outset				
Refer to ESGNS (RLH)	32,601	12.796	5,182	15,428
Remain with stoma	27,419	12.460		
Alternative: inpatient costs based on other ESGNS centres				
Patients managed medically at outset				
Refer to ESGNS	30,210	12.796	9,901	29,476
Convert to stoma	34,043	12.460	13,734	Not defined
Remain with medical management	20,309	12.460		
Patients managed with stoma at outset				
Refer to ESGNS	29,091	12.796	1,672	4,977
Remain with stoma	27,419	12.460		

[a] Values are compared with medical management for those managed medically at outset and compared with stoma management for those with stoma at outset.

TABLE 41 *Model-based results: sensitivity analysis*

Input parameter altered	Initially medically managed		Initial stoma	
	Incremental cost (£)	Cost per QALY gained (£)	Incremental cost (£)	Cost per QALY gained (£)
Base case (25 years)	*13,412*	*39,927*	*5,182*	*15,428*
Alternative costs (using inpatient costs from other ESGNS centres)	*9,901*	*29,476*	*1,672*	*4,977*
5-year time horizon (base case 25 years)	9,397	142,679	6,200	94,135
No discounting (base case costs 6%, health outcomes 1.5%)	17,668	44,046	4,130	10,297
Alternative utility values (excluding 5 patients with missing baseline values) – see *Table 38*	13,412	48,418	5,182	18,708
Rate of ESGNS replacement set to 5% p.a. (base case 14% p.a.)	12,609	37,537	4,380	13,038
Rate of late failure after 5 years of ESGNS set to 0% (base case 5%)	13,488	40,154	5,342	15,904
Age at start: 35 years (base case 45 years)	13,559	38,632	5,143	14,654
Age at start: 55 years (base case 45 years)	13,017	43,682	5,284	17,732

obtained by excluding all measurements for the five ESGNS patients with no EQ-5D measurement at baseline slightly worsens the ICERs. The cost-effectiveness result was not very sensitive to assumptions about ESGNS replacement rates and late failure (after 5 years). The results were not very sensitive to the starting age of patients (this only influences on the mortality parameter in the model and not any clinical effectiveness parameters) with slightly worse ICERs for older patients.

Summary of results and discussion

Summary

The mean cost of the ESGNS intervention in patients managed at the Colorectal Development Unit, RLH, was estimated to be £23,253, including work-up at the unit and use of other NHS services during the intervention period (mean duration 156 days). Over 90% of this cost was for inpatient ward use, theatre use and devices. Patients on average experienced 2.9 admissions resulting in 35 bed-days during the intervention. The mean cost of inpatient care (ward use, theatre use, devices only) for ESGNS patients treated elsewhere was estimated to be £11,731, resulting from less than two admissions and 15 bed-days per patient. The mean cost of assessment of RLH patients who did not proceed to surgery was £509.

The mean healthcare cost of patient management for all ESGNS patients after the intervention itself declined to £1864 per PY, based on reported patient experience ≥3 years after the start of the intervention. The cost for patients with surgical success was lower at £1512 per PY, which excludes the future cost of planned replacements of the stimulator.

An analysis of comparable patients who did not proceed to ESGNS surgery or from centres where it was not offered has reported a mean cost per patient year of £2125 for those with stoma and £442 for those managed medically.

In total, 17 out of 48 ESGNS patients managed at the RLH experienced a surgical failure during the course of follow-up, equivalent to a failure rate (in those remaining free of failure) of about 10% per PY. A similar rate of about 8% per PY was reported for other ESGNS centres. A small gain from the baseline value in QALYs (derived from successive responses to the EQ-5D instrument) from baseline was reported for RLH ESGNS patients. The baseline utility score was 0.633. Estimated QALYs were <0.600 in the first year (year of intervention) but increased to >0.700 per PY for years 3 and beyond.

An economic model has been used to integrate the results from these analyses for two decision contexts: patients being managed medically (refer

to ESGNS, form stoma, continue with medical management) or patients with prior stoma (refer to ESGNS or continue stoma). Over 25 years of follow-up it was estimated that for patients with prior medical management the decision to refer to ESGNS resulted in an extra cost (discounted) of £13,412, for an estimated QALY gain (discounted) of 0.336, an ICER of about £40,000 per QALY gained. Using inpatient care costs based on the other ESGNS centres reduced this value to around £30,000 per QALY gained. The choice of stoma for these patients resulted in a slightly higher cost than ESGNS.

For patients with prior stoma, referral to ESGNS resulted in an extra cost of £5182 for an ICER of ~£15,000 per QALY gained, reducing to £5000 per QALY gained when alternative inpatient costs were used. The results were relatively robust to most modelling assumptions.

Discussion

The costs reported in the analysis of ESGNS patients did not include patients' own costs (transport, over-the-counter medications, laundry, etc., and other materials) and 'indirect' costs associated with improved ability to work or undertake usual activities. Assuming that stoma patients require more of these resources, it is likely that in the long term the excess costs for ESGNS patients from a broader perspective will be less than those reported here. However, in the short term adding travel costs (average in excess of 15 outpatient visits for ESGNS patients) would increase the cost for these patients.

ICERs of ~£30,000 per QALY gained or less are generally regarded as being reasonably attractive in the UK NHS context. This would imply that a strategy to refer patients for ESGNS surgery would be regarded as cost-effective for patients already with stoma, and on the margin of being regarded as cost-effective for patients initially being managed medically. Cost-effectiveness in the second group is substantially improved, although still on the margin if the lower inpatient costs calculated for patients treated at northern ESGNS centres are used.

Any conclusion from the economic evaluation should, however, be treated with caution as the interpretation of the reported relatively small QALY gains reported for ESGNS patients is not straightforward. The estimated QALY gains were based from a relatively small number of patients (44, 32 of whom contributed at least 3 years of experience), and it has not been possible to assess the probability of the reported QALY gain being obtained by chance. As discussed in Chapter 7, the EQ-5D instrument may not be sufficiently sensitive to represent gains in QoL associated with improved faecal continence. As observed, more condition-specific instruments showed larger changes. No information has been obtained to permit a realistic comparison of the options of stoma formation and continued medical management in patients with refractory FI.

On the other hand, the utility values reported for ESGNS patients behaved as expected, with an initial drop followed by an increase over subsequent years. The values for comparison group patients, although slightly higher at baseline, remained steady over 2 years. The economic model that the long-term utility tariff used for ESGNS patients was the lower value calculated for surgical 'successes' rather than the cohort value, which is probably a conservative assumption, tending if anything to give an underestimate of potential QALY gains.

Finally, as in most modelling studies of this kind, much of the cost differences and QALY gains reported from the economic model is based on assumptions about projected rates and costs measured in the short term. However, the univariate sensitivity analysis reported here suggests that the results are not very sensitive to individual parameter assumptions.

Appendix 1 (*Tables 51* and *52)* gives mean costs per patient by category of cost, time period and presence of prior stoma and success of ESGNS (RLH).

Chapter 7
Discussion

This study compares the outcomes and costs of an invasive surgical procedure with the outcomes and costs of two conventional alternatives – the formation of a stoma or continued conservative management of FI. There are several outcomes that have been evaluated, including: (1) clinical success or failure; (2) symptomatic outcomes concerning pain, continence, and evacuation; (3) QoL (generic, psychological and bowel specific); (4) patients' estimates of the success of surgery; and (5) cost comparisons of various alternatives. Because of the complicated nature of the comparisons described in this study, we have discussed separately some of the major limitations of the methods used. Regardless of the measures used, because of the long study interval, changes in surgical technique and patient selection may have affected the observed changes. One variable, duration of follow-up, influenced some findings. Overall, the interpretation of the findings in the surgical group is strengthened by comparison with findings from two other patient groups: those not offered surgery and those who chose not to undergo the procedure. We have included in this report the results of a study from other surgical centres in the UK, and also commented on use of all UK data together. We have compared our results with those of other published series. Although not directly a part of our study, we have added a discussion of the administrative implications of our findings concerning the future management of refractory FI.

Limitations of study methods

Numbers of patients and length of follow-up

The continuing recruitment of patients during a 5-year period has led to cohort effects, which result in diminishing numbers of before-and-after comparisons at the longer follow-up periods. Assessment of study power indicates that we had sufficient numbers to detect between-group differences of ≥20% at 2 years of follow-up for most main outcome measures and between-group differences in excess of this magnitude were observed for the bowel-specific scales and the Cleveland Clinic incontinence scale. At 3 years postoperation, numbers were sufficient to detect within-group differences of 20% and there is a consistent trend to detect significant improvements, some as large as 40%, for all main outcome measures at this 3-year follow-up point. Our sample, although small, has demonstrated improvements up to 4 years of follow-up for the ESGNS group. Large changes are unlikely to be due to chance. The study of the northern centres' patients supported the findings from the RLH prospective study. In spite of the small numbers, there were sufficient data to draw conclusions concerning most outcomes being evaluated.

Comparability of comparison groups

Although we attempted to recruit patients into our two comparison groups with bowel disorders suitable for ESGNS if it were offered, we cannot be certain that the bowel disorders in the comparison group patients were strictly comparable to those who received ESGNS. The process of recruitment into the comparison groups was cumbersome, involving many letters, and, for the not-offered surgery group, letters to surgeons, then GPs and then the patients, all without personal contact or discussion of any questions. Overall, about half of those contacted were willing to receive further contact. Once contacted, however, they continued to participate. Those who participated were similar in age, gender and cause of incontinence to those who did not. Patients in the not-accepting surgery group may have chosen not to proceed to ESGNS because they did not feel that the impact of their bowel disorder was sufficiently severe to warrant such major surgery. This is borne out by their better scores on the bowel-specific measures. Not-accepting surgery patients may also have been more likely to be actively seeking alternative ways of managing their bowel disorders and during the study follow-up period may have achieved some symptomatic or QoL improvements as a result of advice received during assessments for ESGNS. They may have tried dietary manipulation, biofeedback and/or medications. Some chose to undergo colonic conduit or stoma formation and, in one case, formation of an ABS. Patients in the not-offered surgery group were perhaps more likely to have reached a stable phase in adapting to their bowel disorder, although their bowel-specific scores were also significantly better than those of the ESGNS group. In spite of these

considerations concerning recruitment to the study, the generic QoL and symptom measures did not detect significant differences between the three groups.

Some caution is needed when comparing changes between groups over time, especially where baseline scores are dissimilar; those with 'better' baseline scores will have less potential for improvement over time and this could lead to exaggeration of between-group differences. However, such floor effects do not appear to have resulted in limited improvements for the comparison groups, apart from the NHP social isolation scale, which affected all groups similarly.

The effort to recruit comparison groups was not encouraged by our initial ethics committee or by the funding bodies. Recruitment was difficult, and required much time and effort. The comparison groups were initially included because of the consideration that since the ESGNS patients were at the extreme end of a continuum, it would be difficult to evaluate their outcomes and changes in QoL unless they were from the same end of a continuum. As we complete this analysis, we believe the value of the comparison group data justifies the extra work involved

Weaknesses of quality of life and symptom measures

As previously observed, in the absence (at the start of the study) of well-validated condition-specific measures of QoL and symptoms, we opted to employ a battery of measures which covered general health status in addition to the specific domains previously known to be associated with living with FI or stomas. There are many difficulties in assessing QoL and these are compounded by the fact that, in this study, some patients had stomas and some had FI both before surgery and during the follow-up period, body states which are not directly comparable. We did our best to devise a condition-specific measure (the RLH measure) that reflected the concerns of patients living with either disorder. This measure had to be produced rapidly and in suboptimal circumstances, as the surgical programme was already under way before the outcomes assessment study started. We know that the RLH measure should ideally have been further refined and tested prior to its introduction into the study. However, in spite of the late start, we have demonstrated that the RLH measure has internal consistency within two subscales, is responsive to change following surgery, discriminates between cases and comparison patients and correlates well with the appropriate domains of other standardised measures.

Generic and domain-specific measures of QoL, even when well validated and widely used, have their problems. This study, as most other published reports of QoL after ESGNS, failed to demonstrate more than small improvements in QoL following surgery. It is not possible to know whether this reflects a real absence of overall improvement in QoL following surgery or is due to lack of sensitivity in the measures used. Substantial 'floor' effects were observed in the EQ-5D and NHP generic measures, which mean that for a proportion of patients it was not possible to demonstrate improvements, because the score was already at the best end of the scale at baseline. This floor effect was particularly marked in the NHP social isolation scale. The improvements that were demonstrated within the RLH ESGNS group at 3 years postoperation were statistically significant, even if only small or moderate in size. Importantly, none of the generic or domain-specific measures detected any substantial deterioration for the RLH ESGNS group during the study period.

Symptom measurement problems

The Cleveland Clinic score,[44] which is a quantifying measurement of symptoms, is widely used in assessing FI, although it has been superseded since the start of this study. It arbitrarily imposes a scoring system which equates the burden of incontinence to solid stool to that of incontinence to flatus, or the need to wear pads or an inability to carry out usual activities. The Cleveland Clinic score is opaque in its interpretation. For example, a score of 10 could indicate daily incontinence to solid and liquid stool and frequent inability to carry out usual activities; it could also indicate monthly incontinence to solids, liquids and flatus, together with monthly wearing of a pad and monthly inability to carry out usual activities. To give a more transparent picture of symptomatic outcome, we have also reported frequency of incontinence to solid or liquid stool, since the primary aim of ESGNS is to improve this symptom. There are no validated measures of evacuatory disorders, which are appropriate for this patient group, and we have aimed to produce a simple and transparent indication of frequency of severe evacuation difficulty.

