Practical methods for handling missing summary statistics in meta-analysis of continuous outcomes

Cochrane Webinar, 5 February 2019

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Personal Chair in Medical Statistics & Clinical Trials

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Acknowledgements

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Stroke association

Rosetrees Trust
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- Co-Investigators
  - Steff Lewis, Gordon Murray — University of Edinburgh
  - Peter Langhorne — University of Glasgow
  - Marian Brady — Glasgow Caledonian University
- Researchers
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- Collaborators
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Outline

- Background to the issue
- Survey of Cochrane systematic review authors
- Systematic review of methods
  - Recovering missing SD value
  - Recovering missing mean value
- Real-world application of methods
- Conclusions and future work

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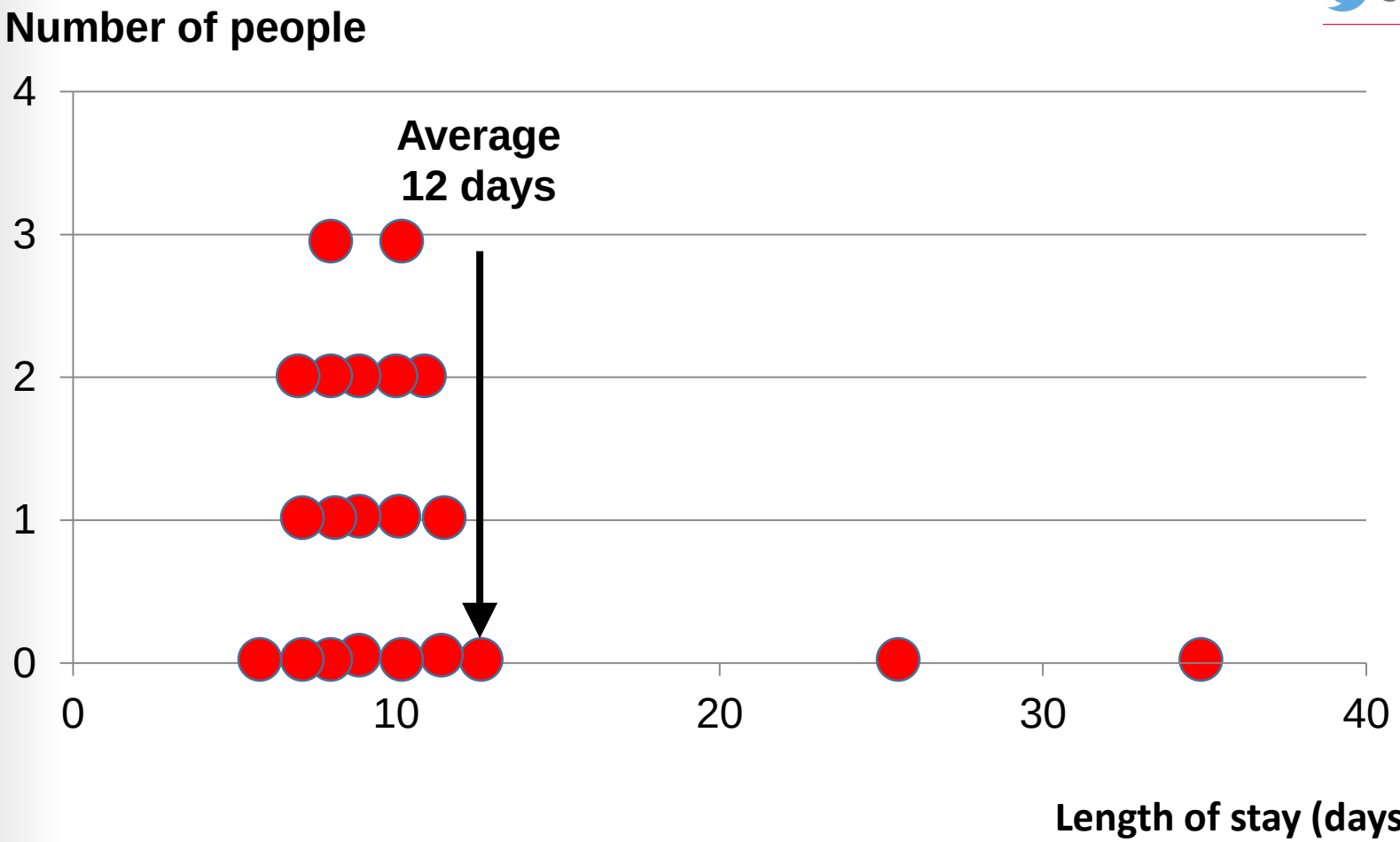

