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Abstract

North of England and Scotland Study of Tonsillectomy and Adeno-tonsillectomy in Children (NESSTAC): a pragmatic randomised controlled trial with a parallel non-randomised preference study

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Objectives: To examine the clinical effectiveness and cost-effectiveness of tonsillectomy/adeno-tonsillectomy in children aged 4–15 years with recurrent sore throats in comparison with standard non-surgical management.
Design: A pragmatic randomised controlled trial with economic analysis comparing surgical intervention with conventional medical treatment in children with recurrent sore throats (trial) and a parallel non-randomised cohort study (cohort study).
Setting: Five secondary care otolaryngology departments located in the north of England or west of Scotland.
Participants: 268 (trial: 131 allocated to surgical management; 137 allocated to medical management) and 461 (cohort study: 387 elected to have surgical management; 74 elected to have medical management) children aged between 4 and 15 years on their last birthday with recurrent sore throats. Participants were stratified by age (4–7 years, 8–11 years, 12–15 years).
Interventions: Treatment was tonsillectomy and adeno-tonsillectomy with adenoid curettage and tonsillectomy by dissection or bipolar diathermy according to surgical preference within 12 weeks of randomisation. The control was non-surgical conventional medical treatment only.
Main outcome measures: The primary clinical outcome was the reported number of episodes of sore throat in the 2 years after entry into the study. Secondary clinical outcomes included: the reported number of episodes of sore throat; number of sore throat-related GP consultations; reported number of symptom-free days; reported severity of sore throats; and surgical and anaesthetic morbidity. In addition to the measurement of these clinical outcomes, the impact of the treatment on costs and quality of life was assessed.
Results: Of the 1546 children assessed for eligibility, 817 were excluded (531 not meeting inclusion criteria, 286 refused) and 729 enrolled to the trial (268) or cohort study (461). The mean (standard deviation) episode of sore throats per month was in year 1 – cohort medical 0.59 (0.44), cohort surgical 0.71 (0.50), trial medical 0.64 (0.49), trial surgical 0.50 (0.43); and in year 2 – cohort medical 0.38 (0.34), cohort surgical 0.19 (0.36), trial medical 0.33 (0.43), trial surgical 0.13 (0.21). During both years of follow-up, children randomised to surgical management were less likely to record episodes of sore throat than those randomised to medical management; the incidence rate ratios in years 1 and 2 were 0.70 [95% confidence interval (CI) 0.61 to 0.80] and 0.54 (95% CI 0.42 to 0.70) respectively. The incremental cost-effectiveness ratio was estimated as £261 per sore throat avoided (95% confidence interval £161 to £586). Parents were willing to pay for the successful treatment of their child's recurrent sore throat (mean £8059). The estimated incremental cost per quality-adjusted life-year (QALY) ranged from £3129 to £6904 per QALY gained.

Conclusions: Children and parents exhibited strong preferences for the surgical management of recurrent sore throats. The health of all children with recurrent sore throat improves over time, but trial participants randomised to surgical management tended to experience better outcomes than those randomised to medical management. The limitations of the study due to poor response at follow-up support the continuing careful use of 'watchful waiting' and medical management in both primary and secondary care in line with current clinical guidelines until clear-cut evidence of clinical effectiveness and cost-effectiveness is available.

Trial registration: Current Controlled Trials ISRCTN47891548.

Contents

List of abbreviations

CI	confidence interval
CONSORT	Consolidated Standards of Reporting Trials
ENT	ear, nose and throat
HTA	Health Technology Assessment
ICER	incremental cost-effectiveness ratio
IRR	incidence rate ratio
NESSTAC	North of England and Scotland Study of Tonsillectomy and Adeno-tonsillectomy in Children
nvCJD	new variant Creutzfeldt–Jakob disease
PedsQL™	Pediatric Quality of Life Inventory™
QALY	quality-adjusted life-year
RCT	randomised controlled trial
RGN	registered general nurse
RR	relative risk
WTP	willingness to pay

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 in the notes at the end of the table.

Executive summary

Background

Tonsillectomy and adeno-tonsillectomy have been widely used surgical procedures for the treatment of children with recurrent sore throat in the UK. The incidence of tonsillectomy has declined in recent years to some 50,000 tonsillectomy procedures carried out on children per year. There remains little clear evidence of clinical effectiveness and cost-effectiveness of surgical or medical management (Burton et al., 2008) that would guide clinicians in treatment decisions or commissioners in commissioning decisions.

Objectives

To examine the cost-effectiveness of tonsillectomy/adeno-tonsillectomy in children aged 4–15 years with recurrent sore throats in comparison with standard non-surgical management.

Design

A pragmatic randomised controlled trial with economic analysis comparing surgical intervention with conventional medical treatment in children with recurrent sore throats (trial) and a parallel non-randomised cohort study (cohort study).

Setting

Five secondary care otolaryngology departments located in the north of England or west of Scotland.

Participants

Two hundred and sixty-eight (trial) and 461 (cohort study) children aged between 4 and 15 years on their last birthday with recurrent sore throats.

Interventions

The treatment arm consisted of tonsillectomy and adeno-tonsillectomy with adenoid curettage and tonsillectomy by dissection or bipolar diathermy according to surgical preference within 12 weeks of randomisation. The control arm consisted of non-surgical conventional medical treatment only.

Main outcome measures

The primary clinical outcome was the reported number of episodes of sore throat in the 2 years after entry into the study. Secondary clinical outcomes included: the reported number of episodes of sore throat; number of sore throat-related GP consultations; reported number of symptom-free days; reported severity of sore throats; and surgical and anaesthetic morbidity. In addition to the measurement of these clinical outcomes, the impact of the treatment on costs and quality of life was assessed.

Analysis

An intention-to-treat analysis was performed according to the original protocol.

Economic evaluation

An intention-to-treat cost-effectiveness analysis, willingness-to-pay survey and cost–utility analysis were undertaken to estimate the incremental cost-effectiveness ratio, how much parents would be willing to pay and the incremental quality-adjusted life-years (QALYs) gained.

Results

Of the 1546 children assessed for eligibility, 817 were excluded (531 not meeting inclusion criteria, 286 refused) and 729 enrolled to the trial (268) or cohort (461).

Patient preferences

Sixty-three per cent (461/729) of children and parents participating in the study stated a preference for medical or surgical management: 16% (74/461) of these who were recruited to the cohort study opted for continuing medical management and 84% (387/461) for surgical management. Prior to recruitment to the cohort study, participants opting for surgical management reported more sore throat episodes and that progress at school was impeded compared with cohort participants opting for medical management and trial participants.

Response rates at baseline and outcome

Eighty-eight per cent (642/729) of all study participants completed and returned baseline questionnaires. The response rate to self-completed outcome questionnaires was 56% at 3 months, 38% at 12 months and 33% at 24 months. At 12 months, the response was 48% for the trial and 33% for the cohort; at 24 months, trial response was 44% and cohort 27%. Each participant was sent 24 4-weekly diaries; there was a poor diary response rate: trial 41% and cohort 29%. The mean number of diaries returned per child was 9.9 for the trial and 6.8 for the cohort. The percentage of GP records accessed was 69 for the trial and 31 for the cohort.

Primary outcome

The primary outcome was the number of episodes of sore throat experienced during 2 years of follow-up by each participating child recorded each day in health diaries. The mean (standard deviation) episode of sore throats per month differed between years and treatment groups, and was in year 1: cohort medical 0.59 (0.44); cohort surgical 0.71 (0.50); trial medical 0.64 (0.49); and trial surgical 0.50 (0.43). Year 2: cohort medical 0.38 (0.34); cohort surgical 0.19 (0.36); trial medical 0.33 (0.43); and trial surgical 0.13 (0.21). During both years of follow-up, children randomised to surgical management were less likely to record episodes of sore throat than those randomised to medical management; the incidence rate ratios in year 1 and year 2 were 0.70 [95% confidence interval (CI) 0.61 to 0.80] and 0.54 (95% CI 0.42 to 0.70) respectively.

Secondary outcomes

The mean (standard deviation) number of sore throats differed between years and treatment groups, and was: year 1: cohort medical 30.6 (28.7); cohort surgical 42.8 (7.5); trial medical 49.1 (7.3); and trial surgical 31.0 (5.0). Year 2: cohort medical 20.4 (2.5); cohort surgical 10.5 (1.5); trial medical 20.2 (3.2); and trial surgical 8.0 (0.9). During both years of follow-up, children randomised to surgical management recorded less sore throats than children randomised to medical management; the incidence rate ratios were: year 1: 0.67 (95% CI 0.52 to 0.85) and year 2: 0.27 (95% CI 0.16 to 0.46).

The mean (standard deviation) number of recorded GP consultations for sore throats differed between years and treatment groups. Year 1: cohort medical 1.6 (2.0); cohort surgical 1.9 (2.2); trial medical 2.4 (2.4); and trial surgical 1.9 (2.8). Year 2: cohort medical 1.5 (2.1); cohort surgical 0.8 (1.3); trial medical 1.3 (1.6); and trial surgical 0.9 (1.4). During both years of follow-up, children randomised to surgical management recorded less sore throat-related consultations than children randomised to medical management; the incidence rate ratios were: year 1: 0.81 (95% CI 0.59 to 1.10) and year 2: 0.67 (95% CI 0.46 to 0.97).

The incremental cost-effectiveness ratio was estimated as £261 per sore throat avoided (95% CI £161 to £586). Parents were willing to pay for the successful treatment of their child's recurrent sore throat (mean £8059). The estimated incremental cost per QALY ranged from £3129 to £6904 per QALY gained.

Conclusions

Children and parents exhibited strong preferences for the surgical management of recurrent sore throats. The health of all children with recurrent sore throat improves over time, but trial participants randomised to surgical management tended to experience better outcomes than those randomised to medical management. The limitations of the study due to poor response at follow-up support the continuing careful use of 'watchful waiting' and medical management in both primary and secondary care in line with current clinical guidelines until clear-cut evidence of clinical effectiveness and cost-effectiveness is available.

Implications for practice

- There are clinical benefits of tonsillectomy that persist for at least 2 years.

- Participants were more likely to express a preference for tonsillectomy if they had experienced more severe symptoms of sore throat.
- There is a strong parental preference for tonsillectomy.
- The findings support careful use of 'watchful waiting' and medical management in both primary and secondary care until clear-cut evidence of effectiveness is available.

Recommendations for research

- Exploratory secondary analysis to estimate the impact at surgical management on study participants whose tonsils were surgically removed.
- Methodological research of alternative methods of data collection.
- Larger utility elicitation/willingness-to-pay studies.

Trial registration

This trial is registered as ISRCTN47891548.

Chapter 1
Background and introduction

In 1999, the NHS Research and Development Health Technology Assessment (HTA) programme identified that original research was necessary to investigate the key research question: 'What is the cost-effectiveness of tonsillectomy/adeno-tonsillectomy in children with recurrent throat infections?' The research brief specified the requirement for a randomised controlled trial (RCT) with economic analysis.

Scientific background

In the UK, sore throats cost the NHS an estimated £60 million per annum in GP consultations, result in 90,000 tonsillectomy procedures, approximately half of which are in children, and result in a loss of more than 35 million school or work days annually.[1] The incidence of tonsillectomy has risen since the early 1990s, although levels are still much lower than in the 1930s, when 100,000 operations were performed on UK school children.[2] Adenoidectomy is performed with tonsillectomy in about one third of patients. Private medical insurance is associated with higher selective surgical rates for tonsillectomy or adeno-tonsillectomy in children under the age of 7 years[3] and 16% of all UK ear, nose and throat (ENT) surgical activity is in the independent sector. Therefore, figures based purely on NHS returns inevitably underestimate the total activity. In addition to the health-care costs, tonsillectomy incurs parental costs as one parent usually resides in hospital overnight. Thereafter the average time to return to normal activity for children under 15 years of age is 12 days.[4]

There is a broad similarity in the criteria for tonsillectomy in clinical guidelines in the UK[5,6] and North America.[7] The minimum criteria are typically a 2-year history of three to four sore throats of moderate severity (5-day duration) per annum. This is despite evidence that even histories that seem impressive may not be confirmed on close scrutiny in the majority of cases.[8] The complex psychosocial influences on tonsillectomy rates include parental enthusiasm for intervention,[9] lack of information[10] and maternal use of psychotropic drugs which increases twofold the rate of consultation for childhood sore throat.[11,12] Guidelines may not be uniformly implemented, even when locally derived. Surgeons tend to break guidelines more often in favour of performing surgery than withholding surgery.[5]

National and international variations in the rates of adeno-tonsillectomy have been recognised for decades. Even in the 1930s, 50% of children in the UK and the USA received a tonsillectomy, while the rate was 0.5% or lower in Germany.[2] A survey of such variation in Quebec, highlighted the importance of clinical uncertainty among physicians about the recommendation for surgical intervention,[13] providing further support for conducting primary research. The Scottish National Tonsil Audit showed that rates of tonsillectomy in childhood varied from less than 4 per 10,000 children in the Forth Valley to almost 10 per 10,000 children in Dumfries and Galloway.[14]

Differential costs and benefits of surgery at different age groups are not known. The tonsils are traditionally thought to undergo a period of physiological enlargement around the age of school entry. Older children and adolescents may have a somewhat different natural history, and illness at higher ages has rather different (educational) implications.

Mortality from tonsillectomy has been estimated at between 1 per 16,000 and 1 per 35,000 operations,[15] but surgical risk at this level is hard to measure, conceptualise and convey. The major non-fatal complications are infection, haemorrhage (2.15%) and pain, which lasts on average 5–6 days[16,17] and may be inadequately treated in children.[18] Haemorrhage is unpleasant, it requires intravenous fluid administration, with or without blood transfusion, and a return to theatre. The reported rate of second anaesthetic for haemostasis varies widely from 0.75% in one British review[4] to as low as 0.06% in a study of almost 9409 children in Toronto.[19] In the UK, post tonsillectomy, it has been reported that the readmission rate is as high as 7%,[4] but an internal audit found that in Newcastle it was only 2.3% for children receiving adeno-tonsillectomy (unpublished data; Department of Clinical Effectiveness, Freeman Hospital, Newcastle, 1999). The overall reported

complication rate ranges from 8%[14] to 14%,[17] the majority of complications being relatively minor such as sore throat, nausea, fever and dysphagia. Most 2–10 year olds undergoing surgery show behavioural changes such as attention seeking, temper tantrums and night waking and there is also anecdotal evidence for depression after tonsillectomy.[20] Younger children, because of cognitive immaturity, seem less able to adapt to hospitalisation.[21,22] Late sequelae may include lower postoperative serum immunoglobulin levels, but these have been ascribed to reduction in antigen stimulation.[23] There is continuing debate about the suggestion that tonsillectomy increases the risk of Hodgkin's lymphoma;[24] a large Scandinavian population cohort study found an increased risk of Hodgkin's disease, especially in younger children.[25] The risk of transmission of new variant Creutzfeldt–Jakob disease (nvCJD) from contaminated tonsillectomy instruments remains quite unquantified. Some UK centres continue to use disposable tonsillectomy sets.

Despite the frequency of tonsil dissection for recurrent sore throats in children, there is a remarkable lack of robust evidence for its efficacy. Uncontrolled patient reports suggest the procedure to be very effective, but recurrent sore throat, particularly in childhood, may be a self-limiting illness. Where non-intervention control groups have been studied, the benefits of adeno-tonsillectomy seem almost to disappear after 2 years. Available studies are either 20–30 years old or confined to small numbers of severely affected individuals with limited general applicability. The Cochrane Review concluded that there is no evidence from RCTs to guide the clinicians in formulating the indications for surgery in children or adults.[26] The authors surmised that there is a need for high quality evidence from RCTs to establish the effectiveness of (adeno-)tonsillectomy and that these should assess the effectiveness of the procedure in patients with throat infections of differing severity and frequency. A recent Dutch RCT of adeno-tonsillectomy versus watchful waiting reported no differences between treatment arms for children with mild symptoms, and only a small difference of less than one episode of fever a year between treatment arms for children with moderate symptoms.[27]

The Scottish National Tonsillectomy Audit[14] showed high levels of patient satisfaction and revealed that 80% of subjects did not consult a doctor in the subsequent 12 months. However, over the past 30 years a number of controlled studies with longer follow-up indicates marginal and diminishing levels of clinical benefit over a period of non-intervention. There are no substantial claims for the benefit of childhood tonsillectomy after 2 years. Roos and colleagues[28] assessed the benefit to be 1.0–1.5 fewer sore throats (0.5–1.0 episodes per annum) over the first 2 years after surgery in those with three to four episodes per annum preoperatively. Other studies[29–31] showed benefits of the order of 1.5 fewer sore throats versus controls in the first postoperative year and, on average, one fewer episode in the second year. All of these and other available studies provide inadequate evidence due to poor definition of entry and outcome criteria, failure to include intention-to-treat calculations and small or skewed samples.[32] Even the only generally acceptable scientific study by Paradise and colleagues[17] suffered from having comparatively small numbers of participants drawn form a skewed population of more severely affected children. The benefits of surgery were more marked (approximately 1.75 fewer episodes in year 1, 1.50 in year 2) but equally short lived. The drop-out rate was 34% by the end of year 2, and one in three of the control group underwent surgery and were excluded from the analysis. Also, the very active therapy of the control arm may have mitigated any impact of surgery. The Paradise group went on to study a more typical, i.e. less severely affected, group of children, but the full results of this study, near completion in 1992, have never been reported.

Weight gain is a cited supplementary benefit of tonsillectomy. Two studies showed accelerated weight gain postoperatively, but as the children were shown to be of normal or above average height and weight preoperatively, this effect may be undesirable.[33]

A straw poll of consultant otolaryngologists asked what level of reduction in sore throat would justify removal of the tonsils? Replies were remarkably consistent – at least two sore throats fewer per annum. No published trial to date shows a benefit of this magnitude, even in the first year after surgery.

We therefore designed a pragmatic RCT to answer the key research question: 'What is the effectiveness and cost-effectiveness of (adeno-)tonsillectomy in comparison with standard non-surgical management in children aged under 16 with recurrent throat infections?' Assessment of outcome emphasised those that were important to children themselves and their parents or carers. Our specific research questions were:

- Does tonsillectomy or adeno-tonsillectomy reduce the number of episodes of recurrent sore throats among children to a clinically significant extent?
- Are there differences in clinical outcome for the age groups: 4–7, 8–11 and 12–15 years?
- What is the cost-effectiveness of tonsillectomy/adeno-tonsillectomy for children, and what are the costs and benefits to families?
- What are the important outcomes of tonsillectomy/adeno-tonsillectomy for children and their parents/carers, and what is the importance of these to children and their parents' quality of life?
- What are parents' (and older children's) preferences for different treatment options for recurrent sore throat?
- How representative of the target population are trial participants?

Structure of this report

This report contains eight chapters and eight associated appendices. The original study protocol is reproduced in Appendix 1. In Chapter 2 we describe the methods used in the study. This includes a comprehensive account of the rationale and methods used in the prospective pragmatic RCT and prospective non-randomised cohort study of non-trial participants comparing surgical intervention with conventional medical treatment and changes to the original protocol. Chapter 3 provides the main results of the trial and cohort study using the analysis strategy described in the original protocol. Chapter 4 describes a small qualitative study of parents and teenagers to identify the experience of recurrent sore throat and their preferences for different treatment options; the study was used to confirm person-centred outcomes and the development of a utility study. Chapter 5 describes a small utility study to assess the preferences of parents and children for the treatment of recurrent sore throat. Chapter 6 describes the economic analysis. Chapter 7 discusses the implications of the study results for the NHS, and Chapter 8 provides conclusions for practice, policy and further research.

Chapter 2
Methods of research

The design of this study was a pragmatic RCT with economic analysis comparing conventional surgical intervention with conventional medical treatment for children with recurrent sore throats (here after referred to as the trial). Eligible subjects who declined participation in the trial were offered their preferred treatment and invited to participate in a parallel non-randomised cohort study (hereafter referred to as the cohort). The analyses of the trial and cohort data are reported in Chapter 3. The economic analysis is reported in Chapter 6. A small qualitative study to investigate treatment and outcome preferences was undertaken prior to commencement of the trial and cohort (see Chapter 4). A small utility study was undertaken once recruitment to the cohort was halted (see Chapter 5).

Rationale for design

Randomised controlled trials are the gold standard study design for the evaluation of health-care interventions in an evidence-based health-care system. The assessment of clinical effectiveness and cost-effectiveness of health technologies that are well established and widely used in clinical practice is particularly challenging in HTA where patients (or clinicians) express preferences for particular treatment regimes and are not in treatment equipoise. Standard RCT designs used where there are strong patient preferences experience high non-participation (refusal) rates and, consequently, increased confounding and decreased generalisability. Patient preference trial designs that combine the RCT with a non-randomised experimental design are increasingly used where there are strong patient preferences.[34,35]

Tonsillectomy and adeno-tonsillectomy for the treatment of children with recurrent sore throat has been routine clinical practice for over 50 years. When developing the study, we anticipated patient preferences to increase the non-participation rate in a standard RCT design, although there was little evidence that there was parental enthusiasm for surgical intervention.[9] We therefore designed a study that combined a pragmatic RCT[36] with a parallel non-randomised cohort.

Patient preference trials of interventions for childhood conditions also raise the question of 'whose preference?', particularly where teenage children are participating. Although we did not attempt to differentiate between the preferences of parents and children, when recruiting participants to the study we did collect 'patient-reported' outcome data from both parents and teenage children.

Trial and cohort

Interventions

Surgical treatment consisted of tonsillectomy and adeno-tonsillectomy with adenoid curettage, and tonsillectomy by dissection or bipolar diathermy according to surgical preference. In the trial, surgical interventions were required to take place within 12 weeks of randomisation.

Medical treatment consisted of conventional treatment. There was no active intervention protocol as no single prescribing strategy would be able to cover all participants.[37] The referring GP was free to treat as in his or her current practice.

Participants

Study subjects were children aged between 4 and 15 years on their last birthday with recurrent sore throats, referred from primary care to the five secondary care otolaryngology departments located in the north of England or west central Scotland; Freeman Hospital, Newcastle upon Tyne (from 13 May 2002 to 31 July 2006); Alder Hey Children's Hospital, Liverpool (from 11 November 2002 to 30 June 2005); Booth Hall Children's Hospital, Manchester (from 8 November 2002 to 30 May 2006); Bradford Royal Infirmary (from 7 December 2004 to 31 July 2006); Royal Hospital for Sick Children, Glasgow (from 4 March 2005 to 31 July 2006). The study inclusion and exclusion criteria are shown in Box 1.

BOX 1 *Inclusion and exclusion criteria*

Inclusion criteria

4+ episodes of sore throat within each of the preceding 2 years

6+ episodes of sore throat within the last year

Exclusion criteria

Previous tonsillectomy

Hospitalisation due to tonsillitis

Quinsy

Marked obstructive airway during attack

Comorbidity affecting ability to undergo surgery within 6 months

Bleeding disorder

Otitis media with effusion

Sleep apnoea syndrome

Rare medical condition (e.g. glomerulonephritis or Henoch–Schönlein purpura)

Suspected velopharyngeal insufficiency

Congenital/valvular heart disease

Mid way through the study, the recruitment process was reviewed. This involved a discussion about the application of the eligibility criteria with the participating surgeons and, as a result, the inclusion criteria were simplified in an attempt to further harmonise the process of recruitment (see Summary of changes to study protocol). Thus two different sets of criteria were used. Recruitment to the study took place in secondary care between May 2002 and July 2006. All primary care referrals of children with recurrent sore throats to the five study centres were considered by participating surgeons. Trained research nurses [Grade F registered general nurses (RGNs) with at least 2 years postregistration experience in ENT and research] introduced the study to children and their parents who were shown a video (see Appendix 2 for the script of the video) describing the main aspects of the study. Printed information sheets were also provided (see Appendix 3). In light of this information the research nurses discussed the study with children and their parents, who then went on to have a further, informed, discussion with the participating surgeon. For children and parents willing to participate in either the trial or the cohort study the research nurses then obtained written consent and collected baseline data. The video transcript, information sheets and consent forms (see Appendix 4) were translated into Bengali, Punjabi, Gujarati and Urdu.

Randomisation

Independent World Wide Web-based computer randomisation allocated trial participants to interventions while cohort participants elected their treatment. Children recruited to either the trial or the cohort were stratified by hospital and by age at their last birthday into three groups (4–7 years, 8–11 years and 12–15 years). Blocked randomisation was used to ensure that within each centre and within each of the three age groups children were allocated in equal numbers to each arm of the trial. Where study centres were unable to access the World Wide Web they telephoned the co-ordinating centre in order for web-based randomisation to be completed on their behalf.

Data collection

The primary clinical outcome was the reported number of episodes of sore throat in the 2 years after entry into the study. Secondary clinical outcomes included the reported number of episodes of sore throat, otitis media and upper respiratory tract infection that invoked a GP consultation; reported number of symptom-free days; reported severity of sore throats; and surgical and anaesthetic morbidity. In addition to the measurement of these clinical outcomes, the impact of the treatment on costs and quality of life was assessed. Quality of life was assessed

using the Pediatric Quality of Life Inventory™ (PedsQL™).[38–40]

At baseline, an anonymised eligibility form was completed by the surgeon for each child approached about the study, recording demographic characteristics (gender, age) along with reported history of sore throats. A baseline questionnaire (see Appendix 5) was completed by participants upon recruitment to the study. All participants were followed up for 24 months from the date of initial randomisation. To minimise recall bias, data on sore throats were gathered by a simple structured daily health diary (see Appendix 6), which was completed and returned by participants on a monthly basis for 24 months. In addition, simple outcome questionnaires based on the baseline questionnaire (see Appendix 5) were administered to study participants at 3, 12 and 24 months into the study. Data on consultation rates and prescribed medication were gathered from GP medical records by manual abstraction by trained researchers at the end of follow-up for all trial participants and a sample of cohort participants.

Diaries

Data on sore throats were gathered by a simple structured daily health diary, which was completed and returned by participants on a monthly basis for 24 months. The diary for month 1 was given to participants by research nurses at the clinic and returned by post after 4 weeks in a prepaid envelope addressed to the study centre. Subsequent diaries were posted to participants directly from the study centre 5 days in advance of the new diary start date, with a letter reminding participants to return the previous diary. Research nurses and, later on, researchers reminded diary non-responders to return diaries by telephone on a monthly basis.

Questionnaires

Outcome questionnaires were administered to participants at 3, 12 and 24 months after randomisation. A baseline questionnaire was completed by participants upon recruitment to the trial. Baseline questionnaires were given to participants by research nurses at the clinic and were either returned immediately at the clinic or taken away and returned by post in prepaid addressed envelopes to the study centre. On their due date, 3-, 12- and 24-month questionnaires were posted to participants directly from the co-ordinating centre. First reminders were sent to non-responders 2 weeks after the initial questionnaire (letter and envelope only). Second reminders were sent 4 weeks after the initial questionnaire (letter, questionnaire and envelope). Third reminders were carried out 6 weeks after the initial questionnaire (telephone reminder which could include further letters, a questionnaire and envelopes).

For children under the age of 8 years, parents completed all outcome measures. For children over the age of 8, children completed the diary and the PedsQL™ section of the questionnaire, while their parents completed the remainder of the questionnaire. If a child turned 16 during the course of the trial he or she was then asked to complete all the outcome measures. All outcome measures were anonymous.

Study power

In this trial we anticipated a fairly large difference in the primary clinical outcome (the reported number of episodes of sore throat in the 2 years after randomisation) with an effect size of around 1.0, but a smaller difference in a number of psychosocial outcomes, including health-related quality of life, with an effect size of 0.33. No standard sample size formula is available for economic evaluations, and a number of methods were proposed.[41–43] The information that was available limited the use of such methods in practical applications. Published data[17] suggested that tonsillectomy may lead to a reduction of approximately 1.5 days per year in missed schooling. Given a reported standard deviation of 4.5, to detect this difference with 80% power we needed approximately 142 children in each arm of the trial assuming a significance level of 5%. A sample size of 142 children in the cohort group opting for surgery would allow us to detect similar differences between the cohort group and propositi. The sample was stratified by age (4–7 years, 8–11 years, 12–15 years). With a total of 284 children, we had approximately 47 randomised to each treatment arm in each stratum. Given that the standard deviation of the number of sore throats per year was 2.018, we were able to estimate the difference between treatments in each strata with a standard error of 0.41. (Equivalently we had 90% power to detect a difference of 1.35 episodes of sore throat per year in each stratum assuming a type 1 error of 0.05.) It was anticipated that the clinically important difference in outcome between the two arms of the trial would be approximately two episodes in the second year of follow-up. A sample size of 142 children in each arm enabled us to measure this difference with sufficient precision to undertake a meaningful economic analysis.

Blinding

The trial was conducted in normal clinical practice and the blinding of health professionals and participants to the intervention was not possible. However, all researchers who conducted interviews or processed self-completed questionnaires and diaries were blind to the interventions of all trial and cohort participants. This was facilitated by separating the responsibility for recruitment and randomisation from outcome assessment. Furthermore, participants were encouraged to respond to questions without describing their treatment regime. In this way, we minimised subjective bias towards a given treatment.

Ethical approval

This study was approved by the Northern & Yorkshire Multicentre Research Ethics Committee and associated Local Research Ethics Committees. The study received a clinical trial authorisation from the Medicines and Healthcare products Regulatory Agency. The study was approved by the NHS Research and Development department and a Caldicott Guardian from each participating secondary care site. Primary care trust support was provided regarding collection of data from GP records.

Adverse events

Adverse events were recorded in self-completion daily diaries and GP records. Expected adverse events included infection, haemorrhage and pain following tonsillectomy, with possible hospital readmission as well as sore throat, nausea, fever and dysphagia. No reporting of serious adverse events was required. All adverse events were managed as per normal care as the intervention did not deviate from normal care.

Summary of changes to study protocol

In order to increase recruitment to the trial, inclusion criteria were amended in May 2004 from 'children (or carers) reporting experience of mild symptoms, 6 or more episodes within 2 years or 8 or more episodes within 1 year, and children reporting experience of moderate symptoms (sore throat for 5 days or more), 6 or more episodes within 2 years or 6 or more within 1 year' to 'children (or carers) reporting experience of 4 or more episodes of sore throat within each of 2 years or 6 or more episodes of sore throat within 1 year'.

Exclusion criteria were also amended in May 2004 in order to increase safety from 'children will be excluded if they require hospitalisation due to tonsillitis or quinsy; have obstructive symptoms suggestive of clinically significant sleep apnoea syndrome or rare medical conditions such as glomerulonephritis or Henoch–Schönlein purpura; or have previously had a tonsillectomy; or have suspected velopharyngeal insufficiency' to 'Children will be excluded if they require hospitalisation due to quinsy; have obstructive symptoms suggestive of clinically significant sleep apnoea syndrome, have rare medical conditions such as glomerulonephritis or Henoch–Schönlein purpura; have previously had a tonsillectomy; have suspected velopharyngeal insufficiency, have co-morbidity that means they are unable to undergo the operation within the next 6 months, have a bleeding disorder, or have congenital/valvular heart disease'.

In July 2004 the project was extended from 5 to 7 years to increase patient recruitment.

Two additional study centres: Royal Hospital for Sick Children, Glasgow and Bradford Royal Infirmary were added in September 2004.

The title of the study was amended in September 2004 from NESTAC: North of England Study of Tonsillectomy and Adeno-tonsillectomy in Children to NESSTAC: North of England and Scotland Study of Tonsillectomy and Adeno-tonsillectomy in Children, with the addition of Glasgow as a study centre.

Postal questionnaires became interview administered in October 2006 in an attempt to improve response rates.

Statistical methods

Main analysis

An intention-to-treat analysis was performed according to the original protocol. The primary clinical outcome measure was the number of episodes of sore throat. This variable was analysed using generalised linear modelling assuming a Poisson error structure with a log link function.[44] By fitting the difference between the two experimental groups as a fixed effect, interval estimates of the effect of tonsillectomy (in each of the first 2 years of follow-up) were generated. These estimates were then used in the economic analysis. The same approach was used to analyse the other outcomes. A Poisson error structure was assumed for data

in the form of a count (such as the number of episodes of absence from school), and normal error structure adopted for continuous variables (such as the quality of life indices).

Secondary analysis

The aim of secondary analysis was to determine whether we could identify groups of children who had benefited from surgical treatment. It was hypothesised that disease severity may be an important factor. A severity index based on history of the condition during the year before entry to the study was derived using data recorded in GP records. The relationship between severity and the effect of tonsillectomy was then investigated using the modelling approach described above.

Cohort analysis

Data from participants who declined to be randomised were used to assess the external validity of the main study. Baseline characteristics of the cohort were compared with those of the study population using standard tests for the comparison of two independent samples (e.g. the t-test or Mann–Whitney test as appropriate). Outcome for the cohort was compared with outcome for the two groups of study participants using the modelling approach described above.

Summary of changes to the protocol for analysis

In the original protocol we specified that 'secondary clinical outcomes included reported numbers of episodes of sore throat, otitis media and upper respiratory tract infection which invoked a GP consultation'. In practice it has not been possible to uniquely determine the cause of each individual GP consultation. The two variables that have been analysed are the number of GP consultations in which a sore throat was mentioned and the total number of GP consultations.

In the protocol we also specified that we would analyse our primary outcome measure – the number of episodes of sore throat – using Poisson regression models. After inspection of the data prior to breaking the blinding it was decided to extend this approach to include negative binomial regression models to allow us to take into account over-dispersion in the data.

In addition to the pre-specified secondary analysis we also examined whether the effect of tonsillectomy varied for the different age strata (as this was specified as one of the study objectives) and whether there was a difference between boys and girls. After observing how the response rate varied with time we decided to adjust all the secondary analyses to take into account when diaries were returned for each child.

When the analysis plan for the cohort study was written it was envisaged that all the children in the cohort would opt to have a tonsillectomy. Thus we specified that cohort and trial children would be compared using methods appropriate for comparing two independent samples (t-tests and Mann–Whitney tests). In practice, a sample of parents/children opted for medical management of their sore throats. We have therefore used methods appropriate for comparing three groups – one-way analysis of variance and chi-squared tests.

Chapter 3
Trial and cohort results

In this chapter we report the main results from the pragmatic RCT (trial) and the parallel prospective cohort study (cohort). The chapter is divided into five sections. First we describe the Consolidated Standards of Reporting Trials (CONSORT) flow chart and review the response and completion rates for each data collection method over the life of the study. Second we describe the baseline characteristics of trial and cohort participants. In the next two sections we report our primary analysis on the impact of the interventions on primary and secondary outcomes. Finally we report a secondary analysis to determine the characteristics of those groups of children who benefited from surgical treatment.

Participant flow

Figure 1 shows the CONSORT flow chart of children in the study.

Eligibility

Five centres assessed 1546 children for eligibility for the study. Five hundred and thirty-one were not eligible. Of these, 328 (62%) did not meet the inclusion criteria and 162 (31%) were excluded because of the exclusion criteria (see Box 1). Other reasons for exclusion included communication difficulties (n = 29), being involved in another RCT (n = 2), and emigrating (n = 1). No reasons were recorded for nine children.

Enrolment

Of 1015 eligible children, 286 (28%) refused to participate in the study. Of the remaining 729, 268 (37%) agreed to participate in the trial and 461 (63%) agreed to participate in the cohort.

Allocation

Trial participants were randomly allocated to surgical (n = 131) or medical (n = 137) management. Of those randomised to surgery, 120 (92%) had an (adeno-)tonsillectomy within 24 months of randomisation, and of those randomised to medical management, 36 (26%) had an (adeno-) tonsillectomy within 24 months of randomisation.

Cohort participants selected surgical (n = 387) or medical (n = 65) management. Of those selecting surgery, 374 (97%) had an (adeno-)tonsillectomy within 24 months of randomisation, and of those selecting medical management, nine (14%) had an (adeno-)tonsillectomy within 24 months of randomisation.

The number of children recruited by each centre broken down by study group is given in Table 1.