Management of faecal incontinence during 5 years of study

Since the start of this 5-year study, surgeons performing ESGNS may have become more

skilled and some modifications to techniques have been introduced, although the procedure had already been performed for 10 years at RLH prior to the start of this study. Our experience of comparison of RLH results with those from other centres gives us some indication of how the selection of patients has become more refined, resulting from the growing experience of multidisciplinary teams, and we are aware that there are some differences in techniques between centres, although the basic principle of the surgery is the same. Centres of excellence in the management of FI have reduced the numbers of people for whom the ESGNS procedure is needed. Although each of the four centres that we observed is different, all have common themes in providing nurse- and/or physiologist-led education prior to consideration of further surgery. The education encourages patients to take control of their bowel disorder by dietary modification, medication or exercises and may be sufficient in itself for many patients, sometimes even for those who have severe anatomical or physiological defects.

Availability of a new intervention, SNS, which is less invasive, but still costly, means that in the future it may be possible for some patients with refractory FI who have already tried medical management to consider SNS before being considered for ESGNS. Although initial SNS results are promising, the procedure has so far undergone only short-term and limited evaluation.

Difficulties associated with the evaluation of a surgical innovation

Wherever appropriate, practical and ethical, the study design of choice of a new procedure should be an RCT. However, it is clear that the gold standard of the RCT is often impossible for invasive interventions. For ESGNS, an RCT was considered ethically and surgically inappropriate, since the surgical alternative would be to form a stoma – a very different outcome to that anticipated when ESGNS is performed.

Early evaluation is important in order to prevent an unevaluated procedure from becoming diffused into widespread practice without rigorous assessment. However, early evaluation also involves the potential that the intervention changes during the evaluation. Also, if it is necessary to do an evaluation over a long period, this not only increases costs, but also involves further difficulties when the intervention is changing. As with this study, occasionally time is needed to develop and test condition-specific, patient-based outcome measures, as these are seldom available 'off the shelf'. We were lucky in the timing of our evaluation that the changes in the intervention were minimal. However, it is unfortunate that a significant new intervention, SNS, was being frequently considered only after our study had begun.

The best available alternatives to RCTs in multiple centres come with the price of selection and observer biases and differences in skills and patient management procedures of different surgeons. They also involve many more ethics committees. We hope that this study, predominantly in one centre, but using some data from other centres, has gone some way towards an adequate evaluation of the ESGNS intervention, notwithstanding the limitations.

The prevalence and character of refractory faecal incontinence

In designing this study, we considered that a major source of patients would be those dissatisfied with a stoma formed after colonic surgery. However, such patients appeared rare, not only in London, but also in the three regional centres. Useful data concerning FI in the UK were collected in Leicester by Perry and colleagues[22] during a large, community-based study of urinary incontinence. From the data of Perry and colleagues, we might expect to see both men and women in the age group over 60 years, with an excess of women in younger age groups. Although about one-quarter of our patients were male, few were elderly. It is unclear whether, in the presence of refractory incontinence, males do not present to the GP. In planning for the future, although the total numbers with FI will increase with the ageing of the population, it is difficult to assess the numbers with refractory incontinence.

Long-term funding for specialist centres for the management of refractory faecal incontinence

Refractory FI presents a continuing medical care problem, occasionally involving surgery. The care involved continuing contact with medical support teams, themselves with access to specialist services, including physiology, psychology and often stoma care.

A surgical intervention to deal with the problem adds a further dimension to the clinical care problem. Not only is surgery expensive, but also the follow-up care adds to the continuing care

need. It is important to realise that even following clinically successful ESGNS, patients will need lifelong access to specialist care and that complications and device failure can occur many years after the initial surgery

A well-planned tertiary refractory incontinence service can reduce the use of surgery. This will be the result by making available, at the time of referral, nurses with the ability to teach about dietary and lifestyle changes and biofeedback, psychologists available to explore the basis of the response to the medical problem, physiologists able to evaluate sphincter problems, in addition to a surgical team with the experience needed to consider surgical options.

All in all, the most cost-effective way to deal with the surgical option of ESGNS is to have a tertiary funded team, within a colorectal service. As a result of the funding of such a team, surgery costs will be minimised, overall costs reduced and the quality of patient care increased. Such a team can take a significant role in teaching, both of the patients, throughout their programme of care, and also of the involved medical staff, house officers and the surgical team.

Comparison of our results with previously published series

Criteria for success of ESGNS varied between studies. All published studies used continence levels to define success. Most studies defined a successful outcome as requiring at least continence to solid stool;[34] Wexner and colleagues[31] required a 50% reduction in the frequency of incontinent episodes.

No published study has compared the QoL of patients following ESGNS with that of a comparison group who did not undergo surgery. Baeten and colleagues[46] compared QoL and psychosocial outcomes between a group of successfully treated ESGNS and a group of unsuccessfully treated ESGNS patients and found that the successfully treated patients had significantly better scores for anxiety, work, usual activities and sexual and social function than the unsuccessfully treated patients. This finding was not replicated in our study, where members in the unsuccessful group were as likely to improve as to deteriorate. However, we used a clinical definition of success rather than a continence-based one and the numbers of 'failures', however defined, are small in both studies.

Hill,[47] in a retrospective outcome study, reported body pain in 24 out of 45 respondents (53%) and severe body pain in six (13%). In our study, 70% reported any pain on the EQ-5D scale and 8% reported severe pain at 2 years postoperation. Hill's sample was cross-sectional and used a different measurement scale, which may account for the difference. It is also notable that patients in the prospective RLH study showed, following surgery, almost no change on either the NHP or EQ-5D pain scales, and that both comparison groups had similar pain scores throughout their 2-year follow-up period.

Satisfaction with graciloplasty was high in 52% and medium in 23% of patients in Hill's study and this compares with 60% of patients <3 years postoperation in our study who said that their bowel condition had got better or much better and with 49% of patients who were between 3 and 6 years postoperation.

A later multicentre study by Baeten and colleagues[48] reported moderate and significant improvements at 12 months in three of eight domains of the Short Form 36 (SF-36) and no change in anxiety levels. A bowel-specific measure (TyPE specification) recorded significant and large improvements in all categories of activities of daily living. A reduction in frequency of incontinent episodes by 50% (or number of continent stools ≥50% for patients with preoperative stomas) was defined as the criterion of success and was achieved in 63% of non-stoma patients and in 57% of stoma patients at 18 months postoperation.

Wexner and colleagues[31] reported that at 2 years postoperation, out of 115 patients from a multicentre study, 15% were completely continent and 42% had 50–99% continence; it is not clear whether 'continence' implied continence to solid and liquid stool. This compares with the RLH ESGNS study where, at 2 years, 17% were never incontinent to solid or liquid stool and 47% were incontinent less than once per week. However, there is some overlap between the patients included in Wexner and colleagues' study and that of Baeten and colleagues[46] above. Rongen and colleagues[32] (Maastricht) reported success of 72% at a median of 5 years for 200 patients, success being defined as continence to all bowel contents or incontinent to flatus only. This compares with 23 and 22% who were never incontinent to solid or liquid stool at 4 and 5 years, respectively, in the RLH study together with 36 and 33% who were incontinent less than once per week. It is not clear how continence was assessed in the Dutch study

and it seems likely that there are some differences in the methods of measurement which may account for their apparently very high level of success. Rongen and colleagues reported chronically disturbed evacuation in 16%, a comparatively low figure compared with our study, where at least one-third of patients had ongoing problems throughout the follow-up period; again, it is not clear how evacuation disturbance was measured or how it was defined.[32]

There are important differences between the outcome study, which is the subject of this report, and those previously published. Previously published studies have all been conducted by clinicians involved in ESGNS patient care, whereas in this study, patients were aware that the investigators were independent and that their responses would not be revealed to the teams who had treated them. It is likely that some patient responses to their healthcare professionals may be biased towards giving a more favourable picture of outcomes than would be revealed to an independent investigator; there may also be some investigator bias in recording responses. These sources of bias may be responsible for the more favourable findings reported in some other studies.

Chapter 8
Conclusions

Evaluating a surgical intervention without an RCT is difficult enough, but in addition this evaluation faced other limitations in the fulfilment of its objectives, principally relating to insufficient numbers of patients. A separate limitation became evident during the study, when it was observed that outcomes of surgery were unstable for several years in some patients, suggesting that a longer than planned follow-up was important. To deal partially with these difficulties, the study period was extended and limited data from patients from the northern areas were collected. A third limitation, associated with the time period, involved dealing with changes in the management of incontinence and the growing expertise of teams in selecting patients and in performing the surgical procedure. Further limitations apply to the economic analyses, where caution is needed in interpreting cost-effectiveness ratios owing to the small numbers of patients and very small changes observed in the EQ-5D measure on which the QALY calculations are based.

Although these methodological limitations are significant and the conclusions must be interpreted with caution, we believe that, without the option of an RCT we have come as close as is possible to providing robust evidence concerning the outcomes of the procedure.

The report presented here, of work predominantly carried out at RLH, is the result of a study independently funded, initially by NHS London R&D, and independently directed. It is prospective, and includes, in addition to other data, information from the patients concerning their anticipation of success before surgery, and reports of their evaluations subsequently, over periods up to 5 years. As a result, the data in this report give a more comprehensive picture of the outcomes of an innovative surgical procedure than could be expected from those directly involved in the surgery. Although those who did the evaluation were not part of the surgery department, the study was initially and continually supported by the administration and staff of the surgery department at RLH, and could not have been completed without their cooperation.

Although predominantly a study of work done in one hospital, data are also included of work done in three other hospitals, during a comparable time period. These data support the results obtained at RLH, and make up, in part, for slow recruitment at RLH. We are very grateful for the warm welcomes and support which we received from the clinical teams in the surgical departments at Edinburgh, Hull and Newcastle.

The analysis was strengthened by the development, early in the study, of disease-specific measures of QoL for use with patients with refractory FI. This was because generic QoL measures are often insensitive in measuring disease-specific changes.

Studies such as this could form an integral part of efforts of the Health Technology Assessment Programme, NSCAG and NICE to develop useful evaluations of innovative procedures.

A summary of our findings follows. This should be considered in the light of the limitations discussed in Chapter 7 and summarised on the previous pages.

1. One view is that this treatment has limited long-term benefit. There may also be pain and difficulty with evacuation. Improved continence is of measurable benefit in some patients, but is achieved at considerable cost and has not achieved a cure in sufficient numbers to justify its continuation.

   An alternative view is that there is a place for ESGNS, but it is at the extreme end of the treatment spectrum for refractory FI. It is a complex operation associated with a high incidence of morbidity and a high incidence of failure in the long term. However, as an option for patients who have considered other conventional treatments and are facing the formation of a permanent stoma or continuing to live with a debilitating, socially disabling disorder, the procedure deserves consideration. It may be the only alternative for patients intolerant of a stoma. Previous studies have indicated a high level of long-term serious complications associated with stomas. Patients should be given a realistic picture of the possible outcomes of ESGNS.

2. Based on the findings of this study, a realistic expectation might be that 3 years postoperation, approximately three-quarters of all patients will still have a functioning neosphincter. Nearly two-thirds of all patients will have a satisfactory continence outcome at 3 years of follow-up, although half of them will have ongoing evacuatory difficulties. Bowel-related QoL and continence, when measured between 1 and 3 years postoperation, improve significantly and in excess of 20% when compared with preoperative status for nearly two-thirds of all the patients who undergo the surgery. The findings indicate that these improvements in QoL and symptoms are maintained in the smaller cohort of patients who have reached 4 and 5 years of follow-up, even though the clinical success rate has fallen somewhat at this length of follow-up.

   Addition of cross-sectional data from the three northern centres' ESGNS patients confirmed the findings recorded for the RLH patients in the postoperative period. Similar, but not identical, surgical techniques were used in the four centres. Patients with similar bowel disorders who did not undergo surgery did not experience significant changes in symptoms or QoL over a 2-year follow-up period.

3. Patients whose disorders are caused by anorectal agenesis (congenital anomalies) pose awkward surgical challenges. The outcomes for this group were poor; two-thirds of procedures failed during the study period.

4. The mean cost of patient care at RLH during and before the intervention itself was £23,253, 91% of which was for inpatient ward use, theatre use and devices. The estimated cost per PY was higher for patients with prior stomas than for patients without prior stomas. Costs of patient care for those with stomas who did not undergo ESGNS were estimated at £2125 per PY and for those who remained with severe FI costs were estimated at £442 per PY.

   In the northern UK centres, the estimated mean cost of the intervention per patient was lower at £11,731. This lower value reflects differences in technique for performing ESGNS, requiring fewer repeat admissions and operations.

   Over 25 years of follow-up, it was estimated that for patients with prior FI the decision to refer to ESGNS at RLH resulted in an ICER of about £40,000 per QALY gained. Using inpatient care costs based on the three northern ESGNS centres, this value reduced to around £30,000 per QALY gained. The choice of stoma for these patients resulted in a slightly higher cost than ESGNS.