Background

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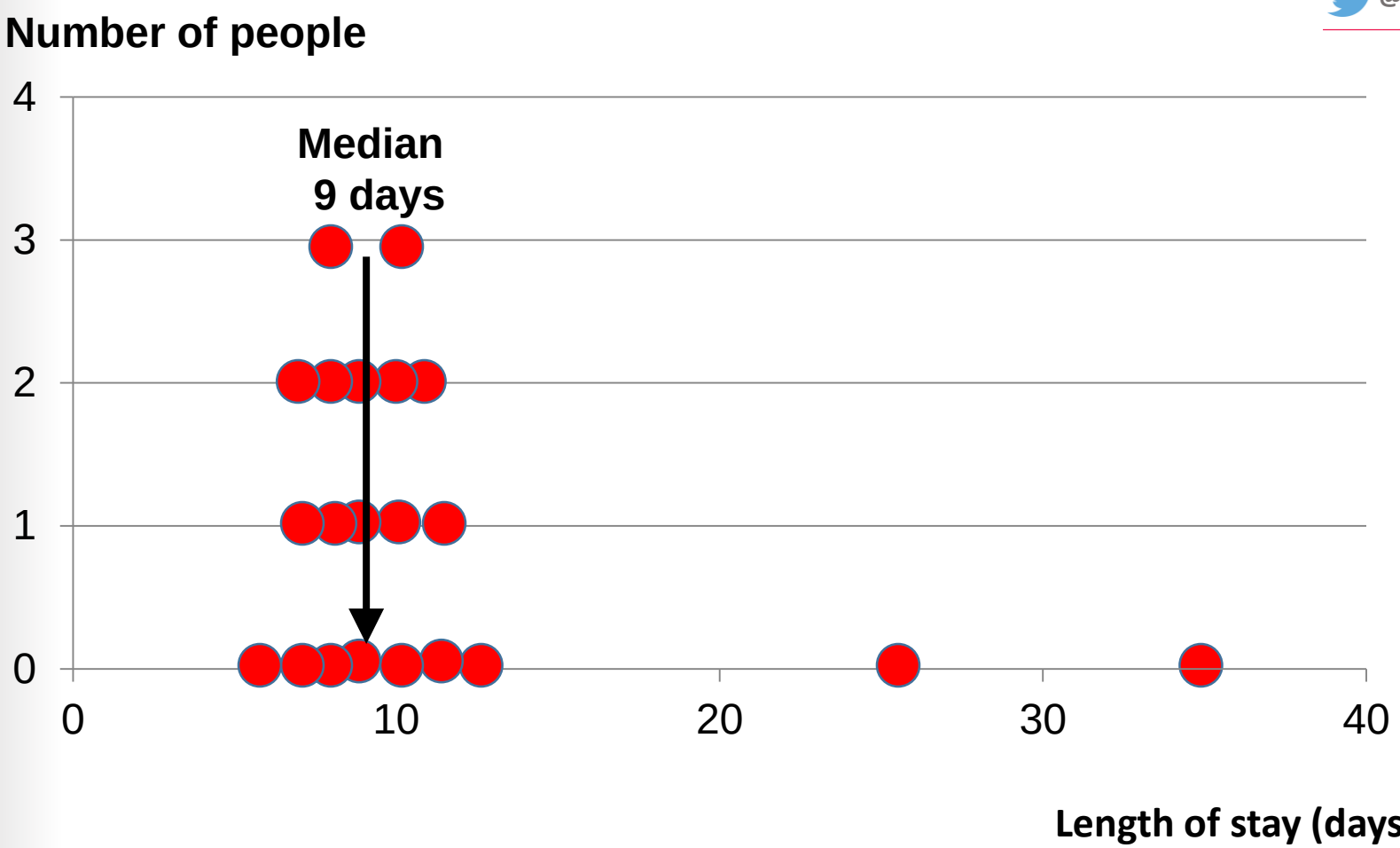

Consequences

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Issue 1
Some trial reports do not contain the summaries of outcome measures (mean and standard deviation) needed in a meta-analysis. Trials have to be left out of the meta-analysis.

