STATISTICS SOP

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Implementation plan

For studies that are being set up, the BTC-SOP-ST-001 Statistics SOP applies.

For ongoing studies applicable sections of this Standard Operating Procedure (SOP) (e.g. study monitoring) should be implemented as far as possible immediately after the implementation date, unless impractical for the circumstances e.g. too close to the end of study.

If unsure, the BTC Director and/or Quality Assurance Manager should advise.

Note to User:

It is your responsibility to ensure that you are using the latest approved version of this SOP. Please note that versions may be superseded before their planned review date.

THIS IS AN UNCONTROLLED VERSION WHEN PRINTED.

If you are reading this document in printed form, please check that the version number and date match the most recent SOP's details. Current versions of all Bristol Trials Centre (BTC) SOPs and accompanying documents are available on the BTC Teams channel.

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1 PURPOSE

This Standard Operating Procedure (SOP) describes the statistical work normally conducted for Bristol Trials Centre (BTC) adopted studies, with the aim of standardising statistical tasks. Many of the procedures followed by the BTC are in line with published guidelines issued by the International Conference of Harmonisation (ICH).

2 SCOPE

This SOP covers the areas of blinding, randomisation, sample size, data management, statistical work for grant applications, study protocols, statistical analysis plans, Trial Steering Committee (TSC) and Data Monitoring and Safety Committee (DMSC) reports, publications resulting from the research, including end of study reports to funders and archiving. Analysis techniques, outcome measurements and secondary analyses of study data after all the planned analyses are completed and the study is archived are not covered.

NB: Throughout this document the terms ‘research’, ‘trial’, and ‘study’ will be used interchangeably to denote those projects which fall under the remit of the UK Policy Framework for Health and Social Care Research 2017.

3 DEFINITIONS, ACRONYMS AND ABBREVIATIONS

Any individual may take on more than one of the statistical roles in a study.

Supervisory Statistician: An appropriately qualified statistician named in the study protocol who will often be involved during the design phase and will then support the Study Statistician throughout the rest of the study, as required.

Study Statistician: An appropriately qualified statistician who has overall responsibility for statistical analyses of the study data. The study statistician may be blinded or unblinded to the study allocation whilst the study is ongoing; the blinding (or not) of the study statistician should be documented.

Safety Statistician: For studies where the study statistician is to remain blinded, another appropriately qualified statistician who is unblinded, who undertakes activities that would unblind the Study Statistician.

Quality Assurance statistician: An appropriately qualified statistician who is responsible for checking the accuracy of reports and analyses.

Note: **The supervisory statistician or safety statistician may undertake the role of quality assurance statistician**. This should be documented.

For studies where the study statistician is unblinded to the study allocation whilst the study is ongoing; the study statistician may undertake the role of the safety statistician. This should be documented.

NB: For definitions, acronyms and abbreviations relevant to statistics please refer to the BTC-RES-ST-001 Definitions and Acronyms (Statistics) available on the BTC Teams channel. For all other definitions, acronyms and common abbreviations relevant to research projects and general

management of research refer to the BTC-RES-TM-001 Definitions and Acronyms document, also available on the BTC Teams channel.

4 RESPONSIBILITIES

4.1 Supervisory Statistician

It is the responsibility of the supervisory statistician to:

- Ensure that the sample size calculation is performed and documented. Note that these tasks can be delegated to other appropriately qualified statisticians, but final responsibility lies with the Supervisory statistician. It is also their responsibility to approve any amendments to the sample size.
- Ensure that an appropriate randomisation system is developed, and that appropriate documentation are completed prior to the start of the study.
- Ensure that that the statistical analysis plan (SAP) is written. Ensure the SAP is reviewed by appropriate members of the study team including the CI and once finalised, sign off this SAP.
- Have oversight of the data management process, including data management plans.
- Review open DMSC and TSC reports for accuracy.

