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| **Template for Writing Non-Randomised Clinical Trial Protocol for PhD Degrees**  **General information:**  1-The protocol should be written in “Times new Roman” Font 12, with normal page layout margins, justified paragraph style and line spacing of 1.15. Titles should be written in Bold “Times new Roman” Font 14 and subtitles in Bold “Times new Roman” Font 12.  2-Each section of the protocol (Introduction, Aim, Methods,…) should start in a separate page.  3-The page numbering of the protocol should be at the bottom center of each page.  4-Title page and protocol checklist should not be numbered.  5- The candidate should add the page number of each item in the checklist.  6- The reviewer checks each item in the checklist and writes ✓ if the item is fulfilled.  7- Words in blue are to be replaced by the relevant data. Title (The population/problem, intervention, control/comparator, primary outcome & study design) **Arabic Title: An Arabic translation of the English title**  Protocol submitted to  Faculty of Dentistry, Cairo University  for partial fulfillment of the requirements for the PhD Degree in ……….. By(Name, Affiliation and degrees)   **2018**  Code:   |  |  | | --- | --- | | Supervisors’ signature | Head of department’s signature | | 1- |  | | 2- |  | | 3- |  | |  |  | | Date |  | |  |  | | | | | |
| **Protocol checklist** | | | | |
| **Section and topic** | **Item no.** | **Checked item** | **Reported on page No.** | **Reviewer’s check** |
| **I. Administrative information** | 1 | Title |  |  |
| 2 | Protocol registration |  |  |
| 3 | Protocol version |  |  |
| 4 | Funding |  |  |
| 5 | Roles and responsibilities |  |  |
|  | | | | |
| **II. Introduction** | | |  |  |
| **A) Background and Rationale** | 6 a | Research question |  |  |
| Statement of the problem |  |  |
| Rationale for carrying out the trial |  |  |
| Review of literature |  |  |
| 6 b | Choice of comparators |  |  |
| **B) Objectives** | 7 | Aim of the study |  |  |
| Hypothesis |  |  |
| **C) Trial design** | 8 | Trial design |  |  |
|  | | | | |
| **III. Methods** | | |  |  |
| **A) Participants, interventions & outcomes** | 9 | Study setting |  |  |
| 10 | Eligibility criteria |  |  |
| 11 | Interventions |  |  |
| 12 | Outcomes |  |  |
| 13 | Participant timeline |  |  |
| 14 | Sample size |  |  |
| 15 | Recruitment |  |  |
| **B) Data collection, management, and analysis** | 16 | Data collection methods |  |  |
| 17 | Data management |  |  |
| 18 | Statistical methods |  |  |
| **C) Monitoring** | 19 | Data monitoring |  |  |
| 20 | Harms |  |  |
| 21 | Auditing |  |  |
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| **IV. Ethics and dissemination** | 22 | Research ethics approval |  |  |
| 23 | Protocol amendments |  |  |
| 24 | Informed Consent |  |  |
| 25 | Confidentiality |  |  |
| 26 | Declaration of interests |  |  |
| 27 | Access to data |  |  |
| 28 | Ancillary and post-trial care |  |  |
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| **V. Appendices** | 30 | Informed consent materials |  |  |
|  | 31 | Biological specimens |  |  |
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| **VII. References** |  |  |  |  |
|  | | | | |
| **Evidence based committee (Reviewers)** | | | | |
| **Name** | | **Signature** | **Date** | |
| **1.** | |  |  | |
| **2.** | |  |  | |
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| **Research plan committee** | | | | |
| **Name** | | **Signature** | **Date** | |
| **1.** | |  |  | |
| **2.** | |  |  | |

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| **I. Administrative information:**  **1. Title:**  Descriptive title identifying the population/problem, intervention, control/comparator, primary outcome & study design.  **2. Protocol Registration:**  Site and registration number of the protocol should be reported before final approval of the protocol (e.g. Clinicaltrials.gov: NCT01066572).  **3. Protocol version:**  Date and version identifier. (e.g. 25 Jul 2018 Protocol number: 5)  **4. Funding:**  A description of the sources of financial and non-financial (material) support.  **5. Roles and responsibilities:**  Names, affiliations, and actual roles of candidate and all supervisors.  Roles: e.g. main supervisor, co-supervisor  Responsibilities: e.g. initiated the study design will provide statistical expertise in clinical trial design.  Name and contact information for trial sponsor (Cairo University)  **II. Introduction:**  **6. Background and rationale:**  -Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished).  This section should clearly include the following titles separately:  **Research question:**  Research question should be clear, properly formulated and well-structured followed with a question mark at the end (PICO format).  **Statement of the problem**:  The research problem should be clearly identified, stating its prevalence whenever applicable.  An understanding of how it is original and relevant.  How the proposed study will help fill the gap of knowledge in the literature.  **Rationale for conducting the research:**  Detailed justification for the trial should be clearly stated including why the research needs to be conducted in the selected population based on the currently available evidence.  Explanation of potential benefits to patients/ health service, relevance to current policies and community priorities.  It is strongly recommended that an up-to-date systematic review of relevant studies be summarized and cited in the protocol.  **Review of literature:**  Review briefly the existing body of knowledge on the topic (but not in details).  Description of the current treatment options and their limitations.  Description of the treatment under investigation including; any available data regarding the effects and mechanism of action of the interventions (published and unpublished) and reference to any previous evidence of its usefulness.  Examining benefits and harms for each intervention (summarize the known and potential risks of the intervention, giving a clear description of any expected adverse reactions).  Outline the rationale for the route of administration, dosage, regimen and period selected for the proposed study based on available non-clinical and clinical data.  Explain how the study will substantially add to science, change practice, save money, save lives and/or improve quality of life.  This section should be backed up by a brief and focused literature review of previous related studies highlighting inadequacies in the body of evidence.  **Explanation for choice of comparators:**  Selection of control/comparator should be justified with reference including data from an up-to-date systematic review.  Comparator may be:  Placebo, no treatment, gold standard, standard of care, another active drug, same drug with a different route or dose of administration.  **7. Objectives:**  Objectives: include aim of the study and hypothesis.  Aim of the study reflects the research questions to be answered by the trial.  Should be clear & very precise, only a few sentences long.  Use neutral words (e.g. “to compare effect of treatment A vs. treatment B on outcome X”) rather than in terms of a particular direction of effect.  Outcome “X” is the primary outcome.  **Hypothesis:**  A hypothesis states the predicted effect of interventions on trial outcomes.  Avoid biased statements, suggesting the author has prejudged the outcome.  Stated as a Null or alternative hypothesis.  **8. Trial design:**  Description of trial design, including the type of trial (e.g. non-randomised clinical trial with parallel group or split-mouth design).  Framework of a trial is objective to test superiority, non-inferiority, or equivalence of one intervention with another.  **III. Methods**  **A) Participants, interventions & outcomes**  **9. Study settings:**  Description of the environment in which a trial will be conducted (e.g, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained.  **10. Eligibility criteria**:  Eligibility criteria for potential trial participants i.e. Inclusion and exclusion criteria for participants.  They can relate to demographic information; type or severity of the health condition; previous or current treatment; diagnostic procedures; pregnancy; or other relevant considerations.  In trials of operator-dependent interventions such as surgery, it is usually important to promote consistency of intervention delivery by also defining the eligibility criteria for care providers and centers where the intervention will be administered.  Try to avoid restrictive participant selection. When trial participants differ substantially from the overall population to whom the intervention will be applied, the trial results may not reflect the impact in real world practice settings thus affecting the external validity (generalizability or applicability)  **11. Interventions**  -Description of Intervention/Control, including how and when it will be administered, with sufficient detail to allow replication.  For drugs, biological agents, or placebos, the protocol description should include:  Generic name, manufacturer, constituent components, route of administration & dosing schedule.  The description of non-drug interventions—such as devices, surgical procedures needs additional details about the settings and individuals administering the interventions. e.g., the level of individuals administering these interventions (e.g, for surgeons).  When intervention delivery is subject to variation, it is important to state whether the same individuals will deliver the trial interventions in all study groups, or whether different individuals will manage each study group.  Interventions that consist of “standard of care” require further elaboration in the protocol, as this care can vary substantially across centers and patients.  -Strategies used to improve adherence to intervention protocols, and procedures used to monitor these strategies (e.g. Pill count, adherence reminder sessions).  -Relevant care/interventions that will be permitted or prohibited during the trial.  -Criteria for discontinuing allocated interventions for a participant, if applicable, e.g. allergic reactions have been observed in rare cases. If this is suspected withdraw the trial medication from the patient.  **12. Outcomes:**  Primary, secondary and other outcomes should be described, with specific and measurable assessment unit.  It is important to explain the rationale for the choice of trial outcomes.  **4 components** should be defined for each outcome:   1. How the outcome variable will be measured, i.e. the data collected directly from participants (e.g., pain score, index, survival, pocket depth, mobility, patient satisfaction…etc.); 2. When the outcome data that will be collected from each participant for analysis (e.g., change from baseline, final value, time to event). 3. The method of aggregation (e.g., mean, median, %....) 