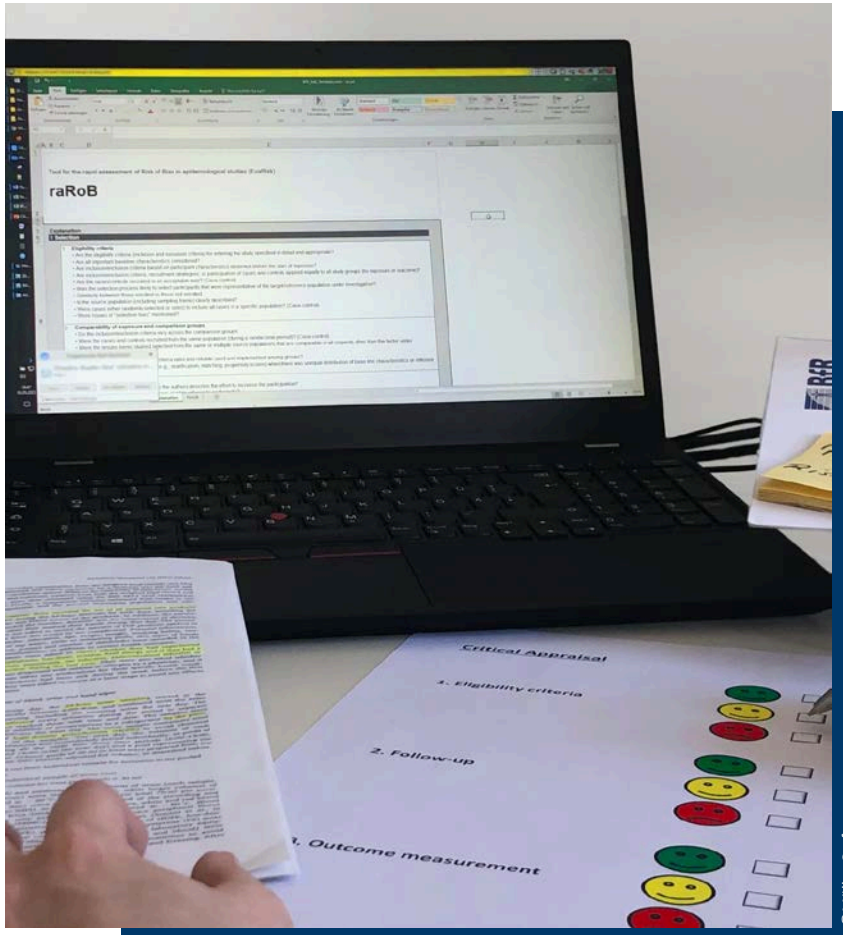
A tool for rapid assessment of Risk of Bias (raRoB) in observational epidemiological studies



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November 10, 2023

International Conference on Using epidemiological studies in health risk assessments

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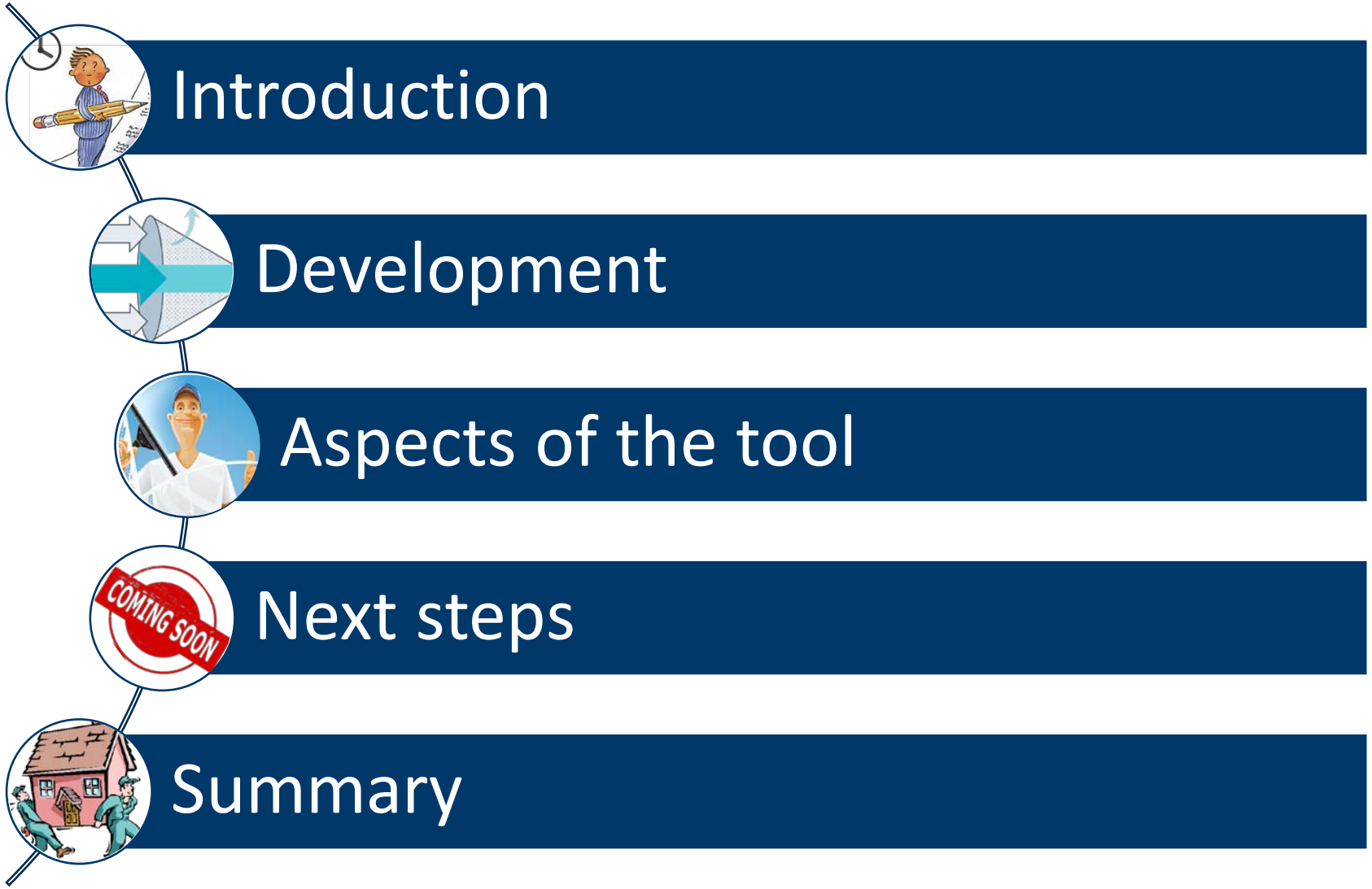
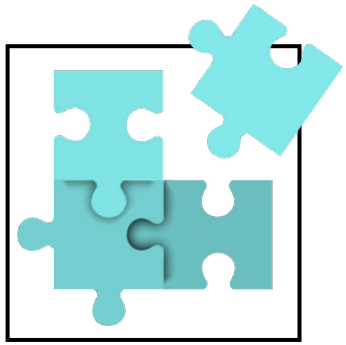
Outline


