


The TYPHOON Study Protocol

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor’s SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

Chief Investigator:	
Signature: 	Date: 28/7/2025
Name: (please print): CATRIONA DOUGLAS	

LIST of CONTENTS

	Page No.
TITLE PAGE	i
RESEARCH REFERENCE NUMBERS	i
HRA PROTOCOL COMPLIANCE DECLARATION	ii
LIST OF CONTENTS	iii
KEY STUDY CONTACTS	iv
STUDY SUMMARY	v
FUNDING	v
ROLE OF SPONSOR AND FUNDER	vi
ROLES & RESPONSIBILITIES OF STUDY STEERING GROUPS AND INDIVIDUALS	vi
STUDY FLOW CHART	ix
SECTION	
1. BACKGROUND	1
2. RATIONALE	2
3. THEORETICAL FRAMEWORK	2
4. RESEARCH QUESTION/AIM(S)	2
5. STUDY DESIGN/METHODS	3
6. STUDY SETTING	6
7. SAMPLE AND RECRUITMENT	7
8. ETHICAL AND REGULATORY COMPLIANCE	8
9. DISSEMINATION POLICY	11
10. REFERENCES	11
11. APPENDICES	11

KEY STUDY CONTACTS

<p>Chief Investigator</p>	<p>Name: Professor Catriona Douglas Role: Consultant ENT/Head and Neck Surgeon Address: NHS Greater Glasgow and Clyde 1355 Govan Road Glasgow G51 4TF Email: catriona.douglas@ggc.scot.nhs.uk Phone: 0141 211 3212</p>
<p>Sponsor</p>	<p>Organisation: Greater Glasgow and Clyde Name: Adam Wade Role: Sponsor Research Co-ordinator Address: NHS GG&C Research and Innovation Ward 11 Dykebar Hospital Grahamston Road Email: Adam.wade@ggc.scot.nhs.uk Phone: 0141 211 6389</p>
<p>Funder(s)</p>	<p>ENT UK Foundation Grant (£1500)</p>
<p>Key Protocol Contributors</p>	<p>Name: Miss Lucy Li Role: Otolaryngology Registrar Address: NHS Greater Glasgow and Clyde 1355 Govan Road Glasgow G51 4TF Email: lucy.li@nhs.scot Phone: 07722052123</p> <hr/> <p>Name: Mr Andrew Williamson Address: The Royal Marsden NHS Foundation Trust 203 Fulham Road London SW3 6JJ</p>

The TYPHOON Study Protocol

	Email:	Andrew.williamson2@rmh.nhs.uk
	Phone:	07595944828
	Name:	Professor Catriona Douglas
	Address:	NHS Greater Glasgow and Clyde 1355 Govan Road Glasgow G51 4TF
	Email:	catriona.douglas@ggc.scot.nhs.uk
	Phone:	0141 211 3212
	Name:	Mr James O'Hara
	Address:	Department of ENT The Freeman Hospital Newcastle upon Tyne NE7 7DN
	Email:	James.o'hara@newcastle.ac.uk
	Phone:	0191 213 7170
Committees	Name:	INTEGRATE (see committee members below)
	Email:	Info@entintegrate.co.uk
	Website:	https://entintegrate.co.uk/

STUDY SUMMARY

Study Title	Tonsillectomy Postoperative Haemorrhage Outcomes and Observations National Cohort Study
Internal ref. no. (or short title)	The TYPHOON study
Study Design	Multicentre prospective national cohort study
Study Participants	Adults patients undergoing tonsillectomy
Planned Size of Sample (if applicable)	No sample size calculation as exploratory study
Follow up duration (if applicable)	28 days
Planned Study Period	1st of August 2025 to 31st of July 2026
Research Question/Aim(s)	To investigate the causes for readmission and bleeding following tonsillectomy

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	FINANCIAL AND NON FINANCIAL SUPPORT GIVEN
ENT UK Foundation Grant	£1500

ROLE OF STUDY SPONSOR AND FUNDER

For this trial, some of the duties of the sponsor have been delegated to the Chief Investigator (CI), for example the CI has overall responsibility for the design and development of the protocol. The sponsorship agreement describes the allocation of such responsibilities, and a summary of this can be provided by the sponsor upon request.

