APPENDIX 1: Risk of bias Assessment

Source of risk of bias assessment tool: Pillay-van Wyk V, Roomaney RA, Awotiwon OF, et al. Burden of Disease Review Manager for Systematic Review of Observational Studies: Technical Report Version 1. Cape Town: South African Medical Research Council; 2017.

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.

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
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.
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) $\geq$80% is excellent (ii) 60%-79% is average (iii) <60% is poor. (If response rate is $\geq$80% score 2; if 60-79% score 1; if <60% score zero; if response rate cannot be determined score 0.)

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
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.
		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”.
		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)

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
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)
	UNCERTAINTY:	
33		If uncertainty estimates were reported for all or at least one of the parameters, select Yes. (Yes=1, No=0)

RISK ASSESSMENT - CROSS-SECTIONAL STUDY		
	Was the parameter of interest reported with uncertainty, i.e. Standard Deviation (SD) or Standard Error (SE) or 95% Confidence Interval (CI)?	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.

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)
27.1	Name the other sampling strategy (e.g. non-random, consecutive, convenience, case by case)? Describe.	Describe the sampling strategy used.

RISK ASSESSMENT - POPULATION-BASED SURVEY		
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:
		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) $\geq$80% is excellent (ii) 60%-79% is average (iii) <60% is poor. (If response rate is $\geq$80% score 2; if 60-79% score 1; if <60% score zero; if response rate cannot be determined score 0)

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		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".
		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)
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	DATA COLLECTION:	

RISK ASSESSMENT - POPULATION-BASED SURVEY		
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		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		If the numbers used to estimate the parameter of interest were appropriate, select Yes.

RISK ASSESSMENT - POPULATION-BASED SURVEY		
	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 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