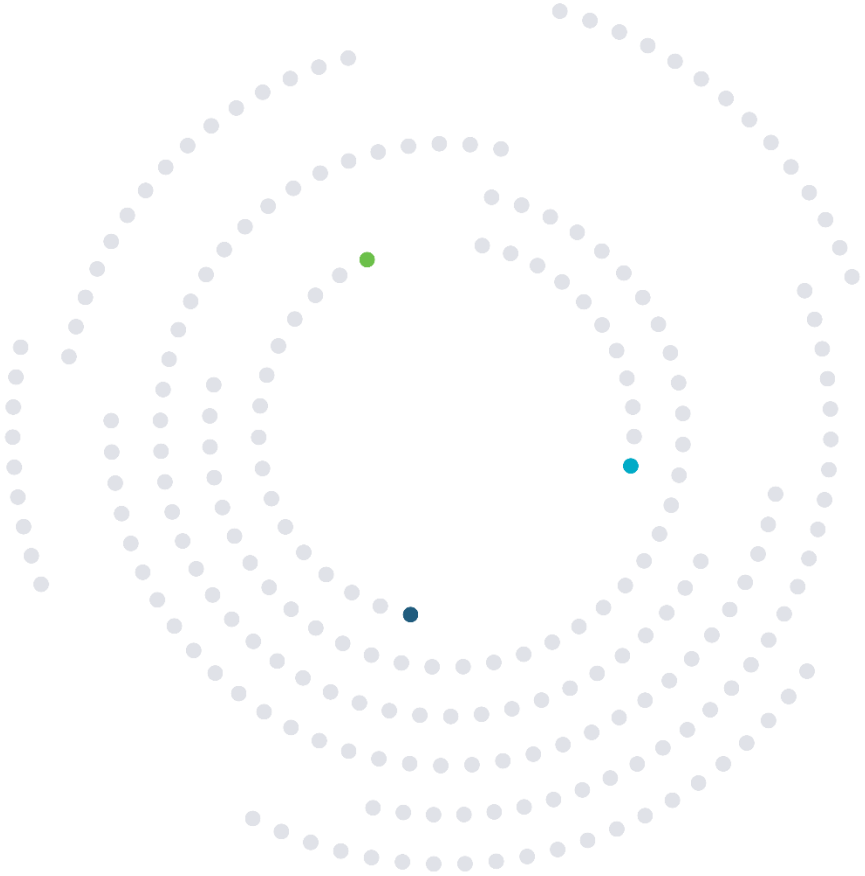
A Guide for Creating a Comprehensive Research Protocol for a Clinical Trial, Observational Study or Qualitative Study



nova scotia health innovation hub

The aim of this guide is to help researchers write a research protocol for an observational study, a clinical trial, as well as a qualitative or mixed methods study. This guide will take you through each section of the protocol giving advice on what should be included in that section.

Many of the methodological aspects of designing a research study and writing the protocol can benefit from the advice of a statistician. Such advice should be sought at an early stage and is available to NSH-affiliated researchers through the Research Methods Unit.

Contents

Research protocols involving human research participants should contain the following core components as appropriate for the specific study you are developing:

1. Administrative Information

1.1. Protocol title

The protocol must include a title. A good title is short, accurate, and concise. The central objectives and variables of the study should be clear to the reader. The title provides the "key words" for the classification and indexing of the project. If it is possible without undue length, the title can give a preview of the protocol.

1.2. Clinical Trials

1.2.1. Trial Registration

When developing a clinical trial, the protocol must provide the trial identifier and registry name, which should be prominently placed in the protocol, such as on the cover page. If the trial is not yet registered, the name of the intended registry must be provided.

1.2.2. Committees

The protocol must provide a description of the composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable.

1.3. Protocol Version

The protocol must contain a date and version identifier.

1.4. Funding Sources

The protocol must include a description of the sources of financial and non-financial support.

1.5. Names (Titles), Responsibilities and Contact Details

The protocol must list author, investigators, experts, advisors, and sponsors involved in the. This must include their names, titles, contact information, affiliation with specific departments and institutions, as appropriate.

1.5.1. Clinical Trials

For clinical trials, the protocol must also contain the Name, title, address, and telephone number(s) of the qualified physician (or dentist, if applicable), who is responsible for all trial-site related medical (or dental) decisions (if other than investigator) and the name(s) and address(es) of the clinical laboratory(ies) and other medical and/or technical department(s) and/or institutions involved in the trial.