Follow-up

Trial and cohort participants were followed up for up to 2 years from time of randomisation. Follow-up was undertaken in three ways:

1. Self-completion health diaries (see Appendix 6). These took the form of booklets, each corresponding to a time period of 28 days (4 weeks). A total of 24 booklets were sent out to study participants at 4-weekly intervals.
2. Telephone prompt interviews were introduced part-way through the study because of concern about the low response rates to the health diary. If a due diary was not returned within 28 days, a telephone call was made to the relevant study participant who was then asked to provide a limited amount of information about the child's health.
3. Self-completed postal outcome questionnaires (see Appendix 5) were administered at 3, 12 and 24 months after entry into the study.

Health diaries

Each participant was sent 24 4-weekly diaries. There was a poor response rate for both trial and cohort participants. Of trial participants, 81.7% (219/268) returned at least one diary. The mean number of diaries returned per child in the trial was 9.91. The overall diary response rate for trial participants was 41.3%. Of cohort participants 65.5% (302/461) children returned at least one diary. The mean number of diaries returned per child in the cohort was 6.84. The overall diary response rate for cohort participants was 28.5%.

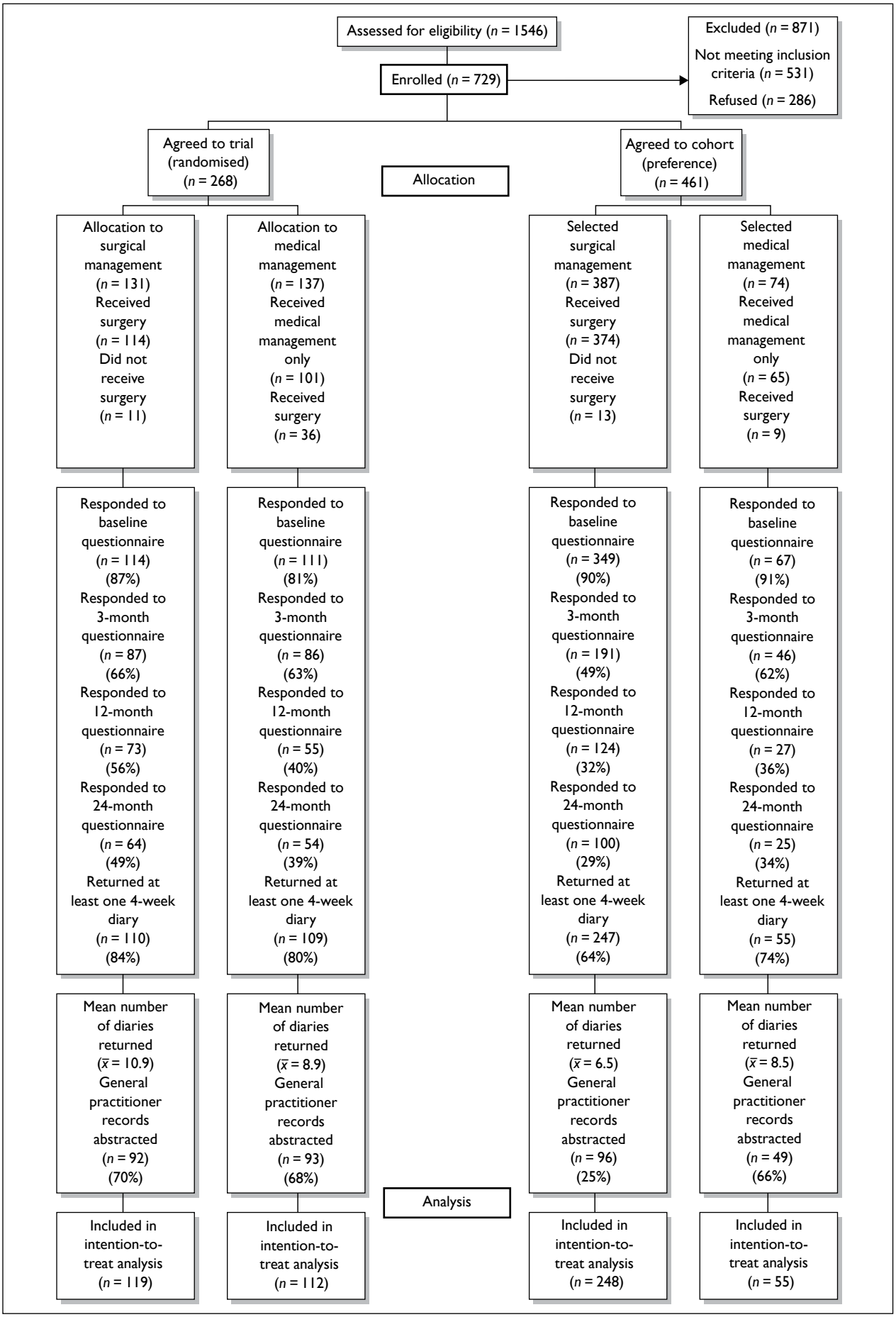

FIGURE 1 *CONSORT flow chart.*

TABLE 1 *Recruitment by centre*

	Study group			
Centre	**Cohort medical**	**Trial**	**Cohort surgical**	**Total**
Newcastle	23 (8.5%)	140 (51.7%)	108 (39.9%)	271
Liverpool	36 (17.6%)	23 (11.3%)	145 (71.1%)	204
Manchester	8 (6.0%)	39 (29.3%)	86 (64.7%)	133
Bradford	0 (0)	39 (69.6%)	17 (30.4%)	56
Glasgow	7 (10.8%)	27 (41.5%)	31 (47.7%)	65
Total	74 (10.2%)	268 (36.8%)	387 (53.1%)	729

Numbers in parentheses are percentages of the total.

Trial participants were significant more likely to respond than cohort participants [relative risk (RR) 1.24; 95% confidence interval (CI) 1.16 to 1.81]. There was no evidence that response rates differed between types of management (surgical versus medical: RR 0.97; 95% CI 0.76 to 1.24).

In Figure 2, diaries are numbered sequentially by month from randomisation (1–24). The figure clearly shows that response rates declined over the 24-monthly follow-up period for both trial and cohort participants. For trial participants only, adding responses from telephone interviews that corresponded to a missing diary provided an average of 1.6 additional monthly measurements. This equates to an overall response rate for the selected primary outcome variable of 47.8% for trial participants.

Self-completion postal questionnaires

There was a poor response rate for both trial and cohort participants (Table 2). At 12 months, 47.8% of trial and 32.8% of cohort participants responded. There was a further decline by 24 months, with 44.0% of trial and 27.1% of cohort participants responding.

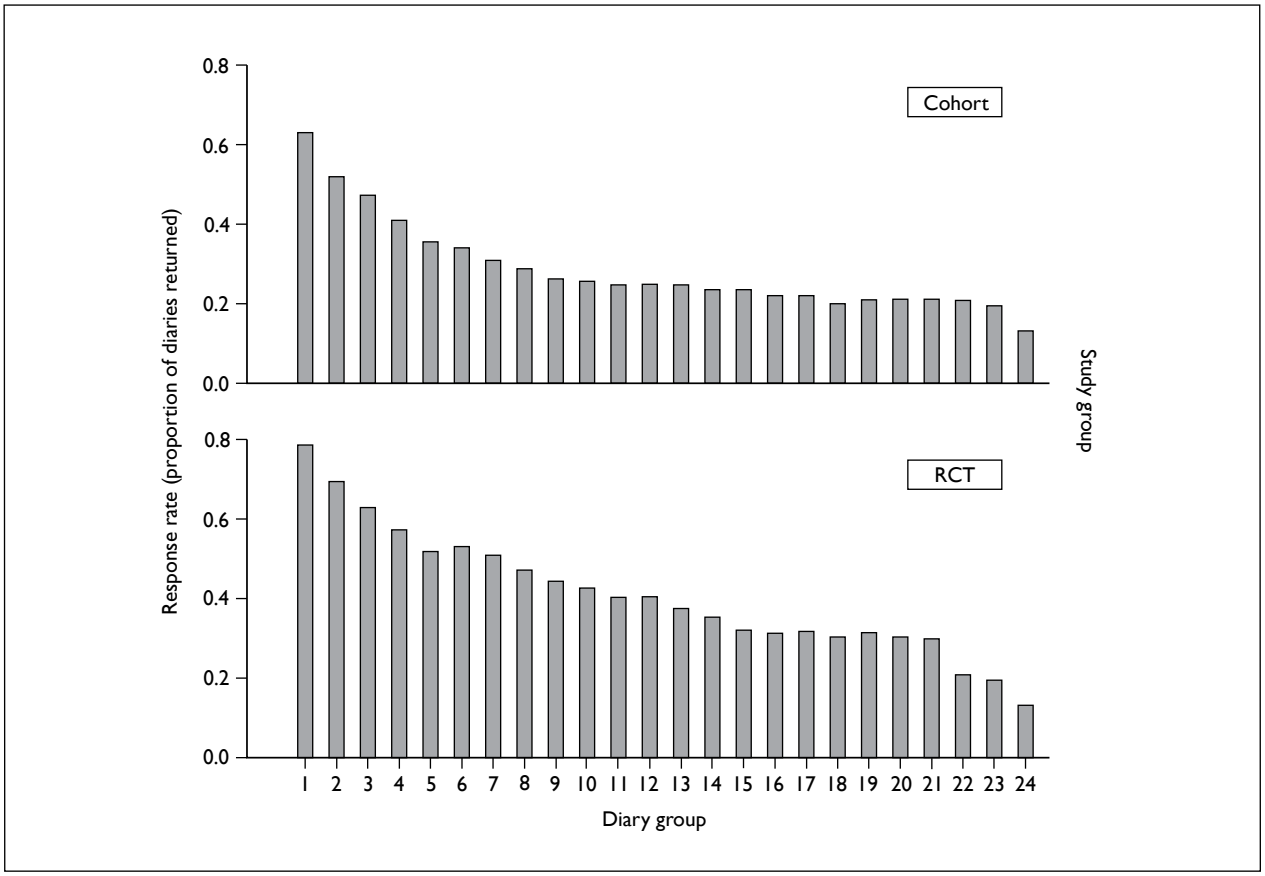

FIGURE 2 *Response rates by diary number for the trial and cohort overall.*

TABLE 2 *Participants' response rates to 12- and 24-month questionnaires by study group*

	Trial			Cohort		
	Surgical management *n* (%)	**Medical management *n* (%)**	**Total *n* (%)**	**Surgical management *n* (%)**	**Medical management *n* (%)**	**Total *n* (%)**
Number of participants	131	137	268	387	74	461
Returned 12-month questionnaire	73 (58%)	55 (40%)	128 (48%)	124 (32%)	27 (36%)	151 (33%)
Returned 24-month questionnaire	64 (49%)	54 (39%)	118 (44%)	100 (26%)	25 (34%)	125 (27%)

Trial participants were much more likely to return their 12-month questionnaire than cohort participants [RR 1.46 (95% CI 1.22 to 1.75) in year 1 and RR 1.62 (95% CI 1.33 to 1.99) in year 2]. Among trial participants the difference in response rates between the two arms was statistically significant (p = 0.014) in year 1; children randomised to tonsillectomy were more likely to respond than other children (RR 1.39; 95% CI 1.08 to 1.79). The corresponding RR in year 2 was 1.24 (95% CI 0.94 to 1.63).

Abstraction of general practitioner records

We attempted to approach all GPs of trial participants and, because of resource constraints, sampled the GPs we approached for cohort participants. Table 3 shows the number of GP records sampled and examined for trial and cohort participants. Not all records were accessible because the research team failed to make contact within the time available (n = 85), the participant was no longer registered with the practice and the research team were unable to trace him or her via the tracing service (n = 40), and practices denied access, either requesting payment or a more recent participant consent record (n = 31).

Baseline characteristics of study participants

Trial and cohort participants (n = 729) were invited to complete and return by post a baseline self-completed questionnaire (see Appendix 5). The baseline questionnaire was completed by 87.9% (641) of participants. Table 4 compares the characteristics of responders and non-responders. Trial participants had a higher non-response rate than cohort surgical or cohort medical participants.

Table 5 shows the demographic characteristics of study participants who responded to the baseline survey. There was some evidence that the proportion of boys was higher in the group opting for medical managements than in the other two groups ($\chi^2_2 = 8.3$; p = 0.02). There was no evidence that age influenced choice of group.

Health during 3 months prior to baseline survey

Responses to questions relating to the child's health over the 3 months prior to the baseline survey are summarised in Table 6. Most of the children (97%) in the study reported at least one sore throat. Although the difference between groups was not significant at the 5% level ($\chi^2_2 = 5.3$; p = 0.07), the trend across the study groups was replicated in the other variables relating to sore throats (where the difference between groups was significant). In general, children who opted to retain their tonsils had fewer and shorter sore throats than other children. Children who opted to have their tonsils removed tended to report the most frequent and most severe sore throats. Children who consented to be randomised were somewhere in the middle. The same response pattern was observed in the questions relating to interruption of schooling and quality of life: children opting for surgery reported the greatest perceived disruption and poorest quality of life; children opting for medical management reported the least perceived disruption and best quality of life (Table 7).

TABLE 3 *Number of study subject's general practice records from which data were collected*

	Trial			Cohort		
	Medical *n* (%)	**Surgical *n* (%)**	**Total *n* (%)**	**Medical *n* (%)**	**Surgical *n* (%)**	**Total *n* (%)**
Number of participants	137	131	268	74	387	461
Number for whom an approach was made to their GP	137 (100%)	130 (99%)	267 (99%)	73 (99%)	146 (38%)	219 (48%)
Number of those for whom an approach was made whose GP record was accessible	93 (68%)	92 (70%)	185 (69%)	49 (66%)	96 (24%)	145 (31%)

TABLE 4 *Gender and study group of questionnaire responders compared with questionnaire non-responders*

	Responders (*n* = 641)	**Non-responders (*n* = 88)**	**Test of difference between groups**
Gender, n (%)			
Male	243 (89%)	29 (11%)	$\chi^2 = 0.812$, df = 1, $p = 0.367$
Female	398 (87%)	59 (13%)	
Study group, n (%)			
All trial participants	225 (84%)	43 (16%)	$\chi^2 = 6.311$, df = 2, $p = 0.043$
Cohort surgical management	349 (90%)	38 (10%)	
Cohort medical management	67 (91%)	7 (9%)	

df, degrees of freedom.

TABLE 5 *Age and gender of study subjects by study group*

Variable	**Cohort medical (*n* = 67)**	**Trial (*n* = 225)**	**Cohort surgery (*n* = 349)**	**Test of differences between groups**
Males, *n* (%)	36 (54%)	76 (35%)	129 (37%)	$\chi^2_2 = 8.3$; $p = 0.016$
Age group, n (%)				
Age: 4–7 years, *n* (%)	28 (42%)	80 (36%)	126 (36%)	$\chi^2_4 = 4.24$; $p = 0.375$
Age: 8–11 years, *n* (%)	24 (36%)	81 (36%)	108 (31%)	
Age: 12–16 years, *n* (%)	15 (22%)	64 (28%)	115 (33%)	

Factors influencing the choice of group to which the child was entered were investigated using multinomial regression. The dependent variable was the choice of study group: 1 = cohort medical, 2 = trial, 3 = cohort surgical. All the variables listed in Table 8 were investigated as potential explanatory variables. Significance tests were based on changes in log likelihood. The greatest change in log likelihood was obtained by fitting the variables described in Tables 5–7.

The most important predictor of choice of group was whether it was perceived that the child's progress at school was being affected by their condition in the 3 months prior to the baseline survey. The second most important predictor was

TABLE 6 *Sore throat symptoms by study group*

Variable	Cohort medical (*N* = 67)	Trial (*N* = 225)	Cohort surgery (*N* = 349)	Test of differences between groups
Any sore throats? *n* (%)	63 (94%)	219 (97%)	341 (99%)	$\chi^2_2 = 5.26$; $p = 0.067$
Mean number of sore throats lasting less than 2 weeks (SD)	2.7 (1.6)	3.2 (2.4)	3.6 (2.5)	$F_{2,630} = 4.92$; $p = 0.008$
Mean length (days) last sore throat (SD)	5.3 (3.2)	7.2 (5.5)	7.8 (4.6)	$F_{2,630} = 8.14$; $p < 0.001$
Any chronic (for longer than 2 weeks) sore throat? *n* (%)	13 (19%)	65 (30%)	155 (46%)	$\chi^2_2 = 22.23$; $p < 0.001$
Sore throat resulted in ear infection? *n* (%)	20 (30%)	76 (35%)	153 (45%)	$\chi^2_2 = 7.79$; $p = 0.021$

n, number of children giving indicated response; *N*, total number of children in each group; SD, standard deviation. Maximum non-response to that question: cohort medical (2), trial (10), cohort surgical (15).

TABLE 7 *School activity and quality of life over the last 3 months*

Variable	Cohort medical (*N* = 67)	Trial (*N* = 225)	Cohort surgery (*N* = 349)	Test of differences between groups
Any days off school? *n* (%)	52 (79%)	187 (87%)	320 (93%)	$\chi^2_2 = 13.15$; $p = 0.002$
Mean number of days off school (SD)	6.6 (6.4)	8.3 (7.9)	11.2 (9.0)	$F_{2,632} = 13.17$; $p < 0.001$
Progress at school affected *n* (%)	19 (29%)	84 (39%)	215 (62%)	$\chi^2_2 = 42.33$; $p < 0.001$
PedsQL: Mean Physical Health Summary Score (SD)	77.2 (18.5)	77.5 (18.8)	71.1 (22.3)	$F_{2,621} = 7.21$; $p = 0.001$
PedsQL: Mean Mental Health Summary Score (SD)	76.6 (13.2)	72.4 (14.5)	68.9 (15.4)	$F_{2,620} = 9.03$; $p < 0.001$

n, number of children giving indicated response; *N*, total number of children in each group; SD, standard deviation. Maximum non-response to that question: cohort medical (2), trial (10), cohort surgical (15).

TABLE 8 *Multinomial regression: sequential fitting of key explanatory variables*

			Model selection: likelihood ratio tests		
Step	Explanatory variable	–2 Log likelihood	χ^2	df	*p*
0	Intercept	136.5			
1	Progress at school affected?	92.5	44.1	2	< 0.001
2	Any chronic sore throats?	80.3	12.2	2	0.002
3	Gender	71.9	8.4	2	0.015

df, degrees of freedom.

whether the child had experienced any chronic sore throats in the 3 months prior to the baseline survey. The final explanatory variable that entered the model was gender. Once these variables were included in the model, none of the other explanatory variables (age, number of episodes and duration of sore throats, ear infection or time off school) produced a significant reduction in –2 log likelihood. Similarly, none of the two-way interactions between any of the explanatory variables produced a significant improvement in the fit of the model.

TABLE 9 *Multinomial regression of choice of group: parameter estimates*

	Group						
	Cohort medical				Cohort surgical		
Explanatory variable	**OR**	**95% CI**		***p***	**OR**	**95% CI**	***p***
Progress at school affected	0.67	0.36	1.25	0.207	2.40	1.67 to 3.44	<0.001
Chronic sore throat experienced	0.60	0.30	1.20	0.151	1.57	1.08 to 2.28	0.018
Child is a girl	0.45	0.25	0.79	0.005	0.94	0.65 to 1.36	0.748

CI, confidence interval; OR, odds ratio; *p*, two-tailed probability that OR differs from 1 based on a Wald test – the comparison group is the randomised trial.

TABLE 10 *Mean number of GP consultations in 2 years prior to entry to study*

	Cohort medical (*n* = 49)	**Trial (*n* = 185)**	**Cohort surgery (*n* = 96)**
Total number of GP consultations Mean (standard deviation)	10.3 (6.9)	10.3 (6.3)	8.6 (5.8)
Number of GP consultations for sore throat Mean (standard deviation)	6.2 (4.2)	6.0 (3.7)	5.4 (3.4)

The parameter estimates of the multinomial regression of choice of group are shown in Table 9. These estimates revealed that children were more likely to be entered into the cohort surgical group than into the trial if it was perceived that their progress at school was being affected by their symptoms (odds ratio = 2.40; 95% CI 1.67 to 3.44). Children were more likely to be entered into the cohort surgical group than the trial if they had experienced a chronic sore throat prior to the baseline survey (odds ratio = 1.57; 95% CI 1.08 to 2.28). Boys were more likely than girls to be entered into the cohort medical group rather than the trial (odds ratio = 0.45; 95% CI 0.25 to 0.79).

Health in 2 years prior to study

We did not ask parents or teenagers to recall the health of participants in the 2 years before the baseline survey because of the limitations of retrospective data over this time frame. Using data abstracted from GP records Table 10 shows the number of GP consultations in the 2 years prior to the study, the average number of these per participant was 9.8. The mean number of consultations at which a sore throat was mentioned was 5.8.

A comparison of the change in –2 log likelihood with the appropriate percentage points of a chi-squared distribution with two degrees of freedom using a negative binomial regression indicated that the difference between groups was not significant ($\chi^2_2 = 5.36$; p = 0.07 and $\chi^2_2 = 2.13$; p = 0.34 for total number of consultations and consultations with sore throats respectively).

Comparison of the two randomised groups

The baseline characteristics of children who agreed to be randomised are summarised in Table 11. Overall, the two groups were evenly balanced with respect to case-mix and history of sore throats.

Primary outcome

The primary outcome was the number of episodes of sore throat experienced during 2 years of follow-up by each participating child. In the diary, the parent or child was asked to indicate the days on which the child had experienced a sore throat. Box 2 describes the algorithm for defining an episode of sore throat used in the following analysis.

Using the algorithm described in Box 2, Table 12 shows in each year of follow-up the mean number of episodes of sore throat per month for the four trial and cohort groups.

TABLE 11 *Baseline characteristics of children recruited to the trial by treatment to which randomised*

Variable		Statistic	Group	
			Medical	Surgical
Number randomised		*n*	137	131
Gender	Male	*n*[a] (%)	49 (35.8)	44 (33.4)
	Female	*n*[a] (%)	88 (64.2)	87 (66.4)
Age band (years)	4–7	*n*[a] (%)	50 (36.5)	50 (38.2)
	8–11	*n*[a] (%)	47 (34.3)	48 (36.6)
	12–15	*n*[a] (%)	40 (29.2)	33 (25.2)
Returned baseline survey		*n*[a] (%)	111 (81.0)	114 (87.0)
Responded to question about sore throats		*n*[b] (%)	109 (98.2)	111 (97.4)
Experienced one or more sore throats in previous 3 months		*n*[c] (%)	102	110
Number of sore throats in previous 3 months		Mean (SD)	3.34 (2.63)	3.09 (2.08)
Duration of last sore throat		Mean (SD)	7.31 (6.04)	7.12 (4.85)
Responded to question about whether child experienced a sore throat lasting longer than 15 days		*n*[b] (%)	107 (96.4)	110 (96.5)
Experienced a sore throat lasting longer than 15 days in the previous 3 months		*n*[c] (%)	34 (31.8)	32 (29.1)
Responded to question about ear infection		*n*[b] (%)	108 (97.3)	109 (95.6)
Experienced an ear infection in previous 3 months		*n*[c] (%)	37 (34.3)	40 (36.7)
Responded to question about time off school		*n*[b] (%)	109 (98.2)	106 (93.0)
Experienced time off school		*n*[c] (%)	90 (82.6)	97 (91.5)
Number of days of school in previous 3 months		Mean (SD)	7.66 (8.24)	8.98 (7.51)
Responded to question about progress at school		*n*[b] (%)	109 (98.2)	107 (93.9)
Felt that progress at school was affected by sore throats		*n*[c] (%)	36 (33.0)	48 (44.9)

SD, standard deviation.
a The number of children randomised to treatment arm.
b The number of children for whom a questionnaire was returned.
c The number of children for whom a valid response was given for the relevant question.

Estimated effect of tonsillectomy based on trial participants

The number of episodes of sore throat was analysed using a Poisson regression model. Our pre-specified primary analysis was to estimate the effect of tonsillectomy in each of the 2 years of follow-up based on responses corresponding to children enrolled in the trial. The model parameters corresponding to this analysis are given in the first column of Table 13.

During both years of follow-up, children randomised to surgical management were less likely to record episodes of sore throat than those randomised to medical management; the incidence rate ratio (IRR) was 0.70 (95% CI 0.61 to 0.80) and 0.54 (95% CI 0.42 to 0.70) in years 1 and 2 respectively. Adjusting for the strata used in randomisation (by fitting centre and age effects) resulted in only small changes in the magnitude of the estimates of tonsillectomy. Similarly adjusting for over-dispersion (by fitting a negative binomial regression model) made some difference to the point estimate in the second year and resulted in wider CIs in both years.

Comparing children in the trial with children in the cohort

The outcome for children in the trial and children in the corresponding cohort group was compared using a negative binomial regression model (Table 14).

Children randomised to tonsillectomy reported fewer episodes of sore throat than children who opted for tonsillectomy. The difference was greatest in the first year of follow-up (IRR = 0.63; 95%

BOX 2 *Defining an episode of sore throat*

The minimum number of consecutive days on which a sore throat is recorded that can constitute an episode is 3

The maximum number of consecutive days is not defined – i.e. 30 consecutive days of recorded sore throat would still count as one episode

Any consecutive recording of sore throat interrupted by 4 days of non-recording constitutes a new episode

Periods of sore throat separated in time by less than 4 days with no recording of sore throat were pooled before application of the above criteria

For example:

Suppose X is a day of sore throat and + is a day where no sore throat symptoms are reported. Then:

++++X X X++++ would be classed as an episode of sore throat of 3 days

++++X+X +X X X++++ would be classed as an episode of sore throat of 5 days

++++X+X++++ would not be classed as an episode of sore throat

++++X++ X++ X+X++++ would be classed as an episode of sore throat of 4 days

++++X X+++X X X X X+X++++ would be classed as a single episode of sore throat of 8 days

++++X X+X X+X X+X X++++ would be classed as a single episode of sore throat of 8 days

++++X X X++++ X X X++++ would be classed as two episodes of sore throat each of 3 days

TABLE 12 *Mean number of episodes of sore throat per month*

	Year 1			Year 2		
	Mean	Standard deviation	Number of respondents	Mean	Standard deviation	Number of respondents
Cohort medical management	0.59	0.44	55	0.38	0.34	27
Cohort surgical management	0.71	0.50	248	0.19	0.36	111
Trial medical management	0.64	0.49	112	0.33	0.43	74
Trial surgical management	0.50	0.43	119	0.13	0.21	83

TABLE 13 *Estimated effect of tonsillectomy by year of follow-up*

	Year 1				Year 2			
Model	IRR	95% CI		*p*	IRR	95% CI		*p*
Poisson regression model	0.70	0.61	0.80	< 0.001	0.54	0.42	0.70	< 0.001
Poisson regression model adjusting for strata (centre and age)	0.70	0.61	0.80	< 0.001	0.51	0.39	0.66	< 0.001
Negative binomial regression model (adjusting for over-dispersion)	0.70	0.58	0.85	< 0.001	0.49	0.33	0.73	< 0.001
Negative binomial regression model adjusting for strata (centre and age)	0.71	0.59	0.85	< 0.001	0.48	0.32	0.70	< 0.001

IRR, incidence rate ratio (usually referred to as the relative risk).

CI 0.53 to 0.74). The difference was smaller in the second year and not statistically significant (IRR = 0.85; 95% CI 0.57 to 1.25), although because of the reduced amount of data the CIs were wider. The difference in outcome between children randomised to medical management and those children who opted for medical management was not significant in either year of follow-up, although

TABLE 14 *Comparing outcome for trial participants with cohort participants*

	Year 1			Year 2		
Model	**IRR**	**95% CI**	***p***	**IRR**	**95% CI**	***p***
Children randomised to tonsillectomy compared with children who opted to have a tonsillectomy	0.63	0.53 to 0.74	< 0.001	0.85	0.57 to 1.25	0.406
Children randomised to medical management compared with children who opted for medical management	1.12	0.88 to 1.42	0.353	0.74	0.46 to 1.19	0.208

IRR, incidence rate ratio (usually referred to as the relative risk).

TABLE 15 *Mean number of sore throats lasting less than 2 weeks based on questionnaire responses*

	Year 1			Year 2		
	Mean	**Standard deviation**	**Number of respondents**	**Mean**	**Standard deviation**	**Number of respondents**
Cohort medical management	1.60	2.37	25	1.09	1.35	23
Cohort surgical management	1.12	1.63	113	0.45	0.86	96
Trial medical management	1.37	1.52	54	1.15	1.83	53
Trial surgical management	0.93	1.33	69	0.81	1.72	59

the width of the CIs means that we can not exclude the possibility that a clinically important difference may exist.

Estimating the effect of tonsillectomy based on self-completion questionnaires

Table 15 shows the mean number of sore throats that lasted less than 2 weeks reported by trial and cohort participants in the 12-month and 24-month follow-up questionnaires according to whether they were in the medical or surgical management group.

Effect of tonsillectomy based on responses from trial participants

Although during the first year children randomised to surgical management were less likely to record a sore throat than children randomised to medical management, negative binomial regression suggests that the difference was not statistically significant (IRR = 0.68; 95% CI 0.42 to 1.08). The corresponding result for year 2 was very similar (IRR = 0.71; 95% CI 0.37 to 1.35).

Comparison of children in the trial with children in the cohort

Although during the first year participants randomised to surgical management in the trial were less likely to record a sore throat than cohort participants who opted for surgical management, negative binomial regression suggests that the difference was not statistically significant (IRR = 0.83 with 95% CI 0.53 to 1.31). The rate of recording of sore throats in year 1 was similar for children randomised to medical management and children who opted for medical management (IRR = 0.86; 95% CI 0.47 to 1.55). The corresponding figures for year 2 were: surgical management IRR = 1.82 (95% CI 0.93 to 3.53) and medical management IRR = 1.06 (95% CI 0.51 to 2.18).

Estimate of number of episodes of sore throat over the 2 years of follow-up for inclusion in economic evaluation

For the economic analysis (see Chapter 6) an estimate of the number of episodes of sore throats over the 2 years of follow-up was required for each

trial participant. These estimates were based on the returned diaries. The estimates were obtained using the following procedures:

1. For each child we calculated the mean number of sore throats per diary returned and multiplied this by 26 to give an estimate of the total number of sore throats over the 2 years of the study. (This is referred to below as the unadjusted estimate.)
2. For each child, for each diary returned, we calculated a diary number – equal to the number of months from the start of the study for that particular child. For each child the first diary had a diary number of 1. For a child who returned all 24 diaries, the diary number of the final diary was 24.
3. For each child we then calculated the mean of these diary numbers. For a child who returned all 24 diaries the mean diary number was 12.5. While it was theoretically possible that this mean could take any value between 1 and 24, in practice more diaries were missing from the second year than the first and thus the mean diary number for most children was less than 12.5. Across all children in the two randomised groups the mean figure was 8.6.
4. We then looked at the relationship between the number of episodes of sore throat reported and mean diary number using a weighted linear regression procedure. The dependent variable was the estimated number of sore throats obtained in step 1 above. Two explanatory variables were included: the mean diary number calculated in steps 2 and 3; and a binary indicator of the group to which the child was randomised (tonsillectomy or medical management). The regression weights were the number of diaries returned by that child (we had more precise estimates of the number of days of sore throat for children who returned more diaries). The estimated regression coefficients were: intercept 23.5 (95% CI 20.3 to 26.7); mean diary number –1.16 (95% CI –1.44 to –0.88); and group –3.51 (95% CI –5.19 to –1.83). The associated R-squared value was 0.27.
5. For each child we then calculated an adjusted estimate of the number of sore throats for the 2 years of the study using:
   adjusted number = observed number – 1.16 × (mean diary number – 12.5)

The weighted mean of these adjusted and unadjusted estimates are given in Table 16.

Using a weighted least squares regression procedure, the estimated effect of tonsillectomy (intention to treat) over the 2 years of the study was a reduction of 3.5 episodes (95% CI 1.8 to 5.2).

Secondary outcomes

Days with sore throat

Table 17 shows the mean number of recorded days of sore throat and the mean number of sore throat days per returned diary for each year of follow-up.

Effect of surgical management

Using diary data (see Table 17) a number of negative binomial regression models were developed to consider the effects of tonsillectomy (intention to treat). The results are summarised in Box 3. For each comparison, models were developed separately for the effect in the first and second years of follow-up. The models estimated the likelihood of a participant in one group recording a day of sore throat compared with the likelihood of a participant in the comparator group recording a day of sore throat.

The models suggest that trial participants in the surgery group were less likely than trial participants in the medical group to record a day of sore throat during both years of the study. Trial participants

TABLE 16 *Weighted mean number of sore throats for trial participants*

	Group			
	Medical management		Surgical management	
Variable	Mean	Standard deviation	Mean	Standard deviation
Unadjusted estimate	11.4	8.7	7.4	6.1
Adjusted estimate assuming a linear trend	9.0	7.7	5.5	5.2

Weights used were the number of diaries returned by each child.

TABLE 17 *Mean number of days of sore throat and mean number of days of sore throat per returned diary*

	Year 1			Year 2		
	Mean days of sore throat (SD)	**Mean days of sore throat per returned diary (SD)**	**Number of respondents**	**Mean days of sore throat (SD)**	**Mean days of sore throat per returned diary (SD)**	**Number of respondents**
Cohort medical management	30.56 (28.67)	4.95 (4.95)	55	20.44 (21.90)	2.52 (2.32)	27
Cohort surgical management	42.77 (44.61)	7.47 (6.04)	247	10.45 (19.48)	1.46 (2.81)	111
Trial medical management	49.11 (54.62)	7.28 (6.74)	107	20.16 (40.79)	3.17 (5.78)	55
Trial surgical management	31.00 (29.25)	4.97 (4.38)	110	8.00 (12.61)	0.86 (1.18)	62

SD, standard deviation.

BOX 3 *Effect of surgical management*

Trial participants

Effect in year 1: IRR = 0.67 (95% CI 0.52 to 0.85)

Effect in year 2: IRR = 0.27 (95% CI 0.16 to 0.46

Comparison of trial and cohort surgical arms

Effect in year 1: IRR = 0.65 (95% CI 0.54 to 0.78)

Effect in year 2: IRR = 0.60 (95% CI 0.37 to 0.97)

Comparison of trial and cohort medical arms

Effect in year 1: IRR = 1.48 (95% CI 1.08 to 2.04)

Effect in year 2: IRR = 1.23 (95% CI 0.63 to 2.42)

in the surgery group were less likely to record a day of sore throat than cohort participants in the surgery group during both years of the study. Trial participants in the medical group were more likely to record a day of sore throat than cohort participants in the medical group during both years of the study, although the difference in incidence rates in year 2 was not statistically significant (p = 0.53). The very wide CI for the IRR in year 2 reflects the comparatively small number of children who returned diaries in this period.

GP consultations

Table 18 shows the mean number of recorded GP consultations and the mean number of recorded consultations for sore throat for each year of follow-up.

TABLE 18 *Mean number of recorded GP consultations and mean number of recorded consultations for sore throat*

	Year 1		Year 2		
	Mean number of consultations (SD)	**Mean number of sore throat consultations (SD)**	**Mean number of consultations (SD)**	**Mean number of sore throat consultations (SD)**	**Number of records**
Cohort medical management	3.16 (3.14)	1.63 (1.98)	3.12 (3.10)	1.45 (2.07)	49
Cohort surgical management	3.69 (3.33)	1.86 (2.23)	2.71 (3.51)	0.78 (1.31)	96
Trial medical management	4.38 (3.48)	2.35 (2.35)	3.40 (3.20)	1.33 (1.56)	93
Trial surgical management	3.99 (3.74)	1.90 (2.84)	2.84 (2.90)	0.89 (1.44)	92

SD, standard deviation.

All consultations

Using consultation data from the available GP records about all consultations for trial participants, the estimated effects of tonsillectomy in years 1 and 2 are given by IRRs of 0.91 (95% CI 0.71 to 1.17) and 0.83 (95% CI 0.63 to 1.10) respectively. The incidence rate of consultations for any reason was similar for trial participants randomised to surgical management and cohort participants who opted for surgical management with IRRs of 1.08 (95% CI 0.84 to 1.40) and 1.05 (95% CI 0.76 to 1.45) in years 1 and 2 respectively. The incidence rate of consultations for any reason may have been a little higher for trial participants randomised to medical management than for cohort participants who opted for medical management in year 1 (IRR = 1.38; 95% CI 1.01 to 1.88), but there was little difference in year 2 (IRR = 1.09; 95% CI 0.79 to 1.50).