NHS Greater Glasgow and Clyde (NHS GGC) will sponsor this study. The study sponsor will take on overall responsibility for proportionate, effective arrangements being in place to set up, run and report the research project. The sponsor will delegate specific roles to the Chief Investigator, and other third parties.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITTEES/GROUPS & INDIVIDUALS

Name	INTEGRATE (UK ENT Trainee Research Network) Project Management Team <ul style="list-style-type: none"> ● Lucy Li ● Andrew Williamson ● Alison Lim ● Christy Moen ● Ying Ki Lee ● Olivia Wharf ● Freddie Green ● Rishi Vasanthan ● Jeremy Wong
Responsibilities	Including but not limited to: <ul style="list-style-type: none"> ● Generation of patient facing documents ● Receipt of submitted data ● Database building and cleaning

Name	Professor Catriona Douglas
Role(s)	Chief Investigator Senior author

The TYPHOON Study Protocol

	Consultant Head and Neck Surgeon
Responsibilities	Including, not limited to: <ul style="list-style-type: none"> • Oversight of project design, conduct and reporting. • Ensure adherence to protocol. • Final review of drafted manuscript(s)

Name	Miss Lucy Li
Role(s)	Associate Chief Investigator First author Otolaryngology Registrar
Responsibilities	Including, not limited to: <ul style="list-style-type: none"> • Oversight of project design, conduct and reporting. • Liaison ethic committees, and other review bodies, during the application process, and where necessary during the conduct of the research. • Ensure adherence to protocol. • Analysis and write up • Drafting and submission of manuscript

Name	Mr Andrew Williamson
Role(s)	Associate Chief investigator Clinical Research Fellow / Otolaryngology Registrar
Responsibilities	Including, not limited to: <ul style="list-style-type: none"> • Project design and recruitment of patients. • Coordination of data governance and control of the study eCRF. • Data interpretation and statistical analysis • Design of dataset and analysis strategy • Analysis and write up.

Name	Miss Ying Ki Lee
Role(s)	Associate Chief investigator Otolaryngology Registrar
Responsibilities	Including, not limited to: <ul style="list-style-type: none"> • Liaison ethic committees, and other review bodies, during the application process, and where necessary during the conduct of the research. • Ensure adherence to protocol • Project design and recruitment of patients. • Coordination of data governance and control of the study eCRF. • Analysis and write up.

Name	Miss Alison Lim
Role(s)	Associate Chief investigator Otolaryngology Registrar
Responsibilities	Including, not limited to:

The TYPHOON Study Protocol

	<ul style="list-style-type: none"> ● Liaison ethic committees, and other review bodies, during the application process, and where necessary during the conduct of the research. ● Ensure adherence to protocol ● Project design and recruitment of patients. ● Coordination of data governance and control of the study eCRF. ● Analysis and write up.
--	---

Name	Mr James O'Hara
Role(s)	Co-investigator Senior author Consultant Head and Neck Surgeon
Responsibilities	Including, not limited to: <ul style="list-style-type: none"> ● Data interpretation and statistical analysis ● Oversight of project design, conduct and reporting. ● Final review of drafted manuscript(s)

Name	Dr David Young
Role(s)	Senior statistician
Responsibilities	Including, not limited to: <ul style="list-style-type: none"> ● Oversight of project design and statistical plan. ● Oversight of data interpretation and statistical analysis

PROTOCOL CONTRIBUTORS

Name	Miss Lucy Li
Position	Otolaryngology Registrar, West of Scotland Deanery
Email	Lucy.li@nhs.scot

Name	Mr Andrew Williamson
Position	Head and Neck Research Fellow Otolaryngology Registrar, The Royal Marsden Hospital
Email	Andrew.williamson2@rmh.nhs.uk

Name	Miss Ying Ki Lee
Position	Otolaryngology Registrar, West of Scotland Deanery
Email	Yingki.lee@nhs.scot

Name	Professor Catriona Douglas
Position	Consultant Head and Neck Surgeon
Email	Catriona.douglas@ggc.scot.nhs.uk

