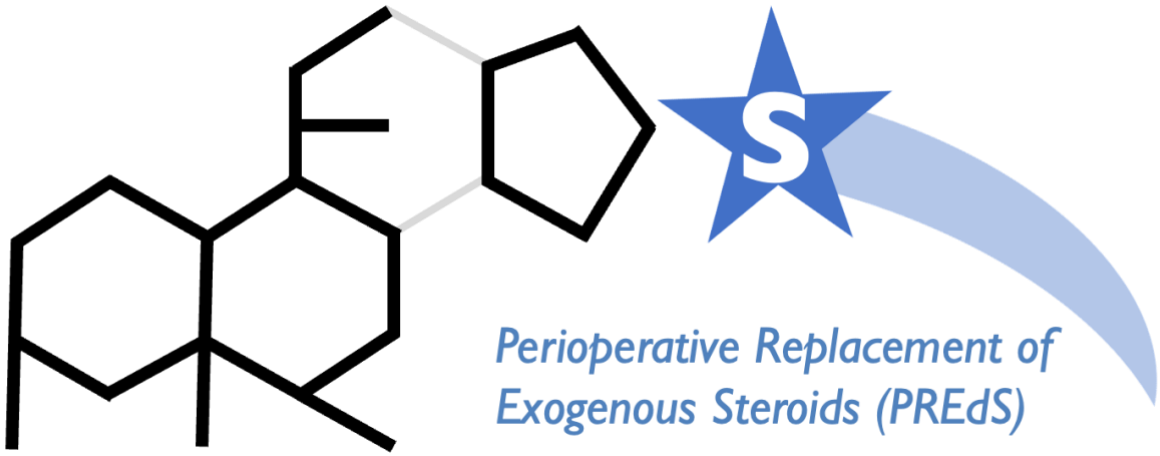
The Perioperative Replacement of Exogenous Steroids (PREdS) Study: Preliminary data collection of patients presenting for surgery with potential adrenal insufficiency

Phase A1: A multi-centre audit of current practise and collection of patient data for future analysis



Sponsor

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ABSTRACT

Introduction: **Oral corticosteroids are prescribed to approximately 1% of the UK population. Indications are broadly split into two groups; those deficient in corticosteroid who require replacement, or those taking therapeutic corticosteroid for a range of inflammatory conditions. Therapeutic treatment can induce (tertiary) adrenal insufficiency with the subsequent inability to increase production at times of physiological stress, such as surgery, potentially leading to major complications. Current guidance therefore recommends steroid supplementation in the perioperative period. Replacement therapy for primary and secondary insufficiency will always be required, but the degree of adrenal suppression is not well understood in the therapeutic patient group. Consensus guidelines exist for such patients but are based on limited evidence. This audit of UK practise is designed to assess compliance with current guidelines. The data gained from the audit will then be used to guide design of a randomised clinical trial.**

Methods and analysis: **This prospective audit will invite all 19 Anaesthetic Trainee Research Networks within the United Kingdom to participate, working across more than 150 NHS Acute Trusts. Data will be collected over a two-week period using a combination of paper and digital case record forms (CRF), with data stored on a secure database. Descriptive statistics for the use of/compliance with existing guidelines will be performed, with additional data collected for secondary analysis to include the number of patients presenting for surgery receiving therapeutic corticosteroids, diagnoses, demographics and planned procedure.**

Ethics and dissemination: **Ethical approval is not required for this audit as defined by the NHS Health Research Authority Defining Research and Ethics tool. All participating centres will be expected to register their involvement with local audit departments and comply with local data protection policy. Results will be reported to Trainee Research Networks who will in turn disseminate results to individual Trusts. Data will undergo secondary analysis to inform the design of a randomised controlled trial assessing peri-operative corticosteroid supplementation regimens. The results of this audit will be disseminated by peer-reviewed manuscript, conferences, and will inform future guidance.**

1. Introduction

Corticosteroid use is common. Initial 'scoping' work for this project (interrogating the Clinical Practice Research Datalink (CPRD)), showed that around 1% of the UK population, takes oral corticosteroids for ≥28 days each year and there were roughly 8 million prescriptions for oral corticosteroids in 2020.[1] Although individual prescriptions are inexpensive, the volume means corticosteroids are one of the 20 highest prescription costs in the UK.[2] Patients prescribed corticosteroids comprise those:

- Deficient in corticosteroids who require replacement (e.g. primary pituitary or adrenal insufficiency)

- Taking therapeutic corticosteroids for a range of inflammatory conditions (e.g. asthma, autoimmune diseases)

This audit is concerned only with those taking therapeutic corticosteroids, who form by far the largest group. This patient group potentially present more frequently than the general population for surgery with indications related to their diagnosis (e.g. bowel resection for inflammatory bowel disease, joint replacement for inflammatory arthritis), or the consequences of corticosteroid use (e.g. bone fracture due to demineralisation, accelerated coronary artery disease etc). There are currently no data quantifying this relationship.

Administering exogenous corticosteroids can reduce production of adrenocorticotropic hormone (ACTH) from the pituitary gland due to negative feedback, which in turn can lead to the adrenal gland being unable to produce enough cortisol in response to stressful stimuli such as surgery. Without adequate corticosteroid supplementation, such patients may develop potentially fatal circulatory failure, hypoglycaemia and other metabolic derangements. Patients on therapeutic corticosteroids are often given 'extra' corticosteroids to ensure their physiological needs are met. This action however should be taken after weighting potential benefits against the risks of administering supplementary steroids (e.g. poor wound healing, infection, hyperglycaemia and other morbidity). Our previous work shows that the dose of peri-operative corticosteroid supplementation in current guidelines, is 10x the 'normal' daily production of cortisol on the day of major surgery.[3-4]

In 2012, the Association of Anaesthetists of Great Britain and Ireland (AAGBI), the Society for Endocrinology UK (SfE), the Royal College of Anaesthetists (RCoA) and the Royal College of Physicians (RCP) received a 'Report to Prevent Future Deaths' from HM Coroner expressing concern about care standards for patients with potential adrenal insufficiency undergoing surgery.

The Coroner's notification led to the first national consensus guidelines generated by the joint Royal Colleges.[3] Literature reviews to inform this guidance highlighted a paucity of evidence about which

patients taking therapeutic corticosteroids need supplementation around the time of surgery, and how much steroid they should take, if any. This is echoed in the United States, as well as by the Cochrane Collaboration.[5-6] Studies were mechanistic and not powered for robust, clinical endpoints. To gain further information about potential supplementation regimens, we performed an RCoA sponsored survey of >1200 UK anaesthetists shortly after publication of the guidance, which showed no consensus regarding whether patients needed supplementation and if so, which patients and at what dose, frequency and duration.[7] The aim is therefore to audit compliance with the guidelines on an individual basis and use the data gained to inform the design of an RCT that seeks to evaluate the impact of steroid supplementation on clinical outcomes.

2. Aims and scope

Audit objectives

The objectives of this audit are to assess compliance with national clinical guidance governing supplementary steroid use, and estimate the prevalence of patients receiving therapeutic glucocorticoids who present for procedures.

Primary objective

To assess compliance with current glucocorticoid supplementation consensus guidelines.

Secondary objectives

We will also be able to describe patient demographics, indication for glucocorticoid therapy, prescribed dose (to include medication, dose, duration, route, and frequency), planned operation, peri-operative supplementation practices, and the number of patients presenting for procedures who are taking therapeutic glucocorticoids.

3. The PREdS Audit – Multi-centre steroid supplementation evaluation

3.1 Audit design

This is a prospective audit of practise. It will collect data on the number of patients presenting for both planned and unplanned procedures receiving any dose of oral steroids, for any duration, with or without a diagnosis of adrenal insufficiency. Data will be eligible to be collected over a window of two months, with fourteen days of consecutive data recorded, at the discretion of the enrolled Trust.

3.2 Eligibility

All patients under the care of an anaesthetist (including those performed under general anaesthesia, regional anaesthesia, and/or sedation with monitoring), ≥18 years of age, presenting for elective, urgent or emergency procedures performed by any medical or surgical specialty at each centre will be eligible to be included in the audit.

3.3 Identification of procedures

Patients will be identified at each centre by the local team, utilising local systems for theatre list scheduling.