Consultations for sore throat

Using consultation data from the available GP records about consultations for sore throat for trial participants, the estimated effects of tonsillectomy in years 1 and 2 are given by IRRs of 0.81 (95% CI 0.59 to 1.10) and 0.67 (95% CI 0.46 to 0.97) respectively. The incidence rate of consultations for sore throat was fairly similar for trial participants randomised to surgical management and cohort participants who opted for surgical management, with IRRs of 1.02 (95% CI 0.73 to 1.41) and 1.14 (95% CI 0.72 to 1.80) in years 1 and 2 respectively. The incidence rate of consultations for sore throat may have been a little higher for trial participants randomised to medical management than for cohort participants who opted for medical management in year 1 (IRR = 1.44; 95% CI 0.98 to 2.13), but there was little difference in year 2 (IRR = 0.92; 95% CI 0.61 to 1.39).

Quality of life

The PedsQL 4.0[38–40] was included in the self-completed questionnaires at baseline, 3 months, 12 months and 24 months. PedsQL has two generic core scales that assess physical health and psychosocial health. Higher scores indicate better self-rated health-related quality of life. Table 19 shows the mean scores for each scale at the four follow-up points.

TABLE 19 *Mean PedsQL subscale scores for physical health and psychosocial health at baseline, and at 3 months', 12 months' and 24 months' follow-up*

	Baseline (*n* = number of respondents) Mean (SD)	**3 months (*n* = number of respondents) Mean (SD)**	**12 months (*n* = number of respondents) Mean (SD)**	**24 months (*n* = number of respondents) Mean (SD)**
Physical health				
Cohort medical management	(*n* = 65)	(*n* = 44)	(*n* = 27)	(*n* = 25)
	77.17 (18.7)	85.66 (16.44)	84.66 (16.00)	91.88 (9.59)
Cohort surgical management	(*n* = 338)	(*n* = 177)	(*n* = 117)	(*n* = 96)
	71.10 (22.33)	74.37 (18.17)	87.15 (15.00)	91.35 (14.48)
Trial medical management	(*n* = 108)	(*n* = 85)	(*n* = 52)	(*n* = 53)
	76.26 (19.50)	74.66 (21.56)	85.34 (17.86)	88.05 (12.76)
Trial surgical management	(*n* = 111)	(*n* = 86)	(*n* = 71)	(*n* = 63)
	78.75 (18.01)	83.70 (16.75)	89.95 (16.37)	88.79 (17.66)
Psychosocial health				
Cohort medical management	(*n* = 66)	(*n* = 45)	(*n* = 27)	(*n* = 25)
	76.58 (13.22)	80.08 (15.55)	82.78 (16.12)	87.46 (10.38)
Cohort surgical management	(*n* = 334)	(*n* = 176)	(*n* = 118)	(*n* = 95)
	68.87 (15.44)	70.51 (17.83)	82.27 (15.83)	85.85 (13.78)
Trial medical management	(*n* = 110)	(*n* = 85)	(*n* = 52)	(*n* = 53)
	72.33 (14.86)	73.34 (17.96)	79.97 (17.49)	83.87 (12.95)
Trial surgical management	(*n* = 111)	(*n* = 85)	(*n* = 71)	(*n* = 63)
	70.95 (14.18)	77.37 (15.07)	83.81 (15.31)	84.30 (15.02)

SD, standard deviation.

Effect of surgical management

Based on the responses summarised in Table 19, the estimated effect of surgical management on trial participants was 4.62 (95% CI –1.53 to 10.76) and 0.74 (95% CI –5.02 to 6.50) in years 1 and 2 respectively on physical health, and 2.97 (95% CI –2.03 to 9.72) and 0.43 (95% CI –4.78 to 5.64) in years 1 and 2 respectively on psychosocial health. Adjusting for baseline assessment (analysis of covariance) the corresponding figures were 3.08 (95% CI –3.11 to 9.27) and 0.31 (95% CI –5.74 to 6.37) in years 1 and 2 respectively for physical health, and 2.43 (95% CI –3.08 to 7.03) and 0.39 (95% CI –4.52 to 5.29) in years 1 and 2 respectively for psychosocial health. In terms of effect size these would be classed as small effects, being around 0.25 or less.

Comparison of outcome for cohort with outcome for trial participants

Outcome was similar for trial participants randomised to surgical management and cohort participants who opted for surgical management. The mean differences in quality of life scores were 2.80 (95% CI –1.81 to 7.41) and –2.56 (95% CI –7.62 to 2.50) in years 1 and 2 respectively for physical health, and 1.55 (95% CI –3.09 to 6.18) and –1.55 (95% CI –6.13 to 3.03) in years 1 and 2 respectively for psychosocial health. Adjusting for baseline quality of life, the corresponding mean differences were 1.24 (95% CI –3.60 to 6.08) and –2.77 (95% CI –8.00 to 2.47) in years 1 and 2 respectively for physical health, and 0.62 (95% CI –5.09 to 3.84) and –1.82 (95% CI –6.20 to 2.57) in years 1 and 2 respectively for psychosocial health. Again, these estimates reflect relatively small effect sizes (less than 0.25).

Outcome was similar for trial participants randomised to medical management and cohort participants who opted for medical management. The mean differences in quality of life scores were 0.68 (95% CI –7.47 to 8.83) and –3.82 (95% CI –9.55 to 1.91) in years 1 and 2 respectively for physical health, and –2.81 (95% CI –10.86 to 5.24) and –3.59 (95% CI –9.48 to 2.30) in years 1 and 2 respectively for psychosocial health. Adjusting for baseline quality of life, the corresponding mean differences were 0.00 (95% CI –7.47 to 7.48) and –3.68 (95% CI –9.28 to 1.93) in years 1 and 2 respectively for physical health, and –1.04 (95% CI –8.29 to 6.21) and –1.81 (95% CI –7.08 to 3.46) in years 1 and 2 respectively for psychosocial health. Again, these estimates reflect relatively small effect sizes (less than 0.25).

Secondary analysis

All secondary analysis was 'intention to treat' and restricted to trial participants. The aim of secondary analysis was to determine whether we could identify groups of participants who benefited from surgical treatment. In the main analysis it was noted that the number of reported sore throats was fewer in year 2 than in year 1. It was also noted that there was a reduction in the proportion of diaries returned as time passed during the follow-up period (see Figure 2). It was decided that the secondary analysis should take these factors into account. This was done by setting the dependent variable to be the number of episodes of sore throat reported by the participant during the 2-year follow-up period, and including as a covariate the mean 'diary number' (diaries having been numbered sequentially from 1 to 24). This covariate proved to be highly significant and was retained, along with a general effect of surgical management, as the reference model with which the other models were compared. Fitting a negative binomial regression model, including the number of diaries returned as an exposure variable, yielded the following estimates:

- Effect of surgical management: IRR = 0.68 (95% CI 0.58 to 0.81).
- Effect of change of 1 in mean diary number: IRR = 0.90 (95% CI 0.88 to 0.92).

Severity of symptoms prior to entry into study

The only measure of symptom severity available from the GP records was the number of consultations for sore throat during the 2 years prior to entry. This was included as an explanatory variable; the number of episodes of sore throat reported during follow-up was not associated with the number of consultations for sore throat prior to entry to the study. The effect of one additional consultation is estimated as: IRR = 0.99 (95% CI 0.96 to 0.02).

Fitting an interaction between this severity index and surgical management did not significantly improve the fit of the model (change in –2 log likelihood = 0.24 for the loss of 1 degree of freedom; p = 0.625).

An alternative measure of symptom severity was available from the baseline questionnaire – the number of sore throats reported in the 3 months

prior to entry into the study. This explanatory variable significantly improved the fit of the model; the greater the number of sore throats reported in the 3 months prior to entry to the study, the greater the likelihood of a sore throat being recorded during follow-up. The effect of one additional sore throat reported at baseline is estimated as: IRR = 1.07 (95% CI 1.03 to 1.11).

However, the interaction between the effect of surgical management and the number of sore throats reported at baseline was not significant (change in –2 log likelihood = 2.60 for the loss of 1 degree of freedom; p = 0.107). The effect of one additional sore throat reported at baseline on the effect of surgical management is estimated as: IRR = 0.94 (95% CI 0.87 to 1.01).

Age group

The sampling strategy for the trial stratified the sample by age group in anticipation of age differences. Table 20 shows the mean number of episodes of sore throat per diary returned by age group and treatment group.

There were three age strata. The number of reported episodes of sore throat was analysed using negative binomial regression. There was no evidence that the number of sore throats reported during follow-up differed by age group (change in –2 log likelihood was 3.79 for the loss of two degrees of freedom; p = 0.150). However, fitting an interaction between the effect of age and the effect of surgical management does produce a significant improvement in the fit of the model (when compared with the main effects model, the change in –2 log likelihood was 9.57 for the loss of two degrees of freedom; p = 0.008; alternatively when compared with the more parsimonious model with just the main effect of surgical management, the change in –2 log likelihood was 9.77 for the loss of four degrees of freedom; p = 0.040). The parameter estimates corresponding to this model are given in Table 21.

Overall, children aged between 8 and 11 years were more likely to report an episode of sore throat than other children during the period of follow-up and it is in these children that we saw the largest effect of surgical management. Trial participants aged 8–11 years randomised to medical management tended to report more sore throats than participants in other age groups randomised to medical management. Participants aged 8–11 years randomised to surgical management tended to report similar levels of sore throat during follow-up to participants in other age groups randomised to surgical management. These results are consistent with the summary statistics presented in Table 20.

TABLE 20 *Mean number of episodes per diary returned by age band and treatment group*

			Outcome: episodes of sore throat					
			Episodes per diary returned			Adjusted[a] number of episodes per diary returned		
	Age (years)	*n*	Mean	SD	95% CI[b]	Mean	SD	95% CI[b]
Medical management	4–7	42	0.33	1.03	0.24 to 0.43	0.27	0.89	0.18 to 0.35
	8–11	40	0.55	1.20	0.45 to 0.65	0.45	1.16	0.36 to 0.54
	12–15	35	0.43	1.13	0.32 to 0.55	0.32	0.97	0.21 to 0.42
	Total	117	0.44	1.16	0.38 to 0.49	0.35	1.04	0.30 to 0.39
Surgical management	4–7	47	0.28	0.84	0.21 to 0.35	0.21	0.73	0.15 to 0.27
	8–11	43	0.28	0.78	0.20 to 0.35	0.21	0.78	0.15 to 0.27
	12–15	31	0.32	1.03	0.22 to 0.41	0.20	0.74	0.12 to 0.28
	Total	121	0.28	0.87	0.23 to 0.34	0.21	0.74	0.17 to 0.25

SD, standard deviation.
a Adjusted to allow for diary response pattern assuming a linear trend in the incidence rate of sore throat across the 2-year period of follow-up.
b 95% confidence for estimated marginal means based on one-way analysis of variance model fitted using weighted least squares (weight = number of diaries returned).

TABLE 21 *Negative binomial regression of number of episodes of sore throat with interaction between age and effect of surgical management: parameter estimates*

Effect	IRR	95% CI	*p*
Change of +1 in mean diary number	0.90	0.88 to 0.92	< 0.001
Effect of being in age group 8 to 11 years (compared with 4 to 7 years)	1.51	1.16 to 1.98	0.002
Effect of being in age group 12 to 15 years (compared with 4 to 7 years)	1.13	0.85 to 1.51	0.409
Effect of tonsillectomy for child aged 4 to 7 years	0.85	0.64 to 1.11	0.243
Effect of tonsillectomy for child aged 8 to 11 years	0.53	0.41 to 0.70	< 0.001
Effect of tonsillectomy for child aged 12 to 15 years	0.76	0.55 to 1.04	0.088

Exposure variable is the number of diaries returned.

TABLE 22 *Mean number of episodes per diary returned by gender and treatment group*

			Outcome: episodes of sore throat					
			Episodes per diary returned			Adjusted[a] number of episodes per diary returned		
	Gender	*n*	Mean	SD	95% CI[b]	Mean	SD	95% CI[b]
Medical management	Male	41	0.36	1.11	0.26 to 0.45	0.27	0.95	0.18 to 0.36
	Female	76	0.48	1.16	0.41 to 0.56	0.39	1.06	0.32 to 0.46
	Total	117	0.44	1.16	0.38 to 0.49	0.34	1.04	0.30 to 0.39
Surgical management	Male	37	0.25	0.78	0.18 to 0.32	0.18	0.66	0.12 to 0.24
	Female	84	0.30	0.90	0.25 to 0.36	0.23	0.77	0.18 to 0.27
	Total	121	0.28	0.87	0.23 to 0.34	0.21	0.74	0.17 to 0.25

SD, standard deviation.
a Adjusted to allow for diary response pattern assuming a linear trend in the incidence rate of sore throat across the 2-year period of follow-up.
b 95% confidence for estimated marginal means based on one-way analysis of variance model fitted using weighted least squares (weight = number of diaries returned).

TABLE 23 *Percentage of days on which a symptom was recorded for days when no sore throat was recorded and for days when a sore throat was reported, based on all diaries returned*

	Sore throat also recorded? (*N* = 521)					
	No			Yes		
	Mean	*n*[a]	SD	Mean	*n*[b]	SD
Sore ear	2.7	516	8.5	15.9	508	21.1
Difficulty swallowing	2.1	516	6.9	34.5	508	26.1
Nausea or vomiting	2.6	516	7.5	12.4	508	16.8
Diarrhoea	1.1	516	3.5	3.6	508	9.8
Aches and pains	1.8	516	4.9	11.5	508	17.4
Fever or temperature	1.5	516	4.7	16.1	508	18.9
No appetite	2.6	516	7.0	19.8	508	22.2
Felt tired	5.8	516	11.6	27.6	508	25.9

SD, standard deviation.
a For five children there were no reported days free of sore throat in any of the diaries returned.
b For 13 children there were no days of sore throat reported in any of the diaries that they returned.

TABLE 24 *The percentage of days on which a symptom was experienced based on all the diaries that were returned over the 2 years of the study*

	Participant type				Comparisons between groups						
	Trial		Cohort		Trial participants: surgical vs medical			Surgical: trial vs cohort		Medical: trial vs cohort	
Symptom	Medical (*n* = 109)	Surgical (*n* = 110)	Medical (*n* = 55)	Surgical (*n* = 247)	RR	95% CI	*p*	RR	95% CI	RR	95% CI
Sore ear	5.7	4.2	3.8	7.2	0.70	0.44 to 1.11	0.13	0.56	0.38 to 0.80	1.48	0.80 to 2.75
Difficulty swallowing	10.5	6.1	5.8	11.9	0.55	0.40 to 0.77	<0.001	0.47	0.39 to 0.65	1.84	1.18 to 2.86
Nausea or vomiting	4.1	4.2	3.0	5.4	0.98	0.67 to 1.43	0.91	0.75	0.54 to 1.04	1.44	0.90 to 2.33
Diarrhoea	1.5	1.4	1.3	2.1	0.86	0.44 to 1.69	0.66	0.64	0.34 to 1.08	1.25	0.59 to 2.62
Aches and pains	4.3	2.6	2.2	4.6	0.56	0.35 to 0.91	0.02	0.51	0.35 to 0.76	1.86	1.08 to 3.23
Fever or temperature	3.7	2.6	3.6	5.0	0.67	0.47 to 0.95	0.03	0.50	0.37 to 0.69	1.03	0.66 to 1.61
No appetite	8.5	3.8	3.5	7.2	0.44	0.30 to 0.64	<0.001	0.51	0.38 to 0.69	2.43	1.57 to 2.47
Tired/no energy	10.7	7.2	5.3	11.9	0.64	0.46 to 0.91	0.01	0.58	0.44 to 0.77	2.04	1.34 to 3.11

Medical, participants for whom medical management was intended; RR, relative risk (based on negative binomial regression of the number of days on which symptom was reported); surgical, participants for whom surgical management was intended.

The mean number of episodes per diary returned for participants aged between 8 and 11 years randomised to medical management was 0.55, which was higher than for all other groups. It may be that the higher level of reporting of sore throats by children aged between 8 and 11 years randomised to medical management is a chance anomaly.

Gender

Table 22 shows the mean number of episodes of sore throat per diary returned by gender and treatment group.

Fitting gender as a main effect suggested that female participants tended to report more sore throats over the follow-up period than male participants (IRR = 1.24; 95% CI 1.04 to 1.49). However, the interaction between gender and surgical management was not significant (change in –2 log likelihood = 0.25 for the loss of 1 degree of freedom; p = 0.614). The additional effect of surgical management for a female participant is estimated as IRR = 0.91 (95% CI 0.64 to 1.30).

Potential adverse events of tonsillectomy and of treatment of sore throats using antibiotics

Respondents were asked to indicate whether particular symptoms were observed on each day in each diary. For each child the proportion of days on which each symptom was observed was calculated. In addition this was done separately for days on which a sore throat was reported and other days. In general other symptoms were more likely to be reported on days when the child was also suffering from sore throat (Table 23).

The overall proportion of days with each symptom is broken down by study group can be found in Table 24.

In general, children randomised to surgery reported fewer symptoms than children randomised to medical management. However, these children also reported considerably fewer symptoms than children who (or whose parents) expressed a preference for tonsillectomy.

Chapter 4
The qualitative study

This chapter describes a qualitative study of parents and teenagers undertaken to inform the development of the study and to identify the experience of recurrent sore throat and their preferences for different treatment options. The qualitative study has been used to support the choice of person-centred outcomes in the trial and cohort study and the development of the utility study (see Chapter 5).

Methods

The study design was qualitative. Data were generated through in-depth interviews with dyads of children aged 4–16 years and their parents. The interviews took place in the family home, all of which were based in the north-east of England. Data collection took place between July and August 2002. Interviews lasted between 30 minutes and 1.5 hours and their content was recorded using a digital audio recorder.

Recruitment

A convenience sample was recruited from children and their parent or guardian attending one of two regular ENT outpatient clinics held at one of the trial centres. Children had been referred to these clinics by their GP for recurrent sore throats. One of the study trial managers explained the study to all 16 children and parents/guardians attending the clinics, and asked if they would be willing to be approached to participate in the study and to provide their contact details. A letter, signed by the interviewer, was sent to children and their parent/guardian, inviting them formally to participate in the study. A study information sheet was included with the letter, providing details of the study team, why the children's help was required, how the interviews would proceed and how the information would be handled and ultimately reported. Parents were subsequently telephoned to gain their consent to participate in the interviews. Out of the 16 families originally approached, 12 agreed to take part. Written consent was given by both the child and the parent/guardian involved in each interview.

Interviews

All interviews were carried out by a social scientist with expertise in qualitative interviewing. Semi-structured interviews were based on a flexible topic guide, which highlighted a number of issues considered to be relevant to the study (see Appendix 7). After 12 interviews no new issues were emerging so data saturation was judged to have occurred and no further participants were approached.

Data management and analysis

Digital audio data were transcribed verbatim, by professional transcribers, as soon as possible after each interview. Typed transcripts were then reviewed by the interviewer for transcription errors and to respond to any queries regarding unclear or inaudible words. Data collection and analysis proceeded in an iterative fashion in several closely linked stages as follows: familiarisation with the data by reading transcripts; identification of recurrent or important topics; development of a topic index; use of index to code data on transcripts; extension and elaboration of the topic index; coalescing of related topics into themes; abstraction of data from transcripts into themes; further collapsing and refinement of categories; and finally the interpretation of analysis into a narrative. NVIVO qualitative data management software was used in indexing and coding of data and themes. For ethical reasons, children and their parents were interviewed together therefore the data were analysed together; however, where possible data were reported separately according to children's and parents' responses.

Ethical issues

Children and their parents/guardians were advised that participation was entirely voluntary and had no influence on their treatment, and they could withdraw at any time. All interview transcripts were anonymised and treated in the strictest confidence. All direct identifying information was removed from the transcripts by giving each child a unique code number which was used to attribute comments during analysis. The study received ethical approval from the Multicentre Research Ethics Committee as part of the trial and cohort study.

Findings

The findings from these interviews comprise a brief description of the participants along with a rough evaluation of the parent's and child's contribution to each interview. Data from the interviews are reported under the general themes of: physical and emotional effects of recurrent sore throat; impact of recurrent sore throat on education, social life and family; and management of this chronic condition. Anonymised quotations, from the interviews, are included in the text to illustrate points made.

Participants

The sample consisted of 12 parents and children (eight male and four female) aged between 4 and 16 years with recurrent sore throats who had recently been referred to ENT (Table 25).

At the time of interview, six of the participants were on the hospital waiting list to have their tonsils removed, four were waiting to see if the frequency of their sore throats improved with time while two had already had their tonsils removed (one as an NHS patient and one privately). In all interviews the child's mother was present and on two occasions the father was also present. On one occasion the father was present in order to translate for both the mother and the child.

Parent/child contributions to the data

Word count was used as a proxy for contribution to the interview by participants. Overall, parents dominated the interviews, taking on average 84% of the interview (range 44–99%). Children's contributions ranged from 1% to 56% of the interview. Children dominated only one interview (56%); this was the oldest child (16 years) in the sample. While there were two other teenagers in the sample, only one made a substantial contribution to the interview (31% versus 4%). For the younger children, age did not appear to be related to contribution during the interview.

Effects of recurrent sore throat

Physical

There was a rich description of the physical symptoms that participants associated with their own or their child's sore throat. While children naturally tended to use less mature language to describe their symptoms, their descriptions were no less colourful than those given by their parents. Although some of the children found their symptoms difficult to articulate:

> Well it does hurt a little bit … [it's] sore.
>
> (01, male, age 6)

TABLE 25 *Characteristics of participants in the qualitative study*

Interview number	Gender	Child's age (years)	Parent(s) present	Tonsillectomy
09	Male	4	Mother and father[a]	Yes (privately)
04	Male	5	Mother	Wait and see
10	Male	5	Mother	On waiting list
01	Male	6	Mother	On waiting list
07	Male	7	Mother and father	On waiting list
03	Male	10	Mother	Yes (NHS)
12	Male	10	Mother	Wait and see
05	Male	14	Mother	On waiting list
11	Female	10	Mother	On waiting list
02	Female	12	Mother	On waiting list
08	Female	15	Mother	Wait and see
06	Female	16	Mother	Wait and see

a Father present to translate for mother and child.

This was not necessarily associated with the age of the child:

> It's like swollen and when I cough it's like dead loud and horrible and like it croaks a little bit … it hurts when I kind of cough in my throat … it hurts a little bit when I swallow … I wanted to say, sometimes at night when I'm breathing it sometimes stops my breathing … and I feel sick through the night too
>
> (04, male, age 5)

Most children mentioned the classic sore throat symptoms which are associated with pain and difficulties eating. Children spoke of not being able to eat, not feeling hungry and finding it hard or impossible to swallow food. Most children said that it hurt or was painful having sore throats, and one child talked of associated ear pain. About half of the children mentioned abnormalities of the tonsils such as being big and/or red, and half of the children described abnormalities of the throat such as sore throat, dry throat and tickly throat. The use of the voice (such as it being difficult to talk, having a croaky voice or cough and loss of speech) was also frequently mentioned. Other less frequently quoted symptoms included aches, temperatures, sickness, tiredness, general feelings of being unwell, and problems with breathing, snoring and bad breath (Box 4).

Similarly, all parents mentioned sore throat symptoms surrounding food (loss of appetite, poor eating and problems swallowing), but in contrast to the children's' responses all parents also discussed abnormalities of the tonsils, describing visible symptoms such as spots or pus on the tonsils. Pain was mentioned much less frequently by the parents than by their children perhaps because this was a less visible symptom, but many talked about their child feeling 'sore' in the throat. Again, in contrast to their children, the majority of parents listed changes in temperature as a symptom of sore throat. About half of the parents felt that energy levels and sleep patterns were affected and half said their children either felt sick or actually vomited. Just under half of the parents talked about a change in the voice. Parents mentioned all of the other less frequently disclosed symptoms that had been listed by the children; however, parents occasionally listed other less common symptoms such as prominent glands in the neck, cold sores, scarlet fever, pallor and anaemia (Box 5).

Emotional

Although there was much less data relating to the emotional consequences of chronic sore throats, at least one of each parent–child dyad mentioned some emotional effect or change in personality which they associated with having chronic sore throats. The over-riding theme was one of moodiness, general lethargy, withdrawal and clinginess.

> Well he's normally a happy go lucky bairn but as I say, when he's got the tonsillitis he's really withdrawn in himself and he's, very, very, quiet, you know he's in pain
>
> (Mother of 05, male, age 14)

> It was kind of depressing at one point … I had worked so hard … for the Drama and then it was kind of all getting messed about with my tonsils.
>
> (06, female, age 16)

More worrying emotional responses were bed wetting (which was only mentioned by parents and not children) and embarrassment and alienation because of smelly breath. It must be noted, however, that the children's responses may have been inhibited by the presence of their parents or other family members.

Impact of recurrent sore throat

Education

All of the children in this sample had had time off school because they were sent home by their teachers or kept out of school by their parent(s) because they either were too ill or had related medical appointments to attend. All of the parents in this sample were concerned regarding the amount of schooling that had been missed by their child, with this concern increasing during important (exam) school years. There were mixed views among the children as to whether missing school was a positive or negative experience, although many children complained about having to catch up on missed work. On a number of occasions the school itself had cited concern regarding the child's attendance, and on one occasion the education authority had become involved.

> Well apart from, me form tutor she was doing that and she was like, well you've missed quite a bit of school through your tonsils, she was like are you not, are you not going to see the doctor

BOX 4 *Children's descriptions of the symptoms associated with chronic sore throat*

Big tonsils (02, female, age 12); (04, male, age 5); (06, female, age 16); (08, female, age 15)

Sore throat (01, male, age 6); (03, male, age 10); (08, female, age 15); (10, male, age 5)

Can't swallow (04, male, age 5); (08, female, age 15); (09, male, age 4); (11, female, age 10)

Painful (06, female, age 16); (08, female, age 15); (09, male, age 4); (10, male, age 5)

Can't eat (01, male, age 6); (03, male, age 10); (11, female, age 10)

Not hungry (01, male, age 6); (08, female, age 15); (10, male, age 5)

Being/feeling sick (02, female, age 12); (04, male, age 5); (10, male, age 5)

Difficult to talk (01, male, age 6); (03, male, age 10); (06, female, age 16)

It hurts (01, male, age 6); (03, male, age 10); (04, male, age 5)

Red tonsils (06, female, age 16); (08, female, age 15)

Headaches (08, female, age 15); (11, female, age 10)

Tired (01, male, age 6); (06, female, age 16)

Get hot (04, male, age 5); (11, female, age 10)

Temperature (08, female, age 15); (09, male, age 4)

Dry throat (02, female, age 12)

Tickling in throat (06, female, age 16)

Neck aches (01, male, age 6)

Sore neck (10, male, age 5)

Croaky voice (04, male, age 5)

Loss of voice (06, female, age 16)

Loud cough (04, male, age 5)

Snoring (01, male, age 6)

Stops me breathing (04, male, age 5)

Hard to breathe (06, female, age 16)

Ear pain (11, female, age 10)

Don't feel well (04, male, age 5)

Feel run down (08, female, age 15)

Bad breath (11, female, age 10)

> and I was like, well not really we're going, we'll go to the hospital, ask them about getting them took out, but some of the teachers were having problems 'cause I was missing some of the lessons
>
> (06, female, age 16)

Social life

The social life of all of the children in this sample had been negatively affected by recurrent sore throats.

> You feel you are missing out sometimes like when people go out like to somewhere … and you can't because you're bad [ill].
>
> (02, female, age 12)

None of the children would go out and play or be with friends during an episode of sore throat, either because they were not allowed to or because they did not feel able to. Many children had hobbies that they were unable to perform such as singing, karate, swimming, drama, dancing and sport. Most of the children would rest or sleep

BOX 5 *Parents' descriptions of the symptoms associated with chronic sore throat*

Loss of appetite/poor eating (01, male, age 6); (02, female, age 12); (03, male, age 10); (04, male, age 5); (05, male, age 14); (07, male, age 7); (09, male, age 4); (10, male, age 5); (11, female, age 10)

Sore throat (01, male, age 6); (02, female, age 12); (04, male, age 5); (05, male, age 14); (06, female, age 16); (07, male, age 7); (10, male, age 5); (11, female, age 10)

High temperature/sweating/fever/shivering (01, male, age 6); (02, female, age 12); (03, male, age 10); (04, male, age 5); (07, male, age 7); (08, female, age 15); (09, male, age 4); (10, male, age 5)

Feeling sick/vomiting (02, female, age 12); (04, male, age 5); (07, male, age 7); (08, female, age 15); (09, male, age 4); (10, male, age 5)

Very large (swollen) tonsils (01, male, age 6); (02, female, age 12); (04, male, age 5); (06, female, age 16); (08, female, age 15); (10, male, age 5)

Lack of energy/need to sleep/drained (01, male, age 6); (02, female, age 12); (04, male, age 5); (07, male, age 7); (11, female, age 10)

Problems swallowing (01, male, age 6); (02, female, age 12); (03, male, age 10); (07, male, age 7); (09, male, age 4)

Red tonsils (01, male, age 6); (02, female, age 12); (06, female, age 16); (11, female, age 10)

Bad breath (01, male, age 6); (09, male, age 4); (11, female, age 10); (07, male, age 7)

Problems with ears (02, female, age 12); (10, male, age 5)

Ear infections (06, female, age 16)

Prominent glands in the neck (01, male, age 6); (06, female, age 16)

Swollen (puffed up) face (02, female, age 12); (05, male, age 14)

Headache/aches (01, male, age 6); (04, male, age 5)

Cough (09, male, age 4); (11, female, age 10)

Snoring (01, male, age 6); (07, male, age 7)

Stomach pains (03, male, age 10); (10, male, age 5)

Red blotches (rash) on face/arms (02, female, age 12); (04, male, age 5)

Pallor (07, male, age 7); (10, male, age 5)

'Thick' voice (01, male, age 6)

Croaky voice (10, male, age 5)

Problems breathing (02, female, age 12); **(specifically at night)** (04, male, age 5)

Little white deposits (on tonsils) (01, male, age 6)

Yellow poisoney colour (in back of throat) (03, male, age 10)

Yellow spots (in back of throat) (04, male, age 5)

White spots (in the mouth) (09, male, age 4)

Feeling 'something' in throat (04, male, age 5)

Hoarse/barking cough (04, male, age 5)

Problems sleeping (07, male, age 7)

In pain (05, male, age 14)

General feeling of being unwell (10, male, age 5)

Sneezing/sniffling (01, male, age 6)

Scarlet fever (04, male, age 5)

Cold sores (07, male, age 7)

Anaemia (10, male, age 5);

and perform sedentary activities (such as watching television, reading or drawing) during an episode of sore throat. Many of the participants had missed or caused the cancellation of family days out or special events because of their sore throat. Two participants had experienced disruption to their holiday as a result of their recurrent sore throat.

Family

Naturally, any recurrent health complaint is likely to take its toll on the sufferer's family. All of the parents were frustrated at the consequences of the recurrent nature of their child's ill health. All of the working parents had, at some point, needed to take time off work to look after their child or to make visits to health professionals. On two occasions this was cited as the reason for leaving or losing jobs.

> I've lost jobs because of him having been off school… I don't think that sometimes people believe you, you know?
>
> (Mother of 10, male, age 5)

Non-working parents were equally frustrated about being tied to the house or concerned about how they would cope if they went back to work.

> Ah it's terrible, you have to stay in the house all week and she does, does your head in… she does – she just does your head in… because you can't go anywhere… she cannot go shopping and I've got to get my brother or her nana to come and you know sit with her but it does your head in doesn't it.
>
> (Mother of 02, female, age 12)

Many of the parents used their extended family (aunts, uncles, grandparents, siblings) as an alternative source of care when taking time off work became difficult or they became ill. A lot of the parents said they experienced periods of tiredness because they had been kept awake during the night or had tried to sleep with their ill child. The social lives of families, including family holidays, days out and evenings out, were also affected by their child's recurrent sore throats, and some felt that their other children suffered from lack of attention as a consequence. Parents and siblings also had to deal with the associated emotional problems described above.

Management of recurrent sore throats

Throughout the interviews, a number of themes arose regarding how the families managed the chronic problem of recurrent sore throats.

Requesting tonsillectomy

The over-riding theme was the need to request or even demand the surgical removal of the child's tonsils. There was a general feeling that parents might have to fight to get this treatment and that there was an increasing reluctance to remove tonsils in recent years which was understood to be largely because of costs. However, parents were unconvinced that their children would simply 'grow out of ' recurrent sore throats or 'grow into' their tonsils, and surgery was often thought to be the only long-term solution.

> Yeah his brother had his took out and he's been brilliant since he got his done… it was the best thing I could have done for him… that's why we are trying to push to get his done because it's just recurring all the time, every couple of months or so and it's not fair on the bairn and it's not fair on his education either because he's having to have the time off school because he's just, well he wouldn't be any good at school.
>
> (Mother of 05, male, age 14)

However, it must be made clear here that there were substantial differences between children and their parent(s) regarding their views on surgery. On only three occasions were parent(s) and child in agreement regarding their desire, or lack of desire, to have surgery. On two other occasions the child exhibited a strong desire for surgery while their parent(s) was less sure; these were the two oldest children in the sample.

> I was a bit disappointed actually because I just wanted to get rid of it [sore throat] straight away.
>
> (08, female, age 15)

In all other cases it was the parent(s) who desired surgery while the child was either 'worried', 'scared', 'panicked' or adamant that they did not want surgery.

'Playing' the surgical waiting list

For parents who were more cautious about surgery, perhaps because their child's symptoms had improved, there was a strategy of 'playing' the surgical waiting list. This involved joining the list for tonsillectomies, but using the time to wait and see whether the symptoms improved. Once the child reached the top of the waiting list the parents would then choose whether or not to go ahead with the surgery. However, if the decision was made not to have surgery at that time, the parents suggested that they would be able to ask for their child to be put back on the bottom of the waiting list just

in case their symptoms got worse again. This was viewed as the best use of the waiting time.

> Well, it's like the consultant said, if for one reason you don't want the operation, go on the waiting list again for the 10 months, and it starts reoccurring, obviously just get in touch with him and hopefully get it done eventually, you know, it's just the waiting list again and another 10 months.
>
> (Father of 07, male, age 7)

Self-referring to secondary health care

Once families had been referred to secondary care but had agreed to wait and see if their child's symptoms would improve with time, there was a general agreement that they could then self-refer direct to secondary care if the child's symptoms worsened. This gave parents the reassurance that they could seek direct help without having to 'fight' their way through the referral system.

> I was really surprised … she said that … actually if he ever got that again ring us up direct and we will take him straight in and have them done, which I thought was good.
>
> (Mother of 04, male, age 5)

Having a tonsillectomy 'just in case'

Even though symptoms were improving for some of the children, some of the parents thought that their child's tonsils should be removed as a precaution against the sore throat symptoms reoccurring.

> If it come to the 10 month up and he didn't need it done, my wife says, 'Oh I might get it done anyway, just in case'.
>
> (Father of 07, male, age 7)

Using the experience of others

As a result of the lack of evidence relating to the best treatment for recurrent sore throats, parents relied heavily on their own or others' experience.

> His brother had his [tonsils] took out and he's been brilliant since he got his done – it was the best thing I could have done for him.
>
> (Mother of 05, male, age 14)

The majority of parents interviewed either had had their own tonsils removed or knew of someone else who had had their tonsils removed with great success, and used this knowledge to decide on the best course of treatment for their child. However, two parents had also heard about tonsillectomy operations 'going wrong', which left them scared and worried. However, after raising these concerns with the consultant, the parents felt that the risks were small enough for them to still request the operation. None of the parents or children related experiences of others successfully 'growing out' of sore throats.

Requesting prescriptions for antibiotics

Another popular strategy in coping with recurrent sore throat was requesting repeat prescriptions for antibiotics from the GP. Often this was dependent on seeing the 'right' GP in the practice or visiting an out-of-hours service. However, many parents preferred not to see the GP but to request prescriptions over the telephone. This allowed parents to receive the desired outcome from a trip to the GP without having to actually attend an appointment. It appeared to be a solution for some GPs as well as parents.

