BURDEN OF DISEASE REVIEW MANAGER FOR SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES

Technical Report and User Guide

Burden Of Disease Research Unit
South African Medical Research Council

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A copy of this report is available on the Internet at: www.mrc.ac.za/bod/bod.htm

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Acronyms

BODRevMan	Burden of Disease Review Manager
BODRU	Burden of Disease Research Unit
CRA	Comparative Risk Assessment Study
DALY	Disability Adjusted Life Years
DISMOD	Disease modelling software
GBD	Global Burden of Disease
ICD-10	International Statistical Classification of Disease and Related Health Conditions 10th revision
NBD	National Burden of Disease
RHIS	Routine Health Information System
SA	South Africa
SA NBD 2	South African Second National Burden of Disease Study
SA CRA 2	South African Second Comparative Risk Assessment Study
SR	Study review
WHO	World Health Organization
YLD	Years of Life lived with Disability
YLL	Years of Life Lost

Definitions

Adequate sample-size calculation	This is the process by which we calculate the optimum number of participants required to arrive at ethically and scientifically valid results. Generally, the sample size for any study depends on the: acceptable level of significance, power of the study, expected effect size, underlying event rate in the population, and standard deviation in the population.
Case-control study	Instead of identifying people on the basis of their exposure status and waiting to see who develops the disease, a case-control study effectively starts from the end and works backwards. People who have developed the disease of interest (cases) and a representative sample of people from the same population who do not have that disease (controls) are selected and then asked about their previous exposure.
Case-fatality rate	Case fatality is a measure of disease severity and is defined as the proportion of cases with a specified disease or condition who die within a specified time. It is usually expressed as a percentage (Portia *et al*, 2014).
Cohort study	A cohort study tracks two or more groups from exposure to outcome. This type of study can be done by going ahead in time from the present (prospective cohort study) or, alternatively, by going back in time to establish the cohorts and following them up to the present (retrospective cohort study). A cohort study is the best way to identify the incidence and natural history of a disease, and can be used to examine multiple outcomes after a single exposure.
Community-based study	Community-based studies recruit subjects from the general population - usually a subgroup - rather than from a clinical/hospital population.
Cross-sectional study	Sometimes termed a frequency survey or a prevalence study, cross-sectional studies are done to examine the presence or absence of disease and the presence or absence of an exposure at a particular time (snapshot in time). The focus is on prevalence.
Data extraction	The process of retrieving relevant information or data from data sources in a specific manner for further data processing or storage.
Duration	An amount of time or time interval.
Exposure	The exposure of interest may be associated with either an increased or a decreased occurrence of disease or other specified health outcome, and may relate to the environment, lifestyle, or inborn/inherited characteristics.
Facility-based study	Facility-based studies recruit subjects from a clinical/hospital population rather than from the general population. Hospital-based differ from population-based studies because the study base is defined secondarily to the identification of cases. Cases are selected regardless of the population from which they arise (e.g. all cases from a given hospital receiving patients from different settings).

Guest user	An individual who is not a part of the study collaboration but is given permission by the principal investigator (PI) to view Stage 2 reviews only.
Guest reviewer	An individual who is part of the study collaboration but is not working on a specific condition. However, is reviewing the same article/study in their work. This person is given permission by the PI to view Stage 1 and 2 reviews of articles/studies relevant to their work.
Hazard Ratio	This is a ratio of instantaneous risk in two groups at any given point in time. It is a measure of relative risk, and is essentially the same as an incidence-rate ratio. It is often calculated in cohort studies.
Incidence	The incidence of disease represents the rate of occurrence of new cases arising in a given period in a specified population.
Incidence-rate Ratio	The incidence-rate ratio (also called the rate ratio or incidence-density ratio) is used to compare the incidence rates of events occurring at any given point in time. It is calculated by dividing the incidence rate of disease in a group of people exposed to the condition of interest by the incidence rate in the unexposed group.
Mean	This is the average of a sample or set of data.
Meta-analysis	A technique for combining the results of multiple different studies into a single estimate, basically presenting a graphic weighted average of the study-specific results with greater reliance on bigger studies with more precise estimates.
Metadata	Provides a summary of the articles screened both outside and within BODRevMan, details on included/excluded studies, the reasons for exclusions at each stage, and the number of articles/studies that had data extracted for a specific condition of interest in BODRevMan.
Odds Ratio	The ratio of the odds of exposure among the cases to the odds of exposure among the controls.
Outcome	The outcome of a study is a broad term for any defined disease, state of health, health-related event or death.
Parameters	A set of standard variables used to measure exposure, frequency, occurrence and distribution of disease conditions in a specified population.
Population-based study	The term population-based is traditionally used to describe a study that involves a defined general population, as opposed to hospital-based or occupation-based populations. We use this to denote a national community-based survey.
Prevalence	The frequency of existing cases in a defined population at a given point in time.
Project administrator	The person responsible for all administrative functions on the system including of the loading of articles onto the system.
Power user	An individual who is given a “read only” permission to access all levels of BODRevMan.
Reference group	This is the comparison group.

Register (not population-based)	A disease registry is a database that contains information about people diagnosed with a specific type of disease. Most disease registries are either hospital or population based. A hospital-based registry contains data on all the patients with a specific type of disease diagnosed and treated at that hospital.
Register (population-based)	A population-based registry aims to include everyone with the disease in the population, be it self-reported, clinically diagnosed or detected at screening. It is a registry that aims to cover all residents in a given geographic area within a specific time period.
Relative Risk	The relative risk (also called the risk ratio) is the ratio of the risk of occurrence of a disease among exposed people to that among the unexposed.
Relative-risk mortality	This is the mortality of diseased divided by the mortality of non-diseased.
Reports	Relevant information is captured in BODRevMan throughout the review and data-entry process and generated as several reports.
Remission	A period during which symptoms of disease are reduced (partial remission) or disappear (complete remission).
Reviewer	An individual who critically evaluates a study and reports on the vital information and parameters of interest.
Risk-of-bias assessment	A systematic process of identifying, evaluating and/or estimating the potential risks that may be present in a study.
Routine health information data	Ongoing data collection of health status, health interventions and health resources. Routinely collected data include: health-unit based, community-based, civil registration and vital events, and sentinel reporting.
Sampling	Selection of a portion of the population, in the research area, which is representative of the whole population.
Severity	The degree or level of seriousness of a condition.
Study Review Form	The Study Review Form is a key feature in the web-based BODRevMan system and consists of three major inter-linked sections namely, the Eligibility Assessment, Risk-of-Bias Assessment and Data Extraction, risk-of-bias assessment and data extraction.

Overview of the Burden of Disease Review Manager

Burden of Disease studies aim to provide a comprehensive assessment of mortality, ill-health and disability experienced in the population. The Disability Adjusted Life Year (DALY) is a summary measure that combines the health loss from premature mortality (Years of Life Lost [YLLs]) as well as the loss from disability associated with non-fatal outcomes (Years of Life Lived with Disability [YLDs]) (Murray *et al*., 1996; Mathers et al., 2001).

Certain epidemiological parameters are required for estimating YLDs and attributable burden of modifiable risk factors; these are prevalence, incidence, case-fatality rate, relative risk, odds ratio, hazard ratio, mean, incidence ratio, severity, duration and remission.

To ensure the use of quality estimates, a systematic review, including a risk-of-bias assessment of studies producing these estimates may be useful (Mathers et al., 2001). While critical appraisal of randomised control trials is well established by the Cochrane Collaboration (Higgins et al., 2011), similar tools across other study designs are not standardised.

The Burden of Disease Research Unit (BODRU) of the South African Medical Research Council has developed a standardised risk-of-bias tool that can be used for cross-sectional (including population-based surveys) studies, case-control studies, cohort studies and surveillance. A risk-of-bias score (0-20) can be obtained based on a set of defined criteria to assess the external and internal validity of a study. This tool can be applied to assess the risk-of-bias of observational studies and guide the decision on whether to use or disregard the epidemiological parameters from that particular study. The risk-of-bias-score can also guide statisticians on the size of the weight (based on the quality) that can be applied to estimates from various studies pooled in a meta-analysis. A web-based system, the Burden of Disease Review Manager (BODRevMan), has been developed to manage the systematic review process, including the risk-of-bias assessment and summary of data extracted from articles/studies.

The aim of this report

Part A of this report provides information on the technical aspects of the systematic review process, application of the risk-of-bias assessment, data extraction and how to summarise information per study or condition investigated. Part B of this report is an End-User Guide that focuses on the preparation of data and gives general guidelines for entering data into the BODRevMan system, including specific instructions and tips to aid data flow.

PART A

Technical Report

1 Overview of the Systematic Review Process

A systematic review is a review of existing literature, using a clearly formulated research question and critical-appraisal process. It uses explicitly predetermined selection criteria to identify eligible articles/studies for inclusion in a review and defined criteria for critical evaluation of the risk-of-bias in these articles/studies (Higgins *et al.*, 2011). One of the key components of a systematic review is independent assessment of studies by at least two reviewers and a process to reach consensus. A meta-analysis can be done to pool results from more than one article/study depending on the heterogeneity between identified studies.

The key features of a systematic review include:

- A clearly stated research question and objectives.
- Predefined eligibility criteria for articles/studies to be included.
- An explicit, step-by-step, transparent, reproducible methodology.
- A systematic search that attempts to identify all studies that meet the eligibility criteria.
- Assessment of the risk-of-bias of articles/study findings that meet inclusion criteria through risk-of-bias assessment.
- Synthesis and summary of findings.

Two reviewers perform a systematic search, screen articles/studies and agree on which of these should be assessed. An eligibility and risk-of-bias assessment of each included article/study is necessary to determine if the study was conducted using rigorous methods and whether the results are of a quality that can be used in meta-analysis to synthesis and summarise findings.

2 Risk-of-bias assessment tool for observational studies

Study design and methodology are crucial for a valid result. A bias is a deviation from the truth. Risk may result in a systematic error and therefore an invalid study result. Therefore, it is important to assess the risk-of-bias of each study included in the systematic review using a standardised risk-assessment tool that can be applied across all observational study designs.

A comprehensive search of three databases (PubMed, Scopus, Web of Science) and a search engine (EBSCOhost) was conducted to identify any checklist or quality assessment tools that assessed the risk-of-bias and methodological quality of observational studies. The reference lists of the articles retrieved were also screened and experts in the field were contacted (Global Burden of Disease Group, Society for Epidemiological Research). Three relevant checklists were obtained from the search (Wells *et al.*, 2011, Hoy *et al.*, 2012, Shamliyan *et al*, 2011). The risk-of-bias tool by Hoy *et al.* (2012) is an improvement on the checklist described by Shamliyan *et al.* (2011). However, none of these checklists can be applied in a standardised manner to assess the risk-of-bias across all observational studies. Therefore, we developed a standardised risk-of-bias tool for cross-sectional (including population-based) studies, cohort studies, case-control studies, and surveillance.

2.1 Development of a standardised risk-of-bias assessment for observational study designs

The questions in the new tool were developed using the framework of Hoy *et al* (2012) with the New Castle Ottawa (Wells *et al.*, 2011) phrasing to guide questions for cohort and case-control studies in particular. Furthermore, some of the questions were developed using general criteria provided by the Global Burden of Disease Group (personal communication; Prof. Theo Vos; June 2014). A more nuanced scoring system was created and standardised across all study designs.

The new risk-of-bias assessment tool consists of two major domains (internal and external validity) which are further sub-divided into criterion. Each criteria has specific questions that assess the risk-of-bias within the criteria. Each question is scored based on the responses.

The scoring system (maximum=20) categorises studies as low risk (14-20), moderate risk (7-13) or high risk (0-6) based on the answers provided for each question. Table 2.1 reports the dimensions and criteria assessed, and the questions that were relevant for the different study designs. For each question answered, guidelines are provided to the reviewer on how to answer that question (see Appendices A-E). Questions have been standardised for scoring taking into account the different elements of study design for each criterion.

Table 2.1: Risk-of-bias tool for observational studies

DOMAIN	CRITERIA	STANDARD QUESTION	STUDY DESIGN				SCORE
			Population-based survey/ cross-sectional study	Cohort Study	Case-control Study	Surveillance System	
External validity (9)	Representativeness (5)	Was a sample-size calculation conducted and is it adequate?	Standard	Standard	Standard	Auto-scoring	1
		Was a clear definition of study population (e.g. inpatient/ outpatient/ register/community) provided?	If it is a population-based survey, is the study population a close representation of the target population (e.g. national population) in relation to relevant variables (e.g. age, sex, or other demographic characteristics)?	Standard	Standard	Standard	1
		Were the controls selected from the same source population as the cases/exposed?	Was the sampling frame a true or close representation of the population/community in which the study is conducted? (Consult with content expert.)	Standard	Standard	Does the sentinel site(s) cover the target population and can this be generalised to the overall population?	1
		Was a form of random selection (e.g. simple random, stratified, cluster and systematic) used to select the sample or was a census undertaken?	Standard	Standard	Standard	Standard	2

DOMAIN	CRITERIA	STANDARD QUESTION	STUDY DESIGN				SCORE
			Population-based survey/ cross-sectional study	Cohort Study	Case-control Study	Surveillance System	
		Name the other sampling strategy (e.g. non-random, consecutive, convenience, case by case)? Describe.	Standard	Standard	Standard		
		Was the sampling method appropriate for the research question?	Standard	Standard	Standard		
	Non response bias (4)	Different questions for each study design	Were there similarities between participants and non-participants in relation to demographic characteristics? (See Help for retrospective review of records.)	From those individuals who met the inclusion criteria, were there no significant differences by demographic characteristics between those who agreed to participate and those who refused to participate? (See Help for retrospective review of records.)	From those individuals who met the inclusion criteria, did the authors describe any significant differences in demographic characteristics between those who agreed to participate and those who refused to participate? (See Help for retrospective review of records.)	Were all eligible participants included in the surveillance?	4

DOMAIN	CRITERIA	STANDARD QUESTION	STUDY DESIGN				SCORE
			Population-based survey/ cross-sectional study	**Cohort Study**	**Case-control Study**	**Surveillance System**	
			If it is a population-based survey, was the overall survey response rate reported for this condition of interest? If cross-sectional study, was the response rate for the study reported?	Was an effort made to limit loss to follow-up?	Among those who participated in the study, were the cases and controls similar in terms of demographic characteristics?	Was the response rate reported for the surveillance?	
			If it is a population-based survey, what was the overall response rate for this condition of interest? If it is a cross-sectional study, what was the response rate for the study?	Was the differential loss to follow-up <20% between the exposed and unexposed groups?		What was the response rate for the surveillance?	
			If it is a population-based survey, was the overall response rate for this condition of interest adequate? If it is a cross-sectional study, was the response rate adequate? Excellent ≥80%, Average 60-79%, Poor <60%	Was the follow-up of participants (cohorts) adequate? Adequate loss to follow-up if <20% and not adequate if ≥20%.		Was the response rate adequate? Excellent ≥90%, Average 70-89%, Poor <70%	

DOMAIN	CRITERIA	STANDARD QUESTION	STUDY DESIGN				SCORE
			Population-based survey/ cross-sectional study	Cohort Study	Case-control Study	Surveillance System	
Internal validity (11)	Case definition (3)	Were the cases classified using the ICD codes or was an acceptable case definition used? (Consult with content expert.)	Standard	Standard	Standard	Standard	1
		What is the case definition?	Standard	Standard	Standard	Standard	
		Were the study instruments used to measure the parameter of interest shown to have reliability and validity in this study or in a previous study, via piloting, test-retesting? (Consult with content expert.)	Standard	Was the ascertainment of outcome done from medical records? Select from the following: (A) diagnostic/laboratory test, (B) Medical records/ clinical assessment, (C) structured interview/self-report, (D) no description.	Was the ascertainment of exposure done from medical records? Select from the following: (A) diagnostic/laboratory test, (B) medical records/clinical assessment, (C) structured interview/self-report, (D) no description.	Standard	2
	Data collection (2)	Were data collected directly from the participants or if a proxy (a representative of the participant) was used, was it appropriate?	Standard	Standard	Standard	Standard	1
		Was the same method used for data collection for all participants for the condition of interest? If a different method was used, was it adequate?	Standard	Standard	Standard	Standard	1

DOMAIN	CRITERIA	STANDARD QUESTION	STUDY DESIGN				SCORE
			Population-based survey/ cross-sectional study	Cohort Study	Case-control Study	Surveillance System	
	Uncertainty of estimation (1)	Was the parameter of interest reported with uncertainty, i.e. standard deviation (SD) or standard error (SE) or 95% confidence interval (CI)?	Standard	Standard	Standard	Standard	1
	Appropriateness of time factor for outcome measure (2)	Was the length of recall period for the parameter of interest appropriate to ascertain outcome/exposure? (Consult with content expert.)	Standard	Was the follow-up period long enough to ascertain the outcome of interest? (Consult with content expert.)	Was the recall period appropriate to ascertain the outcome/exposure of interest? (Consult with content expert.)	Auto-scoring	2
	Appropriateness of numerator and denominator in calculation of estimate (2)	Were the numerator and the denominator for the parameter of interest appropriate? If not, can these be extracted to recalculate the parameter of interest?	Standard	Standard	Standard	Auto-scoring	2
	Confounding (1)	Were potential confounding factors sought and controlled for in the analysis for odds ratios/relative risks/hazard ratios/incidence-rate ratio?	Standard	Standard	Standard	Auto-scoring	1

Table 2-2 reports the differences in the domains for each of the checklists identified in the literature and the newly developed BODRevMan risk-of-bias assessment tool.

Table 2-2: Overview of different risk-of-bias tools from literature and BODRU risk-of-bias tool

	Risk-of-Bias Tools			
	New Castle Ottawa Scale by Wells *et al.*, (2009)	**New Castle Ottawa Scale by Wells *et al.*, (2009)**	**Risk-of-bias tool by Hoy *et al.*, (2012)**	**BODRU risk-of-bias tool (2015)**
STUDY TYPE	**Case-control**	**Cohort**	**Population-based**	**All observational**
Domain 1	Selection	Selection	External validity	External validity
Questions	4	4	4	6
Domain Score	***4***	***4***	***4***	***9***
Domain 2	Comparability	Comparability	Internal validity	Internal validity
Questions	1	1	6	8
Domain Score	*2*	*2*	*6*	*11*
Domain 3	Exposure	Outcome	-	-
Questions	3	3	-	-
Domain Score	*3*	*3*	-	-
OVERALL SCORE	**9**	**9**	**10**	**20**

Notes: Hoy *et al*. deliberately did not include an overall numeric rating of risk of study bias but, instead, made a judgment of the overall risk of study bias based on assessment of risk-of-bias of 10 individual items. The summary assessment is based on the rater's subjective judgment given responses to the preceding 10 items." Newcastle-Ottawa Scale (NCOS): A study can be awarded a maximum of one star for each numbered item within the Selection (maximum four stars) and Exposure (maximum three stars) categories. A maximum of two stars can be given for Comparability.

A literature review on the quality of data collected as part of the routine health information system (RHIS) yielded a paucity of studies (Roomaney *et al*, 2016). These studies, together with personal communication with experts, could not inform on the quality of the RHIS data. In light of this finding, a risk-of-bias assessment of RHIS data is not possible.

While modelled data can be a useful source of information for burden of disease studies, it is not possible to perform a risk-of-bias assessment on these data. Content and method experts would need to determine the coherence and plausibility of these data for inclusion in systematic reviews.

3 Systematic Review in BODRevMan

The web-based BODRevMan system has been created to facilitate, standardise and manage the process of systematic review, the risk-of-bias assessment and summary of data abstracted. A digitised Study Review Form, designed to target the objectives of burden of disease estimation, has been created in the BODRevMan system to ensure that articles/studies are assessed consistently. Furthermore, where deemed necessary, guidance on how to answer the questions in the Study Review Form has been added next to each question.

The Study Review Form is the key feature in the web-based system and consists of three major inter-linked sections namely, the Eligibility Assessment, Risk-of-Bias Assessment and the Data Extraction as shown in Figure 3-1.

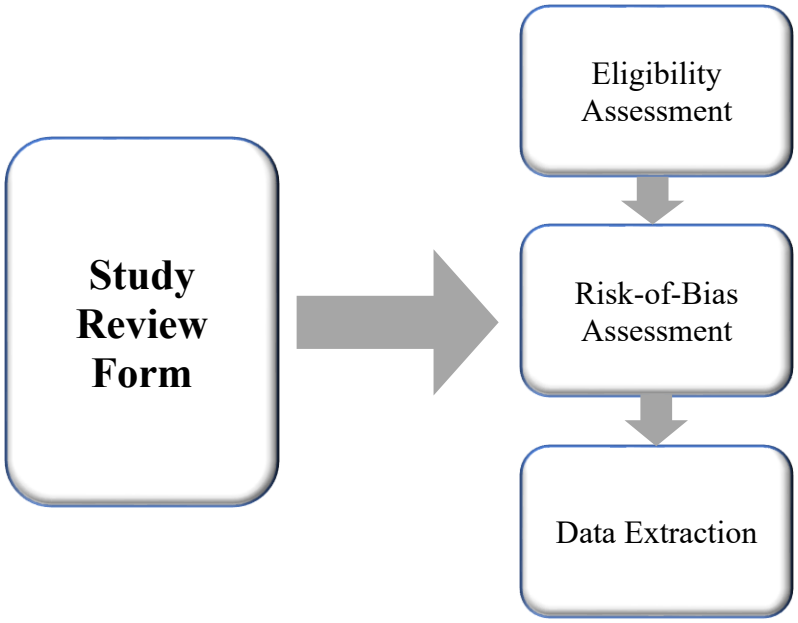


Figure 3-1: Study Review Form

3.1 Eligibility Assessment Section

This section is concerned with identifying articles/studies that do not meet the pre-specified criteria for inclusion in the systematic review. The questions were developed according to the inclusion and exclusion criteria set out in the YLD (Pillay-van Wyk *et al.*, 2015) and CRA protocols (Bradshaw, 2013) and were sequentially designed to allow a coherent flow of information. Questions were structured to elicit sufficient information to enable a valid

judgment on the condition of interest, study design, objectives and methodology at this point in the review process.

Articles/studies that do not satisfy the pre-specified criteria are excluded from further assessment. Information on country of data collection, whether the article-study was conducted within the required period (between 1997 – present year), and availability of the full-text article/study to enable complete data extraction, the sample size, and whether the study design is a randomised-control trial (RCT) is assessed. A sample size of fewer than 100 people is deemed inadequate to reduce the influence of outliers or extreme observations and therefore such articles/studies are excluded. RCTs are not eligible for inclusion because of the presence of an intervention which may influence the true prevalence/incidence of certain conditions. However, in some cases, the sampling strategy and study population used in a RCT could be deemed as representative of the target population under review and baseline information could be used. In these cases, the epidemiologist on the review team should be consulted about including the RCT and assessing the study as a cross-sectional study. If an article/study does not meet the overall eligibility criteria (Figure 3-2) it will be excluded from the systematic review and the reviewer will be able to finish the Study Review Form.

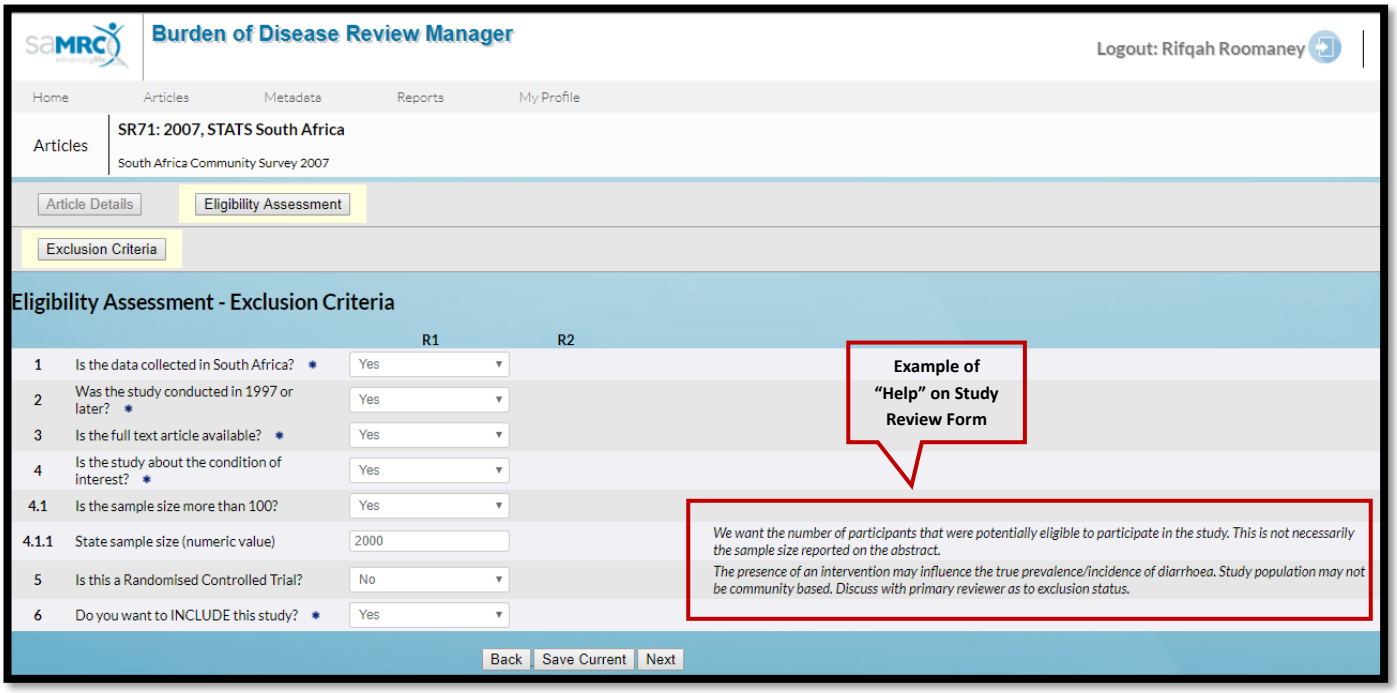


Figure 3-2: Eligibility Assessment Exclusion Criteria

An article/study must report at least one of the epidemiological parameters of interest to be included in the review process; these are prevalence, incidence, case-fatality rate, relative risk, odds ratio, hazard ratio, mean, incidence ratio, severity, duration or remission (Figure 3-3).

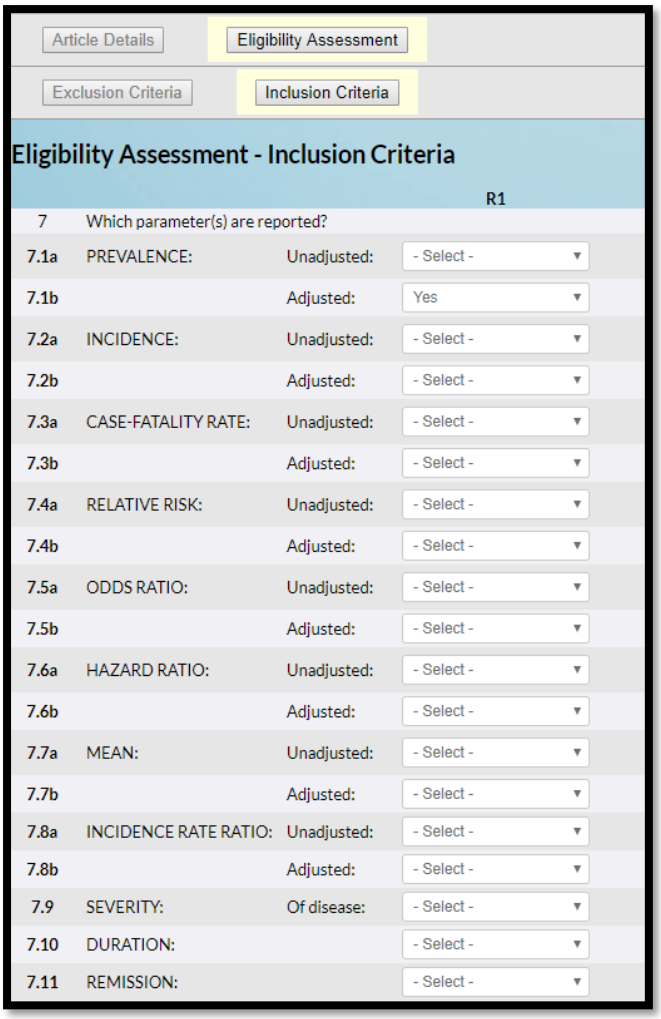


Figure 3-3: Eligibility Assessment Inclusion Criteria

The reviewer can exclude the article/study if none of these parameters are reported. The system enables the reviewer to record whether the selected parameter is adjusted or unadjusted. An example of this would be the weighted (adjusted) versus unweighted (unadjusted) estimates, or crude versus standardised estimates from an article/study.

An article/study can also be excluded if the estimates are not provided by age and sex as this is a requirement for more rigorous disease modelling in DISMOD II (World Health Organization, 2001). Some articles/studies report the regression coefficient (β) instead of the

odds ratio. The odds ratio can be calculated by taking the exponent of the regression coefficient, i.e. exp(β).

Table 3-1 provides detailed information on the the eligibility assessment section.

Table 3-1: Eligibility Assessment Section Overview

Eligibility Assessment		**Notes**
Exclusion criteria	Whether data were collected in South Africa (SA)	According to YLD (Pillay-van Wyk *et al.*, 2015) and CRA protocols (Bradshaw, 2013), any article/study will be excluded if it was not conducted in SA.
	Study conducted in 1997 or later	The National Burden of Disease study time period is from 1997 to 2012 so studies conducted prior to 1997 will be excluded.
	Full text available	If, after much effort, no full text is available, the study will be excluded.
	Sample size	A study with a sample size of <100 participants will be excluded.
	Study is about condition of interest	An article/study not reporting on the condition under review will be excluded.
	Is the study a randomised controlled trial?	In some instances, baseline information from a RCT can be included based on the sampling strategy and type of participants recruited.
Inclusion criteria	Type of parameter reported	According to YLD and CRA protocols, only studies that have data on epidemiological parameters that can be used for burden of disease estimation will be included.
	Data reported by age and sex	Data provided with more than one age-band (and preferably by a sex breakdown) is required for disease modelling.
	If the data can be modelled using DISMOD II	DISMOD II requires more than one age-band for disease modelling.

3.2 Additional study information

Characteristics of the study population and the description of the study setting are vital information that do not form part of the eligibility criteria. Therefore, an Additional Information section was created to extract such information consistently to ensure quality.

Detailed study characteristics such as age range of the participants, study period, the geographical location and study setting (i.e. where the study was conducted) form part of the additional study data extracted. The study period question is a mandatory question as a study's timing may be associated with important disease outbreaks, technology differences or trends over time that could explain changes noted in the profile of the condition of interest. In general, estimates from similar time periods are pooled in the meta-analysis.

3.3 Study types

A wide range of epidemiological study designs provide information on the listed parameters. A risk-of-bias assessment is required before these studies are deemed adequate for inclusion in the systematic review and the burden of disease estimation. BODRevMan includes a risk-of-bias assessment for cross-sectional (including population-based surveys) studies, case-control studies, cohort studies and surveillance study designs. The study designs are described as follows:

- Cross-sectional study: These studies are done to examine the presence or absence of disease and the presence or absence of an exposure at a particular time (snapshot in time). The focus is prevalence. These studies are also referred to as a frequency survey or a prevalence study.
- Case-control study: Instead of identifying people on the basis of their exposure status and waiting to see who develops the disease, a case-control study effectively starts from the end and works backwards. People who have developed the disease of interest (cases) and a representative sample of people from the same population who do not have that disease (controls) are selected and then asked about their previous exposure
- Cohort study: These studies tracks two or more groups from exposure to outcome. This type of study can be done by going ahead in time from the present (prospective cohort study) or, alternatively, by going back in time to establish the cohorts and following them up to the present (retrospective cohort study). A cohort study is the best way to identify the incidence and natural history of a disease, and can be used to examine multiple outcomes after a single exposure
- Population-based survey: Even though this is in essence a cross-sectional study, the term population-based is traditionally used to describe a study that involves a defined "general population", as opposed to hospital-based or occupation-based populations. We use this to

denote a national and/or community-based survey.

3.3.1 Assessing variable response rate before the risk-of-bias assessment

For national population-based surveys, an additional quality check is performed on the variable extracted from the database to ensure an adequate variable response rate irrespective of the overall survey response rate. This is assessed prior to completing the risk-of-bias assessment for the article/study. In general, a variable/item/testing response rate of >80% is regarded as excellent, 60-79% as average, <60% as poor. For our purposes, a variable/item/testing response rate above 80% is deemed adequate for data extraction. However, the reviewer has the option to include the study and extract the data with a low response rate or to exclude the article/study. The former option can be chosen in situations where the data can be adjusted to limit the bias introduced by the low response rate or where a smaller weight is added to the estimate in the meta-analysis.

3.3.2 Risk-of-bias assessment in BODRevMan

The risk assessment section, which refers to the risk-of-bias, is split into two domains namely external and internal validity. External validity is evaluated by assessing the representativeness and non-response bias in the study being appraised. Internal validity is evaluated by assessing the adequacy of the following criterion; case definition, measurement of case, reporting uncertainty of the estimate, appropriateness of time factor for outcome measure, appropriateness of numerator and denominator in calculation of estimate and, where appropriate, if there was an adjustment for confounding (Figure 3-4).

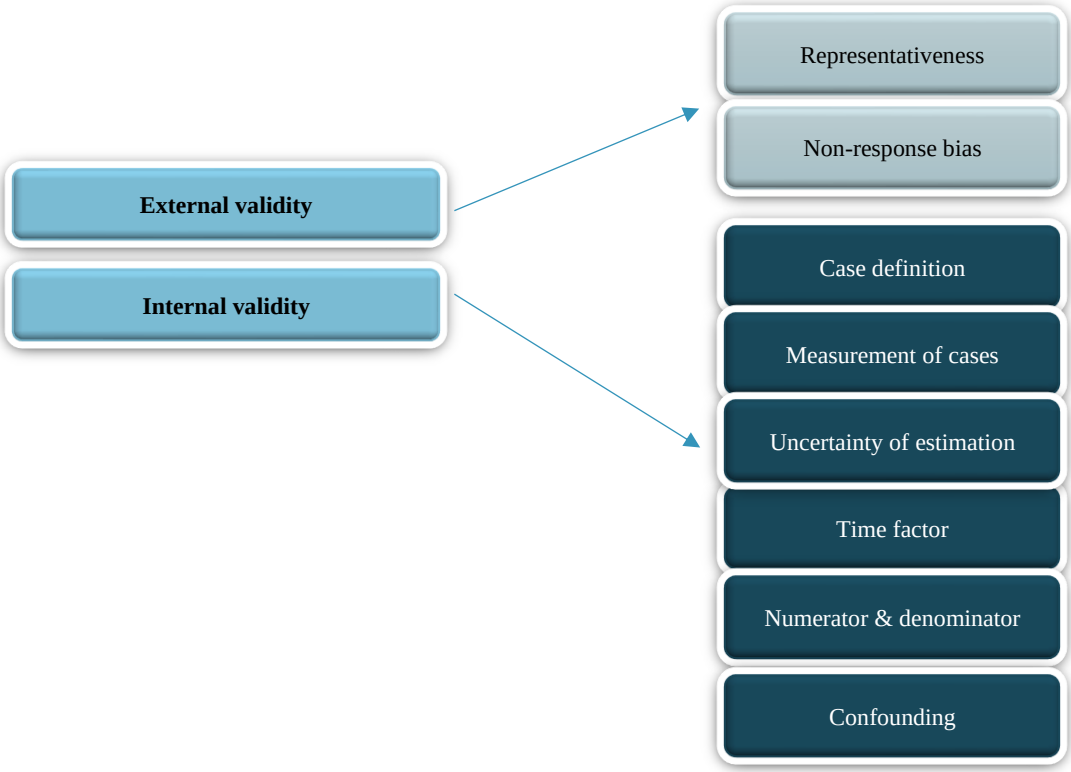
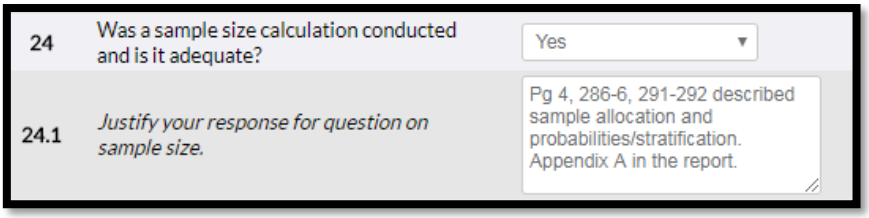


Figure 3-4: Risk-of-bias assessment section

3.3.2.1 Justification of responses to risk assessment

For transparency, justification boxes are provided to substantiate responses to questions on risk-of-bias assessment. The page number and direct quotes from the article being assessed can be copied and pasted in the boxes. Where the response is No or Not reported this should be stated.



