



Systematic reviews of observational data



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“Epidemiologist know a lot about the correct way to conduct a research study but less about how to review and synthesize data from multiple studies and this, I suggest, is a principal source of the public’s confusion when faced with a new result from an epidemiological study”

Bracken MB. IJE 2001:954





What is a systematic review?

A review:

- ✓ clearly formulated question
- ✓ uses systematic and explicit methods to **identify** and **collect** relevant research
- ✓ uses systematic and explicit methods to **select**, **critically appraise** and **analyse** relevant research included.





What is a systematic review?

Statistical methods (meta-analysis) may or may not be used to summarise the results of the included studies





How much work is a systematic review?

~ 1139 hours

~ 30 person-weeks of full-time work

- ✓ 588 for protocol, searching and retrieval
- ✓ 144 for statistical analysis
- ✓ 206 for report writing
- ✓ 201 for administration

Source: Allen IE. JAMA, 1999;282:634





What are observational studies?

- ✓ Data from existing database
- ✓ Cross-sectional study
- ✓ Case series
- ✓ Case-control study
- ✓ Cohort study





RCT

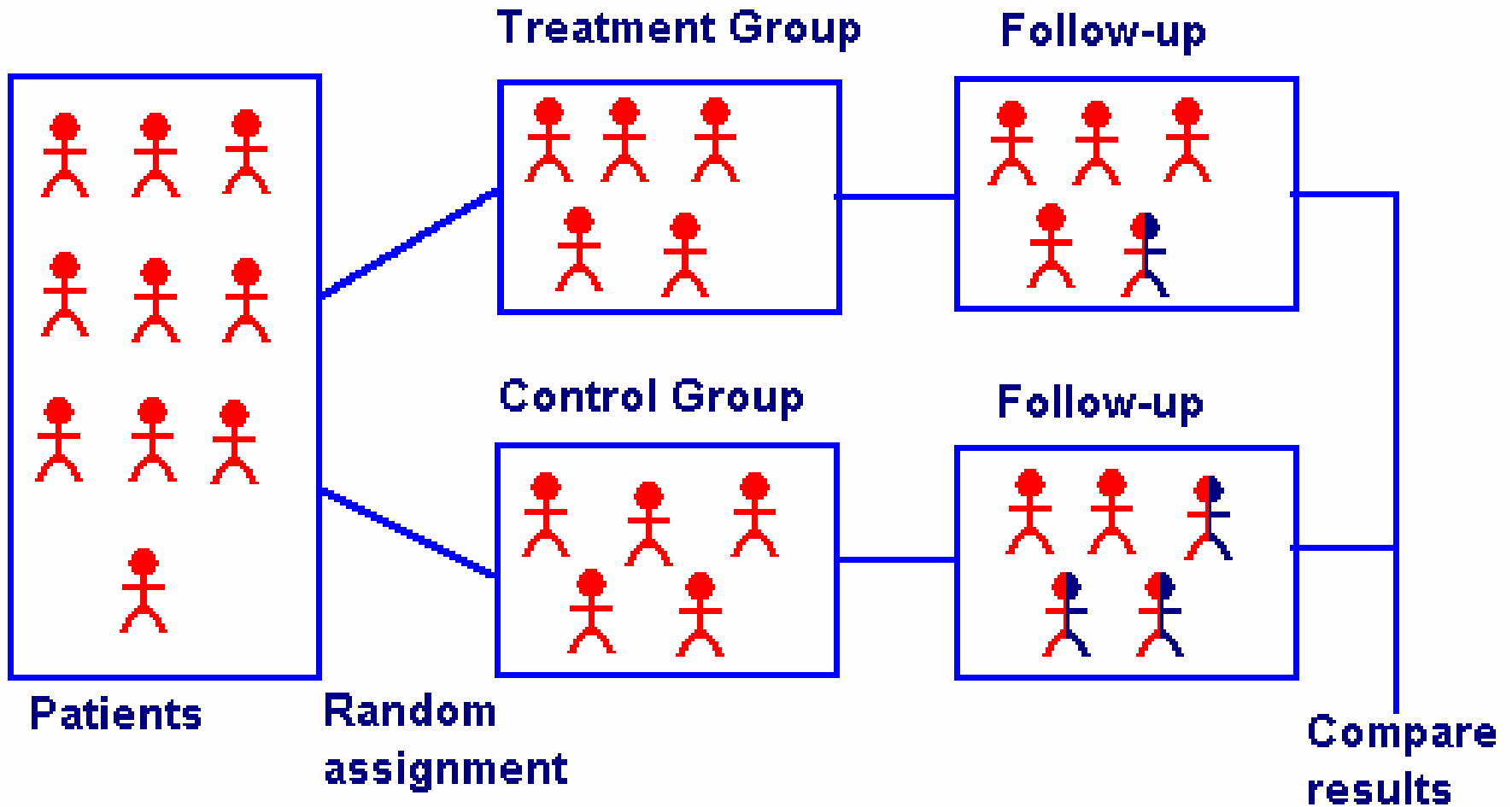


Observational studies





Randomized controlled trials





Why do we need systematic reviews of observational studies?