4.2 Study Statistician

It is the responsibility of the study statistician to:

- Oversee or create a randomisation system, and test that it is working.
- Ensure that, for any study where they must remain blinded, they are not aware of treatment allocations. If, in the absence of others they are required to be unblinded to perform their study duties, this should be documented.
- Draft the SAP with guidance from the supervisory statistician.
- Work with the study team to develop and implement an appropriate data management and monitoring process, documenting this process as required.
- Prepare data summaries for reports to the DMSC and reports to the TSC.
- Conduct the analysis of the study as defined in the SAP. Prepare tables and figures of analyses, and commentary on those analyses, suitable for the results section of any final report and publication of the main results. Prepare material for the methods section and advise the study team on the interpretation of the results for the discussion and conclusions sections.
- Where appropriate, prepare data sets and associated documentation for uploading to a central data repository. This will be the University of Bristol Research Data Storage Facility, unless agreed otherwise with the Sponsor.
- If delegated to the BTC by the Sponsor, work with the Trial Manager to prepare and upload results onto the ISRCTN registry, or ClinicalTrials.gov or equivalent for clinical trials of investigational medicinal products (CTIMPs).

4.3 Safety Statistician

It is the responsibility of the safety statistician to:

- Oversee or create the final randomisation system.
- Review the closed DMSC report, where required.
- Be available to disclose the coding of the allocation groups to the closed DMSC if necessary.

4.4 Quality Assurance Statistician

It is the responsibility of the quality assurance statistician to:

- At minimum, review the code used to derive (if applicable) the primary outcome(s) and the code used to analyse the primary outcome(s) as detailed in the SAP. Check the correct assignment of the groups.

4.5 Bristol Trials Centre, University of Bristol

It is the responsibility of the BTC to:

- Oversee the conduct of the research study ensuring the rights, safety and well-being of participants is maintained and that the integrity of the data is not compromised.
- Facilitate the detection and reporting of deviations and research misconduct and implementation of corrective and preventive actions.
- Report observations of suspected research misconduct, deviations or serious breaches of GCP and/or the protocol and ensure onward reporting in compliance with this SOP and applicable regulations.
- Ensure that members of BTC staff are appropriately trained for their role and maintain individual training records.

4.6 SOP Authors or delegate

It is the responsibility of the SOP author(s) (or delegate) to:

- Generate, finalise and revise the SOP in accordance with the BTC-SOP-QM-001 Development and Management of SOPs.
- Ensure that the SOP remains fit for purpose.
- Provide relevant training and education materials to ensure that staff are aware of their responsibilities in relation to SOP content and management.

4.7 SOP user

It is the responsibility of the SOP user to:

- Ensure compliance with this document.
- Review procedures during use of the SOP and inform the author of any changes required.
- Undertake training on all aspects of this SOP and record training on the BTC Teams channel.

5 SPECIFIC PROCEDURES

5.1 Study design and sample size

5.1.1 Overview

ICH guideline E9 states that the number of subjects in a clinical trial should always be large enough to provide a reliable answer to the questions addressed and is usually determined by the primary objective of the trial.

A BTC supervisory statistician (or delegate) for a study is responsible for writing an outline description of the planned statistical analysis and for conducting/presenting the sample size calculation. The BTC supervisory statistician will meet with the study team at an early stage to review any statistical consequences of the proposed study design.

5.1.2 Design considerations

The following will need to be discussed with the study team and agreed with the Chief Investigator (CI) where appropriate:

- The research question and where applicable the null and alternative hypotheses being tested.
- Study design (e.g. parallel group, cross-over, factorial, cluster randomised etc.)
- The number of comparison groups. The outcome(s) to be considered in the sample size calculation. There will always be a primary outcome, but potentially there could be more than one primary outcome and/or an important secondary outcome as well.
- If more than two study groups, which comparison(s) will be considered in the sample size calculation.
- The minimum clinically important difference (target effect size) for a superiority trial, the non-inferiority margin for a non-inferiority trial or the equivalence bounds for an equivalence trial. Whilst the treatment effect observed in previous studies is a useful indication of what can be achieved, such estimates should not be the basis of sample size calculations.
- All assumptions underpinning the sample size calculation, (e.g. standard deviation, correlations if a repeated measures design, intra-class correlation if a cluster randomised design). Where possible estimates of these parameters should be obtained from the literature or previously published data.
- Proposed levels of statistical significance and power; conventionally the significance level is set at 5%, and the statistical power is set at 80% minimum, although many funders now require 90% power.
- If more than one primary outcome is proposed, or there are more than two groups, any proposed adjustment(s) to minimise the Type I and/or Type II error rates; adjustment will depend on the research question (e.g. superiority required for both primary outcomes versus at least one primary outcome etc).
- Expected rates of missing outcome measures (e.g. due to drop out) and switching between groups should be considered and sample sizes adjusted accordingly.
- Allocation ratio. Most studies have equal allocation to study groups but there can be situations where and alternative ratio (e.g. 1:2) is preferred.

Less commonly, the available sample size is fixed, and the achievable statistical power is to be calculated under various assumptions. The above considerations remain relevant in this situation.

5.1.3 Analysis considerations

For *feasibility studies*, most commonly the feasibility measures (e.g. number of people eligible, proportion randomised and/or completeness of outcome data) will be presented as summary statistics alongside a Consolidated Standards of Reporting Trials (CONSORT) flow chart. The sample size is often chosen to enable the study to estimate feasibility outcomes with sufficient precision. The statistical outline will not include significance testing for the treatment effect, although a preliminary treatment effect estimate with a 95% confidence interval may be presented.

For *full trials* the following should be specified: primary and secondary outcomes and how they will be measured, the analysis principles (e.g. intention to treat), how the treatment effect on the primary outcome will be quantified (e.g. risk ratio, difference in means), how the treatment effect on the primary outcome will be estimated (e.g. Poisson regression model with variables used to stratify the randomisation as covariates), and methods for the analysis of secondary outcomes (often the primary analysis method will be adapted).

Descriptions of how missing data and non-adherence to allocation will be accommodated should not make commitments which may, in the event, be inappropriate. For example, a commitment to multiple imputation should not be made if there is a fair chance that data will be missing not at random. Often the primary analysis will be of the observed data, with a commitment to investigate, in sensitivity analyses, the possible effect of missing data on estimates; this approach is consistent with the ICH Guidelines.

5.1.4 Timing

Sample size calculations following the procedures outlined above should be carried out prior to submission of a final/stage 2 grant application. These calculations should be documented. More informal sample size calculations will be permitted for outline/stage 1 grant applications.

5.1.5 Documentation

All assumptions and decisions made in the sample size calculation should be documented. This documentation should be stored as an electronic file in an appropriate folder. Any papers or references from which assumptions are taken should also be documented.

Any statistical programs (e.g. Stata do files or SAS program files) should be securely stored to enable calculations to be reproduced.

The sample size target should be provided to the CI in writing (e.g. an email), with it made clear whether the sample size is for each study group, or overall for the study. Assumptions underpinning the calculation should be described, and a reference to the method used if not standard. A table showing how the sample size target varies with changes to the assumptions can be useful.

Once agreed with the CI, this same information should be provided in a format suitable for inclusion in the grant application.

The sample size should be clearly and appropriately outlined in the study's protocol.

At the end of the study appropriate details (including any amendments) should be included in the end of study report and any publications. Recommended reporting guidelines (e.g. the CONSORT, Strengthening the Reporting of Observational studies in Epidemiology (STROBE), Standards for

the Reporting of Diagnostic accuracy studies (STARD) statements and Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)) should be followed wherever possible.

5.1.6 Amendments

In accordance with ICH-GCP guidance, sample size calculations can be revisited and amended either before or after the study has started recruiting: For example, this could be done because additional data to inform the calculation becomes available, if the study is adapted to include additional groups or if an interim analysis suggests that the assumptions which underpin the original sample size calculations (e.g. variances, event rates or survival experience) are not as anticipated. This may be particularly important if assumptions have been made based on preliminary and/or uncertain information. The number of data reviews and subsequent sample size amendments should be kept to a minimum. Any sample size amendments should follow the processes outlined above.