3.4 Projected numbers

We aim to recruit as many NHS Trusts (centres) as possible by utilising Anaesthesia Trainee Research Networks (TRN). Within the Severn Trainee Anaesthetic Research (STAR) Network, seven NHS Trusts will be enrolled in this prospective audit. On average each NHS Trust in the UK performs 1000 operations per week, therefore providing a large population for data collection.[8] Each centre is expected to identify all eligible patients and collect contemporaneous data.

3.5 Data Synthesis

The primary measure of this audit will be whether eligible patients undergoing anaesthesia receive appropriate glucocorticoid therapy(s) in compliance with AAGBI guidelines, defined as those taking therapeutic glucocorticoids for >28 days in the period immediately preceding surgery. The primary output of this audit will be the aggregate number of such patients (and the proportion of the total number audited).

The secondary data measures will include:

1. Details of patients': Age, gender, BMI, ASA and NHS Number

2. Details of patients' diagnoses: Known primary adrenal or pituitary insufficiency, any diagnoses requiring therapeutic steroid therapy, current prescribed steroid regime (including medication, dose, duration, route and frequency).

3. Details of patients' procedures: Procedure performed, elective, urgent or emergency

4. Details of peri-operative steroid supplementation

3.6 Additional guideline sharing

Local leads will be encouraged to submit any peri-operative steroid supplementation guidelines that may be in use by the centre that differ from current national consensus guidance. Assessment of peri-operative supplementation will however be measured against the national guidelines.

3.7 Data collection & National Data Opt-Out

All investigators will be required to comply with the requirements of the Data Protection Act 2018 regarding the collection, storage, processing, and disclosure of personal information and will uphold the Act's core principles. Data must also be handled in accordance with the NHS National Data-Opt-Out (NDOO) introduced in May 2018, and compliance must occur prior to data transfer from a participating Trust to UHBW. Data should be recorded contemporaneously onto paper Case Report Forms (CRF) by the clinician delivering care, or local investigators, and a record stored locally. NDOO status will be checked for each record against the NHS Spine in collaboration with the local Business Intelligence Unit (BIU) and/or Clinical Governance (CG) Team. Eligible patient data shall be subsequently uploaded as a digital CRF to our REDCap database (https://redcap.link/PREDS). This database will be held upon a secure server on the Health and Social Care Network (HSCN) at University Hospitals Bristol and Weston (UHBW) and be compliant with standards for collection of sensitive data, thus allowing the collection of patient identifiable information in the form of an NHS number. The primary data set will enable analysis to describe the primary and secondary objectives.

UHBW is registered under the Data Protection Act 2018 with the Information Commissioner's Office (ICO); registration Z7060284. An additional Data Sharing Agreement details the specifics of how patient identifiable data will be securely handled (Appendix D).

Future, secondary analysis of patient demographics and procedures across both patient groups, will utilise Hospital Episode Statistics (HES) and will be requested from the local BIU utilising the compiled NHS numbers for each enrolled Trust. This data will be anonymised at source prior to analysis by the PREdS team, and upon its receipt record of NHS numbers will be removed from the UHBW REDCap database to ensure anonymity. Data will be anonymised in line with the ICO Anonymisation Code of Practice. The specific additional demographic information (e.g. gender, ethnicity), plus further information relating to their admission (e.g. length of stay, geographical distribution), will be analysed in a manner outlined in a further research protocol to follow. This data will facilitate further descriptive analysis of patient demographics, diagnoses and procedures carried out. We anticipate requiring Ethical Approval prior to conducting this analysis.

3.8 Audit management

The audit will be co-ordinated by anaesthetic trainees who are part of the Severn Trainee Anaesthetic Research Collaborative (STAR; https://www.anaesthesiaresearch.org/), with support from the PREdS Chief Investigator and the UHBW Research & Development Centre.

Data will be collected principally by Junior Doctors and Consultants. Local data will be returned to each hospital for audit purposes.

3.9 Data analysis

Descriptive statistics will be produced. Qualitative assessment of guideline use will be undertaken should numbers allow.

3.10 Patient and public involvement

Patient and public involvement (PPI) is not strictly necessary for audits of practice. The wider package of work however, of which this audit is part, was discussed at the Bristol Musculo-skeletal PPI group where many patients had previously taken corticosteroids, or were taking them at the time of surgery. They were supportive of the work in general and understood the rationale challenging perceived wisdom.

3.11 Ethical Considerations

The NHS Health Research Authority Defining Research and Ethics tool (http://www.hra-decisiontools.org.uk/research/) confirms this initial data collection is not defined as research, and therefore does not require Research Ethics Committee Approval. No direct patient contact, nor changes to their care, will occur as part of this study and therefore patient consent is not required. Approval from the Caldicott Guardian at the lead site (UHBW), and audit registration at all enrolled centres will be required prior to commencing the project. The Principal Investigator at each site will be trained with protocol details via virtual seminars prior to recruitment commencing, and are expected to disseminate this information amongst local investigators. Evidence of Ethics Committee Approval will be disseminated prior to requesting anonymised patient data for secondary analysis.

3.12 Financing and insurance

We do not anticipate any additional funding requirements for this audit. All investigators shall be present NHS employees covered by their respective Trust indemnity insurance.

3.13 Dissemination and authorship

It is anticipated that this audit and subsequent data analysis will inform the study design of an NIHR grant application for a randomised-controlled trial. It is anticipated the results of this audit will be presented at national/international meetings and published in a peer reviewed journal. Recognition of contribution for authorship will apply to local Principal Investigators and their team where at least 50 CRF are contributed to the study.

4. Study guide and timeframes for collaboratives and centres

June 2022

- STAR
    - Formally invite all TRNs to participate
    - Distribution of protocol, educational materials, advertising information, and CRF guidance

July 2022

- TRN
    - To formally accept invitation to participate in audit
    - Leads to identify an audit lead within each network
    - Audit lead to publicise protocol and recruit centres
    - Local principal investigator (PI) to be identified at each centre

August 2022

- STAR
    - Organisation of educational webinars and opportunity to answer Q&As
    - Publication of FAQ
    - Protocol revisions (if needed)
- Centre level
    - Local PI to identify team at their centre
    - Local hospital audit department approval must be sought and confirmation of this returned to relevant TRN lead (See Appendix A for example)

September 2022

- TRN
    - TRNs to liaise with local centres and confirm window for data collection
- STAR
    - Repeat educational webinars as necessary

October-November 2022 (Data Collection Window)

- Centre level
    - Local lead to identify eligible patients for data collection

- Local lead to ensure data on all operations performed during audit period is collected and returned via the electronic data collection tool. This will be done by publicising the audit (e.g. via posters, electronic communications, noticeboards, departmental meetings etc) with an anticipation that most data entry will be completed by the responsible anaesthetist.

- STAR/TRN
    - Available for queries, guidance and support throughout

February 2023

- PREdS Study Group
    - Release of provisional data analysis

5. References

1. NHS Business Services Authority. Prescription Cost Analysis – England 2020/21. 2021; https://www.nhsbsa.nhs.uk/statistical-collections/prescription-cost-analysis-england/prescription-cost-analysis-england-202021 (accessed 08/11/2021)
2. Library HoC. Medicine Statistics. In: Library HoC, ed. London, 2015
3. Woodcock T, Barker P, Daniel S et al. Guidelines for the management of glucocorticoids during the peri-operative period for patients with adrenal insufficiency. *Anaesthesia* 2020; **75**: 654-63
4. Gibbison B, Spiga F, Walker JJ et al. Dynamic pituitary-adrenal interactions in response to cardiac surgery. *Critical care medicine* 2015; **43**: 791-800.
5. Liu MM, Reidy AB, Saatee S, Collard CD. Perioperative steroid management: approaches based on current evidence. *Anesthesiology* 2017; **127**: 166-72.
6. Yong SL, Maria, P, Esposito M, Coulthard P. Supplemental perioperative steroids for surgical patients with adrenal insufficiency. *Cochrane Database Syst Rev* 2009: Cd005367.
7. Ramesh AV, Pufulete M, Reeves BC, Fletcher S, Tomlinson JW, Gibbison B. Peri-operative corticosteroid supplementation for patients on therapeutic glucocorticoids: a national survey. *Anaesthesia* 2020; **75**: 1396-8.
8. NHS Digital. Provisional Hospital Monthly Statistics for Admitted Patient Care, Outpatient and Accident and Emergency data April 2019 - March 2020 (M13). 2020; https://digital.nhs.uk/data-and-information/publications/statistical/hospital-episode-statistics-for-admitted-patient-care-outpatient-and-accident-and-emergency-data/april-2019---march-2020-m13 (accessed 08/11/2021)

Appendix A. Example Audit Registration Form

University Hospitals Bristol NHS
NHS Foundation Trust

ID No:
(office use only)

CLINICAL AUDIT PROJECT PLAN

All clinical audit projects should be registered before they start.