HIV prevalence from a national household survey (i.e. a population-based survey) — The South African National HIV Prevalence, HIV Incidence, Behaviour and Communication Survey, 2005 by Shisana *et al* (2005)— is used as an example to illustrate how the risk-of-bias assessment is conducted in the BODRevMan system.

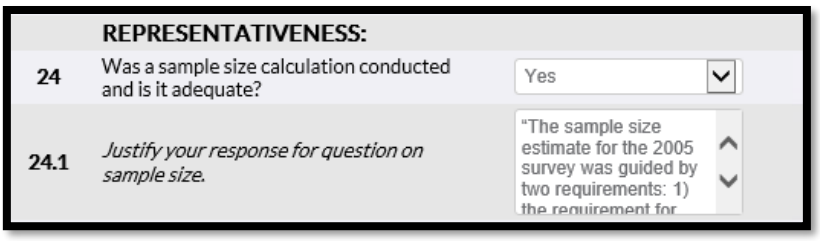
3.3.2.2 External validity

Representativeness

The sampling method used to identify the target population and strategy employed to select the study sample is assessed for representativeness. To enable adequate representation and true inference to the population from where the sample was drawn, sample-size calculation and adequacy are noted. If a sample-size calculation was conducted including the expected uncertainty around the estimate of interest, score Yes, if it is stated that a sample-size calculation was not done score No and if there is no report on a sample-size calculation then score Not reported.

Box 1: Sample-size calculation

"The sample size estimate for the 2005 survey was guided by two requirements: 1) the requirement for measuring change over time, that is, to be able to detect a change in HIV prevalence of 5 percentage points in each of the main reporting domains – gender, age group, race, locality type, and province (5% level of significance, 80% power, two-sided test); and, 2) the requirement of an acceptable precision of estimates per reporting domain – that is, to be able to estimate HIV prevalence in each of the main reporting domains with a precision level of less than ± 4%, which is equivalent to the expected width of the 95% confidence interval (z – score at the 95% level for two-sided test). A design effect of 2 was assumed. The total sample size required for the 2005 survey was the combination of the sample sizes needed for each reporting domain and also taking into account the sampling design and the expected response rate for HIV in a given reporting domain."



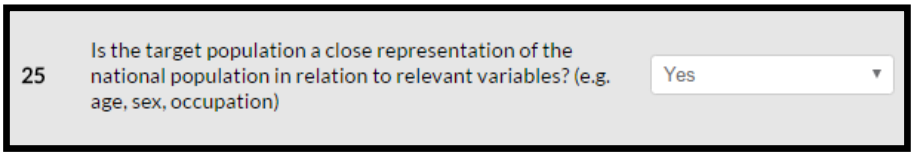
Information on the definition of the target population of interest and whether they are nationally representative is reported in the methods section.

Box 2: Representativity of target population to national population

"The survey sample was inclusive of persons of all ages living in South African households and hostels."

"In the final step, the information at the individual level was integrated and the final sampling weight for each data record was calculated. This weight was equal to the final VP sampling weights multiplied by the selected person's sampling weight per VP per age group. This process produced a final sample representative of the population in South Africa for gender, age, race, locality type and province."

"The socio-demographic characteristics of the weighted sample closely match those of the population estimates in terms of sex, race, and province; less than 1% difference is seen between the sample and the population census. The percentage of those aged 2–14 in the weighted sample is less than that of the population estimates because children younger than 2 were excluded from the survey. These results suggest that the sample is representative of the population from which it was drawn."

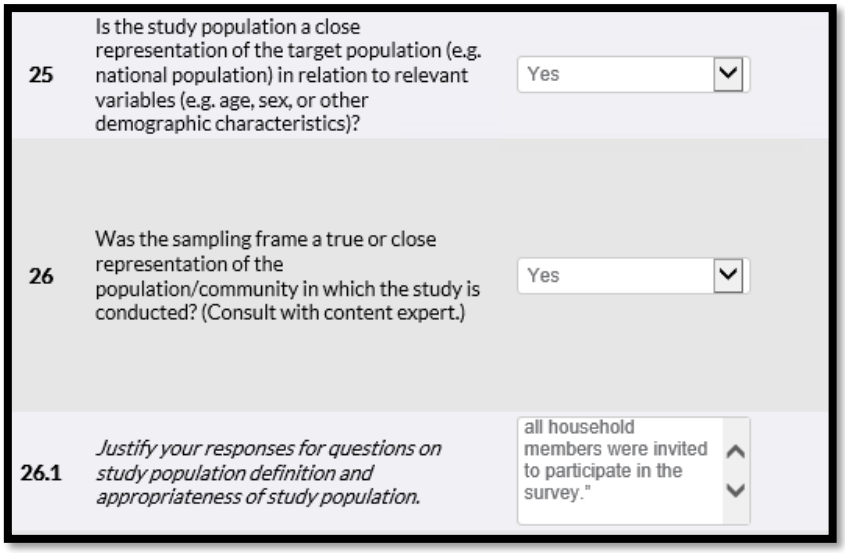


The sampling frame is the list of the items including people forming a population from which a sample is drawn.

Box 3: Sampling frame

"As in 2002, the sampling frame for the 2005 survey was based on a master sample consisting of 1000 enumerator areas (EAs) used by Statistics South Africa (Stats SA) for the 2001 census. The sample was explicitly stratified by province and locality type of the EAs. Locality types were urban formal, urban informal, rural formal (including commercial farms) and rural informal. In the formal urban locality types, race was also used as a third stratification variable (based on the dominant race group in the selected EA)."

"The survey sample was inclusive of persons of all ages living in South African households and hostels. In selected households/hostels, all household members were invited to participate in the survey."

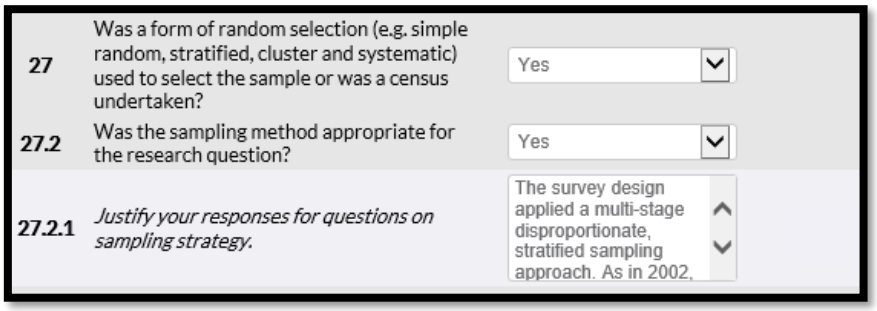


The article/study can report the sampling strategy employed in the study, i.e. if a form of random selection such as simple random, stratified, cluster and/or systematic sampling is used, or if another sampling strategy such as non-random, consecutive, convenient or case-by-case sampling was used to select study participants. This should be described and the

appropriateness of the sampling strategy to the research question should be assessed. Sampling strategies using random selection are regarded as the gold standard.

Box 4: Sampling strategy

"The survey design applied a multi-stage disproportionate, stratified sampling approach. As in 2002, the sampling frame for the 2005 survey was based on a master sample consisting of 1 000 enumerator areas (EAs) used by Statistics South Africa (Stats SA) for the 2001 census. The sample was explicitly stratified by province and locality type of the EAs. Locality types were urban formal, urban informal, rural formal (including commercial farms) and rural informal. In the urban formal areas, race was also used as a third stratification variable (based on the dominant race group in the selected EA). The master sample therefore allowed for reporting of results at the level of province, type of locality, age and race group. The primary sampling unit (PSU) was the EA, the secondary sampling unit (SSU) was the visiting point (VP) or household, and the ultimate sampling unit (USU) was the individual eligible to be selected for the survey. Three persons in each household could potentially be selected, with only one from each of the following age groups: 2–14 years, 15–24 years, and 25 years and older. Fieldworkers enumerated household members, using a random number generator to select the respondent and then proceeded with the interview. The selection procedure was carefully monitored to ensure that fieldworkers followed the sampling protocol and did not bias selection in favour of those present in the house at the time."



Furthermore, the reviewer can assess whether the sampling strategy was adequate for the research question. Answering this question is straightforward in the case of population-based surveys that estimate national HIV prevalence using a multi-stage disproportionate, stratified sampling approach with randomisation at the individual level. However, this is not always the case. The epidemiologist on the review team should be consulted for clarity on how to answer this question.

Non-response bias

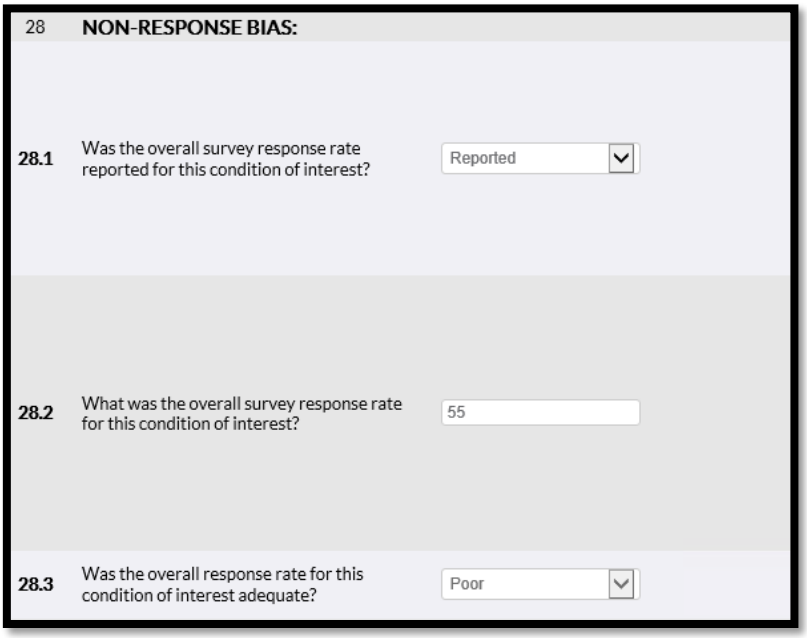
There is more than one level of response in a national household survey; the household response, the individual response and the variable/item/testing response. The household response rate reflects the percentage of households that agreed to participate in the survey from all those households that were potentially eligible. Similarly, the individual interview response rate reflects the percentage of individuals who were interviewed from those who were potentially eligible in each household. Finally, the variable/item/testing response rate is the

number of individuals who answered the questions that were relevant to their condition of interest or were tested for the condition of interest, from those who were interviewed in the survey. The household, individual and variable/item/testing response rates are used to determine the overall response rate for the survey (see formula below).

Overall response rate for the survey= household response rate X individual response rate X variable/item/testing

Box 5: Response rates

"Non-response may occur at the household level. Household non-response relates directly to HIV testing non-response. If the household interview is not completed, HIV testing will not occur. The household response rate is found by dividing the number of households/valid VPs with completed interviews by the number of occupied households/valid VPs. Of 13 422 households (VPs) sampled, 12 581 were valid VPs. Invalid VPs consisted of 473 derelict buildings, and 368 households were clearly abandoned. Of the valid 12 581 households/VPs, 10 584 (84.1%) were interviewed. Thus the household response rate for the 2005 survey is 84.1%. In the 10 584 valid VPs that agreed to participate in the survey, 24 236 individuals (maximum three per household) were eligible for interviews and 23 275 (96.0%) completed the interview. Of the 24 236 eligible individuals, 15 851 (65.4%) agreed to HIV testing and were anonymously linked to the behavioural interviews. The categories of non-response were: 7424 (30.6%) interviewed but refused HIV testing; 359 (1.5%) refused both interview and HIV testing; 602 (2.5%) absent from the household or missing data. Thus the overall response rate for HIV testing in the 2005 survey was 55%. The overall response rate is the product of the household response rate and the individual response rate for HIV testing (84.1% X 65.4% = 55%)."



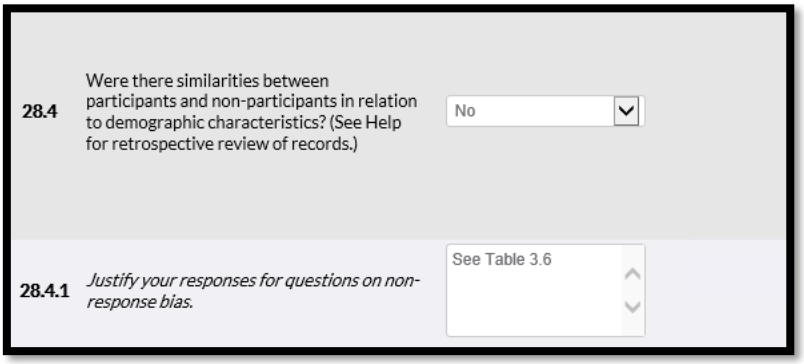
The overall response rate is captured in Question 28.2. The overall variable/item/testing response rate is captured on the Study Types page.

Bias is also introduced when there are significant differences between those who agree to participate in a study and provide information for the variable of interest and those who refuse.

Box 6: Differences between those who agreed to be tested and those who refused

Table 3.6: HIV risk-associated characteristics among respondents aged 15 years and older who were interviewed and tested compared with those who were interviewed but refused HIV testing, South Africa 2005

	Interviewed and tested for HIV		Interviewed but not tested for HIV		Level of significance
	n	%	n	%	
Sex					
Males	4 529	37.6	1 809	41.5	p= 0.003
Females	7 503	62.4	2 554	58.5	p= 0.029
Total	12 032	100.0	4 363	100.0	
Marital status					
Single	5 560	47.0	1 980	46.3	p= 0.663
Married or cohabit	4 773	40.3	1 781	41.7	p= 0.319
Widowed	974	8.2	319	7.5	p= 0.145
Divorced (not married)	530	4.5	194	4.5	p= 0.873
Total	11 837	100.0	4 274	100.0	



Alternatively, in cohort studies, participant loss to follow-up can result in bias. There is no universal consensus for acceptable follow-up rates but a cut-off of 50-80% is considered adequate (Fewtrell, 2013; Kristman, 2004). Furthermore, a loss to follow-up of ≥ 20% is considered a serious threat to validity (although these cut-offs have not been tested) (Fewtrell, 2013; Kristman, 2004).

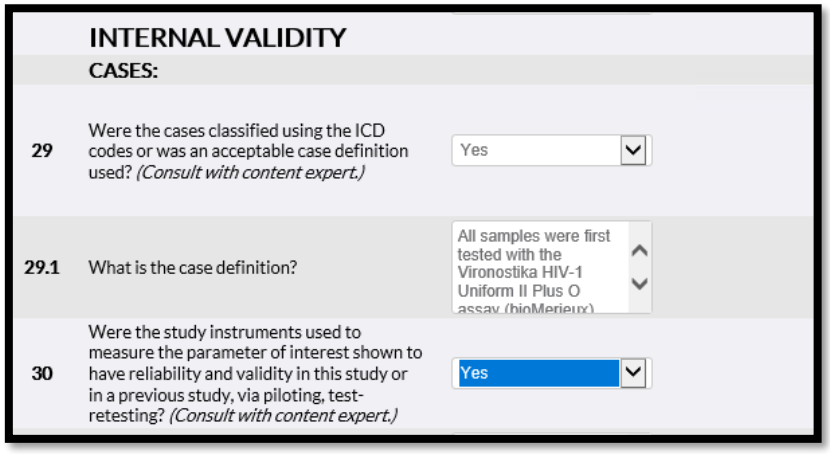
For the purposes of the burden of disease systematic reviews, the follow-up of participants is deemed adequate if there is a loss to follow-up of < 20% for the overall study. If loss to follow-up was not reported or ≥ 20%, it is deemed not adequate (Appendix A).

3.3.2.3 Internal validity

Capturing details on the case definition of the condition of interest and the method used to measure the parameter of interest are required to confirm that the study is reporting relevant information, and is a key comparison when pooling information for the parameter of interest from different studies.

Box 7: Case definition and measurement of cases

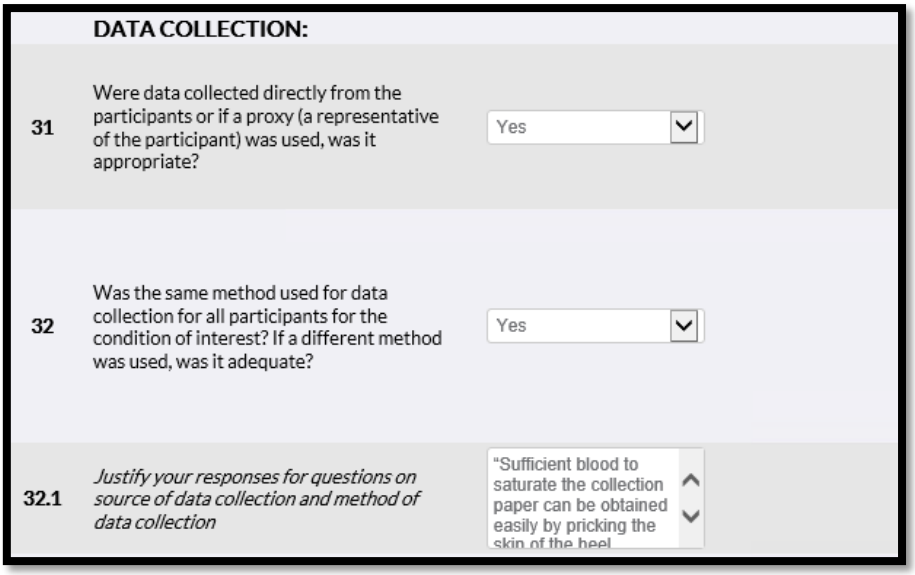
"All samples were first tested with the Vironostika HIV-1 Uniform II Plus O assay (bioMerieux). All HIV-positive samples were retested with a second ELISA test (Vitros ECI, Ortho Clinical Diagnostics). A second test was also conducted for 10% of cases where the first test was negative. Any samples testing positive on ELISA test 1 and negative on ELISA test 2 (producing discordant results) were supposed to be submitted to a third ELISA test (Biorad HIV 1 +2) for final interpretation of discordant samples. However, no discordant samples were identified during the testing procedure."



The manner in which data are collected, be it by questionnaire or by performing a test, should be the same for all participants. However, in population-based surveys, parents are used as proxies for answering questions for young children and blood samples can be collected using the heel of a child <18 months instead of a finger prick as is done with the older participants. Both are regarded as appropriate methods of data collection.

Box 8: Data collection

"Sufficient blood to saturate the collection paper can be obtained easily by pricking the skin of the heel, finger, or ear, thereby eliminating the need for venipuncture. Whole blood obtained by finger prick was spotted onto each of the five circles of the Guthrie card, spotting approximately 50 microlitre of blood per circle."

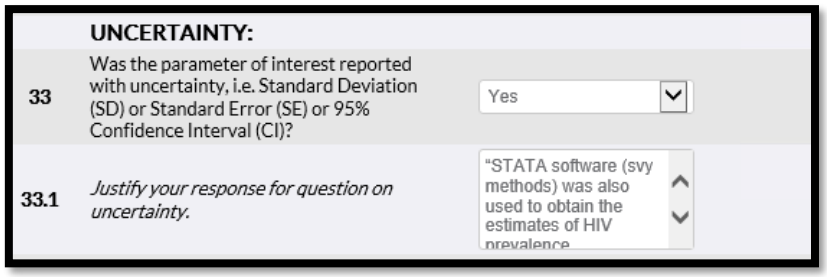


	DATA COLLECTION:	
31	Were data collected directly from the participants or if a proxy (a representative of the participant) was used, was it appropriate?	Yes
32	Was the same method used for data collection for all participants for the condition of interest? If a different method was used, was it adequate?	Yes
32.1	*Justify your responses for questions on source of data collection and method of data collection*	"Sufficient blood to saturate the collection paper can be obtained easily by pricking the skin of the heel

The uncertainty around a parameter indicates how far the estimate might be from the true value. For population-based surveys, a confidence interval is used to measure uncertainty. It is calculated using a model of how sampling, interviewing and measuring contribute to uncertainty about the relationship between the true value of the quantity we are estimating and our estimate of that value.

Box 9: Uncertainty

"STATA software (svy methods) was also used to obtain the estimates of HIV prevalence, significance values (p-values) and confidence intervals (95% CI) that take into account the complex design and individual sample weights."



	UNCERTAINTY:	
33	Was the parameter of interest reported with uncertainty, i.e. Standard Deviation (SD) or Standard Error (SE) or 95% Confidence Interval (CI)?	Yes
33.1	*Justify your response for question on uncertainty.*	"STATA software (svy methods) was also used to obtain the estimates of HIV prevalence

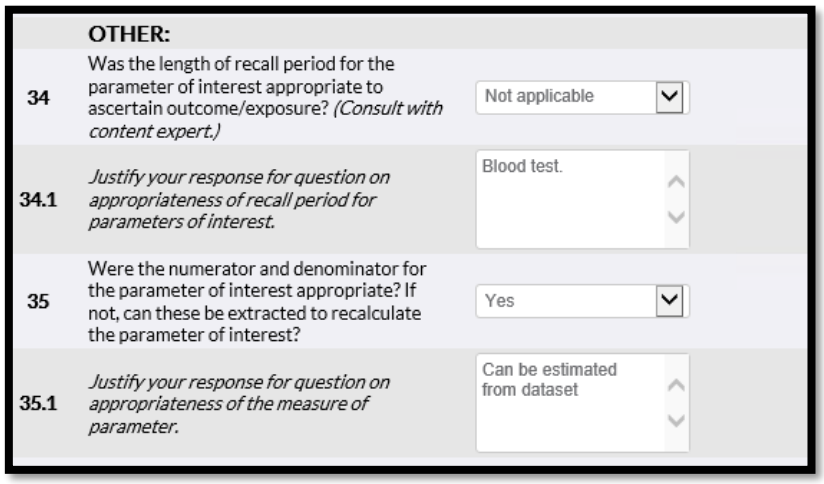
Other information deemed important about the type of information collected and how it was analysed was also assessed. These are whether the length of recall period for the parameter of interest is appropriate to ascertain outcome/exposure? Were the numerator and denominator for the parameter of interest appropriate? If not, can these be extracted to recalculate the

parameter of interest and, were potential confounding factors sought and controlled for in the analysis for odds ratios/relative risks/hazard ratios?

Box 10: Length of recall period and appropriateness of numerator and denominator

"The recall period is important for certain types of self-reported information for particular conditions and if too long may result in recall bias, e.g. time spent sick with an acute illness. As this varies for different types of information, consult with the content expert on the review team for guidance on answering this question. This question is :"Not applicable" for laboratory determined HIV prevalence."

"In some studies, the numerator and denominator used to generate the parameter of interest may not yield the information required for the review. In articles/studies where this is true the reviewer can: i) recalculate the parameter of interest if the correct numerator and/or denominator is reported, ii) contact the author of the article for the information, iii) exclude the article if the information required cannot be obtained."



Confounders are variables associated with both the dependent and independent variables, in a way that influences some or all of the correlation between these variables. Odds/relative ratios, risks/hazard ratios are parameters impacted by confounders, therefore, identifying potential confounders and adjusting for these in the analysis is important to remove their influence. The system has been programmed to only allow the reviewer to answer this question when one of the listed parameters is selected on the Inclusion of Parameters page. Furthermore, when more than one of the parameters of interest are reported in an article/study and if any or all have been adjusted for confounding, then select Yes.

3.3.3 Bypassing the risk-of-bias assessment

Currently, certain study types will not undergo a risk-of-bias assessment as tools to evaluate them are not available. This includes data from grey literature, modelled data, and routine health information systems.

These study types will skip the Risk Assessment and move straight to the Data Extraction section. Some observational studies may also have limited information about data quality, data-collection methods and sampling. The reviewer can still include these data, by selecting the Data not assessed option as the *study type*. Selecting this option will also skip the risk-of-bias assessment. Please note that the Data not assessed option can only be selected if it has been discussed with the Principal Investigator and co-reviewer.

3.4 Data extraction

A Data Extraction page is dynamically generated to provide grids to capture information relevant for each parameter of interest. Data extraction can only be done for parameters selected on the Eligibility Assessment - Inclusion Criteria page. These are prevalence, incidence, case-fatality rate, relative risk, odds ratio, hazard ratio, mean, incidence ratio, severity, duration and remission. Many articles/studies will be excluded before the Data Extraction section due to (a) not meeting the inclusion criteria or (b) having biases that may compromise the data. Data-extraction questions were designed according to the information that would be needed to estimate the burden of disease. The following information is extracted from the article/study for all the parameters of interest excluding severity (which is addressed separately); the unit of measure for the parameter of interest, reported measure of uncertainty, and the total number of participants (see Table 3-2).

Table 3-2: Data extraction overview

Domain		Selected Variables/ information	Notes
Choose parameter		Parameter (prevalence, incidence, etc.)	Parameters will appear based on what was chosen on the Inclusion Parameters page. You may choose more than one parameter.
Unit of measure		Unit of measure (%, per 100 000)	This question reduces manual typing as you only need to confirm in what unit the parameter is being reported once.
Measure of uncertainty		Measure of uncertainty (options)	A measure of uncertainty should be reported with the unit of measure for a parameter. If more than one uncertainty measure is available, the reviewer must choose the best unit of measure.
Population numbers		Number of participants	The total sample size for the population reported in the article/study is captured, i.e. for males and/or females and/or persons separately.
Data grids as per parameter	Data grid for prevalence, incidence, duration, remission, mean, case-fatality rate and incidence ratio	Description of disease or injury, description of the parameter, age-bands, age-band units, number of participants in age-band, measure of parameter, uncertainty estimate.	Data will be recorded in the grid.
	Data grid for odds ratio, relative risk, hazard ratio	All the above mentioned information including exposure, reference group, outcome and description of outcome/exposure.	Data will be recorded in the grid.
	Data grid for severity	Report on whether severity was measured clinically or via laboratory testing or some other method.	Data will be recorded in the textbox.

The information captured in the data grid for the various parameters does differ. For example, for the odds ratio, the data grid is expanded to capture information on exposure, reference group and outcome, as well as a description of the outcome and exposure. For definitions of these

terms see page ix. Using smoking as an example, the exposure can be tobacco smoke; the reference group can be current smokers and/or ever smokers and/or former smokers; the outcome can be lung cancer; and, the description of the outcome/exposure can be for outcome C34 (ICD-10) and, for exposure, those who stopped smoking tobacco five years ago. These descriptions will be completed as reported in the article/study.

The BODRevMan system has been designed to import data from an Excel sheet template, into the Data Extraction grids. Data can also be exported from the grid into an Excel template.

As there is no standard way to report severity, a unique data grid has been designed for this parameter which allows the reviewer to capture information on how severity was measured (i.e. clinically, laboratory-based or some other method) and a text box can be completed to report how the levels of severity were defined.

4 Enabling independent review and subsequent comparison of an article/study

The BODRevMan system has been designed to accommodate independent review of an article/study by two reviewers simultaneously. This is to ensure transparency and minimise human error. Therefore, for each article/study, two Study Review Forms are completed. To facilitate the independent review process, the system is equipped to program the review process into three stages namely Stage 0, Stage 1 and Stage 2 as described in Table 4-1.

Table 4-1: Stages in BODRevMan

Stage	Description
Stage 0: Independent Review	Two reviewers begin to review an article/study independently.
Stage 1: Inter-observer variation	Both reviewers have independently completed the eligibility assessment, risk-of bias-assessment and data extraction for their article/study. Any differences are resolved through discussion.
Stage 2: Final Study Review	Edits are made following discussions between reviewers and the review process is completed.

The flow and stages of the review process are represented in Figure 4-1.

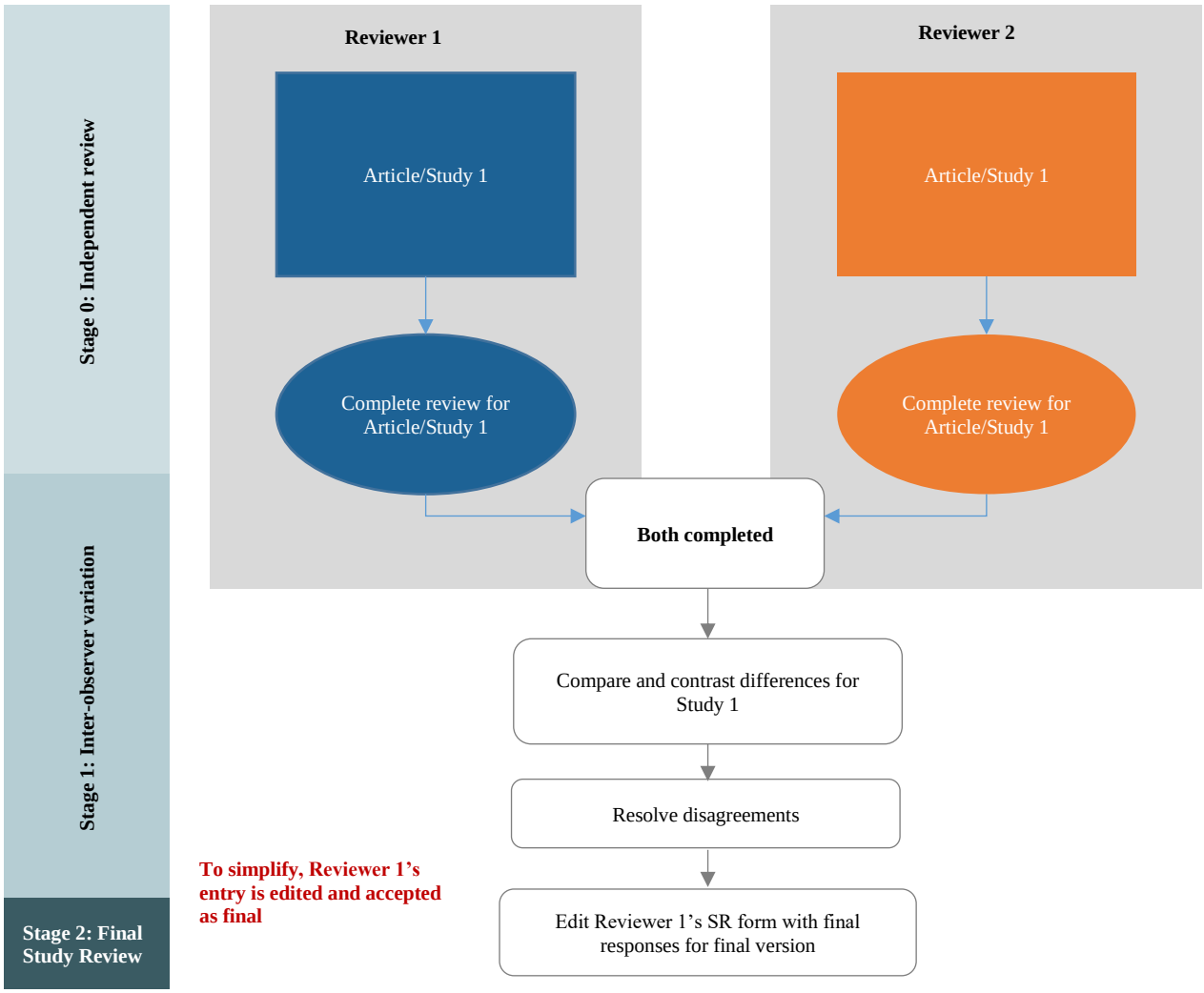


Figure 4-1: Description of stages in the review process

4.1 Independent review: Moving from Stage 0 to Stage 1

Once an article/study has been uploaded into BODRevMan against a reviewer's name that article/study for that reviewer is in Stage 0. The article/study remains in Stage 0 if the reviewer has started but is yet to complete the Study Review Form, or has completed the Study Review Form but did not press the "Finish" button. Once each reviewer completes the Study Review Form for a particular article/study, and clicks the Finish button, they move from Stage 0 to Stage 1. The Study Review Form can no longer be edited by either reviewer.

4.2 Inter-observer variation: Moving from Stage 1 to Stage 2

Once Reviewer 1 (R1) and Reviewer 2 (R2) have completed their reviews, BODRevMan enables inter-observer variation comparison by allowing the viewing of responses and data

extracted at a glance (Figure 4-2). Any differences identified should be discussed and resolved. If agreement cannot be reached, a third reviewer will be engaged to reach consensus. Any required edits are made in R1's Study Review Form.

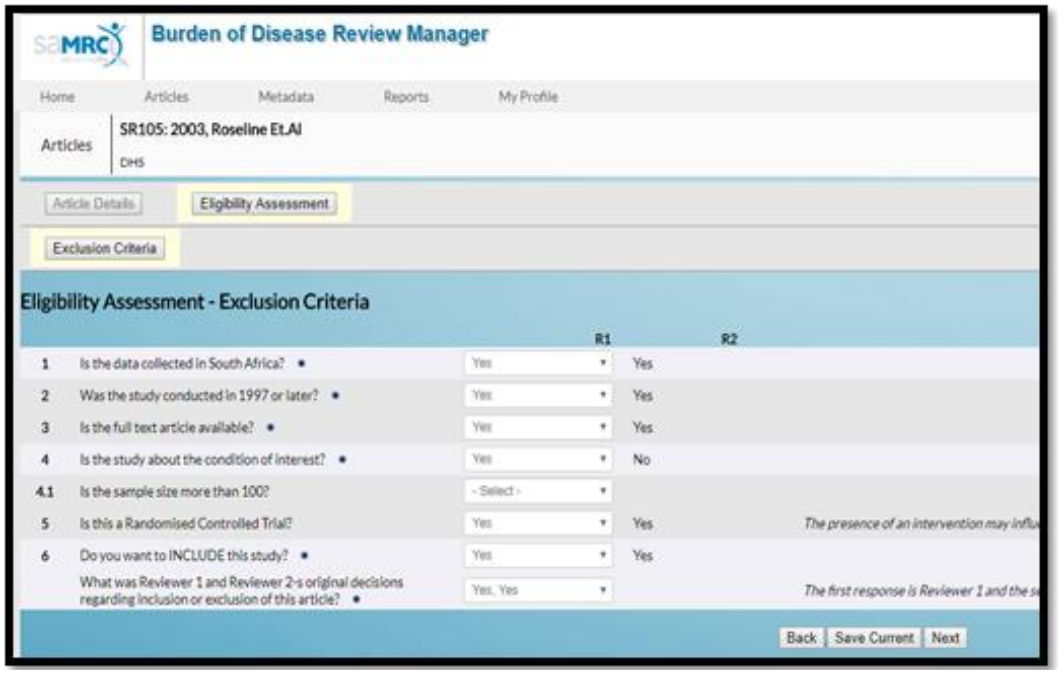


Figure 4-2: Inter-observer variation at a glance

4.3 Final Study Review Form: Stage 2

Once R1's Study Review Form, with R1 and R2's agreed responses, is completed, click the Finish button. The Study Review Form for that particular article/study moves from Stage 1 to Stage 2 and can no longer be edited by the reviewer.

4.4 Moving back a stage

In some instances, the reviewer may need to move back a stage to edit his/her responses. The Project Administrator can kick back the stages for a reviewer upon request.