Introduction
Development
Aspects of the tool
COMING SOON
Next steps
Summary

Background

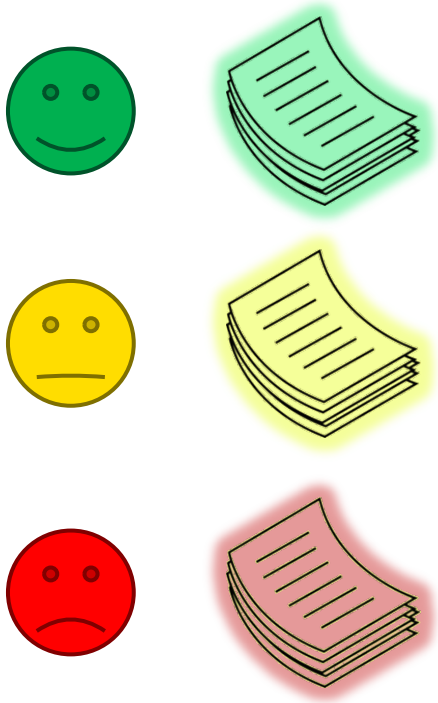
Short-term requests

Risk of Bias assessment



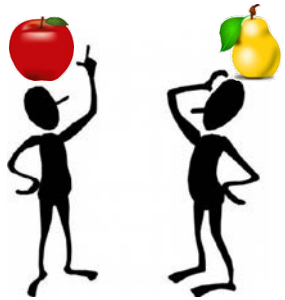
Critical appraisal

Assessments of epidemiological study / publication



Aims of the development of raRoB

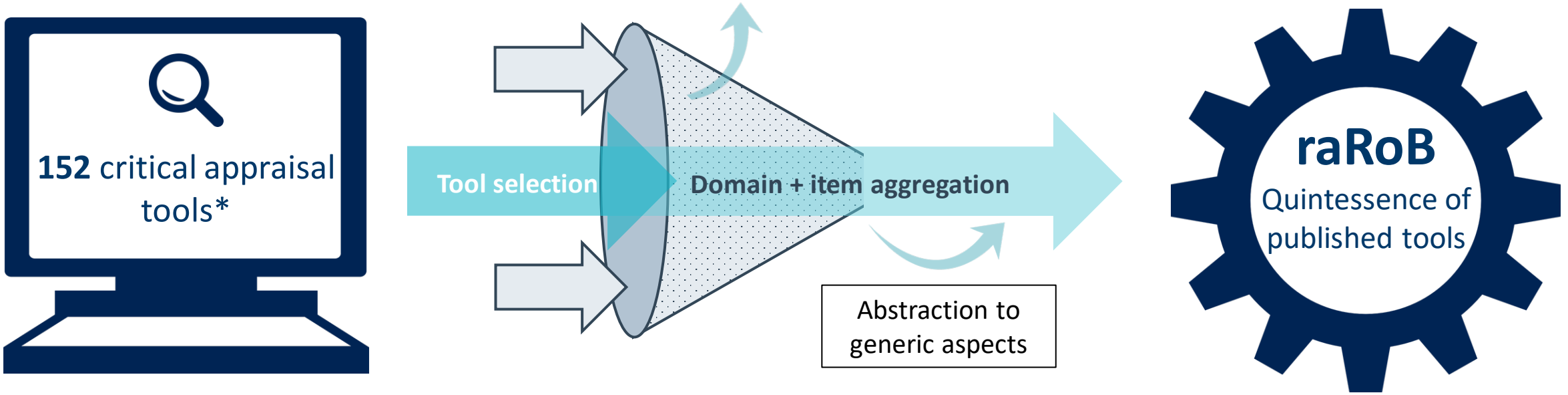
- **Completeness:** all relevant types of biases for main types of observational studies
- **Rapidity:** one concise tool for multiple study types