1.6. Protocol summary

The protocol must include a summary of the proposed research study. The protocol summary is a brief and comprehensive summary of the entire protocol. It should not exceed 200 words in length. It should give a clear idea to the reader of the central question that the research is intended to answer and its justification. It should specify the hypotheses (if applicable) and the research objectives. In addition, the summary should briefly describe the methods and procedures laid out in the chapter on methodology.

2. Background and Rationale

The background section of the protocol should include:

(a) factual information related to the research topic, including a listing of the literature cited;
(b) prior research in the area under investigation;
(c) the reason for conducting the human research in the context of the background information; and
(d) the value that the proposed human research adds to the current knowledge of the research area.

The background is the theoretical framework that supports the central question of the study, states the investigator's reasoning and arguments for the attempt to find the evidence that will offer an answer to the question and/or hypothesis. It also requires an exhaustive bibliographic review. The background should logically progress to the study's research question(s).

2.1. Research Objectives

The protocol must clearly outline the general and specific research objectives. At a minimum, a single research question is needed. If the study is a pilot study or primarily a feasibility or exploratory study, this should be clearly indicted.

General objectives must specify what kind of knowledge the study is expected to obtain. It should give a clear notion of what is to be described, determined, identified, compared, and, in the cases of studies with working hypotheses, confirmed.

Specific objectives are statements of the research question(s). They must disaggregate and follow logically from the general objective(s). Specific objectives should be simple, specific, and stated in advance of the proposed study. There should be a clear link between the literature reviewed and the stated research questions. They should be fact-oriented, information-gathering questions, capable of

being confirmed or refuted. After the statement of the primary objective, secondary and exploratory objectives of the proposed research may be mentioned.

3. Description of Study Methodology

The methodology explains the procedures that will be used to achieve the objectives. In this section the operational definition for the variables used must be specified in detail, along with the type of variables and the ways to measure them. In addition, the methodology should consider the study design and the techniques and procedures used to achieve the proposed objectives.

3.1. Clinical Trials

When developing a clinical trial, the protocol must outline the role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities.

The protocol should also contain the following information:

- Name and description of the investigational product(s).
- A summary of findings from nonclinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.
- Summary of the known and potential risks and benefits, if any, to human subjects.
- Description of and justification for the route of administration, dosage, dosage regimen, and treatment period(s).
- A statement that the trial will be conducted in compliance with the protocol, GCP and the applicable regulatory requirement(s).
- References to literature and data that are relevant to the trial, and that provide background for the trial.

3.2. Study Design

The investigator must clearly state the type of study that will be conducted and provide a detailed explanation of its design, along with details of any matching ad blinding used. This should also include whether the study is retrospective, prospective, longitudinal, or cross-sectional in nature. The protocol should contain a justification with respect to how the proposed study design is adequate to reach each of the stated objectives. The rationale for the choice of a particular design should be clearly explained and justified as well as whether alternatives were explored. The comparison group(s) must be stated explicitly. Definitions should be included for all groups. The feasibility of the proposed study design should be outlined. The investigator should also state the strategies and mechanisms that will be used to reduce or eliminate threats to the validity of the results, i.e., the so-called confounding factors (in the selection and assignment of subjects, the loss of cases, and the control of instruments and observers,

etc.). These factors can be elaborated on when they are taken up in greater depth in their respective sections.

3.1.1. Exposure/Intervention

3.1.1.1. Interventions

If applicable, interventions for each group must be provided with sufficient detail to allow replication, including how and when they will be administered. Criteria for discontinuing or modifying allocated interventions for a given trial participant (e.g., drug dose change in response to harms, participant request, or improving/worsening disease) should be included as well as strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (e.g., drug tablet return; laboratory tests, etc.). Relevant concomitant care and interventions that are permitted or prohibited during the trial should also be outlined.

3.1.1.2. Exposure

For case-control studies, an objective definition for the disease or outcome of interest must be provided and used to define the cases. The appropriate control group for the group of cases should also be provided.

For cohort studies, definition(s) of exposure must be clearly stated, including how they are quantified and measured.

3.1.2. Outcomes

The protocol must outline all primary, secondary, and other outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (e.g., median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended.

The chosen outcomes should be explicitly stated, defined and connected to the research objectives as primary, secondary outcomes or other outcomes. The rationale for the choice of the particular outcome(s) should be clearly explained and justified as well as whether alternatives were explored. The ascertainment methods should be clearly described. Any performance issues, including sensitivity, specificity, positive predictive value of the chosen outcome stated should be carefully addressed.