4.5 Duplicate articles

Duplicate articles can be uploaded in error or intentionally. There are circumstances in which a reviewer may intentionally request a duplicate article(s) to be uploaded as a study reports on more than one risk factor/condition. The BODRevMan system can identify this type of duplicate where only the risk factor/condition differs.

For example, a national survey may report on alcohol use and tobacco use. If one article is uploaded and completed (e.g. for alcohol), some of the information from that article can be duplicated into the smoking SR. Reviewer 1 is notified on their dashboard that a particular study is a duplicate of another study. The reviewer is given the option of copying some of the information into the new SR. Clicking on the notification also copies the data for Reviewer 2. Both Reviewer 1 and 2 can edit the data as needed (Stage 0) and adapt it for their risk factor/condition.

5 Reports

The BODRevMan system generates several reports that capture and, in some instances, summarise the relevant information throughout the review and data-entry process. The report names and the stages in which they are available are given in Table 5-1.

Table 5-1: Overview of reports

Report name	Article/study specific or condition-specific	Available in Stage 0	Available in Stage 1	Available in Stage 2
Inter-observer Variation Report	Article/study	No	Yes	No
Risk assessment per Article report	Article/study	No	Yes	Yes
Condition Variance Report	Condition	No	No	Yes
Parameter per condition Report	Condition	No	No	Yes
All Variables Report	All articles/studies and all conditions	No	No	Yes

5.1 Inter-observer Variation Report

The Inter-observer Variation Report displays the questions where R1 and R2's responses differed at Stage 1. Once both reviewers have completed their independent review of an article/study, differences in the responses, i.e. inter-observer variation can be checked either by viewing the captured data in the system or downloading and viewing the inter-observer-variation report to resolve discrepancies. The aim of the report is to display the initial responses

entered into the BODRevMan system by the reviewers and does not reflect their final responses (Figure 5-1).

Interobserver Variation Report

SR74: 2014,Shisana O, Labadarios D, Rehle T, Simbayi L, Zuma K, Dhansay A, et al

South African National Health and Nutrition Examination Survey (SANHANES-1):2014

Section	QuestionNo	Question	Oluwatoyin	Eunice Turawa
Eligibility Assessment	4.1.1	State sample size (numeric value)	Not reported	16684
Additional Study Infor	10	Age range Start number	0	15
Additional Study Infor	12	Age range End number	35	65+
Study Types	21.2	What was the response rate for the variable of interest?		0
Study Types	21.2.1	Justify your response for the question on variable response rate.	Not reported	Not reported and not explicit to calculate
Risk of Bias Assessme	22	Is this study prospective or retrospective in terms of the data collection process?		Retrospective

Figure 5-1: Inter-observer Variation Report current

5.2 Risk Assessment per Article Report

The Risk Assessment per Article Report displays R1 and R2 response for Stage 1 and Stage 2 for the different criteria of the risk–of-bias scores.

Variance report for Risk of Bias Assessment scores per article with study type

Disease/Injury/Risk Factor: Tobacco Smoking

SR49: 2014,Human Sciences Research Council

South African Social Attitudes Survey, 2010 ddi-documentation

	Name	Study type	Study design	Sample size	Study population definition	Appropriateness of study population	Sampling strategy	Non response bias	Recognized case defintion	Actual case definition	Source of data collected	Mode of data collection	Uncertainty	Appropriateness of recall period	Appropriateness of measure of	Confoundings	Total Score
Reviewer 1 (Stage 1)	Pam Groenewald	Observational study	Population based survey	0	1	1	2	4	1	2	1	1	1	2	2	1	19
Reviewer 2 (Stage 1)	Oluwatoyin Austinen	Observational study	Population based survey	0	1	1	2	2	1	2	1	1	1	2	2	1	17
Difference (0-1)				0	0	0	0	2	0	0	0	0	0	0	0	0	2
Final (Stage 2)				0	1	1	2	4	1	2	1	1	1	2	2	1	19

	Name	Study type	Study design	Sample size	Study population definition and appropriateness of study population	Sampling strategy	Non response bias	Case defintion and instruments used to measure parameter of interest	Source of data collection and method of data collection	Uncertainty	Appropriateness of recall period	Appropriateness of measure of	Confounding
Reviewer 1 (Stage 1)	Pam Groenewald	Observational study	Population based survey	I cannot find a sample size calculation although there is description of the sample design including sampling frame	The sampling frame for the survey is the HSRC's second Master Sample, which was designed in 2007 and consists of 1000 primary sampling units (PSUs). The 2001 population census enumerator areas (EAs) were used as PSUs. Data documentation 2010 02, pg3.	Multistage stratified probability sampling. EA stratified by province, race and gender. The interviewer then selected one	028.2. HHRR and Ind RR: 88.9%; Item RR: 97.78% The weighting reflected the relative selection probabilities of the	Do you ever have you used any of the following tobacco products? Manufactured cigarettes; Roll-your-own cigarettes (Zol); Hubbly or hookah or water pipe; Cigar or pipe. In total, for how long did you ever have you been making regularly?	Questionnaires were administered to all participants	There can be estimated from the data	Questions on current smoking	Can be estimated from dataset	Not applicable
Reviewer 2 (Stage 1)	Oluwatoyin Austinen	Observational study	Population based survey	I cannot find a sample size calculation although there is description of the sample design including sampling frame	The sampling frame for the survey is the HSRC's second Master Sample, which was designed in 2007 and consists of 1000 primary sampling units (PSUs). The 2001 population census enumerator areas (EAs) were used as PSUs. These PSUs (EAs) were drawn, with probability proportional to size, from a sampling frame created by Professor David Stoker containing all 80,787 of the 2001 EAs. This sampling frame was the estimated number of	Multistage stratified probability sampling. Interviewers called at each visiting point selected from the Co-HSRC master sample and listed all those eligible for inclusion in the sample, i.e. all	Not reported	Similar to GATS	The questionnaire contained in SASAS questionnaire number 2010 were asked of a half sample of approximately 3500 respondents. Topics included in the questionnaire are: Environment (ISSP 2010), financial literacy, voting, respondent and household characteristics, personal and household income and other clarificatory variables. Data documentation 2010 02, pg1. Questionnaire 1 did not contain questions	There can be estimated from the data	Questions on current smoking	Can be estimated from dataset	Not applicable
Final (Stage 2)				I cannot find a sample size calculation although there is description of the sample design	The sampling frame for the survey is the HSRC's second Master Sample, which was designed in 2007 and consists of 1000 primary sampling units (PSUs). The 2001 population census enumerator areas (EAs)	Multistage stratified probability sampling. EA stratified by province, race and	028.2. HHRR and Ind RR: 88.9%; Item RR: 97.78% *SASAS 2011 Study	Do you ever have you used any of the following tobacco products? Manufactured cigarettes; Roll-your-own cigarettes (Zol); Hubbly or hookah or water pipe; Cigar or pipe.	Questionnaires were administered to all participants	There can be estimated from the data	Questions on current smoking	Can be estimated from dataset	Not applicable

Figure 5-2: Risk Assessment per Article Report

This report can be used to assess the concordance and discordance in the assessment of the risk-of-bias for a particular article/study (Figure 5-2). Reviewer 1 (Stage 1) and Reviewer 2 (Stage 1) refer to information at Stage 1 for each criterion of the risk-of-bias tool and the overall score is displayed for R1 and R2. Differences (0-1) refer to the difference between R1 and R2's Stage 1 scores. Ideally, this should be zero if no differences were observed. After

resolving differences, final (Stage 2) reports the agreed-upon scores by R1 and R2 for this particular article/study (Figure 5-2).

5.3 Condition Variance Report

This report summarises the variation between R1 and R2 responses for all articles/studies for the specific condition of interest being reviewed. Responses, including the original Stage 1 decision to either include or exclude an article at the end of both Exclusion and Inclusion criteria, and the Risk-of-bias Assessment page are captured. Furthermore, the variation among study designs, study types, the risk-assessment scores and whether data were extracted are also summarised. The Condition Variance Report can be used to assess the overall concordance and discordance for a specific condition at different stages of the review process (Figure 5-3).

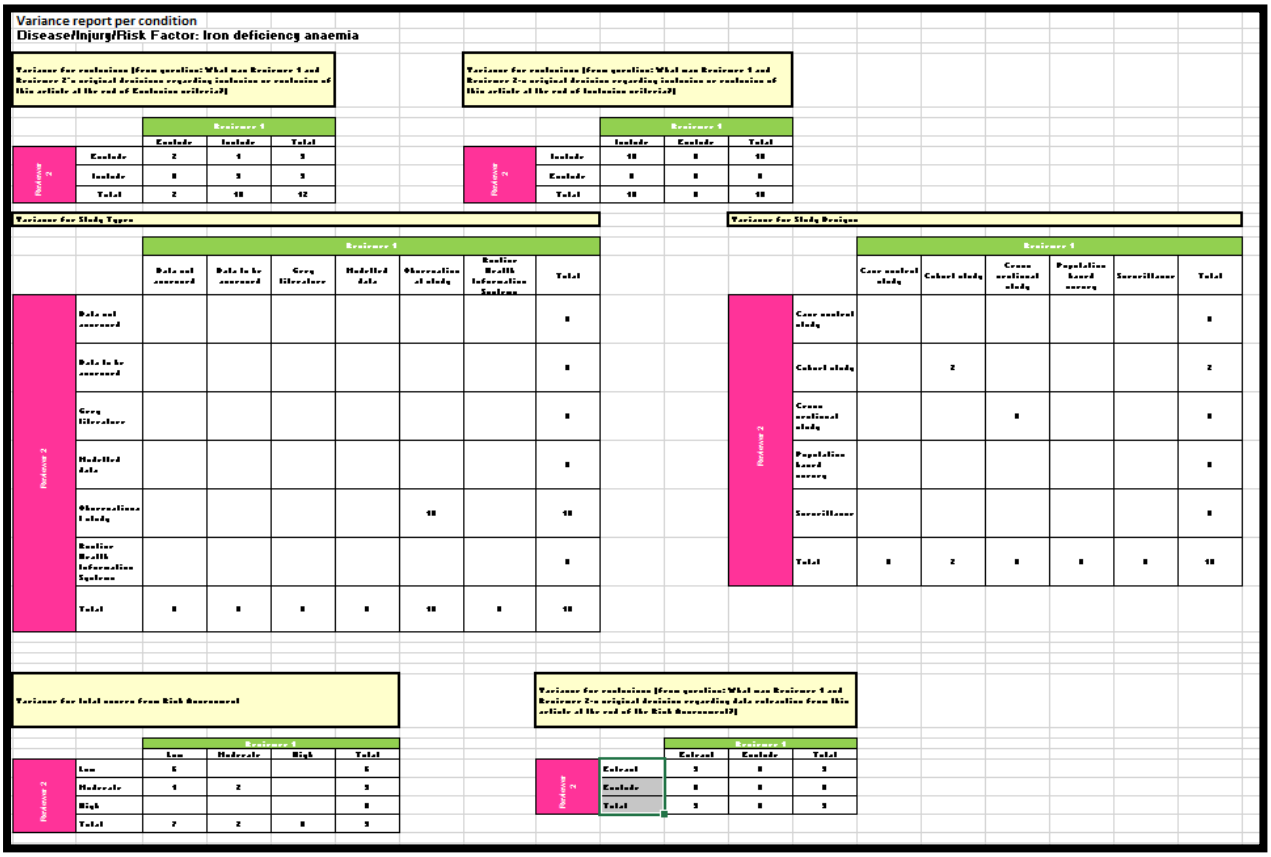
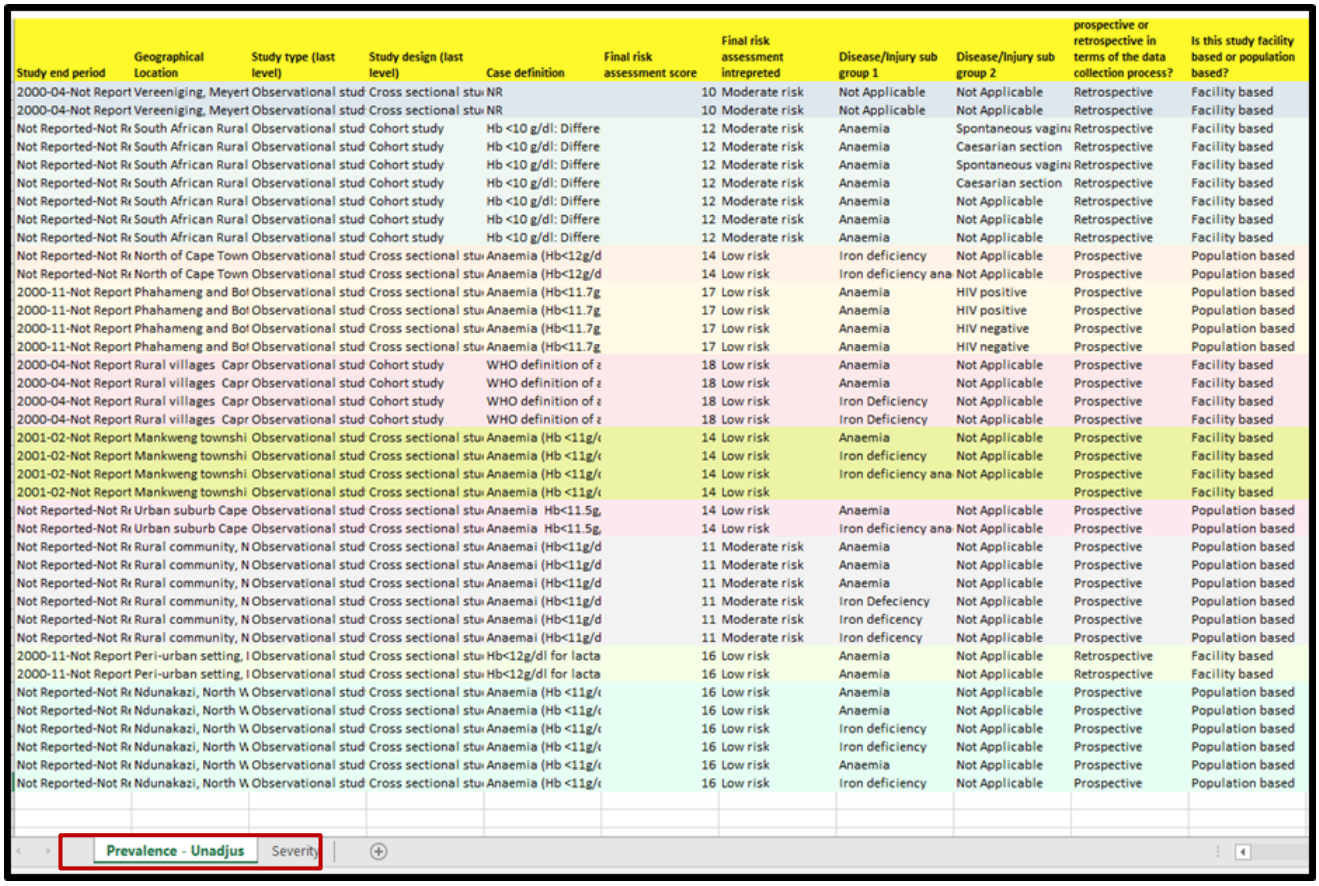


Figure 5-3: Condition Variance Report

5.4 Parameter Information per Condition Report

The Parameter Information per Condition Report provides an extract of the final information captured in the database by R1 in Stage 2 of the study review process and is the information that will be used for burden of disease estimation. Key information collected through the review

process, including those data in the data-extraction grid are available in this report. The information for a specific condition of interest will be presented in an Ms Excel workbook with each sheet reporting all the information for a specific parameter (Figure 5-4).



Study end period	Geographical Location	Study type (last level)	Study design (last level)	Case definition	Final risk assessment score	Final risk assessment intrepreted	Disease/Injury sub group 1	Disease/Injury sub group 2	prospective or retrospective in terms of the data collection process?	Is this study facility based or population based?
2000-04-Not Report	Vereeniging, Meyert	Observational stud	Cross sectional stu	NR	10	Moderate risk	Not Applicable	Not Applicable	Retrospective	Facility based
2000-04-Not Report	Vereeniging, Meyert	Observational stud	Cross sectional stu	NR	10	Moderate risk	Not Applicable	Not Applicable	Retrospective	Facility based
Not Reported-Not Re	South African Rural	Observational stud	Cohort study	Hb <10 g/dl: Differe	12	Moderate risk	Anaemia	Spontaneous vagin	Retrospective	Facility based
Not Reported-Not Re	South African Rural	Observational stud	Cohort study	Hb <10 g/dl: Differe	12	Moderate risk	Anaemia	Caesarian section	Retrospective	Facility based
Not Reported-Not Re	South African Rural	Observational stud	Cohort study	Hb <10 g/dl: Differe	12	Moderate risk	Anaemia	Spontaneous vagin	Retrospective	Facility based
Not Reported-Not Re	South African Rural	Observational stud	Cohort study	Hb <10 g/dl: Differe	12	Moderate risk	Anaemia	Caesarian section	Retrospective	Facility based
Not Reported-Not Re	South African Rural	Observational stud	Cohort study	Hb <10 g/dl: Differe	12	Moderate risk	Anaemia	Not Applicable	Retrospective	Facility based
Not Reported-Not Re	South African Rural	Observational stud	Cohort study	Hb <10 g/dl: Differe	12	Moderate risk	Anaemia	Not Applicable	Retrospective	Facility based
Not Reported-Not Re	South African Rural	Observational stud	Cohort study	Hb <10 g/dl: Differe	12	Moderate risk	Anaemia	Not Applicable	Retrospective	Facility based
Not Reported-Not Re	North of Cape Town	Observational stud	Cross sectional stu	Anaemia (Hb<12g/d	14	Low risk	Iron deficiency	Not Applicable	Prospective	Population based
Not Reported-Not Re	North of Cape Town	Observational stud	Cross sectional stu	Anaemia (Hb<12g/d	14	Low risk	Iron deficiency ana	Not Applicable	Prospective	Population based
2000-11-Not Report	Phahameng and Bot	Observational stud	Cross sectional stu	Anaemia (Hb<11.7g	17	Low risk	Anaemia	HIV positive	Prospective	Population based
2000-11-Not Report	Phahameng and Bot	Observational stud	Cross sectional stu	Anaemia (Hb<11.7g	17	Low risk	Anaemia	HIV positive	Prospective	Population based
2000-11-Not Report	Phahameng and Bot	Observational stud	Cross sectional stu	Anaemia (Hb<11.7g	17	Low risk	Anaemia	HIV negative	Prospective	Population based
2000-11-Not Report	Phahameng and Bot	Observational stud	Cross sectional stu	Anaemia (Hb<11.7g	17	Low risk	Anaemia	HIV negative	Prospective	Population based
2000-04-Not Report	Rural villages Capr	Observational stud	Cohort study	WHO definition of a	18	Low risk	Anaemia	Not Applicable	Prospective	Facility based
2000-04-Not Report	Rural villages Capr	Observational stud	Cohort study	WHO definition of a	18	Low risk	Anaemia	Not Applicable	Prospective	Facility based
2000-04-Not Report	Rural villages Capr	Observational stud	Cohort study	WHO definition of a	18	Low risk	Iron Deficiency	Not Applicable	Prospective	Facility based
2000-04-Not Report	Rural villages Capr	Observational stud	Cohort study	WHO definition of a	18	Low risk	Iron Deficiency	Not Applicable	Prospective	Facility based
2001-02-Not Report	Mankweng townshi	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	14	Low risk	Anaemia	Not Applicable	Prospective	Facility based
2001-02-Not Report	Mankweng townshi	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	14	Low risk	Iron deficiency	Not Applicable	Prospective	Facility based
2001-02-Not Report	Mankweng townshi	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	14	Low risk	Iron deficiency ana	Not Applicable	Prospective	Facility based
2001-02-Not Report	Mankweng townshi	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	14	Low risk			Prospective	Facility based
Not Reported-Not Re	Urban suburb Cape	Observational stud	Cross sectional stu	Anaemia Hb<11.5g,	14	Low risk	Anaemia	Not Applicable	Prospective	Population based
Not Reported-Not Re	Urban suburb Cape	Observational stud	Cross sectional stu	Anaemia Hb<11.5g,	14	Low risk	Iron deficiency ana	Not Applicable	Prospective	Population based
Not Reported-Not Re	Rural community, N	Observational stud	Cross sectional stu	Anaemai (Hb<11g/d	11	Moderate risk	Anaemia	Not Applicable	Prospective	Population based
Not Reported-Not Re	Rural community, N	Observational stud	Cross sectional stu	Anaemai (Hb<11g/d	11	Moderate risk	Anaemia	Not Applicable	Prospective	Population based
Not Reported-Not Re	Rural community, N	Observational stud	Cross sectional stu	Anaemai (Hb<11g/d	11	Moderate risk	Anaemia	Not Applicable	Prospective	Population based
Not Reported-Not Re	Rural community, N	Observational stud	Cross sectional stu	Anaemai (Hb<11g/d	11	Moderate risk	Iron Defeciency	Not Applicable	Prospective	Population based
Not Reported-Not Re	Rural community, N	Observational stud	Cross sectional stu	Anaemai (Hb<11g/d	11	Moderate risk	Iron deficency	Not Applicable	Prospective	Population based
Not Reported-Not Re	Rural community, N	Observational stud	Cross sectional stu	Anaemai (Hb<11g/d	11	Moderate risk	Iron deficency	Not Applicable	Prospective	Population based
2000-11-Not Report	Peri-urban setting, I	Observational stud	Cross sectional stu	Hb<12g/dl for lacta	16	Low risk	Anaemia	Not Applicable	Retrospective	Facility based
2000-11-Not Report	Peri-urban setting, I	Observational stud	Cross sectional stu	Hb<12g/dl for lacta	16	Low risk	Anaemia	Not Applicable	Retrospective	Facility based
Not Reported-Not Re	Ndunakazi, North W	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	16	Low risk	Anaemia	Not Applicable	Prospective	Population based
Not Reported-Not Re	Ndunakazi, North W	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	16	Low risk	Anaemia	Not Applicable	Prospective	Population based
Not Reported-Not Re	Ndunakazi, North W	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	16	Low risk	Iron deficiency	Not Applicable	Prospective	Population based
Not Reported-Not Re	Ndunakazi, North W	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	16	Low risk	Iron deficiency	Not Applicable	Prospective	Population based
Not Reported-Not Re	Ndunakazi, North W	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	16	Low risk	Anaemia	Not Applicable	Prospective	Population based
Not Reported-Not Re	Ndunakazi, North W	Observational stud	Cross sectional stu	Anaemia (Hb <11g/(	16	Low risk	Iron deficiency	Not Applicable	Prospective	Population based

Prevalence - Unadjus | Severity

Figure 5-4: Parameter Information per Condition Report

5.5 All Variables Report

The All Variables Report shows all the information entered into the database for all the articles/studies and conditions reviewed.

6 Metadata

The Metadata page has been created to track screening of articles/studies outside the BODRevMan system, and the screening and eligibility assessment, risk-of-bias assessment and the number of articles/studies that had data extracted for a specific condition of interest in the BODRevMan system.

Condition: Iron-deficiency anaemia

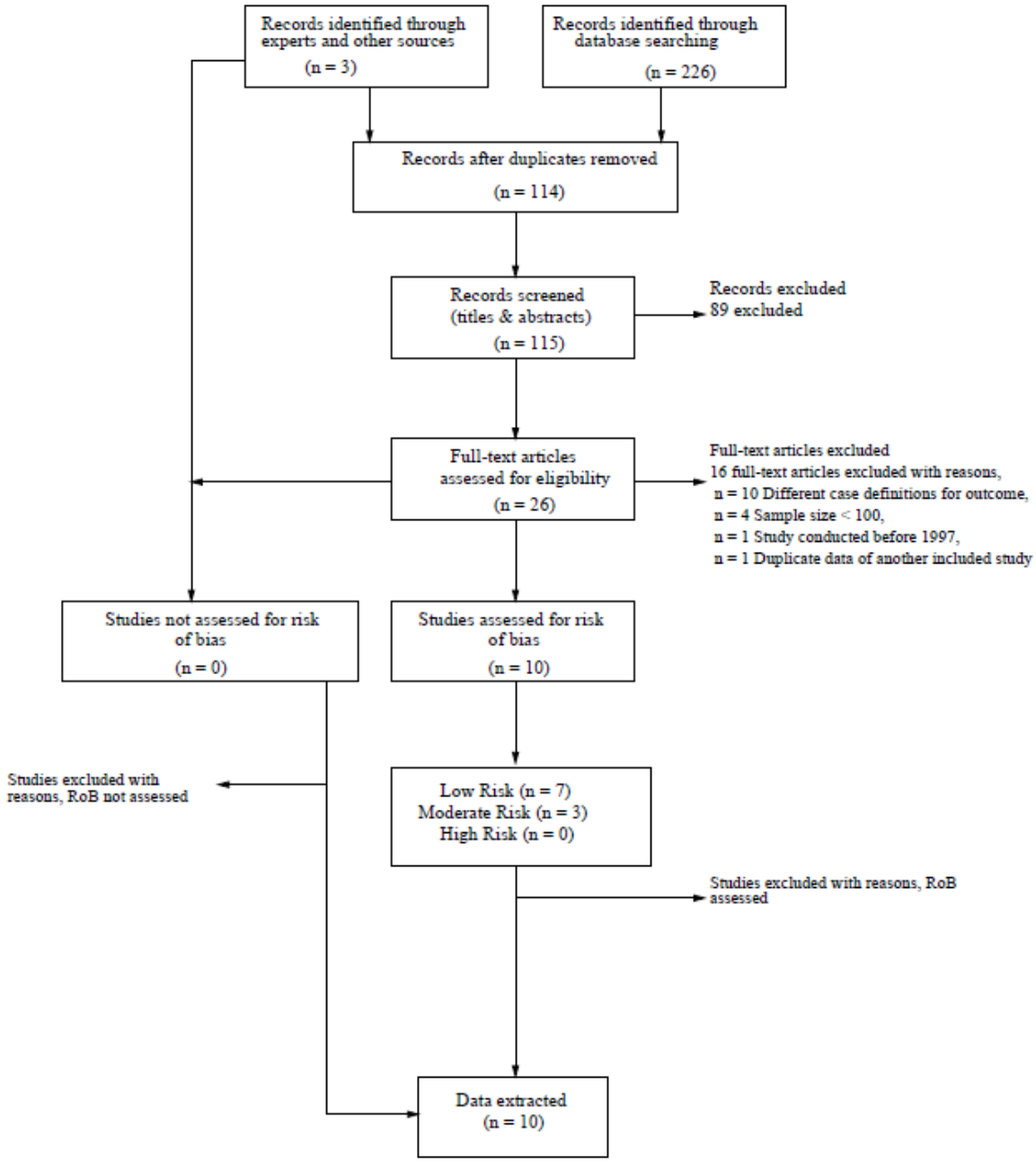


Figure 6-1: Metadata flow chart for iron-deficiency anaemia

A flow-chart reporting this information is displayed as an adapted PRISMA flow-chart (Moher et al., 2009) (Figure 6-1). The original PRISMA flow-chart can be viewed in Appendix F: PRISMA Flow Diagram.

7 Overall roles and responsibilities of BODRevMan users

The BODRevMan system has been set up for different types of users to facilitate the management of burden of disease studies, management of the BODRevMan system and the sharing of information with the necessary security measures. These are reviewers, non-reviewers and administrators (Table 7-1).

Table 7-1: Summary of roles and responsibilities of BODRevMan users

BOD Study Review Permission and Roles					
	Stage 0	**Stage 1**	**Stage 2**	**System**	**Notes**
Power User	Read Only	Read Only	Read Only	Read Only	Access to all but read only
Reviewer	Read /Write	Read /Write	Read Only	None	All reviewers
Guest External	None	None	Read Only	None	Visitor given permission by the PI and project administrator to view Stage 2 reviews only
Guest Reviewer	None	Read Only	Read Only	None	Internal reviewers Only
Project administrator	Read Only	Read Only	Read Only	Read/Write	PI and Administrator
System administrator	Read/Write	Read/Write	Read/Write	Read/Write	First-Line system supporters

7.1 Reviewers

All studies identified from the systematic literature searches for each condition (disease/injury or risk factor) will be uploaded onto the BODRevMan system and assigned to review pairs. The review pair will need to decide who will be assigned Reviewer 1 (main reviewer) and Reviewer 2 (co-reviewer). Reviewer 1 has additional responsibilities as described in Table 7-1. Although Reviewer 1 has more responsibilities, both reviewers need to assess all studies independently to reduce bias. The role of Guest Reviewer has been generated for individuals who are part of the study collaboration, not a reviewer for a specific condition, but would like to access the Study Review Form for studies within a specific condition. This can occur when the same article/study is part of the review for more than one condition. Both Stage 1 and Stage 2 information can be viewed.

7.2 Non-reviewers

The role of Power User has been created so that the Principal Investigators can access the information for any condition under review on the BODRevMan system. The role of Guest External has been generated to share information extracted for a specific condition with an individual who is not a part of the project team. Only Stage 2 information will be made available to Guest External users.

7.3 Administrators

There are two different administrator roles namely a Project Administrator and a Systems Administrator. The Project Administrator is responsible for uploading all identified studies for each condition onto the BODRevMan system and assisting with any system-related queries pertaining to the review process. This individual can also move the article/studies between stages, i.e. from Stage 2 to Stage 1 or Stage 0. The Systems Administrator is responsible for maintenance of the BODRevMan system and all programming and back-end system-related queries including providing support to the Project Administrator.

PART B

User Guide

1 Purpose of user guide

This section of the document is a user guide for BODRevMan. It illustrates the flow of the system, navigation, usability and process from the point of view of the end-user. The end-user should be able to use this guide as a point of reference for using the system or demonstrating the system for training purposes.

2 Understanding the user guide

The User Guide has been set up with screen grabs, red-bordered boxes, and tip boxes to assist with understanding what is being presented in each topic.

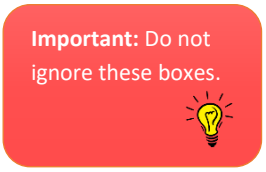
2.1 Emphasised elements

You will notice that the red-bordered boxes highlight an item referred to in the instruction.

2.2 Tip and important boxes

Tip boxes provide helpful tips that can assist in understanding special features and functionality.

Red boxes highlight very important tips that assist in understanding special features and functionality.



2.3 Pop-up boxes/dialogs

Always enable pop-up boxes for BODRevMan. You can enable them in your chrome browser for BODRevMan.

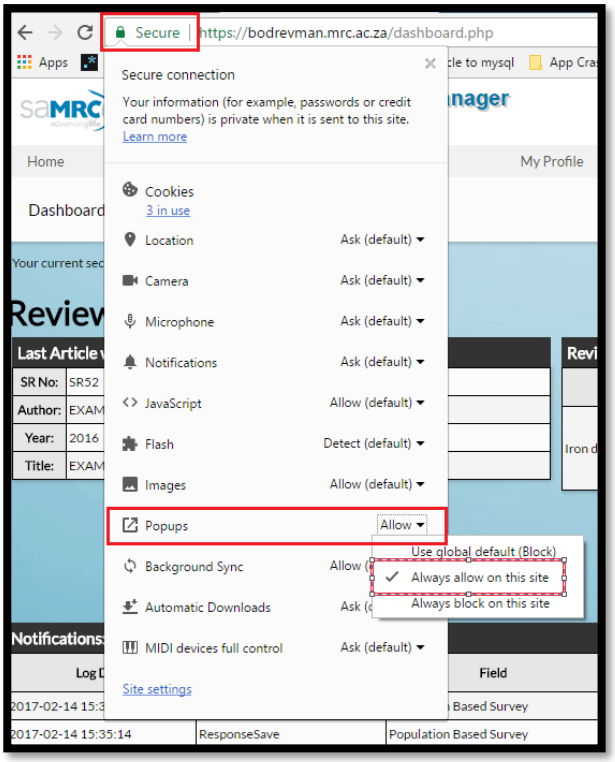


Figure 2-1: Allowing for pop-ups

3 BODRevMan overview

BODRevMan is a web-based system that enables the systematic review of public health research focusing on diseases, injuries and risk factors. The system includes a risk-of-bias tool for assessing the quality of articles reporting on surveillance, population-based, cross-sectional, cohort and case-control studies. BODRevMan manages the assessment of data quality and storage of information for multiple systematic reviews across different study designs and parameters. It also generates summary reports for the systematic review.

There are multiple user roles within the BODRevMan web-based system. These are Reviewer, Power User, Guest Reviewer and Project Administrator. This guide will focus primary on providing guidance for reviewers.

4 System requirements

4.1 Hardware requirements

- 1.6Ghz Core i3 Processor
- 4Gb RAM
- 500GB HDD
- LED screen

4.2 Software requirements

- Windows 8 or newer, MAC OS or Linux
- Google Chrome Web browser
- Microsoft Excel

4.3 Articles/studies for review

This section shows you how to prepare your data for import into BODRevMan. Uploading the articles/studies must be done with support from the Project Administrator.

4.3.1 Create a Condition-specific EndNote database

Reviewer 1 must create and maintain a condition-specific Endnote database to store studies identified in the systematic search. Backup copies of this database should be made regularly. See Table 4-1 for more information on the roles of Reviewer 1 and 2.

Table 4-1: Reviewer responsibilities

Reviewer 1	Reviewer 2
Agree on search terms	Agree on search terms
Conduct systematic search	
Create EndNote database to store search results	
Identify potential studies	Identify potential studies
Note number of studies at each stage	Note number of studies at each stage
Agree with Reviewer 2 about studies that must be sent to the Project Administrator	Agree with Reviewer 1 about studies that must be sent to the Project Administrator
Send predefined sheet to Project Administrator	
Update metadata sheet	
Complete all Study Review Forms	Complete all Study Review Forms
Resolve disagreements with Reviewer 2	Resolve disagreements with Reviewer 1
Update final Study Review Form	

4.3.2 Conduct search and store results in the condition-specific EndNote database

As set out in the condition-specific protocol, Reviewer 1 will conduct the literature search in identified databases (PubMed, EMBASE, Scopus, Web of Science, and African Index Medicus) and store all titles and abstracts in the Endnote database.

4.3.3 EndNote database

Once your EndNote database has been set up and contains all the results from your literature searches, record the total number of records in the database in the “Metadata” page which has

been created in BODRevMan to capture the screening process and decisions made during the review process. This page also automatically records the outcome of the risk-of-bias assessment and final inclusion/exclusion decisions for data extraction for the specific condition. This page displays a flow diagram that is similar to the PRISMA flow diagram. (see Section 12: Metadata).

4.3.3.1 Duplicates

Since several databases will be searched, your results are bound to have duplicate records. These can either be removed manually or by using the de-duplication function in EndNote (References/Find Duplicates). Record the number of duplicates in the Metadata page before deleting the duplicate records. Be sure to save a copy of your EndNote database at each step.

4.3.4 Screening

Screening of an article/study is done both within and outside BODRevMan.

4.3.4.1 Titles and abstracts

Once you have removed the duplicate records, a title and abstract screening should be conducted. If records are clearly not associated with your condition/risk factor, remove these files, and record the number of excluded records in the "Metadata" page.