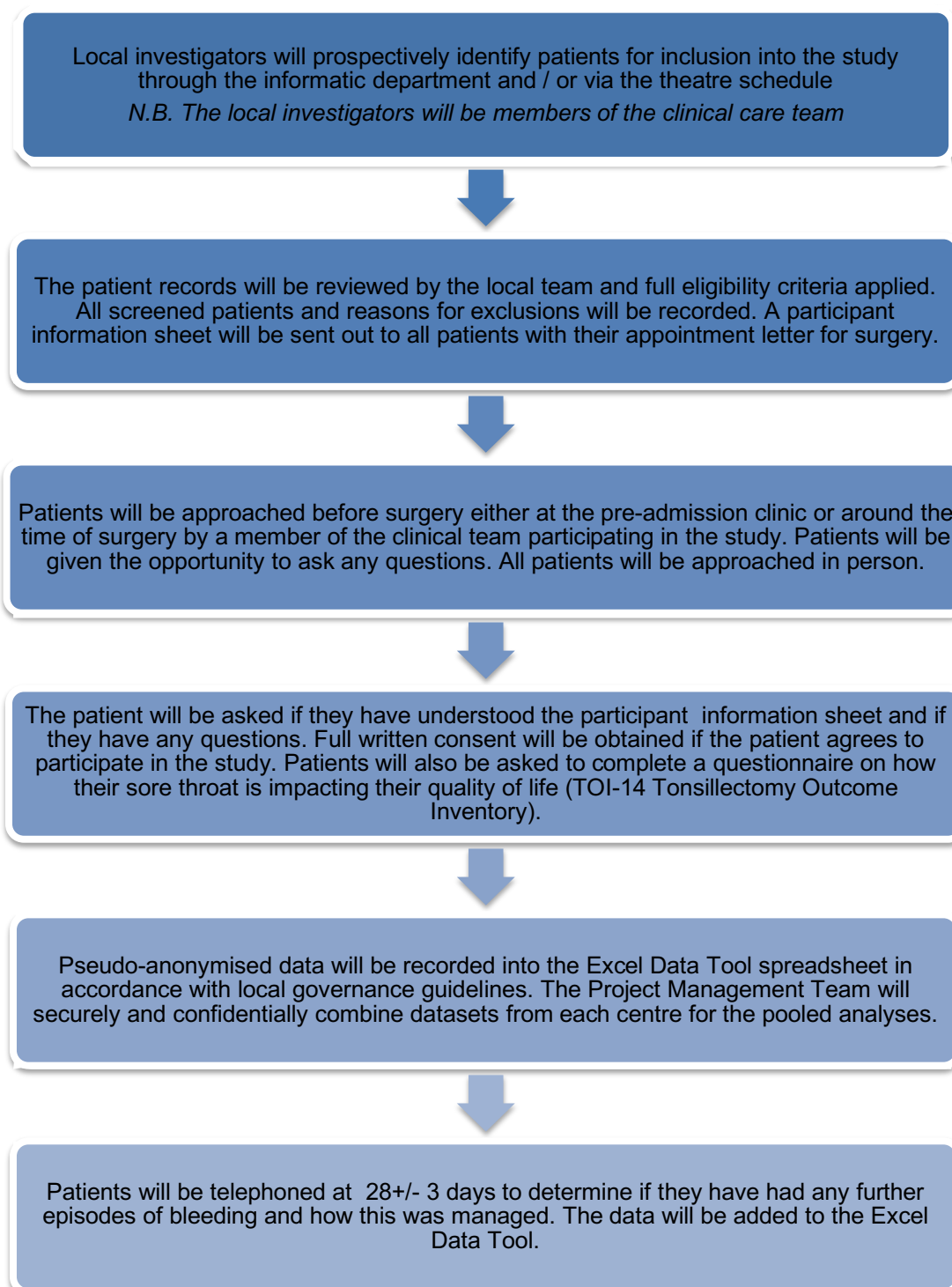
Name	Mr James O'Hara
Position	Consultant Head and Neck Surgeon
Email	James.o'hara@newcastle.ac.uk

KEY WORDS:	Tonsillectomy, Haemorrhage, Complication
-------------------	--

STUDY FLOW CHART

Figure 1: Study flow chart

Upon study enrolment, all participating centres will receive a questionnaire designed to gather information on patient referral pathways and the pathways through which patients with post tonsillectomy bleeding present to the hospital (Appendix 1).