5.2 Randomisation procedure

Randomisation aims to produce treatment groups which are balanced with respect to all prognostic factors (both measured and unmeasured), thus allowing any observed differences to be attributed to treatment. It is important to avoid bias in the conduct of the randomised controlled trial (RCT) by ensuring there is no advanced knowledge of upcoming allocations.

Before a randomisation scheme is developed documentation should be completed which specifies all relevant information. Most of the information required to develop a randomisation scheme should be readily available from the study protocol.

For randomisation schemes developed by a BTC study statistician, they are required to produce a randomisation system, test the system and document the testing done. This documentation should be stored in an appropriate location.

For all studies where the study statistician is blinded, the randomisation system is then required to be updated and tested by another statistician (usually the safety statistician) who is not involved in the study. Details of this testing and a copy of the master randomisation list where appropriate should be stored securely in a restricted access folder and transferred to an appropriate location at the end of the study. Details of where this information is stored during the conduct of the trial should be recorded in an appropriate location.

If appropriate, details on performing an emergency randomisation in the event of system failure will be provided in the relevant study-specific study manual.

5.3 Allocation Concealment and Blinding

Blinding or masking is the procedure by which members of staff, and/or participants, are kept unaware of participants' treatment allocations. Concealment techniques ensure that the person randomising participants cannot predict the allocation of the next recruited participant.

The ICH guideline E9 states that whenever possible, members of a trial team should be blinded to the treatment allocation to minimise the opportunity for conscious or unconscious bias to occur.

The blinding, or not, of study team members, including statisticians, should be documented for each study. Where it is practical to do so, the study statistician and supervisory statistician should

be blinded to the allocation assignment whilst the study is ongoing. The degree of blinding should also be documented (i.e. no access to any information relating to the treatment allocation or group assignment is known but the treatment labels are removed (e.g. groups are coded A, B etc.)).

For randomisation systems developed by the BTC IT team using a randomisation scheme provided by the BTC safety statistician, the BTC IT team could unblind the allocation if unblinding is required and the safety statistician is unavailable.

5.4 Statistical Analysis Plan

5.4.1 Overview

The SAP is intended to be a comprehensive and detailed description of the methods and presentation of data analyses proposed for a study, which will be based on the description of the statistical methods to be used in the protocol. The supervisory and study statistician should have read the protocol and should be asked to contribute to its development. The aim of the SAP is to avoid post hoc decisions that may affect the interpretation of the statistical analysis.

This follows the guidance issued in the GCP Guidelines E3 and E9 section 5.1, and is consistent with recommended reporting guidelines (e.g. CONSORT, STROBE).

A SAP is required for all full RCTs supported by the BTC. For feasibility RCTs, the protocol description of the analysis is normally sufficient, although this may be supplemented by agreement on the tables to be presented in the primary papers. Observational (i.e. non-interventional) studies may not require a SAP. Also, for some studies there may be more than one SAP; for example, SAP or template relating to reports to the TSC and DMSC, interim analyses and a further SAP for the study's final analysis.

5.4.2 Timing

The SAP should be written early in the lifecycle of the study, i.e. ideally during the recruitment phase and before any planned interim comparative analysis of study outcomes, but in all instances it must be written and approved before final database lock and comparative analyses are undertaken.

5.4.3 Scope, Format and Content of the SAP

The scope of the SAP is the analysis to be presented in the final study report and main results paper(s). Planned interim analyses of post-randomisation measures, for the DMSC or publication, may also be described in the SAP. Any changes between the methods in the protocol and analysis plans should be explained in the SAP.

A SAP template is provided for RCTs (BTC-TEMP-ST-001) which should be followed where possible. The SAP should be dated and version controlled following the conventions as described in the BTC-SOP-QM-002 Quality Management SOP. This template is also a useful tool for preparation of a SAP for observational studies, if required.