- ✓ Test aetiological hypothesis
- ✓ Evaluation of interventions designed to prevent rare outcomes
- ✓ Evaluation if outcomes of interest are far in the future
- ✓ Evaluation of effectiveness in a community





MAOS are common

Type of article	Articles (n)
Meta-analysis of:	
Controlled trials	34
Observational studies	25
Methodological article	15
Traditional review	15
Other	11

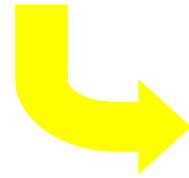
Source: Egger M. Systematic reviews in Health Care. Meta-analysis in context. BMJ Books. 2001



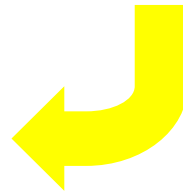


RCT

(Lack of precision)



Meta-analysis



More reliable estimates

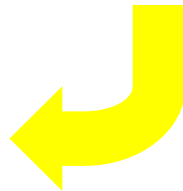
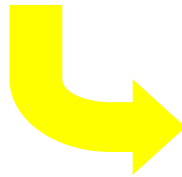




Observational studies

(Confounding, bias)

Meta-analysis



More reliable estimates????





Confounding factors

Smoking



Suicide



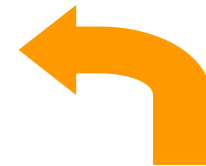
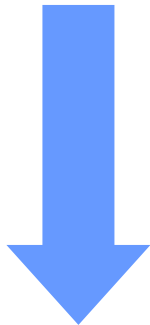
Social/mental states





Confounding factors

Coffee consumption



Risk of myocardial infarction





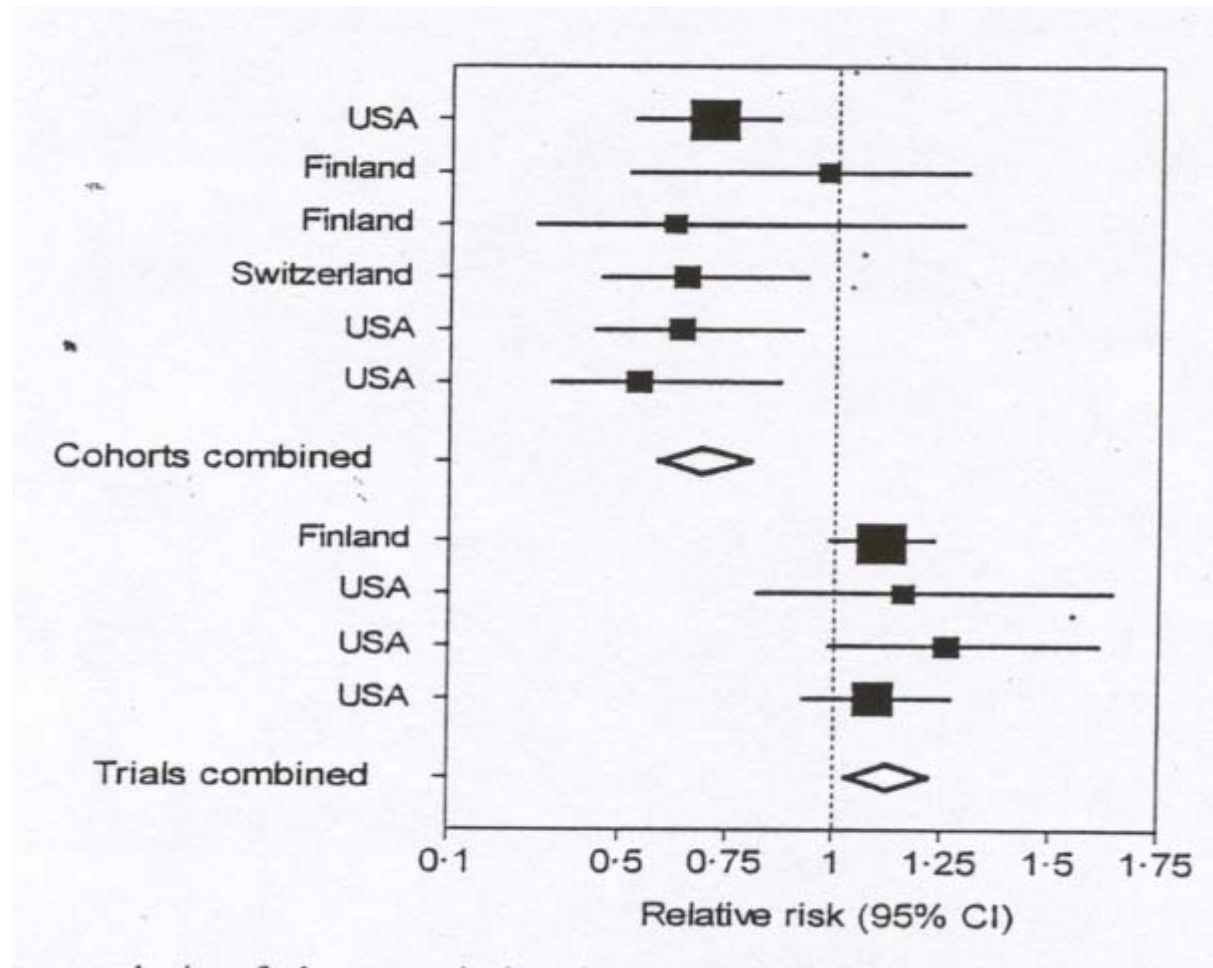
The protective effect of beta-carotene that wasn't