- **Usability:** applicable in interdisciplinary appraisal teams
- **Transparency:** clarity of the assessment

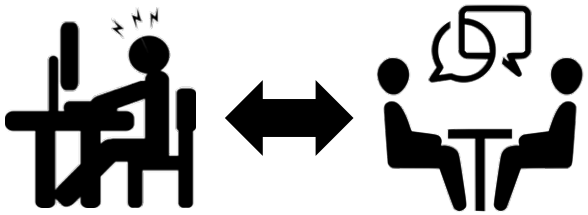
Initial development

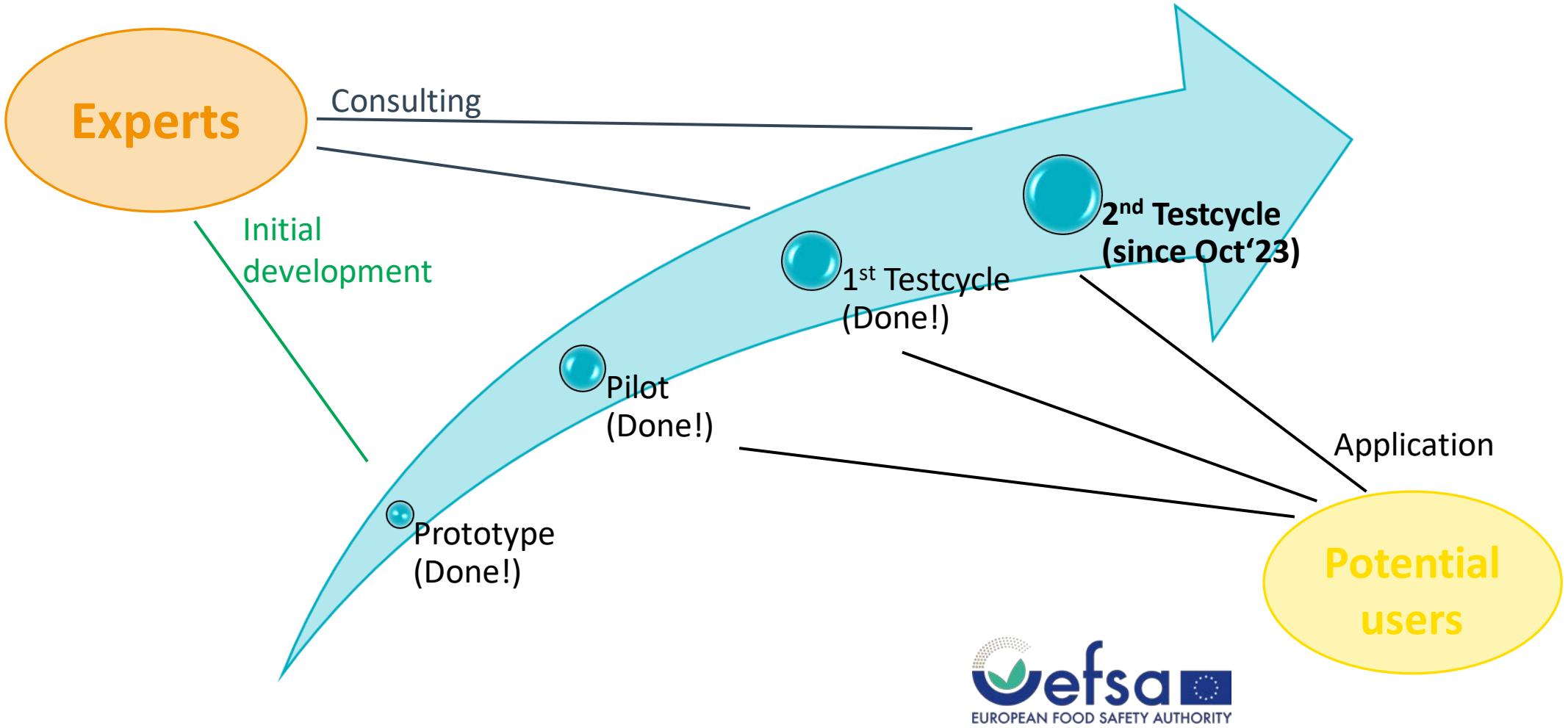
Discarded
- Author guidelines
- Reporting guidelines
- Tools for selective questions
- Tools that are too old or not meeting current standards



*Based on Sanderson et al. (2007), Shamliyan et al. (2010), Wang et al. (2019) or known / used tools by working group members

Development and testing





Compilation of domains (7) and items (15) used by raRoB

1 Selection

- 1 Eligibility criteria
- 2 Comparability of exposures/case and comparison/control groups
- 3 Non-response rate
- 4 Recruitment time frame

2 Exposure

- 1 Accuracy of exposure measurements
- 2 Misclassification of exposure

3 Outcome Assessment

- 1 Accuracy of outcome measurements
- 2 Misclassification of outcome

4 Confounding

- 1 Accounting for confounding
- 2 Accuracy of cofounding variables measurement

5 Loss to follow-up

- 1 Adequacy of length of follow-up
- 2 Amount and handling of loss to follow-up

6 Analysis

- 1 Appropriate statistical methods
- 2 Handling of missing values

7 Selective reporting

- 1 Selective reporting of outcomes

Rapidity + Usability

- Clear user-interface
- Adaption according to study design
- Signalling questions for each item
- Calculation of overall risk of bias

Rapidity + Usability – Clear user-interface

Single RoB items

Selected

high	-
some concerns	+/-
undecided/no judgement	?
low	+
no information	-
not applicable	n.a.