STUDY PROTOCOL

Tonsillectomy Postoperative Haemorrhage Outcomes and Observations National Cohort Study

1 BACKGROUND

Tonsillectomy is one of the most commonly performed surgical procedures in Ear, Nose, Throat (ENT) surgery. It is estimated approximately 20 000 procedures were carried out in children and 7 300 procedures in adults in the UK in 2019/20 (1). Historical data from the UK National Prospective Tonsillectomy Audit in 2005 suggested a post-tonsillectomy bleed (PTB) rate of 4.9% in adults, which has since been widely quoted to patients in the consent taking process. Specifically, the study found a three-times increased risk of PTB with “hot” surgical techniques for both dissection and haemostasis compared to cold steel tonsillectomy without the use of any “hot” techniques (2). National guidance released halfway through the audit changed practice and reduced rates of haemorrhage. However, data collection for this audit concluded over 20 years ago, and recent unpublished data from Hospital Episode Statistics (HES) indicates a significant increase in the PTB rate to 15.6% over the period 2022-2023, the reasons for which are currently unclear (3).

The recently published NATTINA study demonstrated that tonsillectomy was clinically and cost effective at reducing the number of sore throat days than conservative management for adults with recurrent tonsillitis meeting the UK guidelines, providing a landmark contribution to the evidence base for the effectiveness of adult tonsillectomy for recurrent sore throats (4). A huge volume of tonsillectomies are performed each year, therefore there is an urgent need to ensure the procedure is as safe as we can make it. The current bleed rate of 15.6% is concerning and highlights the need for further research to identify the underlying causes and develop strategies to reduce readmission and bleeding rates.

The study will be run by INTEGRATE, the UK ENT Trainee Collaborative Network. There is increasing recognition of the importance of trainee led collaborative networks in the delivery of large scale, meaningful research projects. Involvement in collaborative research has also been recently incorporated into the National ENT ST3 scoring system. By giving trainees the opportunity to be involved in high quality, multi-centre research this strengthens the research culture within ENT and promotes excellence in the specialty. INTEGRATE has successfully delivered multiple national audits that have had a significant impact on current practice including the ENT UK Suspected Head & Neck Cancer Remote Triage Service Evaluation 2020 (10.1002/cncr.33800) and National Epistaxis Audit 2016 (10.1017/S002221511700202X). This project would represent the first cohort study run by INTEGRATE, and has assurances of support from ENT UK, the British Otorhinolaryngology and Allied Sciences Research Society (BOARS) and the Royal College of England research surgical specialty lead.

We plan to conduct an exploratory, national, prospective, multicentre collaborative cohort study of all consecutive adult patients undergoing tonsillectomy over a two-month period. Patients will be expected to fill in a questionnaire on how their sore throat is impacting their quality of life (TOI 14 – Tonsillectomy Outcome Inventory). We will collect granular data on patient characteristics, previous episodes of sore throat, surgical and anaesthetic characteristics and post-operative management including analgesia. We will also telephone the patient at 28 days following surgery to determine if

they have had any episodes of bleeding and how this was managed. The aim of this study is to better understand the risk factors associated with an increased risk of PTB and how we can change our practice to reduce this risk for patients. We hope it may provide the basis for the larger funded study over a longer time frame in the future.

2 RATIONALE

Reducing the rate of PTB is a major national priority, particularly in the context of the trend towards day case procedures and lower readmission, as outlined in the recent Getting It Right First Time (GIRFT) specialty report (5). Understanding the risk factors associated with an increased risk of PTB will inform quality improvement projects that could reduce morbidity for patients and result in significant cost savings to the NHS. We also plan to disseminate our study findings to the wider public to provide patients with the most up-to-date information on the risks associated with tonsillectomy to facilitate the informed decision-making process.

3. THEORETICAL FRAMEWORK

Unpublished data from Hospital Episode Statistics suggests that the current bleed rate amongst adults has dramatically increased to 15.6% in 2022-3 from the 4.9% previously demonstrated in the National Prospective Tonsillectomy Audit in 2005 (2, 3). Reducing the rate of PTB is a major national priority, particularly in the context of the trend towards day case procedures and lower readmission rates, as outlined in the recent Getting It Right First Time (GIRFT) specialty report (5).