Cohorts

- Male health workers
- Social insurance, men
- Social insurance, women
- Male chemical workers
- Hyperlipidaemic men
- Nursing home residents

Trials

- Male smokers
- Skin cancer patients
- (Ex)-smokers, asbestos workers
- Male physicians





There are examples of observational studies producing similar results of those from RCT

But observational studies will always have to deal with **bias** and **confounding** because the intervention was deliberately chosen and not randomly allocated





Benson and Hartz, NEJM, 2000;342:1878-86

The New England Journal of Medicine

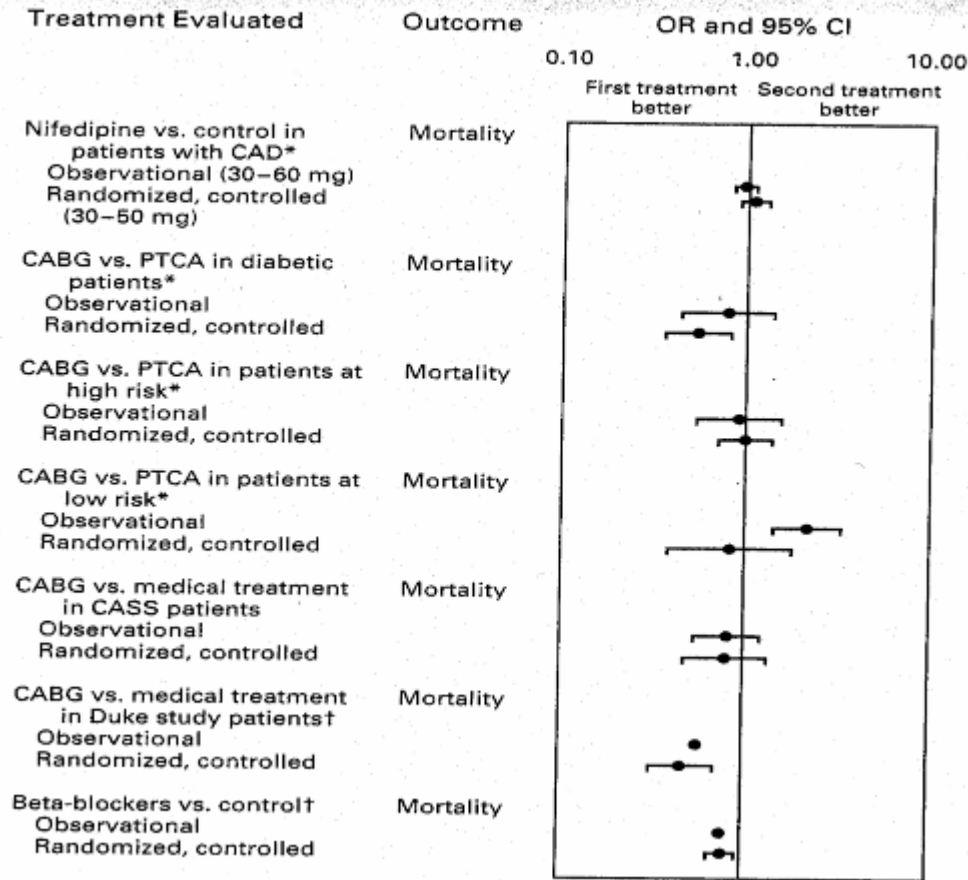
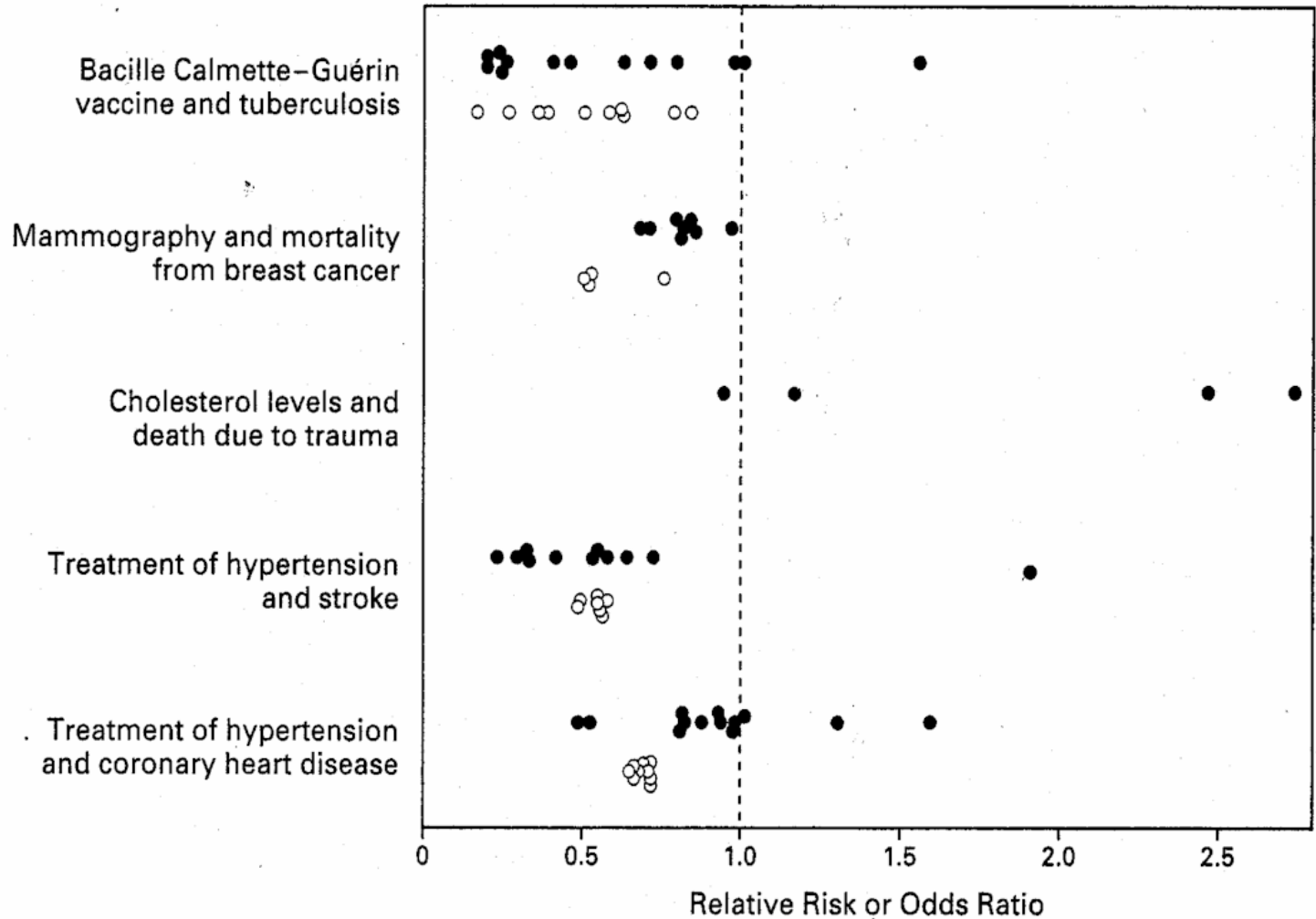