3.1.2.1. Systematic Reviews

The protocol must list and define all outcomes for which data are sought. It should also specify how all results that are compatible with each outcome domain in each study will be sought (for example, for all measures, time points, analyses), and, if not, the methods to be used to decide which results to collect. The protocol should list and define all other variables for which data will be sought (e.g., participant and intervention characteristics, funding sources, etc.). The protocol should include a Description of any assumptions that will be made about any missing or unclear information and specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference, etc.) that will be used in the synthesis or presentation of results.

3.1.3. Qualitative Research Studies

The protocol must include a description of the theoretical framework of the proposed study, including a clear explanation of the proposed approach and why it is suitable to address the gaps outlines in the background section. The protocol should also contain a brief outline of a system of concepts from published literature that frames the study. This can be presented either visually or textually.

3.2. Study Setting

The protocol must contain a description of study settings (e.g., community clinic, academic hospital) and a list of how many sites/countries there are where data will be collected. Where applicable, this should include a reference to where the list of study sites can be obtained. The study setting should be fitted to the study objectives and design, and it should be outlined how the study sites are appropriate to answer the research question. If multiple study sites, the framework for collaboration and the responsibilities of each site should be included in the protocol. This section should also address where and how you are accessing participants, if there are any site-specific requirements to run the study, and, where appropriate, outline if there are different types of activities being undertaken at each site and what the specific requirements are for each.

3.3. Study Population

The protocol must contain a description of the study population that will be studied. The study population is the subset of the target population available for study (e.g., individuals diagnosed with diabetes living in Nova Scotia). The study sample is the sample chosen from the study population. If there is prior knowledge of the total potential population size from which to sample from (e.g., a patient registry, all patients with condition X at hospital, all registered pharmacists in Nova Scotia), this information should be included.

For prospective studies, the expected number of eligible participants available per year and proportion of these expected to take part in the study should be outlined.

The protocol should also include a justification for the selection of research participants, including equity, diversity and other relevant characteristics, such as potential vulnerabilities, accessibility, and willingness to participate in research.

3.3.1. Eligibility Criteria

The protocol must explicitly state the inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (e.g., surgeons, psychotherapists) should also be included.

3.3.1.1. Systematic Reviews

For systematic reviews, the protocol must specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. This should include:

- all study characteristics used to decide whether a study was eligible for inclusion in the review, (e.g., eligible study design(s), setting(s), minimum duration of follow-up, etc.).
- Specifying the eligibility criteria about report characteristics (e.g., year of dissemination, language, report status (i.e., whether reports such as unpublished manuscripts and conference abstracts were eligible for inclusion), etc.).
- Outline any other limits you impose (e.g., language, publication type, study design, etc.).

The protocol should clearly indicate if studies were ineligible because the outcomes of interest were not measured, or ineligible because the results for the outcome of interest were not reported.

Specify any groups used in the synthesis (such as intervention, outcome, and population groups) and link these to the comparisons specified in the objectives.

3.3.3. Sample Size

The protocol must clearly outline the planned number of study participants. The sample size is usually determined using a formal sample size calculation. If the planned sample size is not derived statistically, then this should be explicitly stated along with a rationale for the intended sample size (e.g., exploratory nature of pilot studies; pragmatic considerations for trials in rare diseases, etc.). Even in the case of exploratory research, the details of an anticipated sample size must be provided. If the study has different conditions or groups for comparison, the intended sub-sample sizes should be reported.

This should include details of the precision or power calculation used to estimate the required sample size based on primary outcome, including:

- Assumptions made (i.e., statistical assumptions regarding distribution)
- Estimates of difference to be detected along with appropriate justification
- Chosen levels of significance and power.
- Reference or details of method/formula used for the calculation.

3.3.3.1. Power Calculation

If a power analysis is performed, all input parameters must be included, so that it can be evaluated in its entirety and replicated. If the study is inadequately powered, any design elements or efforts to mitigate the lack of power and/or the potential effect on conclusions and interpretations should be provided. Studies that are known to be underpowered should have an explicit disclaimer that the study is not adequately powered.

3.3.3.2. Qualitative Studies

The protocol must contain a description and justification of how the particular sampling strategy selected answers the research question(s)/aim(s).