Whilst the HES data can provide up to date information on the readmission and rebleed rates, it cannot capture granular data on patient and treatment characteristics that increase an individual's risk of bleeding. Identifying the potential risk factors that may place a patient at an increased risk of PTB may inform national quality improvement projects to produce evidence-based guidance around intra- and post-operative tonsillectomy care. This study also aims to address some of the shortcomings of previous research, specifically by conducting a 28-day telephone follow-up with patients to ensure all cases of PTB are captured to provide a more accurate and comprehensive assessment of the current bleed rate.

4 RESEARCH QUESTION/AIM(S)

To investigate the causes for readmission and bleeding following tonsillectomy

4.1 Objectives

Primary objective

- To better understand the risk factors associated with an increased risk of post-tonsillectomy bleed (PTB) in the first 28 days following tonsillectomy.

Secondary objectives

- Determine readmission and post-operative haemorrhage rate in the first 28 days following tonsillectomy and compare this to Hospital Episode Statistics data.
- Examine frequency and severity of tonsillitis episodes prior to being listed for surgery
- Evaluate differences in intra-operative and post-operative management of tonsillectomy patients
- Examine the management pathways for post-tonsillectomy haemorrhage

4.2 Outcome

Our prospective, multi-centre, collaborative cohort study aims to provide an in-depth assessment of the risk factors associated with post tonsillectomy bleed. Our results have the potential to inform national quality improvement projects to produce evidence-based guidance around intra- and post-operative tonsillectomy care. The results may help guide clinicians on the safest surgical technique as well as identification of patients with a potential to bleed post-operatively. Reducing the number of patients that go back to theatre for surgical arrest of haemorrhage and readmission to hospital could also result in significant savings to the NHS. For example, a ~20% bleed rate among the 12,000 adult tonsillectomies performed each year, with a conservative 1/3 of patients being admitted for one night in hospital at a cost of £1000/night, would equate to a cost of approximately £800,000 pa. We also hope the results of our study can be used to produce up to date and accessible information leaflets for medical professionals to provide to patients. We want to ultimately see the PTB rate reduce to below 10%.

5 STUDY DESIGN and METHODS of DATA COLLECTION AND DATA ANALYSIS

The study methodology is outlined in the flow chart in Figure 1.

5.1 Project registration

This is a local investigator-led, non-commercial, non-interventional national cohort study. No patient identifiable information will be collected by the Project Management Team and data analysis will not identify hospitals individually. As such, the anticipated risks to patient confidentiality are extremely low.

5.2 Patient identification

Local centres will prospectively identify patients for inclusion into the study.

These patients will have

- Undergone tonsillectomy
- Surgery to have taken place between **1st of August 2025 to 31st of July 2026.**

Local investigators are recommended to acquire their patient list via the Informatics departments and / or via the theatre schedule. The clinic notes and investigation results data for these patients will be

The TYPHOON Study Protocol

reviewed by the local team and full eligibility criteria applied. All eligible patients will be recorded onto an Excel Data Tool. All screened patients and reasons for exclusions will be recorded.

A Participant Information Sheet containing a link to the study website will be provided to prospective patients with their appointment letter for surgery to ensure patients have an appropriate amount of time to consider participating in the study. Patients will then be approached in person before surgery or at the time of surgery by a member of their usual clinical team who are participating in the study.

A written consent form will be completed if patients agree to participate in the study. Patients will be allowed to withdraw at any time and the reason for withdrawal will be documented. We will ask all patients to complete a Tonsillectomy Outcome Inventory 14 (TOI-14) to measure disease specific QOL on the day of their surgery.

When necessary, the Project Management Team will be able to provide further guidance to local investigators on request: typhoonstudy@entintegrate.co.uk.

5.3 Anonymisation of patients

The PMT will not request any identifiable data including date of birth, names, addresses, NHS numbers, medical record numbers (MRN) or identifiable dates for any patients. Dates of birth, surgery, discharge and readmission (where applicable) will be used locally to generate durations. Durations (not dates) will then be submitted to the PMT. Reporting and analysis will not identify individual cases in any subsequent reports, presentations or publications. Data flow will be one way, from the Data Discloser to the Data Receiver (i.e. PMT). There will be no traceability from the PMT's spreadsheet to local records. If any identifiable data is received, the files will be deleted and the site will be informed.

5.4 Dataset

All data will be recorded into an Excel Data Tool spreadsheet in accordance with local governance guidelines. This uses restricted data fields and data validation to improve data completeness and homogeneity. This database will collect data on patient characteristics, surgical characteristics, complications during the initial stay and complications within the first 28 days of initial surgery.