Please discuss your proposal with the appropriate Clinical Audit Facilitator. Contact details and guidance on completing this form are available via relevant workspace http://connect/governanceandquality/clinicalaudit/Pages/default.aspx

Title: see note 1
Perioperative Replacement of Exogenous Steroids

Your Details: Audit lead					
Name	Ben Gibbison	**Division**	Specialised Services		
Position/Job Title	Consultant	**Specialty**	Cardiac Anaesthesia		
Email	ben.gibbison@bristol.ac.uk	**Tel**	07931568135	**Bleep**	

Project Team: see note 2			
Name	**Job Title**	**Specialty**	**Role within Project (data collection, Supervisor etc)**
Oliver Barker	Doctor	Anaesthesia	Audit Design
Jon Barnes	Doctor	Anaesthesia	Audit Team
Inthu Kangesan	Doctor	Anaesthesia	Audit Team
Aravind Ramesh	Doctor	Anaesthesia	Audit Team

Participation details: see note 2			
What areas will this audit impact on? (e.g. another profession/specialty/Trust)	Who in this area have you discussed and agreed this audit with?		
	Name	**Job Title**	**Date Agreed**
Theatres	Joe Bloggs	Matron, Theatres	XX/XX

Background: see note 3

Corticosteroid use is common in the UK. In England alone in 2020 over 50 million corticosteroid prescriptions were dispensed, of which over 22 million were inhaled formulations, and around 8 million oral, with use rising in the last decade [1]. Clinical indications for corticosteroid can broadly be divided into two groups; those with endogenous corticosteroid deficiency who require replacement, and therapeutic corticosteroid for a range of diagnoses including inflammatory and malignant conditions, as well as after organ transplantation. Endogenous deficiency may be further classified; primary due to diseases of the adrenal gland, secondary due to reduced pituitary action, or tertiary from reduced hypothalamic release of CRH. Importantly long-term exogenous steroids can result in iatrogenic tertiary adrenal insufficiency in people with previously normal function, and ultimately adrenal atrophy over time. Any patient prescribed equivalent oral daily doses of prednisolone greater than 5mg in adults, or 10-15mg/m^2 in children, when administered for greater than 1 month, may result in tertiary insufficiency [2,3]. When assessed by a short synacthen test, up to a third of patients receiving glucocorticoid therapy can show evidence of adrenal insufficiency when well, but whether this translates into clinical changes is not known [4].

Physiological stresses such as surgery or acute illness induce the hypothalamic-pituitary-adrenal(HPA) axis and daily cortisol production may quadruple in major surgery, with levels typically returning to normal at 24-48 hours [5]. Insufficient production may precipitate metabolic derangements, hypoglycaemia and ultimately life threatening circulatory failure termed an adrenal crisis, mitigated clinically by the concept of supplementary corticosteroids. In theory, a significant proportion of those receiving therapeutic glucocorticoids are at risk of this, and therefore recent consensus guidelines published in the UK by a collaborative of the Association of Anaesthetists, the Society for Endocrinology and the Royal College of Physicians advise additional supplementation for both patient groups in the peri-operative period [6]. The authors acknowledge the paucity of evidence for supplementation in the therapeutic patient group, and the guidelines specifically highlight the need for high-quality studies to inform future guidance. Glucocorticoids have a plethora of side effects including poor wound healing, susceptibility to infections and hyperglycaemia; unnecessary doses peri-operatively may increase the risk of potentially avoidable complications [6].

A survey on behalf of the RCOA in 2019 demonstrated, prior to the present consensus statement, significant heterogeneity in UK anaesthetic practice [7]. This included the dose threshold of routinely prescribed glucocorticoids that triggered supplementation, nature of surgical procedure, and the actual supplementary dose to prescribe. Importantly the majority of respondents would not administer supplementation in those receiving topical or inhaled glucocorticoids, and had an oral dose threshold of 10mg prednisolone, a clear discrepancy from the latest guidelines.

There is no question that those who are glucocorticoid deficient need an increased dose in the peri-operative period. There remains substantial uncertainties however for those patients receiving therapeutic glucocorticoids, including exactly who should receive supplemental dosing, as well as the most appropriate dose and timing. Understanding the number of patients on therapeutic glucocorticoids presenting for surgery who are at risk of adrenal insufficiency, and the true peri-operative consequences, is clearly desirable. Prior to the COVID-19 pandemic greater than 12 million operations were performed in England alone per year, and therefore this presents a potentially very large cohort of patients requiring peri-operative steroid supplementation [8].

1. NHS Business Services Authority. Prescription Cost Analysis – England 2020/21. 2021; https://www.nhsbsa.nhs.uk/statistical-collections/prescription-cost-analysis-england/prescription-cost-analysis-england-202021 (accessed 08/11/2021)
2. Woods CP, Argese N, Chapman M, *et al.* Adrenal suppression in patients taking inhaled glucocorticoids is highly prevalent and management can be guided by morning cortisol. *European Journal of Endocrinology* 2015; **173**(5): 633-642
3. Husebye ES,Allolio B,Arlt W, *et al.* Consensus statement on the diagnosis, treatment and follow-up of patients with primary adrenal insufficiency. *Journal of Internal Medicine* 2014; **275**: 104–15.
4. Bancos I, Hahner S, Tomlinson J, Arlt W. Diagnosis and management of adrenal insufficiency. *Lancet Diabetes and Endocrinology* **2015**; 3: 216–26.
5. Prete A, Yan Q, Al-Tarrah K, *et al.* The cortisol stress response induced by surgery: A systematic review and meta-analysis. *Clinical Endocrinology* 2018; **89**: 554–67.
6. Woodcock T, Barker P, Daniel S *et al.* Guidelines for the management of glucocorticoids during the peri-operative period for patients with adrenal insufficiency. *Anaesthesia* 2020; **75**(5): 654-663
7. Ramesh AV, Pufulete M, Reeves BC, *et al.* Peri-operative corticosteroid supplementation for patients on therapeutic glucocorticoids: a national survey. *Anaesthesia* 2020; **75**: 1394-1397
8. NHS Digital. Provisional Hospital Monthly Statistics for Admitted Patient Care, Outpatient and Accident and Emergency data April 2019 - March 2020 (M13). 2020; https://digital.nhs.uk/data-and-information/publications/statistical/hospital-episode-statistics-for-admitted-patient-care-outpatient-and-accident-and-emergency-data/april-2019---march-2020-m13 (accessed 08/11/2021)

Aim: see note 4

The objectives of this audit are to assess compliance with national clinical guidance governing supplementary steroid use, and estimate the prevalence of patients receiving therapeutic glucocorticoids who present for procedures.

Objectives: see note 4. You may find it is unnecessary to use the "Objectives" section i.e. "**Aim**" and "**Criteria**" may cover all the essential information.

Primary objective

To assess compliance with current glucocorticoid supplementation consensus guidelines.

Secondary objectives

We will also be able to describe patient demographics, indication for glucocorticoid therapy, prescribed dose (to include medication, dose, duration, route, and frequency), planned operation, peri-operative supplementation practices, and the number of patients presenting for procedures who are taking therapeutic glucocorticoids.

STANDARDS

List standards as per example in first row. Be sure data you plan to collect will measure performance against listed standards.

Provide full information on source of standards – Title, website reference etc.

