

# High dropout rates in trials included in Cochrane Reviews

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## Outline

- ◆ Background & Objectives
- ◆ Methods
- ◆ Results
- ◆ Conclusions

## Missing data

- ◆ Potential source of **attrition bias** in primary studies
    - attrition bias in Systematic Reviews
  - ◆ Loss of **internal validity**
- Appropriate handling of missing data should be considered when interpreting results of Systematic Reviews

## What advice is given?

### Cochrane Handbook for Systematic Reviews of Interventions (Version 4.2.5)

- ◆ Section 3 “Guide to the consent of a protocol and review”

“Strategies for dealing with missing data should be described. This will principally include missing participants due to drop-out (whether an intention-to-treat analysis will be conducted) [...].”

- ◆ Section “Missing data” is under construction

### QUOROM statement

- ◆ The section “Methods of a meta-analysis” recommends describing the handling of missing data.

**→ No guidance is given on how to proceed**

## Our research question

- ◆ Is the issue of missing data in clinical trials considered in Cochrane Reviews?

### Other activities in this area, e.g.:

- Gamble and Hollis (Journal of Clinical Epidemiology. 2005)
- Cochrane Workshop by James Carpenter "Missing data in meta-analysis – a practical guide"

## Screening

- ◆ **Random sample**
  - 100 Cochrane Reviews (25/year for 2002-2005)
- ◆ **Inclusion criteria**
  - Any therapeutic intervention
  - Definition of primary outcome measure(s)
  - Inclusion of at least 5 primary trials in the Cochrane Review
- ◆ **Exclusion criteria**
  - Protocols or Updates

## Assessment

- ◆ **Two reviewers independently assessed, whether**
  - ...missing data were reported in the Cochrane Reviews
  - ...high missing data rates were reported in the Cochrane Reviews
  - ...if and how high missing data rates were considered
- ◆ **No standard definition for what is considered a “high” missing data rate**
  - Our question referred to missing data rates > 15%
- ◆ **If at least one primary study included in a Cochrane Review reported a missing data rate > 15%, the Cochrane Review was categorized as “reporting missing data > 15%”.**

## Problems during data extraction

- ◆ **Inconsistent use of terms**
  - Use of inconsistent terms within reviews,
  - Use of inconsistent terms between reviews.