4. The specific measurement time point of interest for analysis.   An ideal outcome is:   1. Valid reproducible 2. Relevant to the target population. 3. Responsive to changes in the health condition being studied.   **Primary outcome should be:**   * Defined in the PICO. * Of greatest therapeutic importance. * Essential for decision-making. * Used in sample size calculation (mostly) * Preferred to be patient oriented or patient-centered or patient-reported.   **Secondary objectives**  Study may not have 2ry objectives.  Include more general objectives.  Explain additional effects of intervention.  Their number should be kept low to enable later analysis of results.   |  |  |  |  | | --- | --- | --- | --- | | **Prioritization of Outcome** | **Outcome** | **Method of Measurement** | **Unit of Measurement** | | Primary outcome | Pain | Visual analogue scale | Numerical |   **13. Participant timeline**  A schematic diagram / table / Gantt chart is used to present the overall schedule for trial participants in each study group.  A clear and concise timeline of the study visits, enrolment process, interventions, and assessments performed on participants.    **14. Sample size:**  Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations. This should include:   1. The primary outcome. 2. Values for outcome (mean & SD). 3. Statistical test used for calculation. 4. Alpha level of significance (5%) 5. Power (80%) 6. The calculated sample size. 7. 20 -30% increase for anticipated missing data depending on nature of study. 8. A reference for outcome assumed.   **15. Recruitment:**  Strategies for achieving adequate participant enrolment to reach target sample size.   1. Where? 2. By whom? 3. When? 4. How? 5. Expected recruitment rates. 6. Duration of recruitment period. 7. Financial/non-financial incentives to investigators/participants.   **B) Data collection, management, and analysis:**  **16. Data collection methods**  Plans for assessment and collection of outcome, baseline and other trial data, including processes used to promote data quality (e.g. duplicate measurements, calibration of assessors)  Description of study instruments used for data collection, along with their reliability and validity.  Describe clearly the data collection process:   1. The personnel (standardized training=consistency). 2. Methods (standardized methods variability). 3. Data collection instruments, valid & reliable (questionnaire). 4. Data collection forms (appendices/reference).   Plans to promote participant retention and complete follow up.  Plans for data collected from participants who discontinue or deviate from intervention protocols  **17. Data management:**  Plans for data entry, coding, security, and storage, including any related processes to promote data quality (e.g., double data entry). Reference to where details of data management procedures can be found should be included.  **18. Statistical methods:**  Statistical methods for analyzing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol.  **C) Data monitoring:**  **19. Monitoring**  In most protocols, no formal data monitoring committee will be needed since the study is with known minimal risks  **20. Harms**  Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct.  **21. Audit**  Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor.  **IV. Ethics and dissemination**  **22. Research ethics approval**  Plans for seeking research ethics committee/institutional review board (REC/IRB) approval  **23. Protocol amendments**  Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses)  **24. Informed consent**  Who will obtain informed consent or assent from potential trial participants.  Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable.  **25. Confidentiality**  How personal information about enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial.  **26. Declaration of interest**  Financial and other competing interests for principal investigators for the overall trial and each study site  **27. Access to data**  Statement of who will have access to the final trial dataset.  **28. Post-trial care**  Provisions, if any, for post-trial care, and for compensation to those who suffer harm from trial participation  **29. Dissemination policy**  -Plans for investigators to communicate trial results to participants, healthcare professionals, the public, groups (e.g., via publication), including any publication restrictions.  -Authorship eligibility guidelines and any intended use of professional writers  -Plans, if any, for granting public access to the full protocol & participant dataset.  **V. Appendices**  **30. Informed consent**  Model consent form and other related documentation given to participants.  **31. Biological specimens**  Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable.  **VI. Statement of originality:**  **32.** **Statement of originality:**  Research point should be novel such as a new intervention, new assessment method, ……… Highlight the originality of your research point. Describe how your research is innovative and original. Explain how it adds to existing literature in your field. e.g. will it extend an area of knowledge, be applied to new contexts, solve a problem, test a theory, or challenge an existing one?  **VII. References**  All references should be written in the same font, and should be written through a citation/reference manager e.g. Mendeley or endnote. All references should follow the same style (author date style or cite-right Harvard is preferred). |