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| **Template for Writing Diagnostic Test Accuracy Protocol for Master Degree**  **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 (identified as a study of diagnostic accuracy using at least one measure of accuracy) **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 Master 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** | 6 | Research question |  |  |
| Rationale |  |  |
| Intended & clinical role of index test |  |  |
| Review of literature |  |  |
| 7 | Study objectives |  |  |
| Hypothesis |  |  |
|  | | | | |
| **III. Methods** | | | | |
| **A) Trial design** | 8 | Prospective or retrospective |  |  |
| **B) Participants** | 9 | Eligibility criteria |  |  |
| 10 | On what bases were participants identified |  |  |
| 11 | Where and when eligible participants were identified |  |  |
| 12 | Did participants form a consecutive, random or convenience series |  |  |
| **C) Test methods** | 13a | Index test, in sufficient detail to allow replication |  |  |
| 13 b | Reference standard, in sufficient detail to allow replication |  |  |
| 14 | Rationale for choosing the reference standard |  |  |
| 15 | Definition and rationale for test positivity cut-offs of the index test & reference standard |  |  |
| 16 a | Whether clinical information & reference standard results will be available to the performers or readers of the index test. |  |  |
| 16 b | Whether clinical information and index test results will be available to the assessors of the reference standard. |  |  |
| **D) Statistical analysis** | 17 | Methods for measuring diagnostic accuracy |  |  |
| 18 | How in determine index test or reference standard will be handled |  |  |
| 19 | How missing data will be handled |  |  |
| 20 | Sample size calculation |  |  |
|  | | | | |
| **IV. Ethics and dissemination** | | | | |
|  | 21 | Research ethics approval |  |  |
|  | 22 | Protocol amendments |  |  |
|  | 23 | Informed Consent |  |  |
|  | 24 | Confidentiality |  |  |
|  | 25 | Declaration of interests |  |  |
|  | 26 | Access to data |  |  |
|  | 27 | Dissemination policy |  |  |
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| **V. Appendices** | | | | |
|  | 28 | Informed consent materials |  |  |
|  | 29 | Biological specimens |  |  |
|  | | | | |
| **VI. References** |  |  |  |  |
|  | | | | |
| **Evidence based committee** | | | | |
| **Name** | | **Signature** | **Date** | |
| 1. | |  |  | |
| 2. | |  |  | |
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| **Research plan committee** | | | | |
| **Name** | | **Signature** | **Date** | |
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| **I. Administrative information:**  **1. Title:**  Descriptive title identified as a study of diagnostic accuracy using at least one measure of accuracy. This can be performed by using terms in the title and/or abstract that refer to measures of diagnostic accuracy, such as ‘sensitivity’, ‘specificity’, ‘positive predictive value’, ‘negative predictive value’, ‘area under the ROC curve (AUC)’ or ‘likelihood ratio’.  **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. Version 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 idea and point of research, will help revise the manuscript, will perform the test, will provide statistical expertise in study.  Name and contact information for trial sponsor (Cairo University)  **II. Introduction:**  **6. Background and rationale:**  -It is a description of the scientific and clinical background of the study  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 (PIRT format).  **Rationale**: Detailed justification for the study should be clearly stated including why the research needs to be conducted. Refer to previous work on the topic, remaining uncertainty and the clinical implications of this knowledge gap. How the proposed study will help fill the gap of knowledge in the literature.  **Intended use of the index test:** Clarify the intended use of the “index test” (test under evaluation). The intended use of a test can be diagnosis, screening, staging, monitoring, prognosis, or treatment selection.  **Clinical role of the index test:** Clarify the clinicalrole of the “index test” under evaluation relative to other tests in the clinical setting, e.g. because it is less costly or burdensome. A new test may be used to replace an existing test.  **Review of literature:** Review briefly the existing body of knowledge on the topic (but not in details). Review previous related studies highlighting inadequacies in the body of evidence.  **7. Study objectives and hypotheses:**  **The aim of the study includes hypothesis and objectives**  -When comparing two or more index tests, statistical hypotheses are defined in terms of superiority, equality or non-inferiority in accuracy.  -For single index tests, statistical hypotheses are defined in terms of acceptability criteria (minimum levels of sensitivity, specificity).  -A hypothesis generally includes a quantitative expression of the expected value of the diagnostic parameter.  -The objectives should be clear & very precise, only a few sentences long.  **III. Methods:**  **A) Trial design**  **8.** Specify whether data collection will be planned before the index test and reference standard be performed (prospective study) or after (retrospective study).  -Sometimes, the idea for a study originates when patients have already undergone the index test and the reference standard. If so, data collection relies on extracting data from patient charts (retrospective study).  **B) Participants:**  **9. Eligibility criteria**:  Eligibility criteria for study participants i.e. Inclusion and exclusion criteria for participants.  Study must include a complete description of the criteria that were used to identify eligible participants. Eligibility criteria are usually related to the nature and stage of the target condition and the intended future use of the index test; they often include the signs, symptoms or previous test results that generate the suspicion about the target condition.    **10. On what basis potentially eligible participants will be identified:**  Describe how the researcher identified eligible participants, such as symptoms, results from previous tests, or searching hospital databases for patients that underwent the index test and the reference standard.  **11. Where and when potentially eligible participants will be identified (setting, location and dates)**  Report the actual setting in which the study will be performed, as well as the exact locations: names of the participating centers, city and country.  Report the anticipated start and end dates of participant recruitment.  **12. Whether participants formed a consecutive, random or convenience series:**  The included study participants will be enrolled in the study either by:  -A consecutive series of all patients evaluated for eligibility at the study location and satisfying the inclusion criteria, where participants will be enrolled based on their accessibility to the clinical investigator.  or  -A subselection of all patients evaluated for eligibility, which can be purely random, by using a random numbers table, or less random, if patients are only enrolled on specific days.  **C) Test method:**  **13. Index test & reference standard in sufficient detail to allow replication**  -Describe the methods for executing the index test and reference standard, in sufficient detail to allow other researchers to replicate the study. The description should cover details of:  A. The preanalytical phase, e.g., patient preparation such as fasting/feeding status prior to blood sampling, the handling of the sample prior to testing, or the anatomic site of measurement.  B. The analytical phase, including materials, instruments and analytical procedures.  C. The postanalytical phase, such as calculations of risk scores.  -Information about the number, amount of training and expertise of the persons who will execute and read the index test and the reference standard as prior training improves interpretation and reduce interobserver variation.  **14. Rationale for choosing the reference standard**  The reference standard is used for establishing the presence or absence of the target condition in study participants. Several reference standards may be available to define the same target condition. Protocol should provide rationale for selecting the specific reference standard from the available alternatives.  **15. Definition and rationale for test positivity cut-offs of the index test & reference standard:**  The threshold (test positivity cut-off) could be either prespecified or explored.  If prespecified, define how this threshold was based on; (1) previous studies, (2) cut-offs used in clinical practice, (3) thresholds recommended by clinical practice guidelines or (4) thresholds recommended by the manufacturer.  If no such thresholds exist, state that the study will explore the accuracy for various thresholds after the data have been collected.  **16 a. Whether clinical information and reference standard results will be available to the performers of the index test**  **16 b. Whether clinical information and index test results will be available to the assessors of the reference standard**  -Some medical tests, such as imaging, require human interpretation and judgment. If the reader of a test has access to information about signs, symptoms and previous test results, the reading may be influenced by this additional information.  -Protocol should specify to which extent such additional information will be available to test readers which may influence their final judgment.  -Protocol should specify whether the assessors of the reference standard will have access to the index test results. Withholding information from the readers of the test is referred to as ‘blinding’ or ‘masking’ which is neither desirable nor undesirable.  **D) Statistical analysis**  **17. Methods for estimating or comparing measures of diagnostic accuracy**  Protocol should describe the methods that will be used for calculating the measures that they considered appropriate for their study objectives.  **18. How indeterminate index test or reference standard results will be handled:**  Indeterminate results refer to those that are neither positive nor negative. A test may fail because of technical reasons or an insufficient sample, for example, in the absence of cells in a needle biopsy from a tumor. Ways for handling indeterminate test results in the analysis when estimating test accuracy should be reported.  -They can be ignored altogether, be reported but not accounted for as a separate test result.  Or  -Reclassify all indeterminate results: as false positives or false negatives, depending on the reference standard result (‘worst-case scenario’), or as true positives and true negatives (‘best-case scenario’).  **19. How missing data on the index test and reference standard will be handled**  -Specify ways to deal with missing data when analyzing them.  -Participants with missing test results can be included in the analysis if missing results are imputed.  Or  -Assess the impact of missing test results on estimates of accuracy by considering different scenarios. For the index test, e.g., in the ‘worst-case scenario, state that all missing index test results will be considered false-positive or false-negative depending on the reference standard result; in the ‘best-case scenario’, all missing index test results will be considered true-positive or true-negative.  **20. Sample size calculation and how it was determined**  -Sample size must be calculated when developing a diagnostic accuracy study to ensure that a sufficient amount of precision is reached.  -Specify how the sample size was determined, and whether the assumptions made in this calculation are in line with the scientific and clinical background, and the study objectives.  **IV. Ethics and dissemination**  **21. Research ethics approval**  Plans for seeking research ethics committee/institutional review board (REC/IRB) approval  **22. Protocol amendments**  Plans for communicating important protocol modifications (e.g., changes to eligibility criteria, analyses)  **23. 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.  **24. Confidentiality**  How personal information about enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial.  **25. Declaration of interest**  Financial and other competing interests for principal investigators for the overall trial and each study site  **26. Access to data**  Statement of who will have access to the final trial dataset.  **27. 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**  **28. Informed consent**  Model consent form and other related documentation given to participants.  **29. 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. 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). |