Issue 2
For some outcomes, the usual approaches to combining the trial results in meta-analysis aren't suitable and alternative methods need to be devised

Polling Question 1

Aims

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- Survey of Cochrane review authors to establish extent of problem
- Investigate (statistical) ways of recovering missing outcome summaries by using other information in the trial report
  - Systematic review of methods to recover missing standard deviation
  - Systematic review of methods to recover missing mean
- Test performance of methods using Cochrane review individual patient data

Survey of Cochrane Reviewers - Design

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- Survey of authors of Cochrane review of stroke rehabilitation intervention
- Sent to lead and second authors (and contact author)
- Invited in covering email to complete survey within 1 month
- Survey in Google Forms
- Questionnaire linked to a specific published review

Survey of Cochrane Reviewers - Results

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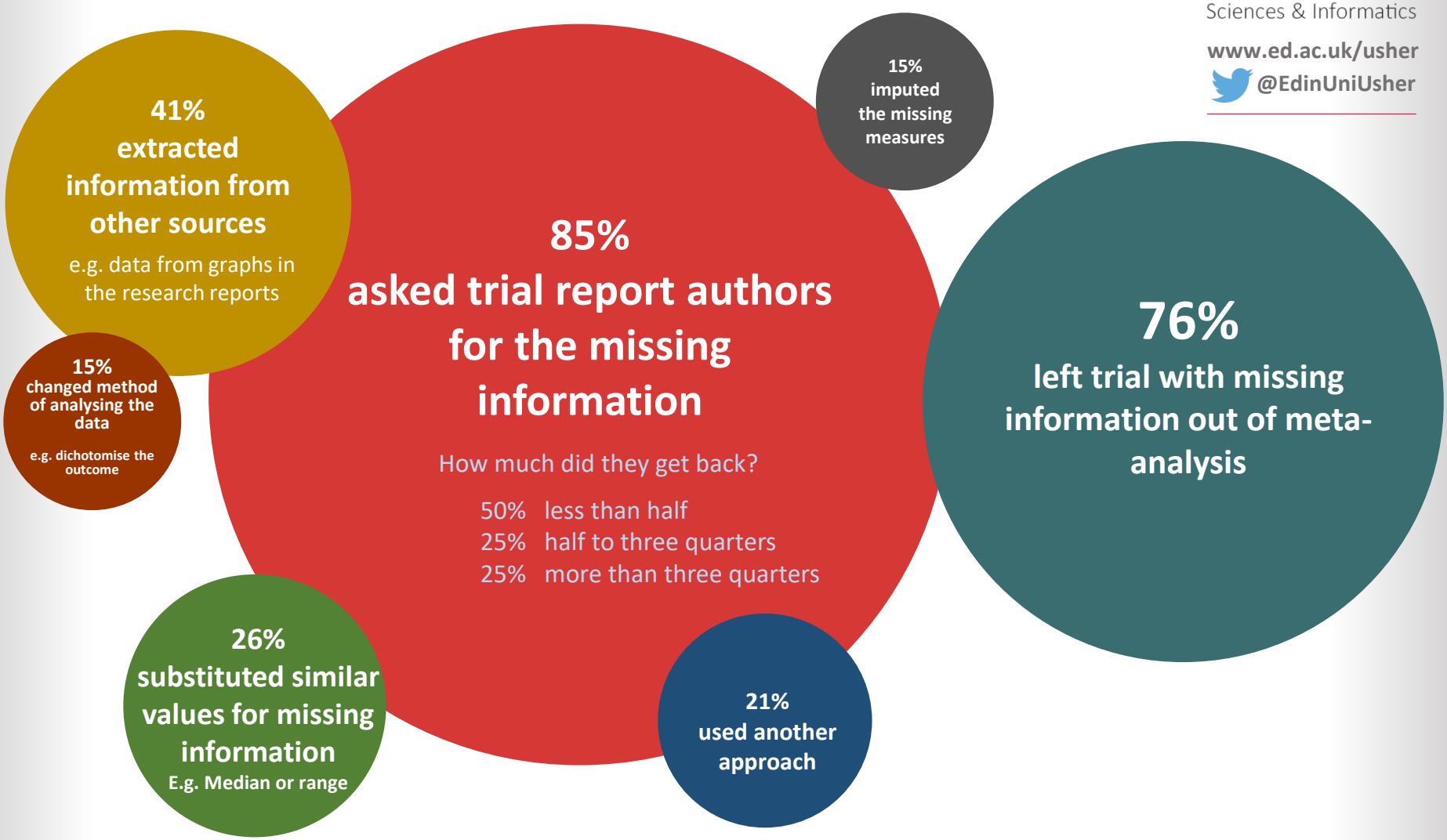
- 177 Cochrane stroke reviews; 70 of rehabilitation interventions
- Sent to 141 authors of 70 reviews
- 63 responses linked to 53 reviews (76%)
- 97% of reviewers who knew details of analysis aimed to extract continuous outcomes
- Of these, 38 (68%) encountered unreported mean or SD values
- 89% of these (34 of 38) still performed a meta-analysis

Survey of Cochrane Reviewers - Results



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Polling Question 2

Systematic Review – Missing Standard Deviation (SD)