> It started a few year ago … he was just constantly sore throats obviously all the time … so we were obviously down the Doctors but the last few month I was just actually phoning the doctor up and asking for a prescription over the phone because they knew what is was and they were well Doctor always just used to say, right we know what's the matter with him … and just give him a prescription over the phone for the last few month.
>
> (Mother of 03, male, age 10)

Attending school with sore throat

In the meantime, while children were experiencing recurrent sore throats, most of the parents at one time or another had sent their child to school while they were ill. This was often in response to increasing levels of absence from school (for the child) and work (for the parents). This strategy sometimes resulted in the child being sent home from school by their teacher; however, this allowed the parent to transfer the responsibility for the child's absence to the teacher or school.

> I mean if I had my way she would be at school with a sore throat, but I mean you cannot … I have been guilty sending her to school because I know that she comes home and I wait here for the phone call and about half eleven or something you'll get a phone call saying … will you be in, she's on her way home, you know … is it alright for her to come home and I'll say well I cannot very leave her there … so she'll end up coming home and she'll be off the rest of the week … and then she'll go back

> to school for a fortnight and then she'll get a sore throat again but I mean as I say she only started there but she missed a lot of school … I mean her attendance was only 55% not on really … I mean she would be there all the time if it wasn't for this you know.
>
> (Mother of 02, female, age 12)

Summary

This small qualitative study provides an understanding of the drivers behind parents seeking a surgical solution to their children's condition. There are a number of caveats that should be made about these data. The study used a convenience sample; the selection of families was based on ease of availability and accessibility rather than using a purposive sample guided by theory. However, the sample broadly reflected the normal range of children seen in ENT outpatient clinics. However, it did not cover the whole range of ages for both boys and girls, with fewer younger girls than might have been expected from normal referral patterns. The interviews provided a rich description of the condition from the perspective of children and their parents and provided an insight into their treatment preferences. These insights were used in the development of the outcome questionnaires and in the construction of the scenarios in the utility study that is described in Chapter 5.

Interviewing dyads presents its own problems as they are jointly created accounts presenting neither the parent's nor the child's version of events. Certainly the percentage contribution of the children to the interviews was much lower than that of the parents. Both contributions may have been inhibited by the presence of others. The presence of parents is likely to affect the accounts given by children as they are tempered by the presence of adults. Similarly, parents are perhaps unlikely to express their deepest fears of the risks of surgery in front of young children. Although young people may have the cognitive skills to form opinions, the adult status of the researcher may cause problems in eliciting, collecting and interpreting their thoughts. In addition, it was parents who took the lead in volunteering and consenting to the study and it is difficult to establish how far this was in collaboration with the child.

Chapter 5

Utility willingness-to-pay study

By estimating the quality of life for different health states associated with tonsillitis and tonsillectomy, it is possible to calculate the number of quality-adjusted life-years (QALYs) that can be gained from treatment using changes in health-related quality of life over time. Participants' ratings of their quality of life were given a score which is anchored at values of zero for death and one for full health. These scores, known as health-state utilities, were used to 'quality adjust' remaining life-years. QALYs are the product of the number of life-years and the quality of those life-years. Therefore, 2 years in a health state valued at 0.5 would be equivalent to 1 QALY, the same as 1 year spent in a health state valued at 1.0. This is useful because, if time in different health states can be empirically assessed and it is feasible to value those different health states on the 0–1 scale, then, using QALYs, the impact of different treatments can be compared on a common unit of assessment that encompasses both quality and length of life.[45]

Objectives

The aim of the utility study was to measure quality of life for health states associated with tonsillitis. The specific objectives were:

- To estimate the health-state utility associated with recurrent sore throat.
- To estimate the health-state utility associated with surgical management.
- To calculate the utility loss or gain associated with surgical management.

Eliciting utility values – the standard gamble method

The standard gamble method was used to elicit utility values for health states associated with recurrent sore throat and medical or surgical management. Standard gamble is a technique used to elicit individuals' preferences.

To measure individuals' preferences for a chronic health state, individuals are offered a choice between two options. Option 1 is some form of treatment that has two possible outcomes: a return to full health for the rest of their life or immediate death. The probability that the treatment will work and they will return to full health is p and the probability it won't and they will die is (1−p). Option 2 is a certain outcome of remaining in the chronic health state (state i) for the rest of their life. The individual is then asked to make a choice between options 1 and 2 as the probability p is varied. The probability p* at which the individual is indifferent between the two options is the utility value of health state i (if measured on a scale where perfect health is p = 1 and death is p = 0).

The scores that are obtained using the standard gamble method for each health state represent the directly derived utility values of those states. The utility value indicates the risk of death a person is willing to take in exchange for perfect health, i.e. a utility value of 0.6 indicates that an individual is willing to take up to a 60% risk of death in exchange for perfect health.

To facilitate the standard gamble exercise a visual aid known as a chance board was used.[46] This presents the probabilities associated with each of the uncertain and certain outcomes as a percentage risk of an event, which is generally more understandable to people.

The chance board

The board is divided into two sections. The top half of the board illustrated the uncertain Option 1 with probability, p, of the most preferred health state and 1−p of the least preferred health state. The probabilities can be changed by turning a wheel underneath the board. On the bottom part of the board is the certain outcome Option 2. The health state placed in this section relates to symptoms that characterise tonsillectomy.

The probabilities were then altered using a ping-pong strategy back and forth between a low and high value until the participant was indifferent to Option 1 or 2. Using the ping-pong strategy reduced the possibility of anchoring bias. It also reduced the risk of a framing effect caused by participants believing that the increases or

decreases in probability were gains and losses subject to a reference point.

Scenario development

Health-state scenarios were developed to be used in the standard gamble exercise. To meet the study objectives two scenarios were developed; one that represented the tonsillitis state and another that represented the outcomes following tonsillectomy. As the alternative treatment for tonsillitis is essentially reactionary, based on prescribing antibiotics when the patient is experiencing an episode of tonsillitis, it was decided not to create a third scenario based on medical management, but instead incorporate this into the tonsillitis health-state scenario. Two sets of scenarios were developed, one that was for parents and the other for teenagers. The scenarios presented an identical list of symptoms but were worded as either 'your child' will experience these symptoms in the scenarios to be presented to parents, or 'you' will experience these symptoms in the scenarios presented to teenagers.

An initial search of the literature indicated that there were no previous studies that had presented health states associated with tonsillitis for use in quality of life surveys. Therefore it was necessary to develop the health states based on the best available evidence at the time on the type of symptoms that a patient with tonsillitis would experience before and after surgery. The information for the scenarios was gathered from the literature on tonsillitis[47–58] and in consultation with the clinicians on the project. As the utility study was being conducted alongside the main trial it was not possible to use the actual number of reductions in sore throats that was reported in the trial, as these data were not available at the time; therefore, we had to use the best available estimates from the literature at the time. Initially the symptoms were presented under five subheadings: physical health; emotional health; behaviour; family activities; and impact on parents' time/emotions. For each scenario, an explanation of how parents' own or their child's health would be affected was presented under each heading. No specific time frame was added to each scenario; however, participants would be informed that the symptoms would last until the child reached 18 years. Although it is known that tonsillitis is essentially a self-limiting disease and is unlikely to last longer than a few years, the standard gamble exercise requires that each scenario lasts for a given time period or it is not a chronic illness. As all of the children who would take part in this study would be of different ages, a pragmatic decision to make the time frame up to the age of 18 years was taken. Two additional scenarios were added to the tonsillitis and tonsillectomy scenarios, these were full health and death. These scenarios were necessary to be able to value the other health states on the 0–1 quality of life scale.

Before piloting of the standard gamble exercise, the scenarios were written as a bulleted list of symptoms without the subheadings included in order to provide concise scenarios that were easy to read. The final scenarios were labelled Health State X, which corresponds to the tonsillitis state, and Health State Z, which is the tonsillectomy state. These labels were used so as not to influence the respondents with the names of the disease and the treatment. A final set of scenarios for parents is shown in Box 6.

Interview materials

The standard gamble exercise was carried out using face-to-face interviews. An interviewer manual was designed to guide the interviewers through the standard gamble exercise (see Appendix 8).

This included an introduction to the study for the interviewer to read out to the participant and then a step-by-step guide to using the chance board to complete the standard gamble exercise. A response booklet was designed to go alongside the interviewer manual so that the interviewer could record the participant's answers to the standard gamble. The response booklet also included a set of demographic questions to be completed after the standard gamble exercise. This was included to be able to present information on the sample and potentially understand the answers given, especially if the parent's employment or income had been affected by his or her child's tonsillitis.

A participant information sheet was designed to give to participants before the exercise to explain the purpose of the study and any potential benefits and disadvantages in taking part. A consent form was also produced. All of these materials were approved by the Newcastle and North Tyneside Research Ethics Committee.

Pilot study

A small pilot study was conducted with members of staff at the Institute of Health and Society, Newcastle University. This pilot study was primarily to test out the materials and provide training to

BOX 6 *NESSTAC scenarios for utility study (for 12–15 year olds)*

Health State X

You get 6–7 sore throats each year; these last 7–10 days each

During this time…

- it hurts to swallow
- you have a temperature
- headache
- feel sick and eat less
- take antibiotics which can give you diarrhoea and a rash
- you feel tired and irritable
- cannot go to school
- cannot do your usual activities
- your parents are worried about you and may not be able to go to work

Health State Z

For up to 2 weeks after the treatment you…

- have a sore throat
- feel sick
- have a temperature
- feel tired and bad-tempered
- small risk (1 in 20) that the tonsils will bleed and you have to have a blood transfusion
- cannot go to school
- cannot take part in family, group or sporting activities
- may wake up in the night
- your parents are more worried and have to stay off work to look after you

After the first 2 weeks you…

- have 1–2 sore throats each year; these last 2–3 days each
- have 2–3 days off school each year when you have a sore throat
- feel ill and tired and bad-tempered when you have a sore throat
- your parents may have to take time off work when you have a sore throat
- when you do not have a sore throat you have no pain or discomfort, behave normally and can take part in your normal activities

Good health

No pain or discomfort and you are full of energy

Behave normally at home and school

Able to go to school and join in classes

Join in family, group or sporting activities

Your parents go to work and carry out their normal activities

the interviewers. Before the pilot study, initial training on using the chance board was provided by a member of the research team with previous experience of using the chance board in a clinical setting (HM). During the piloting process the interviewer manual was updated to make it more naturalistic for the interviewer to read out.

It became clear during the pilot study that when performing the second gamble, which involves trading against death, the participants were reluctant to gamble even at very small risks of death. The nature of the standard gamble exercise means that to be able to place a health-state scenario on the 0–1 scale it must be gambled against death or be chained through a health state that has been gambled against death. Although this could potentially prove problematic in the main study, it was decided to continue with the exercise on the basis that parents and children who had experience of the symptoms of tonsillitis may be more willing to gamble to be free of those symptoms, which the qualitative study had identified as debilitating to children and their parents (see Chapter 4).

Willingness to pay

Willingness to pay (WTP) is another method of preference elicitation which is used to measure a person's 'strength of preference' for, or the value of, a good or service.[59] Maximum WTP represents the maximum amount of other goods an individual is willing to give up (or sacrifice) expressed in monetary terms to gain the benefits of the programme.[60] The contingent valuation method is generally used to elicit individuals' WTP in health care. This involves designing a survey that sets up a hypothetical scenario involving a change in a commodity and eliciting an individual's WTP for it.[61]

One of the main advantages of using WTP is that it can capture more than just the health gain that an individual gains from a service, which is not captured by QALYs. In the case of tonsillitis it is likely that more than the health change that arises from treatment is important to the families, with the type of treatment, the impact on parents' employment and the child's education also likely to be of importance.

As the purpose of the WTP question was to determine how much parents value the provision of a tonsillectomy, it was decided that the WTP question should be answered only by parents who rate Health State Z (tonsillectomy) above Health State X (tonsillitis). The teenagers were not asked the WTP question as it was assumed that they did not have an income from which they could trade. The WTP question was based on the two health states, X and Z, which the participants had previously read as part of the standard gamble exercise and was therefore familiar to them. The WTP question asked the participant to imagine that he or she was in Health State X, but could pay for a treatment which would result in moving to Health State Z. The risks of the treatment were outlined before asking the participant if he or she would be willing to pay for the treatment. The full question is given in Box 7.

To help determine each participant's maximum WTP, a card sorting type exercise was used. This exercise involved 15 small payment cards, each of which was printed with an amount of money ranging from £1 to £20,000. The full set of values was £1, £2.50, £5, £10, £25, £50, £100, £250, £500, £1000, £2000, £3000, £5000, £10,000 and £20,000. Each participant was given a set of payment cards and a template on which to place them. They were asked to shuffle the cards and then take one card at random (to avoid 'starting point bias' whereby participants 'anchor' their subsequent WTP value on a card offered to them by the interviewer) and decide if they would be willing to pay that amount for the intervention described in the question. If yes, they were told to place it on the template in the box marked 'definitely would pay'; if no, they were told to place it in the box marked 'definitely would not pay'; or if they were not sure, to place it in the 'unsure' box.

The participant repeated this exercise for all of the different payment cards, and was then asked to record the highest value placed in the 'definitely would pay' box onto the questionnaire booklet along with the lowest value placed in the 'definitely would not pay' box. Finally, the participant was asked to decide what was the maximum amount he or she would be willing to pay and record this on the questionnaire booklet too. It was stressed to the participant that this may be one of the figures on the payment cards or it may be another value not listed. Each participant was asked to remember when making his or her decision how much they could afford to pay. As an individual's response to a WTP question is constrained by his or her ability to pay, in the demographics section of the questionnaire a question on the participant's current income was also included so that this could be taken into account in the analysis of the WTP questions.

BOX 7 *Willingness to pay question*

For participants who ranked Health State Z above Health State X.

We would like to understand more about how much you value treatment for your child's tonsillectomy. One way of measuring the value to you of the treatment is to ask what you would be willing to pay to receive this treatment. This is simply a way of measuring how strongly you feel about having the treatment for tonsillectomy.

Imagine that your child experienced the symptoms that were presented on the card labelled Health State X. There is a surgical treatment available which would improve your child's symptoms to those presented on the card labelled Health State Z, but it is not yet available on the NHS. So, imagine that, if you would like your child to have this treatment, you would have to pay for it privately. As with all surgical procedures there is a very small risk of death associated with this treatment. For this treatment the risk of death is 1 in 35,000. This means for every 35,000 people who have the operation one person will die as a result of this.

Would you consider paying for this treatment or continue with the scenario described on card X? Bear in mind that any payment you make for this treatment will reduce the amount of money that you have available to you to spend on everything else.

Would pay

Continue with X

If yes, what is the maximum amount you would be willing to pay for this treatment?

(Write in amount here)……

Data collection

Participants were recruited from two of the NESSTAC trial sites: Newcastle and Glasgow. These participants were not in the NESSTAC trial and therefore were not assigned to either medical or surgical management. Interviews took place from March to July 2008.

In Newcastle, participants were recruited to the study through a tonsillectomy preoperative assessment clinic. Patients and their parents visit the paediatric ward for assessment prior to surgery. These clinics operate once a week. Each patient who attended the clinic between May and July 2008 was invited to take part in the study by the nurse conducting the preoperative assessment. If the parents agreed to take part in the study, the nurse introduced the parent to the researcher. If patients were over 12 years old, they were also asked if they would be willing to take part. The researcher outlined the patient information sheet to participants and, if they were still willing to take part, took their consent. The interview was then conducted.

As all patients attending the preoperative assessment clinic in Newcastle were by definition already committed to a tonsillectomy as their means of treatment, it was decided that to gain a wider range of patients whose sore throats were managed in other ways, another clinic should be used. In Glasgow, a children's ENT outpatient clinic was used. Three special sore throat clinics were set up in March and April 2008. Each eligible patient attending these clinics was asked by his or her consultant to take part in the study. The eligibility criteria for the study were that the patient must have suffered with recurrent sore throat in the past year and must be able to complete an interview in English. If the patient agreed the consultant took consent from the parent or teenager and introduced them to the researcher for the interview to take place.

Three interviewers (CL, HM, Marie Poole) conducted the interviews over the 5-month period. Each interviewer was trained using the interviewer manual so as to remove any potential interview bias. Each parent or teenager who agreed to take part in the study was interviewed following his or her clinic appointment. The interviewer followed a set manual (see Appendix 8) so that the same wording was used for each participant. Participants were given further information on the study before moving onto the exercise where they first ranked the health states and then completed the standard gamble questions. If they had ranked Health State Z above X (the tonsillectomy state above the tonsillitis state) they were also asked to answer the WTP question as was outlined above. All participants were then asked to complete the demographic questions and the interview was concluded. Interview data were entered into an EXCEL spreadsheet to aid analysis.

Results

Characteristics of participants

Over the 5-month recruitment period there was a total of 48 eligible parents attending a clinic in either Glasgow (13) or Newcastle (35). From this potential sample, 41 parents agreed to take part. The response rates were 100% for Glasgow and 80% for Newcastle. The most common reason given by parents refusing to take part was that the child had to return to school after the clinic.

There were 12 eligible teenagers, one from Glasgow and 11 from Newcastle. Few teenagers in Glasgow were expected because participants were recruited from a children's hospital which predominately treats children aged 12 years and under. A total of 11 teenagers agreed to take part with one person from Newcastle deciding not to. For all 10 teenagers from Newcastle the exercise was completed by both the teenager and his or her parent.

The characteristics of the children whose parents completed the exercise are given in Table 26. Additional information on how the child's sore throats have affected the parent is also presented in this table.

Table 27 shows the characteristics of teenagers who participated in the study.

TABLE 26 *Characteristics of participating children (patient) and their parents*

Number of participants by gender	
Male	21
Female	20
Mean age (SD)	8 (3.98) years
Age range (SD)	3–17 years
Mean number of sore throats per year (SD)	8.1 (5.48)
Number of parents completing exercise	
Mother	33
Father	7
Mean age of parent (SD)	34 (8.75) years
Mean number of days taken off work (SD)	6.1 (7.50)

SD, standard deviation.

TABLE 27 *Characteristics of participating teenagers*

Number of participants by gender	
Male	4
Female	7
Mean age (SD)	14 (1.97) years
Age range (SD)	12–17 years
Mean number of sore throats per year	9 (5.04)

SD, standard deviation.

Standard gamble results

The first stage of the standard gamble exercise was a ranking where the participant had to rank Health States X and Z. As there were two possible outcomes that participants could choose as their preferred health state, the results are presented in two ways.

It was expected a priori that Health State Z (representing tonsillectomy) would be ranked above Health State X (representing tonsillitis). From the 41 parents completing the ranking, 28 ranked Z above X (68%). For the teenagers, eight ranked health state Z higher (73%). Table 28 presents the results for the two health states when Z was ranked higher than X.

The utility values were elicited using a chaining method where the health state ranked first was scored against full health and the worst ranked health state, this worse health state was then scored against full health and death. The highest ranked state was then rescored using the value that was elicited for the lower ranked state. A chaining exercise was used, as early piloting of the exercise highlighted that participants were not willing to take a risk of death for health states that they perceived were not serious. From the 28 parents who ranked Health State Z highest, 14 were unwilling to take any risk of death even for the health state they ranked worse (Health State X). Only one teenager was unwilling to take any risk of death, perhaps indicating a different attitude to risk to their parents.

TABLE 28 *Utility scores when Z > X*

	Utility Score Z (range)	**Utility Score X (range)**
Parent	0.965 (0.703–1.000)	0.931 (0.65–1.00)
Teenager	0.840 (0.19–1.00)	0.776 (0.1–1.0)

The alternative for participants was to rank Health State X above Health State Z, with 13 parents and three teenagers doing this. Table 29 shows the utility when Health State X was ranked higher than Z.

In this ranking, eight parents were not willing to take any risk of death, but all three teenagers were. Although only three teenagers ranked Health State X above Z, the utility scores elicited from them were substantially lower than those given by the parents.

Willingness to pay results

The WTP question was introduced to complement the standard gamble exercise as it does not ask participants to make any trade-offs between a health state and death, but instead gets them to consider their budget constraints when expressing their value for a health state.

The WTP was only given to parents as most of the teenagers were too young to be in employment and were unlikely to have control over the household budget.

In addition, the WTP was only given to parents who had ranked Health State Z above X, because the aim of the exercise was to find out how much these parents valued tonsillectomy as a treatment for their children.

All 28 parents were willing to complete the WTP question. The mean WTP was £8059 with a range of £100–30,000; therefore, the median of £5000 may be a more representative value. No one gave a zero response, highlighting the importance that parents place on providing a treatment that would move their child from Health State X to Z.

Estimation of quality-adjusted life-years

With these results, it is possible to estimate the QALY gain for the two ranking combinations. Using the mean age of 8 years of the children in this sample and the fact that parents were told to imagine that the symptoms of tonsillitis would last until the child reached 18 years, the time horizon of any potential gain would be 10 years. For those who ranked Health State Z higher than Health State X, the gain in moving X to Z was 0.034. Owing to the design of the standard gamble exercise, the QALY gains estimated were for a longer duration than the cost data and were also longer than would be expected given the nature of the disease. Therefore, these QALY gains should be discounted at 3.5%, which is the current recommended value for discounting by the UK Treasury.[62] This would give QALY gains of 0.3 when Health State Z was ranked above Health State X, and 0.2 when X was ranked above Z. To combine these two values into an overall gain, it is necessary to weight the gains by the proportion of the sample that ranked the health states in each of the two combinations. Approximately 68% of the sample ranked Health State Z above X; therefore, the QALY gain of 0.3 is weighted by this. For those who ranked Health State X above Z, the gain of 0.2 QALYs is weighted by 32%. The overall QALY gain is 0.136 QALYs. Thus, the best QALY gain from treatment for tonsillitis is, based on this study, 0.3 QALYs and at worst is 0.136 QALYs. These gains are relatively small.

For teenagers the gains are larger. For those ranking Health State Z above Health State X, the gain was 0.55 QALYs and was 1.38 QALYs when X was ranked above Z. However, when these values were weighted, the overall gain was 0.28 QALYs. This information was used to calculate an incremental cost per QALY gained (see Chapter 6).

TABLE 29 *Utility scores when X > Z*

	Utility Score X (range)	Utility Score Z (range)
Parent	0.961 (0.73–1.00)	0.938 (0.55–1.00)
Teenager	0.61 (0.45–0.80)	0.450 (0.35–0.55)

Discussion

The sample size of 41 participants may be considered small. However, although a larger sample may have reduced the variance within the results, all of the 41 interviews followed a similar pattern, with parents unwilling to take even quite small risks for either health state, no matter which health state they had ranked first.

The utility values that were elicited are illustrative of the fact that the parents were unwilling to take risks against death, with all of the values being higher than 0.931, which can also be thought of as 93.1% of full health.

For the 28 parents who ranked Health State Z above Health State X, the utility values elicited

from them were 0.965 and 0.931 respectively. These values can also be expressed as: Health State Z was valued as 96.5% of full health and Health State X valued at 93.1% of full health. Both of these values are high, indicating that this sample of parents did not believe that these health states have a large impact on quality of life. The gain in quality of life from Health State Z over Health State X is 0.034.

The remaining 13 parents ranked Health State X higher than Health State Z. This result was less expected as it had been assumed that parents would prefer for their child to have tonsillectomy. This was especially the case for those attending the Newcastle clinics, as these were preoperative assessment appointments on the paediatric ENT ward. There were eight parents from Newcastle who ranked the health states in this way. The main reasons given for preferring Health State X was that they did not like the side effects of Health State Z, especially the risk of bleeding and needing a blood transfusion. The health states were designed in conjunction with clinicians to accurately represent the potential side effects of a tonsillectomy and the potential outcomes that a child might experience following a tonsillectomy. It could also be the case that, as the health states were labelled only X and Z, the parents were unaware that Health State Z represented the tonsillectomy and Health State X presented the common symptoms of recurrent tonsillitis. The health states were purposely not labelled so as to avoid any bias from the participants actively seeking a particular type of treatment.

The utility values elicited from these 13 parents were 0.961 for Health State X and 0.938 for Health State Z, giving a difference of 0.023 between the two health states. Again these values show that these health states were rated highly and did not have a large impact on quality of life.

Just over half of the parents (53%) did not take any risk of death when asked to trade the worst health state against full health and death. This was expected following early piloting. Many of the parents commented that they would not take a risk of death to avoid the worse health state as it was not worth it if the child would grow out of the illness by the age of 18. In the interviews, it was emphasised that the scenarios were hypothetical and that death was not an expected outcome of their child's treatment, but, as with all surgical treatments, there is a small risk of death (estimated at between 1 in 16,000 and 1 in 35,000 for tonsillectomy); however, none of the parents interviewed discussed this risk. This could indicate that they were unaware of the risk or that they considered it to be so small that it did not come into their decision-making when deciding on whether to go ahead with a procedure. This may highlight that the risks need to be more clearly explained to parents, especially when taking into account the non-fatal risks of treatment, which a number of parents seemed to be unaware of.

One of the features of the exercise was that the parent was told that the health states would last until the child reached 18 years. This may have influenced the way in which parents answered the questions, depending on the current age of their child. To see if this made a difference to the values, the data were split by the age categories 4–7, 8–11 and 12–15 years and reanalysed. The results are not presented here as on examination of the values there was no difference in the utility values between each of the age groups. However, there was some difference in the WTP values. Parents of the children aged between 4 and 7 years were willing to pay £10,000 (median) while parents of children in the 8- to 11-year age group were willing to pay £2000 and those in the 12- to 15-year group £3000.

The standard gamble method typically results in higher utility values than would be expected if they had been estimated using another method such as the visual analogue scale or the time trade-off. This is because, with the standard gamble method, to be able to place a health state on the 0–1 scale, at least one of the health states must be gambled against death. With a temporary, non-fatal health state, such as tonsillitis, many people would not take a risk of death to avoid the health state being valued.

If they were asked to rate the same health state using the visual analogue scale, they would likely give a lower valuation to a health state; however, this involves no sacrifice from the participant. In this situation the time trade-off is not appropriate as it involves sacrificing time in the future, which is not realistic in this situation given the young age of the patients and that they are expected to grow out of the illness by the time they reach adulthood. The use of a generic quality of life instrument such as the European Quality of Life-5 Dimensions was also rejected for this study as the five domains are not very applicable to tonsillitis and also the questionnaire would be completed by parents and it is difficult for them to accurately understand how tonsillitis affects their child's quality of life.

There were a smaller number of teenagers who completed the study; however, the results indicate that there could be significant differences in the way in which patients view their quality of life with tonsillitis and the treatment options. The small sample size means that there is less confidence in the results but they do demonstrate that the patients view the quality of life with both tonsillitis and tonsillectomy to be worse than their parents do. The majority of the teenagers ranked Health State Z above X giving a utility score of 0.840 to Health State Z and a score of 0.776 to Health State X. Only one person was unwilling to take any risk of death, this could mean that as the person who suffers with recurrent tonsillitis they believe that this has a serious impact on their quality of life. It could also mean that the risk perceptions and hypothetical risk perceptions of younger people are different to older adults and they may be more risk seeking. Three teenagers ranked Health State X above Health State Z and attached very low utility scores to both health states (0.61 to X and 0.450 to Z). With only three participants it is not possible to draw firm conclusions on whether these results would remain this low if more participants had been recruited to the study.

The health-state utility values indicate that the two health states are not that different, and neither had a great impact on quality of life. However, the WTP results provide a different view suggesting that a treatment for tonsillitis is very important to the parents participating in this study. All parents who were asked the WTP question were willing to pay something. Some of the parents said that they would pay anything and more said that they would pay everything they could. The main reason given was that they could not put a price on their child's health. These results are more in keeping with the qualitative study (see Chapter 4), where the main theme of the interviews was the parents' requests or demands for tonsillectomy. This demand for tonsillectomy appears to be on the basis that the parents interviewed in the qualitative study used their own personal experience or the experience of others they knew that had undergone successful tonsillectomies. This is likely to explain the higher WTP values if the parents believed that the treatment would be successful.

One of the main weaknesses of this study was that it was conducted alongside the trial and therefore it was not possible to use the clinical effectiveness results from the trial in the health-state scenarios. The estimates of the numbers of sore throats that are presented in the health-state scenarios are based on the literature. Following the completion of the trial, the estimates included in the health-state scenarios do not correspond that closely with those found in the trial. Therefore, the QALY calculations reported here are for the health states presented and not the actual health gains experienced by those in the trial.

Chapter 6
Economic evaluation

Economic evaluation

This chapter describes the economic evaluation based on trial participants only, which was conducted as an intention-to-treat cost-effectiveness analysis as described in the original protocol. The perspective for the collection of costs was the UK NHS. The number of episodes of sore throat avoided using the number of reported sore throats by trial participants during the 2-year follow-up period was the primary outcome used in the estimation of cost-effectiveness. A cost-effectiveness analysis was performed following methods outlined by Drummond et al.[63] Costs and outcomes for each of the trial participants were calculated and the mean incremental cost-effectiveness ratio (ICER) was estimated as:

$$E(ICER) = \frac{Ei(cost_{surgical}) - Ej(cost_{medical})}{Ei(n_{surgical}) - Ej(n_{medical})}$$

As the follow-up period of the study was only 2 years, the costs and outcomes were not discounted. Data from the utility study (see Chapter 5) were used to calculate the incremental QALY gain.

Confidence intervals for the cost and outcome data were estimated using a non-parametric bootstrapping method,[64] which accounted for any skewness in the data.[65]

Cost data

The medical resource data required for the cost analysis can be split into two categories: contact with medical professionals and drug prescribing.

Health service unit costs were valued using the most recent Department of Health resource cost data, at 2005–6 UK prices.[66] The items of NHS resources that were included and their unit costs are shown in Table 30, along with the source of cost information. The cost of drugs consumed by participants includes only drugs prescribed by participants' GPs. The 56th edition of the British National Formulary[67] was consulted for the unit cost of individual drugs prescribed to trial participants. Unit cost data were then combined with resource use data to estimate the total NHS resources used by trial participants during the 2-year follow-up.

Resource use

Resources used by trial participants in relation to their recurrent sore throats were recorded in the outcome questionnaires (see Appendix 5) and GP records. Only resource use for the treatment of recurrent sore throat was included in the calculation of cost-effectiveness. The response rates for the return of self-completed questionnaires and abstraction of GP records have been reported in Chapter 3. The resource data have not been adjusted to account for the response rate. The nature of the resource use data, in multiple categories and with varying returns from participants in each section of the trial, does not allow for an accurate transformation of the data similar to that performed for the effectiveness data. In not performing a similar transformation of the resource use data there is likely to be a bias in the overall estimates of the resulting costs for resource use. As it is likely that there will be under-reporting of all resources used it is likely that this will result in a lower overall cost to the NHS than may in fact have occurred. The economic evaluation was performed using only patients who had at least one piece of cost and outcome data. Table 31 shows the total recorded resources used by trial participants randomised to medical management and surgical management.

From Table 31 it can be seen that there are some differences in resource use between the patients in the surgical and medical management groups. Those in the medical management group had more contact with primary care health professionals with more visits to the GP and nurse. Patients in the surgical arm of the trial reported more inpatient visits. However, some caution must be taken in drawing conclusions as to whether surgery increases inpatient visits. The questionnaire asked parents to record any inpatient stays during the previous reporting period but it was not specifically noted that this should not include their inpatient stay for their tonsillectomy procedure. Therefore it is possible that for both arms of the trial patients reported an inpatient stay that was actually their

TABLE 30 *NHS unit costs and source of cost information*

Item	Cost (£)	Source
Primary care		
GP appointment (consultation time of 11.7 minutes)	30.00	PSSRU[68]
GP home visit (visit lasting 23 minutes)	49.00	PSSRU[68]
GP telephone consultation (lasting 7.1 minutes)	18.00	PSSRU[68]
Nurse appointment (per consultation)	9.00	PSSRU[68]
Nurse home visit (per home visit)	17.00	PSSRU[68]
Nurse telephone consultation (lasting 6 minutes)	2.60	PSSRU[68]
Visit to emergency out-of-hours clinic (based on walk-in centre attendance)	27.00	PSSRU[68]
Call to NHS direct (call taken by nurse)	2.69	Richards *et al.*[69]
Secondary care		
Accident and Emergency visit	84.00	Department of Health reference costs, 2006[66]
Outpatient visit[a]	78.00	Department of Health reference costs, 2006[66]
Inpatient stay[b]	1206.00	Department of Health reference costs, 2006[66]
Emergency ambulance	337.00	Department of Health reference costs, 2006[66]
Tonsillectomy	996.00	Specific NHS Trust

PSSRU, Personal Social Services Research Unit.
a Based on follow-up visits for ENT face-to-face consultation.
b Based on non-elective inpatient stay for relevant Healthcare Resource Group C58.

TABLE 31 *Resource use over 2 years of follow-up by group*

Service	Medical management (*n* = 115)	Surgical management (*n* = 120)
Prescription drugs[a]		
Treatment for infection	426, 5 (4.51)	389, 4 (3.77)
Total number of drugs prescribed, mean number of drugs prescribed per patient (SD)		
Analgesics	189, 2 (2.62)	211, 2 (3.13)
Total number of drugs prescribed, mean number of drugs prescribed per patient (SD)		
NHS contacts[b]		
GP contact (number)	571	492
Nurse contact (number)	106	84
Outpatient visits (number)	79	64
Inpatient visits (number)	15	30

SD, standard deviation.
a Prescription drugs as recorded in GP records.
b NHS contacts as reported in outcome questionnaires.

tonsillectomy procedure. If this was the case then, for those in the surgical arm, there will be some double counting of secondary care services. This may mean that the incremental cost between the two groups is lower than reported here.

Costs

NHS costs

The estimated mean costs for trial participants randomised to medical management or surgical management are shown in Table 32. The difference in the mean cost between the surgical group and the medical management group was statistically significant (t-statistic = –9.25: p = $1.41E^{-17}$).

The main factor which influenced the difference in mean total cost was the cost of the tonsillectomy: if this was removed the difference in mean cost between the two groups would be reduced. The mean cost in the surgical group was now lower at £205.92 than the mean cost of £229.99 in the medical management group; however, this was not a statistically significant difference (t-statistic = 0.87; p = 0.379). This indicates that the cost driver was the tonsillectomy.

Patient costs

Indirect patient costs for childhood conditions included loss of earnings and productivity due to the time that parents or carers had to take off work to look after their child and out-of-pocket expenses associated with the child's sore throats such as over-the-counter prescriptions and travel costs.

The time costs of parents were considered for inclusion in the cost-effectiveness analysis. However, when examining the data returned, the numbers of parents who recorded that they had taken time off work because of their child's condition was relatively low. Table 33 presents the mean number of days taken off work as reported by the parents and Table 34 presents the mean number of hours taken off work. As the numbers are small, estimates of the costs to participant have not been estimated or included in the economic analysis.

Information on parents' or carers' out-of-pocket expenses was collected through the questionnaires. These data were collected in three sections: money spent on over-the-counter medications, money spent on any additional expenses caused by the child's condition, and the cost of child care. The mean cost for each of the groups was small at £14 for the medical management group and £18 for the surgical group, the difference between the two was not statistically significant (t-statistic = –0.7, p = 0.473). More data were returned by parents or carers on any out-of-pocket expenses they had incurred, with 190 (71%) reporting that they had some expenses related to their child's condition.

Table 32 *Mean costs (£) (and standard deviation) after 2 years of follow-up by group*

	Medical management (*n* = 115)	**Surgical management (*n* = 120)**
NHS contacts cost	450.38 (6.72)	1390.75 (6.44)
Prescribing costs	12.84 (0.14)	11.40 (0.11)
Total cost	463.22 (6.71)	1402.15 (6.42)

TABLE 33 *Parent-reported mean number of days taken off work over 2 years of follow-up by group*

	Medical management (*n* = 115)		**Surgical management (*n* = 120)**	
Questionnaire	**Mean number (SD)**	**Number of responses (%)**	**Mean number (SD)**	**Number of responses (%)**
Baseline	2.74 (1.87)	35 (30.43)	2.83 (1.71)	36 (30.00)
3 month	2.53 (2.23)	15 (13.04)	3.36 (2.49)	14 (11.67)
12 month	3.22 (4.18)	9 (7.83)	2 (0.00)	5 (4.17)
24 month	3.50 (2.38)	4 (3.48)	1.67 (1.15)	3 (2.50)

SD, standard deviation.

