

# Systematic reviews of diagnostics, prognosis, and prevalence

Eva Denison, senior researcher (and Kjetil G Brurberg)

June 11 2019

# Objectives

- To gain insight in systematic reviews of diagnostics, prognosis, and prevalence
  - How these reviews differ from reviews of effect
  - How to approach the results of such reviews
    - Types of estimates
    - Use of GRADE

# Core questions in health care

Research question	Knowledge	Preferred study design
How many have a problem? (e.g. type 2 diabetes)	Prevalence	Cross-sectional
Why do some have this problem and not others?	Etilogy	Cohort Case-control
How can we decide whether someone has this problem?	Diagnostics	Cross-sectional (with reference standard)
What can we do to prevent or treat this problem?	Effects of interventions	Randomised controlled trials
What is the probable course and outcome of the problem?	Prognosis	Cohort
What hat is it like to have the problem?	Experiences	Qualitative methods
How is the intervention perceived to work?	Mechanisms	

# Steps in conducting a systematic review

- 1. Formulate the question
- 2. Define criteria for inclusion- and exclusion
- 3. Identify (locate) studies
- 4. Select studies
- Assess methodological quality of studies (bias)
- 6. Extract data
- 7. Analyse data
- 8. GRADE
- 9. Present and interpret results



 Where in the process of conducting a systematic review of other core questions would you anticipate differences compared to a review of effect?

#### How can we decide whether someone has a problem?

#### Diagnostics

Important concepts



#### How can we decide whether someone has a problem?

#### Diagnostics

- Important concepts
  - Test accuracy
    - True/false positive and True/false negative
    - Sensitivity and specificity
- Risk of bias assessment
- Data synthesis
- GRADE

#### Not PICO but PICROOS

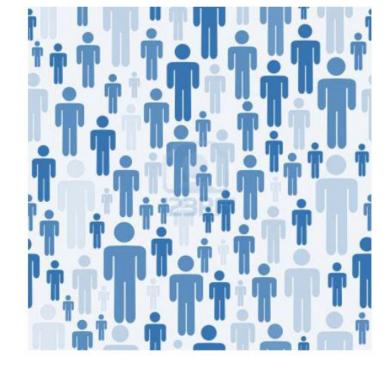
 Patients and setting Index test • Comparator (not always relevant) • Reference test • Outcome (technical) Outcome (patient near) Study design

#### Test accuracy

What proportion of those <u>with</u> <u>the disease</u> does the test correctly identify? (sensitivity)

What proportion of those without the disease does the test correctly exclude? (specificity)

True/False Positive



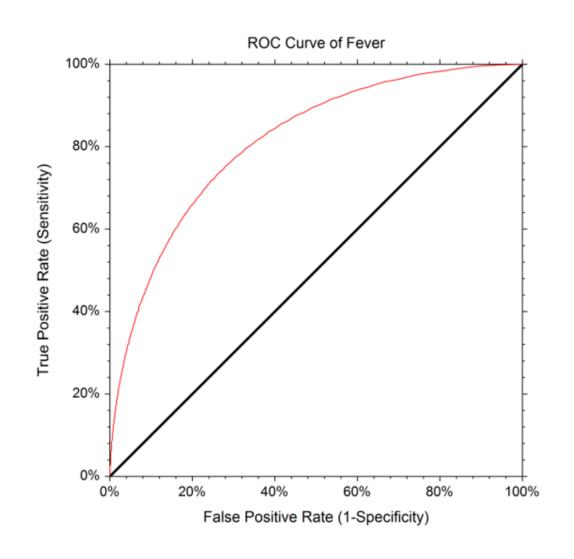
True/False Negative

# **Sensitivity and Specificity**

	Reference standard positive	Reference standard negative	
Index test positive	TP	FP	TP + FP
Index test negative	FN	TN	FN + TN
	TP + FN	FP + TN	TP +FN+FP+TN
Sensitivity = TP	/ (TP+FN)	Specificit	y = TN / (TN+FP)