Project	Example		Project	Example
Assessment		Risk of Bias	Comments	
1 Selection			**1 Selection**	
1	Eligibility criteria	Please select	1	
2	Comparability of exposure/case and comparison/control groups	Please select	2	
3	Non-response rate	Please select	3	
4	Recruitement time frame	Please select	4	
2 Exposure			**2 Exposure**	
1	Accuracy, validity and reliability of exposure measurements	Please select	1	
2	Misclassification of exposure	Please select	2	
3 Outcome Assessment			**3 Outcome Assessment**	
1	Accuracy, validity and reliability of outcome measurements	Please select	1	
2	Misclassification of outcome	Please select	2	
4 Confounding			**4 Confounding**	
1	Accounting for confounding	Please select	1	
2	Accuracy, validity and reliability of confounding variables meas.	Please select	2	
5 Loss to follow-up			**5 Loss to follow-up**	
1	Adequacy of length of follow-up	Please select	1	
2	Amount and handling of loss to follow-up	Please select	2	
6 Analysis			**6 Analysis**	
1	Statistical methods	Please select	1	
2	Handling of missing values	Please select	2	
7 Selective reporting			**7 Selective reporting**	
1	Selective reporting of outcomes	Please select	1	

Rapidity + Usability – Adaption according study design

Item	Cohort study	Case-cohort study	Case-control study	Nested case-control study	Cross-sectional study	Case series
Eligibility criteria	+	+	+	+	+	+
Comparability of exposure/case and comparison/control groups	+	+	+	+	+	-
Non-response rate	+	+	-	+	+	-
Recruitement time frame	+	+	-	+	+	+
Accuracy, validity and reliability of exposure measurements	+	+	+	+	+	+
Misclassification of exposure	+	+	+	+	+	-
Accuracy, validity and reliability of outcome measurements	+	+	+	+	+	+
Misclassification of outcome	+	+	+	-	+	-
Accounting for confounding	+	+	+	+	+	+
Accuracy, validity and reliability of confounding variables meas.	+	+	+	+	+	+
Adequacy of length of follow-up	+	+	-	+	-	+
Amount and handling of loss to follow-up	+	+	-	+	-	+
Statistical methods	+	+	+	+	+	+
Handling of missing values	+	+	+	+	+	+
Selective reporting of outcomes	+	+	+	+	+	+

Rapidity + Usability – Signalling questions for each item

Cohort

4 Confounding

1	Accounting for confounding • Have the authors taken account of the potential confounding factors in the design and/or in their analysis? • Were all important covariates and confounding variables taken into account in the design and/or analysis (restriction, stratification, interaction terms, multivariable analysis, propensity score matching, instrumental variables or other approaches)?
2	Accuracy, validity and reliability of confounding variables meas. • Are the distributions of the principal confounders in each group of subjects to be compared clearly described? • Were the information used to define confounder status independent of exposure and outcome assessment?

5 Loss to follow-up

1	Adequacy of length of follow-up • Was the length of follow-up reported? • Is the follow-up period adequate to allow for the development of the outcome of interest?
2	Amount and handling of loss to follow-up • Were withdrawals and drop-outs reported in terms of numbers and/or reasons per group? • Are the proportion of participants and reasons for missing data similar across exposures/outcomes? • Is the classification of exposed and unexposed person-time free of "immortal time bias"? • Was loss to follow-up taken into account in the analysis?

Rapidity + Usability – Signalling questions for each item

Case-control

4 Confounding

1	Accounting for confounding • Were all important covariates and confounding variables taken into account in the design and/or analysis (restriction, stratification, interaction terms, multivariable analysis, propensity score matching, instrumental variables or other approaches)? • Is there a baseline equivalence of group, i.e. are the groups similar regarding the criteria other than the studied exposures/endpoints? If not, indicate the percentage of controlled relevant confounders (either in design (stratification, matching) or analysis)?
2	Accuracy, validity and reliability of confounding variables meas. • Are the distributions of the principal confounders in each group of subjects to be compared clearly described? • Were the information used to define confounder status independent of exposure and outcome assessment? • Were potential confounding factors comparable for cases and controls? If not, were potential imbalances between cases and controls addressed through statistical measures?