TABLE 34 *Parent-reported mean number of hours taken off work over 2 years of follow-up by group*

	Medical management (*n* = 115)		Surgical management (*n* = 120)	
Questionnaire	Mean number (SD)	Number of responses (%)	Mean number (SD)	Number of responses (%)
Baseline	6.10 (4.38)	10 (7.83)	9.47 (7.70)	15 (12.50)
3 month	8.23 (6.37)	13 (11.30)	11.80 (6.24)	10 (8.33)
12 month	12.67 (11.72)	3 (2.61)	0.00 (0.00)	0 (0.00)
24 month	18.00 (19.70)	3 (2.61)	3.00 (0.00)	1 (0.83)

SD, standard deviation.

Outcomes

Sore throat episodes

As reported in Chapter 3, the mean number of episodes of sore throat per child was less for the surgical management group than for the medical management group over the 2-year follow-up period. As described in Chapter 3, we adjusted the estimate of the number of episodes of sore throat for the reduction in diary response over time. The adjusted mean number of sore throats in the medical management group was 9.0 (standard deviation 7.7) and in the surgical management group 5.5 (standard deviation 5.2). Therefore, the estimated reduction in the mean number of sore throat episodes due to the surgical management group was 3.5 episodes (95% CI 1.8 to 5.2).

To calculate a QALY from the utility value estimated in the utility study, it was necessary to incorporate a time horizon. To calculate this, the average age of the children whose parents took part in the utility study was used; this was 8 years. The health-state scenarios used in the utility study stated that the condition would last until the child reached 18 years of age. Therefore, a 10-year time horizon was used in the calculation of the QALY gain. This is likely to be an over-estimation of the number of years for which the child would either experience the symptoms of tonsillitis or receive benefit from treatment, as we know that tonsillitis is a self-limiting disease. Further explanation of why the time horizon for the standard gamble exercise was chosen can be found in Chapter 5. As the QALY gain is estimated for 10 years, discounting at 3.5%[62] has been applied.

As there were two possible ways (see Chapter 5) in which the health states could be ranked, the best estimate of QALY gain from treatment for tonsillitis based on this study is 0.3 QALYs and the worst estimate is 0.136 QALYs.

Cost-effectiveness

Incremental cost-effectiveness ratio

As reported above, the cost of treatment provided to the surgical management group was higher than that provided to the medical management group. However, the number of episodes of sore throat in the 2 years of follow-up was less. It was therefore necessary to calculate an ICER, as no strategy was dominant.[63] The estimated mean incremental cost for the surgical management group over the medical management group was £939. The estimated mean incremental effectiveness was 3.5 episodes of sore throat avoided. The ICER was therefore £261 per sore throat avoided (95% CI £161 to £586) – numbers may not calculate exactly due to rounding. The CI for the ICER was calculated using the non-parametric bootstrapping method. This method samples with replacement, cost and effectiveness values calculated for the trial participants and calculates the cost-effectiveness ratio. 1000 cost-effectiveness ratios were generated, which were then ordered and the 26th and the 975th percentiles were taken to generate the 95% CI.[64]

Incremental cost per quality-adjusted life year

It was also possible to calculate the incremental cost per QALY. The estimated mean incremental cost of surgical management over medical management was £939. The QALY gain ranged between 0.136 and 0.3 QALYs. Using this information, the incremental cost per QALY ranged from £3129 to £6904 per QALY gained.

Chapter 7
Discussion

Tonsillectomy and adeno-tonsillectomy have been widely used surgical procedures for the treatment of children with chronic tonsillitis or recurrent sore throat in the UK since the 1930s.[2] Although the incidence of tonsillectomy has declined in recent years to some 50,000 tonsillectomy procedures on children per year,[1] there remains little clear evidence of effectiveness and no evidence based on RCTs that might guide clinicians in their decisions about treatment for individual patients or guide NHS commissioners of services in their decisions about the cost-effectiveness of surgical or medical management.[26] This study was commissioned by the HTA programme in order to provide some evidence of clinical effectiveness and cost-effectiveness of tonsillectomy and adeno-tonsillectomy for the treatment of children with recurrent sore throat. The study does not apply to the effectiveness of these surgical procedures for children with obstructive sleep apnoea.

Target population

The true incidence of recurrent sore throat in children is difficult to estimate as it relies on the attitudes and behaviour of parents and children and GPs,[1,11] which are likely to lead to significant variations for parents seeking treatment for their children from their GP in the referral of children with recurrent sore throat by GPs to ENT specialists and for rates of tonsillectomy.[14,70]

Clinical guidelines for the treatment of recurrent sore throat suggest that tonsillectomy is indicated where there is typically a 2-year history of three to four episodes of moderate severity (5-day duration) per annum.[5–7] The impact of these guidelines on clinician behaviour, however, is unclear[71] but they may not be uniformly implemented, and surgeons are more likely to perform tonsillectomies than not on children, whereas guidelines suggest watchful waiting or medical management.[5] Nevertheless, the inclusion and exclusion criteria for the present study were guided by the criteria for tonsillectomy in children indicated in these guidelines. The study therefore does not reflect the outcomes for all children currently undergoing tonsillectomy in the UK for recurrent sore throat.

Patient preference

Parental preference may play an important role in the incidence of tonsillectomy[9] (see Chapter 5). As tonsillectomy has been a routine procedure for over 50 years, we anticipated that some clinicians and parents would not be in equipoise and would favour surgical management of recurrent sore throats in children. In developing the study, we anticipated that patient preference would increase the non-participation rate in a standard RCT design, and therefore combined a pragmatic RCT[36] with a parallel non-randomised cohort in the design of the study[72] (see Appendix 1).

We did not attempt to differentiate between the preferences of parents and children in the study. The proportion of parents and children participating in the study who stated a preference was 63% (461/729) (see Chapter 3). If we assume that all eligible children who declined to participate in the study (286) had a patient preference, this would suggest that the proportion of parents and children stating a patient preference is 74% [(461 + 286)/1015].

Referral from primary care is probably part of the process of stating a preference for a secondary care intervention. The design of the study does not capture the process of self-referral to primary care and the decision-making processes taken by the GP in partnership with parents and children. Therefore, it is not possible to estimate the number of children who would have been eligible for the study but were not referred. Nor is it possible to understand how patient preferences played a role in this process. However, the data revealed a potential gender difference in the demand and referral for secondary care opinion, with girls in the older age group presenting to the study ENT centres more frequently than boys (see Chapter 3). This is consistent with data from Denmark.[73]

Of the 461 cohort participants who were not in 'equipoise', 16% (74/461) opted for medical

management and 84% (387/461) for (adeno-) tonsillectomy. This strong preference for surgical removal was anticipated, given that the procedure is well established in clinical practice and 'expected' by many patients referred to ENT surgeons. Perhaps unanticipated was the minority, but not insignificant number, of participants who opted for medical management following referral to an ENT surgeon and a discussion with the participating consultants and research nurses of the possible risks and benefits of the procedure.

A number of factors may have influenced the 387 cohort participants who had elected for surgery. Earlier studies[10,17,56,74] suggested that in addition to demographic and clinical variables, school attendance and performance were important. Sixty-two per cent of cohort participants opting for surgical management reported that their progress at school was impeded by recurrent sore throats compared with 29% of the cohort participants opting for medical management and 39% of trial participants. A multinomial regression model (see Table 8) confirms the importance of perceptions of school performance, along with the experience of chronic sore throat and female gender.

Characteristics of trial and cohort participants

An examination of participants' reported health in the 6 months before randomisation (trial) or recruitment (cohort) suggests that overall the cohort participants who opted for surgery were likely to experience more of a range of sore throat symptoms than trial participants who in turn were likely to experience more symptoms than cohort participants who opted for medical management (see Table 6). There was a significant association between study group and the number of sore throats, the number of days a sore throat lasted in any one episode, the number of sore throats that lasted more than 2 weeks and the number of sore throats that involved an ear infection.

These findings were also reflected in the effect that sore throats had on school activity and quality of life in the 6 months prior to randomisation or recruitment. Cohort participants opting for surgical management were more likely to have taken days off school, they perceived that progress at school had been affected and scored lower on the PedsQL physical health and mental health summary scores (see Table 7). Sore throat symptoms were more likely to have affected trial participants than cohort participants who opted for medical management, with the exception of their PedsQL physical health scores which were very similar.

Observed differences in the characteristics of participants have an important bearing on the subsequent interpretation of outcome data.

Outcome of surgical or medical management

The key objective of surgical and medical management of recurrent sore throat is to reduce the frequency and severity of sore throats for children to a clinically significant extent. For the purposes of the study, we defined a priori the primary outcome as the reported number of episodes of sore throat in the 2 years after randomisation for trial participants and 2 years after recruitment for cohort participants. The source of these data was self-completed daily diaries returned by participants every 4 weeks for 24 months. In addition we collected information retrospectively about the reported experience of sore throats and other symptoms through telephone contact with participants who had not returned diaries and self-completed postal questionnaires at 3 months, 12 months and 24 months after randomisation (trial participants) or recruitment (cohort participants). A further source of information was abstracted from GP records: the recorded number of GP consultations for sore throat and prescribed medication used in the medical management of recurrent sore throats. The use of these different sources of information about sore throat experience for 24 months' follow-up allowed some triangulation of the data.

External validity

The quality of the evidence reported from the study is seriously compromised by loss to follow-up, the high non-response rate to daily diaries and self-completed questionnaires, and missing data due to incompletion of diary and questionnaires. Figure 2 showed a decline in diary returns for trial and cohort participants over the 24-month follow-up from about 78% to 22% (trial) and from 63% to 15% (cohort). The CONSORT flow chart (see Figure 1) also highlights the significant loss to follow-up through the decline in response rates from 88% for the baseline survey to 33% for the 24-month outcome questionnaire (Table 35).

TABLE 35 *Response rates to baseline and outcome questionnaires*

		Trial		Cohort
	All groups (*n* = 729)	**Surgical management (*n* = 131)**	**Medical management (*n* = 137)**	**Surgical management (*n* = 387)**	**Medical management (*n* = 74)**
Baseline	88%	87%	81%	90%	91%
3 months	56%	66%	63%	49%	62%
12 months	38%	56%	40%	32%	36%
24 months	33%	49%	39%	29%	34%

The quality of evidence from GP records is also impaired by the number of records traced and from which data were abstracted (69% trial; 31% cohort).

Assessment of sore throat outcomes

The primary outcome was the number of reported sore throat episodes in the 24-month follow-up. In clinical guidelines an episode is defined as a period of 4–5 days' duration. Diary reporting of sore throats was not that straightforward, and a period of sore throat reflected in the primary outcome variable was operationalised in the analysis as described in Box 2. This variable was adjusted using data from the telephone contact with non-respondents of diaries. The average number of diaries returned per child in the trial was 9.9. The response rates were very similar for both arms of the trial. By adding in responses to telephone interviews for months during which no diary was returned, we increased the number of responses per child by 1.6 to 11.5. Prior to undertaking the analysis, but in the knowledge of response rates, it was decided that the primary analysis would be based on the pooled data which are those reported in the final report. Because we adopted the same approach for both groups, any bias due to poor recall should be roughly equalised across them. Any bias in the magnitude of the effect of tonsillectomy in terms of episodes of sore throat is likely to be small in comparison with the bias due to the very poor overall diary return rate. The estimates of tonsillectomy using the above approach were consistent with those obtained from the analysis of interviews, which of course are totally based on patient/parent recall.

There was no imputation of missing data. A secondary outcome variable used in the analysis was the number of sore throat days – the number of days for which sore throats were recorded in the diary (or sore throat free days). A second sore throat related secondary outcome variable also used in the analysis was the number of recorded consultations for sore throat abstracted from GP records.

Clinical effectiveness

Primary outcome

Episodes of sore throat

Chapter 3 reports the findings of an intention-to-treat analysis. Analysis of the primary outcome variable, episodes of sore throat, shows that there is a decline in the number of episodes of sore throat across all study groups, reflecting the view that for many children it may be a self-limiting illness.[75] This is shown in Table 12 through a comparison of the mean number of sore throats in the first and second years after randomisation or recruitment – the incidence of sore throats for children receiving medical management was found to be much smaller in the second year than in the first year. Earlier studies[29–31,76] of dubious quality[32] reported that the benefits of tonsillectomy versus medical management controls were higher in the first year after tonsillectomy than in the second year. In one of the few acceptable but underpowered randomised trials,[17] it was reported that the decline in the number of sore throats decreased over time. The intention-to-treat analysis of the present study suggests that surgical management has a larger relative benefit in the second year than in the first year. Comparison with earlier studies, however, is difficult and not to be advised because of their poor quality and the differences in case-mix and the analysis strategy (not an intention-to-treat analysis) in the Paradise trial.[17]

The benefit of surgical management in this study may have been delayed due to the timing of surgery and the effects of surgery. The relatively

high number of sore throat episodes reported in Table 12 for the trial and cohort surgical management groups may include sore throats between the date of randomisation or recruitment and surgery. For the trial participants, tonsillectomy was scheduled to take place within 12 weeks of randomisation, whereas cohort participants would more often be put on the standard waiting list which was normally longer than 12 weeks. The effects of tonsillectomy are well documented,[16,17] with sore throat pain lasting for an average of 5–6 days after the operation.

Reviewing the primary outcome for trial participants only, the intention-to-treat analysis reported in Table 13 that controls for participating centre and age group suggests that surgical management confers a statistically significant benefit and has a larger relative benefit in the second year than the first despite children in the medical management group experiencing fewer episodes of sore throat during that second year. The robustness of this analysis is obviously challenged by the effect of 'patient' preferences (which can be estimated by comparing the outcomes for trial participants with those for cohort participants) and the poor response rate to daily dairies and outcome questionnaires.

Table 14 compares sore throat episodes at outcome for trial and cohort participants. Looking at those children in the trial and cohort in the surgical management groups we find a significant difference in primary outcome during the first year. Cohort participants in the surgical management group had significantly poorer outcomes than trial participants. This difference may reflect differences in trial and cohort participants at baseline: cohort participants in the surgical management group reported more of a range of sore throat symptoms than trial participants in the surgical management group. However, it may also reflect the timing of surgery, with cohort participants having a longer wait for surgery than trial participants. In the second year the difference in primary outcome between trial and cohort participants in the surgical management group was smaller and not statistically significant, although the 95% CI was between 0.57 and 1.25. We therefore cannot discount the possibility that cohort participants in the surgical management group were still reporting worse outcomes in year 2.

Looking at those children in the cohort and trial medical management groups we find that the primary outcome is similar. However, our interval estimates of the difference are fairly wide because of the relatively small number of cohort participants opting for medical management.

Secondary outcomes

Sore throat days

Intention-to-treat analysis of the number of days of sore throat reported in Table 17 and summarised in Box 3 reflects the primary outcome. The statistical models reported suggest that for trial participants those in the surgical management group were less likely than those in the medical management group to record a day of sore throat during both years of the study. Comparisons of trial participants with cohort participants suggest that trial participants in the surgical group were less likely to record a day of sore throat than cohort participants during both years of the study. As with the primary outcome, these differences may reflect differences in baseline characteristics or differences in the length of time that participants waited for surgery. A comparison of trial participants with cohort participants both in the medical management group suggests that trial participants were more likely to record a day of sore throat in both years of follow-up than cohort participants, although differences in the incidence rates in year 2 were not statistically significant. The very wide CI for the incidence rate in year 2 reflects the comparatively small number of children who returned diaries in this period. These differences may also reflect differences in baseline characteristics – cohort participants in the medical management group reporting less sore throat symptoms than trial participants.

GP consultations

Data abstracted from GP records concerning all consultations and consultations for sore throat for the 2 years of follow-up reported in an intention-to-treat analysis in Table 18 show that overall there was little difference between participants in the four groups. The mean number of consultations and sore throat consultations declined for each group between year 1 and year 2. Among trial participants, those in the medical management group had more consultations than those in the surgical management group [year 1, IRR 0.91 (95% CI 0.71 to 1.17); year 2, IRR 0.83 (95% CI 0.63 to 1.10)]. The trial medical management group also had more sore throat consultations than the surgical management group [year 1, IRR 0.81 (95% CI 0.59 to 1.10); year 2, IRR 0.67 (95% CI 0.46 to 0.97)]. These data, which for trial participants are more complete than participant reported data, suggest a similar trend in differences between the

two arms of the trial, as is apparent for the primary outcome.

Quality of life

Assessment of quality of life is based on PedsQL. The analyses reported in Chapter 3 (see Table 19) suggests that trial participants in the surgical management group reported higher scores than participants in the medical management group for both subscales in years 1 and 2 before and after adjustment for baseline assessments. Outcomes were similar for trial and cohort medical and surgical management groups. However, effect sizes were relatively small (less than 0.25). The impact of surgical management on quality of life is more difficult to interpret given that a range of factors may have influenced outcome scores in addition to changes in sore throat experience. The wide CIs reported along with the low response rate to outcome questionnaires suggest that these results should be treated with caution. With these caveats in mind, however, there is some suggestion that surgical management had a more positive effect than medical management among trial participants; an interpretation that is in line with the primary outcome variable. That there was no difference between cohort and trial participants within management strategies suggests that the physical and psychosocial health PedsQL scores are less informative than the primary outcome in the interpretation of clinical effectiveness.

Secondary analysis

An intention-to-treat analysis of trial participants only was undertaken in an attempt to discover whether we could identify groups of participants who benefited from surgical management. The analysis described in Chapter 3 included a covariate to adjust for the poor response to diaries and outcome questionnaires.

In the discussion of primary and secondary outcomes we suggested that the results may have been influenced by the sore throat experience of participants prior to enrolment to the study. The overall effect of surgical management in the trial was estimated as IRR = 0.68 (95% CI 0.88 to 0.92) when fitting a negative binomial regression model. Fitting an interaction with symptom severity using different estimates of symptom severity (number of GP consultations for sore throat in 2 years prior to enrolment; number of sore throats in previous months reported in baseline questionnaire) was found not to have a significant effect.

Age

In Chapter 3 we reported the results of an analysis to identify whether surgical management benefits any particular age group. The results of negative binomial regression analysis using the primary outcome variable (reported number of sore throats episodes) are shown in Table 21. Overall we see a relative benefit for children who are aged 8–11 years. Children in this age group randomised to medical management were more likely to report an episode of sore throat than other children randomised to medical management during the follow-up period. It is in children aged 8–11 years that we see the largest effect of surgical management. However, it may be that the higher level of reporting of sore throats among children of this age group randomised to medical management is a chance anomaly due to the overall poor response rate for diaries.

Gender

We have seen that gender was a factor in patient preferences for surgical management among cohort participants. A secondary analysis that fitted gender as a main effect suggested that girls tended to report more sore throats over the follow-up period than boys. However, the interaction between gender and surgical management was not significant and the additional effect of surgical management for a female participant is estimated as IRR = 0.91 (95% CI 0.64 to 1.30).

Cost-effectiveness

Cost-effectiveness analysis based on intention to treat was performed on trial data using the approach outlined by Drummond *et al.*[63] Resources used by trial participants are reported in Chapter 6 (see Table 31). Prescription data were abstracted from GP records and data on contact with NHS services were collected through the outcome questionnaires. Estimates of NHS service use are therefore subject to the same caveats as the primary outcomes used for the clinical effectiveness analysis. The mean costs for trial participants of treatment for recurrent sore throats were calculated using resource data from participants and standard NHS unit costs. Table 32 reports that the cost of surgical management is significantly higher than that of medical management. The cost of surgery is the cost driver because when the cost of surgery is removed the difference in mean costs is substantially reduced. The estimated mean incremental cost for surgical management over medical management was £939.

For the purposes of the cost-effectiveness analysis, an estimate of the number of sore throats over the 2-year follow-up, adjusted for the reduction in diary response over time, was calculated (see Chapter 3). The estimated reduction in the mean number of sore throat episodes due to surgical management (the estimated mean incremental effectiveness) was estimated as 3.5 episodes (95% CI 1.8 to 5.2). Potentially this is an underestimate of the benefits of surgical management because trial participants reported fewer sore throat symptoms in the 6 months before enrolment to the trial than cohort participants who opted for surgical management. The estimated ICER was therefore estimated as £261 per sore throat avoided (95% CI £161 to £586). This estimate is certainly within the range identified in the WTP study of the amount that parents would be willing to pay for the successful treatment of their child's recurrent sore throat (mean WTP £8059) (see Chapter 5).

Quality-adjusted life-years

The utility study described in Chapter 5 reports the results of preference elicitation using the standard gamble method and the WTP method with a sample of (non-trial) parents and teenagers attending either a tonsillectomy preoperative assessment clinic or an ENT outpatient clinic. Two health-state scenarios were developed; one that represented the experience of recurrent sore throat or tonsillitis (Health State X) and a second that represented possible outcomes following surgery (Health State Z). Each scenario was used in both preference elicitation exercises. In Tables 28 and 29, utility scores for parents and teenagers are reported for the situations in which Z was ranked above X or X was ranked higher than Z. Using these data it is possible to estimate the QALY gain for the two ranking combinations. Adjusting for the proportion of participants who selected each scenario, the estimated gain is between 0.136 and 0.3 QALYs (see Chapter 6). Using these estimates the estimated incremental cost per QALY ranges from £3129 to £6904 per QALY gained. Caution must be used when interpreting the results from the utility study, as the scenarios that were used to describe the health states associated with tonsillitis and tonsillectomy were not based on the clinical outcomes found in the trial. At the time of developing the utility study these data were not available, therefore, values from the literature were used. Following the completion of the trial, it was discovered that the change in the number of sore throats from treatment did not correspond with the numbers in the scenarios. Therefore the cost per QALY estimates do not correspond to the clinical benefits experienced by patients in this trial.

Conclusions

Clinical effectiveness

Overall this study has supported the view that the health of children with recurrent sore throat improves over time. However, trial participants randomised to surgical management tended to experience better outcomes than trial participants randomised to medical management, indicating some relative benefit of surgical management. This may be greatest for children aged 8–11 years. Study participants who expressed a preference for surgical management and experienced more sore throat symptoms prior to enrolment to the cohort study tended to report poorer outcomes than trial participants receiving surgical management. Trial participants who were randomised to medical management had poorer outcomes than children who opted for medical management in the cohort, but this difference decreased over time. The study highlights the role of patient preferences and the importance of taking account of these in the design of the trial.

Cost-effectiveness

The ICER was estimated as £261 per sore throat avoided (95% CI £161 to £586).

Trial quality

These conclusions are subject to a number of caveats. This was an intention-to-treat analysis and may therefore underestimate the effect of surgical management because 36 participants (36%) randomised to medical management received surgery within the 2-year follow-up. This compares with a smaller number of participants randomised to surgical management who had not received surgery at 2-year follow-up (11, 10%).

The main caveats surrounding these analyses, however, concern the poor response rates to daily diaries and self-completed questionnaires, particularly in year 2 of follow-up, which have seriously challenged the external validity of the trial.

Chapter 8
Conclusions

The recently updated Cochrane Review[26] reported that there is no clear evidence of the clinical effectiveness and cost-effectiveness of (adeno-) tonsillectomy in the treatment of recurrent sore throat among children. The limitations of the present study suggest that the next review update will reaffirm the current review's conclusion. The continuing careful use of 'watchful waiting' and medical management in both primary and secondary care is therefore recommended until clear-cut evidence of effectiveness is available.

For children meeting the NESSTAC eligibility criteria, we have shown that there are clinical benefits of tonsillectomy that persist for at least 2 years. Secondary analysis did not really identify subgroups of children for whom tonsillectomy produced greater benefits, but this may be because the study did not have adequate power to detect such effects. Logically there must be a level of disease severity at which the clinical benefits of tonsillectomy are not cost-effective. Current clinical guidelines suggest that (adeno-)tonsillectomy is indicated where there is typically a 2-year history of three to four episodes of moderate severity (episodes of 5-day or longer duration).[5–7] This study provides no evidence for a change in these recommendations in either direction.

Study participants were more likely to express a preference for tonsillectomy if they had experienced more severe symptoms of sore throat prior to entry to the study. Presumably the perceived benefits of the procedure were greater for such participants.

Evidence from this study confirms that there is a strong parental preference for (adeno-) tonsillectomy. A significant minority of study participants, however, opted for medical management within the cohort study, suggesting that consideration needs to be given to ensuring that parents and children are fully aware of the risks and benefits of (adeno-)tonsillectomy and are given an informed choice of what treatment strategy to follow. Surgeons should not assume that referral to ENT is indicative of parents' and childrens' preferences for surgery.

This report has adhered strictly to the principle that an intention-to-treat analysis of complex trials and comprehensive cohort studies is preferred. Secondary analysis is proposed in order to estimate the impact of surgical management on study participants whose tonsils were surgically removed (explanatory analysis[36]).

The poor response rates to postal outcome questionnaires and diaries suggest that other more expensive ways of capturing these data should be considered. Methodological research is recommended that determines the cost-effectiveness of different methods of data collection (e.g. postal questionnaires versus telephone interviews versus face-to-face interviews).

The utility and WTP studies were relatively small and were not based on the clinical outcomes found in this trial. In order to estimate patient preferences for surgical or medical management of recurrent sore throats, further investigation using revised scenarios, which are more reflective of the outcomes found in this trial, could be conducted on a larger sample to determine parent and patient preferences in terms of QALYs and WTP, as well as further work to understand patient preferences for surgical or medical management.

Implications for practice

- There are clinical benefits of tonsillectomy that persist for at least 2 years.
- Participants were more likely to express a preference for tonsillectomy if they had experienced more severe symptoms of sore throat.
- There is a strong parental preference for tonsillectomy.
- Careful use of 'watchful waiting' and medical management in both primary and secondary care is recommended until clear-cut evidence of effectiveness is available.

Recommendations for research

- Exploratory secondary analysis to estimate the impact at surgical management on study participants whose tonsils were surgically removed.
- Methodological research of alternative methods of data collection.
- Larger utility elicitation/WTP studies.

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Contribution of authors

Contribution to the study

Professor John Bond (Professor of Social Gerontology and Health Services Research) was the lead investigator. He was responsible for the overall management of the study, developed the protocol and prepared the report for publication. Dr Katie Brittain (Lecturer in Social Gerontology) was the trial manager (December 2001 to August 2004) and contributed to the qualitative study. Mr Sean Carrie (Consultant Otolaryngologist) recruited participants and assisted in the acquisition and interpretation of data. Mr Ray Clarke (Consultant Otolaryngologist) developed the protocol, recruited participants and assisted in the acquisition and interpretation of data. Professor Martin Eccles (Professor of Clinical Effectiveness and Primary Care) developed the protocol, was responsible for the acquisition of clinical data from general practice and assisted in the analysis and interpretation of data. Mr Haytham Kubba (Consultant Otolaryngologist) recruited participants and assisted in the acquisition and interpretation of data. Dr Catherine Lock (Senior Research Associate) was the trial manager and main researcher on the project (August 2004 to August 2008). She was responsible for the day-to-day management of the trial and the analysis of qualitative data, and prepared the report for publication. Dr Helen Mason (Research Associate – economics from July 2007) was responsible for the economic evaluation and utility study and prepared the report for publication. Mr Chris Raine (Consultant Otolaryngologist) recruited participants and assisted in the acquisition and interpretation of data. Dr Nick Steen (Principal Research Associate – statistics) was the Trial Statistician. He developed the protocol, was responsible for the statistical analysis and prepared the report for publication. Professor Janet Wilson (Professor of Otolaryngology, Head & Neck Surgery and Consultant Otolaryngologist) was the lead clinical investigator, developed the protocol, was responsible for the acquisition of clinical data in secondary care and assisted in the analysis and interpretation of data. Ms Alessandra Vanoli (Senior Research Associate – health economics) was the Trial Health Economist until December 2005. She conceived and designed the economic and utility studies and data collection instruments. Mr Andrew Zarod (Consultant Otolaryngologist) developed the protocol, recruited participants and assisted in the acquisition and interpretation of data.

Contribution to the report

Professor John Bond prepared drafts of Chapters 7 and 8, and edited and finalised the report. Dr Catherine Lock prepared drafts for Chapters 1–3, 5, 7 and 8. Dr Helen Mason prepared drafts for Chapters 4 and 6 and Dr Nick Steen prepared a draft of Chapter 3. All members of the project team contributed ideas to the report, assisted in data analysis and interpretation and were responsible for critical review of the report.

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Appendix 1

Study protocol

Protocol for north of England and Scotland study of tonsillectomy and adeno-tonsillectomy in children (NESSTAC). A pragmatic randomised controlled trial comparing surgical intervention with conventional medical treatment in children with recurrent sore throats

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Abstract

Background: Uncertainties surrounding the effectiveness and cost-effectiveness of childhood tonsillectomy for recurrent sore throat led the NHS Health Technology Assessment Programme to commission this research to evaluate the effectiveness and cost-effectiveness of tonsillectomy and adeno-tonsillectomy in comparison with standard non-surgical management in children aged under 16 with recurrent throat infections. The aim is to evaluate if tonsillectomy and adeno-tonsillectomy reduces the number of episodes of sore throats among children to a clinically significant extent.

Methods/Design: A simple prospective pragmatic randomised controlled trial with economic analysis and prospective cohort study of non-trial participants comparing surgical intervention with conventional medical treatment. The treatment arm will receive tonsillectomy and adeno-tonsillectomy while in the control arm non-surgical conventional medical treatment only will be used. The primary outcome measure will be reported number of episodes of sore throat over two years with secondary outcomes measures of reported number of episodes of sore throat, otitis media and upper respiratory tract infection which invoke a GP consultation; reported number of symptom-free days; reported severity of sore throats and surgical and anaesthetic morbidity. The study will take place in five hospitals in the UK. The trial population will be 406 children aged 4–15 on their last birthday with recurrent sore throat referred by primary care to the five otolaryngology departments. The duration of the study is seven years (July 2001 – July 2008).

Discussion: As with all pragmatic randomised controlled trials it is impossible to control the external environment in which the research is taking place. Since this trial began a number of factors have arisen which could affect the outcome including; a reduction in the incidence of respiratory tract infections, marked socio-economic differences in consultation rates, the results from the National Prospective Tonsillectomy Audit and the Government's waiting list initiatives.

Background

In the UK sore throats cost the NHS an estimated £60 million in GP consultations alone, result in 90,000 tonsillectomy procedures, approximately half of which are in children, and a loss of more than 35 million school or work days annually.[1] The incidence of tonsillectomy has risen since the early 1990s, although levels are still much lower than in the 1930s, when 100,000 operations were performed in UK school children.[2] Adenoidectomy is performed with tonsillectomy in about one-third of patients. Private medical insurance is associated with higher selective ENT surgical rates under the age of seven years[3] and 16% of UK ENT activity is in the independent sector. Therefore figures based purely on NHS returns inevitably underestimate the total activity. In addition to the health care costs, tonsillectomy incurs parental costs as one parent usually resides in hospital overnight. Thereafter the average time to return to normal activity for under 15 year olds is 12 days.[4]

There is a broad similarity in the criteria for tonsillectomy in clinical guidelines in the UK[5,6] and North America.[7] The minimum criteria are typically a two year history of three to four sore throats of moderate severity (five day duration) per annum. This is despite evidence that even histories that seem impressive may not be confirmed on close scrutiny in the majority.[8] The complex psychosocial influences on tonsillectomy rates include parental enthusiasm for intervention,[9] lack of information[10] and maternal use of psychotropic drugs which increases two-fold the rate of consultation for childhood sore throat.[11,12] Guidelines may not be uniformly implemented, even when locally derived. Surgeons tend to break guidelines more often in favour of performing than withholding surgery.[5]

National and international variations in the rates of adeno-tonsillectomy have been recognised for decades. Even in the 1930's, 50% of UK and USA children received a tonsillectomy, while the rate was 0.5% or lower in Germany.[2] A survey of such variation in Quebec, highlighted the importance of clinical uncertainty among physicians about the recommendation of surgical intervention,[13] providing further support for conducting primary research. The Scottish National Tonsil Audit showed that rates of tonsillectomy in childhood varied from <4/10,000 in Forth Valley to almost 10/10,000 in Dumfries and Galloway.[14]

Differential costs and benefits of surgery at different age groups are not known. The tonsils are traditionally thought to undergo a period of physiological enlargement around school entry. At this time also, pathological sequelae may include otitis media. Older children and adolescents, may have a somewhat different natural history, and illness at this age has rather different (educational) implications.

Mortality from tonsillectomy has been estimated at 1/16000 to 1/35000,[15] but surgical risk at this level is hard to measure, to conceptualise and to convey. The major non-fatal complications are infection, haemorrhage (2.15%), and pain which lasts on average five to six days[16,17] and may be inadequately treated in children.[18] Haemorrhage is unpleasant, requires intravenous fluid administration, with or without blood transfusion and return to theatre. The reported rate of second anaesthetic for haemostasis varies widely from 0.75% in one British review,[4] to as low as 0.06% in a study of almost 9409 children in Toronto.[19] The post-tonsillectomy readmission rate is up to 7%,[4] but in Newcastle in childhood is only 2.3% (unpublished data; Department of Clinical Effectiveness, Freeman Hospital, Newcastle). The overall reported complication rate ranges from 8%[14] to 14%,[17] the majority being relatively minor such as sore throat, nausea, fever, dysphagia. Most 2 to 10 year olds undergoing ENT surgery show behavioural changes such as attention seeking, temper tantrums and night waking and there is also anecdotal evidence for depression after tonsillectomy.[20] Younger children, due to cognitive immaturity seem less well able to adapt to hospitalisation.[21,22] Late sequelae may include lower postoperative serum immunoglobulin levels but these have been ascribed to reduction in antigen stimulation.[23] There is continuing debate about the suggestion that tonsillectomy increases the risk of Hodgkin's lymphoma.[24] A substantial Scandinavian population based cohort study found an increased risk of Hodgkin's disease, especially in younger children.[25] The risk of transmission of nvCJD from contaminated tonsillectomy instruments remains quite unquantified. Some centres are costing the use of disposable tonsillectomy sets.

Despite the frequency of tonsil dissection, there is a remarkable lack of robust evidence for its efficacy. Uncontrolled patient reports suggest the procedure to be very effective but recurrent sore throat, particularly in childhood may be a self limiting disease. Where non-intervention control groups have been studied, the benefits of tonsillectomy seem almost to disappear after two years. Available studies are either 20 to 30 years old or confined

to small numbers of severely affected individuals with limited general applicability. The most recently published Cochrane review concludes that there is no evidence from randomised controlled trials to guide the clinicians in formulating the indications for surgery in children or adults.[26] The authors state the need for high quality evidence from randomised controlled trials to establish its effectiveness and that these should assess the effectiveness of the procedure in patients with throat infections of differing severity and frequency. A recent Dutch randomised controlled trial of adenotonsillectomy versus watchful waiting reported no differences between treatment arms for children with mild symptoms and only a small difference of less than one episode of fever a year between treatment arms for children with moderate symptoms.[27]

The Scottish National Tonsillectomy Audit[14] showed high levels of patient satisfaction and that 80% of subjects did not consult a doctor in the subsequent 12 months. However, over the past 30 years a number of controlled studies with longer follow-up indicate marginal and diminishing levels of clinical benefit over a period of non-intervention. There are no substantial claims for the benefit of childhood tonsillectomy after 2 years. Roos[28] assessed the benefit to be 1 to 1.5 fewer sore throats (0.5 to 1 episode per annum) over the first two years after surgery in those with three to four episodes per annum preoperatively. Other studies[29–31] showed benefits of the order of ~1.5 fewer sore throats versus controls in the first postoperative year and on average one fewer episode in the second year. All of these and other available studies provide inadequate evidence because of poor definition of entry and outcome criteria, failure to include intention to treat calculations and small or skewed samples.[32] Even the only scientifically acceptable study by Paradise and colleagues[17] suffered from comparatively small numbers of a skewed population of more severely affected children. The benefits of surgery were more marked (approximately 1.75 fewer episodes in year 1, 1.5 in year 2) but equally short lived. The drop out rate was 34% by the end of year 2 and one in three of the control group underwent surgery and were excluded from analysis. Also, the very active therapy of the control arm may have mitigated any impact of surgery. The Paradise group went on to study a more typical i.e. less severely affected group of children, but the full results of this study, near completion in 1992 have never been reported.