*not stated*

*incomplete*

**dropouts**

**withdrawals**

*defaults*

*excluded*

*incomplete follow up*

*lost*

*not mentioned*

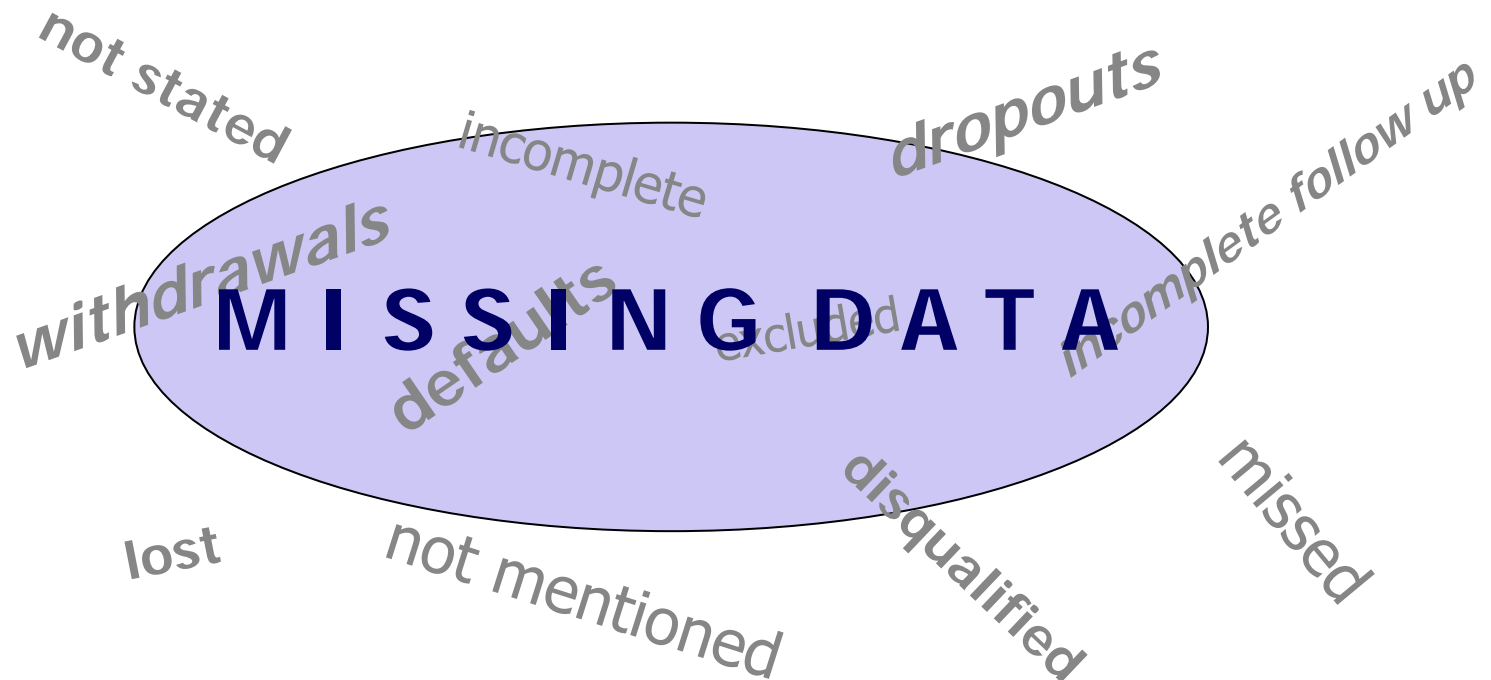
*disqualified*

*missed*



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## Problems during data extraction

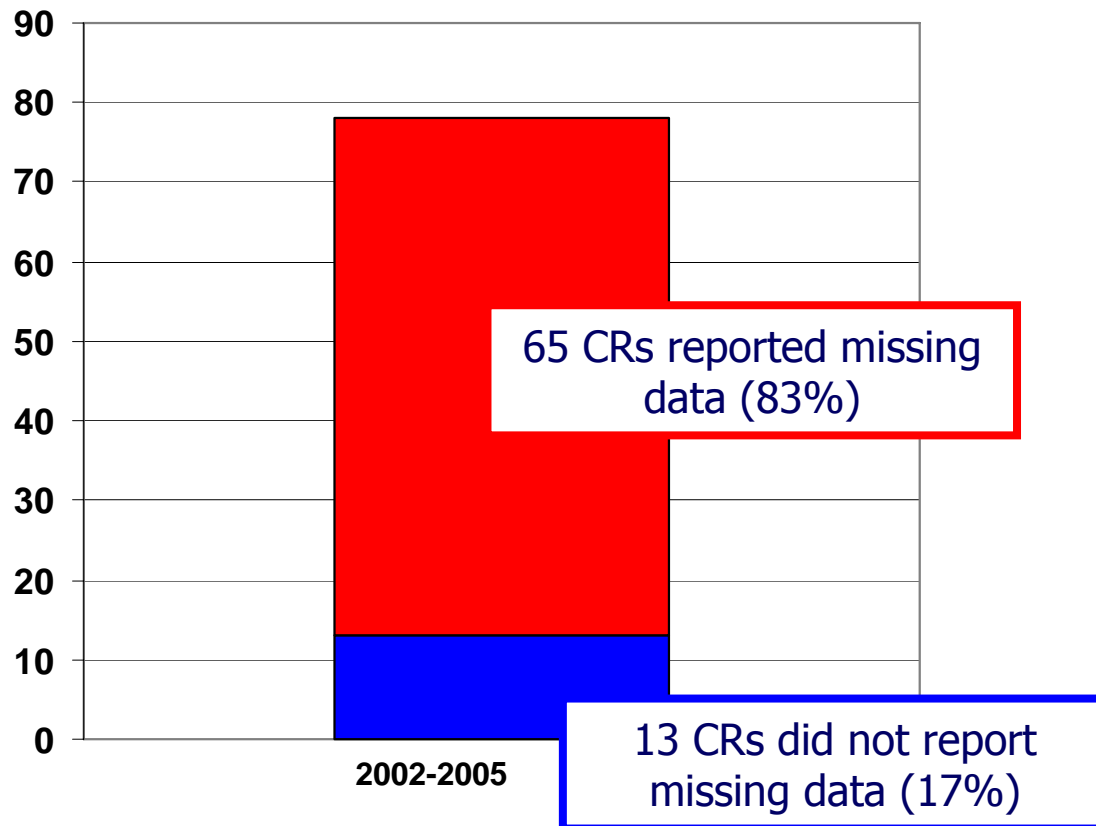
- ◆ **Inconsistent use of terms**
  - ◆ **Missing data in primary trials were not always reported**
  - ◆ **Inconsistent and unclear description of procedures, for dealing with missing data in primary studies included in the review - whether**
    - ...approaches to handle missing data were planned or not,
    - ...approaches were conducted or not,
    - ...there was an impact on results.
  - ◆ **Discrepancies within and between text and tables**
- **Problems were resolved by discussion between the two reviewers**