   For patients with prior stomas, referral to ESGNS at RLH resulted in an ICER of around £15,000 per QALY gained, reducing to £5000 per QALY gained when inpatient costs were based on the three northern ESGNS centres.

   ICERs of around £30,000 per QALY gained or less are generally regarded as being reasonably attractive in the UK NHS context.

5. Because FI is socially debilitating and often of long duration, it is difficult for a patient to make a decision concerning therapy, and this problem is exaggerated when those offered surgery have not previously been offered less complex options. As a result, ESGNS is best offered in a tertiary centre, with facilities available to allow the patient to be considered for conservative and other options. Such a centre will have an experienced and multidisciplinary staff skilled in advising and supporting patients through a range of therapies and ultimately through complex decision-making processes. The staffing of a centre should include nurses, psychologists, physiologists and surgeons capable of dealing with all of the major options for therapy.

6. Because the problem is a chronic one, even with surgical correction, any centre offering ESGNS should have facilities for long-term follow-up and be available to a referring physician as a centre that can handle both technical and psychological problems. Lifelong specialist follow-up is required following ESGNS.

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Contribution of authors

Thérèse Tillin (Study Manager, now Research Fellow, Clinical Epidemiology, Department of Clinical Pharmacology, Imperial College) conducted the study, conducted analyses of symptomatic and patient-based outcomes with guidance from Roger Feldman (Epidemiology), Ken Gannon and Stan Newman (Health Psychology) and Allan Hackshaw (Statistics) and co-authored the Executive Summary and Chapters 1–5 with Roger Feldman.

Roger Feldman (Emeritus Professor of Clinical Epidemiology) designed and supervised the study, wrote Chapters 7–8 and co-authored Chapters 1–5.

Mike Chambers (Health Economics) designed the economic evaluation, supervised resource use data collection, conducted the cost analyses and wrote Chapter 6.

References

1. MacArthur C, Bick ED, Keighley MR. Faecal incontinence after childbirth. *Br J Obstet Gynaecol* 1997;**104**:46–50.
2. Byrne CM, Pager CKB, Rex J, Roberts R, Solomon MJ. Assessment of quality of life in the treatment of patients with neuropathic fecal incontinence. *Dis Colon Rectum* 2002;**45**:1431–6.
3. Sailer M, Bussen D, Debus ES, Fuchs K.-H, Thiede A. Quality of life in patients with benign anorectal disorders. *Br J Surg* 1998,**85**:1716–19.
4. Leigh RJ, Turnberg LA. Faecal incontinence: the unvoiced symptom. *Lancet* 1982;**i**:1349–51.
5. Rintala R, Mildh L, Lindahl H. Fecal continence and quality of life for adult patients with an operated high or intermediate anorectal malformation. *J Pediatr Surg* 1994;**29**:777–80.
6. Crowell MD, Schettler-Duncan A, Brookhart K, Barofsky I. Fecal incontinence: impact on psychosocial function and health related quality of life. *Gastroentereology* 1998;**114**:G3048.
7. National Institute for Clinical Excellence, Interventional Procedures Programme. *Interventional procedure overview of sacral nerve stimulation for faecal incontinence*. London: NICE; 2003.
8. Wade B. *A stoma is for life*. London: Scutari Press; 1989.
9. Thomas C, Madden F, Jehu D. Psychological effects of stomas – 1. Psychosocial morbidity one year after surgery. *J Psychosom Research* 1987;**31**:311–16.
10. White CA, Unwin JC. Post-operative adjustment to surgery resulting in the formation of a stoma: the importance of stoma related cognitions. *Br J Health Psychol* 1998;**3**:85–93.
11. Macdonald L, Anderson HR. Stigma in patients with rectal cancer: a community study. *J Epidemiol Commun Health* 1984,**38**:284–90.
12. Bekkers MJ, van Knippenberg FC, van Dulmen AM, van Berge Henegouwen G. Survival and psychosocial adjustment to stoma surgery and non-stoma bowel resection: a 4-year follow-up. *J Psychosom Res* 1997;**42**:235–44.
13. Bekkers MJ, van Knippenberg FC, van den Borne HW, Poen H, Bergsma J, van Berge Henegouwen GP. Psychosocial adaptation to stoma surgery: a review. *J Behav Med* 1995;**18**:1–31.
14. Shellito PC. Complications of abdominal stoma surgery. *Dis Colon Rectum* 2001;**41**:1562–72.
15. Makela JT, Laitinen ST. Analysis of late stomal complications flowing ostomy surgery. *Ann Chir Gynaecol* 1997;**86**:305–10.
16. Londono-Schimmer EE, Leong APK, Phillips RKS. Life table analysis of stomal complications following colostomy. *Dis Colon Rectum* 1994;**37**:916–20.
17. Park JP, del Pino A, Orsay CP, Nelson RL, Pearl R, Cintron JR, *et al*. Stoma complications: the Cook County Hospital experience. *Dis Colon Rectum* 1999;**42**:1575–80.
18. Porter JA, Salvati EP, Rubin RJ, Eisenstatt TE. Complications of colostomies. *Dis Colon Rectum* 1989;**32**;299–303.
19. Carne PWG, Robertson GM, Frizelle FA. Parastomal hernia. *Br J Surg* 2003; **90**:784–93.
20. Sprangers MA, Taal BG, Aaronson NK. Quality of life in colorectal cancer. Stoma vs non-stoma patients. *Dis Colon Rectum* 1995;**38**:361–9.
21. Grumann MM, Noack EM, Hoffman IA, Sclag PMS. Comparison of quality of life in patients undergoing abdomino-perineal extirpation or anterior resection for rectal cancer. *Ann Surg* 2001;**2**:149–56.
22. Perry S, Shaw C, McGrother C, Matthews RJ, Assassa RP, Dallosso H, *et al*. Prevalence of faecal incontinence in adults aged 40 or more living in the community. *Gut* 2002;**50**:480–4.
23. Williams NS. Surgery of anorectal incontinence. *Lancet* 1999;**353** (Suppl 1):31–2.
24. Pickrell K, Georgiade N, Richard EF, Morris F. Gracilis muscle transplant for the correction of neurogenic faecal incontinence. *Surg Clin North Am* 1959;**39**:1405–15.
25. Salmons S, Vrbova G. The influence of activity on some characteristics of mammalian fast and slow muscles. *J Physiol* 1969;**201**:531–49.
26. Dickson AS, Nixon HH. Control by electronic stimulator of incontinence after operation for anorectal agenesis. *J Paediatr Surg* 1968;**3**:696–701.
27. Baeten CG, Spaans F, Fluks A. An implanted neuromuscular stimulator for fecal incontinence following previously implanted gracilis muscle. Report of a case. *Dis Colon Rectum* 1988;**31**:134–7.
28. Williams NS, Patel J, George BD, Hallan RJ, Watkins ES. Development of an electrically stimulated neoanal sphincter. *Lancet* 1991; **338**:1166–9.
29. Mander BJ, Williams NS. The electrically stimulated gracilis neo-anal sphincter. *Eur J Gastroenterol Hepatol* 1997;**9**:435–41.

30. Madoff RD, Rosen HR, Baeten CG, LaFontaine LJ, Cavina E, Devesa M, *et al*. Safety and efficacy of dynamic muscle plasty for anal incontinence. *Gastroenterology* 1999;**116**:549–56.

31. Wexner SD, Baeten C, Bailey R, Bakka A, Bellin B, Bellivean P, *et al*. Long-term efficacy of dynamic graciloplasty for fecal incontinence. *Dis Colon Rectum* 2002;**45**:809–18.

32. Rongen MJ, Uludag O, El Naggar K, Geerdes BP, Konsten J, Baeten CGMI. Long-term follow-up of dynamic graciloplasty for fecal incontinence. *Dis Colon Rectum* 2003;**46**:716–21.

33. Adang EM, Engel GL, Rutten FF, Geerdes BP, Baeten CG. Cost-effectiveness of dynamic graciloplasty in patients with fecal incontinence. *Dis Colon Rectum* 1998;**41**:725–33; discussion 733–4.

34. Chapman AE, Geerdes B, Hewett P, Young J, Eyers T, Kiroff G, *et al*. Systematic review of dynamic graciloplasty in the treatment of faecal incontinence. *Br J Surg* 2002;**89**:138–53.

35. Kind P, Hardman G, Macran S. *UK Population norms for EQ-5D*. Discussion paper 172. York: University of York, Centre for Health Economics; 1999.

36. European Group for Quality of Life and Health Measurement. *European Guide to the Nottingham Health Profile*. Manchester: Galen Research and Consultancy; 1989.

37. McKenna SP, Hunt SM, Tennant A. The development of a patient completed index of distress from the NHP: a new measure for cost utility studies. *Br J Med Econ* 1993;**6**:13–24.

38. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; **67**:361–70.

39. Derogatis LR. *The Psychosocial Adjustment to Illness Scale – self report version*. Towson, MD: Clinical Psychometric Research Inc.; 1987.

40. Sarason BR, Shearin EN, Pierce GR, Samson IG. Interrelationships of social support. *J Personal Soc Psychol* 1987;**52**:813–32.

41. Carver CS, Schier MF, Weintraub JK. Assessing coping strategies. *J Personal Soc Psychol* 1989;**56**:267–83.

42. Schwarzer R, Jerusalem M. *Measurement of perceived self efficacy: psychometric scales for cross cultural research*. Berlin: Freie Universität; 1993.

43. Partridge C, Johnston M. Perceived control of recovery. *Br J Clin Psychol* 1989;**28**:53–9.

44. Oliveira L, Pfeifer J, Wexner SD. Physiological and clinical outcome of anterior sphincteroplasty. *Br J Surg* 1996;**83**:502–5.

45. (a) Jaeshke R, Singer J, Guyatt GH, (b) Juniper EF, Guyatt GH, Willan A, Griffith LE, (c) Osoba D, Rodrigues G, Myles J, Zee B, Pater J. Cited in Fayers PM, Machin D, editor. *Clinical interpretation, quality of life. Assessment, analysis and interpretation*. New York: John Wiley; 2000. Chapter 16.

46. Baeten CGMI, Geerdes BP, Adang EMM, Heinemann E, Konsten J, Engel GL, *et al*. Anal dynamic graciloplasty in the treatment of intractable fecal incontinence. *N Engl J Med* 1995;**332**:1600–5.

47. Hill H. Quality of life from the patient's point of view. *J Stoma Ther Aust* 1999;**19**:13–15.

48. Baeten CG, Bailey H, Bakke A, Belliveau P. Safety and efficacy of dynamic graciloplasty for fecal incontinence. Report of a prospective, multicentre trial. *Dis Colon Rectum* 2000;**43**:743–51.

Appendix 1

Supplementary tables

Tables 42–50 show comparative findings for the 'not-accepting' surgery group. *Tables 51* and *52* show details of inpatient costs for RLH patients.

TABLE 42 *Questionnaire response rates: RLH ESGNS, not-accepting and not-offered surgery groups*

	Number of patients (% of group)							
	Baseline	**3–5 months**	**6–9 months**	**12 months**	**24 months**	**36 months**	**48 months**	**60 months**
RLH ESGNS group	49	49	47	45	40	31	23	12
Sent questionnaire[a]	45	46	47	45	40	29[b]	21	10
Returned questionnaire	45 (92)[c]	45 (92)	44 (94)	44 (98)	39 (98)	29 (94)	19 (83)	8 (75)
Not-accepting surgery group	42	–	42	42	37	–	–	–
Sent questionnaire	42		42	42	37			
Returned questionnaire	40 (95)[c]		35 (83)	36 (86)	29 (78)			
Not-offered surgery group	45	–	45	45	45	–	–	–
Sent questionnaire	45		45	44	40[d]			
Returned questionnaire	41 (91)[c]		39 (87)	36 (80)	32 (71)			

[a] 4 patients underwent ESGNS prior to the start of the outcomes assessment study.
[b] 2 patients dropped out.
[c] Amongst these, the numbers who returned at least one follow-up questionnaire were 40/45 of the ESGNS group, 38/40 of the not-accepting surgery group and 40/41 of the not-offered surgery group.
[d] 5 previous non-responders not approached.

TABLE 43 *Baseline characteristics: RLH ESGNS, not-accepting and not-offered surgery groups*

Characteristic	**RLH ESGNS group**[a]	**Not-accepting surgery group**[a]	**Not-offered surgery group**[a]	***p*-Value for between-groups difference**
Total who have responded on at least one occasion after baseline (%)	48	38	40	–
Age on recruitment **(years)**				
<20	4 (8)	5 (13)	4 (10)	
20–39	14 (29)	9 (24)	8 (20)	
40–64	28 (58)	22 (58)	21 (50)	
65+	2 (4)	2 (5)	8 (20)	
Mean	42	44	49	0.13[b]
Range	15–71	17–81	16–81	
Gender				
Male	12 (25)	8 (21)	10 (25)	0.89[c]
Female	36 (75)	30 (79)	30 (75)	
Cause of disorder				
Congenital	6 (13)	11 (29)	9 (23)	<0.014[c]
Cancer	1 (2)	4 (11)	8 (20)	
Obstetric trauma	24 (50)	18 (47)	12 (30)	
Other trauma/neuropathic/idiopathic	17 (35)	5 (13)	10 (25)	
Stoma on recruitment				
Yes	18 (38)	10 (26)	21 (53)	0.06[c]
No	30 (63)	28 (74)	19 (47)	
Number of years with disorder **(medium)**				
Congenital disorders	20	25	20	0.4[d]
Acquired disorders	5	7	5	0.9[d]
Previous incontinence-related operations **(non-stoma patients)**.	$n = 30$	$n = 26$	$n = 13$	
Yes	14 (47)	13 (50)	6 (46)	0.87[c]
No	16 (53)	13 (50)	7 (54)	
Not interviewed	–	2	6	

[a] Number (% of respondents) unless indicated otherwise.
[b] Student's *t*-test.
[c] χ^2 test.
[d] Mann–Whitney *U*-test.