5.4.4 SAP approval

Prior to sign-off, the SAP is reviewed by appropriate members of the study team, including the CI for the study. The SAP may also be reviewed by the TSC and/or DMSC in line with the charter for those committees. Sign-off will be by the supervisory statistician for the study and the study CI.

5.4.5 Changes to the SAP

Any modifications to the SAP should be clearly documented, justified and approved. These may then be used when a journal requests an original analysis plan, current analysis plan and a list of the changes made.

5.5 Statistical Quality Assurance

The credibility of the numerical and graphical output of the analysis depends on the method and statistical software used to implement it. All analyses will be conducted in a statistical software package; SAS and Stata are the current standards for clinical trials, but other software packages such as R may be used depending on the type of study and analysis required.. Built-in SAS and Stata commands are deemed appropriately validated and statisticians should use non-validated commands with caution and use validated commands when available.

For all analyses, the package and version number should be recorded, and the sequence of code to be run documented. The statistical code used should also be annotated, so that others could easily follow the approach being used.

Log files including date stamps could be used to document the processes. The output produced of all statistical analyses should be stored in the appropriate secure location for the study.

Data extracts and code used to populate tables and figures for reports, including reports created for external review such as by the TSC and/or DMSC, should be saved to allow any queries raised by the Committee to be checked.

Code used to populate reports and analyses should not be overwritten. Statistical code may be managed through a software versioning and revision control system (e.g. open source software such as Apache Subversion distributed under the Apache License).

Where appropriate the version of the statistical software should be included in the code to ensure it will continue to work as new versions of the software are released. (e.g. in Stata there is an explicit ‘version ‘ command).

Results of all model checking and decisions made in the analysis of outcomes should be documented.

All code used to derive and analyse the primary outcome should be checked by the quality assurance statistician for accuracy and consistency. At minimum this should involve reviewing the code used, but where possible it should include independent coding for the derivation of the outcome and the analysis. The coding and labelling of the treatment groups should also be checked to ensure the codes have been assigned correctly. The level of checking for secondary outcomes and/or other process outcomes should be risk-based (e.g. the derivation of a variable that is particularly complex to code and/or the analysis is complex may also undergo independent statistical review).

5.6 Data Management

5.6.1 Introduction

An essential element of conducting a clinical trial or observational study is efficient data collection and management. Only data that are essential for the purposes of the study should be collected.

ICH GCP guidelines specify that appropriately qualified individuals should supervise the study data handling, verify the data and conduct the statistical analyses.

5.6.2 Data cleaning and validation

Most data checking and cleaning will be done at the data entry stage, and the quality and consistency of the data will be monitored throughout the study in line with the data management plan and risk assessment (see BTC-SOP-TM-001 Study Start Up SOP). Suspected errors in the data discovered through data checks (e.g. impossible combinations of values across variables) will be discussed with the trial manager in the first instance. If confirmed as an error, the correction will be made from within the study database if prior to database lock.

5.6.3 Manipulation of data after export

Data extracts provided to the statistician either whilst the study is ongoing or after database lock (i.e. the finalised dataset) will not be directly modified. All corrections, and all derivations of variables (using derivations detailed in the SAP), and coding or grouping variables will be made from within the statistical programs and this code run each time.

Data extracts (raw data before manipulation) used for reports prepared for either internal team and/or external committee review should be kept and all manipulation should be conducted on copies of this data. Further manipulation will be conducted to provide master data sets (single and multiple row per participant datasets where required) from which subsets of the data may be drawn as appropriate for analysis. All analyses and manipulation of data should be recorded within statistical programs in order that the processing of the data from extract to analysis data set is fully auditable.

5.6.4 Data protection

All data will be stored according to the BTC-SOP-QM-002 Quality Management.