## Post hoc considerations

- ◆ Evaluation of missing data rates not only  $> 15\%$ , but also  $> 10\%$  and  $> 20\%$
- ◆ Exclusion of 21 Cochrane Reviews that defined “dropouts”, “withdrawals”, or “leaving the study early” as outcome measures
- ◆ Exclusion of one Cochrane Review (update)
- ◆ Remaining pool: 78 Cochrane Reviews

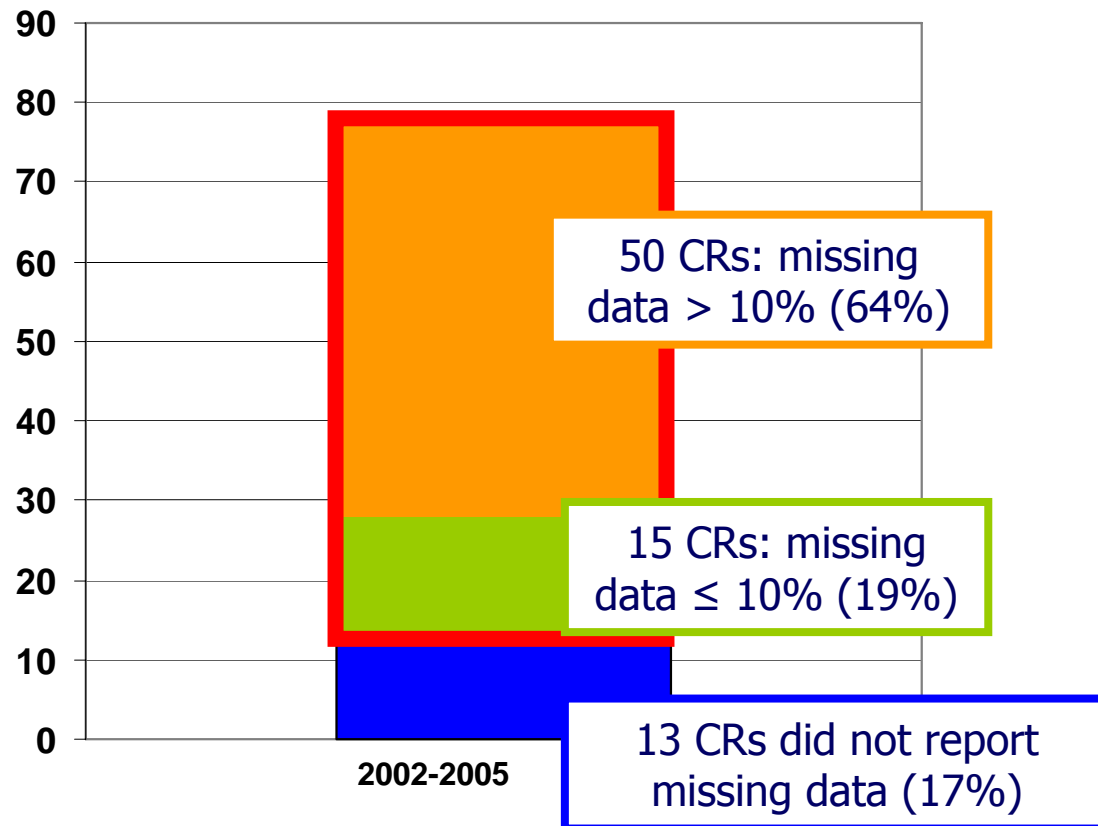
## Of 78 Cochrane Reviews (CRs) investigated....