4.3.4.2 Full-text screening

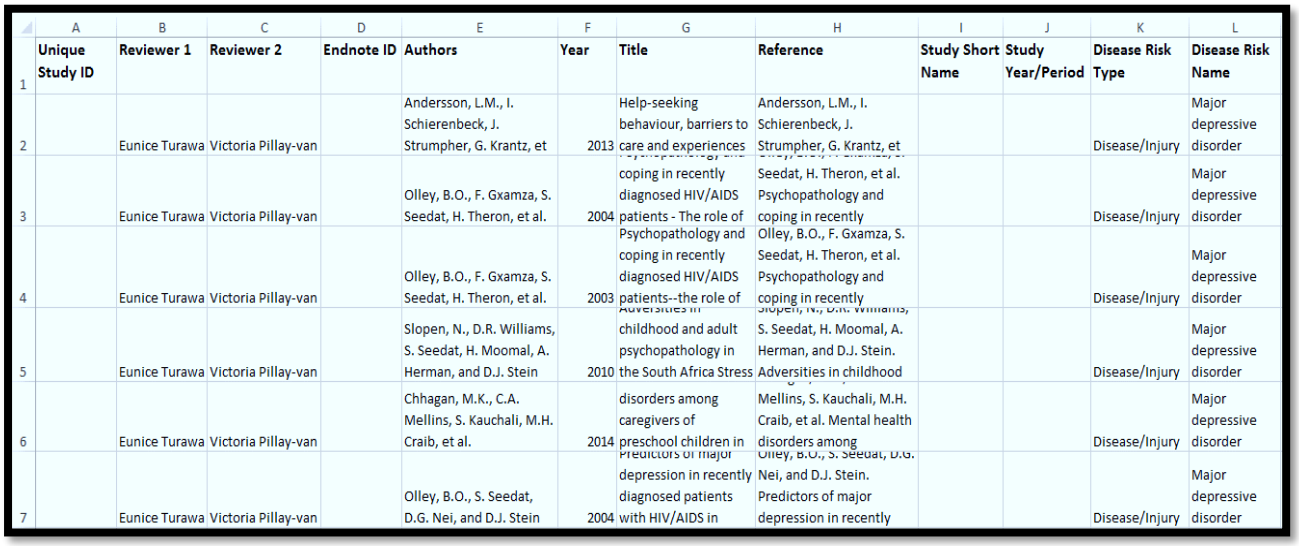
Obtain the full-text articles for the remaining records for screening. These will be uploaded into BODRevMan. At this stage, it is necessary to record the number of excluded records and reasons for exclusion in the "Metadata" page.

Tip: You can export the citations and related articles to an Excel file to more easily record the reasons for exclusion.

4.3.5 Exporting records from EndNote using a predefined sheet

Confirm that your reference style in EndNote is set to "Flagship BoDRU Review". If not, please consult the Project Administrator. This style is used to ensure that your records are exported in the correct format to BODRevMan. For full-text articles that need to be reviewed,

export the relevant citations to Excel. This is done by selecting records in EndNote and right-clicking “Copy Formatted” and then “Paste" to place the records into a predefined Excel spreadsheet.



	A	B	C	D	E	F	G	H	I	J	K	L
1	Unique Study ID	Reviewer 1	Reviewer 2	Endnote ID	Authors	Year	Title	Reference	Study Short Name	Study Year/Period	Disease Risk Type	Disease Risk Name
2		Eunice Turawa	Victoria Pillay-van		Andersson, L.M., I. Schierenbeck, J. Strumpher, G. Krantz, et	2013	Help-seeking behaviour, barriers to care and experiences	Andersson, L.M., I. Schierenbeck, J. Strumpher, G. Krantz, et			Disease/Injury	Major depressive disorder
3		Eunice Turawa	Victoria Pillay-van		Olley, B.O., F. Gxamza, S. Seedat, H. Theron, et al.	2004	coping in recently diagnosed HIV/AIDS patients - The role of	Seedat, H. Theron, et al. Psychopathology and coping in recently			Disease/Injury	Major depressive disorder
4		Eunice Turawa	Victoria Pillay-van		Olley, B.O., F. Gxamza, S. Seedat, H. Theron, et al.	2003	Psychopathology and coping in recently diagnosed HIV/AIDS patients--the role of	Olley, B.O., F. Gxamza, S. Seedat, H. Theron, et al. Psychopathology and coping in recently			Disease/Injury	Major depressive disorder
5		Eunice Turawa	Victoria Pillay-van		Slopen, N., D.R. Williams, S. Seedat, H. Moomal, A. Herman, and D.J. Stein	2010	childhood and adult psychopathology in the South Africa Stress	S. Seedat, H. Moomal, A. Herman, and D.J. Stein. Adversities in childhood			Disease/Injury	Major depressive disorder
6		Eunice Turawa	Victoria Pillay-van		Chhagan, M.K., C.A. Mellins, S. Kauchali, M.H. Craib, et al.	2014	disorders among caregivers of preschool children in	Mellins, S. Kauchali, M.H. Craib, et al. Mental health disorders among			Disease/Injury	Major depressive disorder
7		Eunice Turawa	Victoria Pillay-van		Olley, B.O., S. Seedat, D.G. Nei, and D.J. Stein	2004	depression in recently diagnosed patients with HIV/AIDS in	Olley, B.O., S. Seedat, D.G. Nei, and D.J. Stein. Predictors of major depression in recently			Disease/Injury	Major depressive disorder

Figure 4-1: Example of predefined sheet

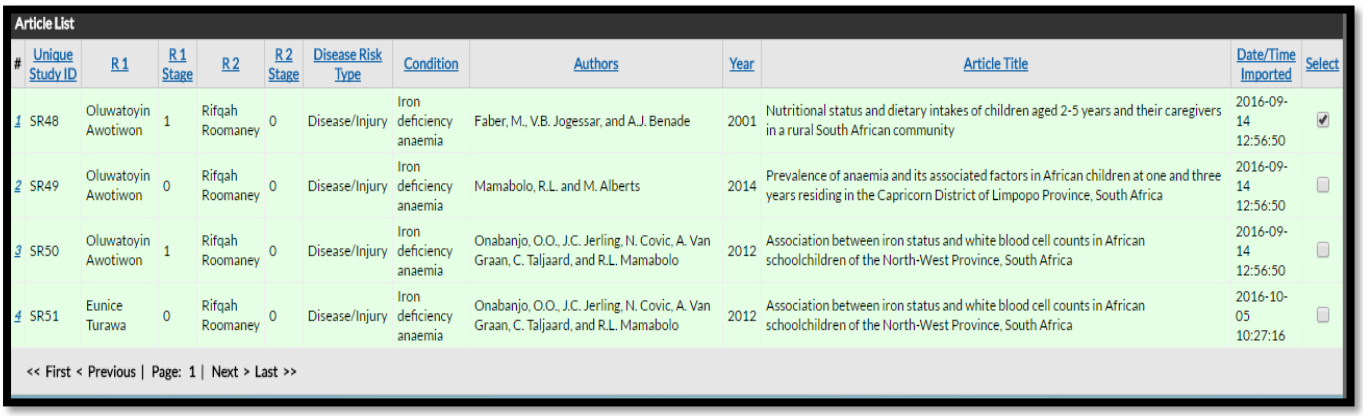
A pre-defined sheet is an Excel spreadsheet, which lists records that need to be sent to the Project Administrator to upload into the BODRevMan. A template will be provided by the Project Administrator.

Once Reviewer 1 has exported the citations to this sheet and filled in the other required information, this sheet can be e-mailed to the Project Administrator.

The columns in the predefined sheet should be completed as indicated below:

- “Unique Study ID” (Column A) should be left blank for the Project Administrator to complete.
- The names of “Reviewer 1” and “Reviewer 2” in (Columns B and C) should be completed by Reviewer 1. Please ensure that names are spelt correctly and reported consistently.
- The “EndNote ID”, “Authors”, “Year”, “Title” and “Reference” columns (Columns D-H) will be automatically completed if you have correctly “Copy Formatted” and “Pasted” the records from EndNote as described.
- “Short Study Name” and “Study/Year Period” (Column I and J) do not need to be completed if the information is not available or does not exist. If you do not have information for these columns, please leave the entries blank (do not delete them).

The column, “Disease Risk Type” (Column K), refers to the condition you are working on. If you are working on a disease (e.g. pneumonia), enter “Disease/Injury”. If you are working on a risk factor (e.g. BMI), select “Risk Factor”. Please ensure the spelling is correct. The column L, “Disease Risk Name”, refers to the name of the condition. Please ensure correct spelling.



Article List

#	Unique Study ID	R 1	R 1 Stage	R 2	R 2 Stage	Disease Risk Type	Condition	Authors	Year	Article Title	Date/Time Imported	Select
1	SR48	Oluwatoyin Awotiwon	1	Rifqah Roomaney	0	Disease/Injury	Iron deficiency anaemia	Faber, M., V.B. Jogessar, and A.J. Benade	2001	Nutritional status and dietary intakes of children aged 2-5 years and their caregivers in a rural South African community	2016-09-14 12:56:50	☑
2	SR49	Oluwatoyin Awotiwon	0	Rifqah Roomaney	0	Disease/Injury	Iron deficiency anaemia	Mamabolo, R.L. and M. Alberts	2014	Prevalence of anaemia and its associated factors in African children at one and three years residing in the Capricorn District of Limpopo Province, South Africa	2016-09-14 12:56:50	☐
3	SR50	Oluwatoyin Awotiwon	1	Rifqah Roomaney	0	Disease/Injury	Iron deficiency anaemia	Onabanjo, O.O., J.C. Jerling, N. Covic, A. Van Graan, C. Taljaard, and R.L. Mamabolo	2012	Association between iron status and white blood cell counts in African schoolchildren of the North-West Province, South Africa	2016-09-14 12:56:50	☐
4	SR51	Eunice Turawa	0	Rifqah Roomaney	0	Disease/Injury	Iron deficiency anaemia	Onabanjo, O.O., J.C. Jerling, N. Covic, A. Van Graan, C. Taljaard, and R.L. Mamabolo	2012	Association between iron status and white blood cell counts in African schoolchildren of the North-West Province, South Africa	2016-10-05 10:27:16	☐

<< First < Previous | Page: 1 | Next > Last >>

Figure 4-2: Example of Articles page

5 Accessing BODRevMan

BODRevMan is accessible from all major browsers, however, it is highly recommended that Google Chrome web browser be used. BODRevMan can be accessed at the following web address https://bodrevman.mrc.ac.za. Contact the Project Administrator to create an account as a reviewer on the BODRevMan system.

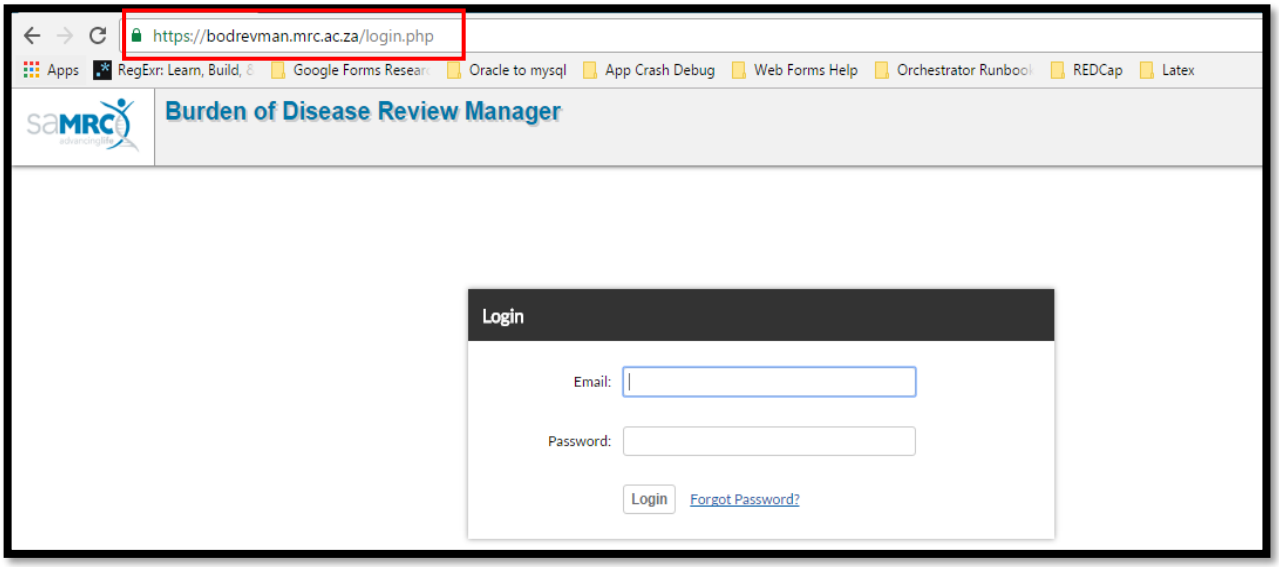


Figure 5-1: Accessing BODRevMan

5.1 Logging in

You can log in by entering your email address and password into the designated fields and clicking the “Login” button.

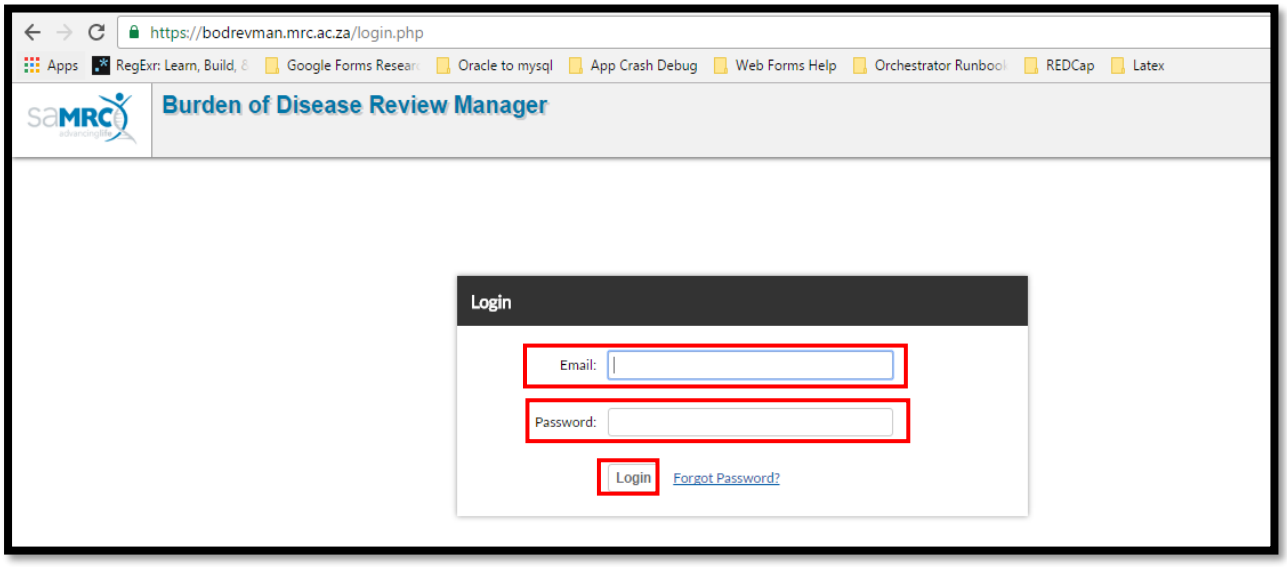


Figure 5-2: Logging in

5.2 Logging out

To log out simply click the “Logout” link in the top right corner. The user will remain logged into the system unless they logout. It is the responsibility of the user to logout.

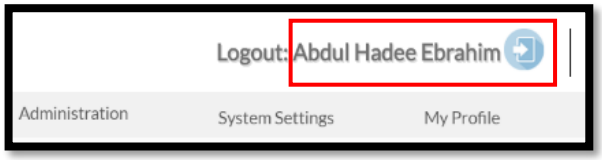


Figure 5-3: Logging out

5.3 Forgot password

If you have forgotten your password, you can click on the “Forgot password” link, then type in your email address and click “Reset Password”.

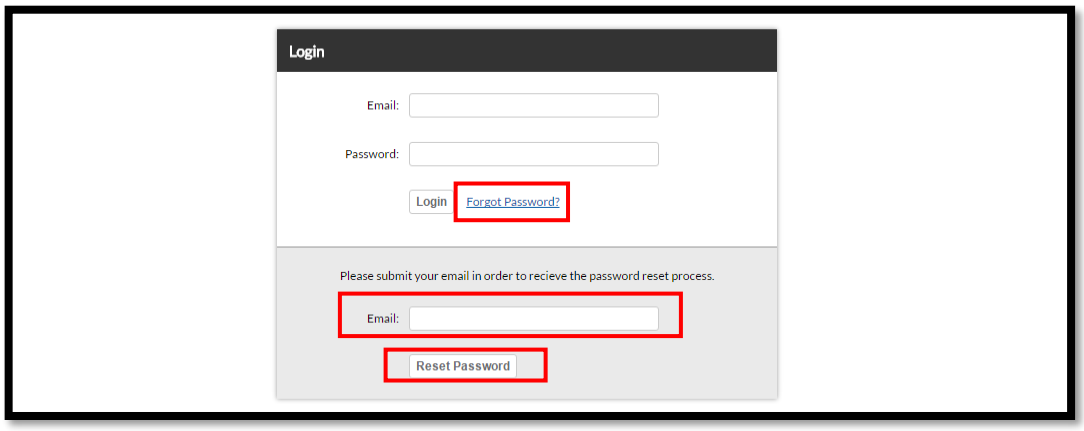


Figure 5-4: Forgot password

5.4 Navigation

Different pages are accessed via the links on the main navigation page.

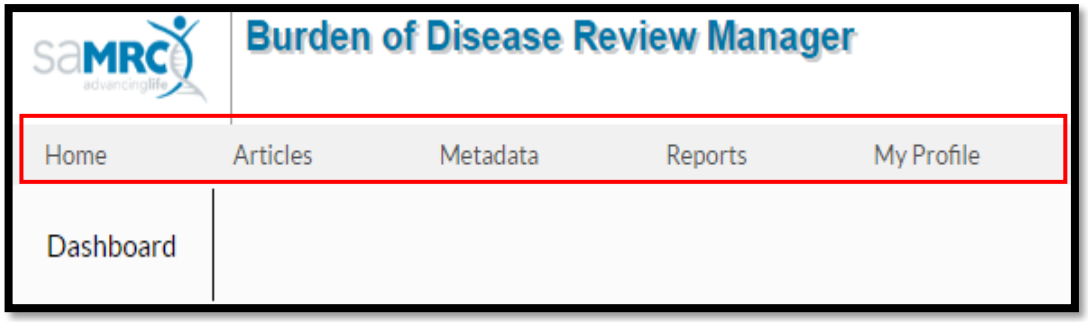


Figure 5-5: Navigation

6 Dashboard

The Dashboard is a significant platform that displays the reviewers' roles, article review progress and system notifications at a glance. The Dashboard displays a summary of all the systematic reviews and the status of articles allocated to you.

6.1 Reviewer Dashboard

The Reviewer Dashboard displays the details of the last article a reviewer worked on and the reviewer's progress summary.

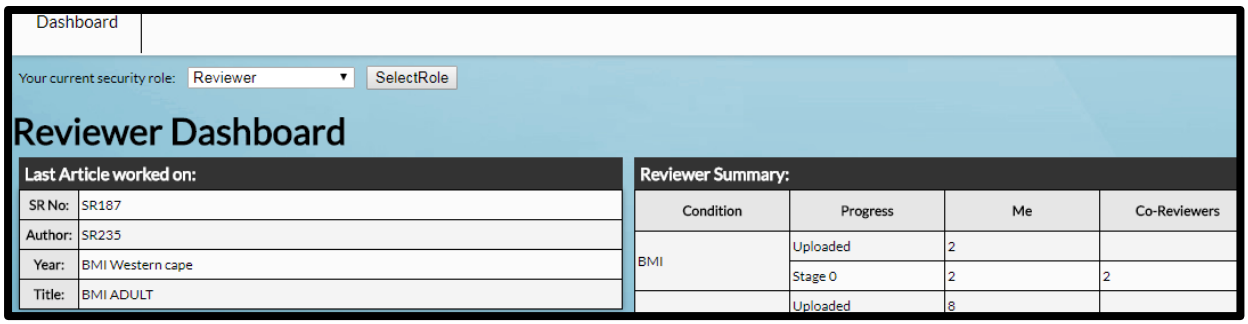


Figure 6-1 Dashboard

6.2 Duplicate notification for Reviewers

Certain studies may report on more than one condition / risk factor of interest e.g. a national survey could report on high blood sugar and low fruit intake. In these circumstances, it is possible to duplicate some of the information from one completed SR to another.

Articles that are loaded on the system under a specific risk factor/condition can be duplicated for review by another risk factor/condition. The project administrator has the responsibility of uploading an article onto the system under a new SR number, condition and reviewers (R1 and R2).

Should the main study be completed (Stage 2) and a duplicate study is uploaded (under a different condition/risk factor and SR number), Reviewer 1's dashboard will display a notification giving Reviewer 1 the option to duplicate the completed SR. The notification will contain the SR number and details of the original article, with a link for Reviewer 1 to click, in order to copy the completed article for their review. When Reviewer 1 clicks the link, the new SR will be pre-populated with data from the original SR up till the point of the Risk-of-Bias Assessment. This duplicated SR will be in Stage 0 and the Reviewer can change the data where

necessary. The data grid information will be blank as it is unlikely that the original SR's data will be needed.

Reviewer 2 does not have the option to duplicate the article on their dashboard. However, when Reviewer 1 clicks the duplication link, Reviewer 2's SR will also be populated with editable data while the SR will remain in Stage 0.

The reviewers will have to navigate through each screen to change responses as they deem fit for their specific risk factor/condition of interest, and extract information into the data grid on the "Data Extraction" screen.

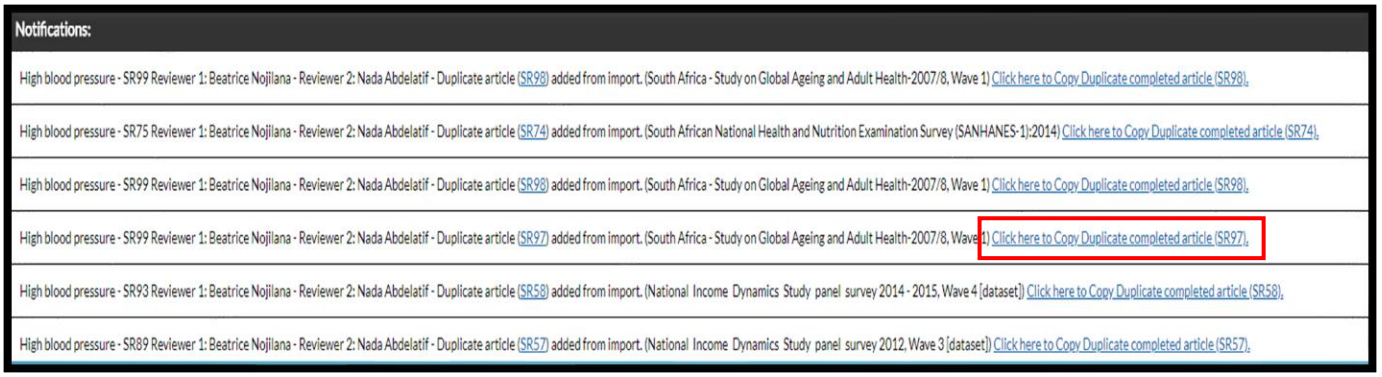


Figure 6-2: Duplicate notification

Tip: If more than one duplicate article is uploaded intentionally, the article that is put into Stage 2 first will be used to pre-populate the duplicate.

6.3 Power- User Dashboard and Notification

The power users' dashboard displays the summary of risk factors and disease conditions uploaded unto the system, the number of article against each risk factors and disease conditions as well as the review progress. The user log emails, notification of activities in the system and dates of activities are displayed.

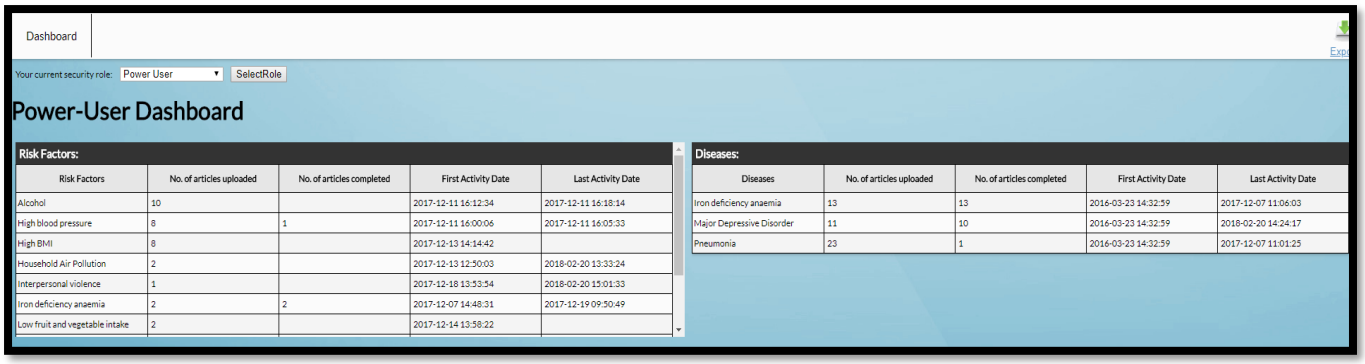


Figure 6-3: Power-User Dashboard

6.4 Role switching

Should you have various roles assigned to you, you can switch between these by selecting the desired role from the list on your dashboard and clicking the “Select Role” button.

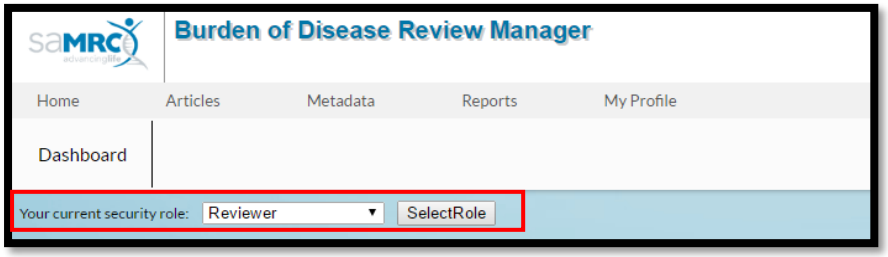


Figure 6-4: Role switching

6.4.1 Reviewer

The Reviewer Summary indicates the progress on the articles/studies in the system, showing how many are in each Stage of the review process and the latest article worked on by the reviewer.

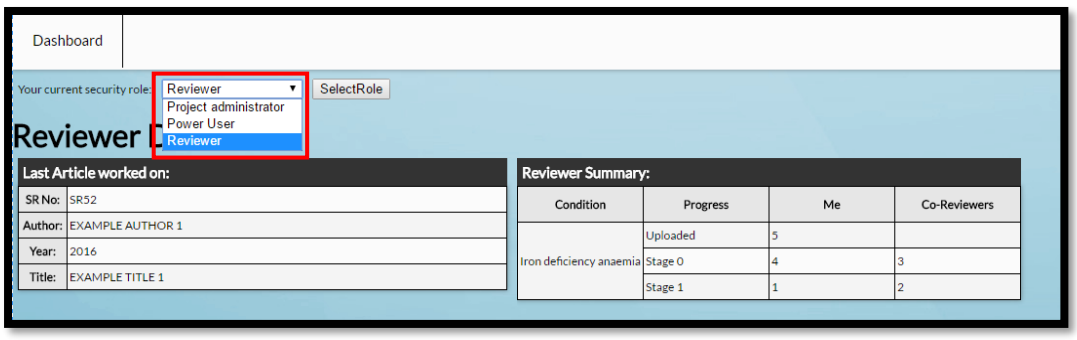


Figure 6-5: Reviewer dashboard

7 Articles screen

Articles can be accessed by clicking the “Articles” link in the main navigation bar.

Figure 7-1: Articles screen navigation

7.1 Filtering articles

Articles can be filtered by utilising the search and filter fields provided on the “Articles” page. To filter or search, type in the phrase to search and select the desired criteria on which to filter.

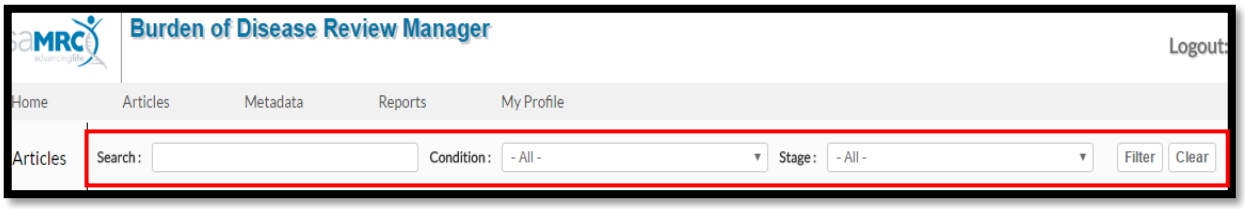


Figure 7-2: Filtering articles

7.2 Exporting an article

To export the article and the information extracted during the review process, check the “Select” checkbox for the desired article and click the “Export” button.

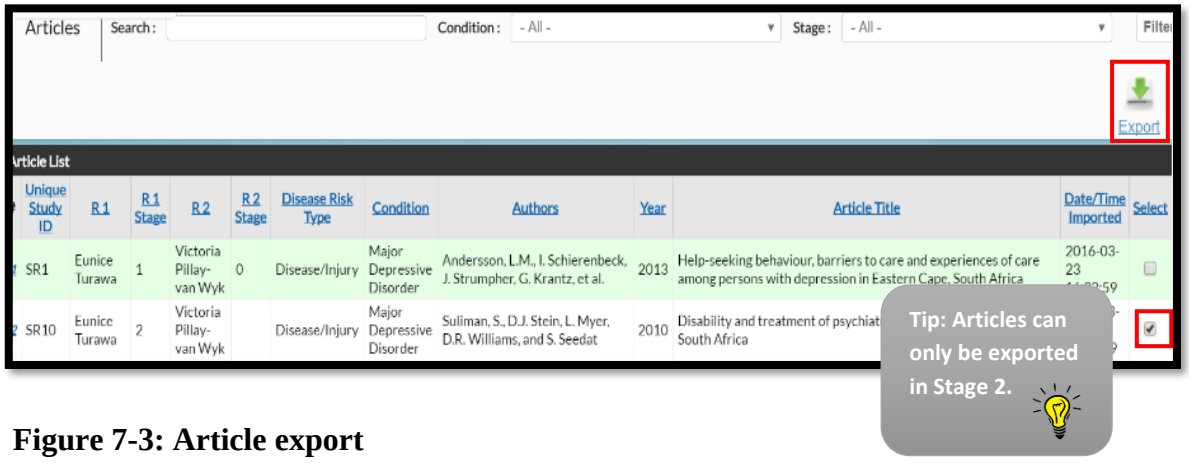


Figure 7-3: Article export

See below for the output of the article export:

Article Details

Article ID	Unique Study ID	Reviewer 1	Reviewer 1 Stage	Reviewer 2	Reviewer 2 Stage	Disagreements Resolved	Disease Risk Type	Disease Risk Name	Authors
33	SR10	Eunice Turawa	2	Victoria Pillay-	1	0	Disease/Injury	Major Depres	Suliman,

Figure 7-4: Export output

7.3 Selecting an article to review

Click on the row to select an article to review.

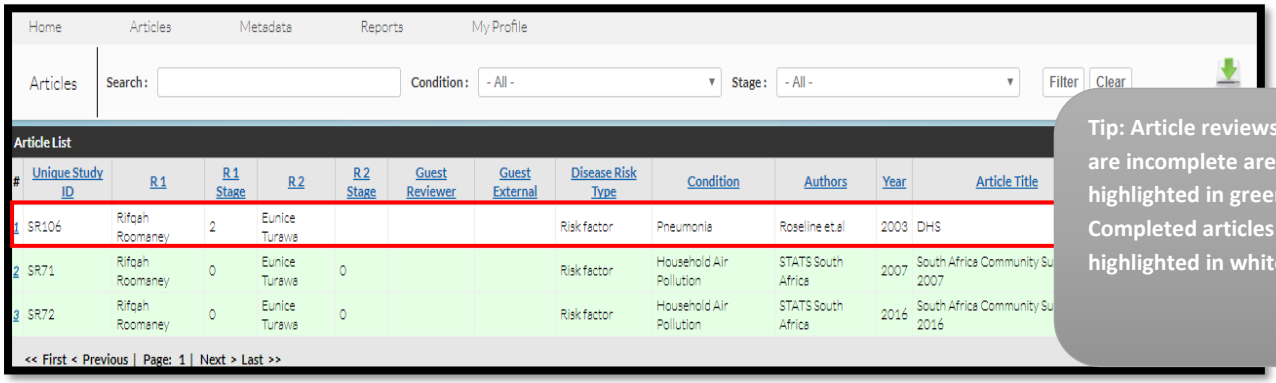


Figure 7-5: Selecting an article to review

8 Article review process

Once you have selected the article to review, you will be presented with the following page. The Article Details page shows the article reference to ensure you are working on right article.

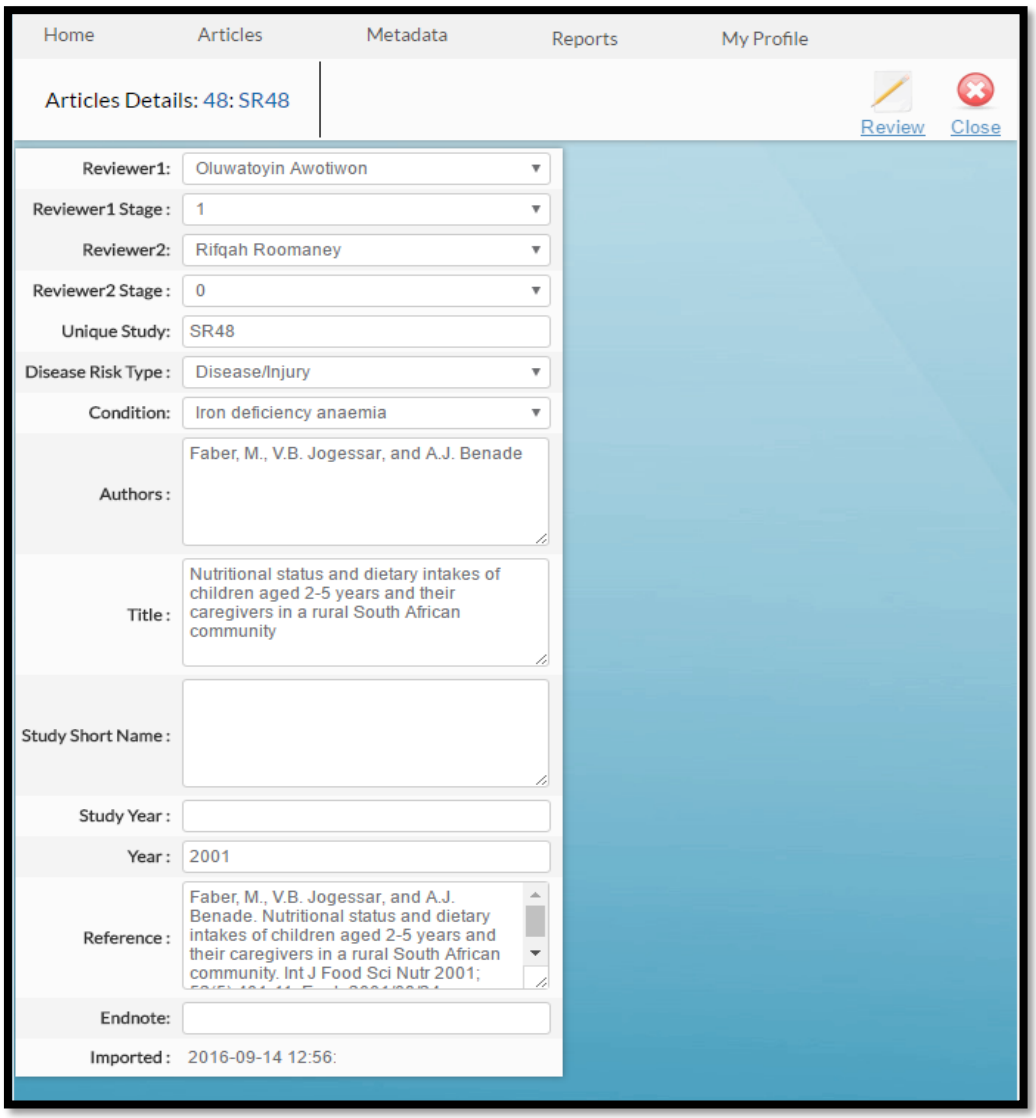


Figure 8-1: Article Details page

8.1 Starting the review process (Data capturing process)

To start the review process, click the "Review" button in the top right of the screen. To close the screen and return to the list click the Close button located next the "Review" button.