3.3.4. Sampling Procedure

The protocol must outline the method for selecting participants (i.e., random sampling vs non-random sampling approach (e.g., quota, purposive, convenience sampling, etc.)). Details on the source of the participants should be provided, including where they will come from (e.g., random sample from a larger

population or obtained from disease registry, etc.) and why this group is appropriate to answer the study question.

Details on what strategies the researcher will employ to obtain a representative sample of their target population, assess the representativeness of their sample, and mitigate loss to follow up should be included here.

If the study is not a randomized controlled trial, details on how the comparison group was selected and how the researcher expects them to differ from the exposed group should be described. For randomized controlled trials, please see section below.

If the study is a multi-centre study, details on the number of centres involved or regional/national limits on possible recruitment should be included.

3.3.4.1. Clinical Trials

The experimental/ treated/ exposed and the control/ comparison group must be introduced here. Method of generating the allocation sequence (e.g., computer-generated random numbers), and a list of any factors for stratification must be included as well as mechanism of implementing the allocation sequence (e.g., central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned. This section should also include who will generate the allocation sequence, who will enroll participants, and who will assign participants to interventions. A description of who will be blinded after assignment to interventions (e.g., trial participants, care providers, outcome assessors, data analysts), and how should be included. If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial should be outlined in this section.

3.3.4.2. Qualitative Studies

The protocol must include a description of the type of non-probability sampling that will be used to recruit potential participants and detail the methods of selection that will be used (e.g., snowball, purposive, etc.).

3.3.5. Recruitment

The protocol must include descriptions of where participants will be recruited (e.g., primary care clinic, community), by whom (e.g., surgeon), when (e.g., time after diagnosis), and how (e.g., advertisements, review of health records, etc.). Other relevant information to explicitly provide in the protocol includes expected recruitment rates, duration of the recruitment period, plans to monitor recruitment during the trial, and any financial or non-financial incentives provided to trial investigators or participants for enrolment. If strategies differ by site in multi-centre trials, these should be detailed to the extent possible.

The protocol also should include details on the following:

- details of procedures, tests, screenings carried out to assess study suitability
- Provision of patient information sheet (include as appendix)

- gaining patient consent (how consent will be obtained, who will gain consent,
- whether a witness will be present, how long the subject will have to decide, the
- arrangements for non-English speakers and special groups (e.g. mentally ill, children, those suffering from dementia, etc.)
- detail of enrolment procedure

All prospective studies (including interventional and non-interventional studies) should describe strategies for achieving adequate participant enrolment to reach the target sample size.

3.3.5.1. Deception

The protocol must contain a description of the elements of partial or full deception, if any, and the plan to debrief the research participants. The protocol should contain a justification of the use of. In particular, the following should be demonstrated:

- The deception is necessary to the effectiveness of the project;
- The deception only extends to the elements of research in which it is necessary; and
- All alternative investigative methods are significantly less satisfactory than the use of deception.

3.4. Engagement with Community or Patient Partners

As appropriate, the protocol should provide information about how the study engages with community or patient partners, including:

- identification of community leadership
- qualification of patient partners (e.g., lived experiences, responsibilities, etc.).

3.5. Measures/Materials

The protocol must include details on the materials and measures needed for the study (e.g., questionnaires, clinical/mechanical apparatuses, etc.).

Where applicable, a clear but concise description of the questionnaire(s) used (e.g., number of items, rating scales, sub-scales, etc.), instruments, key settings, and parameters, and scoring rules must be included. Information regarding their psychometric and biometric properties (i.e., reliability and validity) should be included.

For clinical trials, accountability procedures for the investigational product(s) must be outlined, including the placebo(s) and comparator(s).

3.6. Clinical Trials

The protocol must include a description of the treatment(s) to be administered, including the name(s) of all the product(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial. A list of medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial should also be included.

4. Methods of Data Collection and Data Management

The protocol must include a detailed list of all data (outcome variables, explanatory variables, potential confounding variables, etc.) to be collected, with each description including:

- source of the data (e.g., patient questionnaires, patient notes, electronic data, procedure, etc.)
- time point for collection (baseline, during treatment, at follow-up point)
- who will collect the data
- why the data is being collected (e.g., baseline comparison data, primary outcome, important prognostic / explanatory /confounding variable, etc.)
- whether the data is from a standardised tool (e.g., McGill pain score), involves a procedure (in which case full details should be supplied). If a non-standard tool is to be used, details on reliability and validity should be given.
- what form the data will take (e.g., binary, continuous (numeric), time to event, etc.).
- plan for the termination of the study

If applicable, plans for assessment and collection of outcome, baseline, and other study data, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) and a description of study instruments (e.g., questionnaires, laboratory tests, etc.) along with their reliability and validity, if known, should be included. Methods used to maximise completeness of data must be outlined (e.g., phoning participants who have not returned questionnaires, etc.). A table/diagram describing the schedule for data collection should be provided. Reference to where data collection forms can be found should be made if they are not included in the protocol.