Total number of Cochrane Reviews



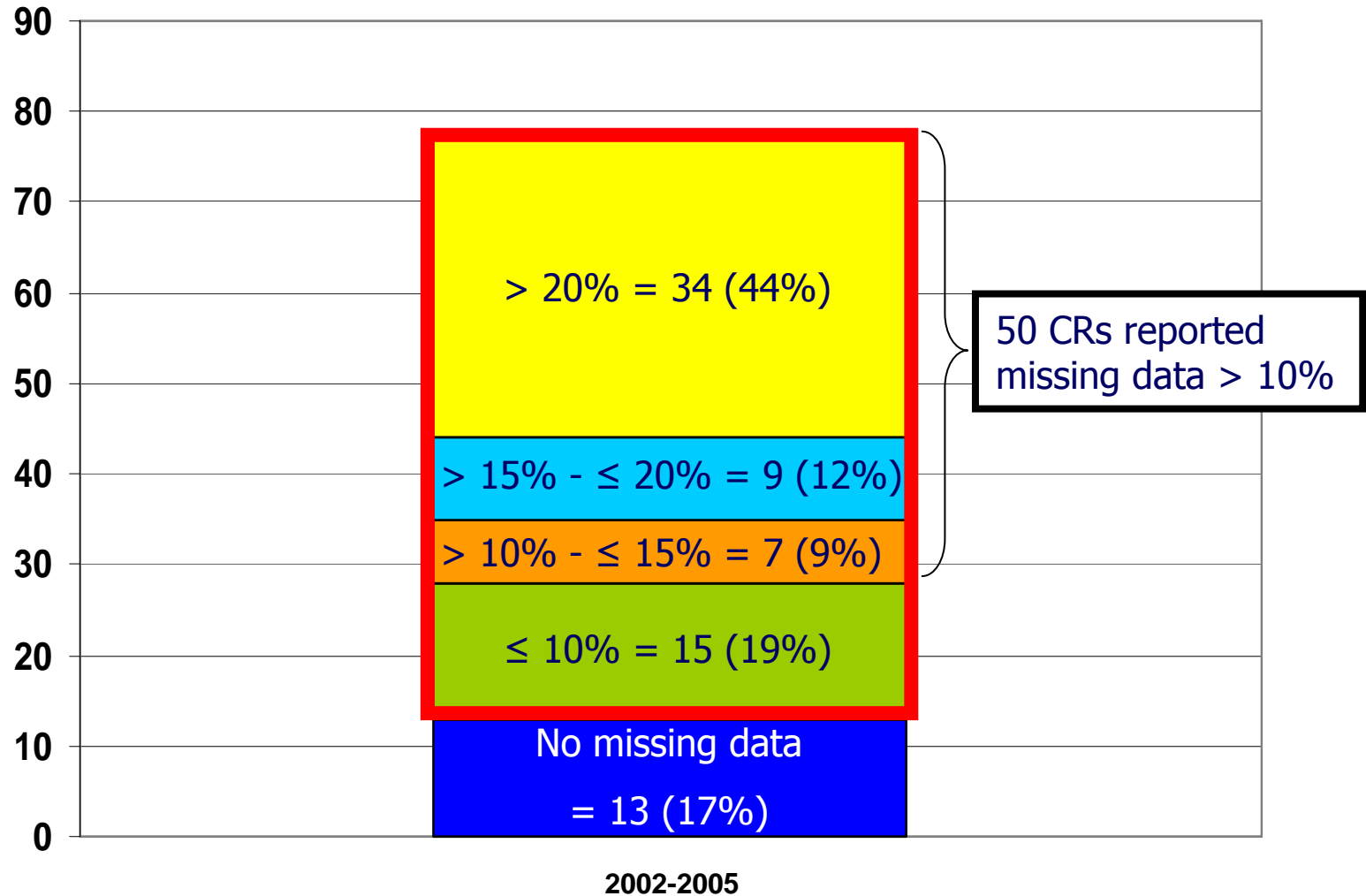