	Criteria	Target (%)	Exceptions	Source & Strength* of Evidence		Instructions for where to find data
E.G.	*At initial assessment urinary incontinence should be categorised as stress/mixed/urge*	*100%*		*NICE Guideline-CG 40* *http://guidance.nice.org.uk/CG40*	*C*	*Medical notes*
1	Assessment of whether patients having surgery are taking exogenous corticosteroids.	100%	Patients receiving replacement corticosteroid therapy			Patients and medical notes

2	Assessment of whether patients on therapeutic corticosteroids are supplemented in the peri-operative periods.	100%		AAGBI Guidance http://dx.doi.org/10.1111/anae.14963	C	Anaesthetic record, patient drug chart and medical notes

***Strength of Evidence**

A At least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation
B Availability of well-conducted clinical studies but no randomised clinical trials on the topic of the recommendation
C Expert committee reports or opinions and/or clinical experience of respected authorities. Absence of directly applicable clinical studies of good quality
D Recommended good practice based on clinical experience (local consensus)

Data Collection Methodology (see note 5)	
Prospective data collection with Clinician-led data entry into a secure REDCap database.	
Further details or other method	UHBW R&D REDCap database with support from Mai Baquedano. REDCap database link: https://redcap.link/PREDS
Please give details of how this has been/will be piloted:	Test database created and pilot data collection by organisers of the audit.
▪ **You must include your data collection form/spreadsheet with this proposed Audit Plan.** ▪ **Be sure the data items you're collecting match the standards set**	

Audit Sample: see note 6	
Sample selection criteria	All patients under the care of an anaesthetist (including general anaesthesia, regional anaesthesia, and/or sedation with monitoring), ≥18 years of age, presenting for elective, urgent or emergency operations.
Time period audited *(i.e. Oct 12- Jan 13)*	14 day period within the **October/November 2022**
Estimated number of cases	>100
Who will provide list of patient (NB – need appropriate hospital / NHS numbers)	Theatre co-ordinators at respective site will provide elective theatre lists for the duration of the audit. Emergency/unscheduled patients will be identified by the local team.
If you are requesting notes through the CA team, where would you like them delivered	N/A

Timescale/Deadlines: see note 6	
Proposed start of data collection	01/09/2022
Proposed date for presentation of results	January 2023
Forum	Divisional audit meeting, national/international meetings, peer-reviewed journal
Proposed finish date *i.e. after report and action plan produced*	Spring 2023

Will you be leaving your current post in the near future?	No
If Yes, please give leaving date	
If your project will not be finished by then, please identify and provide the name and job title of another member of staff who is willing to take over when you go	
Are there any other deadlines you need to take into consideration?	No

You need an appropriate senior clinician / manager to support the project. List below. Helpful to discuss with clinical audit team before seeking approval from senior colleague.

Project Lead: I agree to ensure that this project is completed, the results disseminated, and a report given to my clinical audit facilitator. I understand that non-anonymised (staff/patient) audit data must not be taken outside the Trust. I understand that audit results belong to the Trust and that the project report may be made available to anyone who requests it.

Ben Gibbison	31.11.2021
Project Lead	Date

Senior Clinician / Manager: I confirm that this project has been agreed as part of the Specialty audit programme and that I will give my full support to it. I will ensure the dissemination of audit results and lead on the development and implementation of an action plan (if necessary) in order to obtain improvements in the quality of care provided.

Ben Gibbison	31.11.2021
Senior Clinician/Manager	Date

Clinical Audit Convenor: I approve the project described above and confirm that it has been appropriately reviewed for methodological quality, resource implication and importance to the Trust.

Clinical Audit Convenor	Date

Case Report Form

SITE
Region: _____
Hospital: _____

1.0 PATIENT DETAILS
NHS number: _____

1. Has the patient been on regular **oral** steroids for ≥28 days: YES ☐ NO ☐ **If 'NO' STOP HERE**
If 'YES' move to Section 2.0

2.0 DEMOGRAPHIC DETAILS
Height (m): _____ Weight (kg): _____
ASA grade: 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐
Emergency surgery ☐ Elective surgery ☐
Operation: _____

3.0 REGULAR STEROIDS
1. Diagnosis requiring steroids: _____
2. Name of maintenance steroid: Prednisolone ☐ Hydrocortisone ☐ Dexamethasone ☐ Methylprednisolone ☐ Other: ☐ _____
3. Dose of maintenance steroid (mg): _____
4. Dose frequency of regular oral steroid: OD ☐ BD ☐ TDS ☐ QDS ☐ >QDS ☐ Other: ☐ _____
5. Is patient on 2nd regular oral steroid: YES ☐ NO ☐
6. Name of 2nd maintenance steroid: Prednisolone ☐ Hydrocortisone ☐ Dexamethasone ☐ Methylprednisolone ☐ Other: ☐ _____
7. Dose of 2nd maintenance steroid (mg): _____
8. Dose frequency of 2nd regular oral steroid: OD ☐ BD ☐ TDS ☐ QDS ☐ >QDS ☐ Other: ☐ _____

4.0 PRE/INTRA-OPERATIVE STEROIDS
1. Were additional steroid given either pre-operatively or intra-operatively? YES ☐ NO ☐
If 'NO' move to Section 5.0
2. What was the indication for additional steroids?
☐ Replacement/supplementation of regular maintenance steroid
☐ Other (e.g. PONV) - Please indicate reason: _____
☐ Replacement/supplementation of regular maintenance steroid **AND** another reason
3. What drug and dose were administered for:

a) Replacement/supplementation:

Prednisolone	☐	Dose (mg)____	Methylprednisolone	☐	Dose (mg)____
Hydrocortisone	☐	Dose (mg)____	Other	☐	Drug _____
Dexamethasone	☐	Dose (mg)____			Dose (mg)____

b) Other indication:

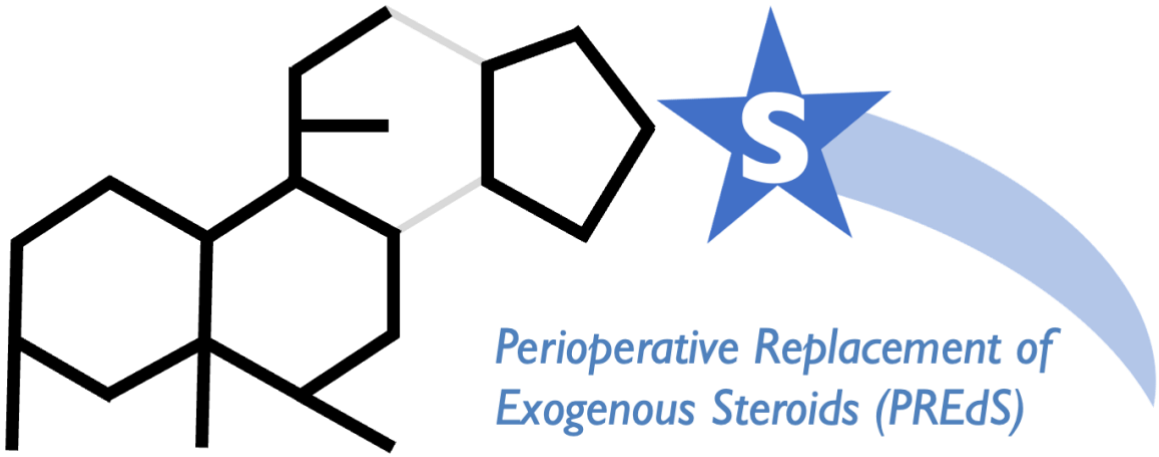
Prednisolone	☐	Dose (mg)____	Methylprednisolone	☐	Dose (mg)____
Hydrocortisone	☐	Dose (mg)____	Other	☐	Drug _____
Dexamethasone	☐	Dose (mg)____			Dose (mg)____

5.0 POST-OPERATIVE STEROIDS
1. Were additional steroids prescribed for the post operative period? YES ☐ NO ☐
If 'NO' move to Section 6.0
2. Please indicate the name, dose, frequency & duration of any additional steroid(s) given post operatively:

Prednisolone	☐	Dose (mg)____	Recovery Only ☐
		OD ☐ BD ☐ TDS ☐ QDS ☐ >QDS ☐	24 Hours ☐
		Continuous Infusion ☐ Other: ☐ _____	> 24 Hours ☐
Hydrocortisone	☐	Dose (mg)____	Recovery Only ☐
		OD ☐ BD ☐ TDS ☐ QDS ☐ >QDS ☐	24 Hours ☐
		Continuous Infusion ☐ Other: ☐ _____	> 24 Hours ☐
Dexamethasone	☐	Dose (mg)____	Recovery Only ☐
		OD ☐ BD ☐ TDS ☐ QDS ☐ >QDS ☐	24 Hours ☐
		Continuous Infusion ☐ Other: ☐ _____	> 24 Hours ☐
Methylprednisolone	☐	Dose (mg)____	Recovery Only ☐
		OD ☐ BD ☐ TDS ☐ QDS ☐ >QDS ☐	24 Hours ☐
		Continuous Infusion ☐ Other: ☐ _____	> 24 Hours ☐
Other	☐	Drug _____	Recovery Only ☐
		Dose (mg)____	24 Hours ☐
		OD ☐ BD ☐ TDS ☐ QDS ☐ >QDS ☐	> 24 Hours ☐
		Continuous Infusion ☐ Other: ☐ _____	

6.0 GUIDELINES
1. Are you aware of any specific trust or national guidelines that were followed to help make these decisions? YES ☐ NO ☐
2. If 'yes' please indicate which guidelines were followed:
_____

Appendix C. Site Data Capture Form



PREdS Audit - Site Data Capture Form

Site Name:

Trust:

Consultant Lead Investigator:

Name:

Email:

Trainee Lead Investigator:

Name:

Email:

Selected Audit Dates:

Investigators List:

(Continue on additional sheets as necessary)

Name:
Email:
Role:

Appendix D. Data Sharing Agreement

University Hospitals Bristol and Weston NHS Foundation Trust

DATA SHARING AGREEMENT

University Hospitals Bristol and Weston NHS Foundation Trust,

whose administrative offices are at

Trust Headquarters, Marlborough Street, Bristol, BS1 3NU

(referred to as 'the Provider')

AND

Insert NAME AND ADDRESS OF OTHER PARTY OR PARTIES],

(Referred to as "the Recipient")

Which are collectively referred to as the "Parties" or individually referred to as a "Party"

NOW

WHEREAS the Provider is an NHS Foundation Trust;

WHEREAS the Recipient is a NHS Organisation;

WHEREAS the Recipient shall use the Data in connection with the Purpose.

The above Parties HEREBY AGREE AS FOLLOWS:

1. DEFINITIONS

The following words and phrases have the following meanings:

Agent(s)	Includes, but shall not be limited to, any person undertaking a function in connection with this Agreement (including the Principal Investigator, any nurse or other health professional), any such person's principal employer in the event it is not the Participating Site and where such person is providing services to a Party under a contract for services or otherwise (including clinical academics), and/or any contracted third party providing services to a Party under a contract for services or otherwise.
Agreement	This agreement, together with the schedules annexed hereto.
Background	Intellectual Property Rights and Know How that are provided by one Party to the other Party for use in the Study (whether before or after the date of this Agreement) that do not themselves arise from the Study.
Confidential Information	All information disclosed, (whether in writing, orally or by another means and whether directly or indirectly) by a Party ("Disclosing Party") to another Party ("Receiving Party") directly relating to the Study including, but not limited to information, the release of which is likely to prejudice the commercial business interests of the Disclosing Party, or which is a trade secret, including Know How and shall also include any data disclosed which is Personal Data and/or special category Personal Data, all as defined in the Data Protection Legislation, and/or information that is otherwise confidential patient information.
Controller	Shall have the meaning set out in the Data Protection Legislation.
Data Protection Legislation	All applicable data protection and privacy legislation, regulations and guidance including but not limited to UK General Data Protection Regulation (UK GDPR), the Data Protection Act 2018 (DPA18), the Privacy and Electronic Communications (EC Directive) Regulations 2003 and any guidance or codes of practice issued by the European Data Protection Board or Information Commissioner from time to time (all as amended, updated or re-enacted from time to time).

Data Subject	As defined in the Data Protection Legislation.
Intellectual Property Rights	Patents, trade marks, trade names, service marks, domain names copyrights, rights in and to databases (including rights to prevent the extraction or reutilisation of information from a database), design rights, topography rights and all rights or forms of protection of a similar nature or having equivalent or the similar effect to any of them which may subsist anywhere in the world, whether or not any of them are registered and including applications for registration of any of them.
Know How	All technical and other information which is not in the public domain, including but not limited to information comprising or relating to concepts, discoveries, data, designs, formulae, ideas, inventions, methods, models, procedures, designs for experiments and tests and results of experimentation and testing, processes, specifications and techniques, laboratory records, manufacturing data and information contained in submissions to regulatory authorities.
NHS Indemnity Scheme	One of the NHS Resolution (Litigation Authority) Clinical Negligence Scheme for Trusts ("CNST") in England; the Clinical Negligence Fund in Northern Ireland; the Clinical Negligence and other Risks Indemnity Scheme (CNORIS) in Scotland; or the Welsh Risk Pool Service (WRPS) in Wales.
Personal Data	Any and all information, data and material of any nature received or obtained by any Party in connection with this Agreement which is personal data as defined in Data Protection Legislation and which relates to any Participant or his or her treatment or medical history.
Process	As defined in the Data Protection Legislation (and "Process" and "Processed" shall be construed accordingly);
Processor	Shall have the meaning as set out in the Data Protection Legislation;
Results	Any outputs arising from the use of the Data.
Purpose	The reason for having the data as described in Schedule 1
Data	The Data described in Schedule 1.

Any reference to a statutory provision, code or guidance shall be deemed to include reference to any subsequent modification or re-enactment of it.

2. DISCLOSURE AND USE OF STUDY DATA OBLIGATIONS OF THE PARTIES

2.1. The Provider shall disclose to the Recipient the Data.

3. LIABILITIES AND INDEMNITY

3.1. Nothing in this clause 3 shall operate so as to restrict or exclude the liability of a Party in relation to statutory or regulatory liability (including but not limited to breach of the Data Protection Legislation), death or personal injury caused by the negligence or wilful misconduct of that Party or its Agent(s), fraud or fraudulent misrepresentation or to restrict or exclude any other liability of a Party which cannot be so restricted or excluded in law.

3.2. Each Party shall maintain all proper insurance or equivalent indemnity arrangements to cover liabilities arising from its rights and obligations under this Agreement. [For the avoidance of doubt, in respect of NHS organisations such indemnity arrangements can include membership of an NHS Indemnity Scheme provided such membership will meet such liabilities.]

3.3. Subject to clauses 3.4, 3.5, 3.6 and 3.7, the Recipient shall indemnify the Provider and its Agents, against any reasonable claims, proceedings and related costs, expenses, losses, damages and demands ("Claims") to the extent they arise or result from the negligent acts or omissions of, or the wilful misconduct of the Recipient, and/or contracted third party, in its performance of this Agreement or use of the Data.

3.4. Subject to clauses 3.3, 3.5, 3.6 and 3.7, the Provider shall indemnify the Recipient against any reasonable claims, proceedings and related costs, expenses, losses, damages and demands to the extent they arise or result from the negligent acts or omissions of, or the wilful misconduct of the Provider in its performance of this Agreement or in connection with the Purpose.

3.5. An indemnity under clauses 3.3 or 3.4 shall only apply if the indemnified Party:

3.5.1. informs the Party providing the indemnity in writing as soon as reasonably practicable following receipt of notice of the claim or proceedings;

3.5.2. upon the indemnifying Party's request and at the indemnifying Party's cost gives the indemnifying Party full control of the claim or proceedings and provides all reasonable assistance; and

3.5.3. makes no admission in respect of such claim or proceedings other than with the prior written consent of the indemnifying Party.

3.6. Any indemnity under clauses 3.3 or 3.4 shall not apply to the extent any claims, proceedings and related costs, expenses, losses, damages or demands arise or result from the negligent acts or omissions or wilful misconduct or breach of statutory duty of the indemnified Party.

3.7. No Party shall be liable to another in contract, tort/delict, breach of statutory duty or otherwise for any loss of profits, revenue, reputation, business opportunity, contracts, or any indirect, consequential or economic loss arising directly or indirectly out of or in connection with this Agreement.