5 Loss to follow-up

1	Adequacy of length of follow-up • Not applicable for retrospective designs
2	Amount and handling of loss to follow-up • Not applicable for retrospective designs

Rapidity + Usability – Calculated overall risk of bias

Project	Example

Assessment results		Risk of Bias
1 Selection		
1	Eligibility criteria	+
2	Comparability of exposure/case and comparison/control groups	+
3	Non-response rate	+/-
4	Recruitement time frame	+/-
2 Exposure		
1	Accuracy, validity and reliability of exposure measurements	-
2	Misclassification of exposure	+
3 Outcome Assessment		
1	Accuracy, validity and reliability of outcome measurements	+
2	Misclassification of outcome	+/-
4 Confounding		
1	Accounting for confounding	?
2	Accuracy, validity and reliability of confounding variables meas.	+/-
5 Loss to follow-up		
1	Adequacy of length of follow-up	+
2	Amount and handling of loss to follow-up	+/-
6 Analysis		
1	Statistical methods	+
2	Handling of missing values	+/-
7 Selective reporting		
1	Selective reporting of outcomes	+

Overall Risk of Bias

Calculation from individual items

Worst rating score	moderate
Ratio score	moderate

Assessor's judgement of overall bias

Assessor 1	high
Assessor 2	moderate

Comment on assessor's judgement of overall bias

The exposure measurement is a crucial part of the research question. If corresponding items are rated with a high sik of bias or without information, the publication is assessed as with a high risk of bias in this context.

Fictional example

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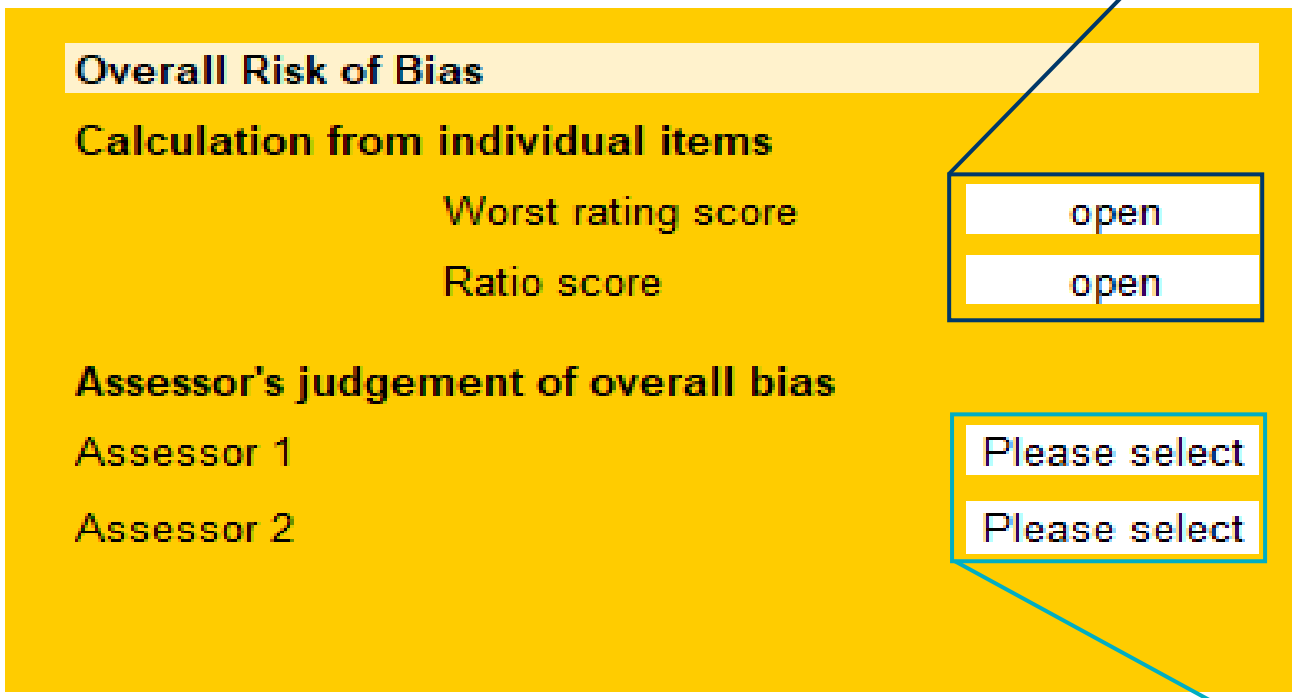
Rapidity + Usability – Calculated overall risk of bias



Calculated

Overall risk of bias

Worst rating score

Ratio score

Scale:

not assessable ○

high 🔴

moderate 🟡

low 🟢

Assessor's judgement

Selected

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Transparency

Project	Example	Project	Example
Assessment	**Risk of Bias**	**Comments**	
1 Selection		**1 Selection**	
1 Eligibility criteria	Low	1	Appropriate: yes, as Type II diabetes is expected to occur later in life. Wanted to have representative population in the exposure group (or at risk group) for a given follow-up period (20yrs).
2 Comparability of exposure/case and comparison/control groups	Low	2	Low, as same individuals are in the comparison groups and were aware of possible differences and accounted for them (confounding)
3 Non-response rate	Some concerns	3	Response rate is reported. Reasons for non-response not reported.
4 Recruitement time frame	Low	4	Relevant dates are clearly described.
2 Exposure		**2 Exposure**	
1 Accuracy, validity and reliability of exposure measurements	High	1	The methods of measurement seemed adequate. We have only information on the selenium at the age of 50 years. However, no further information on selenium concentrations during the observation period of 20 years.
2 Misclassification of exposure	Low	2	It is a prospective cohort study.