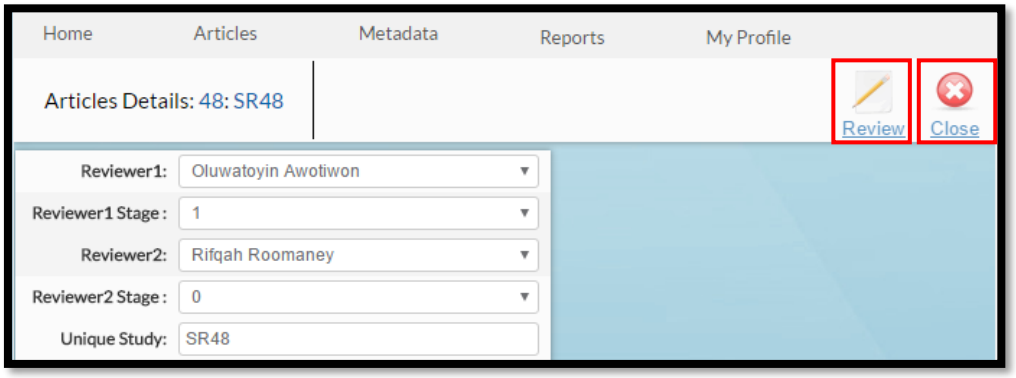


Figure 8-2: Starting the review process

8.2 Data capturing

The Figure 8-3 represents the first of many screens that allow data capturing throughout the review process. You will be required to navigate through and complete the various screens.

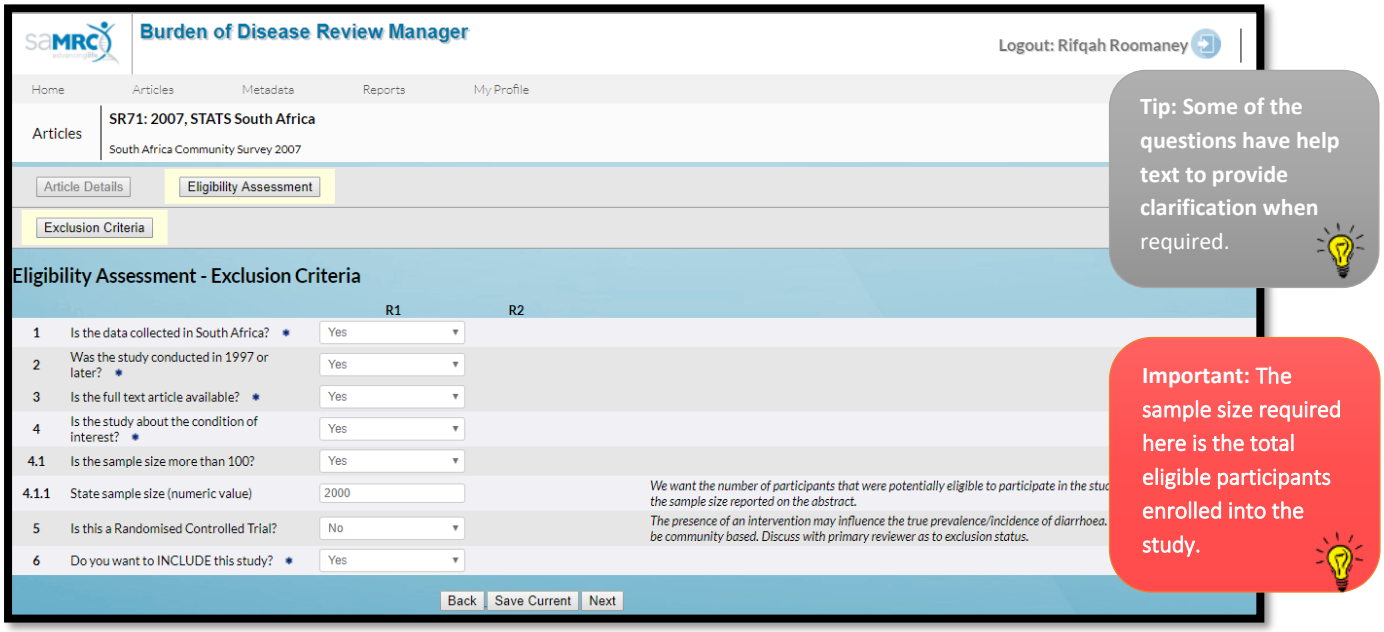


Figure 8-3: Exclusion criteria

8.2.1 Saving current progress

When reviewing an article, **it is recommended that you save your work regularly**; to avoid any loss of data. To save captured data, simply click the Save Current button.

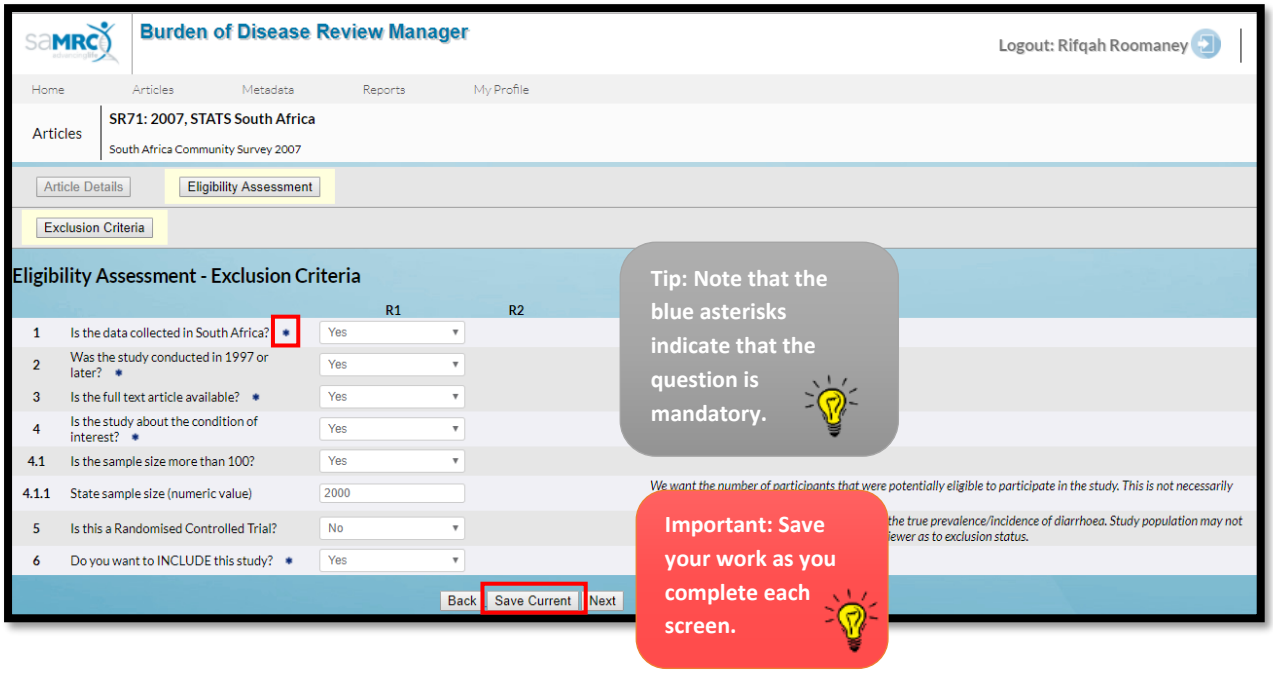


Figure 8-4: Saving progress

8.2.2 Moving to the next screen

Once you have answered all the questions on the screen and are ready to move to the next screen, click the "Next" button.

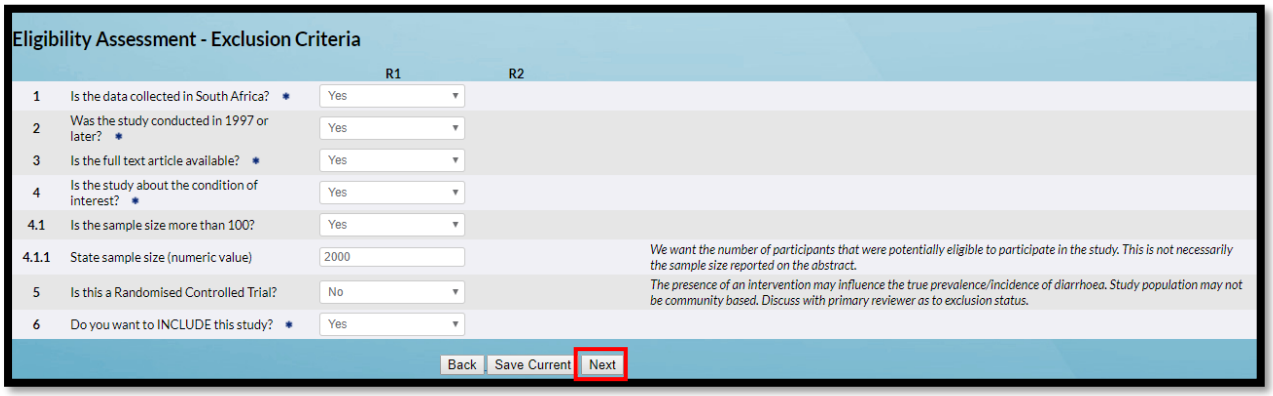


Figure 8-5: Moving to the next screen

To return to the previous assessment screen click the “Back” button.

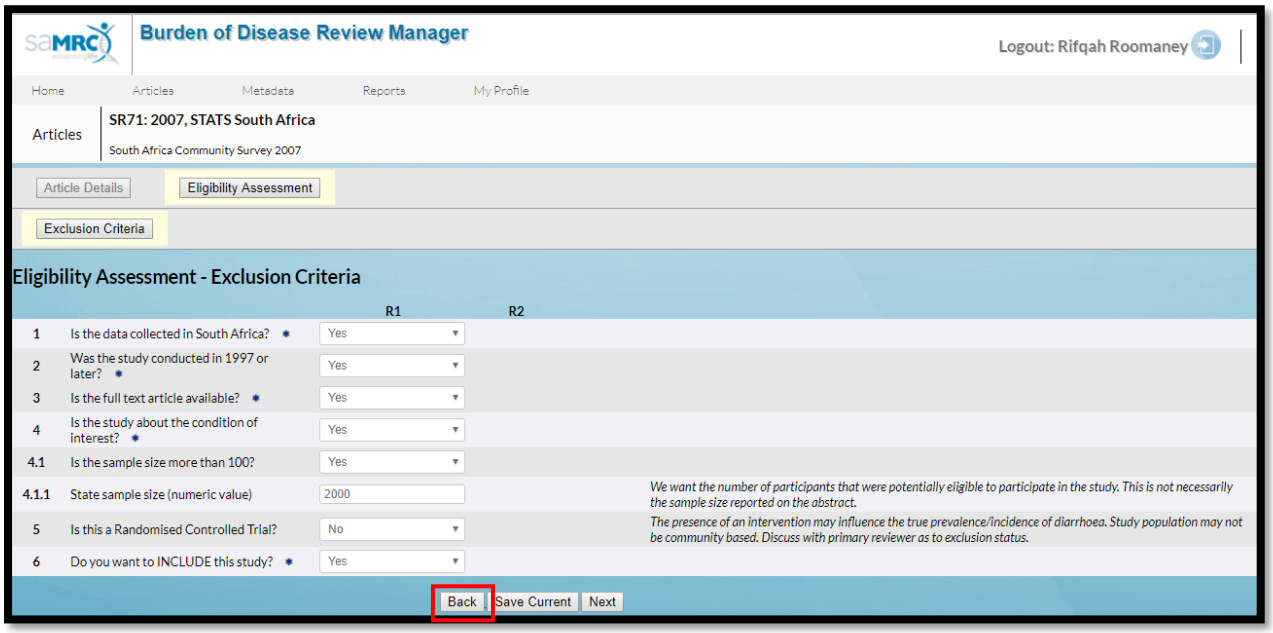
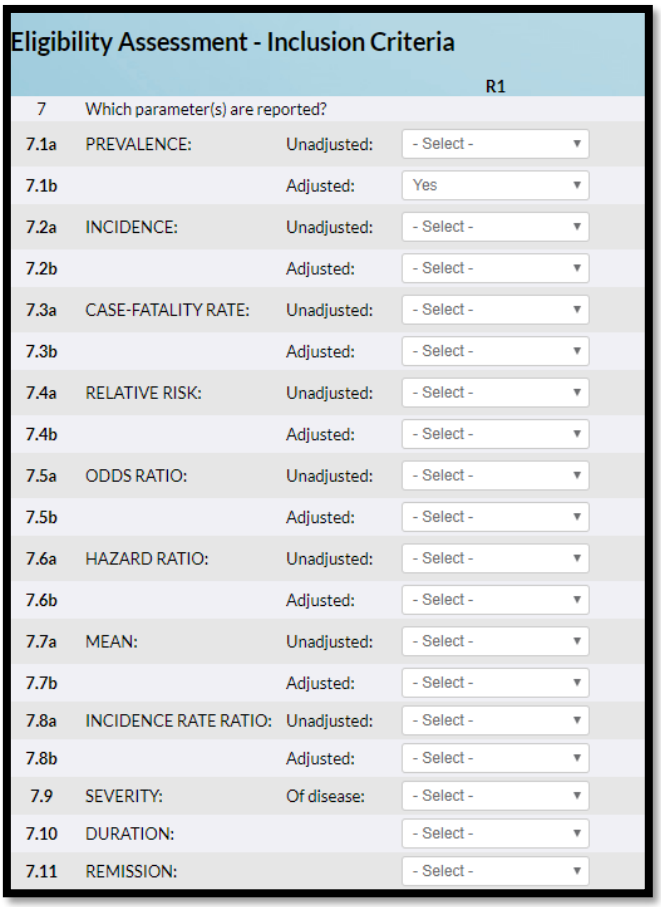


Figure 8-6: Moving to the previous screen

8.3 Choosing parameters for data extraction

This page enables the reviewer to select parameters of interest from which data can be extracted from the article. These include:

- Prevalence
- Incidence
- Case-fatality rate
- Relative risk
- Odds ratio
- Hazard ratio
- Mean
- Incidence-rate ratio
- Severity
- Duration
- Remission



Eligibility Assessment - Inclusion Criteria

			R1
7	Which parameter(s) are reported?		
7.1a	PREVALENCE:	Unadjusted:	- Select -
7.1b		Adjusted:	Yes
7.2a	INCIDENCE:	Unadjusted:	- Select -
7.2b		Adjusted:	- Select -
7.3a	CASE-FATALITY RATE:	Unadjusted:	- Select -
7.3b		Adjusted:	- Select -
7.4a	RELATIVE RISK:	Unadjusted:	- Select -
7.4b		Adjusted:	- Select -
7.5a	ODDS RATIO:	Unadjusted:	- Select -
7.5b		Adjusted:	- Select -
7.6a	HAZARD RATIO:	Unadjusted:	- Select -
7.6b		Adjusted:	- Select -
7.7a	MEAN:	Unadjusted:	- Select -
7.7b		Adjusted:	- Select -
7.8a	INCIDENCE RATE RATIO:	Unadjusted:	- Select -
7.8b		Adjusted:	- Select -
7.9	SEVERITY:	Of disease:	- Select -
7.10	DURATION:		- Select -
7.11	REMISSION:		- Select -

Figure 8-7: Parameters in Inclusion Criteria

Since the information extracted for different parameters varies, customised data-extraction grids are available. (see Section 8.7.4).

8.4 Additional study information screen

The "Additional Study Information" field enables the user to capture relevant additional details relating to the study which is used in the reports.

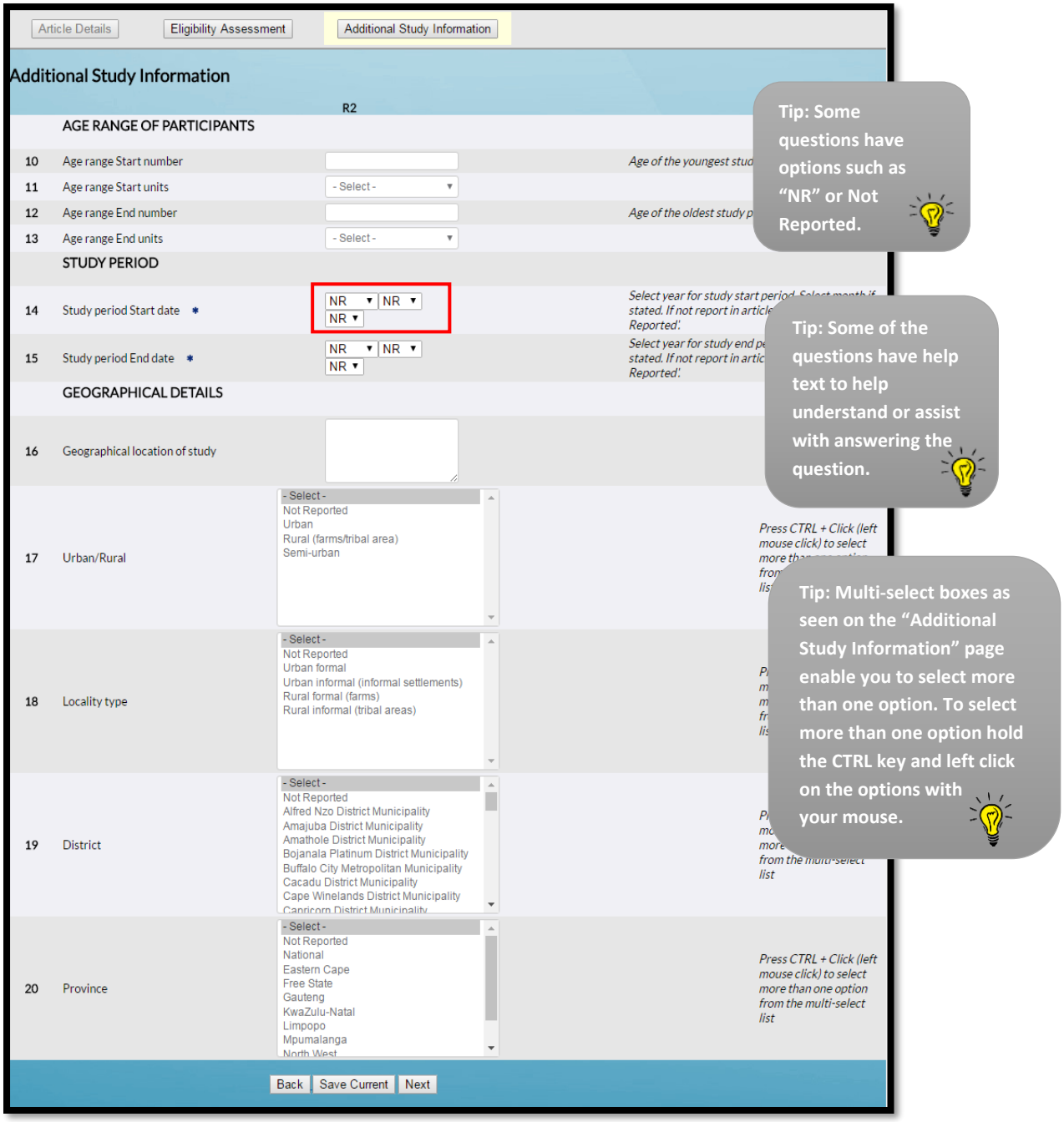
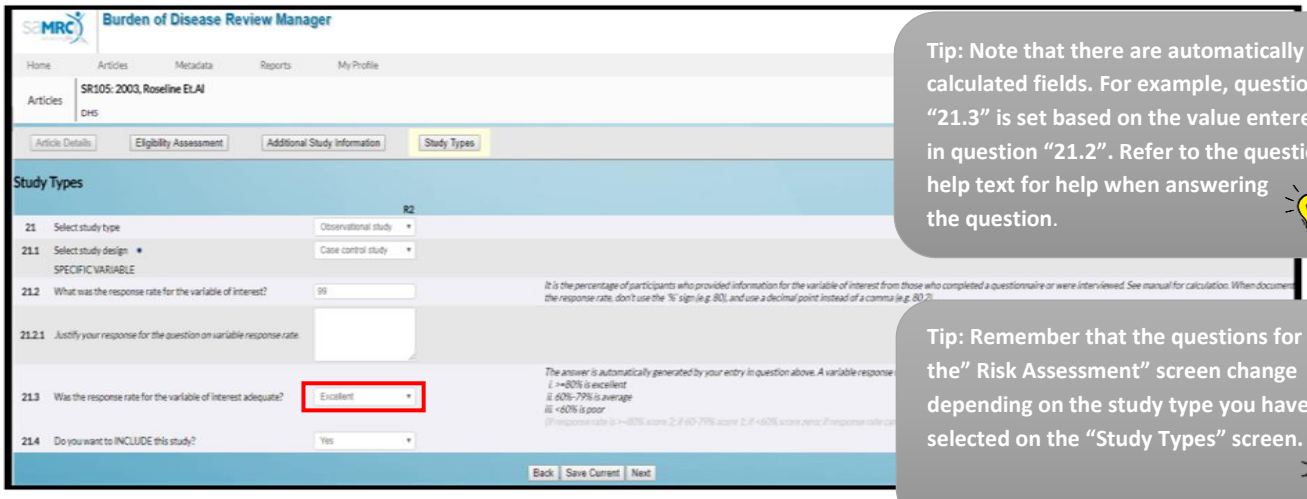


Figure 8-8: Additional Information screen

8.5 Study types screen

The "Study Types" screen enables the user to specify the study type reported in the article. This screen is dynamic and the questions that appear are based on the study type selected.



Tip: Note that there are automatically calculated fields. For example, question "21.3" is set based on the value entered in question "21.2". Refer to the question help text for help when answering the question.

Tip: Remember that the questions for the" Risk Assessment" screen change depending on the study type you have selected on the "Study Types" screen.

Figure 8-9: Study Types screen

8.6 Automated fields

There are fields in the "Study Types" and "Risk Assessment" screens that are completed automatically based on the responses for prior questions. For example, the number entered in question 28.2 determines the auto-generated response in question 28.3. Note that when documenting the response rate, use a decimal point (e.g. 69.3) and do not use the "%" sign (e.g. 69.3%).

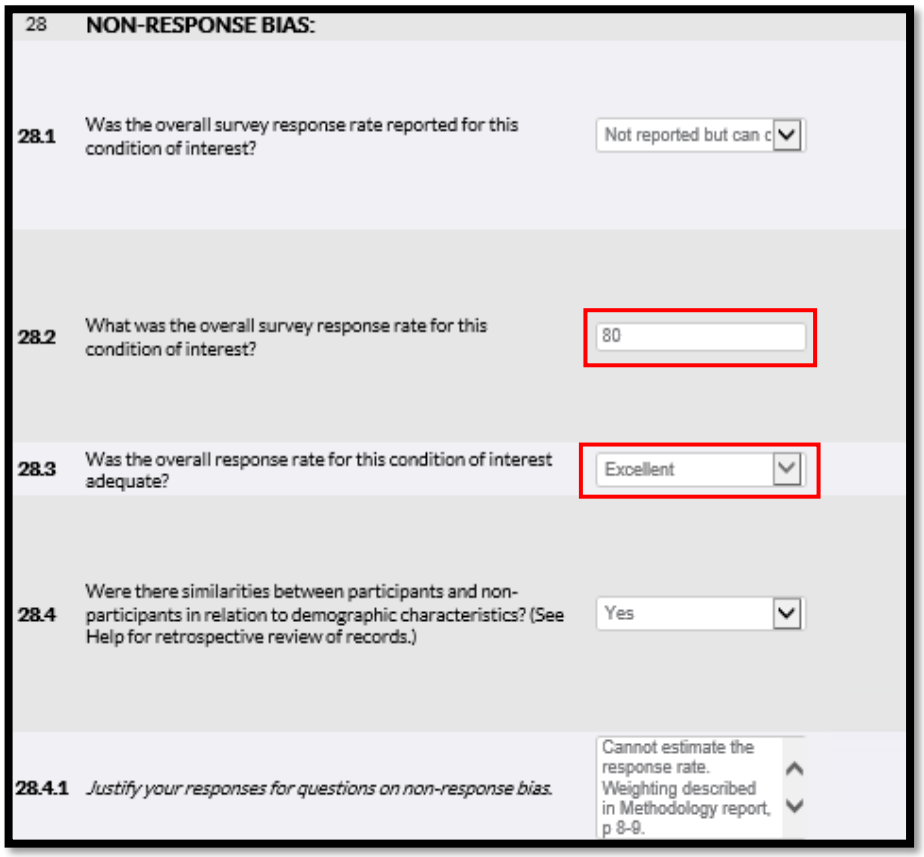


Figure 8-10: Automated fields

The total score for the risk-of-bias assessment is automatically completed based on the responses for the questions, and the quality generated.

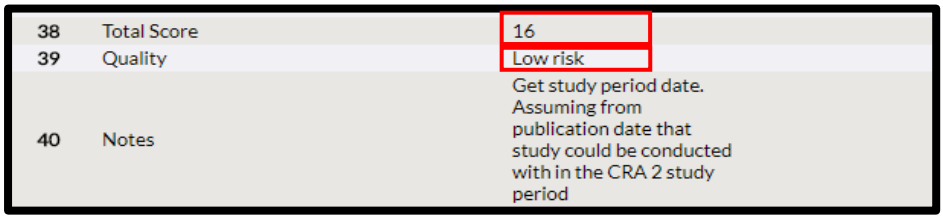


Figure 8-11: Scoring in Risk-of-bias Assessment

8.7 Data Extraction

The “Data Extraction” screen dynamically generates data grids for the parameters of interest that were selected earlier (see Section 8.5: Study types screen). For example, if Prevalence - Adjusted is selected, then Prevalence - Adjusted will be displayed automatically on the “Data Extraction” screen.

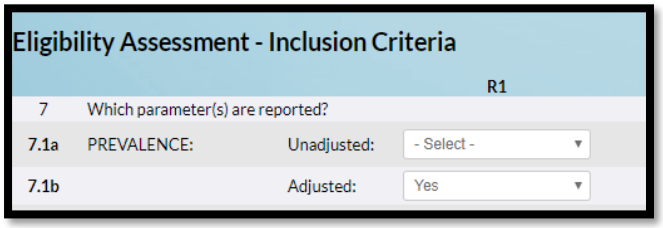


Figure 8-12: Dynamic Data Extraction

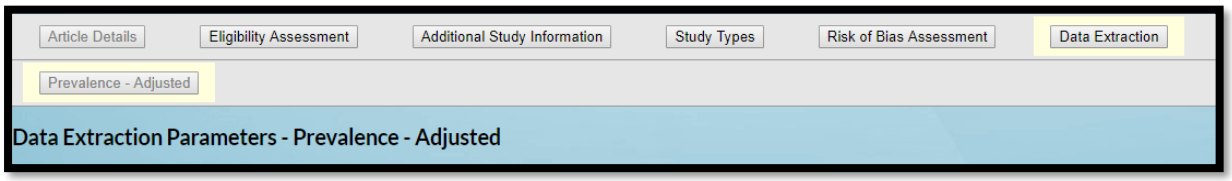


Figure 8-13: Parameter in Inclusion page linked to Data Extraction

Where more than one parameter is selected, all the selected parameters will be displayed on the ribbon.

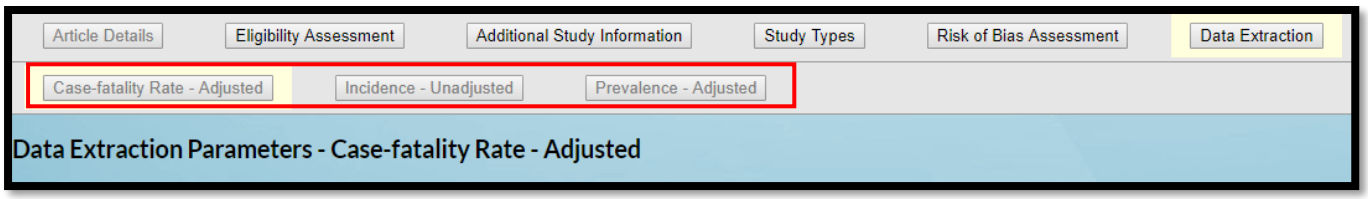


Figure 8-14: Headings of Data Extraction pages

8.7.1 Unit of measure

The screen below displays where the “Unit of measure” for the specific parameter of interest (e.g. Prevalence, Incidence, Relative risk, Odds ratio, etc.) reported by the study is captured. For certain parameters a unit of measure is not available, e.g. Odds Ratio, Relative, Hazard

Ratio and Incidence-Rate Ratio. The unit of measure should be reported as it is referred to in the article/study.

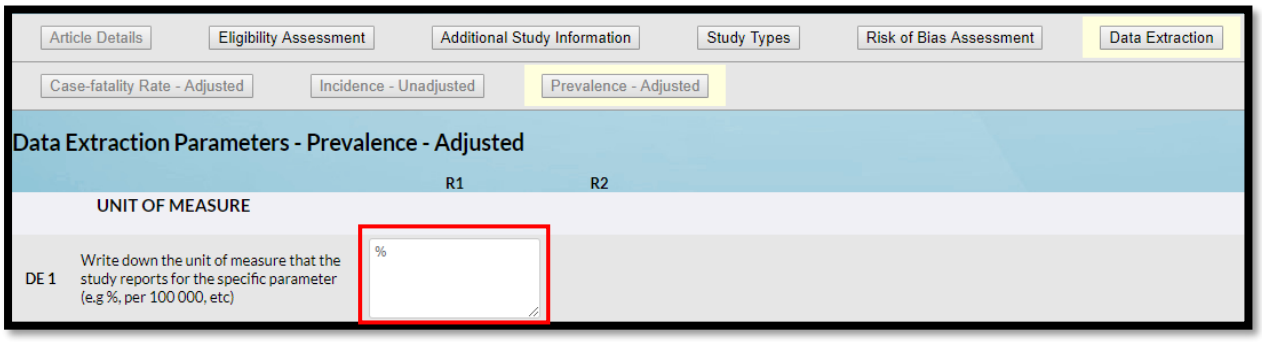


Figure 8-15: Unit of measure

8.7.2 Measure of Uncertainty

Data on the "Measure of Uncertainty" are also captured on the "Data Extraction" screen. If more than one uncertainty measure is reported, choose the best measure, e.g. 95% confidence interval. If the only measure of uncertainty reported in the article is not one of those displayed below (e.g. Inter-quartile Range), select "Other" and report this as text.

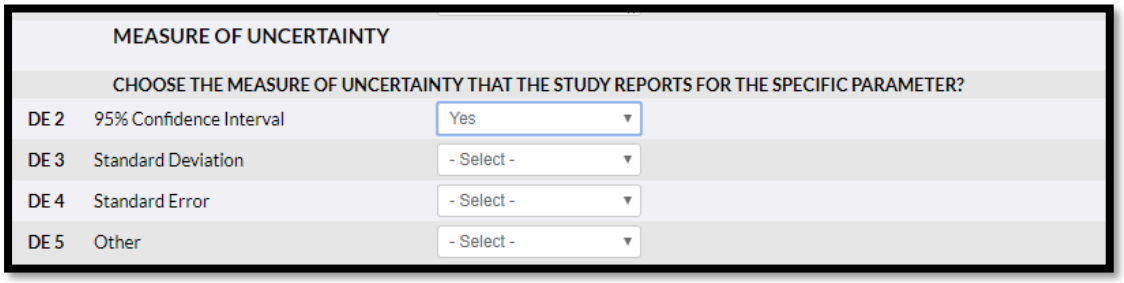


Figure 8-16: Measure of Uncertainty

8.7.3 Population numbers

The "Data Extraction" screen also captures information on the total number of participants by sex (e.g. males, females) or persons, if reported. The data grids are dynamically labelled according to the selected population. If more than one population is selected, a data grid will appear for each one. For ease of data entry, a "Radio" button enables the reviewer to view these grids as desired.

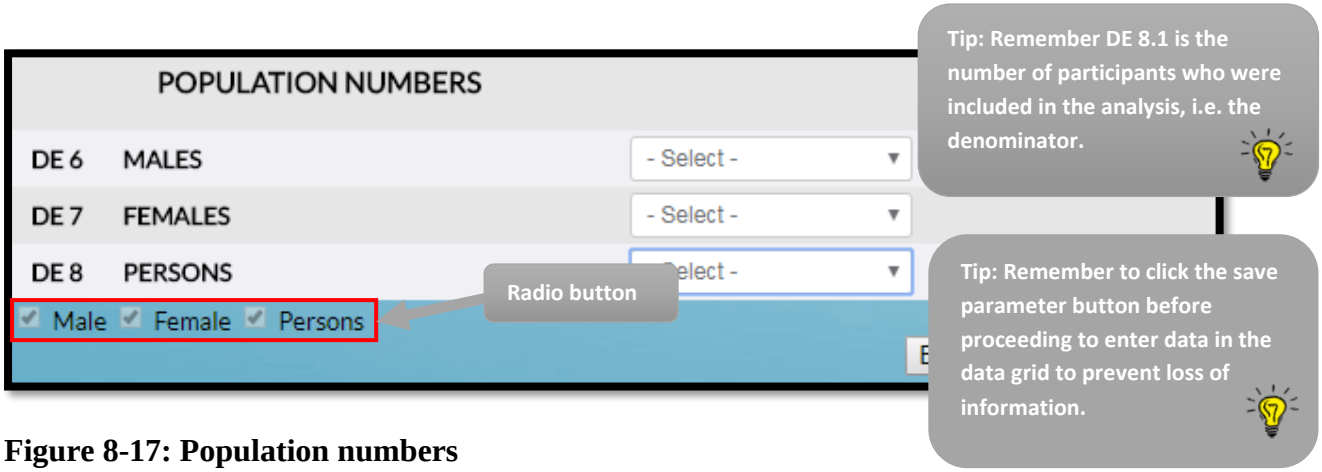


Figure 8-17: Population numbers

8.7.4 Data grids

Data grids are generated based on the selected "Parameter of interest" (e.g. prevalence, Odds Ratio, severity); "Measure of Uncertainty" (e.g. 95% confidence interval, standard deviation) and type of population under "Population numbers".

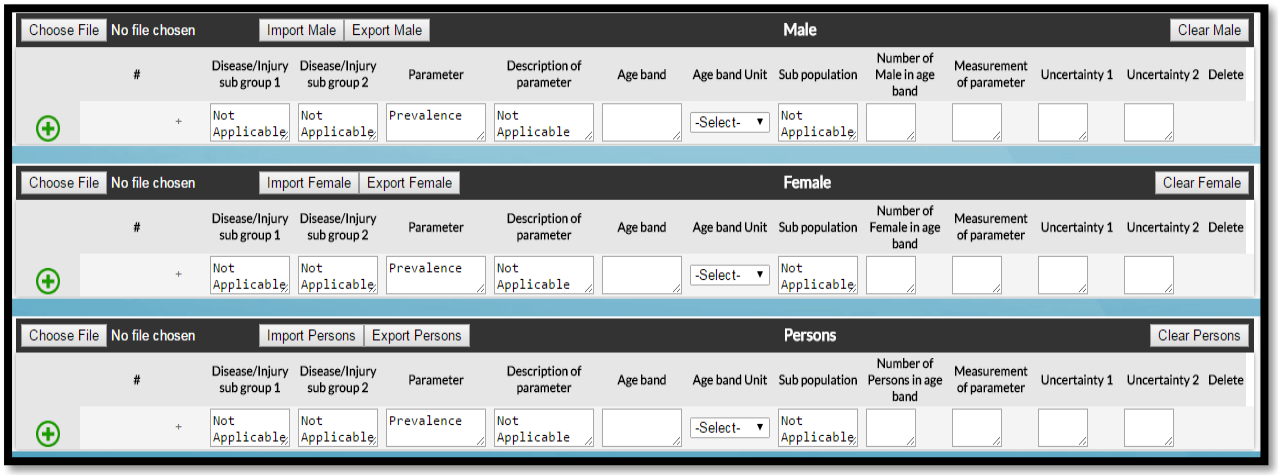


Figure 8-18: Grids in "Data Extraction"

A single field “Uncertainty 1” will be displayed if “Measure of Uncertainty” selected is standard error (SE) or standard deviation (SD).