Study	TP	FP	ΕN	TN	Soneitivity (05% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Innes 2011	206	1	D	294	1.00 [0.98, 1.00]	1.00 [0.98, 1.00]	Sensitivity (95% Ci)	specificity (95% CI)
McCarthy 2005	208	27	D	15	1.00 [0.63, 1.00]	0.36 [0.22, 0.52]		
Innes 2007	31	2/	1	16	0.97 [0.84, 1.00]	0.89 [0.85, 0.99]		
Devos 2013	23	13	i	23	0.96 (0.79, 1.00)	0.64 [0.46, 0.79]		
Nouri 1987	16	1	i	21	0.94 [0.71, 1.00]	0.95 [0.77, 1.00]		
Engum 1989	32	ż	2	40	0.94 [0.80, 0.99]	0.85 [0.77, 1.86]		
McKenna 2004	48	20	4	50	0.92 [0.81, 0.98]	0.71 [0.59, 0.82]		
Devos 2007	10	3	1	26	0.91 [0.59, 1.00]	0.90 (0.73, 0.98)		
Dobbs 2010	53	13	7	48	0.88 [0.77, 0.96]	0.79 [0.66, 0.88]		
Ferreira 2013	22	7	3	18	0.88 [0.69, 0.97]	0.72 [0.51, 0.88]		
Akinwuntan 2013	7	1	1	6	0.88 [0.47, 1.00]	0.86 [0.42, 1.00]		
Devos 2012	13	2	2	13	0.87 [0.60, 0.98]	0.87 [0.60, 0.98]		
Ranchet 2013	6	2	1	30	0.86 [0.42, 1.00]	0.94 [0.79, 0.99]		
Kwok 2015	33	35	6	35	0.86 [0.69, 0.94]	0.50 [0.38, 0.62]		
Lincoln 2008	11	2	2	19	0.85 [0.55, 0.98]	0.90 [0.70, 0.99]		
Nouri 1993	16	2	3	.0	0.84 [0.60, 0.97]	0.75 [0.35, 0.97]		
Lundqvist 1999	21	6	5	25	0.81 [0.61, 0.93]	0.81 [0.63, 0.93]		
Nef 2013	- 8	21	2	49	0.80 [0.44, 0.97]	0.70 (0.58, 0.80)		
Fleitscher 2012	78	- 8	20	10	0.80 [0.70, 0.87]	0.56 [0.31, 0.78]		
Akinwuntan 2006	27	2	7	32	0.79 [0.62, D.91]	0.94 [0.80, 0.99]		
Akinwuntan 2005	23	2	8	7	0.79 [0.60, 0.92]	0.78 [0.40, 0.97]		
Classen 2009	75	59	20	220	0.79 [0.69, D.87]	0.79 [0.74, 0.83]		-
Hoggarth 2013	122	35	33	89	0.79 [0.71, 0.85]	0.72 [0.63, 0.79]		
Myers 2000	28	7	В	43	0.78 [0.61, 0.90]	0.86 [0.73, 0.94]		
Aslaksen 2013	27	6	В	37	0.77 [0.60, 0.90]	0.86 [0.72, 0.95]		
Hargrave 2012	30	19	9	18	0.77 [0.61, 0.89]	0.49 [0.32, 0.66]		
Niewpehner 2012	42	30	1.4	68	0.75 [0.62, 0.86]	0.69 [0.59, 0.78]		
De Raedt 2001	30	5	1 D	35	0.75 [0.59, 0.87]	0.88 (0.73, 0.96)		
Lundberg 2003	14	7	5	23	0.74 [0.49, 0.91]	0.77 [0.58, 0.90]		
Ott 2013	30	11	11	23	0.73 [0.57, 0.86]	0.68 [0.49, 0.83]		
Manning 2014	35	42	14	31	0.71 [0.57, 0.83]	0.42 [0.31, 0.55]		
Bedard 2008	127	58	53	107	0.71 [0.63, 0.77]	0.65 (0.57, 0.72)	-	
Bowers 2013	50	35	21	119	D.70 [0.58, D.81]	0.77 [0.70, 0.84]		-
Classen 2011	55	13	24	59	0.70 [0.58, 0.79]	0.82 [0.71, 0.90]		
Jones 2014	45	22	21	42	0.68 [0.56, 0.79]	0.66 [0.53, 0.77]		
Classen 2013	67	117	32	378	0.68 [0.58, 0.77]	0.76 (0.72, 0.80)	-	-
Oswanski 2007	132	68	70	194	0.66 [0.58, 0.72]	0.74 [0.68, 0.79]	-	
Freund 2005	37	1	20	44	0.65 [0.51, 0.77]	0.98 [0.88, 1.00]		
Vaucher 2014	14	134	В	248	0.64 [0.41, 0.83]	0.65 (0.60, 0.70)		-
Worringham 2006	12	4	- 7	23	0.63 [0.38, 0.84]	0.85 (0.66, 0.96)		
Carr 2011	4.1	2	24	32	0.63 [0.50, 0.75]	0.94 [0.80, 0.99]		
Selander 2010	49	56	42	48	0.64 [0.43, 0.64]	0.46 [0.36, 0.56]		
Korteling 1996	7	5	Ð	20	0.54 [0.25, 0.81]	0.80 (0.59, 0.93)		
Sommer 2010	29	11	25	113	0.64 [0.40, 0.67]	0.91 [0.86, 0.95]		-
Radford 2004	14	8	14	68	0.50 [0.31, 0.69]	0.89 (0.80, 0.95)		-
Schanke 2000	6	6	8	19	0.50 [0.21, 0.79]	0.76 [0.55, 0.91]		
Akinwuntan 2012	10	2	1 D	66	0.60 [0.27, 0.73]	0.97 [0.90, 1.00]		
Bliokas 2011	20	6	21	57	0.49 [0.33, 0.65]	0.90 (0.80, 0.96)		
George 2010	3	7	4	29	0.43 [0.10, 0.82]	0.81 [0.64, 0.92]		
McKenna 2007	61	8	86	236	0.41 [0.33, 0.50]	0.97 [0.94, 0.99]		-
Lincoln 2014	7	5	16	74	0.30 [0.13, 0.53]	0.94 [0.86, 0.98]		-
Hoggarth 2010	4	2	12	42	0.25 [0.07, 0.52]	0.95 (0.86, 0.99)		-
Crizzle 2012	3	3	26	136	0.10 [0.02, 0.27]	0.98 [0.94, 1.00]		0 0.2 0.4 0.6 0.8 1
							0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