Fictional example

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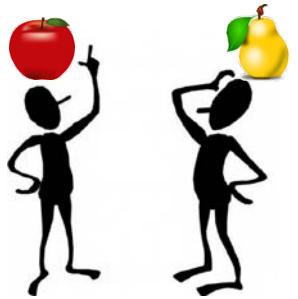
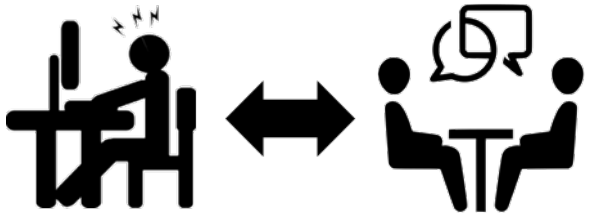
Next steps

- Finalising test phase
- Adapt tool according to results and feedback
- Implementation as a web-based app
- Publication of the tool

Summary – Take-home messages about raRoB

- A tool for short-term and individual RoB assessments
- Rapid usability for researchers in interdisciplinary appraisal teams
- Transparent assessments
- Systematically developed and tested





Cliparts were taken from https://clipart-library.com/

Acknowledgments

BfR Committee for Evidence-Based Methods in Risk Assessment

Kerstin Schmidt (BioMath)

Henning Thole
(KBV, Berlin; SRH University of Applied Health Sciences)

EFSA

Laura Ciccolallo

Marios Georgiadis

BfR

Sven Knüppel

Anselm Hornbacher

Narges Ghoreishi

Christine Müller-Graf

Matthias Greiner

Special thanks to Paul Schmidt (BioMath) for technical support and **all testers of the raRoB tool!**

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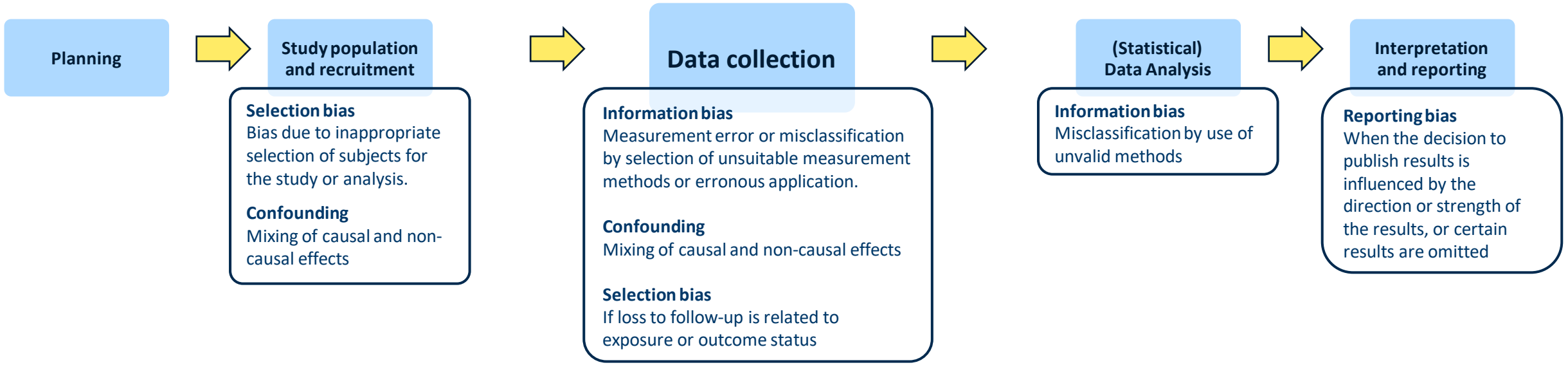
Types of bias



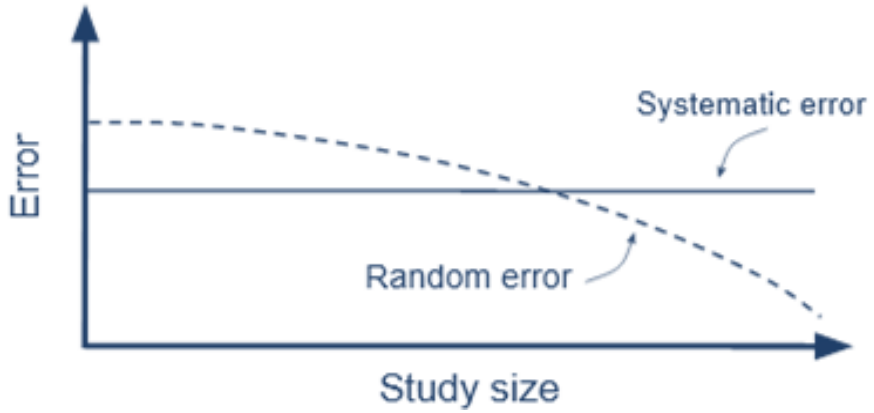
Random error vs. systematic error (bias)