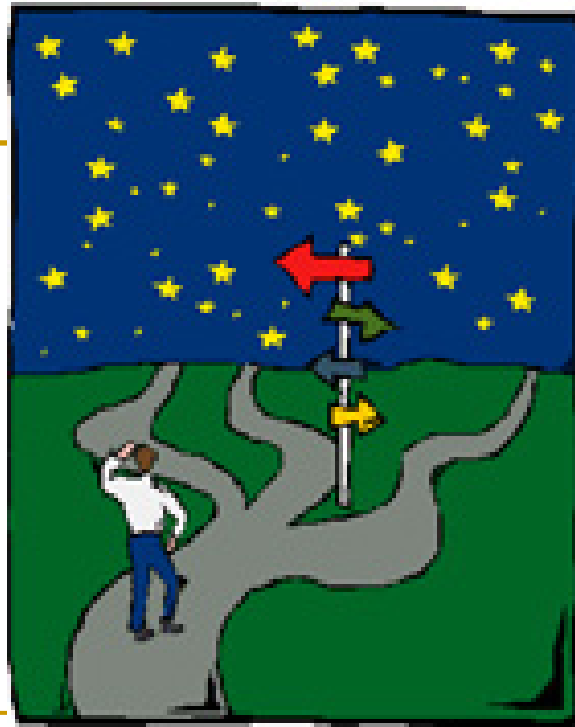
Figure 1. Results of Observational Studies vs. Randomized, Controlled Studies.