## Receiver Operating Characteristic – ROC



#### QUADAS – risk of bias assessement

Domain	Patient Selection	Index Test	Reference Standard	Flow and Timing
Description	Describe methods of patient selection Describe included patients (previous testing, presentation, intended use of index test, and setting)	Describe the Index test and how it was conducted and Interpreted	Describe the reference standard and how it was conducted and interpreted	Describe any patients who did not receive the index tests or reference standard or who were excluded from the 2 × 2 table (refer to flow diagram)  Describe the interval and any interventions between index tests and the reference standard
Signaling questions (yes, no, or unclear)	Was a consecutive or random sample of patients enrolled? Was a case-control design avoided? Did the study avoid inappropriate exclusions?	Were the Index test results Interpreted without know- ledge of the results of the reference standard? If a threshold was used, was it prespecified?	Is the reference standard likely to correctly classify the target condition? Were the reference standard results interpreted without knowledge of the results of the Index test?	Was there an appropriate interval between Index tests and reference standard?  Did all patients receive a reference standard?  Did all patients receive the same reference standard?  Were all patients included in the analysis?
Risk of bias (high, low, or unclear)	Could the selection of patients have introduced blas?	Could the conduct or Interpretation of the Index test have introduced bias?	Could the reference standard, Its conduct, or Its Interpretation have Introduced bias?	Could the patient flow have introduced bias?
Concerns about applicability (high, low, or unclear)	Are there concerns that the included patients do not match the review question?	Are there concerns that the index test, its conduct, or its interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	

Whiting P et al, QUADAS-2: A revised tool for the quality assessment of diagnostic accuracy studies, Ann Intern Med (2011): 155: 529-36

## Diagnostic tests and strategies and GRADE

#### RATING QUALITY OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS

# GRADE: grading quality of evidence and strength of recommendations for diagnostic tests and strategies

The GRADE system can be used to grade the quality of evidence and strength of recommendations for diagnostic tests or strategies. This article explains how patient-important outcomes are taken into account in this process

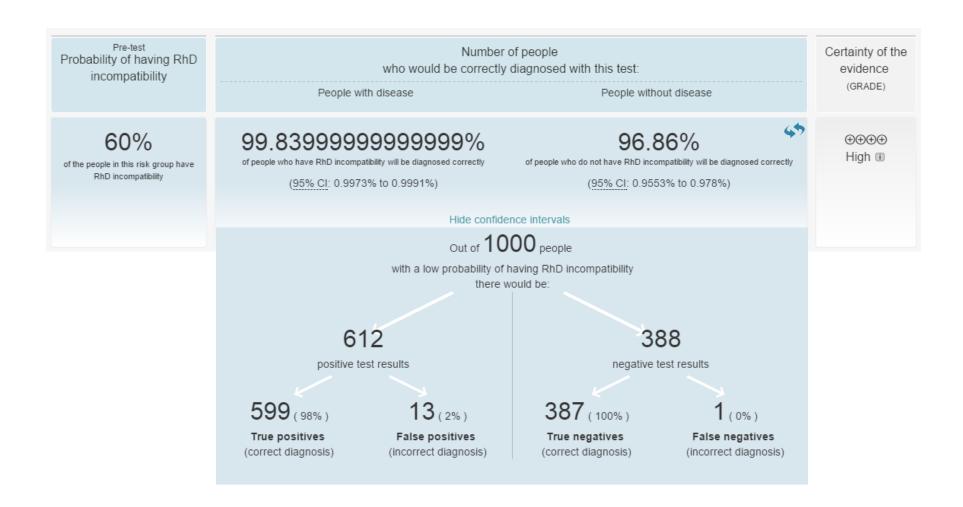
Schünemann et al BMJ | 17 may 2008 | Volume 336

Study design	Initial confidence	Reasons for lowering level of confidence
Cross sectional*	High	Risk of bias**
Cohort*	High	Inconsistency
		Indirectness
		Imprecision
		Publication bias