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- Update to previous review
  - Wiebe N, Vandermeer B, Platt RW, Klassen TP, Moher D, Barrowman NJ. A systematic review identifies a lack of standardization in methods for handling missing variance data. J. Clin. Epidemiol. 2006;59:342–53.
- Methods for determining variance, SD or standard error where unreported
- Parallel group or crossover trials
- Single reviewer screened title and abstract; and full text to identify eligible articles
- Independent reviewer assessed full text to confirm eligibility
- Data sources (searched from 2002 to May 2016)
  - Searched MEDLINE, EMBASE, Web of Knowledge, PsycINFO, Global Health
  - Full text from Journals@Ovid (OVFT), YourJournals@Ovid, PsycARTICLES Full Text, Books@Ovid or via inter-library loan
  - Grey literature – Cochrane Colloquium abstract books, Cochrane Statistics Methods Group mailing list archive, emails to CSMG topic experts

Weir et al. BMC Medical Research Methodology (2018) 18:25
https://doi.org/10.1186/s12874-018-0483-0

BMC Medical Research Methodology

RESEARCH ARTICLE Open Access

Dealing with missing standard deviation and mean values in meta-analysis of continuous outcomes: a systematic review

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Abstract

Background: Rigorous, informative meta-analyses rely on availability of appropriate summary statistics or individual participant data. For continuous outcomes, especially those with naturally skewed distributions, summary information on the mean or variability often goes unreported. While full reporting of original trial data is the ideal, we sought to identify methods for handling unreported mean or variability summary statistics in meta-analysis.

Methods: We undertook two systematic literature reviews to identify methodological approaches used to deal with

Weir et al., *BMC Medical Research Methodology* (2018) 18:25
https://doi.org/10.1186/s12874-018-0483-0

Systematic Review – Missing Standard Deviation (SD)