Random error

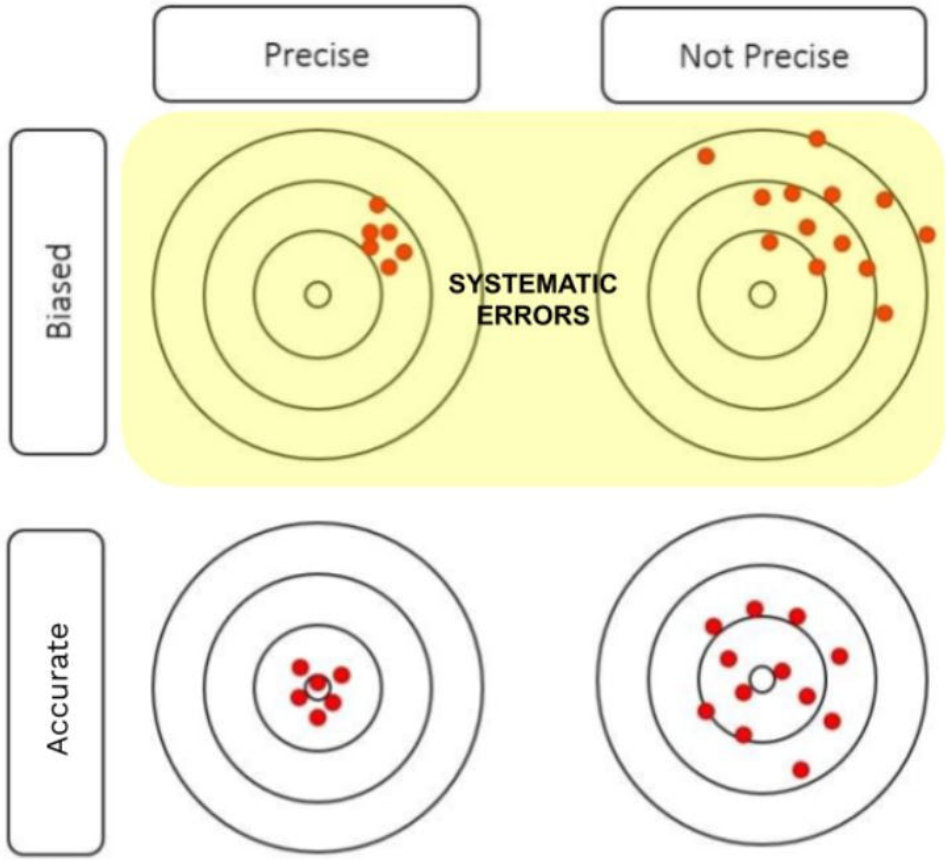
- Resulting from **sampling variability**

Systematic error (bias)

- Resulting from errors in **design and conduct**



According to Rothman (2012). Epidemiology: an introduction.