With appropriate reference standard

<sup>\*\*</sup> e.g. QUADAS

# **Example of GRADE Summary of Findings**



#### What is the probable course and outcome of the problem?

#### Prognosis

Important concepts



#### What is the probable course and outcome of the problem?

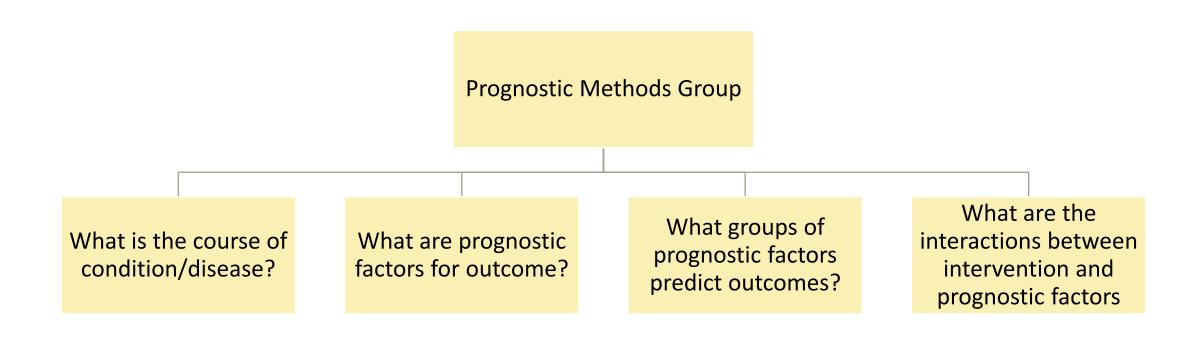
#### **Prognosis**

- Important concepts
  - Course of condition/disease
  - Prognostic factors for outcome
  - Interaction between treatment and prognostic factors
  - Rik of bias assessment
  - Data synthesis
  - GRADE

# Not PICO but...?



# Prognosis: different purposes of questions



#### **Prognostic Methods Group**

What is the course of condition/disease?

What are prognostic factors for outcome?

predict outcomes? HER2 ECD positive (n=23)

Different types of therapy:

No additional

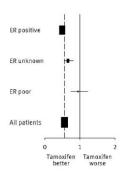
What groups of

prognostic factors

No additional therapy:

- With hormone
- With chemo
- With combined

What are the interactions between intervention and prognostic factors



Benefit of tamoxifen is confined to those with positive oestrogen receptor (ER) status

Breast cancer: variations between countries in age adjusted, five year survival

Cumulative survival HER2 ECD neg/pos

Hemingway et al, Prognosis research strategy (PROGRESS) 1: A framework for researching clinical outcomes, BMJ 2013;346:e5595 doi: 10.1136/bmj.e5595

# QUIPS

#### Table. Summary of the Bias Domains, Prompting Items, and Ratings of the QUIPS Tool\*

Variable		Bias Domains					
	1. Study Participation	2. Study Attrition	3. Prognostic Factor Measurement	4. Outcome Measurement	5.		
Optimal study or characteristics of unbiased study	The study sample adequately represents the population of interest	The study data available (i.e., participants not lost to follow-up) adequately represent the study sample	The PF is measured in a similar way for all participants	The outcome of interest is measured in a similar way for all participants	lm		
Prompting items and considerations†	<ul> <li>Adequate participation in the study by eligible persons</li> </ul>	Adequate response rate for study participants	<ul> <li>A clear definition or description of the PF is provided</li> </ul>	A clear definition of the outcome is provided	a.		
	b. Description of the source population or population of interest	<ul> <li>Description of attempts to collect information on participants who dropped out</li> </ul>	b. Method of PF measurement is adequately valid and reliable	<ul> <li>Method of outcome measurement used is adequately valid and reliable</li> </ul>	b.		
	c. Description of the baseline study sample	c. Reasons for loss to follow-up are provided	<ul> <li>c. Continuous variables are reported or appropriate cut points are used</li> </ul>	c. The method and setting of outcome measurement is the same for all study participants	C.		
	d. Adequate description of the sampling frame and recruitment	d. Adequate description of participants lost to follow-up	d. The method and setting of measurement of PF is the same for all study participants		d.		
	<ul> <li>Adequate description of the period and place of recruitment</li> </ul>	<ul> <li>There are no important differences between participants who completed the study and those who did not</li> </ul>	e. Adequate proportion of the study sample has complete data for the PF		e.		
	f. Adequate description of inclusion and exclusion criteria		f. Appropriate methods of imputation are used for missing PF data		f.		