3.8. Subject to clause 3.1 and 3.7 the liability of the Recipient to the Provider arising out of or in connection with any breach of this Agreement or any act or omission of either Party in connection with the performance of the Purpose shall not be the greater of ten thousand (£10,000 GBP) pounds. For the avoidance of doubt, this cap applies also but not exclusively to the indemnities offered under clause 3.3.

4. CONFIDENTIALITY, DATA PROTECTION AND FREEDOM OF INFORMATION and DATA PROTECTION

Where the Data includes Personal Data, the Parties agree to comply with all applicable statutory requirements and mandatory codes of practice in respect of confidentiality (including medical confidentiality) in relation to Data Subjects.

4.1 Data Sharing Terms

4.1.1. In relation to Personal Data processed by the Recipient in the course of delivering the Services, the Recipient must publish, maintain and operate policies relating to confidentiality, data protection and information disclosures that comply with the Law, the Caldicott Principles and Good Practice;

4.1.2. In the event that the Data is comprised of or includes any Personal Data then the following shall apply:

4.1.2.1. the Parties acknowledge that the factual arrangements between them dictate the role of each Party in respect of the Data Protection Legislation;

4.1.2.2. notwithstanding 4.1.2.1, each Party expects that the Recipient and the Provider shall each be acting as a Data Controller in respect of the disclosure of Personal Data to the Recipient by the Provider in accordance with this Agreement;

4.1.3. Personal Data shall only be disclosed to the Recipient by the Provider where this is required directly or indirectly in connection with the Purpose.

4.1.4. The Recipient agrees to use Personal Data solely in connection with the terms of the Agreement, or otherwise for purposes not incompatible with this original purpose (Article 5, 1 (b) GDPR), and not otherwise. In particular,

4.1.4.1. Not to disclose Personal Data to any person except in accordance with applicable legal requirements and codes of practice; and

4.1.4.2. Not to use Personal Data for commercial purposes.

4.1.5. The Recipient agrees to comply with the obligations placed on a Controller by the Data Protection Legislation. This is not limited to, but includes, being responsible for and able to demonstrate compliance with the principles relating to Processing of Personal Data (Article 5 GDPR)

4.1.6. The Recipient must have in place a communications strategy and implementation plan to ensure that Data Subjects are provided with, or have made readily available to them, Privacy Notices, and to disseminate relevant information materials. Any failure by the Recipient to inform Data Subjects as required by Data Protection Legislation or Data Guidance about the uses of Personal Data that may take place under this Agreement cannot be relied on by the Recipient as evidence that such use is unlawful and therefore not required.

4.1.7. The Recipient agrees to ensure persons processing Personal Data under this Agreement are equipped to do so respectfully and safely. In particular:

4.1.7.1. To ensure any persons (excluding employees, honorary employees, students, researchers, consultants and subcontractors of the

Provider) Processing Personal Data understand the responsibilities for information governance, including their obligation to Process Personal Data securely and to only disseminate or disclose for lawful and appropriate purposes.

4.1.7.2. To ensure any persons (excluding employees, honorary employees, students, researchers, consultants and subcontractors of the Provider) have appropriate contracts providing for personal accountability and sanctions for breach of confidence or misuse of data including deliberate or avoidable data breaches.

4.1.8. The Recipient agrees to proactively prevent data security breaches and to respond appropriately to incidents or near misses. In particular,

4.1.8.1. To ensure that Personal Data are only accessible to persons who need it for the purposes of the Purpose and to remove access as soon as reasonably possible once it is no longer needed.

4.1.8.2. To ensure all access to Personal Data on IT systems processed for Purpose purposes can be attributed to individuals.

4.1.8.3. To review processes to identify and improve processes which have caused breaches or near misses, or which force persons Processing Personal Data to use workarounds which compromise data security.

4.1.8.4. To adopt measures to identify and resist cyber-attacks against services and to respond to relevant external security advice.

4.1.8.5. To take action immediately following a data breach or near miss. The Recipient must report and publish any Data Breach and any Information Governance Breach in accordance with IG Guidance for Serious Incidents. If the Recipient is required under Data Protection Legislation to notify the Information Commissioner or a Data Subject of a Personal Data Breach then as soon as reasonably practical and in any event on or before the first such notification is made the Recipient must inform the Provider of the Personal Data Breach. This clause does not require the Recipient to provide the Provider with information which identifies any individual affected by the Personal Data Breach where doing so would breach Data Protection Legislation.

4.1.9. The Recipient agrees to ensure data are Processed using secure and up to date technology. In particular,

4.1.9.1. To ensure no unsupported operating systems, software or internet browsers are used to support the processing of Personal Data for the purposes of the Purpose.

4.1.9.2. To put in place a strategy for protecting relevant IT systems from cyber threats which is based on a proven cyber security framework such as Cyber Essentials.

4.1.9.3. To ensure IT suppliers are held accountable via contracts for protecting Personal Data they Process and for meetings all relevant information governance requirements.

4.1.10. The Recipient must ensure that its NHS Data Security and Protection Toolkit (or any successor framework) submission is audited in accordance with Information

Governance Audit Guidance where applicable. The Recipient must inform the Provider of the results of each audit and publish the audit report both within the NHS Data Security and Protection Toolkit (or any successor framework) and on its website.

4.2 FREEDOM OF INFORMATION

The Parties acknowledges that the Provider is subject to the requirements of FOIA and EIR. The Recipient must assist and co-operate with the Provider to enable it to comply with its disclosure obligations under FOIA and EIR. The Recipient agrees:

4.2.1. that this Agreement and any other recorded information held by the Recipient on a Provider's behalf for the purposes of this Agreement are subject to the obligations and commitments of the Provider under FOIA and EIR;

4.2.2. that the decision on whether any exemption under FOIA or exception under EIR applies to any information is a decision solely for the Provider;

4.2.3. that where the Recipient receives a request for information relating to the Data provided under this Contract and the Recipient itself is subject to FOIA or EIR, it will liaise with the relevant Provider as to the contents of any response before a response to a request is issued and will promptly (and in any event within 2 Operational Days) provide a copy of the request and any response to the relevant Provider;

4.2.4. that where the Recipient receives a request for information and the Recipient is not itself subject to FOIA or as applicable EIR, it will not respond to that request (unless directed to do so by the Provider) and will promptly (and in any event within 2 Operational Days) transfer the request to the Provider;

4.2.5. that the Provider, acting in accordance with the codes of practice issued and revised from time to time under both section 45 of FOIA and regulation 16 of EIR, may disclose information concerning the Recipient and this Contract either without consulting with the Recipient, or following consultation with the Recipient and having taken its views into account; and

4.2.6. assist the Provider in responding to a request for information, by processing information or environmental information (as the same are defined in FOIA or EIR) in accordance with a records management system that complies with all applicable records management recommendations and codes of conduct issued under section 46 of FOIA, and providing copies of all information requested by that Provider within 5 Operational Days of that request and without charge.

4.2.7. The Parties acknowledge that, except for any information which is exempt from disclosure in accordance with the provisions of FOIA, or for which an exception applies under EIR, the content of this Agreement is not Confidential Information.

4.2.8. Notwithstanding any other term of this Agreement, the Recipient consents to the publication of this Contract in its entirety (including variations), subject only to the redaction of information that is exempt from disclosure in accordance with the provisions of FOIA or for which an exception applies under EIR.

4.2.9. In preparing a copy of this Agreement for publication under the Provider may consult with the Recipient to inform decision-making regarding any redactions but

the final decision in relation to the redaction of information will be at the Provider's absolute discretion.

4.2.10. The Provider must assist and cooperate with the Commissioners to enable the Commissioners to publish this Agreement.

4.3 CONFIDENTIALITY

4.3.1. The Recipient agrees to treat Personal Data and confidential patient information as Confidential Information.

4.3.2. Subject always to clause 4.2 above, the Party receiving Confidential Information shall use all reasonable steps to maintain the confidentiality of the same and shall not disclose it to any third party save as allowed by law.

4.4. The restrictions contained in clauses 4.3 shall remain in force without limit in time.

5. PUBLICITY

Neither Party shall use the name, logo or registered image of the other Party or the employees of such other Party in any publicity, advertising or press release without the prior written approval of an authorised representative of that Party.