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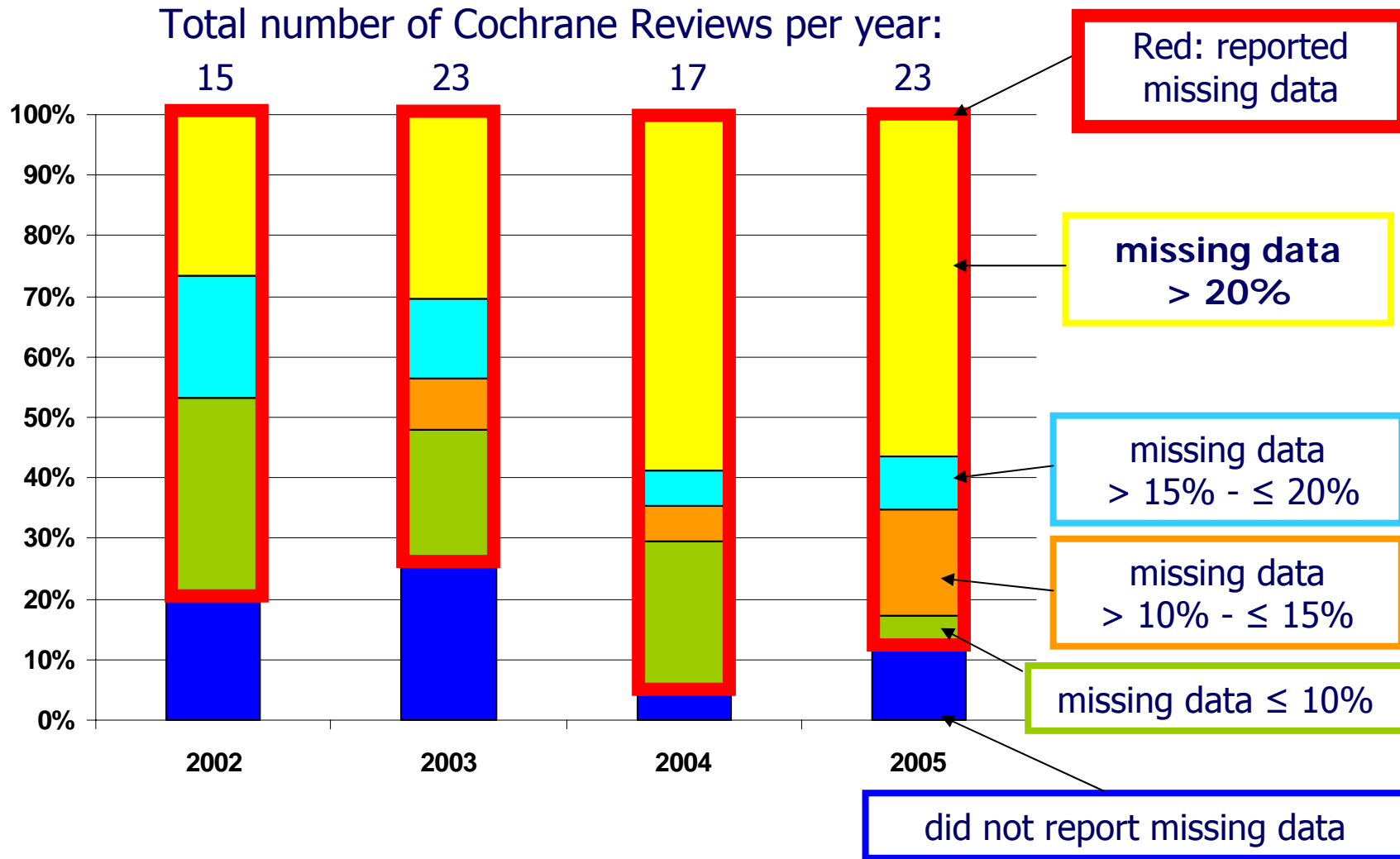