The following time frames will be used to classify primary and secondary post-operative haemorrhage:

- **Primary** Bleeding occurring within 24 hours of tonsillectomy
- **Secondary** Any bleeding occurring more than 24 hours after tonsillectomy

5.5 Follow up

Patient case notes will be reviewed at 28 +/- 3 days to determine if they have represented to hospital following their tonsillectomy,

Patients will also be followed up at 28 +/- 3 days via telephone following the date of their surgery to determine if they have experienced any postoperative bleeding or other complications. The phone call will be attempted up to three times over a 48 hour period. This data will be used as an adjunct to casenote review to ensure no patients who have experienced any bleeding but did not present to the hospital or present to the hospital where they underwent their original procedure are missed.

If patients admit to blood in the saliva, they will be given standard safety netting advice to seek medical attention if it worsens. If patients describe bleeding more than blood in the saliva, they will be advised to seek immediate medical attention if they have not done so already.

5.6 Data collection

All patients will be assigned a Study ID. Local teams will maintain a secure list on an NHS computer to link the Study ID to the patient identifier for the purpose of responding to / correcting any data queries.

Pseudonymised data will be locally entered into the Excel Data Tool in accordance with local governance guidelines. The tool will be available to download from the project website. This uses restricted data fields and data validation to improve data completeness and homogeneity. All submitted records will be pseudonymised and no patient identifiable information will be shared between centres. The Project Management Team will securely and confidentially combine datasets from each centre for the pooled analysis. Only members of the INTEGRATE project management team will be able to view the amalgamated dataset for the purposes of data cleaning and review

The Project Management Team will check the submitted data for completeness and integrity. If necessary, the Project Management Team will give feedback to the local team where any data fields are inadequate. The submitting team will be asked to provide the missing data where possible. If data is not available, the data point will be treated as null, and that record will be excluded from any relevant analysis where necessary.

A pilot study of 10 patients undergoing tonsillectomy in Greater Glasgow and Clyde will be undertaken to assess the adequacy and feasibility of the study. The hospitals will also trial inputting data into the Excel Data Tool. Feedback will be incorporated into improvements to protocol as required.

5.7 Data analysis

Patient demographic data will be presented with mean and SD for continuous variables and counts and proportions for categorical variables. Categorical data will be analysed with the Chi-square or Fisher's Exact test as appropriate. Quantitative continuous variables will be analysed using descriptive statistics such as mean, standard deviation, median, quartiles, minimum/maximum and range.

Complication rates will be expressed as percentages and relative risks calculated as a ratio of the complication rate. Multilevel multiple logistic regression will be used to adjust for potential confounding factors (such as age, sex and grade of operating surgeon). No individual centre will be identifiable from the analysis however we plan to compare regions. P-values of <0.05 will be considered significant.

6 STUDY SETTING

UK hospitals performing adult tonsillectomy procedures. Trainees from the INTEGRATE network will be invited to participate in the study as local site leads.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

7.1.1 Inclusion criteria

All consecutive adult patients undergoing bilateral tonsillectomy in a two-month period between **1st of August 2025 to 31st of July 2026**. Adult patients will be defined as >18 years of age at the time of their surgery. All patients will need to be English speaking.

7.1.2 Exclusion criteria

- Known bleeding disorder
- Tonsillar biopsy
- Tonsillectomy for known or suspected cancer
- Tonsillectomy performed with palatal surgery
- Any second or revision tonsil operation (revision or remnant tonsillectomy)
- Tonsillectomy performed in the private sector

7.2 Sampling

7.2.1 Size of sample

This is an exploratory pilot study therefore no power calculation has been performed. We anticipate our study will be able to demonstrate feasibility of the methodology and provide data for the purposes of larger studies in the future.

The TYPHOON Study Protocol

Based on HES data, we assume between 1000 – 1200 adult tonsillectomies will be performed a month. We expect to capture approximately one quarter of the total, equating to approximately 500 – 600 patients over a two-month period. Based on an expected bleed rate of 20%, we would expect 100 - 120 patients to be readmitted for bleeding.

7.2.2 Sampling technique

All consecutive adult patients undergoing tonsillectomy procedures will be invited to participate in the project.