6. PUBLICATION

For the avoidance of doubt, subject always to all relevant laws (including but not limited to the Data Protection Legislation), regulations and codes of practice and the terms of this Agreement, nothing shall restrict the Recipient's rights to publish or otherwise disseminate any Results arising from its use of the Data or the Data itself.

7. INTELLECTUAL PROPERTY RIGHTS

All Background Intellectual Property Rights (including licences) and Know How and their improvements used in connection with the Purpose shall remain the property of the Party introducing the same and the exercise of such rights for purposes of the Purpose shall not knowingly infringe any third party's right. All Results, Intellectual Property Rights and Know How arising from Purpose, including all Intellectual Property Rights deriving or arising from the Recipient's use of the Data, shall belong to the Recipient. Subject always to all Intellectual Property Rights deriving or arising from the Provider's use of the Data shall belong to the Provider.

8. TERM

This Agreement will commence on the date the final signatory signed the Agreement and shall remain in effect until the expiry of the retention period set out in Schedule 1 or earlier termination in accordance with clause 10 of this Agreement.

9. TERMINATION

This Agreement may be terminated immediately by notice in writing by either Party if the other Party is:

9.1 In material or continuing breach of any of its obligations under this Agreement and fails to remedy the breach (if capable of remedy) for a period of 30 calendar days after written notice by the non-breaching Party; or declared insolvent or has an administrator or receiver

appointed over all or any part of its assets or ceases or threatens to cease to carry on its business.

9.2 The Recipient may terminate this Agreement by notice in writing:

9.2.1 If the regulatory permissions and approvals previously granted to perform the Purpose are withdrawn;

9.2.2 Termination under this clause 10 will be without prejudice to any other rights or remedies of either Party under this Agreement or at law, and will not affect any accrued rights or liabilities of either Party at the date of termination.

9.3 The Recipient may terminate this Agreement by notice in writing:

9.3.1 If the regulatory permissions and approvals previously granted to perform the Purpose are withdrawn;

9.3.2 Termination under this clause 10 will be without prejudice to any other rights or remedies of either Party under this Agreement or at law, and will not affect any accrued rights or liabilities of either Party at the date of termination.

10. AGREEMENT AND MODIFICATION

10.1 Any amendments to this Agreement shall be valid only if made in writing and signed by authorised signatories of the Parties.

10.2 This Agreement including its Schedules contains the entire understanding between the Parties and supersedes all other agreements, negotiations, representations and undertakings, whether written or oral of prior date between the Parties relating to the Purpose.

11. FORCE MAJEURE

No Party shall be liable for any delay in performance or failure to perform its obligations under this Agreement if such delay or failure is due to an occurrence beyond its reasonable control. The Party affected by such occurrence shall promptly notify the other Party. If the circumstances causing the delay or failure to perform continue for longer than thirty (30) calendar days the other Party shall be entitled to terminate this Agreement by notice in writing with immediate effect.

12. NOTICES

12.1 Any notice under this Agreement shall be in writing, signed by the relevant Party to the Agreement and delivered personally, by courier, by recorded delivery post, or by email, providing evidence of receipt.

12.2 Notices to the Recipient and to the Provider shall be delivered to the addressee and at the address specified in Schedule 1 or as may be amended by the Parties during the Purpose.

12.3 Notices:

12.3.1 by post will be effective upon the earlier of actual receipt, or 7 calendar days after mailing;

12.3.2 by hand will be effective upon delivery.

12.3.3 By email will be upon day of sending or next working day if received on a weekend, bank holiday, or otherwise after 5pm.

13. DISPUTE RESOLUTION

13.1 In the event of any dispute or difference between the Parties arising in connection with this Agreement, the authorised representatives of the Parties will discuss and meet as appropriate to try to resolve the dispute within 7 calendar days of being requested in writing by any Party to do so. If the dispute remains unresolved, it will then be referred to the senior manager from each of the Parties who will use all reasonable endeavours to resolve the dispute within a further 14 calendar days.

13.2 If the Parties are unable to resolve a dispute using the procedure outlined in clause 14.1, the Parties will refer the dispute to mediation in accordance with the Centre for Effective Dispute Resolution Model Mediation Procedure

14. GENERAL

14.1 No failure or delay by any Party to exercise any right under this Agreement will operate as a waiver of it, nor will any partial exercise preclude any future exercise of the same.

14.2 If any clause or part of this Agreement is found by any court, tribunal, administrative body or authority of competent jurisdiction to be illegal, invalid or unenforceable then that provision shall, to the extent required, be severed from this Agreement and shall be effective without, as far as possible, modifying any other clause or part of this Agreement and shall not affect any other provisions of this Agreement which shall remain in full force and effect.

14.3 Except as expressly stated nothing in this Agreement shall confer or purport to confer on any third party any benefit or any right to enforce any term of this Agreement.

14.4 This Agreement may be executed in counterparts, each of which when executed (and delivered) will constitute an original of this Collaboration Agreement, but all counterparts will together constitute the same agreement. No counterpart will be effective until each party has executed at least one counterpart. A signed copy of this Agreement delivered by e-mailed portable document format file or other means of electronic transmission

shall be deemed to have the same legal effect as delivery of an original signed copy of this Agreement.

15. SURVIVAL OF CLAUSES

15.1 The following clauses shall survive the termination or expiry of this Agreement: clauses 1 (Definitions), 3 (Liabilities and Indemnities), 4 (Confidentiality, Data Protection and Freedom of Information), 5 (Publicity), 6 (Publication), 7 (Intellectual Property Rights), 9 (Termination), 15 (Survival of Clauses), 16 (Governing Law).

16. GOVERNING LAW

16.1 This Agreement shall be governed and construed in accordance with the laws of England and shall be subject to the exclusive jurisdiction of the English Courts

SIGN OFF*

Each Party represents that it has 'redlined' or otherwise called attention to all changes that it made and sent to the other Party in previously-sent drafts of this Agreement, including but not limited to drafts of the schedules.

Signed by the duly authorised representatives of the Parties.

17. SIGNED ON BEHALF OF THE RECIPIENT

.....	.....	.....	.....
Name	Position	Signature	Date

[REPEAT AS NECESSARY FOR ADDITIONAL RECIPIENTS]

18. SIGNED ON BEHALF OF THE PROVIDER

.....	.....	.....	.....
Name	Position	Signature	Date

* Duly authorised scanned signatures shall be mutually acceptable and email deemed a valid medium for exchanging signed copies of this Agreement, which may be executed in counterpart.

19. SCHEDULE 1

PURPOSE AND SUMMARY OF ARRANGEMENTS

INFORMATION SHARING: SECOND LEVEL PROTOCOL

BETWEEN

		AND:
Name	**University Hospitals Bristol and Weston NHS Foundation Trust**	**[recipient]**
Address	Trust Headquarters, Marlborough Street, Bristol, BS1 3NU	

Purpose for the sharing Agreed purposes for the use of information and a process for agreeing further purposes if necessary	• Only the **minimum necessary data is to be shared** to achieve the secondary outcomes of our study; *"to describe patient demographics, indication for glucocorticoid therapy, prescribed dose (to include medication, dose, duration, route, and frequency), planned operation, length of stay, peri-operative supplementation practices, and the number of patients presenting for procedures who are taking therapeutic glucocorticoids."* • NHS numbers will be stored by the **provider** on a REDCap database stored upon the Health and Social Care Network (HSCN) server. • These numbers will be utilised to request commission returns data **from the recipient** for the secondary analysis of data, including patient demographics. • Commissioning returns data will be

	returned to the **provider** anonymised for the purpose of analysis. • NHS numbers will be removed from the HSCN server following the request of data from the **recipient** Business Intelligence Unit (BIU).
Roles of Partners Definition of who is the controller/processor	• Dr Ben Gibbison is the Chief Investigator and will be responsible for the overall handling of the data and ensuring that minimal patient identifiable data is stored and handled as described herein. • Dr Aravind Ramesh will be responsible for managing the data upon the REDCap database, including its removal following the request of data from the **recipient**. • The **provider** will be the data controller for the data derived as a result of this study. • The **recipient** will remain the data controller for NHS Numbers submitted by its clinical team, the **provider** will only process the NHS number as described in this schedule.
Legal Basis The legal basis for sharing information, in relation to the initiative, based on legal justifications for sharing.	The legal basis for the sharing of the personal data identified as per General Data Protection Regulation 2018 is as follows: • GDPR – Article 6 provides the processing of personal data when: o (1)(e) processing is necessary for the performance of a task carried out in the public interest or in the exercise of official authority vested in the controller • GDPR – Article 9 provides the processing of personal data when: o (2)(h) – processing is necessary for