5.6.5 Outgoing electronic data transfers

All outgoing transfers will be accompanied by information such as file names, number of records and variable names. Data transfer information (for example file format, encryption method used, reason for transfer, and validation procedures undertaken) will be documented. All identifiers (except study IDs) should be removed before transfer unless there is specific agreement and approval to share them. If identifiers are to be shared, files must be encrypted before transfer. Transfers can be sent via e-mail or via the unit's secure study website. Transfers of large files within and outside the University of Bristol can be achieved using the University Facility for the

Upload of Large Files (fluff) service. Confirmation of successful transfer will be requested from recipients.

5.6.6 Incoming electronic data transfers

Where appropriate, incoming data will be transferred via a secure drive on the NHS server, or received via the University fluff service. Successful transfers may be acknowledged via e-mail or as requested by the sender. Data should not include identifying information, such as names and addresses, unless there is specific agreement and approval to receive them.

5.6.7 Adverse event recording

Any recorded data on adverse events stored as free text may be coded if appropriate. The World Health Organisation Adverse Reaction Terminology (WHO-ART) and Medical Dictionary for Regulation Activities (MedDRA) both have a system of coding to assist with this categorised by System Organ Class. Similarly, medication data may be coded, using the WHO Drug Dictionary Enhanced (WHO-DDE). This coding can be done at various stages of the study, details of the classification system to be used and the process for coding free text should be documented.

5.7 Trial Steering, and Data Monitoring and Safety Committees

5.7.1 Overview

A TSC is required for all studies. A Data Monitoring and Safety Committee, also known as DMEC, DMC, IDMC or DMSC, may also be required. Whether an independent DMSC is required for feasibility trials, or for full trials of low-risk service delivery or public health interventions, will be agreed with the study CI, TSC, Sponsor and funder as appropriate. This follows guidance issued in the ICH Guidelines E3 and E9.

Both the TSC and DMSC will have a charter which is agreed at the first meeting, which should be held during the preparatory phase of the study. It is often helpful to have a joint first meeting of the two committees so they can meet, discuss their respective roles and agree the contents of open reports to the committees.

For planned TSC and DMSC meetings the report should be sent out to the relevant attendees in advance of the meeting (if possible, 2-weeks beforehand). Statistical output provided in reports should be reviewed by the supervisory statistician (or delegate) for accuracy and consistency prior to circulation.

5.7.2 DMSC

The DMSC charter will be based on the Damocles DMSC Charter template. Interim analyses should be limited to pre-planned interim analyses specified in the study protocol. The DMSC can request an unplanned interim analysis, but the basis for any request (e.g. due to the emerging data) should be fully documented and agreed by committee.

Each DMSC may have different requirements, therefore if there are differences between guidance in this document and the requirements agreed with the DMSC and documented within the DMSC charter, the requirements within the DMSC charter take precedence.

DMSC meetings usually consist of three sessions:

- Open session where independent members, study and supervisory statisticians and study team members may be present. The report for this open session should not include any details separated by allocation.
- Closed session where only the independent members and the study statistician are present. The report for the closed session will include information separated by allocation. Unless agreed otherwise, non-informative labels (e.g. A and B) will be used to identify groups. The safety statistician will be available to disclose the coding of the allocation groups if required. The supervisory statistician may attend closed sessions if agreed in advance with the DMSC.
- Executive session where only the independent members are present.
- Feedback session (optional) should the DMSC independent members wish to discuss the study further with the study team, then a final feedback session will follow the executive session and the study members will be asked to return.

A typical DMSC open/closed report will have the following data components:

- Recruitment rates and graph (open session)
- Study flowchart (open session)
- Withdrawals, loss to follow up and deaths (open session)
- Treatment compliance, if appropriate (open session)
- Data completion rates (open session)
- Statistical analysis plan (open session)
- Adverse events (open/closed session)
- Sample size assumptions check, if appropriate (open/closed session)
- Some populated outcome tables without any formal analyses conducted, if appropriate (closed session)

Statistical output provided at DMSC meetings will be guided by the SAP/agreed template for DMSC reports.