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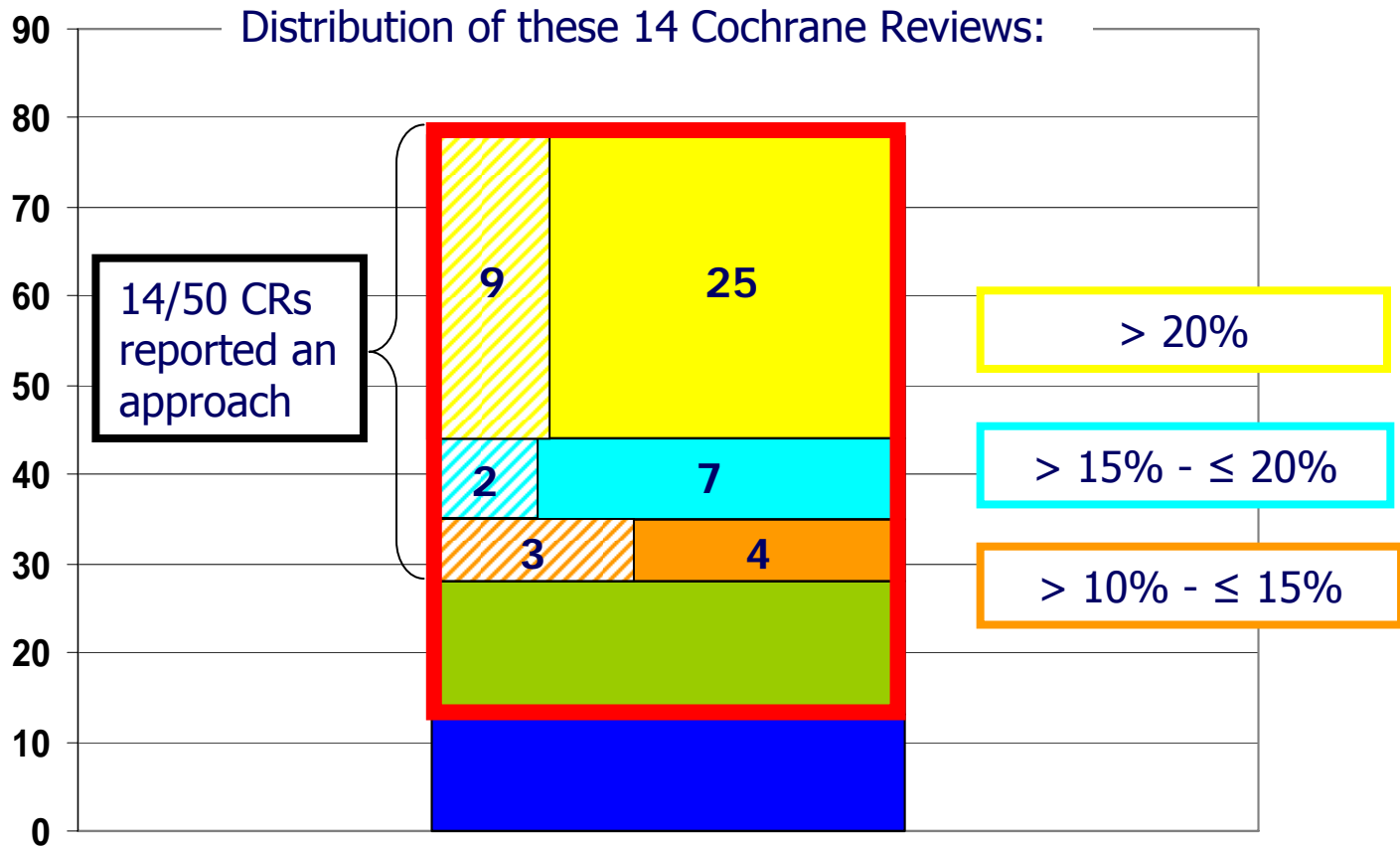