**Hayden et al,** Assessing Bias in Studies of Prognostic Factors, *Ann Intern Med.* 2013;158:280-286.

	Bias Doma	ins
	5. Study Confounding	6. Statistical Analysis and Reporting
1	Important potential confounding factors are appropriately accounted for	The statistical analysis is appropriate, and all primary outcomes are reported
	a. All important confounders are measured	Sufficient presentation of data to assess the adequacy of the analytic strategy
I	b. Clear definitions of the important confounders measured are provided	<ul> <li>Strategy for model building is appropriate and is based on a conceptual framework or model</li> </ul>
•	c. Measurement of all important confounders is adequately valid and reliable	c. The selected statistical model is adequate for the design of the study
•	d. The method and setting of confounding measurement are the same for all study participants	d. There is no selective reporting of results
	e. Appropriate methods are used if imputation is used for missing confounder data	
1	f. Important potential confounders are accounted for in the study design	
	g. Important potential confounders are accounted for in the analysis	
	The observed effect of the PF on the outcome is very likely to be distorted by another factor related to PF and outcome	The reported results are very likely to be spurious or biased related to analysis or reporting
	The observed effect of the PF on outcome may be distorted by another factor related to PF and outcome	The reported results may be spurious or biased related to analysis or reporting
	The observed effect of the PF on outcome is unlikely to be distorted by another factor related to PF and outcome	The reported results are unlikely to be spurious or biased related to analysis or reporting

# Prognosis and GRADE

Use of GRADE for assessment of evidence about prognosis: rating confidence in estimates of event rates in broad categories of patients

Alfonso lorio,<sup>1,2</sup> Frederick A Spencer,<sup>2</sup> Maicon Falavigna,<sup>3</sup> Carolina Alba,<sup>4</sup> Eddie Lang,<sup>5</sup> Bemard Bumand,<sup>6</sup> Tom McGinn<sup>7</sup>, Illi Hayden,<sup>8</sup> Katrina Williams,<sup>9</sup> Beverly Shea;<sup>1,0,1</sup> Robert Wolff;<sup>1,2</sup> Ton Kujpers,<sup>1,3</sup> Pablo Perel,<sup>1,4</sup> Per Olav Yandriki,<sup>1,5</sup> Paul Glasziou,<sup>1,6</sup> Holger Schunemann,<sup>1,2</sup> Gordon Guyatt<sup>1,2</sup>

BMJ 2015;350:h870

Study design	Initial confidence	Reasons for lowering level of confidence	Reasons for raising level of confidence	Final level of confidence rating
Longitudinal cohort study	High	Risk of bias*	Large effect	High ⊕⊕⊕⊕
Control arm of randomized controlled trial	High	Inconsistency	Dose response	Moderate ⊕⊕⊕○
		Indirectness		Low ⊕⊕○○
		Imprecision		Very low ⊕○○○
		Publication bias		

<sup>\*</sup> E.g QUIPS, Newcastle Ottawa instrument

#### **Example of GRADE Summary of Findings**

**Summary of findings 2.** Summary of findings: risk of intermediate hyperglycaemia (IFG5.6 mmol/L definition) versus normoglycaemia for developing T2DM

Outcome: development of T2DM  Prognostic factor: intermediate hyperglycaemia versus normoglycaemia as measured by IFG <sub>5,6</sub>				
No of studies	No of participants with intermediate hyperglycaemia	Geographic region/special population	Estimated effect (95% CI) [95% prediction interval]	Overall certainty of the evidence (GRADE) <sup>a</sup>
HR: 4	HR: 2385	Asia/Middle East	HR: 5.07 (3.41-4.86)	⊕⊕⊝⊝
IRR: 6	IRR: 15,661		[1.07-24.02]	Low <sup>b</sup>
	1111 15,551		IRR: 5.23 (3.77-7.25)	
OR: 10	OR: 6359		[1.72-15.89]	
			OR: 2.94 (1.77-4.86)	
			[0.43-19.93]	

CI: confidence interval; HR: hazard ratio; IFG<sub>5.6</sub>: impaired fasting glucose 5.6 mmol/L threshold; IRR: incidence rate ratio; NA: not applicable; N/M: fewer than 3 studies or calculation of the 95% prediction interval did not provide a meaningful estimate; OR: odds ratio; T2DM: type 2 diabetes mellitus.

Richter B, Hemmingsen B, Metzendorf MI, Takwoingi Y. Development of type 2 diabetes mellitus in people with intermediate hyperglycaemia. Cochrane Database of Systematic Reviews 2018, Issue 10. Art. No.: CD012661. DOI: 10.1002/14651858.CD012661.pub2.

# How many have a problem?

#### Prevalence

Important concepts



#### How many have a problem?

#### Prevalence

- Important concepts
  - Point/Interval estimates
  - Time trends

- Risk of bias
- Data synthesis
- GRADE

# Not PICO but...?



#### Risk of bias

#### Item

#### External validity

- 1. Was the study's target population a close representation of the national population in relation to relevant variables?
- 2. Was the sampling frame a true or close representation of the target population?
- 3. Was some form of random selection used to select the sample, OR was a census undertaken?
- 4. Was the likelihood of nonresponse bias minimal?