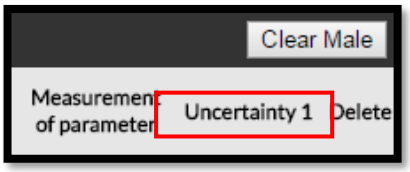


Figure 8-19: Uncertainty options

The data grid will display additonal fields such as exposure, reference group, etc. if Odds Ratio, Relative Risk, Hazard Ratio are the parameters of interest selected.

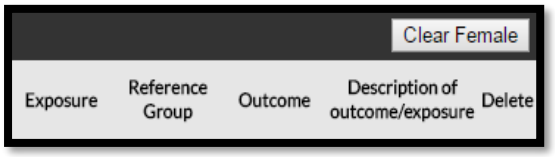


Figure 8-20: Additional columns in data grid

8.7.4.1 Adding data

You can add data to the grids by manually typing or importing. To manually type data, you will require a new row which can be created by clicking on the green plus sign.

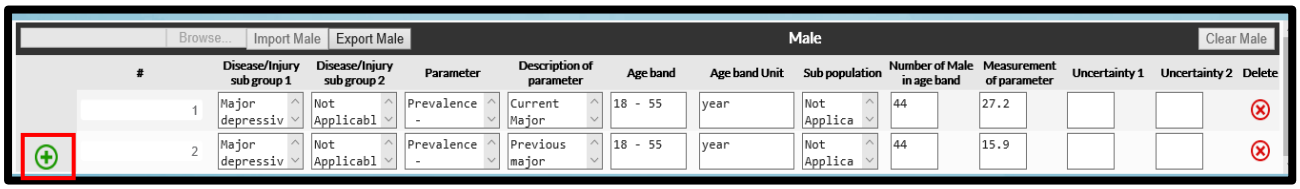


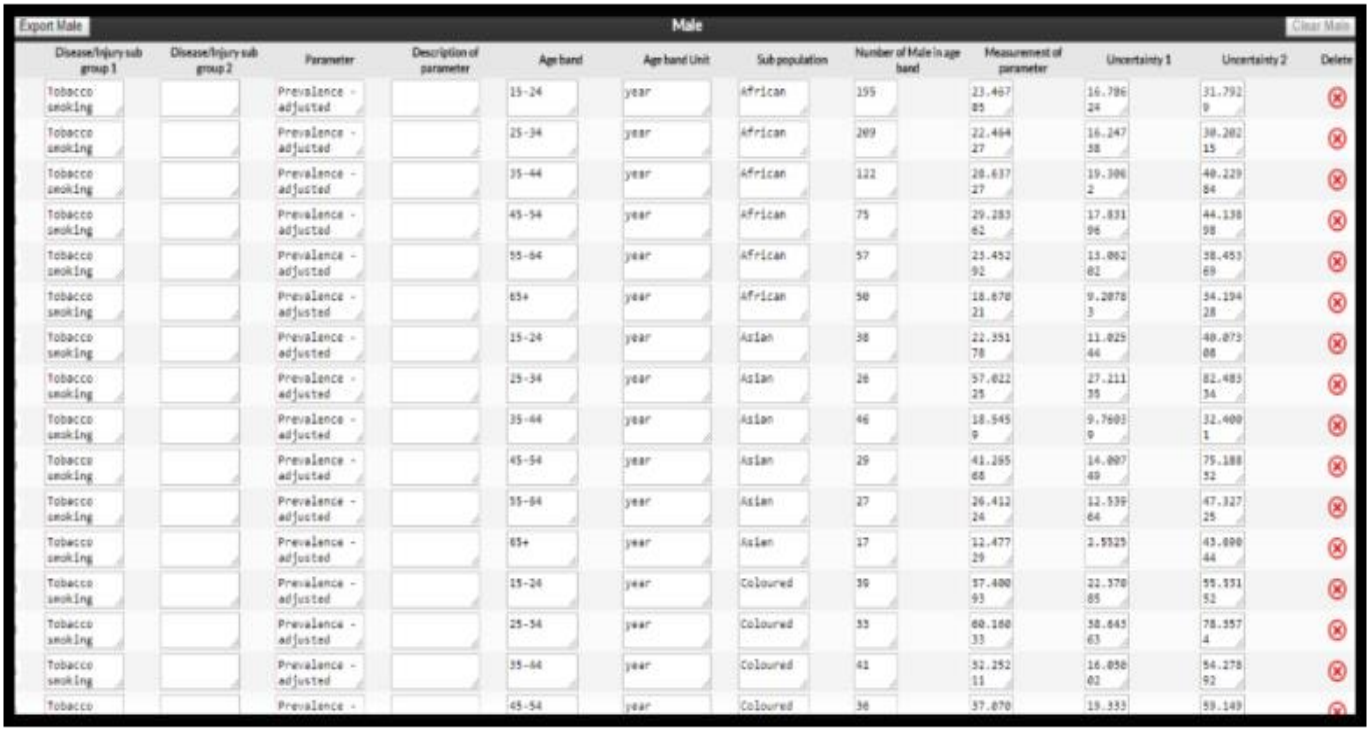
Figure 8-21: Adding data to the grid

The column “Parameter” autocompletes based on the parameters selected in the “Inclusion Criteria” screens and “Description of Parameter” provides the space to report more information on the parameter, e.g. point prevalence or period prevalence. Additionally, information on whether the parameter of interest is adjusted or unadjusted can be reported here, e.g. adjusted prevalence or unadjusted prevalence.

Parameter provides the space to report more information on the parameter, e.g. The columns “Disease/Injury groups”, “Age-band Unit”, “Sub population”, “Exposure”, “Reference group”, “Outcome” and “Description of Outcome” autocomplete as “Not Applicable” when the first

row is generated. Data entered into these columns appear when the next row is added. This will continue with additional rows added until the reviewer changes the information in these columns.

The reviewers should capture the first level of the condition of interest e.g., Tobacco smoking in the "Disease/injury sub group 1" column as reported in the article as close to the National Burden of Disease cause of disease list where possible. Any other disease/injury breakdown (second level of condition of interest) can be added to the column "Disease/injury sub group 2". Sub-population breakdown of race and/or region should be added to the Sub-population column e.g., African, Asian, Coloured etc.



Export Male — Male — Clear Male

Disease/Injury sub group 1	Disease/Injury sub group 2	Parameter	Description of parameter	Age band	Age band Unit	Sub population	Number of Male in age band	Measurement of parameter	Uncertainty 1	Uncertainty 2	Delete
Tobacco smoking		Prevalence - adjusted		15-24	year	African	195	23.46785	16.78624	31.7929	
Tobacco smoking		Prevalence - adjusted		25-34	year	African	209	22.46427	16.24738	30.20215	
Tobacco smoking		Prevalence - adjusted		35-44	year	African	122	28.63727	19.3062	40.22984	
Tobacco smoking		Prevalence - adjusted		45-54	year	African	75	29.28362	17.83196	44.13898	
Tobacco smoking		Prevalence - adjusted		55-64	year	African	57	25.45292	13.86201	38.45369	
Tobacco smoking		Prevalence - adjusted		65+	year	African	50	18.67821	9.20783	34.19428	
Tobacco smoking		Prevalence - adjusted		15-24	year	Asian	38	22.35178	11.02544	40.07388	
Tobacco smoking		Prevalence - adjusted		25-34	year	Asian	28	57.02225	27.21135	82.48334	
Tobacco smoking		Prevalence - adjusted		35-44	year	Asian	46	18.5459	9.76039	32.4001	
Tobacco smoking		Prevalence - adjusted		45-54	year	Asian	29	41.26568	14.00749	75.18852	
Tobacco smoking		Prevalence - adjusted		55-64	year	Asian	27	26.41224	12.53964	47.32725	
Tobacco smoking		Prevalence - adjusted		65+	year	Asian	17	12.47729	2.5325	43.69044	
Tobacco smoking		Prevalence - adjusted		15-24	year	Coloured	39	37.40093	22.37085	55.15152	
Tobacco smoking		Prevalence - adjusted		25-34	year	Coloured	33	60.16033	38.64563	78.3574	
Tobacco smoking		Prevalence - adjusted		35-44	year	Coloured	41	32.25211	16.05002	54.27892	
Tobacco		Prevalence -		45-54	year	Coloured	36	37.870	19.333	59.149	

Figure 8-22: Example data

The column "Age-band Unit" is a drop-down box that provides the options to select whether the data are provided as days, weeks, months, or years.

Figure 8-22 provides an example of tobacco smoking prevalence data among the South African population.

Figure 8-23 provides an example of the Odds Ratio parameter for smoking as a risk factor for lung cancer displaying the extra columns mentioned above.

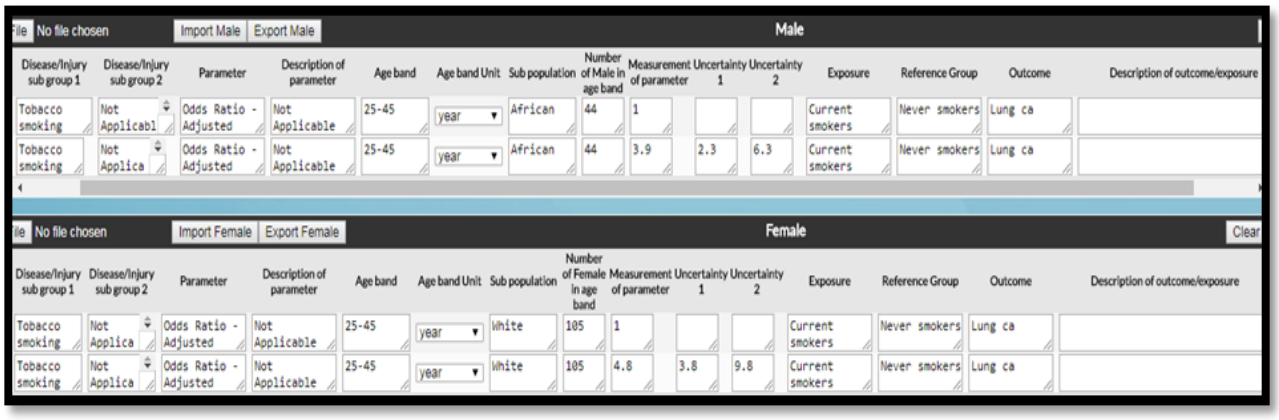


Figure 8-23: Example of the Odds Ratio parameter for smoking as a risk factor for lung cancer

8.7.4.2 Saving and removing data from grids

When adding data to the data grid, it is important to remember to save your captured data. Saving the grid data will also allow you to remove any undesired rows. The removed row buttons will only appear after you have saved your data.

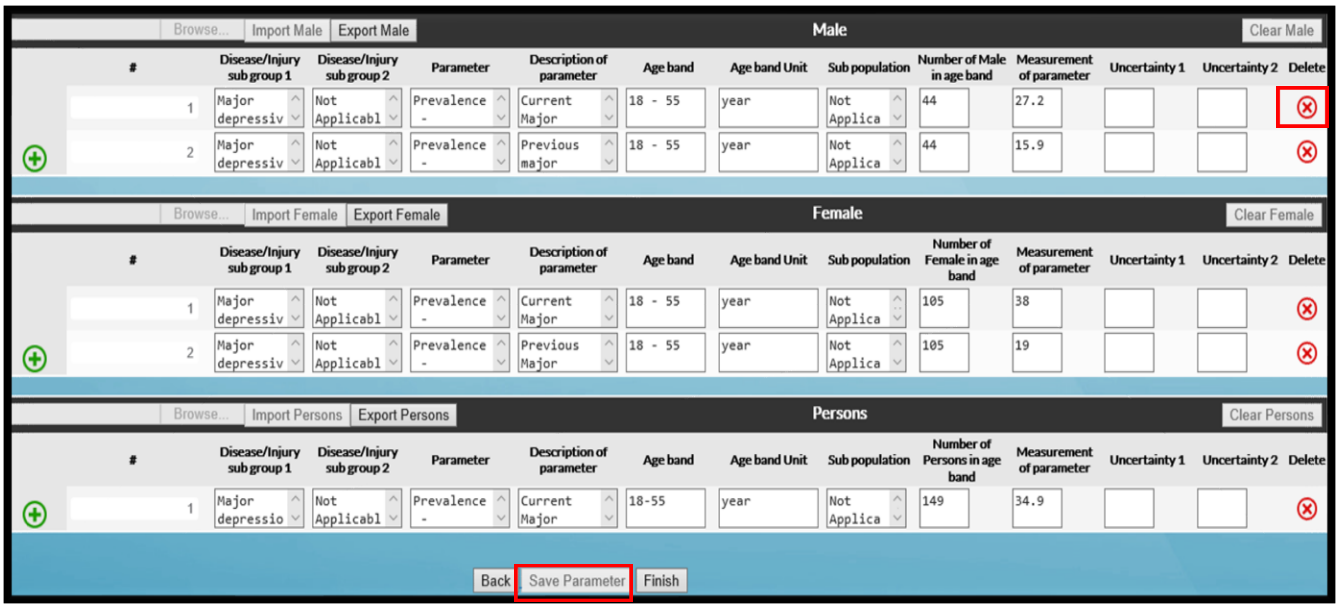


Figure 8-24: Saving data

8.7.4.3 Clearing a data grid

By simply clicking the "Clear" grid button you can clear all data captured in the grid and then click Save Parameter. These buttons will display as either Persons, Males or Females.

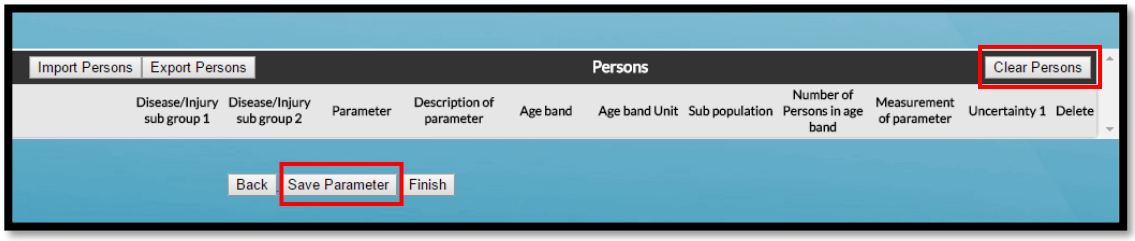


Figure 8-25: Clearing a data grid

8.7.4.4 Importing and exporting data grids

The "Data Extraction" screen also has the ability to import your data grids. However, before you can import you should export the template of the data grid, insert your data into the template and then import the data from the template. See screen below for exporting data:

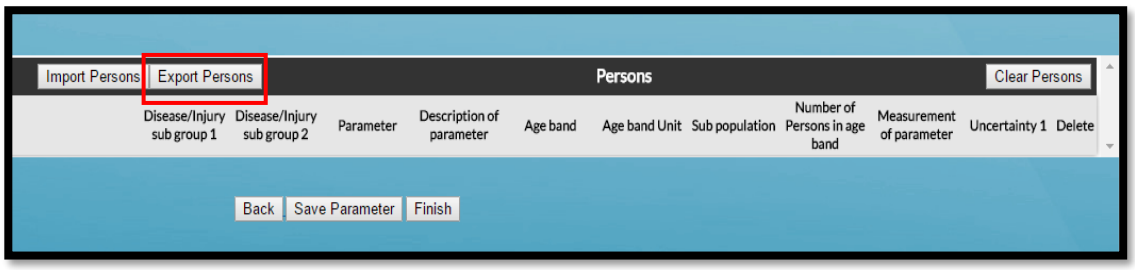


Figure 8-26: Exporting grid template

Once you press the "Export" button, an Excel template will appear at the bottom of the grid. Note that this template will not appear if your pop-ups are not enabled.

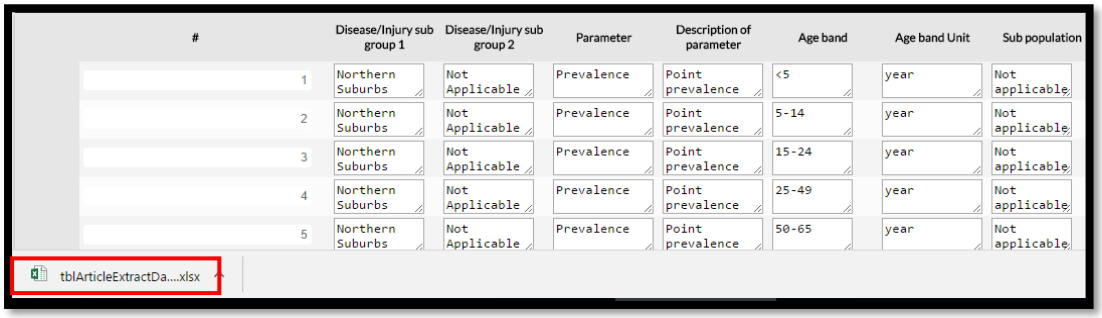
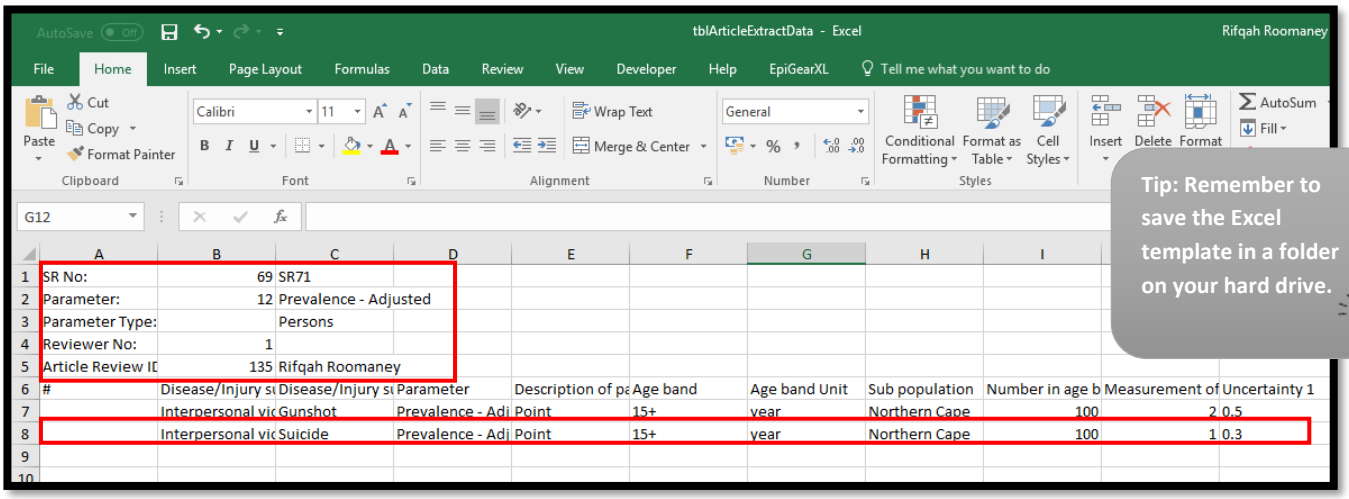


Figure 8-27: Download from web browser

Once you have exported the template, you should be presented with a downloaded Excel spreadsheet into which you can enter your data.



	A	B	C	D	E	F	G	H	I		
1	SR No:	69	SR71								
2	Parameter:	12	Prevalence - Adjusted								
3	Parameter Type:		Persons								
4	Reviewer No:	1									
5	Article Review ID	135	Rifqah Roomaney								
6	#	Disease/Injury s	Disease/Injury s	Parameter	Description of pa	Age band	Age band Unit	Sub population	Number in age b	Measurement of	Uncertainty 1
7		Interpersonal vic	Gunshot	Prevalence - Adj	Point	15+	year	Northern Cape	100	2	0.5
8		Interpersonal vic	Suicide	Prevalence - Adj	Point	15+	year	Northern Cape	100	1	0.3
9											
10											

Figure 8-28: Import template

Do not change the values for cells A1–A6 and B1–B6, as these contain data specific to the grid you have exported.

You can add your data from Columns B–L onwards starting from row 7.

*** Note that you should change the sheet name to "Worksheet 1".**

*** The Age band Unit (Column G) is case sensitive. Only enter "day", "week", "month" or "year" in lowercase.**

*** Do not enter Measurement, Uncertainty 1, Uncertainty 2 (Columns J – L) with any symbols e.g. %. Only enter the relevant number.**

*** Note Cells A7–A* (#) are the unique ID numbers. Should your exported data grid contain data you have manually entered do not delete these unique IDs. Also, leave these cells blank when entering new rows, as unique IDs will be allocated to the new rows when the spreadsheet is imported.**

TIP: If you export R2's data and import it into R1's data grid, make sure that Cells A7–A* (#) are left blank so that the system imports it as new data. If you leave R2's unique IDs in and import it into R1s grid, it will overwrite R2's original data.

Once you have entered your data into your template, you can upload your spreadsheet by clicking “Choose file” and navigating to the physical template file saved on your computer clicking “Open” and then clicking the “Import” button.

The following steps are required to import your data:

1. Select “Choose file” on the “Data Grid” screen.
2. Select the Excel template from the appropriate folder in which you have saved it.
3. Click the “Open” button in the folder.
4. Select the “Import” button on the data grid for the appropriate population to upload the data.

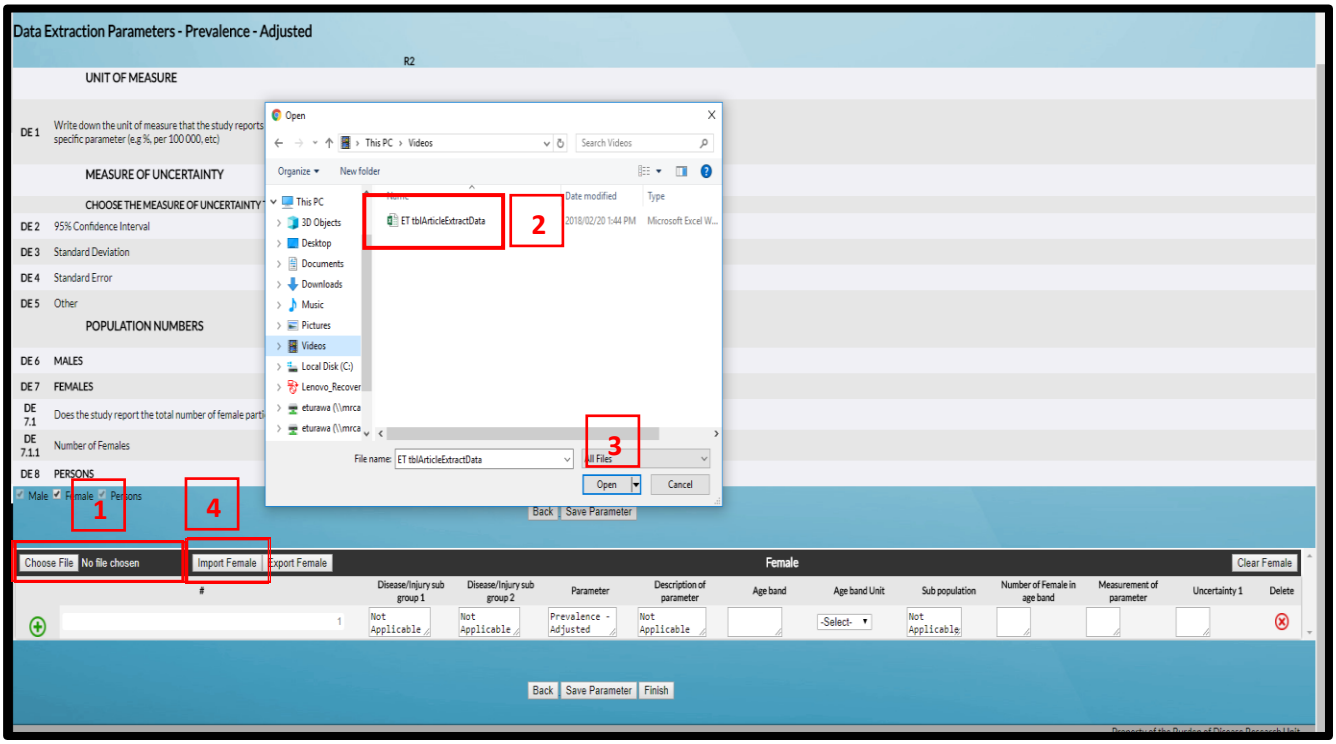


Figure 8-29: Import to grid

You should now be able to see the data you imported into the data grid. As “Age-band Unit” is a drop-down box in the data grid, the information for this column needs to be entered manually.

8.7.5 Severity

As the information required for Severity is different, data entry for this parameter is addressed separately.

The system provides the option to report the Severity of the condition based on an article's definition of severity, e.g. clinical or laboratory based.

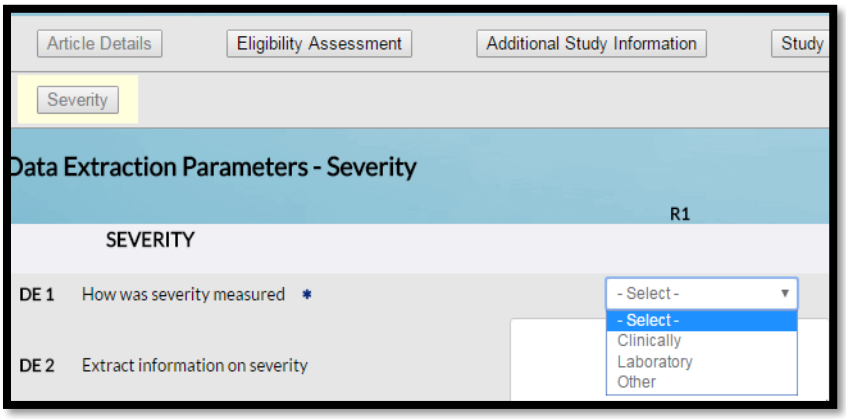


Figure 8-30: Severity data extraction

Information on Severity as reported in the article is captured in a Memo box on the data grid.

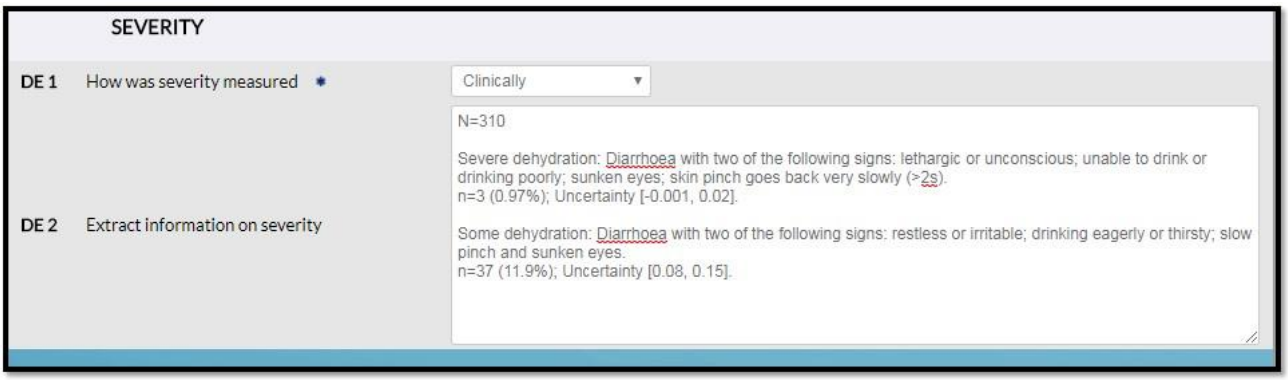


Figure 8-31: Capturing data on Severity

8.8 Moving to Stage 1

Once you have completed your review and all your data is captured, you can then move to the next stage of the review process by clicking the "Finish button". Once in Stage 1, the Study Review Form for the individual Reviewer cannot be amended. Should there be a need to revise your response contact the Project Administrator to move this article/study back to the Stage 0.

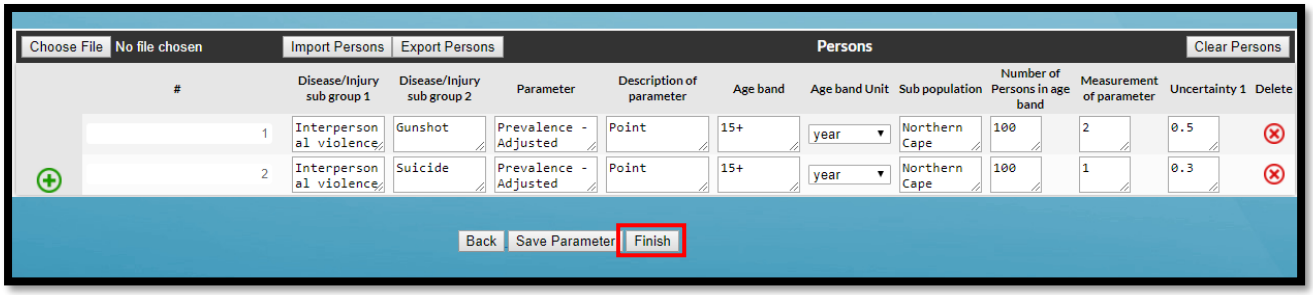


Figure 8-32: Moving into Stage 1

9 Duplicate articles

Duplicate articles may be uploaded in two instances:

I. If an article is uploaded twice for the same condition in error; and,
II. If an article is relevant to more than one condition.

In the first instance, the Project Administrator will be notified that a duplicate article was uploaded and will delete the article.

In the second instance, the Project Administrator and Reviewer 1 will be alerted via a notification on the dashboard and an email with the details of the original article. Note that Reviewer 1 will only be alerted when the original/first article is put into Stage 2. (see Section 6.2: Duplicate notification for reviewers).

Once the first article is in Stage 2, Reviewer 1 will receive a notification on their dashboard. The same information will be copied for Reviewer 1 and Reviewer 2. The duplicate article will then be in Stage 0 and Reviewer 1 (with input from Reviewer 2) will be able to tailor their answers or change responses where necessary.

10 Comparing responses of Reviewers 1 and 2

Once both reviewers have completed Stage 1 (independent review), they can compare their answers. Once consensus is reached on any differences, Reviewer 1 will input (edit) the final responses. Note that both reviewers' responses are visible during the Stage 1 comparison.

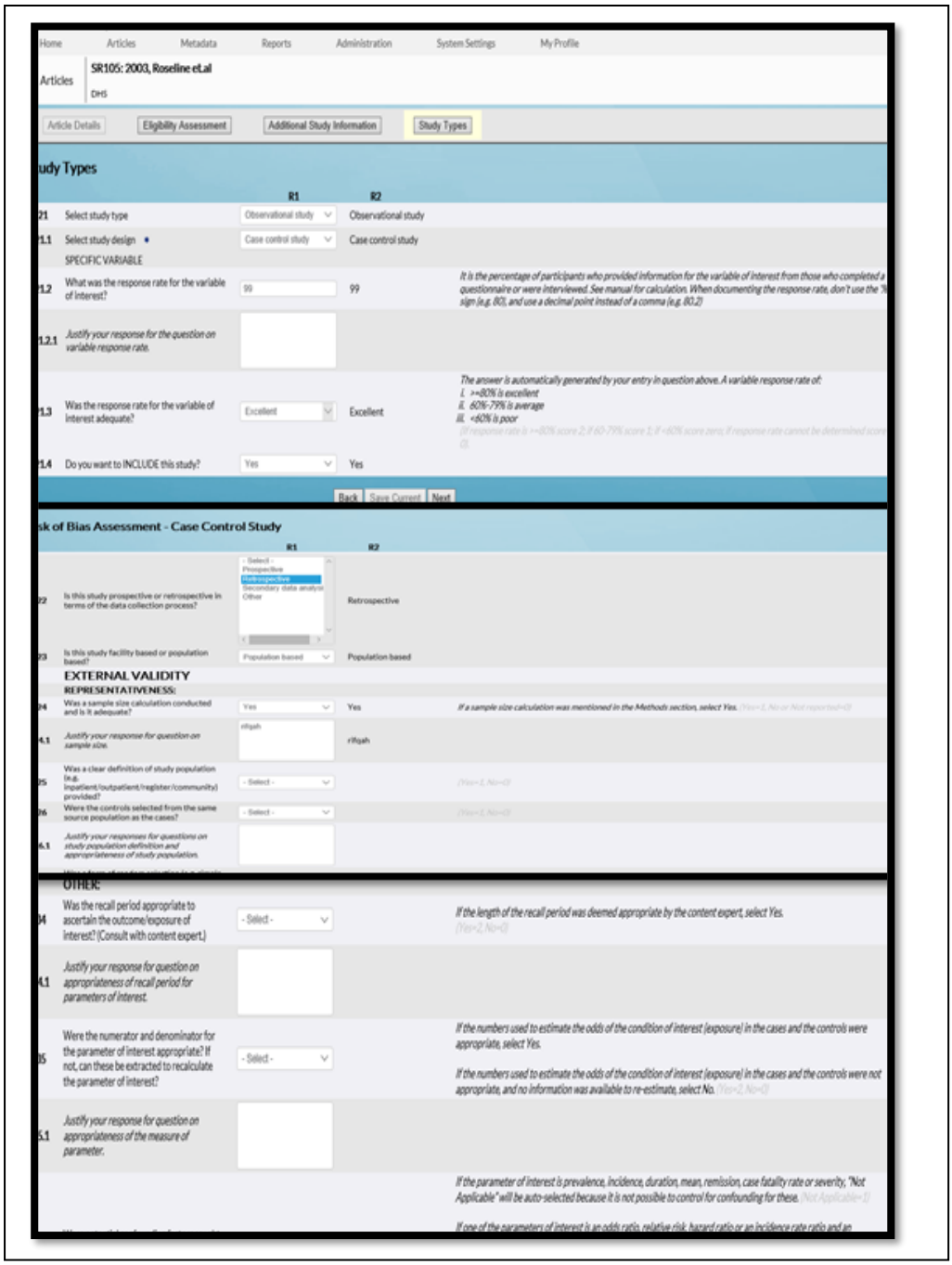


Figure 10-1: Comparing Reviewer 1 and Reviewer 2 answers

10.1 Additional questions on reviewer agreement

At the end of the "Exclusion Criteria", "Inclusion Criteria" and "Risk-of-Bias Assessment" screens, an additional question needs to be answered to capture Reviewer 1 and Reviewer 2's Stage 1 final responses. The answer selected from the drop-down options should be the same as Reviewer 1 and 2's responses in the preceding question indicated by a red outline.