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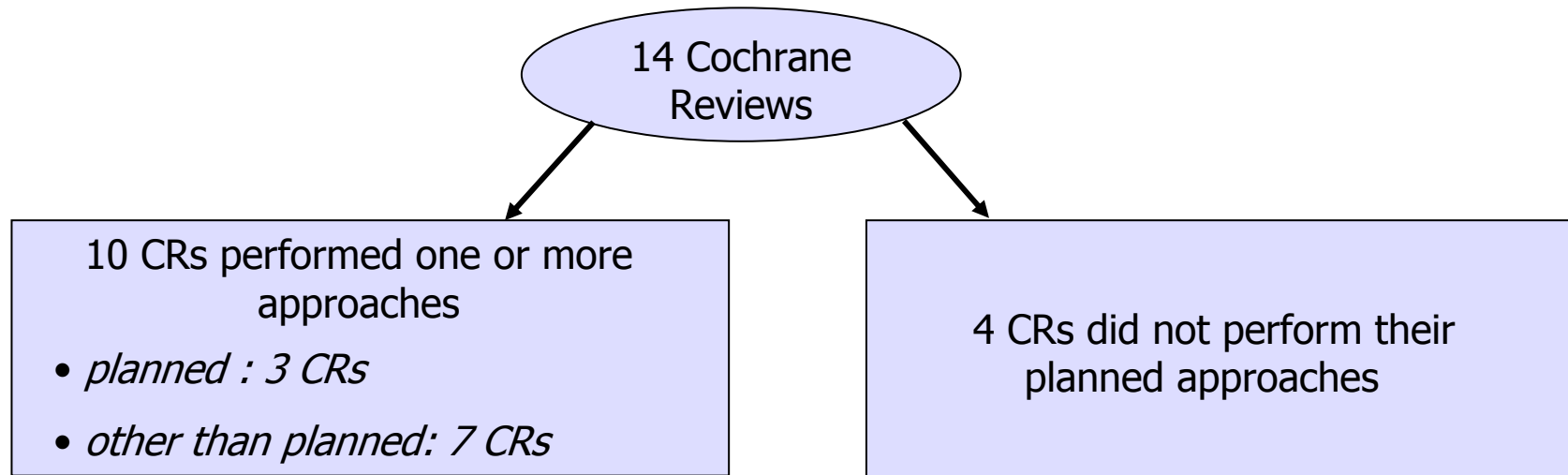
## Number of CRs reporting an approach

- ◆ ...50 Cochrane Reviews reported missing data rates  $> 10\%$
- ◆ ...of which **14 Cochrane Reviews** reported an approach for dealing with these missing data