4.1. Systematic Reviews

The protocol must specify all databases, registers, websites, organizations, reference lists, and other sources that will be searched or consulted to identify studies. This must include a description of the methods that will be used to decide whether a study meets the inclusion criteria of the review, including how many reviewers will screen each record and each report retrieved, whether they will work independently, and, if applicable, details of any automation tools that will be used in the process.

4.2. Retention/Withdrawal

For prospective studies, including qualitative studies, and clinical trials, the protocol must include plans to promote participant retention and complete follow-up, including a list of any outcome data to be collected for participants who discontinue or deviate from study protocols. A description under which circumstances and how participants will be withdrawn from the study, whether and how participants will be replaced, and follow-up on non-compliant as well as details of the documentation to be completed on participant withdrawal must be provided.

4.3. Compliance

Where applicable, the protocol must contain an outline of the procedures for monitoring participant compliance (e.g., exercise diary for participants in a rehabilitation program, etc.), how this compliance information will be recorded and details of follow-up of non-compliant participants.

4.4. Premature Termination or Suspension of Study

For prospective studies, including qualitative studies, and clinical trials, the protocol must outline plans for premature termination or suspension of the study, including notifications, reasons and what criteria or review will be used to determine whether study can resume.

4.5. Data Collection

The protocol must include procedures for data collection and recording, including software to be used, location of the data, etc.). Methods that will be implemented to ensure validity and quality of data (e.g., double entry, cross validation, etc.) must be detailed.

Additionally, this section should include as appropriate:

- Settings and locations in which the data will be collected and securely stored. If electronic data collection and storage is used, as description of the electronic data platform should be provided as well as details on where and how the data is stored on the platform.
- Timelines for when data will be collected including start dates, end dates and number of collection time points if applicable.
- How the data will be securely transferred from one location to another.
- How participants will be recruited (e.g., in person, online, via chart review)
- For chart reviews, a description of the database and how information will be access and extracted should be provided.
- A description of how the data will be recorded, including whether it be transposed directly from a chart to a data file; whether any subjective ratings are to be made by research assistants (if so, a description of the coding scheme should be included
- If manipulations or interventions will be performed, the protocol should describe who will carry the intervention and what their level of training is, and how the conditions will be manipulated or interventions performed (e.g., number of sessions or events, duration, settings, in groups or individually, etc.).
- A description of the “stopping rules or "discontinuation criteria" for individual participants, parts of a clinical trial and entire clinical trial
- A description of how trial treatment randomization codes are maintained and what procedures are in place for breaking the codes.
- A description of the identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data) and considered to be source data.

4.5.1. Qualitative Studies

For qualitative studies, the protocol must contain a description of the data collection methods (e.g., observational methods, interviews, focus groups, etc.), including specific procedures for data collection (e.g., for observations, what will be observed, who will be observing, resources/equipment used). This section should also include procedures for recording data and procedures for preparing transcripts and field notes for analysis, as applicable. How interview and focus group data will be handled should also be outlined where applicable.

4.5.2. Systematic Reviews

For systematic reviews, the protocol must specify the methods that will be used to collect data from reports, including how many reviewers will collect the data from each report, whether they will work independently, any processes that will be used for obtaining or confirming data from study investigators, and, if applicable, details of automation tools that will be used in the process. This should include and outline of what criteria will be used to assess methodological quality and how the quality assessment will be performed.

4.5.3. Procedures to enhance Data Quality

The protocol must contain a description of the procedures to enhance data quality. This includes as appropriate, relevant training for research assistants, reliability of the observers/coders (e.g., inter-rater reliability) and established criteria for successful reliability (e.g., intraclass correlation coefficients, Kappa statistic), use of multiple observations, and data reliability checks, etc.

4.6. Data Management

The protocol must include plans for data entry, coding, security, and storage, including any related processes to promote data quality (e.g., double data entry; range checks for data values). Reference to where details of data management procedures can be found should be provided, if not in the protocol.