7.3 Recruitment**7.3.1 Sample identification**

Local investigators will prospectively identify adult patients for inclusion into the study through the informatic department and / or via the theatre schedule. The local investigators will be members of the usual clinical care team.

7.3.2 Consent

Local site leads will arrange for the Participant Information Sheet (PIS) to be sent to potential participants prior to their admission date for surgery along with any standard clinical documents. They will ensure the details of their local Patient Advice and Liaison Service (PALS) are included in the PIS.

Patients will be consented before surgery either at the preassessment clinic or at the time of surgery. All contact regarding informed consent will be undertaken in person. Patients will be given an adequate period of time to ask questions and consider their involvement in the study before providing consent. Patients will be allowed to withdraw at any time, without reason, and the reason for withdrawal will be documented. As the study does not involve any additional risk for patients, and the only deviation from normal practice is completion of a quality of life questionnaire and a telephone follow up phone call at 28 days post-surgery, we do not anticipate any significant implications associated with participating in the study.

8 ETHICAL AND REGULATORY CONSIDERATIONS

This study will report on the outcomes of tonsillectomy that will take place regardless of inclusion in the study. There will be no effect on the subsequent management of patients as a result of inclusion in the study. All data will be pseudonymised, and no patients will be identifiable in any subsequent reports, presentations or publications.

The protocol will be submitted for ethical review to the Health Research Authority's 'Integrated Research Application System' (IRAS).

8.1 Assessment and management of risk

The sponsor has implemented an audit programme, based on risk, for its non-CTIMPs studies. This study falls under the remit of this programme and therefore may be subject to audit.

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

The study was deemed to require NHS research ethics committee (REC) review for England, Scotland, Wales or Northern Ireland using the NHS REC review decision tool available at <https://www.hra-decisiontools.org.uk/ethics/index.html>.

Substantial amendments that require review by NHS REC will not be implemented until that review is in place and other mechanisms are in place to implement at site. All correspondence with the REC will be retained. It is the Chief Investigator's responsibility to produce the annual reports as required. The Chief Investigator will notify the REC at the end of the study. If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination. Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications / abstracts to the REC.

Regulatory Review & Compliance

Before any site can enrol patients into the study, the Chief Investigator / Principle Investigator or designee will ensure that appropriate approvals from participating organisations are in place. Specific arrangements on how to gain approval from participating organisations are in place and comply with relevant guidance.

Amendments

Amendments to the protocol or associated documentation will be made when necessary and will be agreed by the INTEGRATE head and neck steering committee. The Chief Investigator has responsibility for preparing the protocol and making appropriate amendments. All amendments will be submitted for sponsorship approval prior to making REC and/or HRA applications.

The TYPHOON Study Protocol

Any amendments will be submitted to the sponsor to be categorised as Substantial or non-Substantial. The amendment will be locked via the IRAS Amendment Tool and clearly documented before submission to REC via the IRAS Amendment Portal by the CI (or representative) for approval prior to implementation.

Amendments to the protocol will be summarised Appendix 3.

8.3 Peer review

Will be peer reviewed by Mr David Hamilton and Mr Matt Smith

8.4 Patient & Public Involvement

The study protocol and patient facing documents were reviewed by the patient and public involvement group (PPI) from NHS Research Scotland at the University of Glasgow on the 15th of August 2024. Specifically, there were concerns about the amount of time patients had to consent for the study, therefore the protocol was amended to ensure that the Participant Information Sheet was sent out with the appointment letter for surgery to give patients an appropriate amount of time to consider their participation.

8.5 Protocol amendments and compliance

Any change in the study protocol will require an amendment. If applicable, any proposed protocol amendments will be initiated by the Chief Investigator following continued assessment of the study and any required amendment forms will be submitted to the relevant regulatory authority, ethics committee and sponsor. The Chief Investigator will liaise with the study sponsor to determine whether an amendment is non-substantial or substantial. All amended versions of the protocol will be signed by the Chief Investigator and Sponsor Representative. Before the amended protocol can be implemented favourable opinion / approval must be sought by the original reviewing REC and Research and Development (R&D) office(s).

Accidental protocol deviations will be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately. Deviations from the protocol which are found to frequently recur will receive immediate action and could potentially be classified as a serious breach.