TABLE 44 *Baseline symptoms: incontinence, evacuation and pain for the RLH ESGNS, not-accepting and not-offered surgery groups*

Symptoms	RLH ESGN group[a]	Not-accepting surgery group[a]	Not-offered surgery group[a]	*p*-Value for between-groups difference
Frequency of incontinence to solid or liquid stool	*n* = 48	*n* = 37	*n* = 40	
Never	1 (2)	1 (3)	0 (0)	0.08[b]
<1/month	0 (0)	2 (5)	2 (5)	(non-stoma
<1/week	3 (6)	6 (16)	6 (15)	patients only)
>1/week	6 (13)	9 (24)	5 (13)	
Daily	20 (42)	9 (24)	6 (15)	
Stoma	18 (38)	10 (27)	21 (53)	
Cleveland Clinic incontinence score **(based on respondents without stomas) Scale: 0–20, 20 = worst**	*n* = 27	*n* = 26	*n* = 19	
Median score	14	12.0	11	0.11[c]
Inter-quartile range	11.5–16	10.3–13.8	7–14	
Number (%) with score 9+	24 (89)	21 (81)	14 (74)	
Frequency of evacuatory difficulties[d]	*n* = 37	*n* = 33	*n* = 39	
Never	14 (32)	12 (36)	10 (26)	0.24[b]
<1/month	2 (5)	1 (3)	2 (5)	(non-stoma
<1/week	0 (0)	0 (0)	1 (3)	patients only)
>1/week	0 (0)	5 (15)	2 (5)	
Daily	1 (2)	4 (12)	2 (5)	
Colonic conduit	2 (5)	1 (3)	1 (3)	
Stoma	18 (41)	10 (30)	21 (54)	
NHP pain scale. **(Scale: 0–100, 0 = best)**	*n* = 44	*n* = 35	*n* = 39	
Median score	0	0	0	0.54[e]
Inter-quartile range	0 23	0 23	0 24	
Number (%) at floor (best health)	26 (58)	24 (69)	21 (54)	
Population mean score adjusted for age and gender	*5.7*	*5.9*	*7.4*	
EQ-5D pain/discomfort domain	*n* = 43	*n* = 37	*n* = 39	
Number (%) of patients reporting moderate or severe pain or discomfort	31 (72)	20 (54)	25 (64)	0.28
% of general UK population reporting moderate of severe pain or discomfort	33	33	33	

[a] Number (% of respondents) unless indicated otherwise.
[b] χ^2 test.
[c] Kruskal–Wallis one-way ANOVA test.
[d] Question added after start of study.
[e] One-way ANOVA.

TABLE 45 *Baseline quality of life, anxiety and depression and patients' predictions of success of surgery for the RLH ESGNS, not-accepting and not-offered surgery groups*

Measure	RLH ESGNS	Not-accepting surgery group	Not-offered surgery group	% general UK population reporting moderate or severe problems	*p*-Value for between groups difference
EuroQol (EQ-5D) **weighted index of health status. Scale 0–1, 1 = best health (negative scores are possible)**	*n* = 43	*n* = 37	*n* = 39	–	
Median	0.69	0.76	0.69		0.17[a]
Inter-quartile range	0.59–0.81	0.66–1.00	0.62–0.85		
Number (%) at floor (best health)	5 (11)	10 (27)	8 (21)		
Population mean score adjusted for age and gender	*0.88*	*0.87*	*0.85*		
Number (%) with z scores of ≤ –2 (extreme low) when compared with the population score adjusted for age and gender	15 (34)	8 (21)	12 (30)		0.31[b]
EQ-5D categories: **number (%) who report moderate or severe problems**	*n* = 43	*n* = 37	*n* = 39		[b]
Mobility	16 (37)	10 (27)	17 (43)	19%	0.36
Self-care	7 (16)	2 (5)	6 (15)	4%	0.43
Anxiety/depression	30 (70)	21 (57)	26 (67)	21%	0.55
Pain/discomfort	31 (72)	20 (54)	25 (64)	33%	0.28
Usual activities	32 (74)	15 (41)	23 (59)	16%	0.023
NHP social isolation scale. **Scale 0–100, 0 = best**	*n* = 44	*n* = 37	*n* = 40	–	
Median score	20.2	0	0		0.60[a]
Inter-quartile range	0–44	0–40	0–42		
Number (%) at floor (best health)	19 (42)	22 (59)	22 (55)		
Population mean score adjusted for age and gender	*4.7*	*4.8*	*5.3*		
HADS anxiety score. Scale 0–7 = normal, 8–10 = mild, 11–14 = moderate, 15–21 = severe	*n* = 44	*n* = 38	*n* = 40	–	
Median score	9.0	8.0	8.0		0.48[a]
Inter-quartile range	6.8–10.9	4.8–13	4.3–11		
Number (%) at floor (best health)	1 (2)	2 (5)	3 (7)		
HADS anxiety categories, number (%) in each category					
Normal	14 (32)	18 (47)	19 (48)		
Mild	12 (27)	7 (18)	9 (23)		
Moderate	14 (32)	6 (16)	6 (15)		
Severe	4 (9)	7 (18)	6 (15)		
HADS depression score	*n* = 44	*n* = 38	*n* = 40	–	
Median score	6.8	3.5	4		0.15[a]
Inter-quartile range	2.3–10.9	2.0–9.0	2.3–9.8		
Number (%) at floor (best health)	0	3 (8)	4 (10)		
HADS depression categories, number (%) in each category					
Normal	27 (61)	27 (71)	28 (70)		
Mild	6 (14)	6 (16)	4 (10)		
Moderate	9 (21)	4 (11)	5 (13)		
Severe	2 (5)	1 (3)	3 (8)		

continued

TABLE 45 *Baseline quality of life, anxiety and depression and patients' predictions of success of surgery for the RLH ESGNS, not-accepting and not-offered surgery groups (cont'd)*

Measure	RLH ESGNS	Not-accepting surgery group	Not-offered surgery group	% general UK population reporting moderate or severe problems	p-Value for between groups difference
RLH bowel-specific measure. Psychosocial impact. **Scale 0–10, 0 = best health**	*n* = 41	*n* = 38	*n* = 39	–	
Median score	4.8	2.3	3.3		0.004[a]
Inter-quartile range	2.9–7.3	0.3–5.6	0.3–6.5		
Number (%) at floor (best health)	1 (2)	7 (18)	5 (13)		
Number (%) above overall median (= 4.2)	26 (63)	14 (37)	19 (49)		
RLH bowel-specific measure. Lifestyle impact	*n* = 44	*n* = 38	*n* = 39	–	
Median score	7.3	4.7	4.1		<0.0001[a]
Inter-quartile range	5.3–7.9	2.5–6.9	1.9–6.8		
Number (%) at floor (best health)	0	0	1 (3)		
Number (%) above overall median (= 5.8)	30 (68)	17 (45)	13 (33)		
Patients' predictions of success of surgery in solving their bowel problems (0–100%)	*n* = 36[c]	–	–	–	–
Median prediction	80				
Inter-quartile range	78–100				

[a] Kruskal Wallis, one way ANOVA.
[b] χ^2 test.
[c] Question added after start of the study.

TABLE 46 *Frequency of incontinence to solid or liquid stool: RLH ESGNS, not-accepting and not-offered surgery groups (RLH ESGNS and comparison group cohorts of patients who have both baseline and 2-year follow-up data)*

	RLH ESGNS group[a]		Not-accepting surgery group[a]		Not-offered surgery group[a]	
	Preop.	24 months postop.	Baseline	24 months post-recruitment	Baseline	24 months post-recruitment
Total number of respondents	37	37	31	31	35	35
Number of respondents (% of total)						
Never/<once per week	2 (5)	23 (62)	5 (16)	9 (29)	8 (23)	7 (20)
Several times per week	5 (14)	7 (19)	9 (29)	7 (23)	3 (9)	3 (9)
Daily/stoma	30 (81)	7 (19)[b]	17 (55)	15 (48)[c]	24 (69)	25 (71)[d]

[a] McNemar's test for within-group changes.
[b] $p < 0.0001$ (RLH ESGNS group).
[c] $p = 0.77$ (not-accepting surgery group).
[d] $p = 1.0$ (not-offered surgery group).

TABLE 47 *Percentage changes in main outcome measures at 12, 24 and 36 months of follow-up: RLH ESGNS, not-accepting and not-offered surgery groups*

Measure	Mean % changes compared with baseline (95% CI)[a]							Between-group differences in change in score at 24 months: *p*-Values (one-way ANOVA)
	RLH ESGNS group			Not-accepting surgery group		Not-offered surgery group		
	12 months *n* = 37–40	24 months *n* = 30–35	36 months[b] *n* = 23–24	12 months *n* = 31–35	24 months *n* = 29	12 months *n* = 34–36	24 months *n* = 28–32	
Cleveland Clinic incontinence score	*n* = 23 +5 (+2 to +7)	*n* = 17 +24 (+11 to +37)	*n* = 13 +25 (+16 to +35)	*n* = 17 0 (–1 to +2)	*n* = 15 +5 (–5 to +15)	*n* = 13 –1 (–3 to +1)	*n* = 13 –8 (–19 to +3)	0.001
EQ-5D weighted index of health status	+4 (–5 to +13)	+7 (–3 to +18)	+11 (+2 to +20)	+4 (–10 to +3)	–5 (–15 to +6)	–1 (–8 to +5)	+7 (–3 to +16)	0.21
NHP pain scale	–8 (–18 to +7)	–0.3 (–0.6 to 0)	0 (–13 to 0)[c]	–0.5 (–7 to +6)	0 (–0.2 to +0.2)	–6 (–13 to +2)	0 (–0.2 to +0.2)	0.16[d]
NHP social isolation	+12 (+3 to +20)	+10.2 (+0.4 to +21)	+6 (0 to +22)[c]	+11 (+2 to +19)	+3 (–5 to +11)	0 (0 to +23)	+2 (–4 +9)	0.34[d]
HADS anxiety	+8 (–1 to +16)	+9 (+0.1 to +17)	+11 (+2 to +19)	+8 (+3 to +13)	+2 (–4 to +8)	–2 (–6 to +2)	–3 (–9 to +3)	0.06
HADS depression	+7 (–1 to +16)	+6.0 (–3 to +15)	+18 (+10 to +26)	+5 (+0.5 to +9)	–0.5 (–8 to +7)	–5 (–1 to –8)	–4 (–8 to +1)	0.12
RLH psychosocial scale	+28 (+19 to +38)	+26 (+16 to +36)	+34 (+24 to +44)	+4 (–2 to +11)	+2 (–7 to +11)	+0.2 (–6 to +7)	+0.1 (–8 to +8)	<0.0001
RLH lifestyle scale	+36 (+26 to +46)	+31 (+19 to +43)	+40 (+28 to +52)	+9 (+2 to +16)	+6 (–1 to +14)	–4 (–10 to +2)	–3 (–11 to +5)	<0.0001

[a] Positive changes = improvements in scores.
[b] ESGNS group only (not-accepting surgery and not-offered surgery groups only followed for 24 months).
[c] Medians and 95% CIs of the medians are shown for the NHP pain and social scale at 36 months of follow-up owing to non-normality of distributions.
[d] Kruskal–Wallis ANOVA.

TABLE 48 *Percentage changes in secondary outcome measures at 24 and 36 months of follow-up: RLH ESGNS, not-accepting and not-offered surgery groups*

Measure	Median % changes compared with baseline (95% CI of median)[a]				Between-group differences in change in score at 24 months: *p*-Values (Kruskal–Wallis ANOVA)
	RLH ESGNS group		Not-accepting surgery group:	Not-offered surgery group:	
	24 months	36 months[b]	24 months	24 months	
EQ-5D self-rated VAS score[c]	*n* = 25 +11 (+5 to +25)	*n* = 17 +25 (+1 to +30)	*n* = 29 0 (–15 to +14)	*n* = 29 0 (–9 to +6)	0.06
NHP emotional reaction scale	*n* = 33 +10 (0 to +24)	*n* = 23 +21 (+7 to +34)	*n* = 28 0 (0 to +8)	*n* = 31 0 (0 to +10)	0.03
NHP energy scale	*n* = 34 0 (–18 to +12)	*n* = 23 0 (0 to +24)	*n* = 29 0 (0 to 0)	*n* = 31 0 (0 to 0)	0.70
NHP physical mobility scale	*n* = 35 0 (0 to +21)	*n* = 23 0 (0 to +11)	*n* = 27 0 (0 to 0)	*n* = 31 0 (–9 to +9)	0.72
NHP sleep scale	*n* = 35 0 (0 to +22)	*n* = 23 +13 (0 to +37)	*n* = 29 0 (0 to 0)	*n* = 30 0 (0 to 0)	0.09
RLH scale item: effect on sex life	*n* = 25 +20 (0 to +55)	*n* = 17 +20 (0 to +50)	*n* = 25 0 (0 to +5)	*n* = 28 0 (–10 to +10)	0.01
Satisfaction with life in general[c]	*n* = 25 + 43 (+13 to +55)	*n* = 19 +53 (+29 to +72)	*n* = 19 +1 (+11 to +35)	*n* = 25 +9 (–1 to +15)	0.02

[a] Positive changes = improvements in scores.
[b] RLH ESGNS group only.
[c] EQ-5D self-rated and 'satisfaction with life in general' scales not given to patients in early part of study.