4.6.1. Documentation and Record Keeping

The protocol must include a description of the data retention plan and outline:

- the duration of retention,
- retention location (if electronic data collection and storage is used, as description of the electronic data platform should be provided as well as details on where and how the data is stored on the platform
- any plans for anticipated future uses of research data, if applicable
- responsibilities of personnel
- access management plan

4.7. Data Monitoring

Where appropriate, the protocol should include the composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests. Reference to where further details about its charter can be found should be

provided if they not included in the protocol. Alternatively, an explanation of why a DMC is not needed should also be included.

4.7.1. Interim Analysis

For clinical trials, the protocol must contain a description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial. This should include methods and timing for assessing, recording and analysing efficacy parameters.

4.7.2. Assessment of Safety and Harms

For clinical trials, the protocol must specify the safety parameters, methods and timing for assessing, recording and analysing safety parameters. The protocol should also include a description of the plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct. The type and duration of follow-up of participants after an adverse event must be clearly described.

4.8.3. Auditing

For clinical trials, the protocol should include the frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor.

4.7.4 Description of Quality Management Systems

Where appropriate, the protocol should also outline the quality management systems used for the proposed study and responsibilities of research team, including:

- availability for quality assurance audits
- process for reporting deviations
- process for data quality monitoring

4.8. Access to Source data/documents

For clinical trials, the protocol must specify or contain a reference to another written agreement that the investigator(s)/institution(s) will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspection(s), providing direct access to source data/documents.

5. Analysis Plan

Note: Statistical analysis plans are among the most important elements of a research protocol. It is of upmost importance that an analysis plan be specified in complete detail before collecting or analyzing any data. This avoids the ever-growing problems of p-hacking (conscious or non-conscious changing of analysis and/or methods to produce ideal results, cherry-picking only significant results) or HARKing ("hypothesizing after the results are known", aka, peeking) in research. Even in the case of exploratory research, the details of an analysis plan should be provided.

The proposed data analyses and their importance in understanding how the research question and the data/measures are linked must be clearly and comprehensively outlined. The section should be structured such that each research question is stated again, followed by the description of the proposed statistical analysis plan for each question. Primary and secondary analyses must be clearly marked and described, including which were pre-specified or exploratory (Research studies/questions can be exploratory in nature, but an analysis plan should always be pre-specified). Even with exploratory research, there should be a plan of which variables to analyze and which tests to use. This includes a brief description of the software packages that will be used and their anticipated applications.

This section should also include the following as appropriate:

- Indicate how data will be screened for inaccuracies and statistical model assumptions.
- Indicate if any baseline, demographic, or clinical descriptive statistics will be provided.
- Outline the selection of participants to be included in the analysis (e.g., all randomized participants, all eligible participants, etc.)
- While it can be assumed that the reader has knowledge of common statistical method (e.g., t-tests, correlations, ANOVA models, regression models, chi-square), uncommon methods must include descriptions and citations supporting their relevance, appropriateness, and robustness.
- Each statistical model should include a complete description of what variable will be predictor vs outcome variable, between-subjects and within-subject factors and levels in the case of ANOVA models, etc. The assumed form of the outcome should always be specified (e.g., continuous, linear, etc.)
- For multivariable analyses, the analysis plan must include a detailed plan of how variables will be selected into the model.
- Methods to account for confounding, loss to follow-up and missing data should be included in detail.
- The alpha level must be stated (i.e., p = .05; or justify any modifications such as Bonferroni or Benjamini-Hochberg corrections) and whether confidence intervals (e.g., 95% or 99% confidence interval) or measures of effect size (e.g., Cohen's d, odds ratios) will be reported.
- Describe and justify any procedures for reporting any deviation(s) from the original statistical plan.
- Outline a plan for the dissemination of the research results

5.1. Analysis Population and missing data

For clinical trials, the protocol must include a definition of the analysis population relating to protocol non-adherence (e.g., as randomized analysis), and outline any statistical methods to handle missing data (e.g., multiple imputation).

5.2. Qualitative Studies

For qualitative research, the protocol must include a description of the data analysis procedures, including the type of analysis (e.g., inductive, deductive, etc.) to be used, steps for transcribing and coding information as appropriate, and procedures to maintain trustworthiness of the analysis as it relates to credibility, dependability, conformability, and transferability.

A description of how the analysis will be conducted (e.g., on NVIVO) should be included.