8.6 Data protection and patient confidentiality

The clinical investigator and local site investigators will comply with the requirements of the Data Protection Act 2018 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

The TYPHOON Study Protocol

All study data will be held on NHS systems with password protection and destroyed after 5 years once the study is completed. No patient identifiable data will be accessed outside the initial visit and patients will be pseudonymised during data collection.

8.61 Data handling and record keeping

Each centre will input pseudonymised data into an Excel Data Tool. They will be stored on the Trust password protected shared drive with security to protect against unauthorised access, in line with local data governance protocols. Data from each centre's individual Excel spreadsheet will be amalgamated onto a master spreadsheet, with each update saved as a separate version and old versions retained. Study IDs will be applied on data submission.

8.62 Access to data

Direct access will be granted to authorised representation from regulatory authorities to permit study related monitoring, audits and inspections, in line with participant consent.

8.63 Anonymisation of patients

The Project Management Team will not request the names, addresses, medical record numbers (MRN) or identifiable data for any patients. Dates of birth, surgery, discharge and readmission (where applicable) will be used locally to generate durations. Durations (not dates) will then be submitted to the PMT. Reporting and analysis will not identify individual cases in any subsequent reports, presentations or publications. Data flow will be one way, from the Data Discloser to the Data Receiver (i.e. Project Management Team). There will be no traceability from the Project Management Team's database to local records. If any identifiable data is received, the files will be deleted and the site will be informed and asked to report the breach as per local protocols. Study level IDs will be added on submission, and thus the data will be considered pseudonymised.

8.7 Indemnity

The NHS CNORIS indemnity scheme will apply. CNORIS provides cover for legal liabilities arising from its actions or those of its staff or supervised students in relation to study management, design and conduct (subject to policy and conditions).

8.8 Access to the final study dataset

The INTEGRATE committee will have access to the final dataset.

9 DISSEMINATION POLICY

9.1 Dissemination policy

Data arising from the study are owned by the Sponsor. Findings will be submitted for publication in relevant ENT peer reviewed journals. We also plan to present the results of our audit at a national and international level, including at the ENT UK Research Showcase event and at the British Academic Conference in Otolaryngology (BACO). Results will be promoted on the INTEGRATE website and Twitter pages. Funders and sponsor will be acknowledged in any subsequent reports. Patient participants will not be directly informed of the results of the study.

9.2 Authorship eligibility guidelines and any intended use of professional writers

Authorship will be in line with INTEGRATE policy on multi-centre collaborative projects (<https://entintegrate.co.uk/>). Each Centre will have a named Consultant Lead and a Trainee Lead, in addition to up to two local collaborators.

10 REFERENCES

1. ENT UK RCoS. Commissioning guide: Tonsillectomy. 2021.
2. Lowe D, van der Meulen J, Cromwell D, Lewsey J, Copley L, Browne J, et al. Key messages from the National Prospective Tonsillectomy Audit. *Laryngoscope*. 2007;117(4):717-24.
3. Powell S. Unpublished HES data ed2024.
4. Wilson JA, O'Hara J, Fouweather T, Homer T, Stocken DD, Vale L, et al. Conservative management versus tonsillectomy in adults with recurrent acute tonsillitis in the UK (NATTINA): a multicentre, open-label, randomised controlled trial. *Lancet*. 2023;401(10393):2051-9.
5. Time GIRF. Ear, Nose, Throat Surgery. GIRFT Programme National Specialty Report. 2019.

11. APPENDICES

11.1 Appendix 1- Required documentation

Site questionnaire

Excel data collection proforma

Participant Information Sheet

Patient consent form

TOI-14 (tonsillectomy outcome inventory)

11.2 Appendix 2 – Schedule of Procedures

Procedures	Visits	
	Baseline	28 days
Informed consent	X	
Baseline Data entry	X	
QOL questionnaire	X	X
Telephone Interview		X
Follow-up data entry		X

13.3 Appendix 3 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1	V1	02/07/2024	AW	Change to HRA template
2	V2	02/08/2024	AW	Change to HRA template
3	V3	26/09/2024	LL	Change to Excel from Redcap
4	V4	17/01/2025	YKL	Changes made to Chief Investigator and Associate Chief Investigator, Study Duration, Patient Identification, Inclusion Criteria.
5	V5	28/7/2025	YKL	Changes made to Planned Study Period, Patient Identification, Inclusion Criteria.