Weight gain is a cited supplementary benefit of tonsillectomy. Two recent studies showed accelerated weight gain postoperatively, but as the children were shown to be of normal or above average height and weight preoperatively, this effect may be undesirable.[33] There appears so far to be only minimal additional benefit from adenoidectomy or adenotonsillectomy in recurrent acute otitis media.[16]

A straw poll, for this protocol, of consultant otolaryngologists asked: what level of reduction in sore throat would justify removal of the tonsils? Replies were remarkably consistent – at least two sore throats fewer per annum. No published trial to date shows a benefit of this magnitude, even in the first year after surgery. There is a pressing need for a UK, pragmatic trial to evaluate the effectiveness and cost-effectiveness of childhood tonsillectomy.

The purpose of this study therefore is to answer the key research question "What is the effectiveness and cost-effectiveness of tonsillectomy/adeno-tonsillectomy in comparison with standard non-surgical management in children aged under 16 with recurrent throat infections?" Assessment of outcome will emphasise those which are important to children themselves and their parents or carers. Specific research questions are:

- Does tonsillectomy/adeno-tonsillectomy reduce the number of episodes of recurrent sore throats among children to a clinically significant extent?
- Are there differences in clinical outcome for the age groups: 4–7, 8–11, 12–15 years?
- What is the cost-effectiveness of tonsillectomy/adeno-tonsillectomy among children and what are the costs and benefits to families?
- What are the important outcomes of tonsillectomy/adeno-tonsillectomy for children and their parents/carers and what is the importance of these to children and their parents' quality of life?
- What are parents' (and older children's) preferences for different treatment options for recurrent sore throat?
- How representative of the target population are trial participants?

Methods/Design

Trial design

A simple prospective pragmatic randomised controlled trial with economic analysis comparing

surgical intervention with conventional medical treatment.

Cohort design

We anticipate that a large majority of participants who decline randomisation to the trial will opt for, and receive, surgery. Therefore, in order to assess the external validity of the trial results, we will recruit a cohort of children from those who decline to participate in the trial. The cohort will include both children who opt for surgery and those who choose conventional medical treatment. They will be followed up for 24 months.

Interventions

The treatment arm will receive tonsillectomy and adeno-tonsillectomy while in the control arm non-surgical conventional medical treatment only will be used.

Treatment

Tonsillectomy and adeno-tonsillectomy with adenoid curettage and tonsillectomy by dissection or bipolar diathermy. Most (80%) UK surgeons use the conventional dissection method[4] and the remainder use bipolar diathermy. Both methods will be allowed in the trial according to surgical preference. Surgical intervention will take place within four weeks of randomisation.

Control

Non-surgical conventional medical treatment only will be used. There will be no active intervention protocol since no single prescribing strategy would be able to cover all patients.[34] The referring GP will be free to treat as in their current practice. The use of usual treatment rather than an active intervention protocol is considered important for the implementation of study findings since surgical enthusiasts may argue against the findings were the control group to be atypically and over rigorously treated.

Outcome measurement

The primary clinical outcome is the reported number of episodes of sore throat in the two years after randomisation. Secondary clinical outcomes include reported number of episodes of sore throat, otitis media and upper respiratory tract infection which invoke a GP consultation; reported number of symptom-free days; reported severity of sore throats and surgical and anaesthetic morbidity. In addition to the measurement of these clinical outcomes, the impact of the treatment on costs and quality of life will be assessed. There will also be an economic evaluation.

Setting

Inpatient facilities and outpatient clinics of five hospitals in the North of England and Scotland: Freeman Hospital, Newcastle upon Tyne; Alder Hey Children's Hospital, Liverpool; Booth Hall Children's Hospital, Manchester; Yorkhill Royal Hospital for Sick Children, Glasgow; and Bradford Royal Infirmary and general practices with which study participants are registered. Freeman Hospital, Newcastle is a large teaching hospital with a mixed adult and paediatric ENT unit. The Unit has a wide urban and rural catchment area including Newcastle and Gateshead, Northumberland and north west Durham. Alder Hey Hospital, Liverpool, and Booth Hall Hospital, Manchester, house two of the largest paediatric ENT units in the UK covering catchment areas in and around Liverpool and Manchester. Yorkhill is a busy university hospital with the largest children's ENT unit in Scotland and Bradford Royal Infirmary is one of the major hospitals within West Yorkshire. It has recently obtained teaching hospital status with the opening of its medical school. The ENT unit acts as a hub and supports clinics in Airedale and Dewsbury. The unit supports the majority of adult and paediatric care.

Target population

The trial population will be children aged 4–15 on their last birthday with recurrent sore throat referred by primary care to five otolaryngology departments in Newcastle, Liverpool, Manchester, Glasgow and Bradford. In 1999 a total of 2683 tonsillectomy/adeno-tonsillectomy procedures were done for children in these centres: Liverpool (750), Manchester (440), Newcastle (545), Glasgow (498) and Bradford (450) of which some two-thirds will be referrals for recurrent sore throat.

Inclusion criteria

The study will use entry criteria drawn from the Northern regional guidelines.[5] Children (or carers) reporting experience of four or more episodes of sore throat within each of two years or six or more episodes of sore throat within one year will be eligible. We have considered pre-randomisation prospective data recording to operationalise stricter inclusion criteria for severity, but have rejected these as our aim is to operationalise current UK clinical practice.

Exclusion criteria

Children will be excluded if they require hospitalisation due to quinsy; have obstructive symptoms suggestive of clinically significant sleep apnoea syndrome, have rare medical conditions such as glomerulonephritis or Henoch Schonlein purpura; have previously had a tonsillectomy; have suspected velopharyngeal insufficiency, have co-morbidity that means they are unable to undergo the operation within the next six months, have a bleeding disorder, or have congenital/valvular heart disease.

Number of subjects required

We estimate a completed sample size at follow-up of 284 children. Allowing for an attrition rate of around 30% we will need to recruit a total of 406 children to the trial to achieve the estimated sample of 284 (who will complete the trial). Within the original three study hospitals some 1700 tonsillectomies/adeno-tonsillectomies are currently performed annually. Only two-thirds of these will have recurrent sore throats. In any trial where the intervention is widely used in current practice there are likely to be large numbers of eligible participants who opt for the intervention treatment and decline participation in the trial. We estimate that this could be up to one half of all eligible referrals from primary care. The maximum available for randomisation is therefore estimated as 566 per annum. Loss of eligible subjects in the trial is expected due to holiday periods and 'winter pressures'. On the experience of loss in other trials (50%) a conservative estimate would be 283 per annum. If we assume a conservative rate of attrition of 30% over two years we would expect 198 completing trial participants to be recruited in a 12 month period. Given seasonal effects a full two years would be necessary to recruit the estimated sample size. The cohort sample will be identified from participants who indicated a preference not to be randomised within the trial and who agreed to data collection. An appropriate sampling fraction will be used once non-participation in the trial can be estimated.

Subject recruitment

Recruitment to the study will take place in secondary care. All GP referrals to study centres of children with recurrent sore throat will be considered by participating surgeons. Arrangements are in place in each centre for eligible children to be referred to the clinical applicants. GPs will be informed of this reorganisation. This will facilitate efficient use of outpatients clinics at which trial participants would be recruited. Trained Research Nurses will introduce the trial to patients who will be shown a video regarding the main aspects of the trial. Patients will also receive information sheets. Research Nurses will discuss the trial with patients in light of the information provided in the video and information sheets. Patients will then be able to have an informed discussion with the participating consultant. Research Nurses will obtain written consent from patients willing to participate in the trial. Information sheets and consent forms are provided for all parents involved in the trial however these have been amended accordingly in order to provide separate information sheets and consent form which are suitable for children and teenagers. All information sheets, consent forms and the video transcript have been translated into Bengali, Punjabi, Gujarati, and Urdu. There are also separate information sheets and consent forms for the cohort group.

Randomisation

Independent world wide web based computer randomisation will allocate participants to treatment arms. Randomisation will take place once informed consent to the study has been completed and baseline data collected. The sample will be stratified by age of child at last birthday. Blocked randomisation will be used to ensure that within each centre, within each of the three age groups (4–7, 8–11, 12–15) children will be allocated in equal numbers to each arm of the trial. Where trial sites are unable to access the world wide web they will telephone the coordinating centre (University of Newcastle) in order for web based randomisation to be completed on their behalf. Sampling for the cohort study will similarly be stratified by age.

Blinding

Health technology assessment is essentially a pragmatic activity conducted in normal clinical practice, rather than an exploratory activity conducted in highly controlled settings. It follows that blinding doctors and patients to treatment is not desirable since it distorts normal clinical practice. Nor is it practicable. In contrast, blinding assessors is important because it minimises subjective bias towards a given treatment. All research staff conducting interviews or processing postal questionnaires and diaries will be blind to treatment modalities of all participants. This will be facilitated by separating the responsibility for recruitment and randomisation from outcome assessment. Furthermore, participants will be encouraged to respond to questions without describing their treatment regime. In this way,

we will minimise subjective bias towards a given treatment.

Data collection and follow-up

All participants will be followed up for 24 months from the date of initial randomisation. To minimise recall bias, data on sore throats will be gathered by a simple, structured daily health diary completed and returned by participants on a monthly basis for 24 months. Experience of similar studies suggests that with appropriate telephone reminders 90% of diaries will be returned completed. In addition simple outcome questionnaires, using two postal reminders and a telephone reminder, will be sent to trial and cohort study participants. Overall we anticipate an 80% response rate. Postal surveys will be done at 3, 12 and 24 months after randomisation. A baseline questionnaire will be completed by all participants upon recruitment to the trial. The greater frequency of data collection in the first 12 months is necessary in order to capture data on expected changes in direct and social costs to participants in the first 12 months. Experience also suggests that data on consultation rates and prescribed medication can be gathered most accurately and reliably from medical records. Manual abstraction will be performed by trained research nurses at the end of follow-up for all participants.

Adverse events will be recorded by self completion daily diaries (parent or child) which will be collected four weekly and GP records which will be examined at the end of the 24 months follow-up period. Expected adverse events include infection, haemorrhage and pain following tonsillectomy with possible hospital readmission as well as sore throat, nausea, fever and dysphagia. All adverse events will be managed as per normal care, since the intervention process of this study does not deviate from normal care.

Data handling and record keeping

Only anonymised non-identifiable data will be recorded by the site's research teams from personal medical records. Health diaries and follow-up questionnaires will be anonymous and returned to the trial centre in reply-paid envelopes. For linking purposes these data sets will have unique study identifiers. Only the lead researcher, trial manager and trial administrator will have access to the key which links study identifiers to individual data sets. Personal details (participants full name and address) will be stored on a secure database at CHSR for the purpose of sending out questionnaires and diaries centrally. All data held for analysis will be held in accordance with the Data Protection Act. On completion of the study and associated dissemination the Trial Master File will be archived in the CHSR for 10 years. Trial sites will be responsible for archiving their own documentation.

Economic evaluation

An economic evaluation will be carried out alongside the clinical trial in order to ascertain the cost-effectiveness from a societal perspective with a focus on health service and families.[35] The cohort sample will not be included in the economic evaluation except for the purpose of validation and estimating the representativeness of cost and benefit data for trial participants.

Measure of benefits used and study type

Cost consequences analysis (CCA), cost-effectiveness analysis (CEA) and cost utility analysis (CUA) will be conducted. In CCA, all the outcomes used in the clinical study will be adopted as measures of benefits, including the QoL dimensions. In CEA, the benefits will be measured by the number of events of recurrent sore throat and the number of symptom-free days. In CUA, different health outcomes will be combined with QoL dimensions.

Resources data collected within the trial and costing methods

Medical resource data will relate to the interventions under investigation, any use of health care services due to 'sore throat' episodes not averted, treatment of drug side-effects, surgery complications and long term sequelae. Services to be monitored include: outpatient visits and hospitalisations, investigations, A&E admissions, visits and telephone consultations to and from the GP and any other health care professionals, use of medications (including antibiotics, analgesics, and drugs to manage antibiotic side-effects), and any other use of health care services in both the private and public sectors. Manpower data will be collected separately for each main category of staff. Participants' out of pocket expenses such as over the counter medicines will be reported. Costing of health care resources will be undertaken in a parallel study and a mixed approach using micro-costing and gross-costing methods will be used.[36] We will cost resources using health service pay and price data. Where appropriate, these will be integrated using national published data.[37–39] Where relevant, costs will be broken down into capital, staff, consumable and overhead costs.

This will aid the production of different cost scenarios. The impact of the interventions on the time 'invested' by children and carers because of illness, treatment and rehabilitation will also be assessed. Children's days of restricted activity and their level of functioning; time off school; carers' time off work; children's and carers' time involved in outpatients attendance (such as travel time, waiting time and the duration of the clinical visit) and impact on children's and carers' quality of life will be monitored. For carers' in paid/unpaid work, time will be valued in monetary terms. Costing will be undertaken using the human capital approach and the friction cost method.[40] Those resources for which we find a statistically significant difference between the groups will be costed. Those which show no statistically significant difference but are of practical significance in their contribution to costs, will also be costed. The cost analysis will not differ across the different types of economic evaluations. However in the CUA, when carers' preferences will be assessed, particular caution will be used to avoid double counting the loss of income due to work absences.[41] Whenever applicable, a discount rate of 6% will be used, which is the rate currently used by the public sector in the UK. Costs will be expressed in UK pounds sterling. Costs will be expressed in the prices of the year in which the final analysis will be carried out and if necessary inflation method will be used to update costs data.

Resources/costs data collected outwith the trial

The study is not powered to detect significant differences for rare events. Given the relatively low incidence of surgical complications, long-term sequelae due to surgery and drugs side-effects, data on the related use of resources, costs to the carers and impact on children will be gathered outwith the trial, from the literature and from experts' opinions. Consensus estimates will be obtained by interviewing a panel of experts, including members of the study team and others. The source of the data will always be explicitly stated.

Synthesis of costs and benefits

Depending on the outcome measure, if there is no statistically significant evidence that one treatment strategy is more effective than another, a cost-minimisation framework will be used and the less expensive form of care will be recommended. If one strategy appears to be dominant (i.e. to be more effective and less costly than the alternative), the uptake will be recommended. If one form of care appears to be more effective and more expensive than the comparator, estimates of incremental cost-effectiveness (and cost utility) ratios will be generated. A judgement will be required in a policy making context to establish whether the additional benefits should be achieved sustaining the additional costs. In any case, recommendations will be made taking into account the generalisability of the results.

Sensitivity analysis

To handle uncertainty not related to sampling variations and to enhance the generalisability of the results, one-way; multi-way and extreme scenario analysis will be undertaken as appropriate and confidence intervals for cost-effectiveness ratios will be estimated under different scenarios.[42] A sensitivity analysis taking into account differences in resource use which are practically significant (i.e. potentially costly) but which have not been shown to be statistically significant, will also be undertaken. The sensitivity analysis will also make explicit all the simplifying assumptions made to collect the data.[43] The application of discounting to the benefits will also be tested in the sensitivity analysis, as well as a range of discount rates. Particular attention will also be given to whether the costs data used reflect the true marginal opportunity costs of the resources used. When more than one reliable source of information is available, such data will be used as a term of comparison. The use of different costing methods for multi-centre studies will be explored. Earlier studies[28–31] suggest that longer term outcomes such as reduction in recurrent sore throat may show only marginal benefits. An equivalence trial with a substantially larger sample size would be necessary to capture significant longer-term outcomes. To contain the cost of the trial we have not proposed a three year follow-up. However, the future sequence of clinical events and economic impact will be modelled beyond two-year follow-up. The relevant data will be derived from studies which will be available and experts' opinions.

Measuring participants' preferences and utilities

There is a need to value the effectiveness of interventions taking account of the risk of surgery and its long-term sequelae (e.g. sleep, eating, speech, disturbances, regressive behaviour[44]). The utility assessments will also provide insight into informed choice models.[45] Older children's and carers' values will be used to elicit preferences for trade-off between the perceived risks and benefits of surgery versus drugs treatment. Preferences will relate to temporary and chronic scenarios associated with morbidity and QoL because of

symptoms and treatment complications. The scenarios will be developed selecting the health outcomes and QoL domains relevant to the problem. Interviews will be carried out with a sample of older children and carers from the cohort group, and the Standard Gamble method[46] will be used to derive utilities.

Statistical considerations

Sample size calculation

In this trial we anticipate a fairly large difference in the primary clinical outcome (the reported number of episodes of sore throat in the two years after randomisation) with an effect size of around 1.0, but a smaller difference in a number of psycho-social outcomes including health-related quality of life, with an effect size of 0.33. No standard sample size formula is available for economic evaluations, and a number of methods have been proposed.[47–49] The information which is currently available limit the use of such methods in practical applications. Published data[17] suggest that tonsillectomy may lead to a reduction of approximately 1.5 days per year in missed schooling. Given a reported standard deviation of 4.5, to detect this difference with 80% power we would need approximately 142 children in each arm of the trial assuming a significance level of 5%. A sample size of 142 children in the cohort group will allow us to detect similar differences between the cohort group and propositi. The sample will be stratified by age (4–7, 8–11, 12–15). With a total of 284 children, we will have approximately 47 randomised to each treatment arm in each strata. Given that the standard deviation of the number of sore throats per year is 2.018, we will be able to estimate the difference between treatments in each strata with a standard error of 0.41. (Equivalently we would have 90% power to detect a difference of 1.35 episodes of sore throat per year in each strata assuming a type 1 error of 0.05). It is anticipated that the difference in outcome between the two arms of the trial will be approximately 2 episodes in the second year of follow-up. A sample size of 142 children in each arm should enable us to measure this difference with sufficient precision to undertake a meaningful economic analysis.

Main analysis

An intention to treat analysis will be performed. In particular, children randomised to non-surgical conventional medical treatment will be retained in that group for the analysis even if they subsequently receive a tonsillectomy. The primary clinical outcome measure will be the number of episodes of sore throat. This variable will be analysed using generalised linear modelling assuming a Poisson error structure with a log link function.[50] By fitting the difference between the two experimental groups as a fixed effect, interval estimates of the effect of tonsillectomy (in each of the first two years of follow-up) will be generated. These estimates will then be used in the economic analysis. The same approach will be used to analyse the other outcomes. A Poisson error structure will be assumed for data in the form or a count (such as the number of episodes of absence from school) and normal error structure adopted for continuous variables (such as the quality of life indices).

Secondary analysis

The aim of secondary analysis is to determine whether we can identify groups of children who benefit from surgical treatment. It is hypothesised that disease severity may be an important factor. A severity index based on history of the condition during the year before entry to the study will be derived using data recorded in GP records. The relationship between severity and the effect of tonsillectomy will then be investigated using the modelling approach described above.

Economic analysis

We expect skewness in the distribution of use of resources/costs.[51] In the presence of skewness, the logarithmic transformation of data is not recommended, and the application of non-parametric tests can provide misleading results (economic studies aim to base the analysis on arithmetic means and not median values).[52,53] The non-parametric bootstrap test can be the most appropriate,[53] since it does not require any assumptions about the normality of data and equality of the variance or shape of the distributions. The t-test can be safely used if the sample size is not too small.[52] Depending on the level of skewness of data obtained we will make a judgement on which of these two methods can be safely applied. The mean costs estimates and (incremental) cost-effectiveness ratios, and conventional measures of variances will be reported.[42]

Cohort analysis

The cohort of patients who decline to be randomised will be used to assess the external validity of the main study. Baseline characteristics of the cohort will be compared with those of the study population using standard tests for the

comparison of two independent samples (e.g. the t-test or Mann–Whitney test as appropriate). Outcome for the cohort will be compared with outcome for the two groups of study participants using the modelling approach described above.

Trial steering committee

The study has a Trial Steering Committee which meets 6 monthly. The Trial Steering Committee is responsible for monitoring public interest and ensuring issues relating to research governance are met. The trial does not have a data monitoring committee since it examines routine therapies.

Consumer involvement

Consumer involvement will be encouraged and facilitated throughout the study by the establishment of a consumer advisory panel. We will use the advisory panel to help clarify important outcomes for children and their parents (or carers) and to assist in the development of participant-oriented data-collection methods. By consumer we include here children and their parents as well as representatives of appropriate advocacy groups such as the Patients Association. Our experience of consumer panels in the development and implementation of other studies (e.g. quality of life of people with dementia and treatment for primary biliary cirrhosis of the liver) have highlighted the different types of involvement and the different ways that consumers can be involved in primary research. Parents and children will be involved in an advisory capacity rather than in a full participatory role. We will establish and convene regularly the consumer advisory panel in which the group process will use focus group methods. Throughout the project (at least annually) we will use the advisory panel to voice participants' concerns and to identify participant-oriented solutions to such concerns.

Ethical approval

The conduct of this study will be in accordance with the ethical principles set out in the Declaration of Helsinki. The trial has approval from MREC and all the associated LRECs. The trial also holds a Clinical Trial Authorisation from the MHRA. The trial has NHS R&D and Caldicott Guardian approval from each participating site. There are no particular ethical problems with this trial. The ethical challenge is as with any surgical randomised trial where one arm is an irreversible procedure under general anaesthesia and the other limb effectively maintenance of the status quo with reverting to surgery an outstanding choice. Set against the surgical risk, however, is the essentially curative nature of the intervention – no tonsillitis can occur once the tonsils have been removed. Further, the children under consideration all have qualifying levels of sore throat and would otherwise be eligible for surgery. In other words the issue is more the withholding of tonsillectomy rather than one of random allocation to intervention. All subjects will provide written informed consent before any study procedures are carried out and a participant information sheet will be provided. As part of the consent process participants must agree to researchers and regulatory representatives having access to their medical records. Participants will also be informed that they have the right to withdraw from the study at any time.

The NHS Trust has liability for clinical negligence that harms individuals toward whom they have a duty of care. NHS Indemnity covers NHS staff and medical academic staff with honorary contracts conducting the trial.

Discussion

As with all pragmatic randomised controlled trials it is impossible to control the external environment in which the research is taking place. Since this trial began a number of factors have arisen which could affect the outcome. Firstly there appears to be a reduction in the incidence of respiratory tract infections or at least a reduction in the number of patients presenting to primary health care with respiratory tract infections.[54] This will inevitably lead to a reduction in the number of children being referred to secondary care for recurrent throat infections. Secondly it has come to light that there are marked socio-economic differences in consultation rates in primary health care which are not reflected in operation rates for tonsillitis in secondary care.[55] Lower socio-economic groups use NHS services for tonsillitis less in relation to need than higher socio-economic groups. Again this has implications for the rate of referral to secondary care. The results from the recent National Prospective Tonsillectomy Audit[56] may also have led to an alteration in the surgical techniques favoured by our trial consultants however surgical methods and any associated postoperative complications are recorded for the trial. In addition there is anecdotal evidence that the Government's waiting list initiatives may impact the study by exporting surgery outside the NHS.

List of abbreviations used

Abbreviation	Definition
A&E	Accident and Emergency
CCA	cost consequences analysis
CEA	cost-effectiveness analysis
CHSR	Centre for Health Services Research
CUA	cost utility analysis
ENT	Ear, Nose and Throat
GP	General Practitioner
LREC	Local Research Ethics Committee
MREC	Multi-centre Research Ethics Committee
MHRA	Medicines and Healthcare Products Regulatory Agency
NHS	National Health Service
nvCJD	new variant Creutzfeldt–Jakob Disease
UK	United Kingdon
USA	United States of America

Competing interests

The authors declare that they have no competing interests.

Authors' contibutions

JB, JW, ME, NS, RC, AZ were involved in the original conception and design of the study. AV designed the economic evaluation. CL, KB, CS, NR were involved in the management of the trial including acquisition and interpretation of data. CL drafted the manuscript. All authors were involved in revising the manuscript critically for important intellectual content and have given approval of the final manuscript.

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Appendix 2
Videoscript

NESSTAC patient recruitment video – DIALOGUE, 4 November 2004

Opening credit – NESTAC, North of England Study of Tonsillectomy and Adeno-tonsillectomy in Children.

⇒ Explain addition of sites here, i.e. second text screen NESSTAC with addition of Bradford and Glasgow to x, y and z.

Dialogue: parent, child and doctor

Doctor: Good morning. As you know, your GP has asked you to come up to clinic today so we can discuss the treatment options for John. In children who have recurrent sore throats and tonsillitis there really are two options. The first option, particularly in children who are getting better, is to keep an eye on the episodes of tonsillitis, we need to watch and see what happens. The second option in children who have more severe attacks of tonsillitis or sore throats is to take the tonsils out and this is done with an operation called a tonsillectomy. In some children it's easy to decide what is best to do but in children who are having infrequent episodes of sore throat or tonsillitis or perhaps who are getting less frequent episodes than they had been previously, we can keep an eye on them and watch and wait and see what happens. In children who have more severe episodes of tonsillitis, perhaps those who've been admitted to hospital in the past because of it, then we would think about taking their tonsils out. However, there is a large group of children who are not having those two extremes of sore throats and tonsillitis, in whom we're not so sure what is the best line of management.

Parent: That sounds like John.

Doctor: Yes it's probably the commonest group.

Parent: So what's the best form of treatment for these in-between children?

Doctor: Well, in the UK certainly in the past lots of tonsils have been taken out because it was felt it was the best thing to do. However in Europe the tonsillectomy procedure is actually very uncommon. Tonsillectomy is a safe operation but it's never really been tested to see if it produces long-term benefits for a child's health. On the one hand taking the tonsils out means the child won't get tonsillitis again. But tonsillectomy requires a general anaesthetic and an overnight stay in hospital. In most children who keep the tonsils, the number of episodes of tonsillitis diminishes as time goes on, so we don't really know what the best form of treatment is and that's why the National Health Service have asked us to perform the NESSTAC Trial.

Parent: What sort of trial?

Simple animation showing people going through 2 doors

⇒ Different – little coloured people walking into two groups!

Doctor: Children will be divided into equal groups. Each group will be given one of two different treatments. Both treatments are safe and in common usage and have been used many times in the past, we just don't know which treatment form is best.

Parent: What are the two treatments?

Doctor: The first group is the keep tonsils group. Those children will not have a tonsillectomy and will see their general practitioner as and when required if they have a sore throat. In addition they will also have a hospital follow-up appointment at 9 months to see how they're getting on.

Parent: What's the other treatment?

Doctor: The second group will be placed on a waiting list to have their tonsils out and when they get to the top of the waiting list then they'll be admitted for a tonsillectomy. It may be at that time they also have their adenoids removed as well if the surgeon believes that's the most appropriate treatment.

Parent: So who chooses which children go into which group?

Doctor: No one will choose which group each of the children go into. The decision will be made by random by a computer. That means that each child has a 50/50 chance of going into either the tonsils out group or keeping tonsils group.

Parent: So why has John been chosen to take part in this study?

Doctor: All children who are referred with recurrent tonsillitis or sore throats in the three (five) centres – that's Newcastle, Manchester and Liverpool (and Bradford and Glasgow) – are being invited to take part in the trial. We need approximately 400 children in total.

Parent: Can you tell me a bit more about the keep tonsils group?

Doctor: In the keep tonsils group children who suffer with recurrent episodes of tonsillitis or sore throat will seek the advice of their general practitioner as before. It's quite likely that this group of children will suffer at least one further episode of tonsillitis or sore throat.

Parent: Presumably that would be similar to the usual attacks that John's been getting?

Doctor: Yes. Tonsillitis is unpleasant but it generally clears up within a few days. We know that children who suffer with recurrent sore throats and tonsillitis usually begin to get better after a couple of years or so and we know that hopefully within the next 2 years that John's symptoms will be less severe than they have been previously.

Parent: Are there any risks with this treatment?

Doctor: There are theoretical risks with recurrent tonsillitis but complications are very uncommon indeed. And John has been suffering with recurrent tonsillitis for a long time now and has never had a complication and indeed if he'd had a complication in the past then he wouldn't be considered for the trial.

Parent: So what's involved if the tonsils are taken out?

Doctor: The operation involves coming into hospital usually for an overnight stay. The risks of the procedure are very small indeed and the risks are usually bleeding and infection. Approximately 2 children in every 100 are likely to suffer with an episode of bleeding that would possibly necessitate them having to return to theatre for a further operation. The usual side effects are nausea and vomiting and of course it's normal for children to experience some pain after a tonsillectomy. But that's rather like having another episode of tonsillitis.

Parent: Does having the tonsils out affect the immune system?

Doctor: No, there's no evidence at all that having a tonsillectomy leads to further infections.

Parent: How do I know that John's going to get the best treatment for him?

Doctor: If we knew exactly what the best treatment for John was then we'd offer him that treatment. However John falls into that group of children in whom we're not sure whether a tonsillectomy or whether waiting and seeing is the best form of treatment and that's what we hope to do with the NESTAC trial.

Are there any questions you want to ask, John?

John: Do I have to take any special medicine to take part in the trial?

Doctor: No, there are no special medicines you need to take during this trial. If you have another episode of sore throat or tonsillitis then you may need to go to your general practitioner to get some medicine from him in the normal way. The only other thing we will ask you to do is to complete a diary and some questionnaires. These are to give us an idea of how well you're getting on during the trial period.

Line appears on screen reading 'only children aged 8 and over will be asked to help with the questionnaires and diaries' – move to end for translation

John: What sort of diary?

Doctor: These diaries aren't like a normal sort of diary you keep on holiday where you write whole sentences in the diary. These diaries ask you questions and you ring your response to them. I've got a copy here to show you.

Diary appears full screen with animation showing number being circled as doctor talks.

For example this page asks which symptoms you have had today. If you've had a sore throat and difficulty swallowing you would ring 1 and 3. If you have no symptoms at all then you would ring 10. Do you see what I mean John?

John: Yeah.

Parent: So how long does each child stay in the study?

Doctor: Each child stays in the study for 2 years and during that time we will also ask you to complete four questionnaires.

Parent: What happens if John's condition gets much better or much worse during that time?

Doctor: Well if that happens during the trial it may mean we need to reconsider and take a fresh decision and of course at any stage during the trial you're free to decide to leave the trial if that's what you want to do. If you do agree to let John take part in the trial then you'll be helping us to answer some questions about the treatment of children with recurrent sore throats and tonsillitis in the future. We will ask you to sign a consent form before you take part in the study and we'll also provide an information sheet which you can take home with you. If you have any other questions then you could contact us using the number on the information sheet.

The NESSTAC study team would like to thank you for watching this video.

Screen at end

⇒ Five sites, not three ('In addition to three sites mentioned, the study is now …

⇒ Children over 8 'text' diaries and questionnaires, + parents will be required …

⇒ Keep tonsils group – very few children randomised to the GP have then crossed over and chosen to have their tonsils out 'In the study so far, very few children …

Appendix 3

Patient information sheets

NESSTAC

North of **E**ngland and **S**cotland **S**tudy of **T**onsillectomy and **A**deno-tonsillectomy in **C**hildren

The Tonsil Study Information for Children

How would you like to take part in a research study?

Before you decide, we want to tell you about the study and what taking part in it would mean for you. Please read this leaflet and talk to your parents or other people about it if you want to. Because the leaflet talks about medical treatments, you may not know some of the words. Just ask the nurse or doctor about anything that is not clear. They will be very happy to answer any questions you have. **Thank you for reading this.**

What is the tonsil study?

Having your tonsils out (also called a "tonsillectomy") is a very common operation. But we are not sure whether it is always the best thing to do with children like you. Some doctors think it might be better to wait and see whether children like you get better as they get older rather than having an operation now. At the moment no-one knows the answer. This is what the tonsil study is trying to find out.

Why have I been chosen?

We are asking all children, aged between 4 and 15, who visit this hospital because they get lots of sore throats, to take part in the tonsil study. We need 400 children altogether.

No – you don't have to take part if you don't want to. Nobody will be cross with you if you say that you don't want to take part. If you say yes now but change your mind later, that's OK too. But if you do take part you will be helping to answer an important question which is bothering doctors and nurses around the country.

If you decide to take part you will be put at random into one of two groups. "At random" is like tossing a coin, or pulling a name out of a hat. Except that in this case a computer does it. Neither you nor anyone else will be able to choose which group you get put into.

- The first group is the "wait and see group". This group will carry on seeing their family doctor when they need to for any sore throats or tonsillitis they get. Plus, they will see the hospital doctor in about 9 months time to check how they are doing.

- The second group is the "tonsils out group". This group will be put on the list to have their tonsils out.

You will have the same chance of being in one group as the other.

Whichever group you are in, we will ask you to answer some questions about your health. We will do this by giving you some questionnaires and a diary to fill in. The diary isn't like a diary where you write in sentences about what you did on holiday. In this one we just ask you to circle some numbers. The research nurse can show you the questionnaires and diaries now if you would like to see them. If you decide to take part in the study, the research nurse will show you how to fill in the questionnaires and diaries.

DOI: 10.3310/hta14130

Are there any risks to taking part?

All medical treatments carry some risks. For example, medicine to treat sore throats sometimes gives children an upset tummy. The treatments in the tonsil study are not new and lots of children have had them before. So there are no special risks to taking part. We just don't know which treatment is best. The normal risks that you can expect with the treatments in the tonsil study are:

1. Wait and see group

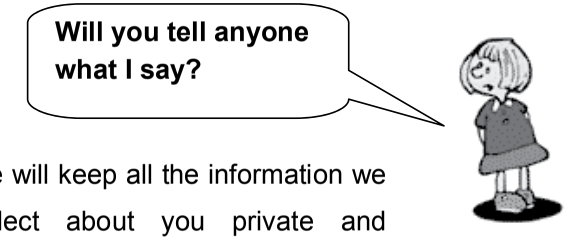
There is a high chance that children who don't have their tonsils out will get at least one extra sore throat or attack of tonsillitis. As you know, this can be unpleasant but it usually clears up within a few days without any serious problems. Sometimes, a sore throat leads onto another problem like an ear infection. Very rarely, a sore throat gets so bad that a child has to go into hospital.

2. Tonsils out group

If you have your tonsils out you will have to have a stay in hospital. You will be put to sleep while the doctor takes your tonsils out. After the operation you will probably feel a bit sick and have a sore throat. You will have to have some time off school. Some children get an infection or have bleeding after the operation.

Will I get anything out of taking part in the study?

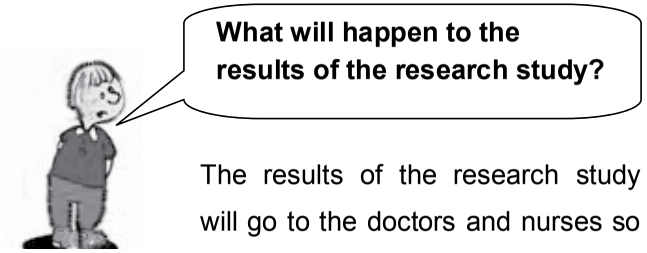
Both the treatments in the tonsil study are safe and help children with sore throats. But you won't get any special treatment because you're taking part in the tonsil study. We hope that you will feel proud to be helping answer an important question about children's health. This will help us to treat children with sore throats and tonsillitis better in the future.



We will keep all the information we collect about you private and confidential.

We will need to tell your family doctor that you are taking part in this study, and that you have said it is OK for us to look at your medical records. But we will not tell your family doctor, or anyone else, anything that you tell us, unless you ask us to.

The only time we might have to tell somebody about something you tell us, is if you tell us something that makes us very worried about you. But we would still try and check with you first before we told anyone.



The results of the research study will go to the doctors and nurses so that they will know better how to treat children with tonsillitis. If you'd like to know the results of the research study please tell us.

Just ask the nurse or the doctor at the hospital. Their names are at the bottom of this page.

Newcastle upon Tyne:
Professor J Wilson and Mr S Carrie
Liverpool: Mr R Clarke
Manchester: Mr A Zarod
Bradford: Mr C Raine
Glasgow: Mr H Kubba

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Newcastle upon Tyne Hospitals NHS Trust
Freeman Hospital

Royal Liverpool Children's NHS Trust
Alder Hey Children's Hospital

Manchester Children's Hospitals NHS Trust
Booth Hall Children's Hospital

Bradford Teaching Hospitals NHS Trust
Bradford Royal Infirmary

NHS Greater Glasgow
Royal Hospital for Sick Children (Yorkhill)
&
Centre for Health Services Research
University of Newcastle

NHS

DOI: 10.3310/hta14130

Teenager trial information sheet

NESSTAC

North of England and Scotland
Study of Tonsillectomy and Adeno-tonsillectomy
in Children

Teenager Information Sheet

Randomised controlled trial
Would you like to take part in a research study? Before you decide we want to tell you why the research is being done and what it will involve. Please read this leaflet and talk to your parents or other people about it if you want to. Ask the nurse or doctor about anything that is not clear. They will be very happy to answer any questions you have. Thank you for reading this.