5.3. Systematic Reviews

The protocol must include the procedures that will be used to analyse and summarise the study results, including whether or not there is a plan to carry out meta-analyses. Details must be provided about how the data will be extracted and how it will be analysed and summarised (i.e., statistical or narrative). If statistical analysis will be conducted, please see further requirements above.

6. Timeframe

The protocol must outline chronology and timelines of what is to be accomplished. This can be done in an appendix. This should include, as appropriate, the following information:

- timeline for research participant recruitment, conduct of the study, and reporting, including
    - dates, workflow and/or schedule of assessments,
    - number of study visits, details of study visits (eg, procedures, assessments),
    - study visit windows and/or follow-up time and/or member checking,
- prospective or retrospective research data collection procedures

7. Risk Management

The protocol must clearly describe all benefits and potential physical and non-physical harms to research participants and non-participants (e.g., families and communities), including, as appropriate:

- how harms to participants are minimized and managed by using procedures and protocols that demonstrate concern for the welfare of the participants;

- how harms to participants are minimized by using procedures already being performed for other purposes (e.g., diagnostics, treatments, etc.);
- how harms to participants are minimized by using procedures that are consistent with a sound research design; and
- an assessment that demonstrates that the benefits of the research outweigh the risks and potential harms to participants are reasonable in relation to anticipated benefits and the importance of the knowledge that may be gleaned from the proposed research study. This should include how participants' perceptions of benefits and harms has been assessed and that there is evidence supporting the described benefits and harms.

This section should also include a description of the process used to provide participants with post-research information (e.g., debriefing, provision of generalized research results in lay language, etc.).

8. Ethical Considerations

The protocol must include a description of the ethical considerations related to the proposed study, as appropriate, including:

- Plans for seeking research ethics committee/institutional review board (REB) approval.
- Plans for communicating important protocol modifications (e.g., changes to eligibility criteria, outcomes, analyses) to relevant parties (e.g., investigators, REB, trial participants, trial registries, journals, regulators).
- Plans for who will obtain informed consent or assent from potential participants or authorized surrogates, and how:
    - If study consent is not possible due to the nature of the study, this should be clearly stated and the reasons why consent cannot be obtained should be outlined.
    - If applicable, additional consent provisions for collection and use of participant data and biological specimens in ancillary studies should be outlined.
- A description of how personal information about potential and enrolled participants will be collected, shared, and maintained to protect confidentiality before, during, and after the study should be provided.
- A brief synopsis of how the research findings will be reported and delivered to the subjects involved in the study or to other interested parties.
- Any financial and other competing interests for principal investigators for the overall study and each study site as applicable.
- Withdrawal of participants (this is different from the requirements outlined in section 4.1.)
- Privacy and confidentiality - indicate how the information obtained from participants in the study will be kept confidential.

- Any other issues that may raise ethical concerns as applicable, such as:
    - Processes for safeguarding the reputation, community standing, and bodily and mental harm of participants.
    - participant compensation, restitution, and incentives - when appropriate, indicate any special incentive or treatment that subjects will receive through their participation in the study. If there is any type of remuneration, specify the amount, method of delivery, time, and reason why payment is required.
    - individuals in situations of vulnerability, including threats to the physical, mental, and social integrity of participants.
    - conflicts of interest or conflicts of roles.
    - financial disclosure.
    - undue influence.
    - misconception regarding the personal benefits of the research (e.g., therapeutic misconception).
    - procedures for incidental findings.

9. Roles and Responsibilities of Team Members

The protocol should include a description of the research team that will be conducting the proposed study, including, as appropriate:

- Identification (names)
- qualifications
- affiliations
- locations
- roles
- contact information
- the experience of the research team with similar research populations.

10. Knowledge Translation Plan

The protocol must include a brief description of how the investigators (and sponsors, if applicable) plan to communicate study results to participants, healthcare professionals, the public, and other relevant groups (e.g., via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions.

11. Conclusion

The protocol should conclude with a short summary of the purpose of the project, what is hoped to achieve, how this will benefit the population (patients and/or staff) of Nova Scotia Health, and its potential implications for theory, research, and practice. Benefits and implications need to be in line with the level of evidence provided by the study (e.g., results from a pilot study will not change clinical practice). Limitations of the proposed research should also be included in this section.

If you require support developing your research protocol, please contact the Research Methods Unit: Research Methods Unit | Nova Scotia Health Innovation Hub (nshealth.ca)