TABLE 49 *Percentage of patients with ≥ 10% improvement at 2 years of follow-up: main outcome measures, RLH ESGNS, not-accepting and not-offered surgery groups*

Measure	RLH ESGNS clinical 'successes'	RLH ESGNS clinical 'failures'	All RLH ESGNS patients	Not-accepting surgery group	Not offered surgery group	*p*-Value[b]
Cleveland Clinic incontinence score[a]						
Number of patients	15	2	17	15	13	<0.0001
% with 10–19% improvement	13	0	12	27	8	
% with ≥20% improvement	67	50	65	20	8	
EQ-5D						
Number of patients	28	7	35	28	29	0.06
% with 10–19% improvement	14	14	14	18	14	
% with ≥20% improvement	36	14	31	7	14	
NHP pain						
Number of patients	27	7	34	27	30	0.72
% with 10–19% improvement	11	0	9	7	7	
% with ≥20% improvement	7	14	9	11	10	
NHP social isolation						
Number of patients	28	7	35	29	30	0.02
% with 10–19% improvement	7	0	9	7	3	
% with ≥20% improvement	39	14	34	17	13	
HADS anxiety						
Number of patients	28	7	35	29	32	<0.0001
% with 10–19% improvement	11	14	9	3	6	
% with ≥20% improvement	32	14	34	10	3	
HADS depression						
Number of patients	28	7	35	29	32	0.001
% with 10–19% improvement	25	14	23	4	3	
% with ≥20% improvement	18	0	14	4	9	
RLH psychosocial impact scale						
Number of patients	23	7	30	29	31	<0.0001
% with 10–19% improvement	13	29	17	7	10	
% with ≥20% improvement	61	43	57	17	19	
RLH lifestyle impact scale						
Number of patients	26	7	33	29	31	<0.0001
% with 10–19% improvement	15	0	12	28	10	
% with ≥20% improvement	65	57	64	14	19	

[a] Only applies to patients who did not have stomas at either baseline or 2 years of follow-up.
[b] χ^2 test comparing those who improved by ≥10% in the total ESGNS group with the combined comparison groups.

TABLE 50 *Percentage of patients with ≥ 10% deterioration at 2 years of follow-up: main outcome measures, RLH ESGNS, not-accepting and not-offered surgery groups*

Measure	RLH ESGN clinical 'successes'	RLH ESGN clinical 'failures'	All RLH ESGN patients	Not-accepting surgery group	Not-offered surgery group	*p*-Value[b]
Cleveland Clinic incontinence score[a]						
Number of patients	15	2	17	15	13	0.08
% with 10–19% deterioration	7	0	6	13	23	
% with ≥20% deterioration	0	50	6	13	23	
EQ-5D						
Number of patients	28	7	35	28	29	0.75
% with 10–19% deterioration	0	0	0	4	10	
% with ≥20% deterioration	14	43	20	21	10	
NHP pain						
Number of patients	27	7	34	27	30	0.03
% with 10–19% deterioration	4	0	3	7	0	
% with ≥20% deterioration	33	29	32	15	10	
NHP social isolation						
Number of patients	28	7	35	29	30	0.47
% with 10–19% deterioration	0	14	3	0	3	
% with ≥20% deterioration	11	29	14	10	10	
HADS anxiety						
Number of patients	28	7	35	29	32	0.78
% with 10–19% deterioration	4	0	3	3	9	
% with ≥20% deterioration	7	29	11	10	9	
HADS depression						
Number of patients	28	7	35	29	32	0.81
% with 10–19% deterioration	14	14	14	14	3	
% with ≥20% deterioration	4	14	6	10	9	
RLH psychosocial impact scale						
Number of patients	23	7	30	29	31	0.03
% with 10–19% deterioration	4	0	3	17	7	
% with ≥20% deterioration	0	14	3	14	16	
RLH lifestyle impact scale						
Number of patients	26	7	33	29	31	0.07
% with 10–19% deterioration	0	14	3	17	16	
% with ≥20% deterioration	12	0	9	3	19	

[a] Only applies to patients who did not have stomas at either baseline or 2 years of follow-up.
[b] χ^2 test comparing those who deteriorated by ≥ 10% in the total ESGNS group with the combined comparison groups.

TABLE 51 *Mean costs per patient by category of cost, time period and presence of prior stoma (RLH)*

		Primary intervention			Year from start of primary intervention						
Category	**Total**	**Before**	**During**	**After**	**Baseline**	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5+**	**Year 3+**
All patient											
RLH: inpatient ward use (£)	15,053	257	9,548	5,249	257	11,725	1,735	432	784	121	1,337
RLH: theatre use (including staff, devices) (£)	12,771	42	10,569	2,161	44	10,999	672	280	629	147	1,056
RLH: outpatient (£)	2,844	692	761	1,391	706	1,252	472	196	141	78	415
Other: inpatient and outpatient (£)	2,039	174	941	924	0	281	245	208	162	140	510
Other: community staff (£)	866	0	271	595	0	181	158	134	104	90	328
Total (£)	33,574	1,164	22,089	10,320	1,006	24,438	3,282	1,250	1,820	577	3,647
Patient years	3.85		0.43	3.43		1.00	0.90	0.76	0.61	0.59	1.96
Cost per patient year (£)	8,710		54,488	3,011		25,472	3,649	1,646	2,984	983	1,864
Patient with stoma before											
RLH: inpatient ward use (£)	14,467	490	9,676	4,301	490	10,967	1,391	371	1,075	173	1,619
RLH: theatre use (including staff, devices) (£)	12,754	95	10,825	1,833	100	11,158	477	205	794	20	1,019
RLH: outpatient (£)	2,402	551	735	1,116	576	1,100	312	149	168	97	414
Other: inpatient and outpatient (£)	1,369	3	692	674	0	205	179	152	118	102	372
Other: community staff (£)	543	0	167	376	0	114	100	85	66	57	207
Total (£)	31,535	1,139	22,095	8,300	1,166	23,544	2,458	962	2,221	448	3,632
Patient years	4.08		0.46	3.62		1.00	0.94	0.79	0.66	0.70	2.14
Cost per patient year (£)	7,729		50,061	2,295		24,727	2,623	1,224	3,388	639	1,694
Patient without stoma before											
RLH: inpatient ward use (£)	15,510	75	9,447	5,987	75	12,314	2,002	479	557	82	1,118
RLH: theatre use (including staff, devices) (£)	12,785	0	10,369	2,415	0	10,875	825	339	500	246	1,085
RLH: outpatient (£)	3,187	806	795	1,586	806	1,423	596	232	73	58	363
Other: inpatient and outpatient (£)	2,561	307	1,135	1,119	0	341	297	252	196	170	617
Other: community staff (£)	1,116	0	352	764	0	232	203	172	134	116	422
Total (£)	35,159	1,188	22,099	11,871	881	25,185	3,922	1,474	1,460	672	3,605
Patient years	3.68		0.40	3.28		1.00	0.87	0.74	0.57	0.50	1.81
Cost per patient year (£)	9,557		58,555	3,618		26,105	4,509	1,995	2,541	1,350	1,991

TABLE 52 *Mean costs per patient by category of cost, time period and success of ESGNS (RLH)*

		Primary intervention			Year from start of primary intervention						
Category	**Total**	**Before**	**During**	**After**	**Baseline**	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5+**	**Year 3+**
Patient with ESGNS success											
RLH: inpatient ward use (£)	12,950	363	9,387	3,200	363	10,714	1,196	453	139	86	678
RLH: theatre use (including staff, devices) (£)	11,920	57	10,603	1,260	68	10,760	365	292	249	186	727
RLH: outpatient (£)	2,851	735	831	1,285	1,390	410	173	88	51	8	147
Other: inpatient and outpatient (£)	1,906	14	829	1,063	0	323	282	239	186	161	587
Other: community staff (£)	684	0	200	484	0	147	128	109	85	73	267
Total (£)	30,310	1,168	21,850	7,292	1,820	22,355	2,144	1,182	709	515	2,406
Patient years	3.47		0.44	3.03	0.00	1.00	0.88	0.67	0.51	0.41	1.59
Cost per patient year (£)	8,744		52,569	2,407		24,192	2,445	1,761	1,383	1,266	1,512
Patient with ESGNS failure											
RLH: inpatient ward use (£)	18,889	63	9,840	8,986	63	13,569	2,717	394	1,961	185	2,540
RLH: theatre use (including staff, devices) (£)	14,324	13	10,507	3,804	0	11,433	1,233	259	1,322	76	1,658
RLH: outpatient (£)	2,832	622	655	1,555	1,084	585	238	161	104	0	265
Other: inpatient and outpatient (£)	2,284	466	1,147	671	0	204	178	151	117	102	370
Other: community staff (£)	1,186	0	401	785	0	239	208	177	137	119	433
Total (£)	39,515	1,165	22,550	15,801	1,147	26,029	4,575	1,142	3,642	483	5,266
Patient years	4.56		0.41	4.16	0.00	1.00	0.94	0.92	0.79	0.91	1.44
Cost per patient year (£)	8,662		58,339	3,803		27,230	4,864	1,240	4,621	528	3,661

Appendix 2

Protocol: quality of life and costs of anorectal reconstruction (electrically stimulated gracilis neosphincter surgery). Planned investigation (revised October 1999)

Introduction

Supra-regional funding has been granted to the Academic Department of Surgery at RLH for a series of more than 100 reconstructive operations, starting from April 1997. The Department of Health NSCAG is funding the service costs of these procedures on the condition that an independent assessment of outcome is undertaken. NSCAG funding was originally agreed for the period April 1997 to March 2000, but has recently been extended for a further 2 years to March 2002, to allow for recruitment of sufficient patients.

The procedure is known as anorectal reconstruction and includes the formation of an electrically stimulated gracilis neosphincter.

This proposal reflects progress and changes in the independent evaluation study after 18 months.

The extended evaluation is being carried out by the Unit for Costs and Outcomes Evaluation (UCOE) based at St Bartholomew's and the Royal London Hospital School of Medicine and Dentistry and led by Professor Roger Feldman. The evaluation is funded for 3 years to October 2000 by North Thames Research and Development Directorate and for $2^1/_2$ years from October 2000 by the Health Technology Assessment Programme.

Background

Stomas and incontinence

A stoma (colostomy or ileostomy) is an incontinent opening of the bowel brought out onto the abdominal wall through which all faecal matter is then collected in a bag applied around the stoma orifice. Most permanent colostomies are needed for one of the following reasons;

- congenital absence of the anorectum
- removal of the lower rectum or anus to treat rectal cancer
- trauma resulting in irreparable damage to the anorectum
- end-stage FI
- idiopathic FI.

It is estimated that 100–150 individuals a year in the UK have a colostomy formed for congenital ano-rectal atresia and that 3000 people have a permanent stoma following an abdomino-perineal resection of the rectum or anus for cancer. As a result of advances in surgery and chemo-radiotherapy, 50% of these cancer patients will be cured, but left with the handicap of a stoma. Increasing use of sphincter-saving surgery for cancer of the rectum and anus, although reducing the numbers of patients with permanent stomas, may result in problems of anal incontinence for up to one-quarter of patients.

Although a permanent stoma is often compatible with a normal life, many patients suffer lifelong physical, mental, sexual and social problems as a result of the incontinence and appearance of the stoma.[1–3]

Patients who live with anal incontinence suffer similar problems to those associated with a stoma.[4]

A community-based survey estimated a prevalence of anal incontinence of 2.2%; independent risk factors were found to be female sex, advancing age, poor general health and physical limitations.[5] The commonest cause of FI among women is obstetric trauma, which is reported to lead to FI in 4% of women up to 2 years after delivery.[6] There are several medical and surgical techniques that may improve continence, but there remains a small group of patients whose incontinence does not respond to such treatments and for whom the only alternative would be a permanent stoma. It is uncertain how many people are living with intractable anal incontinence; anecdotal evidence

from more than 300 surgeons in England and Wales indicated an average of one patient known per consultant (personal correspondence). However, the condition is known to be under-reported and under-diagnosed.[7] The Academic Department of Surgery at RLH is seeing about 50 new referrals per year.