#### Internal validity

- 5. Were data collected directly from the subjects (as opposed to a proxy)?
- 6. Was an acceptable case definition used in the study?
- 7. Was the study instrument that measured the parameter of interest shown to have validity and reliability?
- 8. Was the same mode of data collection used for all subjects?
- 9. Was the length of the shortest prevalence period for the parameter of interest appropriate?
- 10. Were the numerator(s) and denominator(s) for the parameter of interest appropriate?
- 11. Summary item on the overall risk of study bias



Journal of Clinical Epidemiology 65 (2012) 934-939

Journal of Clinical Epidemiology

#### ORIGINAL ARTICLES

Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement

Damian Hoy<sup>a,\*</sup>, Peter Brooks<sup>b</sup>, Anthony Woolf<sup>c</sup>, Fiona Blyth<sup>d</sup>, Lyn March<sup>d</sup>, Chris Bain<sup>a</sup>,
Peter Baker<sup>a</sup>, Emma Smith<sup>d</sup>, Rachelle Buchbinder<sup>e,\*</sup>

"University of Queensland, Herston Road, Herston, Brisbane, QLD 4006, Australia

\*bastralian Heddh Workforce Institute, 766 Elizabeth Street, Melbourne 3010, Australia

\*Peninstala College of Medicine and Dentistry, Truno TRI 311, United Kingdom

\*University of Sydney, Royal North Store Hospital, St Leonards, Sydney 2065, Australia

\*Cabrini Hospital and Monash University, Cabrini Medical Centre 183 Wattletne Rd, Malvern, Melbourne 3144, Australia

\*Cabrini Hospital and Monash University, Cabrini Medical Centre 183 Wattletne Rd, Malvern, Melbourne 3144, Australia

\*Cabrini Hospital and Monash University Cabrini Medical Centre 183 Wattletne Rd, Malvern, Melbourne 3144, Australia

\*Cabrini Hospital and Monash University Cabrini Medical Centre 183 Wattletne Rd, Malvern, Melbourne 3144, Australia

# Data synthesis and GRADE (by us)

Badawi et al. Virology Journal (2018) 15:148 https://doi.org/10.1186/s12985-018-1060-1

Virology Journal

REVIEW Open Access



Systematic review and meta-analysis of HIV, HBV and HCV infection prevalence in Sudan

M. M. Badawi 1\*, M. S. Atif2 and Y. Y. Mustafa2

"The aim of this study was to provide a systematic review and meta-analysis of the results of prevalence studies of the three viruses in different populations and in distinct geographical regions, which will help in determining the population distribution of the viruses."

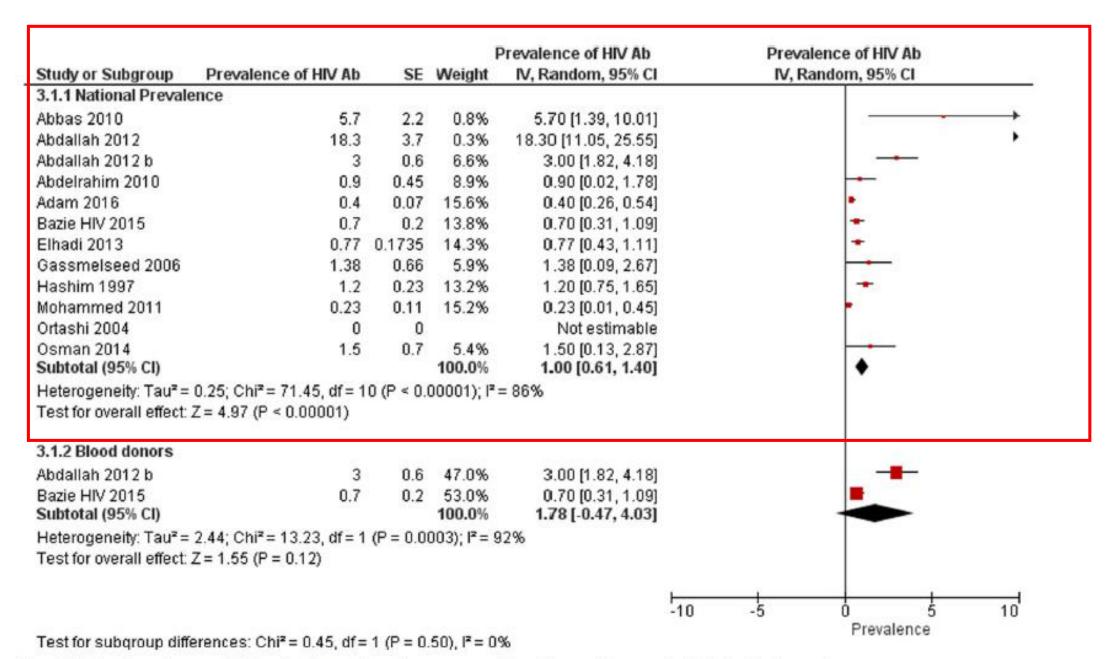


Fig. 2 National prevalence of HIV antibodies and prevalence among blood donors from studies included in the review