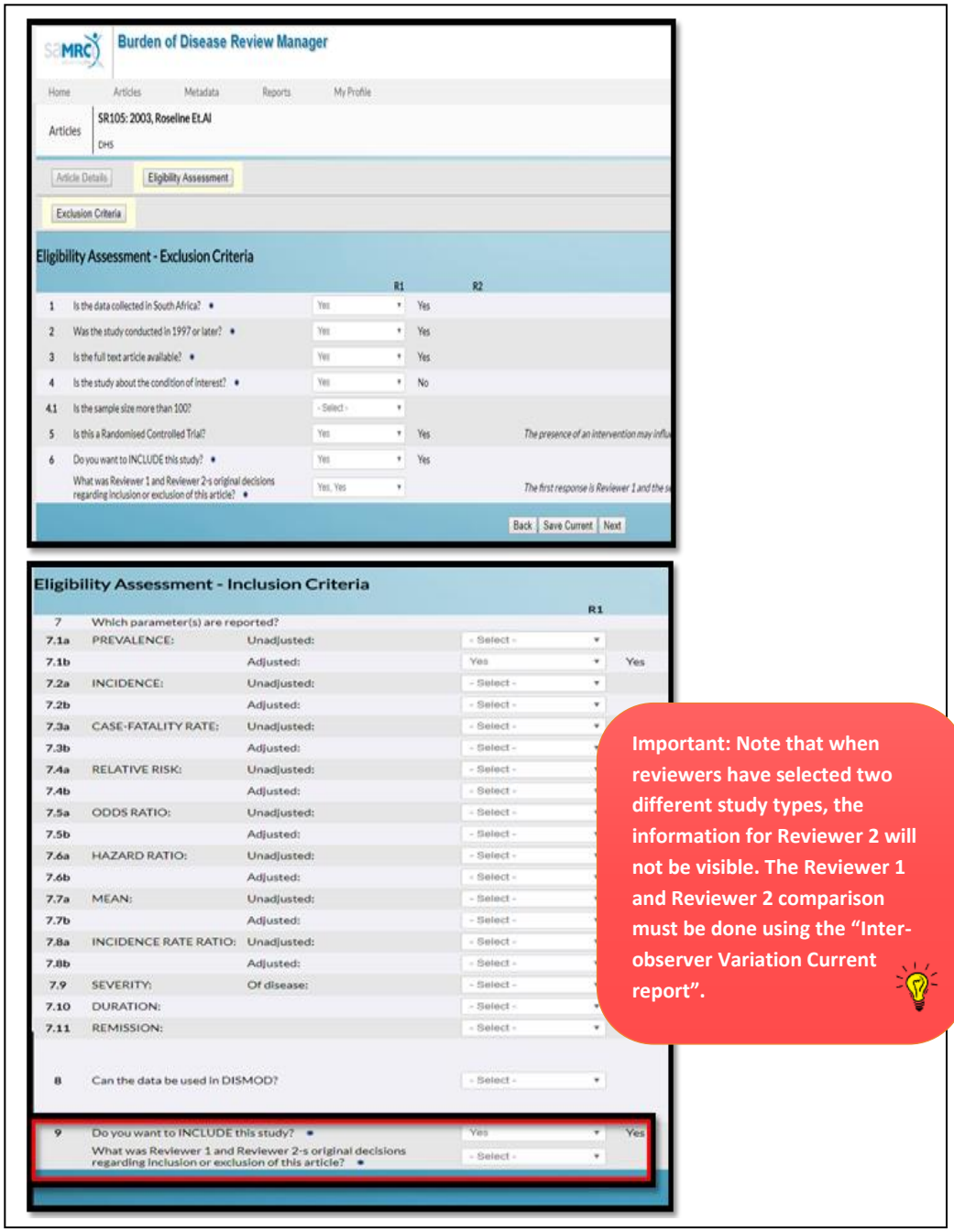


Figure 10-2: Additional questions on reviewer agreement in Eligibility Assessment

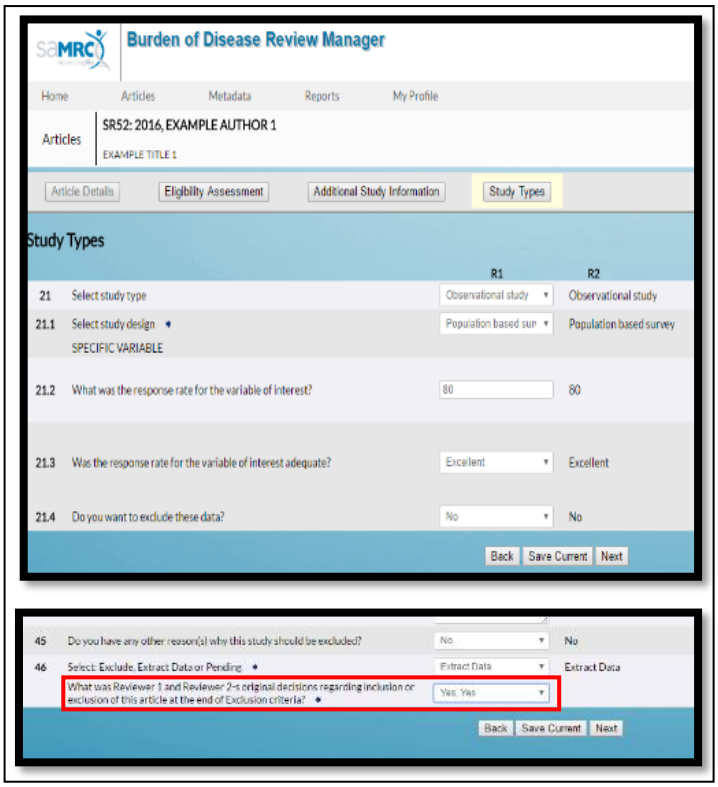
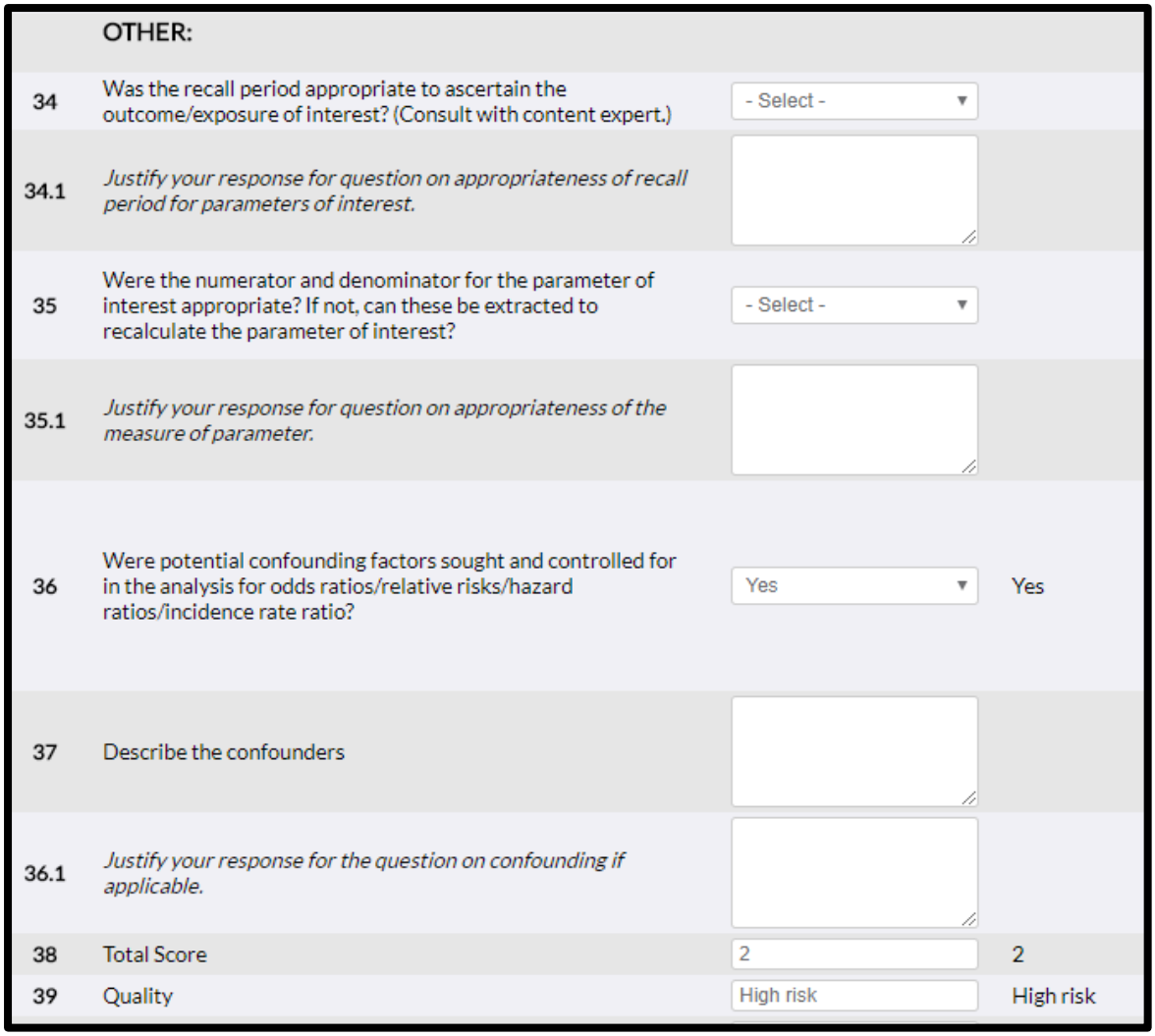


Figure 10-3: Additional question in Study Types

10.2 Data grid display

At this stage, both Reviewers' responses in the data grids become visible. If the responses of Reviewer 2 are more correct, this grid can be exported and imported into the responses of Reviewer 1 (see Section 8.7.4: Data grids). Before importing the correct information into Reviewer 1's data grid, use the "Clear" button to empty the data grid, click the "Save" button and then import the corrected information. Click the Save button after you import the information. In addition to Reviewer 1 and Reviewer 2 responses being displayed in the Study Review Form, differences in their responses can be viewed in the "Inter-observer Variation Report" (see Section 11: Reports).



	OTHER:		
34	Was the recall period appropriate to ascertain the outcome/exposure of interest? (Consult with content expert.)	- Select -	
34.1	*Justify your response for question on appropriateness of recall period for parameters of interest.*		
35	Were the numerator and denominator for the parameter of interest appropriate? If not, can these be extracted to recalculate the parameter of interest?	- Select -	
35.1	*Justify your response for question on appropriateness of the measure of parameter.*		
36	Were potential confounding factors sought and controlled for in the analysis for odds ratios/relative risks/hazard ratios/incidence rate ratio?	Yes	Yes
37	Describe the confounders		
36.1	*Justify your response for the question on confounding if applicable.*		
38	Total Score	2	2
39	Quality	High risk	High risk

Figure 10-4: Both reviewers' grids are visible

10.3 Moving to Stage 2

Once Reviewer 1 has completed the Study Review Form to reflect the final responses, you can then complete the review process by clicking the "Finish" button and move to Stage 2. See below:

Once in Stage 2, the Study Review Form cannot be amended. If there is a need to revise your response, contact the Project Administrator to move this article/study back to the appropriate stage.

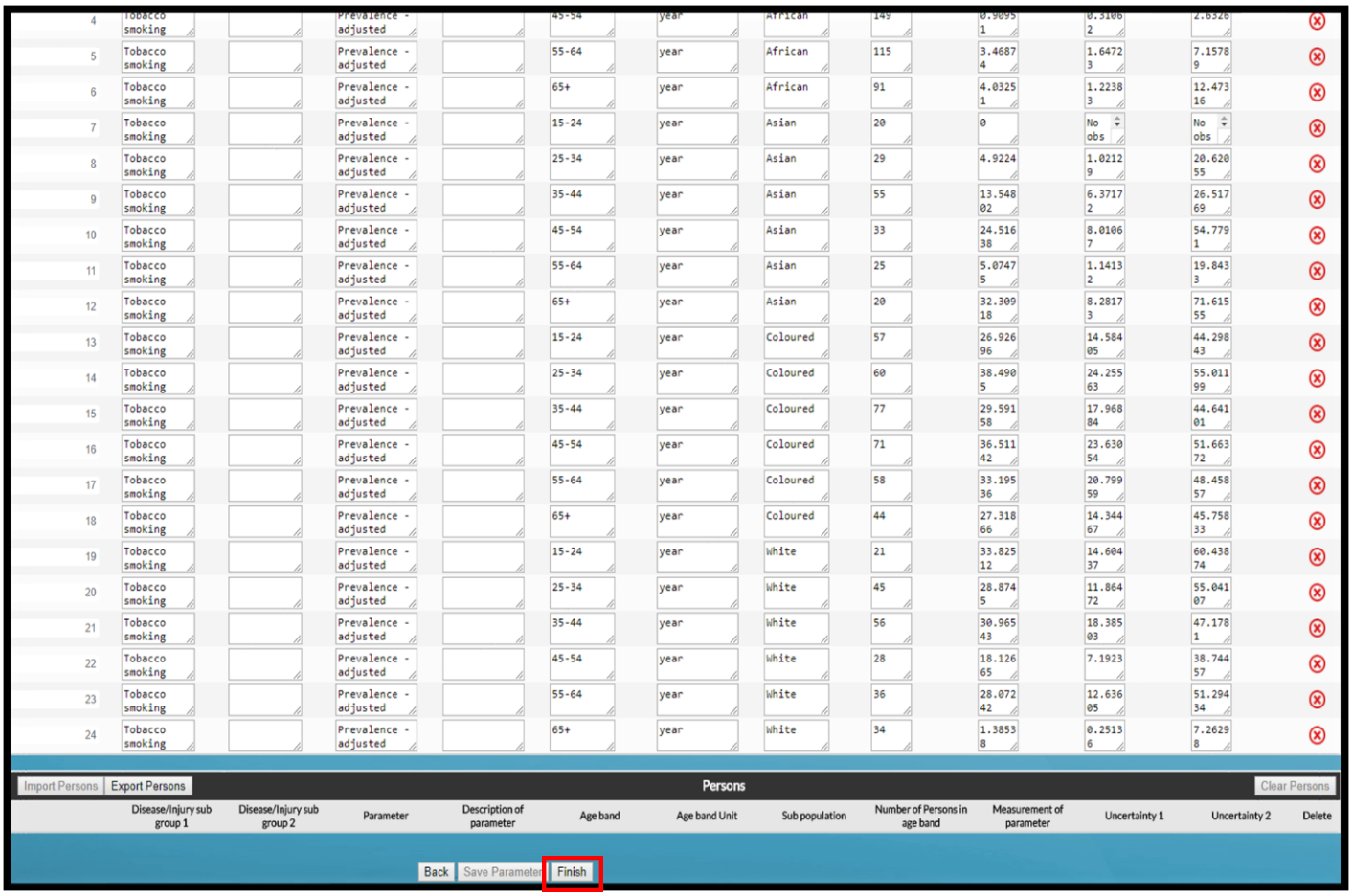


Figure 10-5: Moving to Stage 2

11 Reports

Reports have been set up to assist with presenting a summary of the information entered into the system. Five different reports can be generated displaying available information at different levels of the system. You can access these by clicking on the “Reports” link in the main navigation menu.

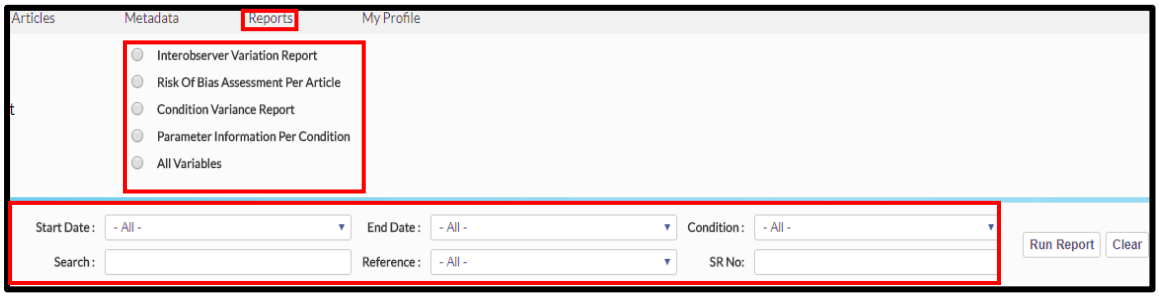


Figure 11-1: Reports

Filters are available to view information in the reports as needed. When running a report for a designated Study Review Form, simply type in the SR number into the “SR No” field located in the filter bar. It is important to type in “SR” followed by the desired SR number with no spacing between “SR” and the number (e.g. SR16). Click the “Run Report” button.

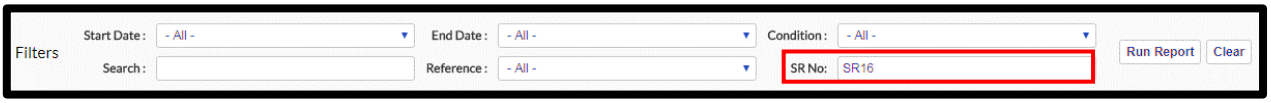


Figure 11-2: Search by study review number

You can view different reports for a specific condition by selecting the desired report first, followed by the condition in the “Condition” filter and click the “Run Report” button. Note that the condition of interest has to be selected in order to download the “Parameter Information per Condition” report.

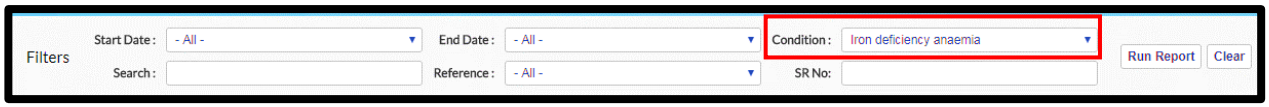


Figure 11-3: Search by specific condition

Similarly, the “Start Date”, “End Date” filter would enable information entered into the system for studies conducted from a particular year to be viewed. Simply type in the “Start Date” and “End Date”, then click the “Run report” button.

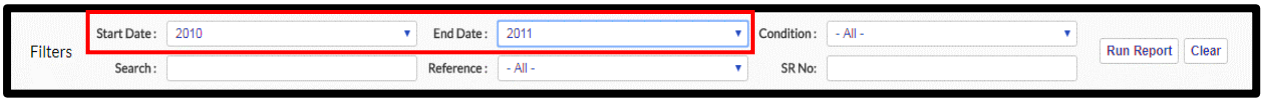


Figure 11-4: Search by study start and end date

The "Search" filter is a universal tool that can be used to generate desired reports by simply typing in a term related to the Study Review Form. This includes the author name, SR No, condition of interest etc. Type in, for example, the desired SR number and click the "Run Report" button.

Figure 11-5: General search

Alternatively, the "Reference" button can be used to generate report(s) for a specific article under review, select the study reference from the "Reference" drop down and click "Run report" to view.

Figure 11-6: Search by reference

Filtered results can be deleted by selecting the "Clear" button.

Figure 11-7: Clear search filters

The "Export" button can be used in place of the "Run Report" button to download reports. Select the desired report and the SR number (e.g. SR16), then click the "Export" button to view.

Figure 11-8: Export report

Reports that can be downloaded include:

- Inter-observer Variation Report
- Risk-of-Bias Assessment per Article Report
- All Variables Report

12 Metadata

The “Metadata” screen displays the list of conditions reviewed and captures important information on the flow of the review process from database searching to data extraction.

12.1 Viewing Metadata

Navigate to the “Metadata” page by clicking on the “Metadata” navigation link.

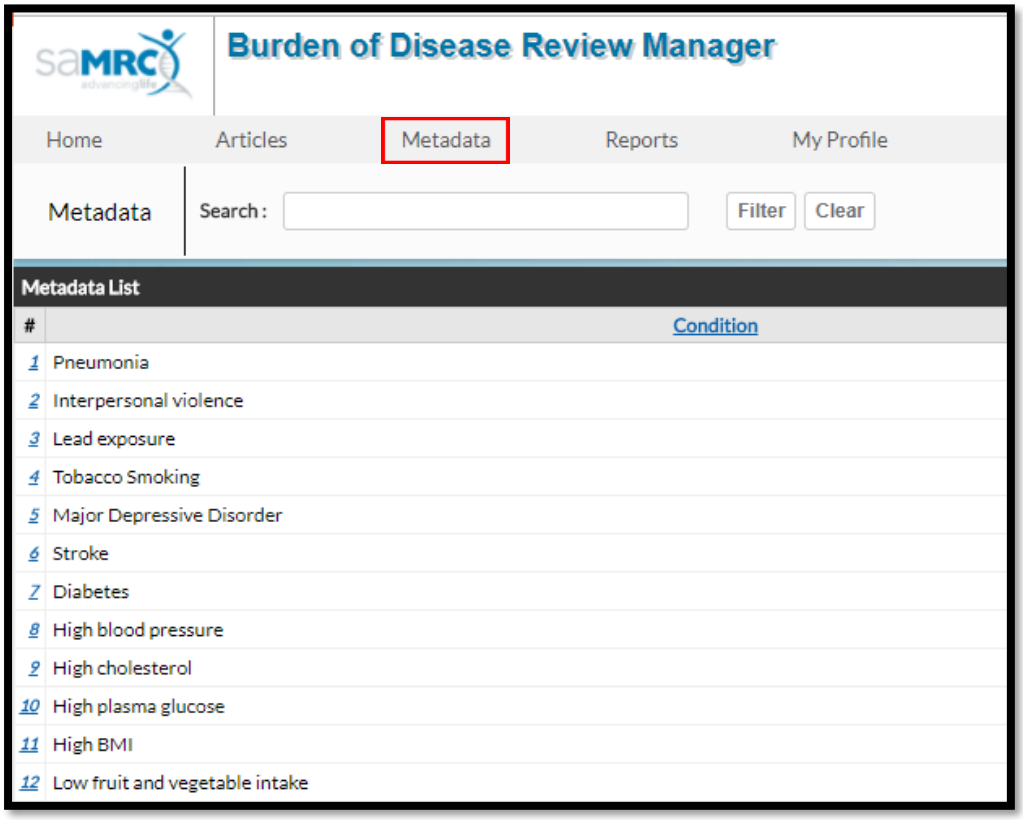
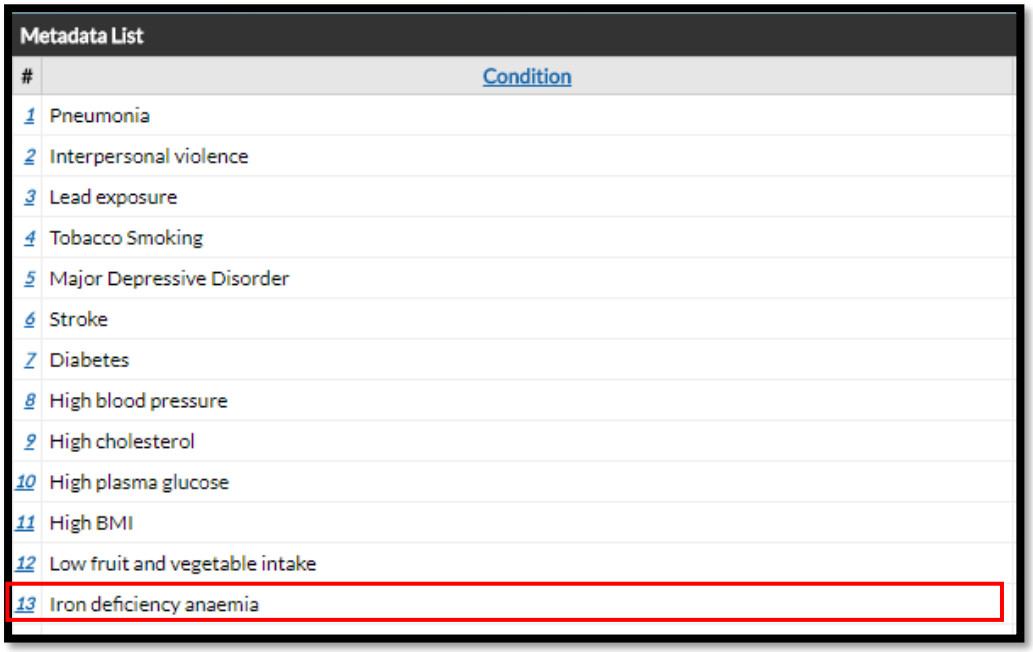


Figure 12-1: Navigation to Metadata

Next, click “Condition” to retrieve the desired metadata. See below:



Metadata List

#	Condition
1	Pneumonia
2	Interpersonal violence
3	Lead exposure
4	Tobacco Smoking
5	Major Depressive Disorder
6	Stroke
7	Diabetes
8	High blood pressure
9	High cholesterol
10	High plasma glucose
11	High BMI
12	Low fruit and vegetable intake
13	Iron deficiency anaemia

Figure 12-2: Condition of interest in Metadata

You will now be able to see the Metadata Details.

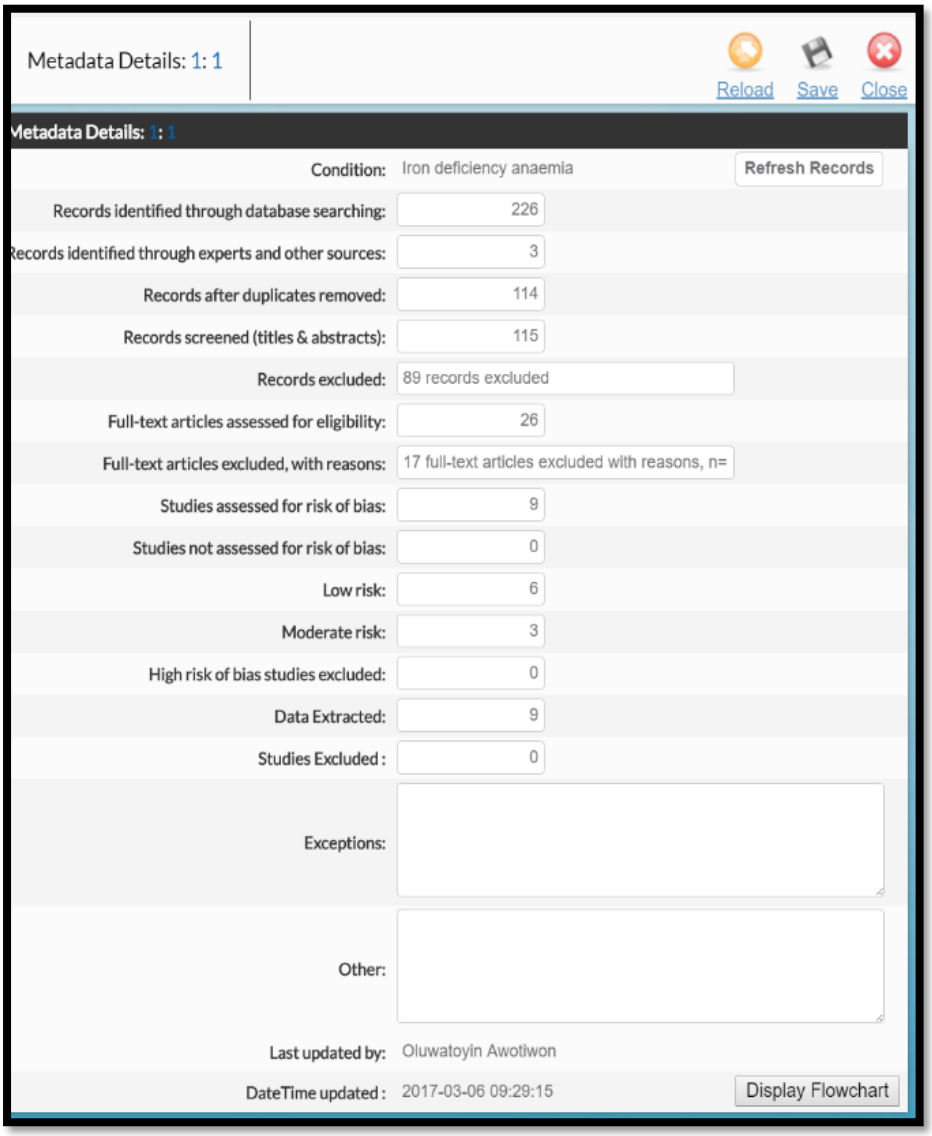


Figure 12-3: Metadata Details page

To update the metadata, simply fill in the desired values in the editable text fields and click the “Save” button.

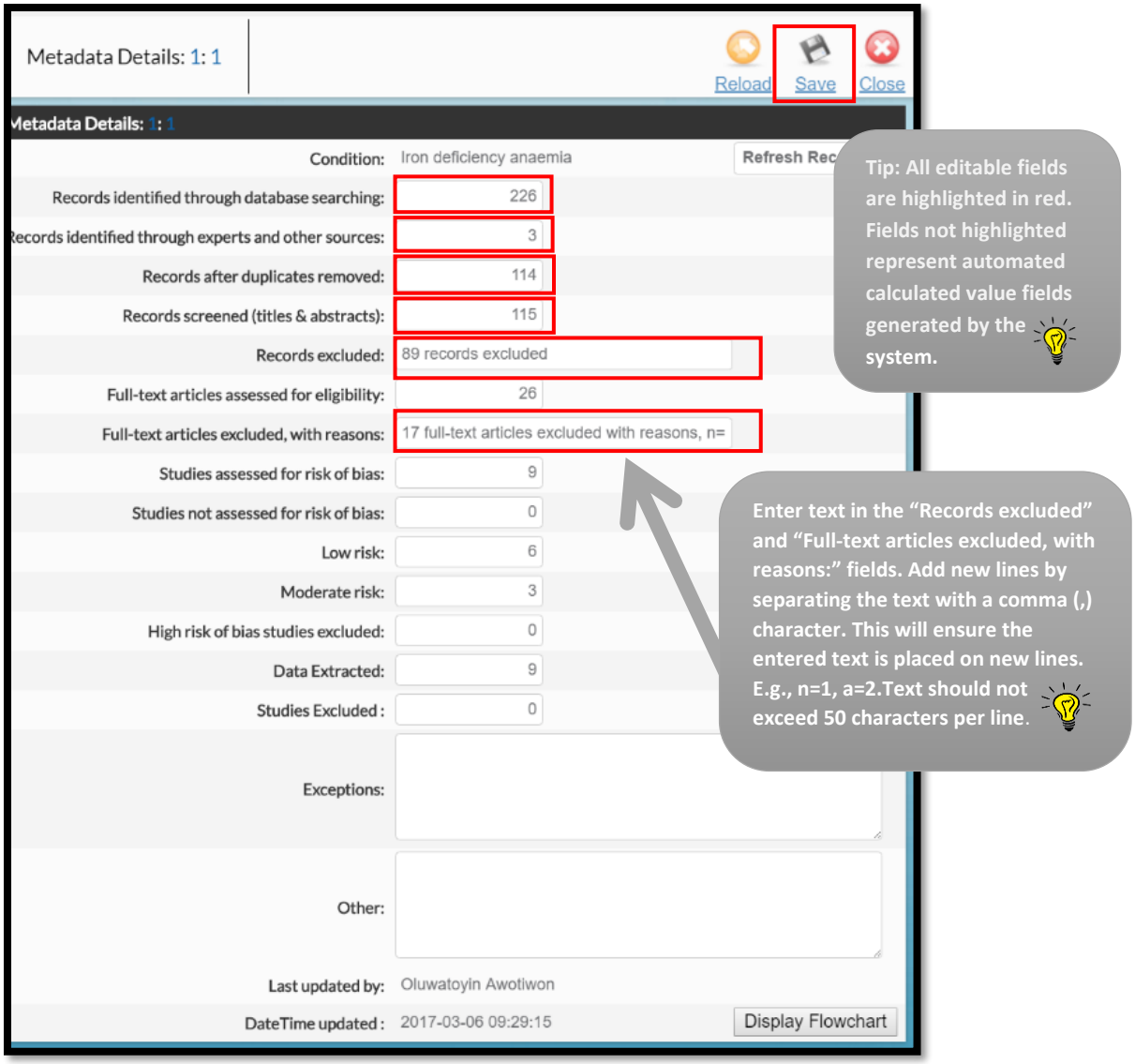


Figure 12-4: Filling in the Metadata Details Page

The “Refresh Records” button is similar to the “Save” button and updates the flowchart with the latest information added to the “Metadata Details” screen. To refresh the metadata, simply click the “Refresh Records” button. To view the flowchart in PDF format, click the “Display Flow Chart” button.

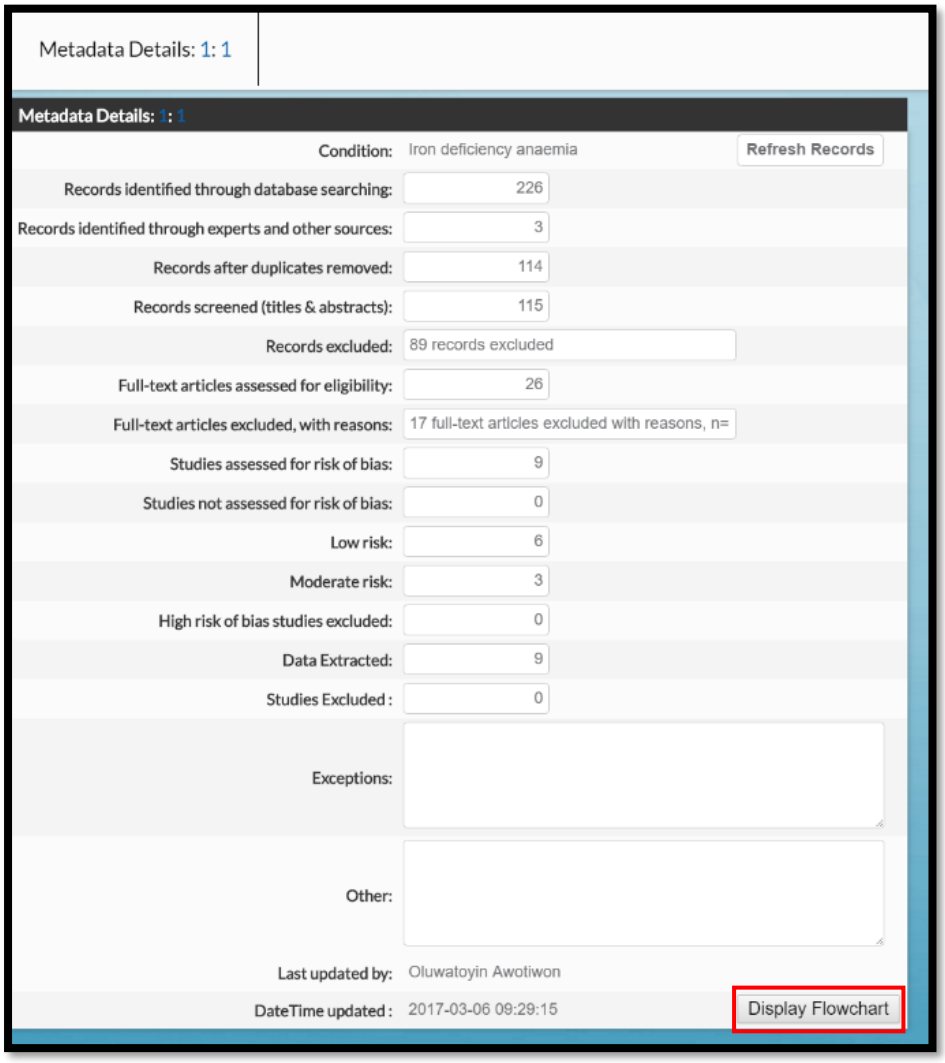


Figure 12-5: Metadata refresh records

To display the printable metadata flow diagram, click the “Display Flowchart” button.