The procedure and current knowledge of outcomes

A procedure to restore near normal bowel function has been developed over the last decade. This involves the transposition of gracilis muscle around the anus, which is then electrically stimulated to provide a continent neosphincter.[8]

A recent worldwide multicentre trial on the safety and efficacy of dynamic muscle plasty for anal incontinence[9] followed 139 patients for a median of 24 months after surgery. Overall, two-thirds of patients maintained a successful outcome over the follow-up period, success being defined as a 70% reduction in solid stool incontinence for patients with baseline incontinence and zero incontinence to solid stool for patients with baseline stomas or undergoing total anal reconstruction. However, major wound complications occurred in one-third of patients and a significant number of patients reported continuing evacuatory difficulties. Other published smaller studies show similar findings.[10]

Little is known about either the cost implications or the effects on QoL of such major reconstructive surgery. The only paper published on cost-effectiveness of this surgery[11] is from The Netherlands; the study prospectively evaluated a group of 43 patients who underwent reconstruction surgery for intractable anal incontinence. The outcomes for these patients were compared with seven patients who had undergone stoma formation some years previously. The conclusion of this paper was that clinical success of dynamic graciloplasty was 74%, and that although dynamic graciloplasty was more expensive than conventional treatments in the short term, it resulted in a significantly better QoL. QoL in the stoma group was not directly assessed owing to small numbers. The paper drew some limited conclusions about long-term cost-effectiveness of the procedure and suggested that stoma formation may be the least attractive option in terms of both QoL and costs.

A prospective study of QoL before and after dynamic graciloplasty in 30 patients carried out as part of the same study[12] found improvements in levels of anxiety, ability to work and carry out usual activities, personal relationships, sexual function and social activity in the 22 patients in whom the operation was clinically successful. However, QoL was followed for 1 year only and there was no prospective study of QoL in patients with similar bowel problems who did not undergo anorectal reconstruction.

There are very few recent published papers that have assessed the overall costs of immediate and long-term stoma care.[13]

Prior to 1997, these operative techniques had been carried out on over 70 patients at the Royal Hospitals NHS Trust. A pilot study in a group of 10 patients suggested that a significant improvement in the QoL (as measured by the NHP, HADS and the EuroQoL) is conferred by reconstruction when compared with preoperative status. There was an improvement of about 25% over a range of dimensions measured up to 1 year after surgery.

Most patients request stoma-avoiding reconstruction to restore normal continence, a procedure for which it is estimated that up to 1000 patients per year in England and Wales are clinically suitable.

The evaluation

Continuing demands on financial resources for healthcare increase the need for evidence about the benefits of treatments in relation to their costs. Benefits and costs of treatment should be viewed from the perspectives of patients, their carers, healthcare professionals and of society as a whole.

It is well recognised that clinically defined outcomes of treatment may not represent the outcomes of concern and importance to the patient. This is particularly relevant in evaluating a major surgical procedure such as anorectal reconstruction, which is performed for non-life-threatening conditions and which is known to have a high risk of major complications and morbidity.

The independent evaluation study aims to provide evidence about patient-based outcomes and the benefits and costs of anorectal reconstruction surgery, to inform decision-making with regard to more widespread adoption of the procedure within the NHS.

Objectives

To test the hypotheses:

1. That anorectal reconstruction surgery leads to a better QoL than continued medical management of anal incontinence or the formation of a permanent stoma.
2. That the long-term costs to society (and to the NHS) of patients undergoing anorectal reconstruction surgery are less than the costs of alternative management options, or are justifiable in terms of improved patient QoL.

Research method

A prospective case-comparison study which will examine QoL and symptoms before and after anorectal reconstruction and compare the findings with those of two groups of people with similar bowel conditions who do not undergo surgery.

Direct and indirect costs incurred by the reconstruction and comparison patients will be assessed.

We cannot carry out an RCT, since it would be impossible to discuss reconstruction procedures with patients and then deny them such surgery. Therefore, the main comparison group (group A) will be selected from a sample of patients who have not, so far, been referred for reconstruction surgery. Although this is not optimal, there is no realistic alternative. An additional comparison group (group B) is described below.

Group size justification

The number of patients to be recruited to the reconstruction and comparison groups was determined as follows.

A power calculation using a power of 80% and a significance of 95% suggested that, predicting a 25% difference between groups (based on reduction in scores for key domains of the NHP, as demonstrated in the pilot study), a minimum group size of 70 patients is required. A drop-out rate of up to 30% was anticipated, hence the aim will be to recruit at least 70 and preferably 100 patients to the case group.

Sample

Case group

The case group will consist of 70–100 people aged ≥16 years who are referred to RLH from all areas of England (and, from 1999, Scotland).

Their bowel disorders are due to:

- congenital anorectal anomalies or
- previous curative surgery for cancer or
- idiopathic or traumatic incontinence

and they have either already undergone permanent stoma formation, or they are living with intractable anal incontinence for which the only other alternative would be the formation of a permanent stoma.

Although recruitment rates have not matched the rates projected at the outset of the surgical programme, an average of 15 patients per year have been recruited to the surgical programme during the first 2 years. New patient referrals remain steady at about four per month and it seems reasonable to predict that at least 70 patients will have been recruited by March 2002. All patients have agreed to take part in the evaluation study and their questionnaire return rate is currently 98%, based on 154 questionnaire administrations (10 May 1999).

Main comparison group A

The main comparison group (A) will consist of patients with similar bowel conditions but who have not been offered reconstruction surgery; these patients will be matched by diagnosis, gender, age (within 5 years) and whether they have a stoma or are incontinent. This group is being recruited with the help of a sample of consultant general surgeons throughout England and Wales who are identifying patients with appropriate bowel conditions. It is hoped that up to four comparison group A patients will be matched to each case patient.

Approach to surgeons

Letters were sent to over 900 general and colorectal consultant surgeons in England and Wales. Over 300 indicated that they would be willing to help identify suitable patients for the comparison group; estimates from these surgeons of numbers of their patients in each category give the following totals:

- patients with stomas due to cancer (treated 1994–97) 5500+
- patients with stomas or incontinence due to anorectal atresia 150+
- patients with stomas due to FI 280+
- patients with otherwise intractable anal incontinence (i.e. no stoma) 270+

Ethical approval

With the advice of the project steering group, it

was decided in the first instance to target surgeons from North and South Thames, for recruitment of comparison patients whose conditions are due to either atresia, cancer or trauma, and from other areas of England and Wales where surgeons indicated that they would be able to identify suitable patients with anorectal atresia. Approval was obtained from North Thames Multi-centre Research Ethics Committee (REC) in April 1998, following the approval of East London and City REC. Fifty-four local RECs have since been approached. Positive replies have now been received from all of these local committees. Letters have been sent to inform local trusts of the study.

In anticipation of possible difficulties in identifying people for comparison group A, a patient support group (InContact), which advises people who have urinary or faecal incontinence, has been approached. InContact will publish a request in their next quarterly newsletter for people who are living with FI to contact the research group.

Comparison group B

A second comparison group (group B) will consist of patients (unmatched) who are referred to RLH for, and who have conditions amenable to, anorectal reconstruction, but who decide not to proceed. This group is expected to be slightly smaller in size than the reconstruction group. To date (10 May 1999) 17 patients have agreed to be part of this comparison arm. It was not possible to recruit patients to this group who were assessed early in the programme and before the evaluation study was in place. It is also a sensitive period for some patients, who may agonise over their decision as to whether to proceed with such major surgery.

Recruitment

Patients who are referred for surgery are contacted by UCOE by letter prior to their first outpatient appointment. They are then given the opportunity to meet a researcher at the time of the first appointment, when the research can be explained. The patient's GP will also be informed at this stage that their patient has been approached. When patients are found to be suitable to undergo reconstruction surgery and they have reached a decision as to whether or not they wish to proceed, their written consent is obtained to allow participation in the evaluation study (whether or not they have decided to undergo surgery). The independent nature of the study is emphasised to all patients.

The matched comparison group A patients are approached with the consent of their GPs, who forward a letter and information booklet to the patients. A second letter is sent to the GP after 1 month if no response has been received.

Lists of suitable patients are now being received from surgeons and the first batch of potential matched comparison patients has been approached via their respective GPs. To date (17 May 1999) 32 patients have been approached to be part of the main comparison group, 12 have agreed to take part, one GP and one patient have refused and replies are awaited from a further 18.

Clinical assessment

The assessment of outcome in each of the above groups will be measured by a researcher from the UCOE, working independently of the surgical team, and supervised by Professor Feldman. The surgical team will provide clinical details of all reconstruction patients at the time of first referral for consideration of surgery and inform the researchers of the clinical progress, including complications, of each patient.

It is difficult to define clinical 'success' for this procedure. Patients choose to undergo reconstruction surgery because of the impact of their bowel condition on their QoL. However, the surgery is complex and major and it is not claimed to restore 'normal' or 'perfect' function. As noted previously, many patients experience complications during and after the treatment period; many will continue to live with evacuatory difficulties even though the neosphincter may function well and some will experience other problems including faecal soiling. Some people are delighted with the improvements gained from even a less than perfect result whereas others may feel that any benefits are outweighed by the trauma of the procedure and some may find their condition worsened as a result of surgery.

Clinical outcomes that may be measured are changes in faecal continence and changes in physiological measurements. There are considerable difficulties in assessing faecal continence. A stoma is completely incontinent, although patients who use irrigation techniques to empty the bowel at regular intervals are often able to achieve a degree of control. For patients without stomas, it is accepted that the most severe disorders involve incontinence to solid bowel motion; however, most patients find leakage of liquid motion more

distressing. Incontinence to flatus is common in all cases and is unlikely to be improved by reconstruction surgery; patients vary widely in their acceptance of incontinence to flatus. Excellent continence may coexist with severe evacuation difficulties. Similarly, physiological measures may not correspond with the functional outcome.

No validated measure of continence currently exists. The Cleveland Clinic scale is widely used, but is not adequate for the purposes of this study. The self-assessed continence and symptom questionnaire used in this study is a locally devised measure, which incorporates the Cleveland Clinic scale, but includes more detail about levels of incontinence in addition to questions on evacuation difficulties. For case group patients, it includes some operation-specific questions in the postoperative period.

Quality of life assessment

Formal assessment of a range of appropriate QoL indices and also physical and psychological symptoms will be carried out in all these groups at regular intervals. Data on the reconstruction group will be obtained both before and after surgical treatment, and data from the comparison groups will be obtained over a period of time after recruitment to the study. It is hoped that patients in all groups will be followed for at least 1 year and preferably 2 years or more following completion of surgery or recruitment.

Subsequent comparisons of QoL will be made using non-parametric statistical techniques:

1. between pre- and postoperative status of the reconstruction group
2. between reconstruction group patients and the matched comparison group, over the study period
3. between reconstruction group patients who proceed to surgery and those who choose not to proceed to surgery, over the study period.

Repeated measures are necessary because QoL may change over time as people adapt to their condition or are affected by treatment complications.

The QoL questionnaires are either sent by post or given when patients visit the hospital.

Semi-structured interviews are conducted with all patients (case and comparison groups) either in person or by telephone. These interviews are conducted on recruitment and 1 year after the final stage of surgery/recruitment. Questions will be asked about QoL and costs to the patients and their families of living with their bowel condition and the treatment for it. The case group and comparison group B patients will be questioned regarding the reasons for their decisions about whether or not to proceed with the surgery. One year after surgery, case group patients will be asked about their overall experience and their assessment of the results.

Surgeons are asked to predict the likely success of the operation in solving the patient's bowel problems before surgery. They are asked again at 1 year postoperation for their impressions of the success of the surgery.

Non-responders will be followed up in all cases. It is our experience that regular contact with reconstruction group patients on their frequent hospital visits ensures good compliance. Non-responding patients will be initially followed up by letter and then by telephone. For case group patients, hospital visits also give opportunities for personal reminders.

The current overall response rate (10 May 1999) based on administration of 197 sets of questionnaires during the study period is >97%.

Measures in use

Questionnaires

The following questionnaires will be administered repeatedly:

- Nottingham Health Profile (NHP).
- EuroQol (EQ-5D).
- Psychosocial Adjustment to Illness Scale (PAIS-SR) for patients with acquired bowel disorders.
- Hospital Anxiety Depression Score (HADS).
- RLH Score, a locally developed questionnaire which examines the impact of the bowel condition on daily life.
- BAC, locally devised questions about general satisfaction with life, body image, sexual function, previous counselling or psychological therapy, membership of self-help groups and expectation of the surgery (as appropriate for patient groups at each stage).
- A questionnaire regarding information received preoperatively about the reconstruction surgery will be given once only, 3 months after the final procedure.

Four questionnaires measuring psychosocial factors known to be related to the impact of and recovery from illness will be administered once only on recruitment:

- short social support questionnaire (SSQ-6)[14]
- COPE, a generic measure of a person's approaches to dealing with stress[15]
- generalised self-efficacy scale[16]
- recovery locus of control scale[17] (reconstruction group only).

All the questions, with the exception of the PAIS-SR, will be combined into one form, and all questions are accessible to people with a standard reading age of 12 years, calculated using the Flesch–Kincaid formula. The total form takes 20–30 minutes to complete and consists mainly of check boxes and visual analogue scales. There are options for respondents to make additional comments in the questionnaires. Formal statistical tests of data validity will be included in the study.

Rationale for use of measures

Quality of life

> "Quality of life in clinical medicine represents the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient."[18]

Table 53 has been adapted from Fitzpatrick and colleagues[19] and draws together the dimensions of health status most commonly identified in the literature as being relevant to patient-based outcome measures. Also shown in the table are the measures employed in this study, which are intended to measure each dimension.