Concato et al., NEJM, 2000;342:1887-92





**This does not mean to return to
narrative reviews**





Benefits of MAOS:

- ✓ Systematic and explicit rules
- ✓ Statistical power
- ✓ Insight into variable interaction
- ✓ Detection of discrepancies
- ✓ Deepness into heterogeneity
- ✓ Identification of gaps in knowledge





Reporting of background should include:

- 1 Problem definition, hypothesis statement
- 2 Description of study outcome(s)
- 3 Type of exposure or intervention used
- 4 Type of study designs used
- 5 Study population





Reporting of search should include:

- 6 Qualifications of researchers
- 7 Search strategy including time period
- 8 Effort to include all available studies
- 9 Databases and registries searched
- 10 Searching software used
- 11 Use of hand searching
- 12 List of citations located and those excluded, including justification
- 13 Methods of addressing articles not published in English
- 14 Methods of handling abstracts and unpublished studies
- 15 Descriptions of any contact with authors





Reporting of methods should include:

- 16** Description of relevance/appropriateness of papers assembled for assessing the hypothesis to be tested
- 17** Rational for the selection and coding of data
- 18** Documentation about how data were classified and coded
- 19** Assessment of confounding
- 20** Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results
- 21** Assessment of heterogeneity
- 22** Description of statistical methods in sufficient detail to be replicated
- 23** Provision of appropriate tables and graphics





Reporting of results should include:

- 24** Graphic summarizing individual study estimates and overall estimate
- 25** Table giving descriptive information for each study included
- 26** Results of sensitivity testing (e.g. subgroup analysis)
- 27** Indication of statistical uncertainty of findings





Reporting of discussion should include:

- 28** Quantitative assessment of bias
- 29** Justification for exclusion
- 30** Assessment of quality of included studies





Reporting of conclusions should include:

- 31** Consideration of alternative explanations for observed results
- 32** Generalization of the conclusions
- 33** Guidelines for future research
- 34** Disclosure of funding source





Quality of reviews in Epidemiology

Breslow R. *AJPH*, 1998;88:475-7

All 1995 issues of 7 widely read epidemiology journals were searched for reviews



29 reviews were found





Reviews following quality guidelines

Guideline	Yes	Unable to determine	No
Search methods stated	6 (21)	1 (3)	22 (76)
Inclusion criteria reported	5 (17)	4 (14)	20 (69)
Bias in selecting studies avoided	3 (10)	26 (90)	0 (0)
Criteria for assessing validity reported	2 (7)	15 (52)	12 (41)
Methods for combining findings reported	10 (34)	6 (21)	13 (45)
Conclusions supported by data	24 (83)	4 (14)	1 (3)





Search restriction:

General medical journal, 2001

Search Procedure	19 meta-analyses	13 systematic reviews
Numerous Databases Searched (versus just MEDLINE)	13 (68%)	6 (46%)
Additional Searches Conducted (e.g., manual search of reference lists or textbooks)	17 (89%)	10 (77%)
Gray Literature Searched (e.g., manual search of conference or dissertation abstracts)	5 (26%)	4 (31%)
Contacted Experts to Find Unpublished Data	7 (37%)	2 (15%)
Cochrane Databases Searched	8 (42%)	4 (31%)
All Methods Employed	4 (21%)	1 (8%)





Search restriction: General medical journal, 2001

Language Restriction	19 meta-analyses	13 systematic reviews
None	6 (32%)	1 (8%)
English plus other lang.	2 (11%)	0 (0%)
English only	7 (37%)	7 (54%)
Unclear	4 (21%)	5 (38%)
Attempted to include unpublished studies	7 (37%)	5 (38%)





Other citations:

- ✓ Mulrow CD. The medical review article: state of the science. *Ann Intern Med* 1987, 6:233-240.
- ✓ McAlister FA, Clark HD, van Walraven C et al. The medical review article revisited: has the science improved? *Ann Intern Med* 1999, 131:947-951
- ✓ Bracken MB. Commentary: towards systematic reviews in epidemiology. *IJE* 2001, 30:954-957.





Summary

- ✓ SR and MA of observational studies are as common as reviews of RCT
- ✓ Confounding and selection bias often distort the findings
- ✓ Danger in producing very precise but spurious results
- ✓ More is gained by examining heterogeneity





WHO Systematic review of incidence/prevalence of maternal mortality and morbidity 1997-2002





Objectives

- To provide a comprehensive, standardised and reliable tabulation of available data on maternal morbidity
- To provide up-to-date data for future maternal mortality estimates
- To provide case-fatality rates





CHARACTERISTICS OF THE STUDY

3. Study design

- (1) Census
- (2) Cross-sectional
- (3) Cohort/longitudinal
- (4) Controlled trial
- (5) Incidence/Prevalence survey
- (6) Unknown
- (7) Other, specify _____

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WHO CODE

4. Sampling

- (1) Random sample
 - 4a. Specify the method of randomization:

WHO CODE

- (2) Non-random sample
 - 4b. Specify the method of sampling:

WHO CODE

- (3) Total population (i.e. census)
- (4) Unknown

WHO systematic review

5. Data source

- (1) Vital statistics/census
- (2) Medical record
- (3) Special survey/interview
- (4) Multiple sources
- (5) Clinical data collected for the study
- (6) Other, specify _____

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WHO CODE

6. Lowest unit of data source

- (1) Cluster
 - 6a. Number of clusters
- (2) Individual
- (3) Other, specify _____