What is the NESSTAC study?
Having your tonsils out (also called a "tonsillectomy") is a very common operation. But we are not sure whether it is always the best thing to do with teenagers like you. Some doctors think it might be better to wait and see whether teenagers like you get better as they get older rather than having an operation now. At the moment no one knows what's best. This is what the NESSTAC study is trying to find out.

Why have I been chosen?
We are asking all children and teenagers, aged between 4 and 15, who visit this hospital because they get lots of sore throats, to take part in the tonsil study. It is important that we have lots of teenagers as well as younger children. We need 400 children and teenagers altogether.

Do I have to take part?
It is up to you to decide whether or not to take part. Nobody will be annoyed with you if you say that you don't want to take part. If you say yes now but change your mind later, that's OK too. We are not paying your doctor to include you in the NESSTAC study. But if you do take part you will be helping to answer an important question which is bothering doctors and nurses around the country.

What is a randomised controlled trial?
When we do not know the best way of helping people with an illness, we need to compare different treatments. For the comparison to be fair, we need to make sure that the sort of people in each group are exactly the same. We do this by putting people into groups "at random" – which is rather like tossing a coin, or pulling a name out of a hat. Except that in NESSTAC a computer does it.

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Newcastle upon Tyne Hospitals NHS Trust
Freeman Hospital

Royal Liverpool Children's NHS Trust
Alder Hey Children's Hospital

Manchester Children's Hospitals NHS Trust
Booth Hall Children's Hospital

Bradford Teaching Hospitals NHS Trust
Bradford Royal Infirmary

NHS Greater Glasgow
Royal Hospital for Sick Children (Yorkhill)

Randomised controlled trials are only ever carried out when doctors are not sure which way of treating people is best – if it were clear that having your tonsils out would be best for you then you would not be being asked to take part in this trial.

What will happen if I take part?
If you decide to take part in the NESSTAC study, you will be put at random into one of two groups.

- The first group is the "wait and see group". This group will carry on seeing their family doctor when they need to for any sore throats or tonsillitis they get. Plus, they will see the hospital doctor in about 9 months time to check how they are doing.

- The second group is the "tonsils out group". This group will be put on the list to have their tonsils out. [It is possible that they may also have their adenoids out at the same time (this is called an adeno-tonsillectomy). Having the adenoids out as well is quite normal when having your tonsils out. If this happens to you it will be because the doctor doing the operation thought it was necessary. This decision has nothing to do with the NESSTAC trial.]

You will have a 1 in 2 (or 50/50) chance of being in either group. Neither you nor anyone else will be able to choose which group you get put into. You therefore need to be happy whichever group you get put into if you are going to take part in the trial.

Whichever group you are in, we will ask you to answer some questions about your health. We will do this by giving you some questionnaires and a diary to fill in. The diary isn't like a diary where you write in sentences about what you did on holiday. In this one we just ask you to circle some numbers. The research nurse can show you the questionnaires and diaries now if you would like to see them. If you decide to take part in the study, the research nurse will show you how to fill in the questionnaires and diaries.

If you do not think you would be prepared to fill in these questionnaires and diaries then you should not agree to take part in the trial.

Are there any risks to taking part?
All medical treatments carry some risks. For example, antibiotics to treat sore throats sometimes gives people an upset stomach. The treatments in the tonsil study are not new and lots of children and teenagers have had them before. So there are no special risks to taking part. We just don't know which treatment is best. The normal risks that you can expect with the treatments in the tonsil study are:

1. Wait and see group
There is a high chance that children and teenagers in the study who don't have their tonsils out will get at least one extra sore throat or attack of tonsillitis. As you know, this can be unpleasant but it usually clears up within a few days without any serious problems. Sometimes, a sore throat leads onto another problem like an ear infection. Very rarely, a sore throat gets so bad that a person has to go into hospital.

2. Tonsils out group
If you have your tonsils out you will have to have a stay in hospital. You will be put to sleep while the doctor takes your tonsils out. After the operation you will probably feel a bit sick and have a sore throat. You will have to have some time off school. It's possible you could get an infection or have bleeding after the operation.

Will I get anything out of taking part in the study?
Both the treatments in the tonsil study are safe and help children and teenagers with sore throats. But you won't get any special treatment because you're taking part in the tonsil study. We hope that you will feel proud to be helping answer an important question about children and teenagers' health. This will help us to treat children and teenagers with sore throats and tonsillitis better in the future.

Will you tell anyone what I say?
We will keep all the information we collect about you private and confidential.

We will need to tell your family doctor that you are taking part in this study, and that you have said it is OK for us to look at your medical records. But we will not tell your family doctor, or anyone else, anything that you tell us, unless you ask us to.

The only time we might have to tell somebody about something you tell us, is if you tell us something that makes us very worried about you. But we would still try and check with you first before we told anyone else.

What will happen to the results of the research study?
The results of the research study will go to the doctors and nurses so that they will know better how to treat children and teenagers with tonsillitis. If you'd like to know the results of the research study please tell us.

I want to ask another question about the tonsil study
Just ask the nurse or the doctor at the hospital. Their names are at the bottom of this page.

For more information please contact:

Newcastle upon Tyne:
Professor Janet Wilson and Mr Sean Carrie

Liverpool: Mr Ray Clarke

Manchester: Mr Andrew Zarod

Bradford: Mr Christopher Raine

Glasgow: Mr Haytham Kubba

Mrs Mary Dickinson
NESSTAC
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Parent trial information sheet

NESSTAC

North of England and Scotland Study of Tonsillectomy and Adeno-tonsillectomy in Children

Parent Information Sheet

Randomised controlled trial
You and your child are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

What is the NESSTAC study?
Tonsillectomy ("having your tonsils out") is a very common operation in Britain and other countries. Usually it is carried out on children who have lots of sore throats or tonsillitis. It is a safe operation but has never been properly tested to see whether it leads to a long-term improvement in children's health. On the one hand having tonsils out clearly means that the tonsils can no longer become infected. On the other hand, tonsillectomy means a general anaesthetic, a stay in hospital and the discomfort associated with having surgery. Children who have their tonsils out may still get other sore throats. And children who suffer from tonsillitis but *don't* have their tonsils out often "grow out" of tonsil infections after a year or two.

At one time it was routine for children suffering from lots of sore throats or tonsillitis to have their tonsils out. Doctors nowadays are not so sure that this is the right thing to do. In the UK an average of 2.3 children in every 1000 children will have their tonsils removed. But within the UK the rate varies a lot from place to place. And in some other countries such as Germany it is much less common to have your tonsils out.

Because of the uncertainty about what is best to do for children who get sore throats and tonsillitis, the National Health Service (NHS) has funded the University of Newcastle, together with hospitals in Newcastle, Manchester, Liverpool, Bradford and Glasgow, to carry out a randomised controlled trial of treatment for sore throat or tonsillitis. This study started in 2001 and should finish in 2008.

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Manchester Children's Hospitals NHS Trust
Booth Hall Children's Hospital

Bradford Teaching Hospitals NHS Trust
Bradford Royal Infirmary

NHS Greater Glasgow
Royal Hospital for Sick Children (Yorkhill)

Why has my child been chosen?
All children aged between 4 and 15 who are referred for sore throats and tonsillitis to the 5 hospitals taking part in the study are being considered for this trial. We need to include 400 children in the trial.

Do I have to take part?
It is up to you to decide whether or not to take part. If you decide to take part you are still free to opt out at any time and without giving a reason (though it may help the researchers if you do give a reason). Your child will get the best possible care as a patient no matter what you decide to do. Your doctor is not being paid to include you in the NESSTAC trial.

What is a randomised controlled trial?
When we do not know the best treatment, we need to compare different approaches. For the comparison to be fair, we need to make sure that there is no difference between the people in the groups that are being compared. We do this by putting people into groups randomly – which is rather like tossing a coin.

In the case of NESSTAC, a central computer is used to decide which group people are put into. Neither you nor your doctor can choose which group your child is put into. You therefore need to be happy with whichever group your child gets put into if you are going to be involved in this trial.

Randomised controlled trials are only ever carried out when doctors are not sure which way of treating people is best – if it were clear that having your tonsils out would benefit your child then you would not be being asked to take part in this trial.

What are the comparison groups in NESSTAC?
In the NESSTAC trial, children will be put, by chance, into one of **two** groups.

- The first group will be medical management. This means that they will continue to have treatment from their GP for any bouts of sore throat or tonsillitis. In addition they will be given a follow up appointment to see the hospital doctor in 9-12 months time to check how they are doing. At this time, you and your hospital doctor can think again about whether having your child's tonsils out would be a good idea. This type of approach is sometimes called "watchful waiting".

- The second group will be surgical treatment. This means that they will be put onto the waiting list to have their tonsils out now. They may also have their adenoids out at the same time (this is called an adeno-tonsillectomy) if the doctor thinks this is necessary. [Having the adenoids out as well is quite normal. If this happens to your child it will be because the surgeon and you are agreed that this is necessary. This decision has nothing to do with the NESSTAC trial.] While children are waiting to have their tonsils out they should see their family doctor or GP as usual for any bouts of sore throat or tonsillitis.

Your child will have a 1 in 2 (or 50/50) chance of being in either group. Once your child has been assigned to one of the groups you are still free to switch to the alternative course of treatment without having to withdraw from the trial.

What will happen if I agree to take part?
First, you will be asked to sign a consent form to show that you are happy to take part in the study. You will also be asked to sign to say that you are happy for a data collector to get some information about your child's sore throats from the GP's records, at the end of the study. If there is anything on the consent form, or in this

information sheet, that you do not understand or agree with please tell the nurse before you sign the form. You will be given a copy of your signed consent form and of this information sheet to keep.

Next your child will be randomised to either the surgical (tonsillectomy) or the medical (GP and hospital follow up) group.

Whichever group you are in, you will be asked to complete 4 questionnaires over the next 2 years. These questionnaires will have questions about your child's health, and the impact of any illnesses they have on both you and your child. Some of these questions will be about the costs to you of your child's illnesses. If your child is aged 8 or over then there will be separate questionnaires for them to fill in. We will also want you to complete weekly diaries of sore throat symptoms. We estimate that the diary will take 5 minutes a week to fill in and that each questionnaire should take no more than 15 minutes to complete. We will post these out to you with a reply paid envelope for you to return them to us. The research nurse can show you the questionnaires and diaries now if you would like to see what they will involve. If you decide to take part in the study, the research nurse will show you how to complete the questionnaires and diaries. If you do not think you would be prepared to fill in these questionnaires and diaries then you should not agree to take part in the trial.

What are the possible disadvantages and risks of taking part?
All the treatments being used in the NESSTAC trial are part of normal medical care – there are no special risks from taking part. The normal risks associated with each of the treatment options are outlined below.

1. Medical management group
There is a high chance that children in the medical management group will suffer at least one additional bout of tonsillitis. As you know, this can be unpleasant but it usually clears up within a few days without any serious problems. There is a small risk that a bout of tonsillitis could lead on to another problem such as an ear infection, and an even smaller risk that a bout of tonsillitis could become more serious and require hospital treatment. It is difficult to give numbers for these risks. Some studies have shown complications happen after tonsillitis in about 1% of cases. But this includes figures for adults and complications are less common in children.

2. Surgical treatment group
As with any operation, there are some risks associated with tonsillectomy but these are small. The main risks are of infection and haemorrhage (severe bleeding) after the operation. Around 2% of children may have a haemorrhage – this means that out of the 200 children who will be in the NESSTAC surgical treatment group we might expect 4 to have a haemorrhage. Some of these children may need another operation. More common side effects include feeling sick or being sick, and minor bleeding after the operation. There is also likely to be a sore throat – typically this may be like that felt during a bout of tonsillitis.

Any person or parent consenting to undergo tonsillectomy should understand that there have been, over the past 20 years in the UK a very small number of cases of fatal haemorrhage following tonsil removal. This is a potential risk in any type of surgical operation and fortunately in the present day is extremely rare indeed.

What are the possible benefits of taking part in the study?
There are no direct benefits to you and your child from taking part in the study. But you will be helping to answer an important question about children's health. The aim of the study is to treat future children with sore throats and tonsillitis better.

Will my taking part in this study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital or the GP surgery will have your name and address removed so that you cannot be recognised from it. (We will need to have a record of your name and address so that we can send you questionnaires and diaries – but this will be kept separate from any other details about you.)

We will need to tell your child's GP that you are taking part in this trial, and to let them know that you have given us permission to look at their medical records. But we will not tell your GP, or anyone else, anything that you say in the diaries or questionnaires, unless you ask us to.

What will happen to the results of the research study?
The results of the research study will go to the National Health Service so that they will know better how to treat children with tonsillitis. No one who reads the results will be able to identify your child. If you would like to know the results of the research study please say so when you fill in the consent form. We will send you a copy of the results at the end of the study – this will be in 2008.

Who can I contact for more information?
You can ask the nurse who gave you this sheet or the doctor you saw at the hospital for more information. Their names are at the bottom of this page. These are the best people to ask if you have any questions about treatments for sore throats or about your child's medical situation. Or, you can contact the NESSTAC study team at Newcastle University on 0191 222 8709 (their address is shown below). Please ask for Mary Dickinson, the project secretary.

Please do not contact the hospital staff if your child gets a sore throat – in this case the best person to contact is your own GP, just as you have done up to now.

For more information please contact:

Newcastle upon Tyne:
Professor Janet Wilson and Mr Sean Carrie

Liverpool: Mr Ray Clarke

Manchester: Mr Andrew Zarod

Bradford: Mr Christopher Raine

Glasgow: Mr Haytham Kubba

Mrs Mary Dickinson
NESSTAC
Centre for Health Services Research
Newcastle University
21 Claremont Place
Newcastle upon Tyne
NE2 4AA

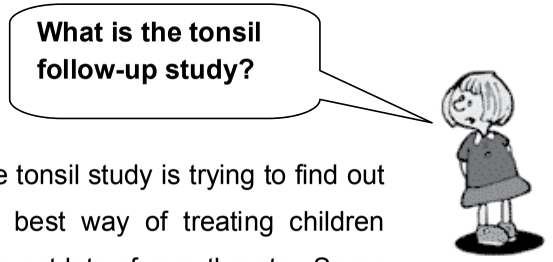
☎ 0191 222 8709

NESSTAC

North of **E**ngland and **S**cotland **S**tudy of **T**onsillectomy and **A**deno-tonsillectomy in **C**hildren

The Tonsil Follow-up Study Information for Children

Before you decide, we want to tell you about the study and what taking part in it would mean for you. Please read this leaflet and talk to your parents or other people about it if you want to. Because the leaflet talks about medical treatments, you may not know some of the words. Just ask the nurse or doctor about anything that is not clear. They will be very happy to answer any questions you have. **Thank you for reading this.**

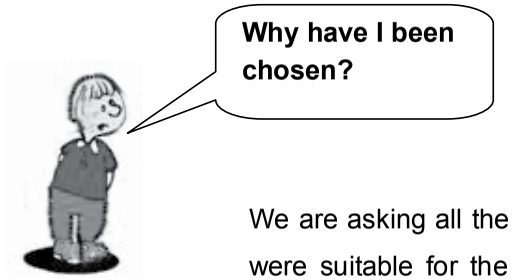


The tonsil study is trying to find out the best way of treating children who get lots of sore throats. Some parents and children have agreed to take part in the main part of the tonsil study. In the main part of the tonsil study, children are put at random in either the "wait and see" group or the "tonsils out" group.

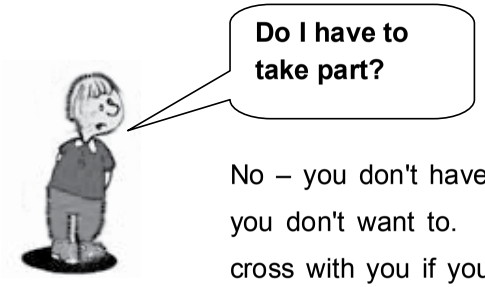
Other parents and children have decided that they would prefer not to take part in the main part of the study. This is fine – no one will be cross with them because of what they decided. However we would like to follow up some of these children too. This is so that we can see what happens normally – when parents and children together with their doctors decide what happens. This is what we are calling the tonsil follow-up study.

DOI: 10.3310/hta14130

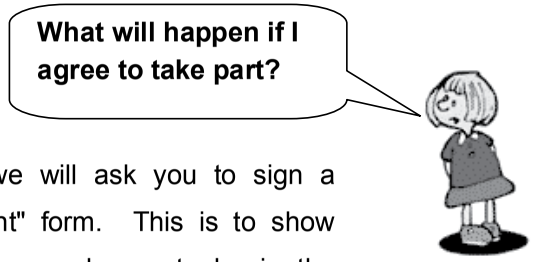
The only thing we want to do with the children taking part in the tonsil follow-up study is to find out about their treatment choices and the illnesses they get. Taking part in the tonsil follow-up study will make no difference at all to your treatment. You and your doctors and parents will be able to choose the treatment you prefer. Just like you would if you weren't taking part in any study.



We are asking all the children who were suitable for the main part of the tonsil study, but chose not to take part, to be in the tonsil follow-up study. We need to include up to 400 children in the tonsil follow-up study.



No – you don't have to take part if you don't want to. Nobody will be cross with you if you say you don't want to take part. If you say yes now but change your mind later, that's OK too. But if you do take part you will be helping to answer an important question which is bothering doctors and nurses around the country.



First, we will ask you to sign a "consent" form. This is to show that you are happy to be in the tonsil follow-up study. We will need to get some information about your sore throats from your doctor's records. The form asks you to say if this is OK. Please tell the nurse before you sign the form if you don't understand, or don't like something in this information sheet or the consent form.

You will then have the treatment that you and your parents and doctor decide is best for you.

We will ask you to answer some questions about your health. We will do this by giving you some questionnaires and a diary to fill in. The diary isn't like a diary where you write in sentences about what you did on holiday. In this one we just ask you to circle some numbers. The research nurse can show you the questionnaires and diaries now if you would like to see them. If you decide to take part in the study, the research nurse will show you how to fill in the questionnaires and diaries.

Are there any reasons why I might not want to take part?

The only downside to taking part is the time taken to fill in the questionnaires and diaries. There are no risks from taking part in the tonsil follow-up study.

Will I get anything out of taking part in the study?

You won't get any special treatment because you're taking part in the tonsil follow-up study. We hope that you will feel proud to be helping answer an important question about children's health. This will help us to treat children with sore throats and tonsillitis better in the future.

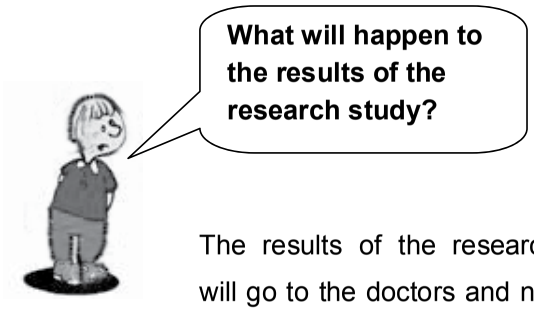
Will you tell anyone what I say?

We will keep all the information we collect about you private and confidential.

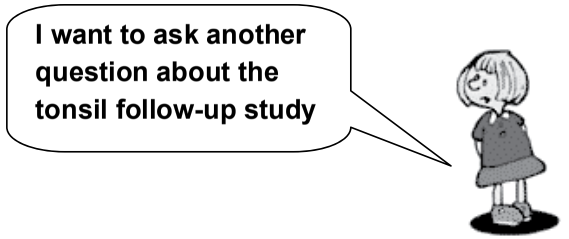
We will need to tell your family doctor that you are taking part in this study, and that you have said it is OK for us to look at your medical records. But we will not tell your family doctor, or anyone else, anything that you tell us, unless you ask us to.

DOI: 10.3310/hta14130

The only time we might have to tell somebody about something you tell us, is if you tell us something that makes us very worried about you. But we would still try and check with you first before we told anyone else.



The results of the research study will go to the doctors and nurses so that they will know better how to treat children with tonsillitis. If you'd like to know the results of the research study please tell us.



Just ask the nurse or the doctor at the hospital. Their names are at the bottom of this page.

Newcastle upon Tyne:
Professor J Wilson and Mr S Carrie
Liverpool: Mr R Clarke
Manchester: Mr A Zarod
Bradford: Mr C Raine
Glasgow: Mr H Kubba

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Newcastle upon Tyne Hospitals NHS Trust
Freeman Hospital

Royal Liverpool Children's NHS Trust
Alder Hey Children's Hospital

Manchester Children's Hospitals NHS Trust
Booth Hall Children's Hospital

Bradford Teaching Hospitals NHS Trust
Bradford Royal Infirmary

NHS Greater Glasgow
Royal Hospital for Sick Children (Yorkhill)
&
Centre for Health Services Research
University of Newcastle

NHS

Teenager cohort information sheet

NESSTAC

North of England and Scotland Study of Tonsillectomy and Adeno-tonsillectomy in Children

Teenager Information Sheet

Follow-up study

Would you like to take part in a research study? Before you decide, we want to tell you about the study and what taking part in it would mean for you. Please read this leaflet and talk to your parents or other people about it if you want to. Ask the nurse or doctor about anything that is not clear. They will be very happy to answer any questions you have. Thank you for reading this.

What is the NESSTAC follow-up study?
The NESSTAC study is trying to find out the best way of treating children and teenagers who get lots of sore throats. Some people have agreed to take part in the NESSTAC randomised controlled trial. In this, children and teenagers are put at random in either the "wait and see" group or the "tonsils out" group.

Other people have decided that they would prefer not to take part in the NESSTAC randomised controlled trial. This is fine – no one will be annoyed with them because of what they decided. However we would like to follow up some of these children and teenagers too. This is so that we can see what happens normally – when parents and teenagers together with their doctors decide what happens. This is what we are calling the NESSTAC follow-up study.

The only thing we want to do with the children and teenagers taking part in the follow-up study is to find out about their treatment decisions and the illnesses they get. Taking part in the NESSTAC follow-up study will make no difference at all to the treatment you get. You and your doctors and parents will be able to choose the treatment you prefer. Just like you would if you weren't taking part in any study.

Centre for Health Services Research
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NHS

Newcastle upon Tyne Hospitals NHS Trust
Freeman Hospital

Royal Liverpool Children's NHS Trust
Alder Hey Children's Hospital

Manchester Children's Hospitals NHS Trust
Booth Hall Children's Hospital

Bradford Teaching Hospitals NHS Trust
Bradford Royal Infirmary

NHS Greater Glasgow
Royal Hospital for Sick Children (Yorkhill)

Why have I been chosen?
We are asking all the children and teenagers who were suitable for the NESSTAC randomised controlled trial, but chose not to take part, to take part in the NESSTAC follow-up study. It is important that we have lots of teenagers as well as younger children. We need to include up to 400 children and teenagers altogether in the follow-up study.

Do I have to take part?
No – you don't have to take part if you don't want to. Nobody will be annoyed with you if you say that you don't want to take part. If you say yes now but change your mind later, that's OK too. But if you do take part you will be helping to answer an important question which is bothering doctors and nurses around the country.

What will happen if I agree to take part?
First, we will ask you to sign a consent form. This is to show that you are happy to be in the NESSTAC follow-up study. We will need to get some information about your sore throats from your doctor's records. The form asks you to say if this is OK. Please tell the nurse before you sign the form if you don't understand, or don't like, something in this information sheet or the consent form.

You will then have the treatment that you and your parents and doctor decide is best for you.

We will ask you to answer some questions about your health. We will do this by giving you some questionnaires and a diary to fill in. The diary isn't like a diary where you write in sentences about what you did on holiday. In this one we just ask you to circle some numbers. The research nurse can show you the questionnaires and diaries now if you would like to see them. If you decide to take part in the study, the research nurse will show you how to fill in the questionnaires and diaries.

Are there any reasons why I might not want to take part?
The only downside to taking part is the time taken to fill in the questionnaires and diaries. There are no risks from taking part in the NESSTAC follow-up study.

Will I get anything out of taking part in the study?
You won't get any special treatment because you're taking part in the NESSTAC follow-up study. We hope that you will feel proud to be helping answer an important question about children and teenagers' health. This will help us to treat children and teenagers with sore throats and tonsillitis better in the future.

Will you tell anyone what I say?
We will keep all the information we collect about you private and confidential.

We will need to tell your family doctor that you are taking part in this study, and that you have said it is OK for us to look at your medical records. But we will not tell your family doctor, or anyone else, anything that you tell us, unless you ask us to.

The only time we might have to tell somebody about something you tell us, is if you tell us something that makes us very worried about you. But we would still try and check with you first before we told anyone else.

What will happen to the results of the research study?
The results of the research study will go to the doctors and nurses so that they will know better how to treat children and teenagers with tonsillitis. If you'd like to know the results of the research study please tell us.

I want to ask another question about the NESSTAC study
Just ask the nurse or the doctor at the hospital. Their names are at the bottom of this page.

For more information please contact:

Newcastle upon Tyne:
Professor Janet Wilson and Mr Sean Carrie

Liverpool: Mr Ray Clarke

Manchester: Mr Andrew Zarod

Bradford: Mr Christopher Raine

Glasgow: Mr Haytham Kubba

Mrs Mary Dickinson
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☎ 0191 222 8709

Parent cohort information sheet

NESSTAC

North of England and Scotland
Study of Tonsillectomy and Adeno-tonsillectomy
in Children

Parent Information Sheet

Follow-up study
You and your child are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Thank you for reading this.

What is the NESSTAC follow-up study?
The NESSTAC study is measuring the effects of removing the tonsils of children with regular sore throats. Some parents and children have agreed to take part in the NESSTAC randomised controlled trial. This will compare surgical treatment (tonsillectomy) with medical treatment from GP and hospital doctors.

Other parents and children have decided that they would prefer not to take part in the randomised controlled trial. This is fine and will in no way affect the standard of care that they will receive. However we would like to follow up some of these children too. This will allow us to compare the trial results with what happens in the usual course of events, outside any trial. This is what we are calling the NESSTAC follow-up study.

The only thing we want to do with the children taking part in the follow-up study is to collect information about the treatment they receive and the illnesses they suffer from. Joining the follow-up study will make no difference whatsoever to the treatment you are offered.

Why has my child been chosen?
All children who are suitable for the NESSTAC randomised controlled trial but have chosen not to take part are being considered for the NESSTAC follow-up study. We need to include up to 400 children in the follow-up study.

Centre for Health Services Research
21 Claremont Place
Newcastle upon Tyne
NE2 4AA

NHS

Newcastle upon Tyne Hospitals NHS Trust
Freeman Hospital

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Manchester Children's Hospitals NHS Trust
Booth Hall Children's Hospital

Bradford Teaching Hospitals NHS Trust
Bradford Royal Infirmary

NHS Greater Glasgow
Royal Hospital for Sick Children (Yorkhill)

Do I have to take part?
It is up to you to decide whether or not to take part. If you decide to take part you are still free to opt out at any time and without giving a reason (though it might help the researchers if you do give a reason). Your child will get the best possible care as a patient, no matter what you decide to do. Your doctor is not being paid to include you in the follow-up study.

What will happen if I agree to take part?
First, you will be asked to sign a consent form to show that you are happy to take part in the NESSTAC follow-up study. You will also be asked to sign to say that you are happy for a data collector to get some information about your child's sore throats from the GP's records, at the end of the study. If there is anything on the consent form, or in this information sheet, that you do not understand or agree with please tell the nurse before you sign the form. You will be given a copy of your signed consent form and of this information sheet to keep.

Your child will then have the treatment that you and your doctor decide is best for him or her. **The NESSTAC study will not influence the treatment that your child gets, in any way.**

You will be asked to complete 4 questionnaires over the next 2 years. These questionnaires will have questions about your child's health, and the impact of any illnesses they have on both you and your child. Some of these questions will be about the costs to you of your child's illnesses. There is also a simple health diary to complete. We estimate that each questionnaire should take no more than 15 minutes to complete. If your child is aged 8 or over then there will be separate questionnaires for them to fill in as well as a diary. We will post these out to you with a reply paid envelope for you to return them to us. The research nurse can show you the questionnaires and diaries now if you would like to see what they will involve. If you decide to take part in the study, the research nurse will show you how to complete the questionnaires and diaries. If you do not think you would be prepared to fill in these questionnaires and diaries then you should not agree to take part in the study.

What are the possible disadvantages and risks of taking part?
Apart from the time taken to fill in the questionnaires and diaries, there are no disadvantages or risks to you and your child from taking part in the NESSTAC follow-up study.

What are the possible benefits of taking part in the study?
There are no direct benefits to you and your child from taking part in the study. But you will be helping answer an important question about children's health. The aim of the study is to treat future children with sore throats and tonsillitis better.

Will my taking part in this study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you that leaves the hospital or the GP surgery will have your name and address removed so that you cannot be recognised from it. (We will need to have a record of your name and address so that we can send you questionnaires and diaries – but this will be kept separate from any other details about you.)

We will need to tell your GP that you have given us permission to look at your child's medical records. But we will not tell your GP, or anyone else, anything that you say in your questionnaires and diaries, unless you ask us to.

What will happen to the results of the research study?
The results of the research study will go to the National Health Service so that they will know better how to treat children with tonsillitis. No one who reads the results will be able to identify your child. If you would like to know the results of the research study please say so when you fill in the consent form. We will send you a copy of the results at the end of the study – this will be in 2008.

Who can I contact for more information?
You can ask the nurse who gave you this sheet or the doctor you saw at the hospital for more information. Their names are at the bottom of this page. These are the best people to ask if you have any questions about treatments for sore throats or about your child's medical situation. Or, you can contact the NESSTAC study team at Newcastle University on 0191 222 8709 (their address is shown below). Please ask for Mary Dickinson, the project secretary.

Please do not contact the hospital staff if your child gets a sore throat – in this case the best person to contact is your own GP, just as you have done up to now.

For more information please contact:

Newcastle upon Tyne:
Professor Janet Wilson and Mr Sean Carrie

Liverpool: Mr Ray Clarke

Manchester: Mr Andrew Zarod

Bradford: Mr Christopher Raine

Glasgow: Mr Haytham Kubba

Mrs Mary Dickinson
NESSTAC
Centre for Health Services Research
Newcastle University
21 Claremont Place
Newcastle upon Tyne
NE2 4AA

☎ 0191 222 8709

Appendix 4
Consent form

Parent/Guardian consent form

NESSTAC patient identification number:

Consent form

NESSTAC

NESSTAC randomised controlled trial

	Please put your initials in the box:
1. I have read and understand the NESSTAC randomised controlled trial information sheet dated ……. and have had the opportunity to ask questions.	
2. I understand that I do not have to take part in the NESSTAC randomised controlled trial. I also understand that I can opt out at any time, without giving a reason, and without this affecting my child's medical care or legal rights.	
3. I understand that sections of my child's medical notes, including their GP records, may be looked at by responsible individuals from Newcastle University. I give permission for these individuals to have access to my child's records.	
4. I agree to my child being included in the NESSTAC randomised controlled trial.	
5. I agree to the information provided in this study being managed by the University of Newcastle.	

Name of parent **(Please PRINT name and give title eg Mr/Mrs/Ms/Miss)**	Date	Signature
Name of person taking consent	Date	Signature

To be filled in by ENT consultant

Name of child……..

Child's hospital:……

Child's hospital number:……..

Child's ENT consultant:……..

Signed:……. Date:…….

1 for patient; 1 for researcher; 1 to be kept with hospital notes

Appendix 5

Baseline and outcome questionnaire

db	cc	pv	va

CONFIDENTIAL

						1	1

1 8

UNIVERSITY OF NEWCASTLE

NESSTAC

North of **E**ngland and **S**cotland **S**tudy of **T**onsillectomy and **A**deno-tonsillectomy in **C**hildren

The Tonsil Study

Parent's Questionnaire

How to answer these questions

Throughout this questionnaire we talk about your child's "condition". By "condition" we mean any **sore throats** your child has had, together with any **complications as a result of the sore throats** and any treatment **side-effects**. We are interested in finding out whether your child's condition has affected everyday life, both for him or her and for you and your family. We would also like to know about any use of health services for your child's condition. **It is important to hear from you even if your child has not suffered any sore throats for a while.**

Some questions ask you to think back over the **last month** and some over the **last three months**. This is because we realise that some things are easier to recall than others. Please read the instructions carefully throughout the questionnaire.

Almost all the questions can be answered simply by ringing a number next to the answer which applies to your child. Occasionally you are asked to write in the answer.

Usually, after answering a question, you should go on to the next one. Sometimes there will be an instruction in a shaded box next to the number you ring, telling you which question to answer next.

Example:	Yes 1	**Answer a)**
	No..... 2	**Go to Q7**

In this example if you circle 1 for 'Yes' you should go on to answer part a).

If you circle 2 for 'No' you should go to question 7.

If you are unsure about how to reply to a particular question, please give the best answer you can and write in any other comments you have. Please contact us if you have any questions – a contact number is given at the end of the questionnaire.

The information you provide will be **strictly confidential**. Your child's name will not appear on the questionnaire and any information you give us will not be used in any way that could identify you or your child personally.

Your child's condition

1. **Over the last three months,** has your child had any sore throats at all?

Yes..... 1 **Answer Q2**

No..... 2 **Go to Q8** 9

---

2. **Over the last three months,** how many sore throats, each lasting **less than two weeks**, has your child had?

☐☐ sore throats 10-11

---

3. How long did your child's **most recent** sore throat last?

☐☐ days 12-13

---

4. **Over the last 3 months,** has your child had any **constant or chronic** sore throats that lasted more than 2 weeks?

Yes..... 1 **Answer a)**

No..... 2 **Go to Q5** 14

If yes, a) How many weeks were they affected in total? ☐☐ weeks 15-16

---

5. Sometimes sore throats can lead on to other problems or complications. Did any of the episodes of sore throat your child had result in any complications?

Yes, ear infection..... 1

Yes, other complications (*please say what these were below)*..... 2

.....

No, no complications..... 3

Please ring <u>all</u> that apply 17 19

6. **Over the last 3 months**, has your child taken any antibiotics to treat his/her sore throats and/or related complications?

Yes..... 1	**Answer Q7**	
No..... 2	**Go to Q8**	20

---

7. Sometimes children get side-effects from the antibiotics they take. **Over the last three months**, has your child suffered any of these symptoms either while they were taking or during the week after taking antibiotics?

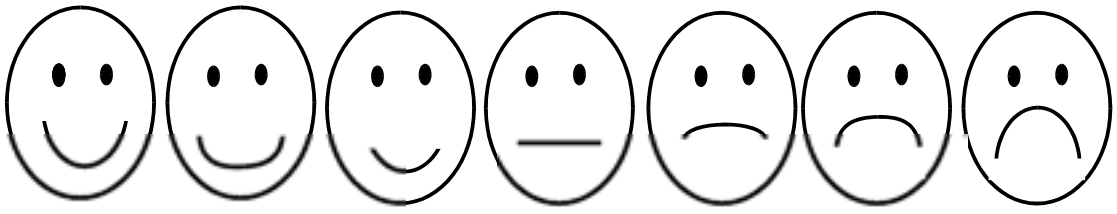
Feeling sick (nausea) and or being sick (vomiting)..... 1	**Please ring <u>all</u> that apply**	21
Diarrhoea..... 2		
Skin rash..... 3		
Thrush (yeast infection)..... 4		
Other side-effects (*please say what these were*)..... 5		
.....		
No, no side effects..... 6		26

The next set of questions asks you to say how much you **agree or disagree** with each of the statements. Please show how much you agree or disagree **by circling one number on each line**.

		Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree	
8.	**Over the last 3 months**, my child has not grown or not put on as much weight as I think he/she should	1	2	3	4	5	27
9.	**Over the last 3 months**, my child has put on too much weight	1	2	3	4	5	
10.	**Over the last 3 months**, my child has missed out on their **usual day to day activities** (eg playing with friends, regular clubs and hobbies) **because of their condition**	1	2	3	4	5	
11.	**Over the last 3 months**, my child has missed out on activities that are **important** to him/her (eg birthday parties, playing sport in a school team, being in the school play, school trips out) **because of their condition**	1	2	3	4	5	
12.	**Over the last 3 months**, the **whole family** has had to reschedule or miss out on activities **because of my child's condition**	1	2	3	4	5	31

13. **Taking everything together**, which of the faces below shows **best** how you feel about your child's life as a whole?