Several different types of instruments are used in this study:

1. Generic (NHP, PAIS-SR)
These can be used to compare outcomes of treatment of a wide range of health problems and have been widely tested in a variety of settings. These instruments may be of value in detecting unexpected effects of the treatment. The sensitivity to change of these instruments to the results of the treatment is necessarily limited by their broad nature.

The NHP is a 36-tick box questionnaire that has been successfully combined with other tools for health economic research,[20] it reflects health-related QoL in five dimensions. It is the instrument used by Baeten and colleagues to evaluate outcome of graciloplasty for FI.[21] Pilot studies suggest significant improvements in the dimensions of energy, emotion and social isolation after reconstructive surgery, and some improvements in sleep and pain.

The NHP has been chosen for this study rather than the recently popularised SF-36 for a number of reasons, for example the NHP includes dimensions of sleep disturbance, which is frequently worsened by a stoma and by surgery and it includes more questions on pain, important in a recovery from major surgery.

The PAIS-SR[22] is designed to assess the quality of a patient's psychosocial adjustment to a current illness or its residual effects. It is therefore not suitable for patients whose bowel conditions have congenital causes. The PAIS-SR reflects psychosocial adjustment to illness via seven primary domains, all of which have been found to be significantly affected in these groups of patients. The PAIS-SR has recently been used successfully in studies of psychosocial adjustment and adaptation to stoma and non-stoma bowel resection.[23]

2. Utility (EQ-5D)
The EQ-5D is a five item instrument that generates a single index of QoL (a utility) in order to compare outcomes between different treatments. The single index is derived from values assigned by population samples to different health states. The five items can be used on their own to describe the individual's health state. It also includes a visual analogue for rating individual overall health state. EQ-5D is designed to complement other QoL measures and it has been combined with other QoL instruments in cost-utility analyses.[24] The pilot studies suggest improvements in health utility from a median of 0.6 ('best imaginable health state' = 1) preoperatively to 0.9 postoperatively following anorectal reconstruction. The EQ-5D scores can be used to determine QALYs directly, although its sensitivity to change is, as yet, unconfirmed in people with these bowel disorders.

3. Condition specific (RLH)
The RLH score has been developed from work carried out in the pilot study using direct questioning of objectives methodology[25] and from discussions with patients and staff. It consists of 25 items representing aspects of daily life that may be affected by the bowel condition; patients are asked to score each item using a linear analogue scale to indicate the severity of the effect of the bowel condition. There are no validated measures of QoL

TABLE 53 *Range of dimensions assessed by patient-based outcome measures, showing measures employed in this study*[a]

Dimension	Measures used in this study
Physical function	
Mobility, dexterity, range of movement, physical activity, activities of daily living: ability to eat, wash, dress	EQ-5D, NHP
Symptoms	
Pain	EQ-5D, NHP, symptom questionnaire
Nausea	–
Appetite	Interviews
Energy, vitality, fatigue	NHP
Sleep and rest	NHP, RLH
Continence/evacuatory difficulties (specific to this study)	Symptom questionnaire, RLH
Global judgements of health	EQ-5D (VAS scale)
Psychological well-being	
Psychological illness: anxiety and depression	HADS, PAIS-SR, EQ-5D, NHP
Coping, positive well-being and adjustment, sense of control, self-esteem	RLH, BAC, PAIS-SR, COPE, recovery locus of control
Social well-being	
Family and intimate contacts	PAIS-SR, RLH, SSQ-6
Social contact, integration, social opportunities	
Leisure activities	–
Sexual activity and satisfaction	–
Cognitive functioning	–
Role activities	
Employment	PAIS-SR, RLH, EQ-5D
Household management	PAIS-SR,
Financial concerns	PAIS-SR
Personal constructs	
Satisfaction with bodily appearance	BAC
Stigma and stigmatising conditions	
Life satisfaction	–
Spirituality	–
Satisfaction with care	Interviews, questionnaire re information received, PAIS-SR

[a] Semi-structured interviews probe all of these dimensions, with the exceptions of cognitive functioning, nausea and spirituality

Adapted from Fitzpatrick *et al*., *Health Technol Assess* 1998;**2**(14).

relating to FI or stomas, although there is some evidence accruing regarding the Gastrointestinal Quality of Life Index (GIQLI).[26,27] However, it is felt that GIQLI does not focus sufficiently on symptoms that would be likely to change as a result of this surgery. It is hoped that the RLH questionnaire may be validated as part of this study.

4. Dimension specific

Psychological distress, perceptions of body image and sense of control are known to be important in patients with these bowel disorders.[1–3,20] The HAD scale[28] has been used widely in surgical practice and as part of several trials of chemotherapy.[29] Pilot work suggests that the anxiety scale of the HAD score improves after surgery, whereas depression scores remain within the normal range throughout.

The BAC questionnaire includes questions developed in collaboration with health psychologists working at Queen Mary and Westfield College. Part of this questionnaire is concerned with body image, sense of control and general satisfaction with life.

Economic evaluation

The economic analysis will:

1. describe the cost of anorectal reconstruction surgery and its consequences
2. provide a cost minimisation analysis comparing the direct and indirect costs of anorectal reconstruction and compare them with those of patients receiving three different types of conventional care: either continuing to live with severe anal incontinence, or undergoing stoma formation for incontinence or receiving care for a pre-existing stoma
3. provide a cost-utility analysis comparing the costs and utility (based on health-related QoL) of patients undergoing anorectal reconstruction with those of patients receiving conventional care as described in 2 above
4. by means of modelling techniques, estimate and compare the long-term costs and utility of anorectal reconstruction and the conventional alternatives.

All direct healthcare costs will be measured which are incurred in reconstruction surgery and stoma formation and in the management of patients with otherwise intractable anal incontinence, with corrections for actual complication and revision rates where appropriate.

Costs of care for people with pre-existing stomas or with intractable anal incontinence are derived via experiences of the comparison group patients, with particular attention to stomal complications and their management. Hospital costs for permanent stoma formation will be assessed for a sample of patients undergoing this procedure for FI at the RLH and at other hospitals.

Assessment of primary care and community costs for all patients, together with direct and indirect costs to patients, will rely on patient recall. There is currently very little published information on these costs and it will be necessary to seek further information from patient support groups and stoma care appliance manufacturers, some of whom are believed to have assessed primary care costs.

Costs will be expressed in both discounted [6% or the recommended rate at the time of data analysis (as recommended by the Department of Health)] and undiscounted formats. The ICER of reconstructive surgery over colostomy formation or life with anal incontinence will be calculated (in this case the measure of effectiveness is a 'utility', i.e. health-related QoL), with results expressed as an incremental value between groups. Incremental cost-effectiveness (utility) will be expressed with respect to each of the QoL indices. A full sensitivity analysis will be used to identify a range of critical cost variables.

In both reconstruction and comparison groups, in-hospital resource use will be identified by a number of routes:

1. examining medical and nursing notes and also drug charts
2. examining hospital computer records.

Examination of medical notes and hospital computer records will identify outpatient resource use in the reconstruction group. In the comparison groups, patient recall of outpatient visits will be the main method; in a sample of patients this will be verified with their hospital records.

Methods and data collection forms for the identification of unit costs are agreed and have been reviewed at an economics steering group meeting. Discussions with the Royal Hospitals Trust contracts and finance departments have taken place to identify areas where they can be of help.

Primary care and community-based resource use will be identified via patient recall at regular intervals using the specially designed ECO1 questionnaire; these data will be verified with a sample of local GP records with regard to GP visits, prescribed medications and appliances.

Direct and indirect patient costs and predicted future economic productivity will be estimated via repeated administration of the ECO1 questionnaire and from semi-structured interviews with patients both on recruitment and one year after recruitment or completion of surgery.

Analysis/dissemination of findings

Interim analysis will be carried out during the second half of 1999, to present QoL changes 1 year after surgery at the Royal College of Nursing Gastroenterology and Stoma Care Nursing Conference in November 1999.

Further analysis will be completed by October 2000, at the end of 3 years of the evaluation study, and findings will be provided to NHS London Regional Office R&D Directorate, to NSCAG (and to NCCHTA if extension of funding is agreed).

This will include data from both the QoL and economic evaluations.

The final analyses will be completed by October 2002 and it is hoped that the results will be presented at professional meetings and that they will be published in the national and international medical literature and nursing literature.

Summary reports will be sent to all the surgeons who have helped in the study, to GPs whose patients have participated and to stoma therapy nurse specialists.

A synopsis of the findings will also be made available to patients who have expressed an interest in the outcome of the study and to self help groups such as 'InContact' and the British Colostomy Association.

Project milestones

Table 54 shows the existing project timeline from the start of the surgical programme in 1997, projected to the end of 2002.

Expertise

The project is supervised by Professor Roger Feldman, whose background is in epidemiological analyses of infectious disease and most recently health service evaluation.

The day-to-day conduct of the project is carried out by Thérèse Tillin, whose previous experience includes management of regional and district wide clinical audit projects in both primary and secondary care settings, including experience and training in questionnaire design and both qualitative and quantitative information gathering techniques.

Project consultants

These have been appointed on a part-time basis, as follows:

Mr Mike Chambers, Health economist, Medtap International. Will work on furthering the economic model, analysis of final data, general project management and data collection monitoring and analysis and report writing.

Dr Ken Gannon, Senior Lecturer in Health Psychology, St Bartholomew's and the Royal London School of Medicine and Dentistry. Provides advice regarding content, design and analysis of QoL questionnaires and interviews and monitoring of interview quality. Ongoing advice and support as required.

Department of Medical Statistics, Wolfson Institute, St Bartholomew's and the Royal London School of Medicine and Dentistry provide statistical advice as required.

Project advisors

These give advice on clinical and surgical matters:

Mr James Eccersley, formerly Lecturer in Surgery, St Bartholomew's and the Royal London School of Medicine and Dentistry, now Specialist Registrar, Department of Surgery, Hinchingbrooke Hospital.

Mr Gunju Ogunbiyi, Lecturer in Surgery, Colorectal Research Fellow, St Bartholomew's and the Royal London School of Medicine and Dentistry.

Miss Barbara Stuchfield, clinical nurse specialist, stoma therapy.

Steering group

The steering group has met once during the first year and is likely to continue to meet yearly and when particular needs arise. The group consists of:

Professor Jack Hardcastle, Emeritus Professor of Surgery, University of Nottingham [to December 1998: Mr Brendan Devlin (deceased), consultant surgeon].

Professor Stan Newman, psychological medicine, University College London.

Dr Jenny Roberts, health economist, Senior Lecturer, London School of Hygiene and Tropical Medicine.

Changes made to the evaluation study

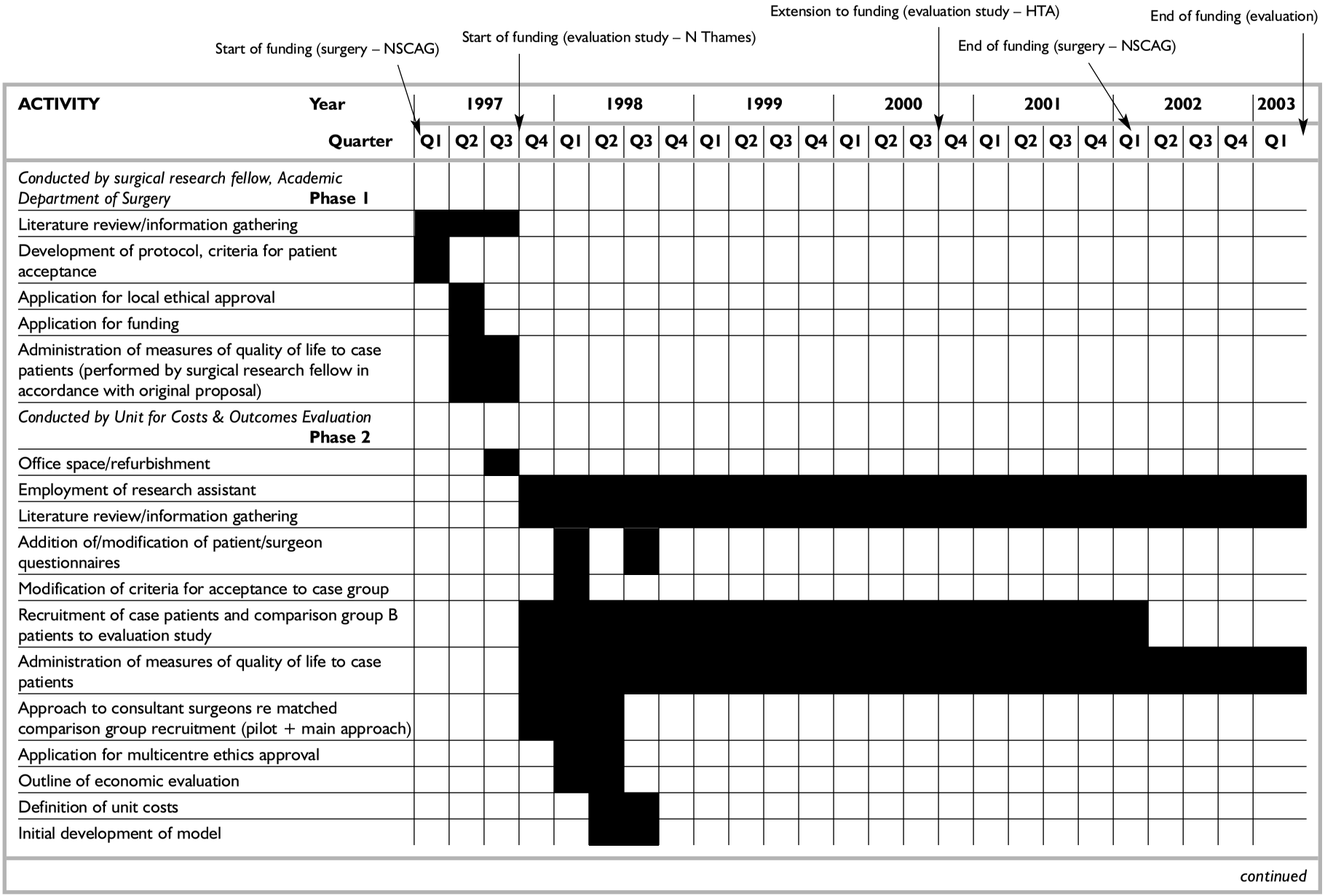
Changes made to the evaluation study since original application to North Thames R&D Directorate are set out in *Table 55*.