Study design	Initial confidence	Reasons for lowering level of confidence	Reasons for raising level of confidence	Final level of confidence rating
	High	Risk of bias		High ⊕⊕⊕⊕
		Inconsistency		Moderate ⊕⊕⊕○
		Indirectness		Low ⊕⊕○○
		Imprecision		Very low ⊕○○○
		Publication bias		

#### Search

"A comprehensive search was conducted in PubMed, Embase, Google scholar, Scopus, Index Copernicus, DOAJ, EBSCO-CINAHL, Cochrane databases as well as Sudan Journal of Medical Sciences without specific time or language limits. The keywords used were Human Immunodeficiency Virus, Hepatitis B, Hepatitis C, Hepatitis B surface antigen, prevalence, Sudan, and similar terms such as HBV, HBsAg, HCV and HIV were also crossed. Moreover, to optimize our search, hand searches of reference lists of included articles were also performed."

#### **Data extraction**

Prevalence data of HIV, HBV or HCV for a defined population group, in a defined region, or combination of two or more of them (co-infectionprevalence) or provision of specific prevalence in one infection under study as Occult Hepatitis B (OBI).

Moreover, data from each method section was extracted using a predefined set of variables; study characteristics, type of participants, study population size, geographical region and the screening protocol used.

Study design	Initial Reasons for lowering confidence level of confidence	Reasons for raising level of confidence	Final level of confidence rating
	Risk of bias		High ⊕⊕⊕⊕
	Inconsistency		Moderate ⊕⊕⊕○
	Indirectness		Low ⊕⊕○○
	Imprecision		Very low ⊕○○○
	Publication bias		

**Table 1** Assessment of quality of general population studies and studies toward specific Populations at risk

Aspect	Score	Description
Age	0	Not determined
	0	Determined with clear bias; not representative to general/targeted population
	1	Determined with no clear bias; can be considered representative
Gender	0	Not determined
	0	Determined with clear bias
	1	Determined with no clear bias; can be considered representative
Coverage	1	Single centre/local
	2	Multi-centre/local
	3	Multi-centre/national
Sample size <sup>a</sup>	0	Less than 150 participants
	1	More than 150 and less than 1000 participants
	2	More than 1000 participants

<sup>&</sup>lt;sup>a</sup>Thresholds were set based on authors opinion solely

Authors	Age bias (0 or 1)	Gender bias (0 or 1)	Population coverage (1, 2 or 3)	Sample size (0, 1	Total Score
Abdallah and Ali [16]	-	-	1	1	2
Osman et al [10]	-	-	1	1	2
Bazie [18]	-	-	1	2	3
Elhadi et al [8]	1	-	3	2	6
Hashim et al [19]	0	1	2	2	5
Abdelrahim et al [17]	1	-	2	1	4
Adam et al [13]	-	-	1	2	3
Mohammed et al [15]	-	-	1	1	2
Gassmelseed et al [9]	-	-	1	1	2
Abbas et al [11]	1	1	1	0	3
Ortashi et al [12]	-	-	1	1	2
Abdallah et al [14]	1	1	1	0	3

<sup>&</sup>quot;A total score for risk of bias was calculated by adding up the scores in all four domains, resulting in a score of between 0 and 7. The highest score indicates the lowest risk of bias."

Study design	Initial Reasons for lowering level of confidence	Reasons for raising level of confidence	Final level of confidence rating
	Risk of bias		High ⊕⊕⊕⊕
	Inconsistency		Moderate ⊕⊕⊕○
	Indirectness		Low ⊕⊕○○
	Imprecision		Very low ⊕○○○
	Publication bias		