	the purposes of preventive or occupational medicine, for the assessment of the working capacity of the employee, medical diagnosis, the provision of health or social care or treatment or the management of health or social care systems and services on the basis of Union or Member State law or pursuant to contract with a health professional
Data Description • Who are the Data Subjects? • What Level of identity will be shared? • What fields of data will be shared? • What is the source of the data? • Will multiple datasets be linked?	• The **subjects** are eligible patients as per the study protocol; *"All patients under the care of an anaesthetist (including those performed under general anaesthesia, regional anaesthesia, and/or sedation with monitoring), ≥18 years of age, presenting for elective, urgent or emergency procedures performed by any medical or surgical specialty at each centre will be eligible to be included in the audit."* • The **NHS number** will be shared. This will not be utilized to identify any patient by the **provider** but solely for retrieval of data at a later point by the **recipient**. • Data will be **shared** from the commissioning reports; including but not limited to height, weight, gender, age, ASA and procedure performed. • Data **source** will be that of NHS numbers entered into the REDCap Case Report Forms (CRF) by Clinicians providing care at each eligible patient episode.

	the purposes of preventive or occupational medicine, for the assessment of the working capacity of the employee, medical diagnosis, the provision of health or social care or treatment or the management of health or social care systems and services on the basis of Union or Member State law or pursuant to contract with a health professional
Data Description • Who are the Data Subjects? • What Level of identity will be shared? • What fields of data will be shared? • What is the source of the data? • Will multiple datasets be linked?	• The **subjects** are eligible patients as per the study protocol; *"All patients under the care of an anaesthetist (including those performed under general anaesthesia, regional anaesthesia, and/or sedation with monitoring), ≥18 years of age, presenting for elective, urgent or emergency procedures performed by any medical or surgical specialty at each centre will be eligible to be included in the audit."* • The **NHS number** will be shared. This will not be utilized to identify any patient by the **provider** but solely for retrieval of data at a later point by the **recipient**. • Data will be **shared** from the commissioning reports; including but not limited to height, weight, gender, age, ASA and procedure performed. • Data **source** will be that of NHS numbers entered into the REDCap Case Report Forms (CRF) by Clinicians providing care at each eligible patient episode.

	• **No** data will be collected that is not already recorded in the practice of routine care.
Date of Sharing • When will sharing commence/cease? • How frequently will information be shared?	• Data sharing will **commence** on a date chosen by the **recipient** within the data collection window of September 26th 2022 to December 4th 2022. • Information will be collected for a consecutive 14 day period, and will be shared as CRF entered onto the database. • Sharing will **cease** once NHS numbers have been returned to the **recipient** and anonymised data returned to the **provider** from the commission reports. • The data sharing is a one-off event.
Transparency and Rights • How individuals will be informed of the sharing and use of data where required? • How will individuals' information rights be upheld?	• Data collected does not differ from that routinely stored by the Health Care Provider and additional information for patients are not envisioned. • Those patients who have 'opted-out' via the NHS Digital National Data Opt-Out will be flagged by the **recipients** Business Intelligence Unit when data is requested, and it is anticipated they will uphold their rights as per the **recipients** local policy.
Security/method of secure transfer • Physical Security • Electronic security (access control, secure transfer, encryption levels)	• NHS Numbers shall be securely transferred digitally to the **providers** HSCN REDCap instance by use of the digital CRF. • In the instance of paper forms used locally for data capture, these will be disposed of locally as per the **recipients** local policy following transcription to the digital REDCap CRF. • When requestioning commissioning report data the NHS numbers will be transferred

	back to the designated **recipient** project lead via encrypted NHS email.
Quality A commitment to accuracy and completeness of data exchanged, including a process for informing all relevant parties of any inaccuracies identified including any verification procedures (e.g. reconciled against SPINE etc.)	• NHS numbers will not be verified by the **provider**. • Should they be recorded inaccurately and it not prove possible to reconcile against commissioning report data, these patients will be recorded and reported in the final publication as 'data lost to follow-up'.
Retention Agreement to the period of retention of data with reference to organisational retention schedules and the longest applicable period, unless there is reason for destruction of copies of data.	• NHS numbers will be removed from the REDCap database once commission report data has been requested.
Training Additional/specialist training needs	• All participants in the project are expected to be up-to-date with mandatory training for Information Governance. • Additionally they will practice in accordance to **Good Clinical Practice** as outlined by the National Institute for Health and Care Research (NIHR).
Monitoring and Review • Who will monitor that the processes above are taking place and are effective? • What checks will be made? • How often will this agreement be reviewed? • Who will ensure that the review takes place?	• **Dr Ben Gibbison** as the Chief Investigator. • **Joe Ellis** as the Information Governance Manager at the **provider**. • Removal of data from the REDCap database upon requesting commissioning report data will be monitored by those named above.

Incident Management • How will any breaches of principles be reported and managed? • What will be the procedure to update this protocol in the light of any findings?	• Breaches of security, confidentiality and other violations of this agreement must be reported in line with each partner organisation's incident reporting procedure. In addition, the Information Governance lead from the respective partner organisation must be informed of any such breaches. • This agreement will be reviewed and redistributed should changes be required.

20. SIGNED ON BEHALF OF THE RECIPIENT

.....	.....	.....	.....
Name	Position	Signature	Date

21. SIGNED ON BEHALF OF THE PROVIDER

.....	.....	.....	.....
Name	Position	Signature	Date

22. NOTICES

Notices to the Recipient shall be addressed to:

[Insert JOB TITLE OR POSITION]

[Insert NAME OF NHS BODY]

[Insert ADDRESS]

[Insert EMAIL]

Notices to the Provider shall be addressed to:

Dr Ben Gibbison

University Hospitals Bristol and Weston NHS Foundation Trust
R&D Office
Level 3, Education Centre
Upper Maudlin Street
Bristol BS2 8AE

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Appendix E. Protocol Revision History

Status	Version	Date	Contributors	Change Log
	1.0	17/01/2022	Dr Oliver Barker Dr Jonathan Barnes Dr Aravind Ramesh Dr Inthu Kangesan Dr Ben Gibbison Professor Barney Reeves	Pending Final Approval
	1.1	13/04/2022	Dr Oliver Barker Dr Jonathan Barnes Dr Aravind Ramesh Dr Inthu Kangesan Dr Ben Gibbison Professor Barney Reeves	1. Amendments to 3.7, 3.9, 3.10, 3.11 regarding data collection, ethical considerations, and financing. 2. Addition of Appendix B, C, D
	2.0	14/04/2022	Dr Oliver Barker Dr Jonathan Barnes Dr Aravind Ramesh Dr Inthu Kangesan Dr Ben Gibbison Professor Barney Reeves	1. Amendments to formatting and grammatical changes 2. Refined 2.0 aims and scope 3. Updated objectives language in 3.5
	3.0	23/05/2022	Dr Oliver Barker Dr Jonathan Barnes Dr Aravind Ramesh Dr Inthu Kangesan Dr Ben Gibbison Professor Barney Reeves	1. Grammatical and formatting adjustments throughout 2. Revision of 2.0 and removal duplicated objectives (previously 3.5) 3. Addition of abstract 4. Addition of 3.10 PPI 5. Updated 4.0
	4.0	08/08/2022	Dr Oliver Barker Dr Jonathan Barnes Dr Aravind Ramesh Dr Inthu Kangesan Dr Ben Gibbison Professor Barney Reeves	1. Removal of 'last 3 months' in 3.5. 2. Updated Appendix B to latest version.
Current	5.0	22/10/2022	Dr Oliver Barker Dr Jonathan Barnes Dr Aravind Ramesh Dr Inthu Kangesan Dr Suzanne Harrogate Dr Ben Gibbison	1. Significant amendments to 3.7 and considerations for the National Data Opt-Out 2. Replacement of CRF with Paper CRF in Appendix B 3. Addition of Data Sharing Agreement as Appendix D