References

1. Wade B. *A stoma is for life*. London: Scutari Press, 1989.

2. Devlin HB. Aftermath of surgery for anorectal cancer. *BMJ* 1971;**3**:413–18.
3. Macdonald L. Stigma in patients with rectal cancer: a community study. *J Epidemiol Commun Health* 1984;**38**:284–90.
4. Rintala R, *et al*. Fecal incontinence and quality of life in adult patients with an operated low anorectal malformation. *J Pediatr Surg* 1992;**27**:902–5.
5. Nelson R, *et al*. Community-based prevalence of anal incontinence. *JAMA* 1995;**274**:559–61.
6. MacArthur C, *et al*. Faecal incontinence after childbirth. *Br J Obstet Gynaecol* 1997;**104**:46–50.
7. Madoff RD, *et al*. Fecal incontinence. *N Engl J Med* 1992;**326**:1002–7.
8. Williams NS, *et al*. Development of an electrically stimulated neoanal sphincter. *Lancet* 1991;**338**:1166–9.
9. Madoff RD, *et al*. Safety and efficacy of dynamic muscle plasty for anal incontinence. *Gastroenterology* 1999;**116**:549–56.
10. Mander BJ, *et al*. The electrically stimulated gracilis neo-anal sphincter. *Eur J Gastroenterol Hepatol* 1997;**9**:435–41.
11. Adang EMM, *et al*. Cost-effectiveness of dynamic graciloplasty in patients with fecal incontinence. *Dis Colon Rectum* 1998;**41**:725–34.
12. Baeten CB, *et al*. Anal dynamic graciloplasty in the treatment of intractable fecal incontinence. *N Engl J Med* 1995;**332**:1600–5.
13. Laucks SS, *et al*. An assessment of colostomy irrigation. *Dis Colon Rectum* 1988;**31**:279–82.
14. Sarason, *et al*. Interrelationships of social support. *J Pers Soc Psychol* 1987;**52**:813–32.
15. Carver, *et al*. Assessing Coping strategies. *J Pers Soc Psychol* 1989;**56**:267–83.
16. Schwarzer, Jerusalem. *Measurement of perceived self efficacy: psychometric scales for cross cultural research*. Berlin: Freie Universität, 1993.
17. Partridge *et al*. Perceived control of recovery. *Br J Clin Psychol* 1989;**28**:53–9.
18. Schipper, *et al*. Quality of life studies: definitions and conceptual issues. In Spilker B, editor. *Quality of life and pharmacoeconomics in clinical trials* Philadelphia: Lippincott-Raven; 1996. pp. 11–23.
19. Fitzpatrick, *et al*. Evaluating patient-based outcome measures for use in clinical trials. *Health Technol Assess* 1998;**2**(14).
20. Alonso J, *et al*. *European Guide to the Nottingham Health Profile*. Manchester: Galen Research; 1989.
21. Baeten C, *et al*. Graciloplasty in the treatment ... *N Engl J Med* 1995;**332**:1600–5.
22. Derogatis LR. The Psychosocial Adjustment to Illness Scale – self report version. *Clin Psychom Res* 1997
23. Bekkers MJTM, *et al*. Survival and psychosocial adjustment to stoma surgery and nonstoma bowel resection. *J Psychosom Res* 1997;**42**;234–44.
24. Brazier J, *et al*. Testing the validity of the EuroQoL. *Qual Life Res* 1993;**2**;169–80.
25. O'Boyle CA. Assessment of quality of life in surgery. *Br J Surg* 1992;**79**:395–8.
26. Eyspach E, *et al*. Gastrointestinal quality of life index: development, validation and application of a new instrument. *Br J Surg* 1995;**82**:216–22.
27. Sailer M, *et al*. Quality of life in patients with benign anorectal disorders. *Br J Surg* 1998; **85**:1716–19.
28. Snaith RP, Zigmond AS. *The hospital anxiety and depression manual*. Windsor: NFER-Nelson; 1994.
29. Slevin M. Quality of life... *BMJ* 1992;**305**:466–9.

TABLE 54 *Quality of life and costs of anorectal reconstruction project timeline (draft)*



ACTIVITY	Year	1997				1998				1999				2000				2001				2002				2003
	Quarter	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1
Conducted by surgical research fellow, Academic Department of Surgery **Phase 1**																										
Literature review/information gathering		■	■	■																						
Development of protocol, criteria for patient acceptance		■																								
Application for local ethical approval			■																							
Application for funding			■																							
Administration of measures of quality of life to case patients (performed by surgical research fellow in accordance with original proposal)			■	■																						
Conducted by Unit for Costs & Outcomes Evaluation **Phase 2**																										
Office space/refurbishment				■																						
Employment of research assistant					■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Literature review/information gathering					■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Addition of/modification of patient/surgeon questionnaires					■		■																			
Modification of criteria for acceptance to case group					■																					
Recruitment of case patients and comparison group B patients to evaluation study					■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■				
Administration of measures of quality of life to case patients					■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■
Approach to consultant surgeons re matched comparison group recruitment (pilot + main approach)					■	■	■																			
Application for multicentre ethics approval						■	■																			
Outline of economic evaluation						■	■																			
Definition of unit costs							■	■																		
Initial development of model							■	■																		

continued

TABLE 54 *Quality of life and costs of anorectal reconstruction project timeline (draft) (cont'd)*

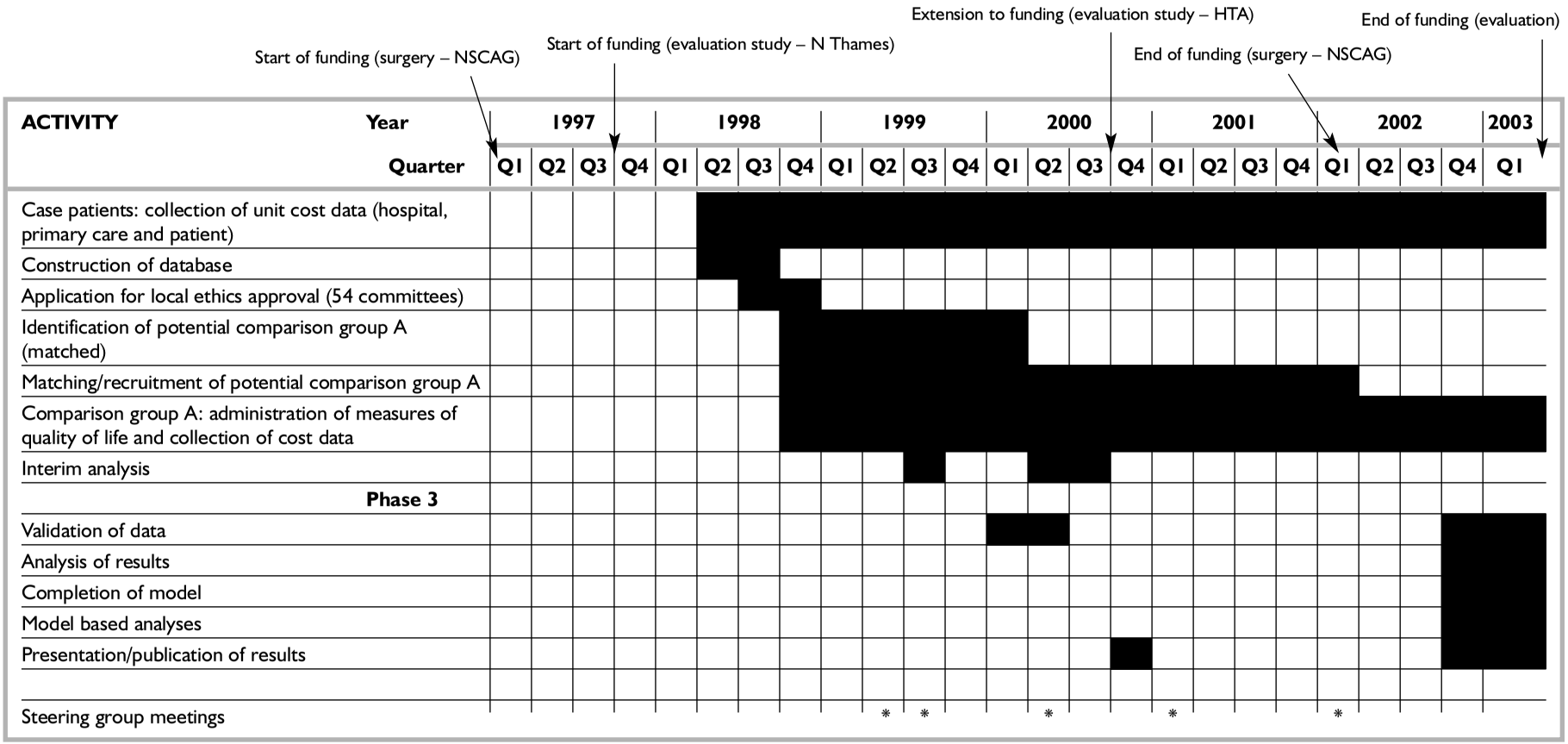


TABLE 55 *Changes made to the evaluation study since original application to North Thames R&D Directorate*

	Original proposal, April 1997	Amended proposal, May 1999	Reason for change/comments
Period of NSCAG funding for surgical programme	3 years to March 2000	5 years to March 2002	Very slow recruitment. Extension agreed by NSCAG (December 1998) to allow time for sufficient patients to undergo surgery to enable evaluation study to reach a conclusion
Period of time needed for evaluation study	3 years to October 2000	$5^1/_2$ years to March 2003	As above, see also project timeline, appended. Additional 6 months to ensure minimum follow-up period for all of 1 year
Criteria for patient inclusion (case and comparison groups)	Patients with stomas due to anorectal agenesis or to carcinoma	Patients with stomas or severe anal incontinence which is refractory to conventional treatments, due to anorectal agenesis, carcinoma, trauma, either obstetric or other cause of trauma	Referrals of patients for consideration of surgery did not follow the anticipated pattern. The majority of referrals have been patients with anal incontinence due to trauma. Changes in these criteria were agreed with NSCAG at the end of the first year of the surgical programme
Comparison group composition	Recruit one group of matched patients (A) who have not been referred for surgery	Recruit an additional, unmatched, comparison group (B) consisting of referred patients who are suitable for surgery, but who decide not to proceed	To obtain additional information, particularly with regard to the reasons why patients decide to undergo this complex surgery. Cost and QoL data will also be gathered for these patients
Main comparison group (A) size	Aim to match 1 comparison per case. Match by age, gender, cause of disorder, length of time with stoma	Aim to match at least 2 and preferably 4 comparisons per case Match by age, gender and cause of disorder	To increase power of study in order to compensate for slow recruitment of cases. Could enable close matching on some characteristics, e.g. baseline QoL
QoL measures (generic)	EQ-5D, NHP, HADS	As original, with addition of PAIS-SR scale for patients with acquired disorders	Recommended by project steering group, PAIS-SR more sensitive and detailed in areas of particular importance to these patients
QoL measures (condition specific)	BAC, RLH score	Both measures added and modified	Based on early responses and discussions with patients and staff. No validated measures available for these conditions
Continence/symptom measures	Not included	Questionnaire devised	To assess continence, evacuatory problems for all patients without stomas, plus pain and other problems which may occur postgraciloplasty. No validated measures available
Patient's perceptions of information received preoperation	Not included	Questionnaire devised, given 3 months postoperation	Important aspect of patient expectations of outcome

continued

TABLE 55 *Changes made to the evaluation study since original application to North Thames R&D Directorate*

	Original proposal, April 1997	**Amended proposal, May 1999**	**Reason for change/comments**
Surgeon predictions and assessment of outcome	Not included	Questionnaire devised	To record surgeons' preoperative expectations and assessment of outcome
Semi-structured interviews	One interview during study period	Two interviews, first preoperation/on recruitment, second 1 year postoperation/recruitment	To record information about reasons for decision whether or not to proceed with surgery, satisfaction with outcome, additional information re costs and to aid validation of non-standardised measures

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We look forward to hearing from you.

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