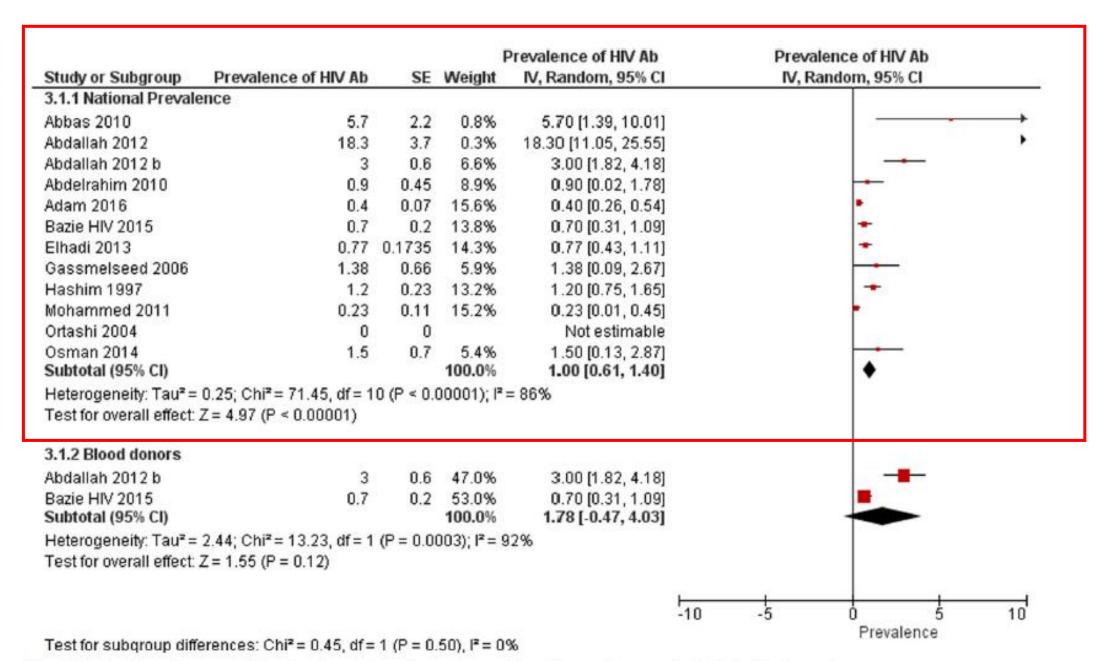


Fig. 2 National prevalence of HIV antibodies and prevalence among blood donors from studies included in the review

Study design	Initial confidence	Reasons for lowering level of confidence	Reasons for raising level of confidence	Final level of confidence rating
		Risk of bias		High ⊕⊕⊕⊕
		Inconsistency		Moderate ⊕⊕⊕○
		Indirectness		Low ⊕⊕○○
		Imprecision		Very low ⊕○○○
		Publication bias		

Author(s)	City/State	Study population	Age group	Sample size	Screening protocol
Abdallah and Ali [16]	Kassala / Kassala	Blood donors	19-58	810	ELISA
Osman et al [10]	Khartoum / Khartoum	Pregnant women	20-40	285	ELISA and Confirmed
Bazie et al [18]	Kosti/ White Nile	Blood donors	18-65	1204	ICT
Elhadi et al [8]	National <sup>a</sup>	Female sex workers	15-49	4220	Confirmed ICT
Hashim et al [19]	Khartoum / Khartoum	Children	<16 years	1118	ELSIA / Western blot
Abdelrahim et al [17]	Khartoum / Khartoum	Female sex workers	18-49	321	ELSIA
Adam et al [13]	Gadarif / Gadarif	Pregnant women	Not specified	6420	Confirmed ICT
Mohammed et al [15]	Kassala / Kassala	Pregnant women	16-40	430	Confirmed ICT
Gassmelseed et al [9]	Khartoum / Khartoum	Pregnant women	Not specified	305	ELISA
Abbas et al [11]	Omdurman / Khartoum	Children with acute medical illnesses	18 months -14 years	106	Confirmed ICT
Ortashi et al [12]	Khartoum / Khartoum	Pregnant women	25±2.6 <sup>d</sup>	151	ELISA
Abdallah et al [14]	Kassala / Kassala	TB patients	18-62	109	ELISA

Study design	Initial confidence	Reasons for lowering level of confidence	Reasons for raising level of confidence	Final level of confidence rating
		Risk of bias		High ⊕⊕⊕⊕
		Inconsistency		Moderate ⊕⊕⊕○
		Indirectness		Low ⊕⊕○○
		Imprecision		Very low ⊕○○○
		Publication bias		

"Publication bias assessment indicated no major asymmetry (data not shown)."

Study design	Initial confidence	Reasons for lowering level of confidence	Reasons for raising of confidence	Final level of confidence rating
		Risk of bias	?	High ⊕⊕⊕⊕
		Inconsistency		Moderate ⊕⊕⊕○
		Indirectness		Low ⊕⊕○○
		Imprecision		Very low ⊕○○○
		Publication bias		

Study design	Initial confidence	Reasons for lowering level of confidence	Reasons for raising level of confidence	Final level of confidence rating
		Risk of bias	?	High ⊕⊕⊕⊕
		Inconsistency		Moderate ⊕⊕⊕○
		Indirectness		Low ⊕⊕○○
		Imprecision		Very low ⊕○○○
		Publication bias		

# Summary of Findings table

 What do you suggest we report in a Summary of Findings table on prevalence?

# Let's recap: Steps in conducting a systematic review of diagnostics/prognosis/prevalence

- 1. Formulate the question
- 2. Define criteria for inclusion- and exclusion
- 3. Identify (locate) studies
- 4. Select studies
- Assess methodological quality of studies (bias)
- 6. Extract data
- 7. Analyse data
- 8. GRADE
- 9. Present and interpret results

# Thank you for your attention and collaboration!