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WHO CODE





WHO systematic review

9. Population studied	<input type="checkbox"/>			
(1) Urban				
(2) Rural				
(3) Mixed				
(4) Unknown				
10. Description of the characteristics of the population studied (e.g. socio-economic status, ethnic group, age group, etc.)	<table border="1"><tr><td><input type="text"/></td><td><input type="text"/></td><td><input type="text"/></td></tr></table> WHO CODE	<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>		





WHO systematic review

MATERNAL MORTALITY (cont.)			
26a. Cause distribution of maternal mortality			
Condition	(i) WHO code	(ii) No. of deaths	(iii) Percentage
26a.1) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.2) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.3) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.4) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.5) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.6) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>
26a.7) _____	<input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/>





WHO systematic review

32. Infections	
32a) Condition _____	WHO code <input type="text"/> <input type="text"/> <input type="text"/>
32b) Does the study include a definition?	Yes <input type="checkbox"/> No <input type="checkbox"/>
32c) If definition is included, please specify: _____ _____	WHO code <input type="text"/> <input type="text"/> <input type="text"/>
32d) Does the study explain the method of assessment of the infection?	Yes <input type="checkbox"/> No <input type="checkbox"/>
32e) If method of assessment is explained, please specify: _____ _____	WHO code <input type="text"/> <input type="text"/> <input type="text"/>





MATERNAL MORTALITY

25a. Maternal mortality estimates

i) Year

From		To	

ii) Age group

From		To	

iii) No. of deaths

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iv)

Denominator							

v)

- 1. Live births
- 2. Pregnancies
- 3. Deliveries

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vi)

MM Rate			

vii)

CI (95%)			

-

CI (95%)			

viii)

MM Ratio			

ix)

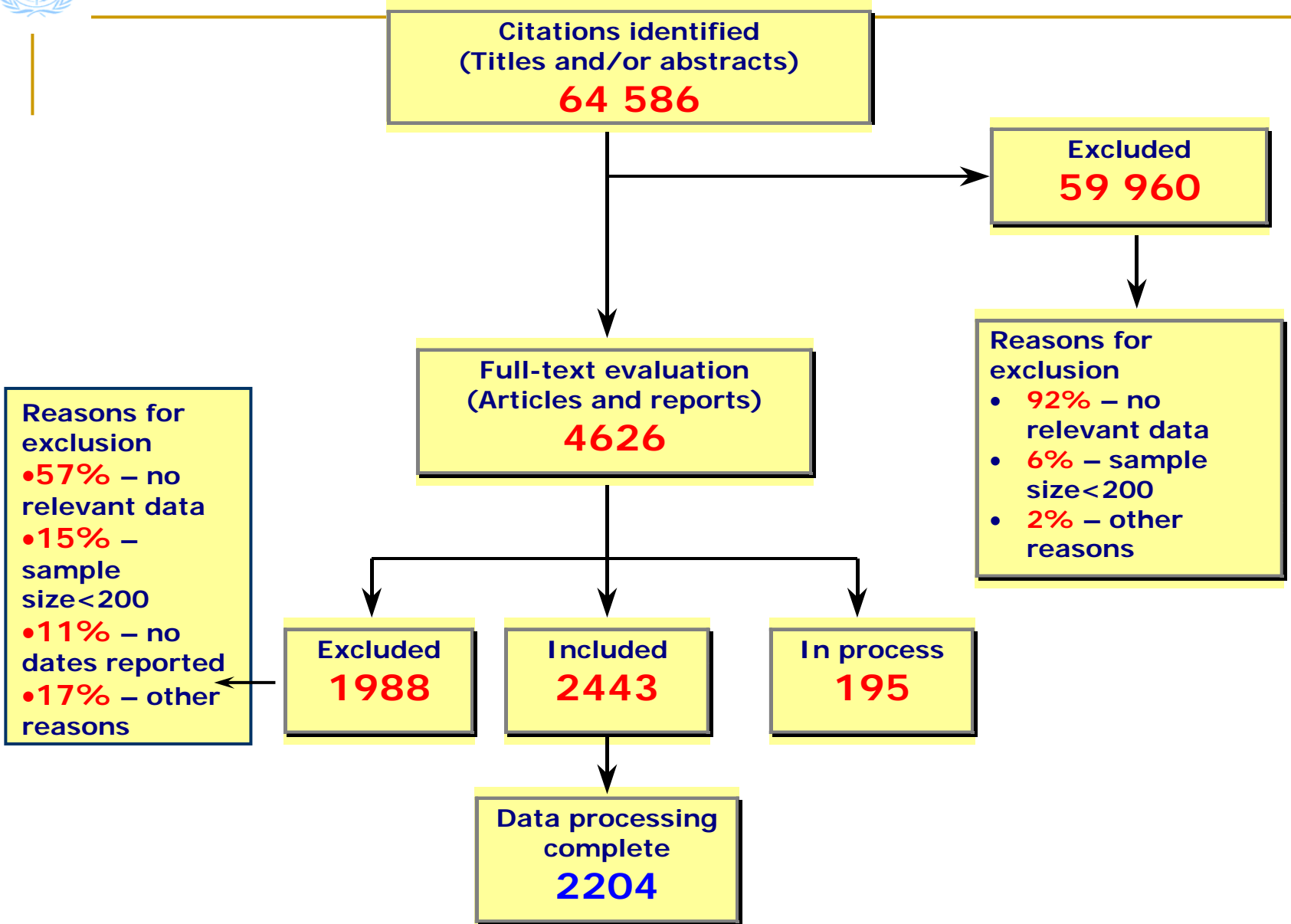
CI (95%)			