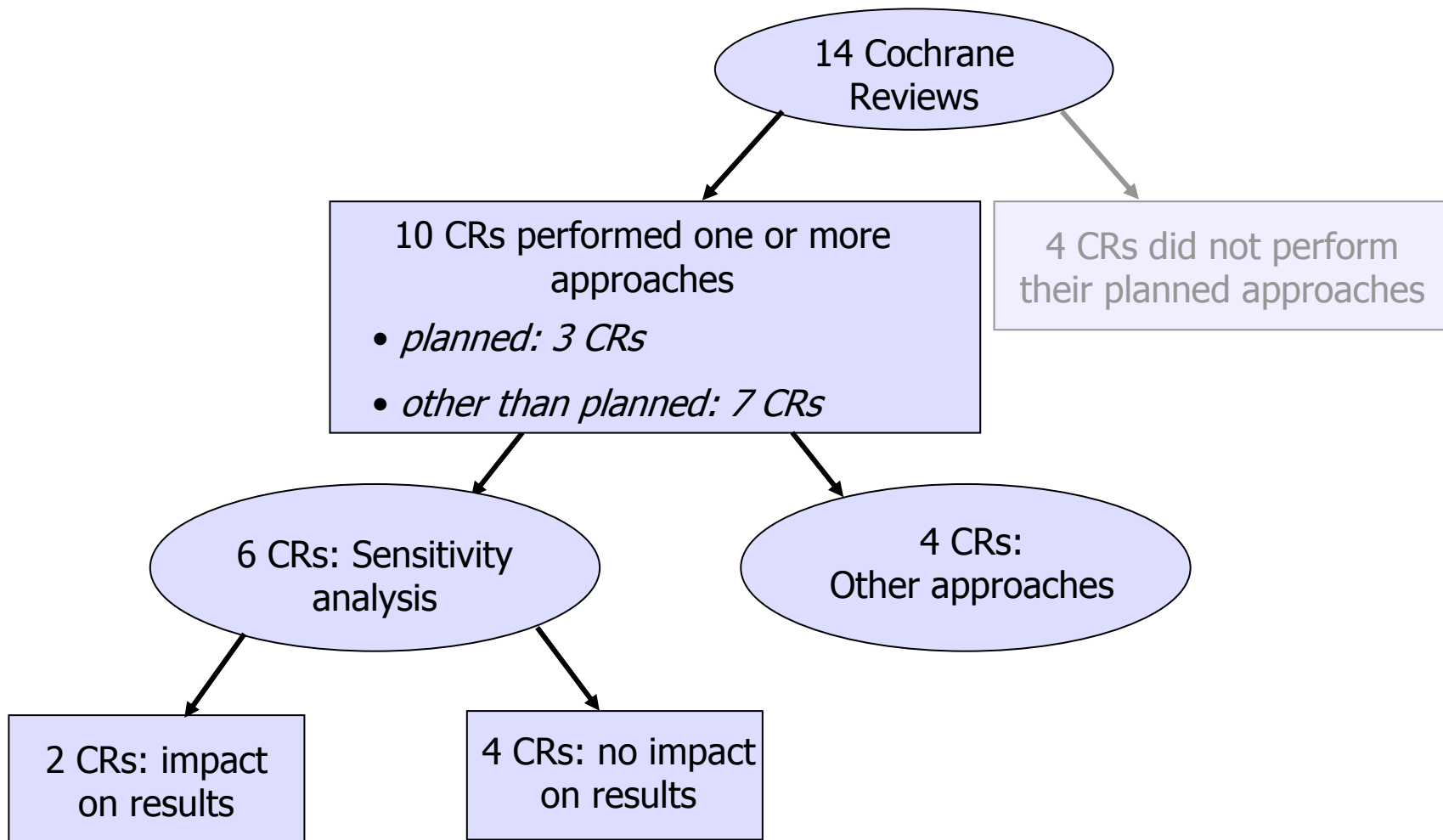




## ...of these 14 Cochrane Reviews (CRs)...



## ...of these 14 Cochrane Reviews (CRs)...



## Summary

### ◆ Problems during data extraction

- Inconsistent & unclear presentation of data
  - inconsistent use of terms
  - insufficient reporting of missing data and approaches for dealing with missing data (within & between Reviews)
  - discrepancies between text and tables

### ◆ Only 65 of 78 CRs reported missing data of primary studies

- 50 CRs reported rates of missing data > 10%
  - Only 14 CRs reported an approach for dealing with missing data
  - Only 10 of 14 CRs actually performed an approach

→ **Generalization of results is limited**

## → Suggestions:

- ◆ **Standardisation of terms used to describe missing data**
  - Cochrane Reviews should at least provide a definition of the term used
- ◆ **Standardisation of reporting missing data in Cochrane Reviews (Cochrane Handbook for Systematic Reviews of Interventions )**
  - Inclusion of table to describe missing data
- ◆ **Methods section: clear description of procedures planned**
  - Planned or unplanned consideration of missing data
  - Definition of a “high” rate of missing data
- ◆ **Results section: clear description of procedures conducted**
  - Was a planned or unplanned approach conducted or not (if not, why not?)
  - Impact on results of review

Thank you for your attention



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**The Cologne Cathedral**