5.7.3 TSC

TSC meetings are typically held soon after the DMSC meeting has taken place. The DMSC chair is required to send a letter to the chair of the TSC to make them aware of any problems and whether they feel the study is safe to continue.

A TSC report will typically contain most, if not all, of the elements of the DMSC open report. The open DMSC report can form the report for both committees. The primary focus for the TSC is on recruitment and study progress. This meeting should include independent members, including lay members, supervisory statisticians and study team members.

At the end of the study the DMSC and TSC may be invited to the final results meeting so they can partake in discussions around data interpretation.

5.8 End of study report

Good Clinical Practice (GCP) guidelines state that when a study is closed, the Sponsor should ensure that the End of Study Report (ESR) is prepared and provided to the regulatory agency/agencies and Research Ethics Committee (REC), as required. This SOP follows guidance issued in ICH Guidelines E3 and E9

Statistical output presented in the end of study report will follow those set out in the SAP. Where an analysis has not been able to follow the SAP, details of the discrepancy and the reasons for it should be provided. Post-hoc analyses may be added as long as they are clearly defined as 'post-hoc' within the text. Findings from such analyses are normally defined as 'hypothesis-generating' rather than confirmatory results, to reduce bias.

The exact format of the ESR is decided by the study team based on the type of study, any funder obligations and the intended recipients of the report. RCTs should be reported in accordance with the CONSORT statement and its extensions (e.g. feasibility and cluster studies). Observational studies should be reported in accordance with the STROBE guidelines.

The ESR is reviewed by appropriate members of the study team including the trial manager, study and supervisory statistician, CI and other reviewers as required by the publication policy. Some funding bodies specify their own ESR template to be used; where this is the case that template should be followed. Previously published reports can be sourced within the BTC and may also be found on the funder's website.

5.9 Archiving

5.9.1 Analysis files and programs

Statistical program and analysis files need to be archived. All relevant statistical documentation needs to be archived in the same way as the other study paperwork. Statistical programs for processing and analysing the study data also require archiving. This involves checking that all files and folders are clearly named and ordered in a logical way, so that recreation of the study analyses for final analyses and if appropriate, various reports, could be recreated from these files. Along with any electronic aspects of the statistical documentation, these electronic files need to be archived by being moved to an appropriate location.

5.9.2 Data sharing

Responsibility for meeting the requirement for open access to the final study data rests with the study CI. As appropriate, the BTC statisticians will assist in preparing data sets for uploading to the University of Bristol Research Data Storage Facility (RDSF) or other repository as agreed with the Sponsor. The RDSF is a secure archive, with a clear process for researchers to request access to study data. Relevant information is provided in the BTC-WI-TM-005 Data Sharing Guidance document

6 SUPPORTING DOCUMENTS TO BE USED

Number	Title
BTC-RES-ST-001	Definitions and Acronyms (Statistics SOP)
BTC-RES-TM-001	Definitions, Acronyms and Abbreviations Relevant to Research Projects and Management of Research
BTC-RES-ST-002	Website References (Statistics SOP)
BTC-TEMP-ST-001	Statistical Analysis Plan template
BTC-SOP-TM-001	Study Start Up SOP
BTC-SOP-QM-001	Development and Management of SOPs
BTC-SOP-QM-002	Quality Management SOP
BTC-WI-TM-005	Data Sharing Guidance

7 CHANGE HISTORY

Previous version and date	New version and date	Brief summary of review
NIL		New document
Version 1 23 July 2021	Version 2 9 February 2022	Clarified that the IT team may facilitate unblinding if the study statistician is unavailable Randomisation procedure clarified
Version 2 9 February 2022	Version 3 26 February 2024	Clarified several areas of text, including responsibilities of specific statistical roles Removed EudraCT as no longer required Updated all instances of BTC intranet to BTC teams channel References to “statistical site file” have been updated to refer to saving in appropriate locations to reflect working practices Added reference to the BTC-WI-TM-005 Data Sharing Guidance