(Please ring the number under the face which shows **best** how you feel)



1 2 3 4 5 6 7

About the next set of questions

Please tell us **how much of a problem** each one has been for your child during the past **ONE month** by circling:

0 if it is **never** a problem
1 if it is **almost never** a problem
2 if it is **sometimes** a problem
3 if it is **often** a problem
4 if it is **almost always** a problem

There are no right or wrong answers.

Physical functioning (problems with…)	**Never**	**Almost Never**	**Some -times**	**Often**	**Almost Always**
14. Walking down the road a little bit	0	1	2	3	4
15. Running	0	1	2	3	4
16. Participating in sports or running games	0	1	2	3	4
17. Lifting heavy things	0	1	2	3	4
18. Having a bath or shower by him or herself	0	1	2	3	4
19. Doing chores, like picking up his or her toys	0	1	2	3	4
20. Having hurts or aches	0	1	2	3	4
21. Feeling very tired	0	1	2	3	4

Emotional functioning (problems with…)	**Never**	**Almost Never**	**Some -times**	**Often**	**Almost Always**
22. Feeling afraid or scared	0	1	2	3	4
23. Feeling sad or unhappy	0	1	2	3	4
24. Feeling angry or cross	0	1	2	3	4
25. Trouble sleeping at night	0	1	2	3	4
26. Worrying about what will happen to him or her	0	1	2	3	4

Social functioning (problems with…)	**Never**	**Almost Never**	**Some -times**	**Often**	**Almost Always**	
27. Getting on with other children	0	1	2	3	4	46
28. Other children not wanting to be his or her friend	0	1	2	3	4	
29. Getting bullied by other children	0	1	2	3	4	
30. Not able to do things that other children his or her age can do	0	1	2	3	4	
31. Keeping up when playing with other children	0	1	2	3	4	50

School functioning (problems with…)	**Never**	**Almost Never**	**Some -times**	**Often**	**Almost Always**	
32. Paying attention in class	0	1	2	3	4	51
33. Forgetting things	0	1	2	3	4	
34. Keeping up with schoolwork	0	1	2	3	4	
35. Having days off school because of not feeling well	0	1	2	3	4	
36. Having days off school to go to the doctor or hospital	0	1	2	3	4	55

2

8

Use of NHS health services

The next set of questions asks you about your child's use of NHS health services **over the last three months**. We are interested **both** in **overall** use of NHS health services and in use of NHS health services **for the condition**. **Remember – by condition we mean any sore throats, complications of sore throats, and any side-effects of treatment.**

37. **Over the past three months**, have you done any of the following because of your child's **condition** or **other health reasons**?
If yes, please tell us the number of times. (Please be sure to answer either 'yes' or 'no' to every item.)

a) **Has your child been seen by the family doctor or another GP at a doctor's surgery?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 9-11
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 12-14
No 3 15

b) **Has your child been seen by a nurse at a surgery?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 16-18
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 19-21
No 3 22

c) **Did you speak to a nurse from a doctor's surgery about your child on the telephone?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 23-25
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 26-28
No 3 29

d) **Did you speak to a doctor about your child on the telephone?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 30-32
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 33-35
No 3 36

e) **Did you phone NHS Direct about your child?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 37-39
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 40-42
No 3 43

f) **Has your child been seen by a nurse at home?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 44-46
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 47-49
No 3 50

g) **Has your child been seen by a doctor at home?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 51-53
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 54-56
No 3 57

h) **Has your child visited an emergency doctor at an "out of hours" clinic?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 58-60
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 61-63
No 3 64

i) **Has your child been to a hospital casualty (A&E) department?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 65-67
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 68-70
No 3 71

j) **Has your child been seen by a doctor at a hospital clinic, hospital ward or outpatient department?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 72-74
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 75-77
No 3 78

k) **Has your child been admitted to hospital as an in-patient or a day patient?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 79-81
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 82-84
No.....3 85

l) **Did your child make use of the emergency ambulance service at all?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 86-88
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 89-91
No 3 92

m) **Has your child had some other contact with the NHS?**

Yes, because of their condition ..... 1 → Please write in no. times ☐☐ 93-95
Yes, because of other health reasons .. 2 → Please write in no. times ☐☐ 96-98
No 3 99

3 8

Costs of your child's condition

The next set of questions are about the costs of your child's **condition** and of any **treatment for their condition**. **Remember – by condition we mean any sore throats, complications of sore throats, and any side-effects of treatment.**

38. **Over the last three months**, have you bought any medicines (for example Calpol, throat sweets, herbal remedies) for your child from a pharmacy or other shop? **Do not include prescription medicines like antibiotics as we are getting this information from your doctor.**

Yes..... 1 **Answer a)**

No..... 2 **Go to Q39** 9

If yes, a) Please write down the name of each medication you bought for your child **over the last three months**, and how much you spent on it.

Please give the name(s) of the medication *(Brand name if possible)*	How much did you pay for it overall?		Did they take this medication **for their condition**? (please tick if yes)	
	£	**p**		
				10-16
				17-23
				24-30
				31-37
				38-44

39. **Over the last three months**, has your child missed any days at school **because of his/her condition**?

Yes..... 1	**Answer a)**	
No..... 2	**Go to Q40**	
Does not apply – my child is not yet at school..... 3	**Go to Q42**	45

If yes, a) How many days of school has your child missed in the last three months **because of their condition**?

Number of days missed *(please write in)* ☐☐ days 46-47

---

40. **Over the last three months**, do you think **your child's condition** has affected his/her progress at school?

Yes, progress has been affected..... 1	**Go to Q41**	
No, progress has not been affected..... 2	**Go to Q42**	
Not sure..... 3		48

---

41. **Over the last three months**, has your child had any private tuition/coaching because his/her progress at school has been affected **due to their condition**?

Yes..... 1	**Answer a)**	
No..... 2	**Go to Q42**	49

If yes, a) How much did you pay for this?

£☐☐☐☐•☐☐ p 50-55

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42. **Over the last three months**, did you have any other extra expenses **because of your child's condition**?

Yes..... 1 **Answer a)**

No..... 2 **Go to Q43** 56

If yes, a) Please tell us the reason and how much you have spent on each item:

Item 1: Reason for expense 57-58

Amount spent overall £ | | • | | | p 59-62

Item 2: Reason for expense 63-64

Amount spent overall £ | | • | | | p 65-68

Item 3: Reason for expense 69-70

Amount spent overall £ | | • | | | p 71-74

Item 4: Reason for expense 75-76

Amount spent overall £ | | • | | | p 77-80

4 8

Your child and your work

The next set of questions are about the impact of your child's **condition and treatment** on your employment. **Remember – by condition we mean any sore throats, complications of sore throats, and any side-effects of treatment.**

43. Which of the following **best** describes your current position about paid work?
*Please ring **one** number only.*

Full or part time..... 1

Retired..... 2

At home and not looking for paid employment..... 3
(eg looking after your home, family or other dependants)

Unable to work due to illness or disability..... 4

Unemployed and looking for work..... 5

In full time education..... 6

Other *(please write in)*..... 7 9

.....

The next set of questions asks about you and your work**. If you are not working at present for any reason then please tell us about your last main job.**

44. **IF YOU ARE WORKING**, please answer a) to f) below about your **present** job.

IF YOU ARE RETIRED OR ARE NOT WORKING AT PRESENT, please answer a) to f) below about your **last main** job.

IF YOU HAVE NEVER WORKED, please tick this box ☐ and go to Q52. 10

a) How many hours do you/did you work? ☐☐ hours per week 11-12

b) Please write in your job title:

13-16

c) What do/did you actually do?

17-18

d) What does the firm or organisation you work(ed) for make or do?

19

e) Are/were you?

An employee..... 1

or self-employed..... 2 20

f) Are/were you a manager, foreman or supervisor of any kind?

Yes, manager..... 1

Yes, supervisor..... 2

No, neither..... 3 21

45. **Over the last three months**, have you been in paid employment/self employment **at all**?

Yes..... 1 **Answer Q46**

No..... 2 **Go to Q49** 22

---

46. **Over the last three months**, have you taken any time off **work because of your child's condition** *(eg to look after your child when they were ill or to go with them to the doctor or hospital*)? **Do not include times when you took work home or made up the time later.**

Yes..... 1 **Answer Q47**

No..... 2 **Go to Q49** 23

---

47. How many days or hours did you take **altogether** in that time?

☐☐ days **or** ☐☐ hours 24-27

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48. Did you lose any earnings while off work to look after your child in that time?

Yes..... 1 **Answer a)**

No..... 2 **Go to Q49** 28

If yes, a) Please write in the amount of earnings you lost: £ ☐☐☐☐•☐☐p 29-34

---

49. **Over the last three months**, has your work **situation** been affected in any way **by your child's condition** (including changes due to an **improvement** in your child's condition)? *(please ring **all** that apply)*

No, no effect on my work at all..... 1

I took some time off work to look after my child but **no other effect**..... 2

Go to Q52

35

Yes, I have not been able to work at all over the last 3 months 3

Yes, I stopped working and haven't started again..... 4

Yes, I was not working but I am now..... 5

Yes, I changed the type of job or tasks I do..... 6

Yes, I changed my place of work..... 7

Yes, I changed the number of hours I work..... 8

Yes, I retired early from work..... 9

Other *(please write in what)*..... 0

.....

Go to Q50

44

50. **Over the last three months,** has there been any change in your earnings **from paid or self employment** because **of your child's condition**?

Yes, earnings have changed..... 1 **Answer a) b) and c)**

No, no change..... 2 **Go to Q51** 45

If your earnings have changed,

a) What were your earnings before the change? *(please give the amount before tax)*

£ | | | | | | • | | | p

Was that per … *(please circle the one that applies)*

week 1 month 2 year 3 46-53

and b) What are your earnings now? *(please give the amount before tax)*

£ | | | | | | • | | | p

Is that per … *(please circle the one that applies)*

week 1 month 2 year 3 54-61

and c) Was the change in your earnings due to:

A change in the number of hours you work..... 1 **Answer a)**

An increase in your wage..... 2

A decrease in your wage..... 3 **Go to Q51**

Loss of a job..... 4 62

If hours changed,

a) How many hours per week were you working **before the change**? ☐☐ hours 63-64

How many hours per week do you work **now**? ☐☐ hours 65-66

51. **Over the last three months**, have you been unemployed at any time **because of your child's condition**? *Please include all times when you were not working* ***even if you were not eligible for unemployment benefits****.*

Yes..... 1	**Answer a) and b)**	
No..... 2	**Go to Q52**	67

If yes, a) Altogether, how many days were you unemployed in that time?

☐☐ days 68-69

and b) What were your earnings before you lost or gave up work?

£☐☐☐☐☐•☐☐p

Was that per … *(please circle the one that applies)*

week	month	year	
1	2	3	70-77

5 8

52. Are you:

Married or living with a partner..... 1 — **Answer Q53**

Divorced or separated..... 2

Widowed..... 3 — **Go to Q62**

Single..... 4

9

The next set of questions are about the impact of your child's condition and treatment on your **spouse or partner** and their employment. **(Remember – by condition we mean any sore throats, complications of sore throats, and any side-effects of treatment).**

53. Which of the following **best** describes your spouse or partner's current position about paid work? *Please ring **one** number only.*

Full or part time..... 1

Retired..... 2

At home and not looking for paid employment..... 3
(eg looking after your home, family or other dependants)

Unable to work due to illness or disability..... 4

Unemployed and looking for work..... 5

In full time education..... 6

Other *(please write in)*..... 7

..... 10

The next set of questions asks about your spouse or partner and their work. **If they are not working at present for any reason then please tell us about their last main job.**

54. **IF YOUR** SPOUSE OR PARTNER IS **WORKING**, please answer a) to f) below about their **present** job.

IF YOUR SPOUSE OR PARTNER IS RETIRED OR NOT WORKING AT PRESENT, please answer a) to f) below about their **last main** job.

IF YOUR SPOUSE OR PARTNER HAS NEVER WORKED, please tick this box ☐ and go to Q62. 11

a) How many hours does/did your partner work? ☐☐ hours per week 12-13

b) Please write in your spouse or partner's job title:

14-17

c) What do/did they actually do?

18-19

d) What does the firm or organisation they work(ed) for make or do?

20

e) Are/were they?

An employee..... 1

or self-employed..... 2 21

f) Are/were they a manager, foreman or supervisor of any kind?

Yes, manager..... 1

Yes, supervisor..... 2

No, neither..... 3 22

55. **Over the last three months**, has your spouse or partner been in paid employment/self employment **at all**?

Yes..... 1 **Answer Q56**

No..... 2 **Go to Q59** 23

---

56. **Over the last three months**, has your spouse or partner taken any time off work **because of your child's condition** *(eg to look after your child when they were ill or to go with your child to the doctor or hospital*)? **Do not include times when they took work home or made up the time later.**

Yes..... 1 **Answer Q57**

No..... 2 **Go to Q59** 24

---

57. How many days or hours did your spouse or partner take **altogether** in that time?

☐☐ days **or** ☐☐ hours

25-28

---

58. Did your spouse or partner lose any earnings while off work to look after your child in that time?

Yes..... 1 **Answer a)**

No..... 2 **Go to Q59** 29

If yes, a) Please write in the amount of earnings they lost: £ ☐☐☐☐•☐☐ p 30-35

---

59. **Over the last three months**, has your **spouse or partner's** work **situation** been affected in any way **by your child's condition** (including changes due to an **improvement** in your child's condition)? *(please ring **all** that apply)*

No, no effect on their work at all 1

They took some time off work but **no other effect** 2

Go to Q62

36

Yes, they have not been able to work at all over the last 3 months 3

Yes, they stopped working and haven't started again 4

Yes, they were not working but they are now 5

Yes, they changed the type of job or tasks they do 6

Yes, they changed their place of work 7

Yes, they changed the number of hours they work 8

Yes, they retired early from work 9

Other *(please write in what)* 0

.....

Go to Q60

45

60. **Over the last three months,** has there been any change in your spouse or partner's earnings **from paid or self employment** because **of your child's condition**?

Yes, earnings have changed..... 1 — **Answer a) b) and c)**

No, no change..... 2 — **Go to Q61**

46

If your spouse or partner's earnings have changed,

a) What were their earnings before the change? *(please give the amount before tax)*

£ ☐☐☐☐☐•☐☐ p

Was that per … *(please circle the one that applies)*

week 1 month 2 year 3

47-54

and b) What are their earnings now? *(please give the amount before tax)*

£ ☐☐☐☐☐•☐☐ p

Is that per … *(please circle the one that applies)*

week 1 month 2 year 3

55-62

and c) Was the change in your spouse or partner's earnings due to:

A change in the number of hours they work..... 1 — **Answer a)**

An increase in their wage..... 2

A decrease in their wage..... 3 — **Go to Q61**

Loss of a job..... 4

63

If hours changed,

a) How many hours per week were they working **before the change**? ☐☐ hours 64-65

How many hours per week do they work **now**? ☐☐ hours 66-67

61. **Over the last three months**, has your spouse or partner been unemployed at any time **because of your child's condition**? *Please include all times when they were not working* ***even if they were not eligible for unemployment benefits***.

Yes..... 1 **Answer a) and b)**

No..... 2 **Go to Q62** 68

If yes, a) Altogether, how many days were they unemployed in that time?

☐☐ days 69-70

and b) What were their earnings before they lost or gave up work?

£☐☐☐☐☐•☐☐p

Was that per … *(please circle the one that applies)*

week month year

1 2 3 71-78

---

62. **Over the last three months,** has anybody else other than you and your spouse or partner looked after your child **because of his/her condition**?

Yes..... 1 **Answer Q63**

No..... 2 **Go to Q64** 79

---

6 8

63. Can you please tell us about the people who looked after your child? *Please provide as much information as you can in the box below.*

If you paid anything for that help, please tell us how much you paid **altogether** over the last three months.

Who looked after your child?	Please tick all that apply.	How long did they look after your child **altogether** over the last three months? (Days **or** Hours)		If you paid anything for that help, please tell us how much you paid **altogether** over the last three months.		
		Days	**Hours**	**£**	**p**	
A grandparent						9-17
Another relative						18-26
A friend						27-35
A child minder						36-44
A nanny						45-53
Other *(please write in who)*						54-62

About you and your child

64. What is your relationship to your child? Are you:

His/her mother..... 1
His/her father..... 2
His/her step-mother..... 3
His/her step-father..... 4
Other (*please write in relationship*)..... 5 63

.....

---

65. What is his/her date of birth? *(please write the date in the boxes provided)*

day	**month**	**year**

64-69

---

66. What is your date of birth?

day	**month**	**year**

70-75

---

67. When did you answer these questions? *(please write the date in the boxes provided)*

day	**month**	**year**

76-81

68. If there is anything else you would like to tell us about your child's condition and any related costs you have had to meet, or this questionnaire, please write it in the space below.

82-83

84-85

Thank you for taking the time to fill in the questionnaire. We are very grateful for your help.

Please return the questionnaire in the envelope provided. No stamps are needed.

If you have any questions about the questionnaire, or about the NESSTAC study in general, please contact **Mary Dickinson** at:

Centre for Health Services Research
21 Claremont Place
Newcastle upon Tyne
NE2 4AA

☎ 0191 222 8709

Appendix 6
Health diary

About this Diary

We would like you to keep this diary for four weeks to tell us about your child's health over that time.

We would like you to tell us any symptoms your child has each day. We also want to know about what your child was able to do each day.

Please try to fill in the diary at the end of each day all through the four weeks.

If you forget to fill in the diary sometimes, don't worry! Just start again at whichever day in the week it is when you remember. It may help to put the diary somewhere where you will see it easily.

Please start filling in the diary on a Monday. To help you remember which Monday you started, please fill in the date you started below.

Date: ☐☐ / ☐☐ / ☐☐

10 15

If you have any problems filling in the diary, please give us a ring. Our phone number is 0191 222 8709. Please ask for Cheryl Wiscombe.

Thank you for your help

Is there anything else you would like to tell us about your child or your child's sore throats? If there is, please write it in the space below.

WEEK 1

MON

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	16
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	25

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	26

WEEK 1

TUES

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	27
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	36

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	37

WEEK 1

WED

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	74
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	83

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	84

WEEK 1

THURS

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	63
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	72

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	73

WEEK 1

FRI

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	38
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	47

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	48

DOI: 10.3310/hta14130

WEEK 1

SAT

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	49
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	58

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	59

WEEK 1

SUN

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	52
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	61

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	62

WEEK 2

MON

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	41
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	50

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	51

WEEK 2

TUES

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	60
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	69

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	70

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WEEK 2

WED

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	71
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	80

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	81

WEEK 2

THURS

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	30
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	39

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	40

WEEK 2

FRI

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	19
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	28

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	29

WEEK 2

SAT

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	82
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	91

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	92

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WEEK 2 4 (7)

SUN

1. Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)

Sore throat..... 1 (8)

Sore ear..... 2

Difficulty swallowing 3

Feeling sick (nausea) or being sick (vomiting) 4

Diarrhoea..... 5

Aches and pains all over 6

Having a fever/temperature..... 7

Didn't want to eat food/no appetite 8

Felt tired/no energy 9

None of these symptoms..... 0 (17)

2. What did your child do today? (*please ring only <u>one</u>*)

They carried on with their usual activities..... 1

They were not able to do as much as usual..... 2

They had to stay at home, but not in bed 3

They had to stay at home in bed 4

They had to stay in hospital..... 5 (18)

WEEK 3 2 (7)

MON

1. Was your child bothered by any of the following today? (*please ring all that apply*) (8)

Sore throat 1
Sore ear 2
Difficulty swallowing 3
Feeling sick (nausea) or being sick (vomiting) 4
Diarrhoea 5
Aches and pains all over 6
Having a fever/temperature 7
Didn't want to eat food/no appetite 8
Felt tired/no energy 9

None of these symptoms 0 (17)

2. What did your child do today? (*please ring only one*)

They carried on with their usual activities 1
They were not able to do as much as usual 2
They had to stay at home, but not in bed 3
They had to stay at home in bed 4
They had to stay in hospital 5 (18)

WEEK 3

TUES

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	19
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	28

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	29

WEEK 3

WED

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	74
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	83

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	84

WEEK 3

THURS

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	63
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	72

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	73

WEEK 3

FRI

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	30
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	39

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	40

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WEEK 3

SAT

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat 1 41
Sore ear 2
Difficulty swallowing 3
Feeling sick (nausea) or being sick (vomiting) 4
Diarrhoea 5
Aches and pains all over 6
Having a fever/temperature 7
Didn't want to eat food/no appetite 8
Felt tired/no energy 9

None of these symptoms 0 50

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities 1
They were not able to do as much as usual 2
They had to stay at home, but not in bed 3
They had to stay at home in bed 4
They had to stay in hospital 5 51

WEEK 3

SUN

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat 1 52
Sore ear 2
Difficulty swallowing 3
Feeling sick (nausea) or being sick (vomiting) 4
Diarrhoea 5
Aches and pains all over 6
Having a fever/temperature 7
Didn't want to eat food/no appetite 8
Felt tired/no energy 9

None of these symptoms 0 61

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities 1
They were not able to do as much as usual 2
They had to stay at home, but not in bed 3
They had to stay at home in bed 4
They had to stay in hospital 5 62

WEEK 4

MON

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat 1 41
Sore ear 2
Difficulty swallowing 3
Feeling sick (nausea) or being sick (vomiting) 4
Diarrhoea 5
Aches and pains all over 6
Having a fever/temperature 7
Didn't want to eat food/no appetite 8
Felt tired/no energy 9

None of these symptoms 0 50

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities 1
They were not able to do as much as usual 2
They had to stay at home, but not in bed 3
They had to stay at home in bed 4
They had to stay in hospital 5 51

WEEK 4

TUES

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat 1 52
Sore ear 2
Difficulty swallowing 3
Feeling sick (nausea) or being sick (vomiting) 4
Diarrhoea 5
Aches and pains all over 6
Having a fever/temperature 7
Didn't want to eat food/no appetite 8
Felt tired/no energy 9

None of these symptoms 0 61

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities 1
They were not able to do as much as usual 2
They had to stay at home, but not in bed 3
They had to stay at home in bed 4
They had to stay in hospital 5 62

DOI: 10.3310/hta14130

WEEK 4

WED

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	63
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	72

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	73

WEEK 4

THURS

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	30
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	39

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	40

WEEK 4

FRI

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	19
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	28

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	29

WEEK 4

SAT

1. **Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)**

Sore throat	1	74
Sore ear	2	
Difficulty swallowing	3	
Feeling sick (nausea) or being sick (vomiting)	4	
Diarrhoea	5	
Aches and pains all over	6	
Having a fever/temperature	7	
Didn't want to eat food/no appetite	8	
Felt tired/no energy	9	
None of these symptoms	0	83

2. **What did your child do today? (*please ring only <u>one</u>*)**

They carried on with their usual activities	1	
They were not able to do as much as usual	2	
They had to stay at home, but not in bed	3	
They had to stay at home in bed	4	
They had to stay in hospital	5	84

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WEEK 4 3 7

SUN

1. Was your child bothered by any of the following today? (*please ring <u>all</u> that apply*)

Sore throat..... 1 8

Sore ear..... 2

Difficulty swallowing 3

Feeling sick (nausea) or being sick (vomiting) 4

Diarrhoea..... 5

Aches and pains all over 6

Having a fever/temperature..... 7

Didn't want to eat food/no appetite..... 8

Felt tired/no energy 9

None of these symptoms..... 0 17

2. What did your child do today? (*please ring only <u>one</u>*)

They carried on with their usual activities..... 1

They were not able to do as much as usual..... 2

They had to stay at home, but not in bed 3

They had to stay at home in bed 4

They had to stay in hospital..... 5 18

Appendix 7

Topic guide for qualitative study

The outline below represents the topics we aim to cover in the qualitative interviews and examples of questions we will ask. The language and way in which we get to the information will depend on the age and ability of the child/ young person, and interviews will be flexible and responsive.

Explain that we are interested in talking to children/ young people about sore throats
Getting participants used to talking and the microphone/ tape recorder etc.,
What do you like to do? Hobbies etc?
Do you like school, what's your favourite thing at school?
Have you got any brothers or sisters?

Experience of sore throats

What's it like to have sore throats?

- Do you get them often?
- **How does it make you feel?**

  Probe self esteem, behaviour etc
- When did you last have a sore throat?
- What was that like?
- Who takes care of you when you have a sore throat?

- Have you been off school with your sore throat?
- Do you mind having time off school?

Treatments and surgery

- Do you have any treatment when you get a sore throat? *(medicines etc)*
- What is that like?
- Are there any good things and bad things about having treatment?
- Are you going to have any other sort of treatment either at home, at the doctors or at the hospital? (*What did the doctor say?)*
- How do you feel about that? *(looking forward to it? Worried about it?)*

- Have you had any operations on your throat?
- What was it like?
- Were there any good or bad things about having surgery?
- How did it make you feel?

Differentiating between severity of sore throats

- Are there different kinds of sore throats?
- In what ways are they different?

Impact on the individual

- Did having a sore throat stop you from doing anything you wanted to do?
- Does anything good come from having a sore throat?

Impact on others

- Has it affected the rest of the family in any way?

Appendix 8

Utility study interview manual

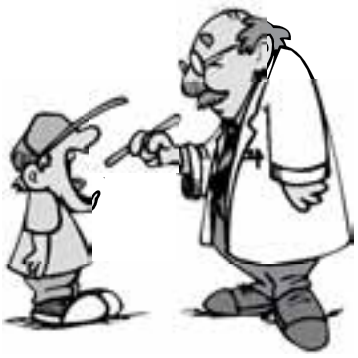
UNIVERSITY OF NEWCASTLE

NESSTAC

North of **E**ngland and **S**cotland **S**tudy of **T**onsillectomy and **A**deno-tonsillectomy in **C**hildren

The Tonsil Study

Parent/Guardian's Interview Handbook



INTRODUCE SELF

Thank you for agreeing to be interviewed

INTRODUCTION

- This research is a project to find out more about tonsils and sore throat in children

- We want to find out people's opinions of the quality of life associated with tonsillitis and sore throat

- In this interview I will ask for your opinions about children's quality of life associated with tonsillitis and sore throat. There are no right or wrong answers. We are interested in your opinion

- Your answers will be treated in the strictest confidence. They will not be made available to anyone not involved in the project. Your name and address do not appear on the forms used during the interview

- Throughout the interview we will be talking about serious problems associated with illness and treatment including death. Sometimes, people are upset reading and talking about illness. However I would like to take this opportunity to reassure you that this is only being done to find out your attitudes to risk. Death is NOT an expected outcome of your child's treatment. We have to include it in this exercise as it helps us to understand how much you value the health descriptions we are going to give you that's all. If you find that you feel uncomfortable answering any of our questions, please don't feel that you have to go on with the interview. We can talk about it, and stop, if you want to

- Throughout the interview I will use a set form of wording, although it may seem repetitive and impersonal it will make the interview easier for both of us. Please give comments as we go along and there will be time at the end of the interview if you have any final comments on the whole exercise.

RANKING PROCEDURE - PART I

- Before we go on I would like you to read these two cards, each of which describe the possible effects tonsils and sore throat can have on a child's life

- Each of these two imaginary descriptions show different kinds of experiences that a child with tonsils and sore throat may have

➔ *Show person cards*

- Please read these two descriptions, taking your time, and tell me when you've finished. You don't need to memorise the details

➔ *Give person time to consider descriptions*

- Is there anything about the descriptions that is not clear?

➔ *If 'yes', give brief explanation making sure information is understood*

- I would also like you to read the description of Good Health

➔ *Give person time to consider description*

I want you to imagine how a child like yours would feel in the two descriptions as described on the green cards. Imagine how their relationships with family and friends, how their home, school and social life could be affected and how they would feel having the different symptoms. The symptoms described on these cards would last until your child reaches 18. After this time try to imagine that the child would return to full health. I would like you to choose which description you think is best – what you would choose for your child if you were faced with these 2 options.

➔ *Continue, allow time to think about the ranking*

➔ *Affirm ranked order of descriptions allowing a change to ranked order if required*

➔ *Record ranked order (1: best, 2: worst). If descriptions are ranked as equal, tick appropriate box*

- In a moment I am going to ask you to make some choices between 2 treatment options where the outcomes of the treatments will be the same as the symptoms on the cards you have just looked at.

- One choice will involve a risk and the other choice will be definite. The amount of risk will be changed until we find out how much risk you will take to avoid the definite choice. This may seem complicated but once we have gone through it, it will make a lot more sense

- As before there are no right or wrong answers, only what you think

- To make this easier to understand we are going to use a chance board

➔ *Place chance board on table, set choice A to pink 90/10 blue*

➔ *Turn to table 2 of response booklet (page 3)*

- It's called a chance board because it indicates the chance or how likely it is that a certain event will happen. As you can see the top part of the board is labelled Choice A

➔ *Point finger at "Choice A"*

- and the lower part of the board is labelled Choice B

➔ *Point finger at "Choice B"*

- You will be asked to pick Choice A or Choice B.

- Now the best way to explain how a chance board works is to work through an example together. Let's imagine you were in an accident and hurt your leg. When you see the doctor, she explains that you have two choices. Here are the descriptions for this example

➔ *Place example cards in chance board pockets*

- Choice A is an operation and Choice B is to let your leg heal by itself. If you were to let your leg heal by itself, choice B, you would definitely have a limp. You would be able to walk, but you would **not** be able to run. Everyone who lets their leg heal by itself will have these health outcomes. If something is definite it is a 100%. On the other hand, you can choose the operation. The operation, choice A, is risky. It doesn't always work. If the operation **did** work, your leg would be fixed and you would walk and run normally. If the operation **didn't** work, you'd have to use crutches

➔ *Point to the pink section of circle*

- The chance of walking and running normally after the operation is shown by the pink amount of circle you can see. 90% of the circle is pink so the chances are that the treatment would work, and you would be able to walk and run after the operation

➔ *Point to the blue section of circle*

- The chance of having to use crutches after the operation is shown by the amount of blue colour you can see. 10% of the circle is blue so it is not very likely that you would have to use crutches, but there is still a chance

- Here, the chances of walking and running normally are 90% with a 10% chance of having to use crutches. Another way to think of it is that, on average, for

every 100 people who choose A, the operation, 90 will walk and run normally afterwards but 10 will have to use crutches to get around after the operation

➔ *Change spinner and board to 50/50*

- Now I've changed the chances.

- The chance that the operation will go well is the same as the chance that the operation won't go well. There is an **equal** amount of pink and blue showing on the circle. So now if I were to ask you if you would choose A or B, your answer might be different because there is a bigger chance that the operation would leave you having to use crutches. Do you think you understand how the chance board works?

➔ *If 'yes', continue below. If 'no', return to beginning of chance section and repeat the exercise.*

Before we continue I just want to remind you of the two cards that you ranked before.

➔ *hand green cards to respondent and give them time to re-read.*

We'll work through the first question together. Imagine that there are two types of treatment; treatment A and treatment B. With treatment A the outcome of the treatment is uncertain, you could either return to good health if it works or you could have the symptoms which are shown on the blue card if it doesn't. On the other hand you could opt for treatment B where you are certain of what will happen and you will definitely have the symptoms which are displayed on the green card – in this first question this is the health state that you said was best.

- ➔ *Hand respondent "ranked 1" card*

- Please can you read over the description and when you are finished I'll put it next to the board

➔ *Place "…" card next to board when respondent is finished*

➔ *Be sure wheel is set to 100/0*

STEP 1

- Now we are ready to begin. As you can see choice A is now a 100% chance of good health and a zero chance of the worst health state (HEALTH STATE XXXX). Choice B is 100% chance of the health described on the card you have just finished reading. If I was to ask you to choose between Choice A and Choice B, Which would you choose? This is a pretty unrealistic situation to start with as its unlikely that there would be 2 treatments both of which would offer you a 100% chance of the outcomes presented here but it helps us to get into the exercise.

➔ *A - Go to step 2*

➔ *B - Circle response (?), Ask "why…" and record response verbatim*

STEP 2

Move wheel to 10/90

- Now I've changed Choice A to show there is a 10% chance of good health and a 90% chance of HEALTH STATE XXXX. Choice B is still a 100% chance of the health described on the card. Would you pick treatment A or B now?

➔ *B – Go to step 3*

➔ *A?? - Prompt "Do you mean that you would prefer your child to have a 90% chance of being in the health state you ranked worst and a 10% chance of good health rather than living in the state of health described on the cards in choice B"*

➔ *No - Repeat choices shown on board*

➔ *Yes - ask "If choice A was certain death with no chance of good health, do you think this would be better than living as choice B or worse than living as choice B?"*

➔ *Better - Mark response (negative)*

➔ *Equal - mark response (0.00)*

➔ *Worse - Mark response (0.05)*

➔ *State "Thank you that ends this question"*

STEP 3

Move wheel to 90/10

- The board now shows choice A to be a 90% chance of good health with a 10% chance of HEALTH STATE XXXX and Choice B remains the same as before Which treatment would you prefer now, A or B?

➔ *A – Go to step 4*

➔ *B -Ask what if the odds were changed to 95% good health with a 5% chance of health state XXX. (if accept, mark response 0.975) If still prefer choice B ask what they would choose if the odds were 99% good health and 1% health state XXX (if accept mark response 0.99. if still prefer choice B, mark response as 1. Finish by saying "Thank you that ends this question*

STEP 4

Move wheel to 20/80,

- Now I've changed choice A to a 20% chance of good health with an 80% chance of HEALTH STATE XXXX Choice B is still a 100% chance of the health state described. Which treatment would you prefer, A or B?

➔ *B -Go to step 5*

➔ *A - Mark response (0.15) and state "Thank you that ends this question"*

STEP 5

Move wheel to 80/20

- Choice A is now an 80% chance of good health with a 20% chance of the worse health state HEALTH STATE XXXX. Choice B is still the same as before. Would you prefer treatment A or B?

➔ *A - Go to step 6*

➔ *B - Mark response (0.85) and state "Thank you that ends this question"*

STEP 6

Move wheel to 30/70

- The choices have now been changed so that Choice A has a 30% chance of good health but a 70% chance of the worse health state HEALTH STATE XXXX. Choice B is still the same. Which treatment would you prefer now?

➔ *B – Go to step 7*

➔ *A - Mark response (0.25) and state "Thank you that ends this question"*

STEP 7

Move wheel to 70/30

- Now I've changed Choice A to a 70% chance of good health and a 30% chance of HEALTH STATE XXXX. As before Choice B remains the same. Which treatment would you prefer now?

➔ *A – Go to step 8*

➔ *B - Mark response (0.75) and state "Thank you that ends this question"*

STEP 8

Move wheel to 40/60

- Choice A has now been adjusted to indicate a 40% chance of perfect health and a 60% chance of the worse health state HEALTH STATE XXXX. Would you prefer treatment A or B?

➔ *B – Go to step 9*

➔ *A- Mark response (0.35) and state "Thank you that ends this question".*

STEP 9

Move wheel to 60/40

- If Choice A had a 60% chance of good health and a 40% chance of HEALTH STATE XXXX as shown on the board would you pick A or B?

➔ *A – Go to step 10*

➔ *B - Mark response (0.65) and state "Thank you that ends this question"*

STEP 10

Move wheel to 50/50

- Now I have changed Choice A to a 50% chance of good health and a 50% chance of HEALTH STATE XXXX. Choice B remains the same. Which choice would you prefer now?

➔ *A-Mark response (0.45)*

➔ *B- Mark response (0.55)*

- Thank you, that ends this question

We are now going to run through this exercise again but this time we are going to change the health states that you will have to make choices between. One of the health states that will be included this time is death. I would just like to say again that death is not an expected outcome of your child's treatment. We have to use it in this exercise as it helps us to understand how much you value the different health states that you see.

➔ *Go back to step 1 and repeat exercise using good health and death in choice A and the worst ranked health state in choice B.*

➔ *At the end of the SG exercise for all respondents who ranked health state Z above health state X complete WTP question in response booklet.*

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The HTA programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (www.hta.ac.uk) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

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