-

CI (95%)			

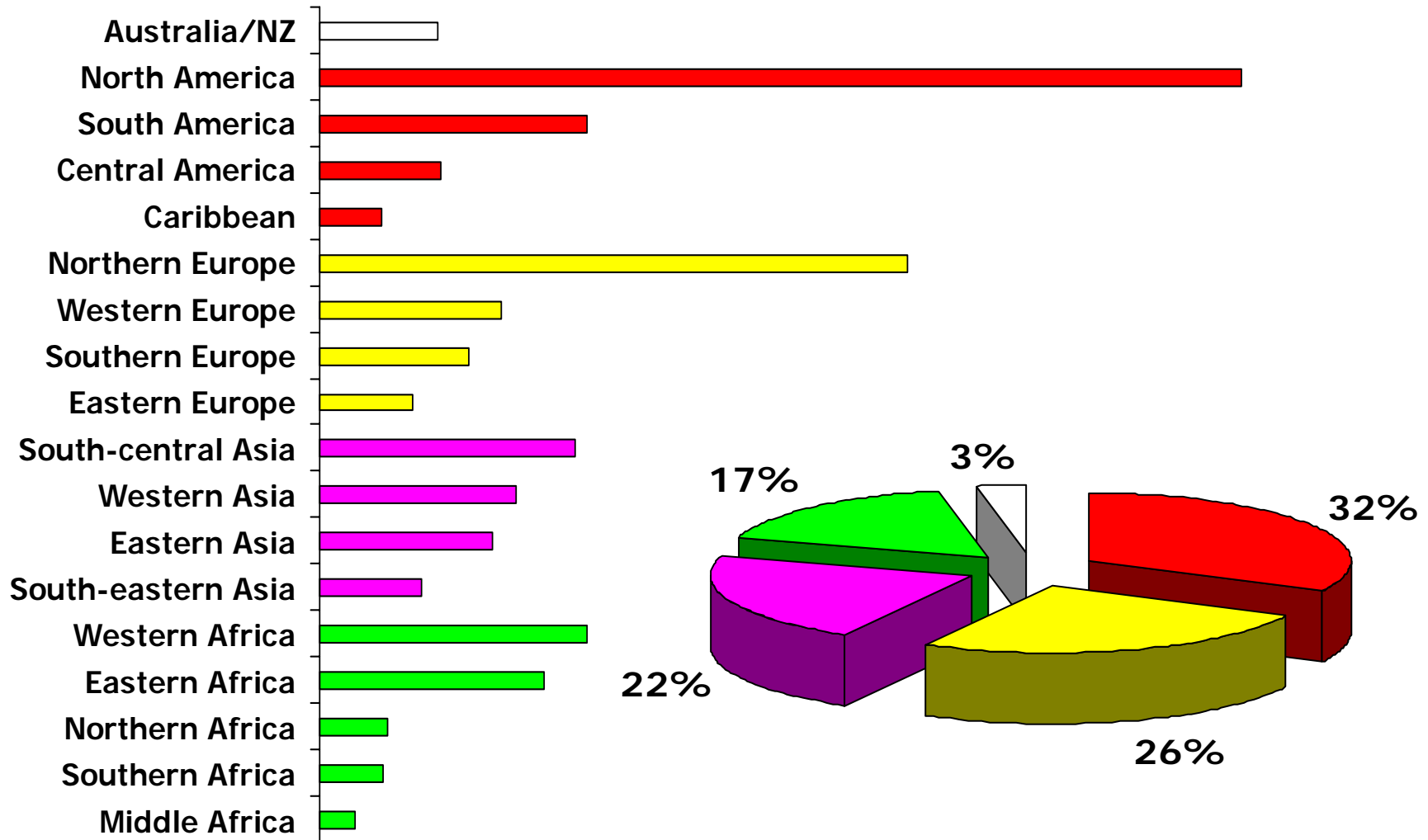
WHO systematic review





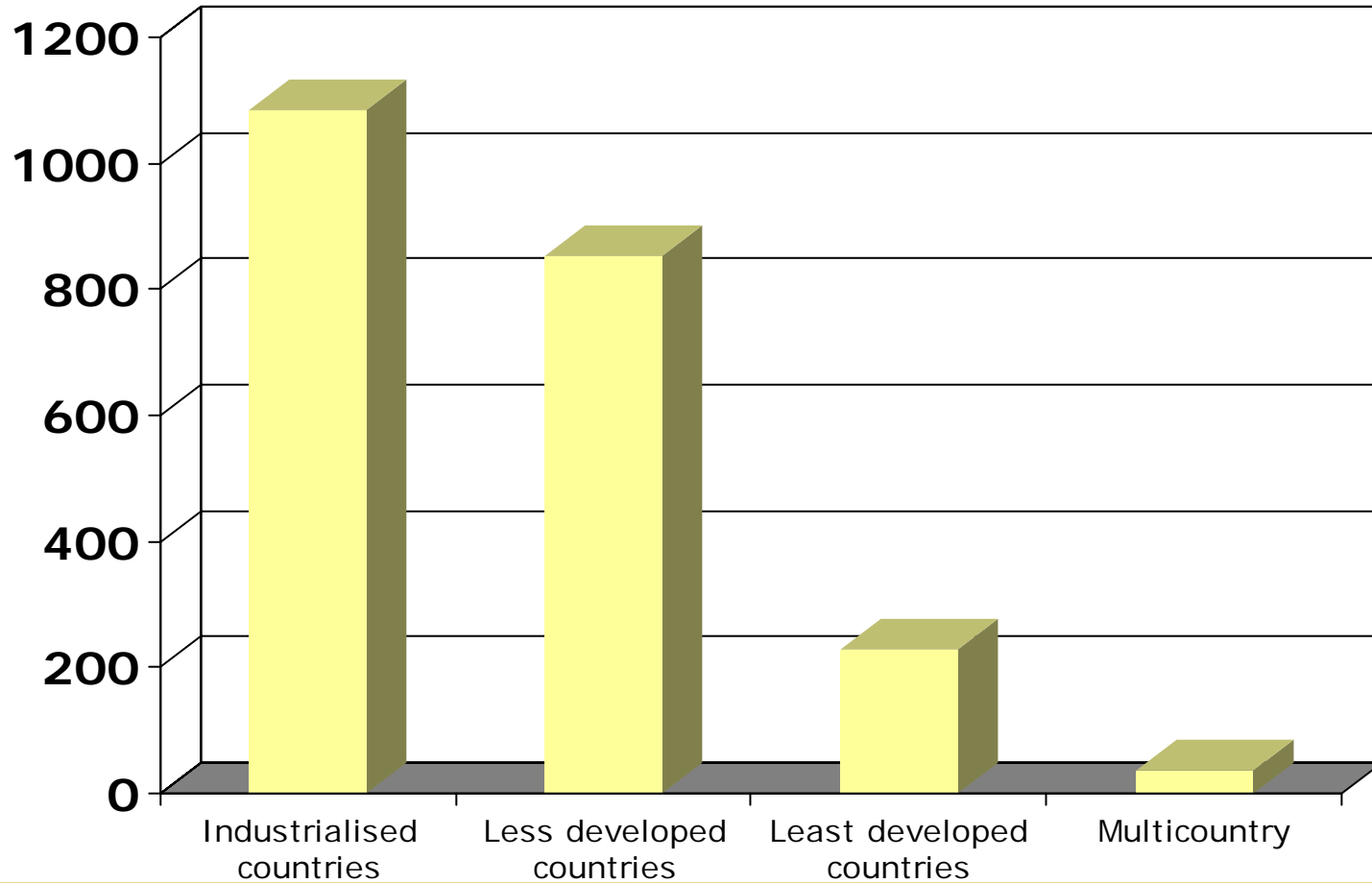


Regional distribution (n=2204)





Development status (n=2204)





Results: methodological quality of reported data

	Morbidity (n = 3215)	Mortality (n = 335)	Total (n = 3550)
High	103	8	111
Medium	1670	250	1920
Low	1442	77	1519





Reported morbidities (n=3215)

- ✓ Hypertensive disorders of pregnancy (16.3%)
- ✓ Haemorrhage (11.1%)
 - ✓ postpartum - 2.7%
 - ✓ antepartum / intrapartum - 2.2%
 - ✓ placenta praevia - 1.8%
 - ✓ abruptio placenta - 2.6%
 - ✓ other haemorrhage / unspecified - 1.8%
- ✓ Abortion (10.7%)
- ✓ Preterm delivery (8.3%)
- ✓ Stillbirth (6.3%)
- ✓ Diabetes in pregnancy (4.4%)
- ✓ Anaemia in pregnancy (4.3%)
- ✓ Ectopic pregnancy (3.0%)
- ✓ Perineal tears (2.6%)
- ✓ PROM (2.6%)
- ✓ Uterine rupture (2.1%)
- ✓ Postpartum sepsis (1.6%)
- ✓ Depression (1.9%)
- ✓ Obstructed labour (1.8%)





*"And it was so typically brilliant of you
to have invited an epidemiologist."*