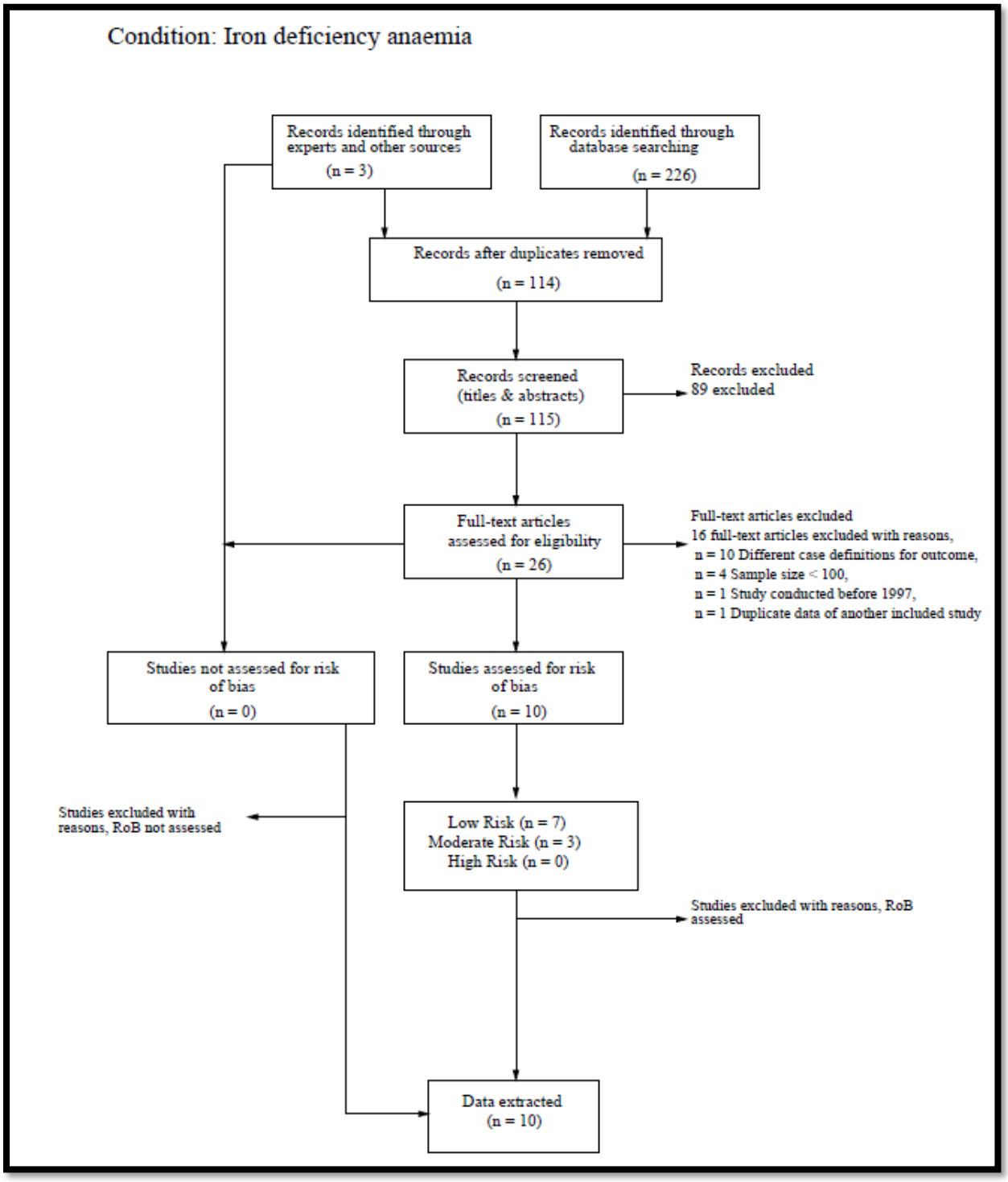


Figure 12-6: Metadata PDF

References

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Appendices

Appendix A: Cohort study

RISK ASSESSMENT - COHORT STUDY		
EXTERNAL VALIDITY		
	REPRESENTATIVENESS:	
24	Was a sample-size calculation conducted and is it adequate?	If a sample-size calculation was mentioned in the Methods section, select Yes. (Yes=1, No or Not reported=0)
25	Was a clear definition of study population (e.g. inpatient/outpatient/register/community) provided?	(Yes=1, No=0)
26	Were the controls selected from the same source population as the exposed?	(Yes=1, No=0)
27	Was a form of random selection (e.g. simple random, stratified, cluster and systematic) used to select the sample?	If a form of random selection was done, select Yes. (No score)
27.1	Name the other sampling strategy (e.g. non-random, consecutive, convenience, case by case)? Describe.	Describe the sampling strategy used.
27.2	Was the sampling method appropriate for the research question?	If the sampling strategy used was appropriate for the research question described for your condition of interest in the protocol, select Yes. (Yes=2, No=0)
28	***NON-RESPONSE BIAS AND LOSS TO FOLLOW-UP:***	
28.1	From those individuals who met the inclusion criteria, were there significant differences by demographic characteristics between those who agreed to participate and those who refused to participate? (See Help for retrospective review of records.)	If authors reported no significant differences between participants and non-participants, select Yes.
		If there were significant differences between the participants and non-participants, and the authors adjusted for this in the analysis, select Yes.

RISK ASSESSMENT - COHORT STUDY		
		If no adjustment was done, select No.
		If this is a retrospective review of medical records, and the authors have reported the number of missing folders for the exposed and the unexposed during the study period, select Yes. (Yes=1, No or Not reported=0)
28.2	Was an effort made to limit loss to follow-up?	If the authors made an effort to prevent loss to follow-up in the design of their study, select Yes. (Yes=1, No=0)
28.3	Was there no differential loss to follow-up between the exposed and unexposed groups?	If there was no difference in the percentage of loss to follow-up between the exposed and the unexposed groups, select Yes.
		If there was a difference in the percentage of loss to follow-up between the exposed and the unexposed groups, did the authors establish whether the loss to follow-up was related to the exposure and/or outcome?
		(i) If a sensitivity analysis was performed to assess the impact of loss to follow-up in both groups, select Yes.
		(ii) If such an analysis was not performed, select No. (Yes=1, No=0)
28.4	Was the follow-up of participants (cohorts) adequate?	If loss to follow-up for the overall study was <20%, this is adequate, select Yes.
		If loss to follow-up was not reported or $\geq$ 20%, this is not adequate, select No.
		Note: If the information is available, calculate the percentage loss to follow-up and select your response based on the instructions given above (Yes=1, No=0)
INTERNAL VALIDITY		
	CASES:	
29	Were the cases classified using the ICD codes or was an acceptable case definition used? (Consult with content expert.)	Most conditions have an international/recognised definition, e.g. a case of diarrhoea is defined by WHO as “the passage of 3 or more loose or liquid stools per day”.

RISK ASSESSMENT - COHORT STUDY		
		If such a definition was used, select Yes. Consult with your content expert if you are unclear on what the international or recognised definition is for your condition of interest. (Yes=1, No=0)
29.1	What is the case definition?	Write out the case definition and ICD code (if stated) for the condition of interest as reported by the authors.
30	Was the ascertainment of outcome done from medical records? Select from the following: (A) diagnostic/laboratory test, (B) medical records clinical assessment, (C) structured interview/self-report, (D) no description.	A/B=2, C=1, D=0
	DATA COLLECTION:	
31	Were data collected directly from the participants or if a proxy (a representative of the participant) was used, was it appropriate?	If data were collected directly from the participants, select Yes.
		If the primary caregiver responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select Yes.
		If the respondent was not the primary caregiver and responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select No. (Yes=1, No=0)
32	Was the same method used for data collection for all participants for the condition of interest? If a different method was used, was it adequate?	The mode of data collection is the method used for collecting information from the participants. If the same method was not used for all participants for the condition of interest, select No. For example, a sphygmomanometer was used to establish a blood-pressure measurement for some participants and other participants self-reported on their last blood-pressure measurement.
		If the same method was not used for all participants for the condition of interest but justifiable and acceptable methods were used, select Yes. For example, a finger prick was used to obtain blood samples from older participants, while a heel or toe prick was used for infants. (Yes=1 No=0)

RISK ASSESSMENT - COHORT STUDY		
	UNCERTAINTY:	
33	Was the parameter of interest reported with uncertainty, i.e. Standard Deviation (SD) or Standard Error (SE) or 95% Confidence Interval (CI)?	If uncertainty estimates reported for all or at least one of the parameters, select Yes. (Yes=1, No=0) Note: For surveys where uncertainty was not reported but can be calculated, select Yes.
	OTHER:	
34	Was the follow-up period long enough to ascertain the outcome of interest? (Consult with content expert.)	If the duration of the follow-up was deemed appropriate by the content expert, select Yes. (Yes=2, No=0)
35	Were the numerator and denominator for the parameter of interest appropriate? If not, can these be extracted to recalculate the parameter of interest?	If the numbers used for the numerator and denominator to estimate incidence, or the numbers used for the exposed and unexposed groups to estimate relative risk or hazard ratio were appropriate, select Yes. If the numerator and the denominator used to calculate the incidence, or the numbers used for the exposed and unexposed groups for the estimation of relative risk or hazard ratios were not appropriate, and no information was available to re-estimate, select No. (Yes=2, No=0)
36	Were potential confounding factors sought and controlled for in the analysis for odds ratios/relative risks/hazard ratios/incidence-rate ratio?	If the parameter of interest is prevalence, incidence, duration, mean, remission, case fatality rate or severity, “Not Applicable” will be auto-selected because it is not possible to control for confounding for these. (Not Applicable=1) If one of the parameters of interest is an odds ratio, relative risk, hazard ratio or an incidence-rate ratio and an adjustment was done for potential confounders, select Yes. If one of the parameters of interest is an odds ratio, relative risk, hazard ratio or an incidence-rate ratio and no adjustment was done for potential confounders, select No. (Yes=1, No=0)

RISK ASSESSMENT - COHORT STUDY		
		Note: Where appropriate, when potential confounders were controlled for in the analysis for either all or at least one of the parameters, select Yes.

Appendix B: Case-control study

RISK ASSESSMENT - CASE-CONTROL STUDY		
EXTERNAL VALIDITY		
	REPRESENTATIVENESS:	
24	Was a sample size calculation conducted and is it adequate?	If a sample-size calculation was mentioned in the Methods section, select Yes. (Yes=1, No or Not reported=0)
25	Was a clear definition of study population (e.g. inpatient/ outpatient/ register/ community) provided?	(Yes=1, No=0)
26	Were the controls selected from the same source population as the cases?	(Yes=1, No=0)
27	Was a form of random selection (e.g. simple random, stratified, cluster and systematic) used to select the sample?	If a form of random selection was done, select Yes. (No score)
27.1	Name the other sampling strategy (e.g. non-random, consecutive, convenience, case by case)? Describe.	Describe the sampling strategy used.
27.2	Was the sampling method appropriate for the research question?	If the sampling strategy used was appropriate for the research question described for your condition of interest in the protocol, select Yes. (Yes=2, No=0)
28	***NON-RESPONSE BIAS:***	
28.1	From those individuals who met the inclusion criteria, did the authors describe any significant differences by demographic characteristics between those who agreed to participate and those who refused to participate? (See Help for retrospective review of records.)	Among those who participated, were the cases and controls similar in terms of demographic characteristics? If there was a difference in the non-response rate between the cases and the controls, did the authors establish reasons for non-response?
		(i) If a sensitivity analysis was performed to assess the impact of non-response in both groups, select Yes.

RISK ASSESSMENT - CASE-CONTROL STUDY		
		(ii) If such an analysis was not performed, select No. (Yes=2, No=0)
28.2	Among those who participated in the study, were the cases and controls similar in terms of demographic characteristics?	If the response rate for the overall study was less than 60%, select No.
		If there was no difference in the non-response rate between the cases and the controls, select Yes.
		If there was a difference in the non-response rate between the cases and the controls, did the authors establish reasons for non-response?
		(i) If a sensitivity analysis was performed to assess the impact of non-response in both groups, select Yes.
		(ii) If such an analysis was not performed, select No. (Yes=2, No or Not reported=0)
	INTERNAL VALIDITY	
	CASES:	
29	Were the cases classified using the ICD codes or was an acceptable case definition used? (Consult with content expert.)	Most conditions have an international/recognised definition, e.g. a case of diarrhoea is defined by WHO as “the passage of 3 or more loose or liquid stools per day”.
		If such a definition was used, select Yes. Consult with your content expert if you are unclear on what the international or recognised definition is for your condition of interest. (Yes=1, No=0)
29.1	What is the case definition?	Write out the case definition and ICD code (if stated) for the condition of interest as reported by the authors.
30	Was the ascertainment of exposure done from medical records? Select from the following: (A) diagnostic/laboratory test, (B) medical records/clinical assessment, (C) structured interview/self-report, (D) no description.	A/B=2, C=1, D=0

RISK ASSESSMENT - CASE-CONTROL STUDY		
	DATA COLLECTION:	
31	Were data collected directly from the participants or if a proxy (a representative of the participant) was used, was it appropriate?	If data were collected directly from the participants, select Yes.
		If the primary caregiver responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select Yes.
		If the respondent was not the primary caregiver and responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select No. (Yes=1, No=0)
32	Was the same method used for data collection for all participants for the condition of interest? If a different method was used, was it adequate?	The mode of data collection is the method used for collecting information from the participants. If the same method was not used for all participants for the condition of interest, select No. For example, a sphygmomanometer was used to establish a blood-pressure measurement for some participants and other participants self-reported on their last blood-pressure measurement.
		If the same method was not used for all participants for the condition of interest but justifiable and acceptable methods were used, select Yes. For example, a finger prick was used to obtain blood samples from older participants, while a heel or toe prick was used for infants. (Yes=1 No=0)
	UNCERTAINTY:	
33	Was the parameter of interest reported with uncertainty, i.e. Standard Deviation (SD) or Standard Error (SE) or 95% Confidence Interval (CI)?	If uncertainty estimates were reported for all or at least one of the parameters, select Yes. (Yes=1, No=0)
		Note: For surveys where uncertainty was not reported but can be calculated, select Yes.
	OTHER:	

RISK ASSESSMENT - CASE-CONTROL STUDY		
34	Was the recall period appropriate to ascertain the outcome/exposure of interest? (Consult with content expert.)	If the length of the recall period was deemed appropriate by the content expert, select Yes. (Yes=2, No=0)
35	Were the numerator and denominator for the parameter of interest appropriate? If not, can these be extracted to recalculate the parameter of interest?	If the numbers used to estimate the odds of the condition of interest (exposure) in the cases and the controls were appropriate, select Yes.
		If the numbers used to estimate the odds of the condition of interest (exposure) in the cases and the controls were not appropriate, and no information was available to re-estimate, select No. (Yes=2, No=0)
36	Were potential confounding factors sought and controlled for in the analysis for odds ratios/relative risks/hazard ratios/incidence-rate ratio?	If the parameter of interest is prevalence, incidence, duration, mean, remission, case fatality rate or severity, “Not Applicable” will be auto-selected because it is not possible to control for confounding for these. (Not Applicable=1)
		If one of the parameters of interest is an odds ratio, relative risk, hazard ratio or an incidence-rate ratio and an adjustment was done for potential confounders, select Yes.
		If one of the parameters of interest is an odds ratio, relative risk, hazard ratio or an incidence-rate ratio and no adjustment was done for potential confounders, select No. (Yes=1, No=0)
		Note: Where appropriate, when potential confounders were controlled for in the analysis for either all or at least one of the parameters, select Yes.

Appendix C: Cross-sectional study

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
EXTERNAL VALIDITY		
	REPRESENTATIVENESS:	
24	Was a sample-size calculation conducted and is it adequate?	If a sample-size calculation was mentioned in the Methods section, select Yes. (Yes=1, No or Not reported=0)
25	Was a clear definition of study population (e.g. inpatient/outpatient/register/community) provided?	(Yes=1, No=0)
26	Was the sampling frame a true or close representation of the population/community in which the study is conducted? (Consult with content expert.)	The sampling frame is the list from which the potential respondents are drawn. It must be representative of the target population.
		If the sampling frame is a true or close representation of the target population, select Yes. If not, select No.
		For example, the study was a national health survey of people 15 years and over and the sample was drawn from a list that included all individuals in the population aged 15 years and over. Select Yes. (Yes=1, No=0)
		Note: If a comparison was performed between the study population and the target population, there should not be more than a 5% difference between these for the various reporting domains.
27	Was a form of random selection (e.g. simple random, stratified, cluster and systematic) used to select the sample or was a census undertaken?	If a form of random selection was done, select Yes. (No score)
27.1	Name the other sampling strategy (e.g. non-random, consecutive, convenience, case by case)? Describe.	Describe the sampling strategy used.

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
27.2	Was the sampling method appropriate for the research question?	If the sampling strategy used was appropriate for the research question described for your condition of interest in the protocol, select Yes. (Yes=2, No=0)
28	***NON-RESPONSE BIAS:***	
28.1	Was the response rate for the study reported?	If the response rate was not reported and there is insufficient information to estimate the response rate, select Not Reported.
		If the response rate was not reported and there is sufficient information to estimate the response rate, select Not reported but can calculate.
		If the response rate was reported, select Reported. (No score)
28.2	What was the response rate for the study?	If response rate is not reported for the study, use the number of people who participated in the study as the numerator, and the number of people who were eligible to participate as the denominator, to estimate the response rate (as a percentage).
		For a retrospective review of medical records or case notes: If the authors reported the number of missing cases for the study period, estimate the percentage of included cases reviewed over expected cases.
28.3	Was the response rate adequate?	The answer is automatically generated by your entry for the question above. A response rate of: (i) ≥80% is excellent (ii) 60%-79% is average (iii) <60% is poor. (If response rate is ≥80% score 2; if 60-79% score 1; if <60% score zero; if response rate cannot be determined score 0.)
28.4	Were there similarities between participants and non-participants in relation to demographic characteristics? (See Help for retrospective review of records.)	If the authors reported that there were no significant differences with respect to demographic characteristics between participants and non-participants, select Yes.

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
		If the authors reported there were significant differences between participants and non-participants, and the authors adjusted for this in the analysis, select Yes. If no adjustment was done, select No.
		If the authors reported that there were no significant differences with respect to demographic characteristics between participants and non-participants, select Yes.
		If the authors reported there were significant differences between participants and non-participants, and the authors adjusted for this in the analysis, select Yes. If no adjustment was done, select No.
		For a retrospective review of medical records or case notes:
		(i) If the authors reported that there were no significant differences with respect to demographic characteristics between missing and included cases that were eligible for inclusion in the study, select Yes.
		(ii) If the authors reported there were significant differences with respect to demographic characteristics between missing and included cases that were eligible for inclusion in the study, and the authors adjusted for this in the analysis, select Yes. If no adjustment was done, select No. (Yes=2, No or Not reported=0)
	INTERNAL VALIDITY	
	CASES:	
29	Were the cases classified using the ICD codes or was an acceptable case definition used? (Consult with content expert.)	Most conditions have an international/recognised definition, e.g. a case of diarrhoea is defined by WHO as “the passage of 3 or more loose or liquid stools per day”.

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
		If such a definition was used, select Yes. Consult with your content expert if you are unclear on what the international or recognised definition is for your condition of interest. (Yes=1, No=0)
29.1	What is the case definition?	Write out the case definition and ICD code (if stated) for the condition of interest as reported by the authors.
30	Were the study instruments used to measure the parameter of interest shown to have reliability and validity in this study or in a previous study, via piloting, test-retesting? (Consult with content expert.)	Each parameter measure should have a standard recognised method used for measurement. The content expert will be able to advise on whether the mode of measurement is acceptable. (Yes=2, No=0)
	DATA COLLECTION:	
31	Were data collected directly from the participants or if a proxy (a representative of the participant) was used, was it appropriate?	If data were collected directly from the participants, select Yes.
		If the primary caregiver responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select Yes.
		If the respondent was not the primary caregiver and responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select No. (Yes=1, No=0)
32	Was the same method used for data collection for all participants for the condition of interest? If a different method was used, was it adequate?	The mode of data collection is the method used for collecting information from the participants. If the same method was not used for all participants for the condition of interest, select No. For example, a sphygmomanometer was used to establish a blood-pressure measurement for some participants and other participants self-reported on their last blood-pressure measurement.

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
		If the same method was not used for all participants for the condition of interest but justifiable and acceptable methods were used, select Yes. For example, a finger prick was used to obtain blood samples from older participants, while a heel or toe prick was used for infants. (Yes=1 No=0)
	UNCERTAINTY:	
33	Was the parameter of interest reported with uncertainty, i.e. Standard Deviation (SD) or Standard Error (SE) or 95% Confidence Interval (CI)?	If uncertainty estimates were reported for all or at least one of the parameters, select Yes. (Yes=1, No=0)
		Note: For surveys where uncertainty was not reported but can be calculated, select Yes.
	OTHER:	
34	Was the length of recall period for the parameter of interest appropriate to ascertain outcome/exposure? (Consult with content expert.)	If the length of the recall period was deemed appropriate by the content expert, select Yes. (Yes=2, No=0)
35	Were the numerator and denominator for the parameter of interest appropriate? If not, can these be extracted to recalculate the parameter of interest?	If the numbers used to estimate the parameter of interest were appropriate, select Yes.
		If the numbers used to estimate the parameter of interest were not appropriate, and no information was available to re-estimate, select No. (Yes=2, No=0)
36	Were potential confounding factors sought and controlled for in the analysis for odds ratios/relative risks/hazard ratios/incidence-rate ratio?	If the parameter of interest is prevalence, incidence, duration, mean, remission, case fatality rate or severity, “Not Applicable” will be auto-selected because it is not possible to control for confounding for these. (Not Applicable=1)
		If one of the parameters of interest is a relative risk, hazard ratio or an incidence-rate ratio and an adjustment was done for potential confounders, select Yes.

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
		If one of the parameters of interest is a relative risk, hazard ratio or an incidence rate ratio and no adjustment was done for potential confounders, select No. (Yes=1, No=0)
		Note: Where appropriate, when potential confounders were controlled for in the analysis for either all or at least one of the parameters, select Yes.

Appendix D: Population-based survey

RISK ASSESSMENT - POPULATION-BASED SURVEY		
EXTERNAL VALIDITY		
	REPRESENTATIVENESS:	
24	Was a sample size calculation conducted and is it adequate?	If a sample size calculation was mentioned in the Methods section, select Yes. (Yes=1, No or Not reported=0)
25	Is the study population a close representation of the target population (e.g., national population) in relation to relevant variables (e.g. age, sex, or other demographic characteristics)?	The target population refers to the group of people or entities to which the results of the study will be generalised. For example, if you are investigating burn-out in economically active individuals and your study population is comprised of retirees post-60 years of age, then this does not represent your target population. (Yes=1, No=0)
26	Was the sampling frame a true or close representation of the population/community in which the study is conducted? (Consult with content expert.)	The sampling frame is the list from which the potential respondents are drawn. It must be representative of the population.
		If the sampling frame is a true or close representation of the target population, select Yes. If not, select No.
		For example, the study was a national health survey of people 15 years and over and the sample was drawn from a list that included all individuals in the population aged 15 years and over. Select Yes. (Yes=1, No=0)
		Note: If a comparison was performed between the study population and the target population, there should not be more than a 5% difference between these for the various reporting domains.
27	Was a form of random selection (e.g. simple random, stratified, cluster and systematic) used to select the sample or was a census undertaken?	If a form of random selection was done, select Yes. (No score)

RISK ASSESSMENT - POPULATION-BASED SURVEY		
27.1	Name the other sampling strategy (e.g. non-random, consecutive, convenience, case by case)? Describe.	Describe the sampling strategy used.
27.2	Was the sampling method appropriate for the research question?	If the sampling strategy used was appropriate for the research question described for your condition of interest in the protocol, select Yes. (Yes=2, No=0)
28	***NON-RESPONSE BIAS:***	
28.1	Was the overall survey response rate reported for this condition of interest?	If the response rate was not reported and there is insufficient information to estimate the response rate, select Not Reported.
		If the response rate was not reported and there is sufficient information to estimate the response rate, select Not reported but can calculate. Overall survey response rate for this condition of interest = Household response rate multiplied by Individual (interview) response rate multiplied by the variable/item response rate.
		If the response rate was reported, select Reported. (No score)
28.2	What was the overall survey response rate for this condition of interest?	If response rate is not reported for the survey then calculate using the following formula: (i) the household response rate = the number of households who participated in the survey/ number of households that were potentially eligible to participate in the survey; (ii) the individual interview response rate = the total number all the individuals who were interviewed/ the total number of all the individuals in each household that were eligible to be interviewed; and, (iii) the variable/item response rate = the total number of individuals who provided information for the variable/item of interest/ the total number of individuals who completed a questionnaire or where interviewed. Estimate the response rate as a percentage. When documenting the response rate, use a decimal point e.g. 69.3. Do not use the % sign (e.g. 69.3%).
		For a retrospective review of medical records or case notes:

RISK ASSESSMENT - POPULATION-BASED SURVEY		
		If the author reported the number of missing cases for the study period, estimate the percentage of included cases reviewed over expected cases.
28.3	Was the overall response rate for this condition of interest adequate?	The answer is automatically generated by your entry for the question above. A response rate of: (i) ≥80% is excellent (ii) 60%-79% is average (iii) <60% is poor. (If response rate is ≥80% score 2; if 60-79% score 1; if <60% score zero; if response rate cannot be determined score 0)
28.4	Were there similarities between participants and non-participants in relation to demographic characteristics? (See Help for retrospective review of records.)	If authors reported that there were no significant differences with respect to demographic characteristics between participants and non-participants, select Yes.
		If authors reported there were significant differences between participants and non-participants, and the authors adjusted for this in the analysis, select Yes. If no adjustment was done, select No.
		For a retrospective review of medical records or case notes:
		(i) If the authors reported that there were no significant differences with respect to demographic characteristics between missing and included cases that were eligible for inclusion in the study, select Yes.
		(ii) If the authors reported there were significant differences with respect to demographic characteristics between missing and included cases that were eligible for inclusion in the study, and the authors adjusted for this in the analysis, select Yes. If no adjustment was done, select No. (Yes=2, No or Not reported=0)
INTERNAL VALIDITY		
	CASES:	
29	Were the cases classified using the ICD codes or was an acceptable case definition used? (Consult with content expert.)	Most conditions have an international/recognised definition, e.g. a case of diarrhoea is defined by WHO as “the passage of 3 or more loose or liquid stools per day”.

RISK ASSESSMENT - POPULATION-BASED SURVEY		
		If such a definition was used, select Yes. Consult with your content expert if you are unclear on what the international or recognised definition is for your condition of interest. (Yes=1, No=0)
29.1	What is the case definition?	Write out the case definition and ICD code (if stated) for the condition of interest as reported by the authors.
30	Were the study instruments used to measure the parameter of interest shown to have reliability and validity in this study or in a previous study, via piloting, test-retesting? (Consult with content expert.)	Each parameter measure should have a standard recognised method used for measurement. The content expert will be able to advise on whether the mode of measurement is acceptable. (Yes=2, No=0)
	DATA COLLECTION:	
31	Were data collected directly from the participants or, if a proxy (a representative of the participant) was used, was it appropriate?	If data were collected directly from the participants, select Yes.
		If the primary caregiver responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select Yes.
		If the respondent was not the primary caregiver and responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select No. (Yes=1, No=0)
32	Was the same method used for data collection for all participants for the condition of interest? If a different method was used, was it adequate?	The mode of data collection is the method used for collecting information from the participants. If the same method was not used for all participants for the condition of interest, select No. For example, a sphygmomanometer was used to establish a blood pressure measurement for some participants and other participants self-reported on their last blood pressure measurement.
		If the same method was not used for all participants for the condition of interest but justifiable and acceptable methods were used, select Yes. For example, a finger prick was used to obtain blood samples from older participants, while a heel or toe prick was used for infants. (Yes=1 No=0)

RISK ASSESSMENT - POPULATION-BASED SURVEY		
	UNCERTAINTY:	
33	Was the parameter of interest reported with uncertainty, i.e. Standard Deviation (SD) or Standard Error (SE) or 95% Confidence Interval (CI)?	If uncertainty estimates were reported for all or at least one of the parameters, select Yes. (Yes=1, No=0)
		Note: For surveys where uncertainty was not reported but can be calculated, select Yes.
	OTHER:	
34	Was the length of recall period for the parameter of interest appropriate to ascertain outcome/exposure? (Consult with content expert.)	If the length of the recall period was deemed appropriate by the content expert, select Yes. (Yes=2, No=0)
35	Were the numerator and denominator for the parameter of interest appropriate? If not, can these be extracted to recalculate the parameter of interest?	If the numbers used to estimate the parameter of interest were appropriate, select Yes.
		If the numbers used to estimate the parameter of interest were not appropriate, and no information was available to re-estimate, select No. (Yes=2, No=0)
36	Were potential confounding factors sought and controlled for in the analysis for odds ratios/relative risks/hazard ratios/incidence rate ratio?	If the parameter of interest is prevalence, incidence, duration, mean, remission, case fatality rate or severity, “Not Applicable” will be auto-selected because it is not possible to control for confounding for these. (Not Applicable=1)
		If one of the parameters of interest is a relative risk, hazard ratio or an incidence rate ratio and an adjustment was done for potential confounders, select Yes.
		If one of the parameters of interest is a relative risk, hazard ratio or an incidence rate ratio and no adjustment was done for potential confounders, select No. (Yes=1, No=0)
		Note: Where appropriate, when potential confounders were controlled for in the analysis for either all or at least one of the parameters, select Yes

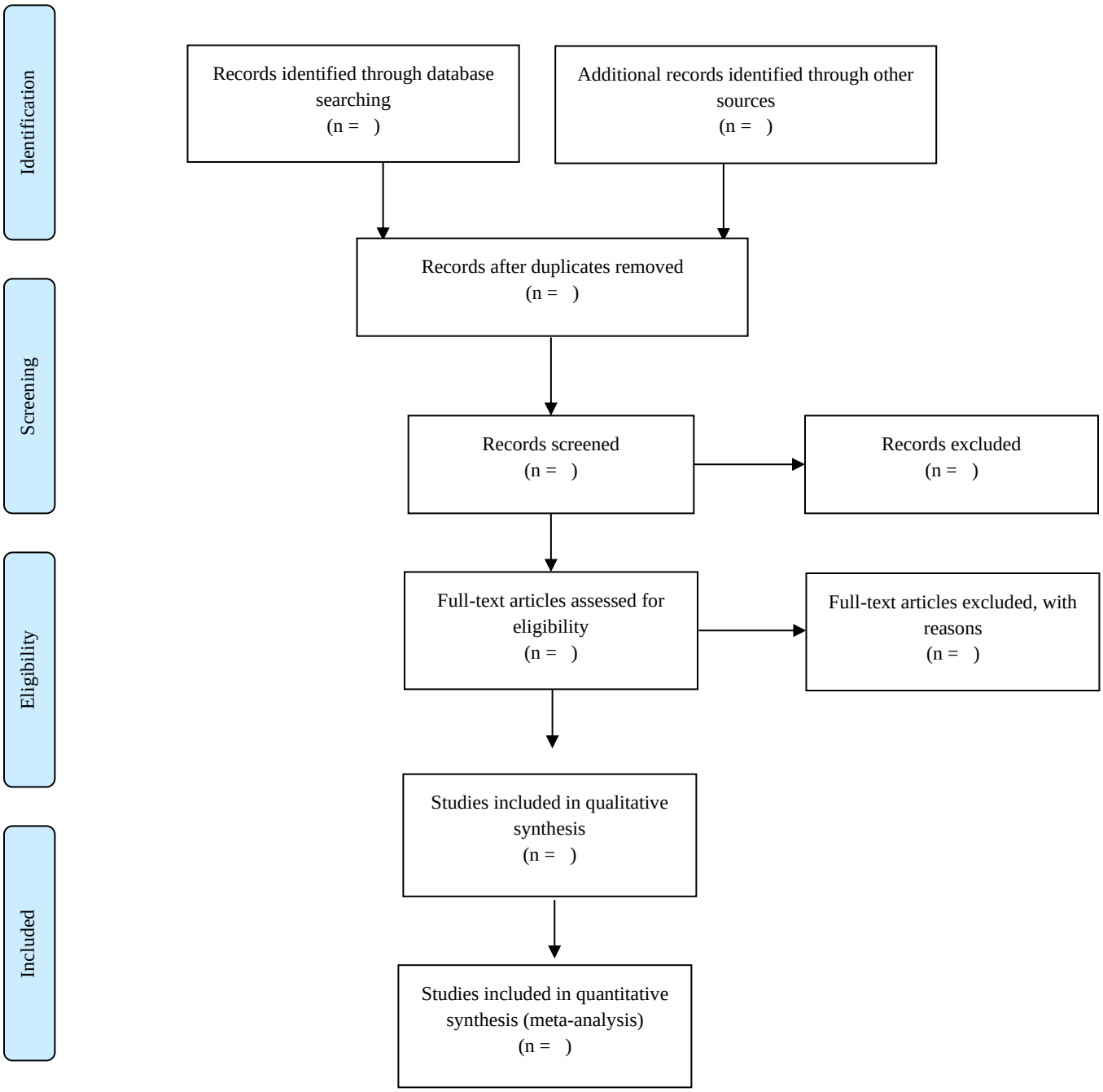
Appendix E: Surveillance study

RISK ASSESSMENT - SURVEILLANCE STUDY		
EXTERNAL VALIDITY		
	REPRESENTATIVENESS:	
25	Was a clear definition of study population (e.g. inpatient/outpatient register/community) provided?	(Yes=1, No=0)
26	Does the sentinel site(s) cover the target population and can this be generalised to the overall population?	(Yes=1, No=0)
27.2	Was the sampling method appropriate for the research question?	If the sampling strategy used was appropriate for the research question described for your condition of interest in the protocol, select Yes. (Yes=2, No=0)
28	***NON-RESPONSE BIAS:***	
28.1	Were all eligible participants included in the surveillance?	Were there any aspects of the selection and recruitment processes that could have resulted in eligible participants refusing to participate in the surveillance? For example, individuals refuse to participate in the surveillance because specimens are required that are not a part of routine care or the condition under surveillance is stigmatised.
		If the surveillance system excluded eligible participants, select No. (Yes=2, No=0)
28.2	Was the response rate reported for the surveillance?	If the response rate was not reported and there is insufficient information to estimate the response rate, select Not Reported.
		If the response rate was not reported and there is sufficient information to estimate the response rate, select Not reported but can calculate.
		If the response rate was reported, select Reported. (No score)

RISK ASSESSMENT - SURVEILLANCE STUDY		
28.3	What was the response rate for the surveillance?	If the response rate was not reported, use the number of people who were included in the surveillance as the numerator, and the number of people who were eligible as the denominator, to estimate the response rate (as a percentage).
		For retrospective review of medical records or case notes: If the authors reported the number of missing cases for the study period, estimate the percentage of included cases reviewed over expected cases.
		Note: If the information is available to estimate the response rate, perform the calculation and select your response based on instructions given above.
28.4	Was the response rate adequate?	The answer is automatically generated by your entry for the question above. A response rate of (i) ≥90% is excellent (ii) 70%-89% is average (iii) <70% is poor. (If response rate is ≥90% score 2; if 70-89% score 1; if <70% score zero; if response rate cannot be determined score 0)
INTERNAL VALIDITY		
	CASES:	
29	Were the cases classified using the ICD codes or was an acceptable case definition used? (Consult with content expert.)	Most conditions have an international/recognised definition, e.g. a case of diarrhoea is defined by WHO as "the passage of 3 or more loose or liquid stools per day".
		If such a definition was used, select Yes. Consult with your content expert if you are unclear on what the international or recognised definition is for your condition of interest. (Yes=1, No=0)
29.1	What is the case definition?	Write out the case definition and ICD code (if stated) for condition of interest as reported by the authors.
30	Were the study instruments used to measure the parameter of interest shown to have reliability and validity in this study or	Each parameter measure should have a standard recognised method used for measurement. The content expert will be able to advise on whether the mode of measurement is acceptable. (Yes=2, No=0)

RISK ASSESSMENT - SURVEILLANCE STUDY		
	in a previous study, via piloting, test-retesting? (Consult with content expert.)	
	DATA COLLECTION:	
31	Were data collected directly from the participants or if a proxy (a representative of the participant) was used, was it appropriate?	If data were collected directly from the participants, select Yes.
		If the primary caregiver responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select Yes.
		If the respondent was not the primary caregiver and responded on behalf of an individual classified as part of a vulnerable group (children less than 12 years of age), select No. (Yes=1, No=0)
32	Was the same method used for data collection for all participants for the condition of interest? If a different method was used, was it adequate?	The mode of data collection is the method used for collecting information from the participants. If the same method was not used for all participants for the condition of interest, select No. For example, a sphygmomanometer was used to establish a blood-pressure measurement for some participants and other participants self-reported on their last blood-pressure measurement.
		If the same method was not used for all participants for the condition of interest but justifiable and acceptable methods were used, select Yes. For example, a finger prick was used to obtain blood samples from older participants, while a heel or toe prick was used for infants. (Yes=1 No=0)
	UNCERTAINTY:	
33	Was the parameter of interest reported with uncertainty, i.e. Standard Deviation (SD) or Standard Error (SE) or 95% Confidence Interval (CI)?	If uncertainty estimates were reported for all or at least one of the parameters, select Yes. (Yes=1, No=0)
		Note: For surveys where uncertainty was not reported but can be calculated, select Yes.

Appendix F: PRISMA Flow Diagram[1]



[1] Prisma Flow Diagram: http://prisma-statement.org/documents/PRISMA%202009%20flow%20diagram.pdf