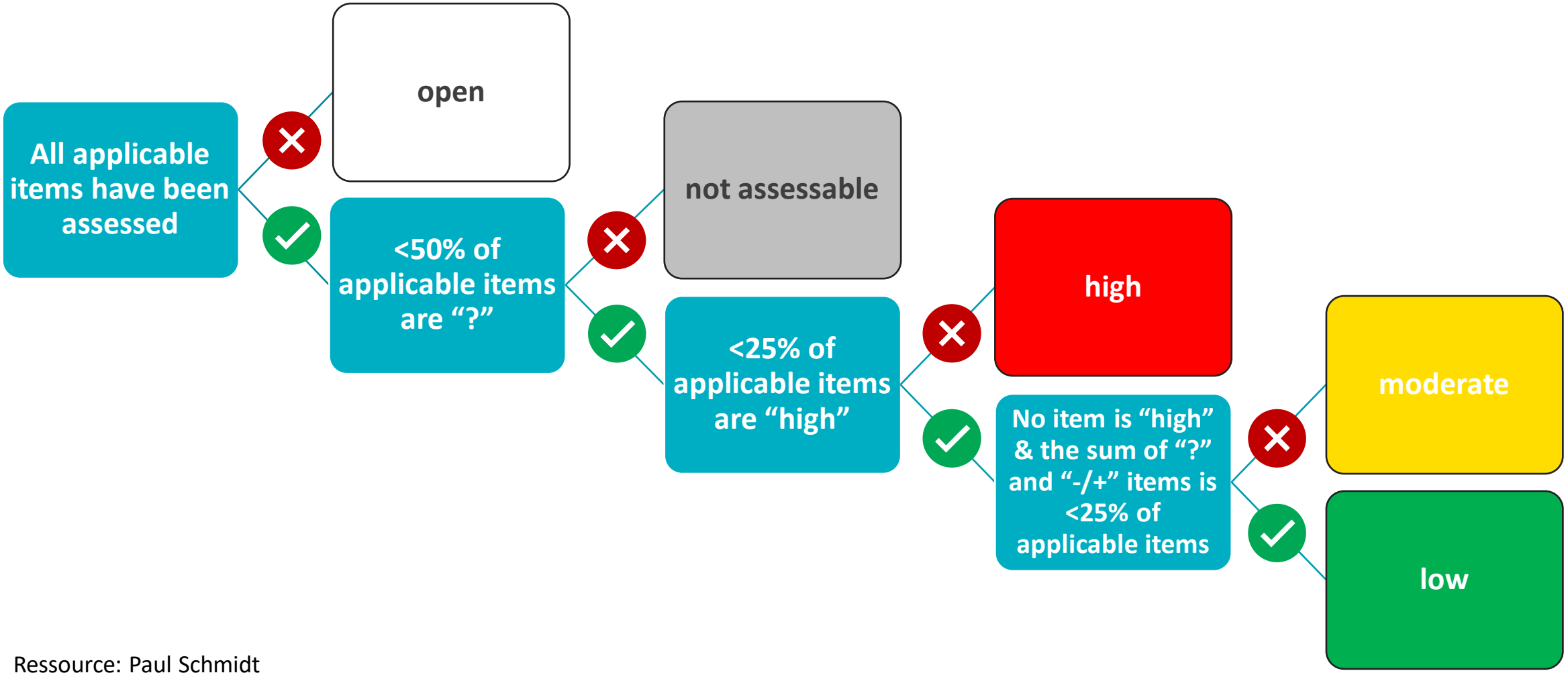


https://www.biologyforlife.com/error-analysis.html

Comparision of domains of raRoB to other established RoB tools

raRoB	ROBINS-E	OHAT
1 Selection	Risk of bias in selection of participants into the study (or into the analysis)	Selection Bias
2 Exposure	Risk of bias arising from measurement of the exposure	Detection Bias
3 Outcome Assessment	Risk of bias arising from measurement of the outcome	Detection Bias
4 Confounding	Risk of bias due to confounding	Confounding Bias
5 Loss to follow-up	Risk of bias due to missing data	Attrition/Exclusion Bias
6 Analysis	Risk of bias due to missing data	Attrition/Exclusion Bias Other sources of Bias
7 Selective reporting	Risk of bias in selection of the reported result	Risk of bias due to missing data
Overall risk of bias	Overall risk of bias	
	Risk of bias due to post-exposure interventions	

Assessment scheme
Overall Risk of Bias – Worst rating score

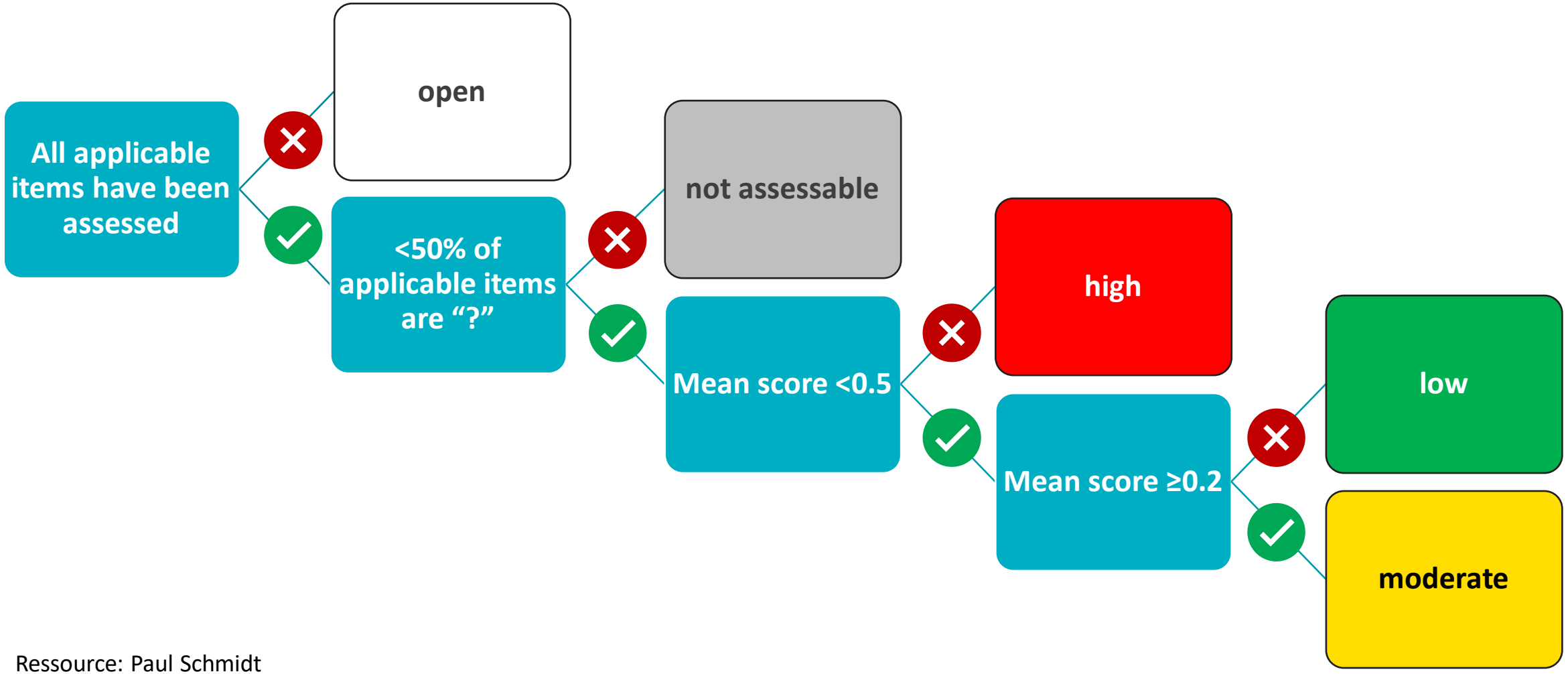


Ressource: Paul Schmidt

"?" – undecided/no judgement

High/no information = 1
Some concerns = ½
Low/undecided/no judgement = 0

Assessment scheme
Overall Risk of Bias – Ratio score



Ressource: Paul Schmidt

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