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4. clinical trial/ or controlled clinical trial/ or Clinical Trials as Topic/ or (clinical adj3 trial$1).tw. or controlled clinical trial.mp.
5. randomized controlled trial/ or "randomized controlled trial (topic)"/ or (randomi#ed adj5 trial$1).tw.
6. *data analysis/ or *data extraction/ or *data synthesis/
7. *statistics as topic/ or *statistical parameters/ or *variance/ or *statistical analysis/ or *"analysis of covariance"/ or *"analysis of variance"/ or *attributable risk/ or *bootstrapping/ or *canonical analysis/ or *chi square test/ or *cohort analysis/ or *correlation analysis/ or *correspondence analysis/ or *effect size/ or *etiologic fraction/ or *fisher exact test/ or *frequency analysis/ or *friedman test/ or *geostatistical analysis/ or *inferential statistics/ or *instrumental variable analysis/ or *intention to treat analysis/ or *jackknife test/ or *kaplan meier method/ or *kappa statistics/ or *kolmogorov smirnov test/ or *kruskal wallis test/ or *latent structure analysis/ or *life table method/ or *log rank test/ or *loglinear model/ or *mantel haenszel test/ or *maximum likelihood method/ or *mcnemar test/ or *median test/ or *meta analysis/ or *"meta analysis (topic)"/ or *monte carlo method/ or *most probable number method/ or *multilevel analysis/ or *multivariate analysis/ or *nonparametric test/ or *numbers needed to treat/ or *one tailed test/ or *ordination analysis/ or *parametric test/ or *post hoc analysis/ or *power analysis/ or *"power of a test"/ or *principal coordinate analysis/ or *rank sum test/ or *rasch analysis/ or *redundancy analysis/ or *regression analysis/ or *risk benefit analysis/ or *sequential analysis/ or *sign test/ or *spatial analysis/ or *spatial autocorrelation analysis/ or *student t test/ or *temporal analysis/ or *two tailed test/ or *univariate analysis/ or *wilcoxon signed ranks test/ or *yates continuity correction/ or *youden index/
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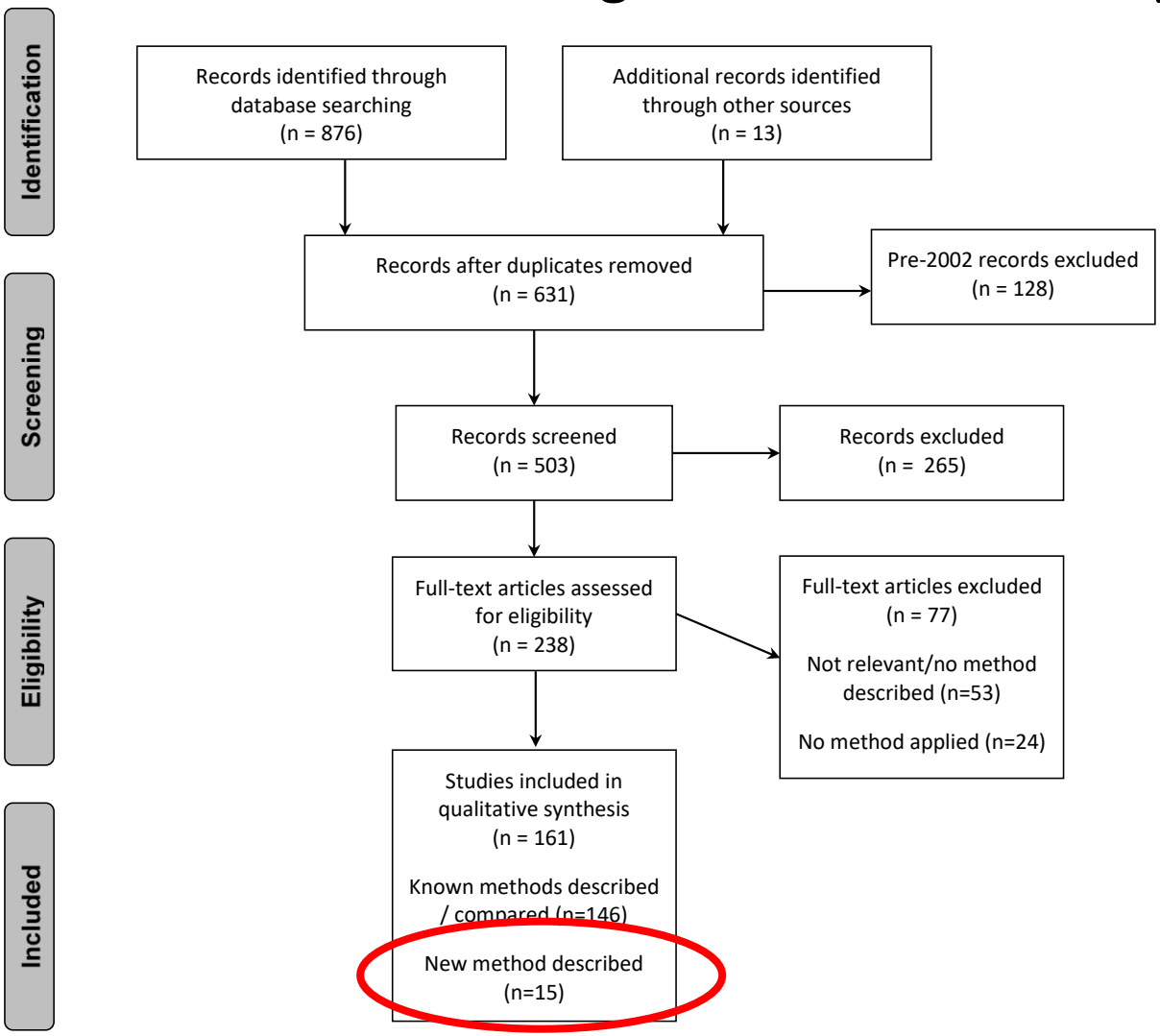
19. 18 not 15

Systematic Review – Missing Standard Deviation (SD)



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Systematic Review – Missing Standard Deviation (SD)

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Authors	Description	Statistics required
Abrams et al (2005)	Bayesian meta-analysis	Baseline, follow-up and change from baseline mean/SD
Hozo et al (2005)	Formulae provided	Min, Max, Median, N
Sung et al (2006)	Bayesian meta-analysis	Variances in other studies
Walter and Yao (2007)	Look-up table	Min and Max (or Range), N
Ma et al (2008)	Weighted average	Variances in other studies, N
Nixon et al (2009)	Bayesian meta-analysis	Baseline SD, Follow-up SD
Dakin et al (2010)	Bayesian meta-analysis	SDs in other studies
MacNeil et al (2010)	Bayesian meta-analysis	SDs in other studies
Stevens (2011)	Bayesian meta-analysis	Variances in other studies
Stevens et al (2012)	Bayesian meta-analysis	Variances in other studies
Boucher (2012)	Emax model of SDs	Observed SDs over time (longitudinal study)
Wan et al (2014)	Formulae provided	Lower and Upper Quartile, N
Bland (2015)	Formulae provided	Min, Max, Lower and Upper Quartile, Median, Mean, N
Kwon and Reis (2015)	Approximate Bayesian computation	Available summary statistics
Choudhry et al (2016)	Meta-regression of variances	Variances in other studies

Systematic Review – Missing Mean

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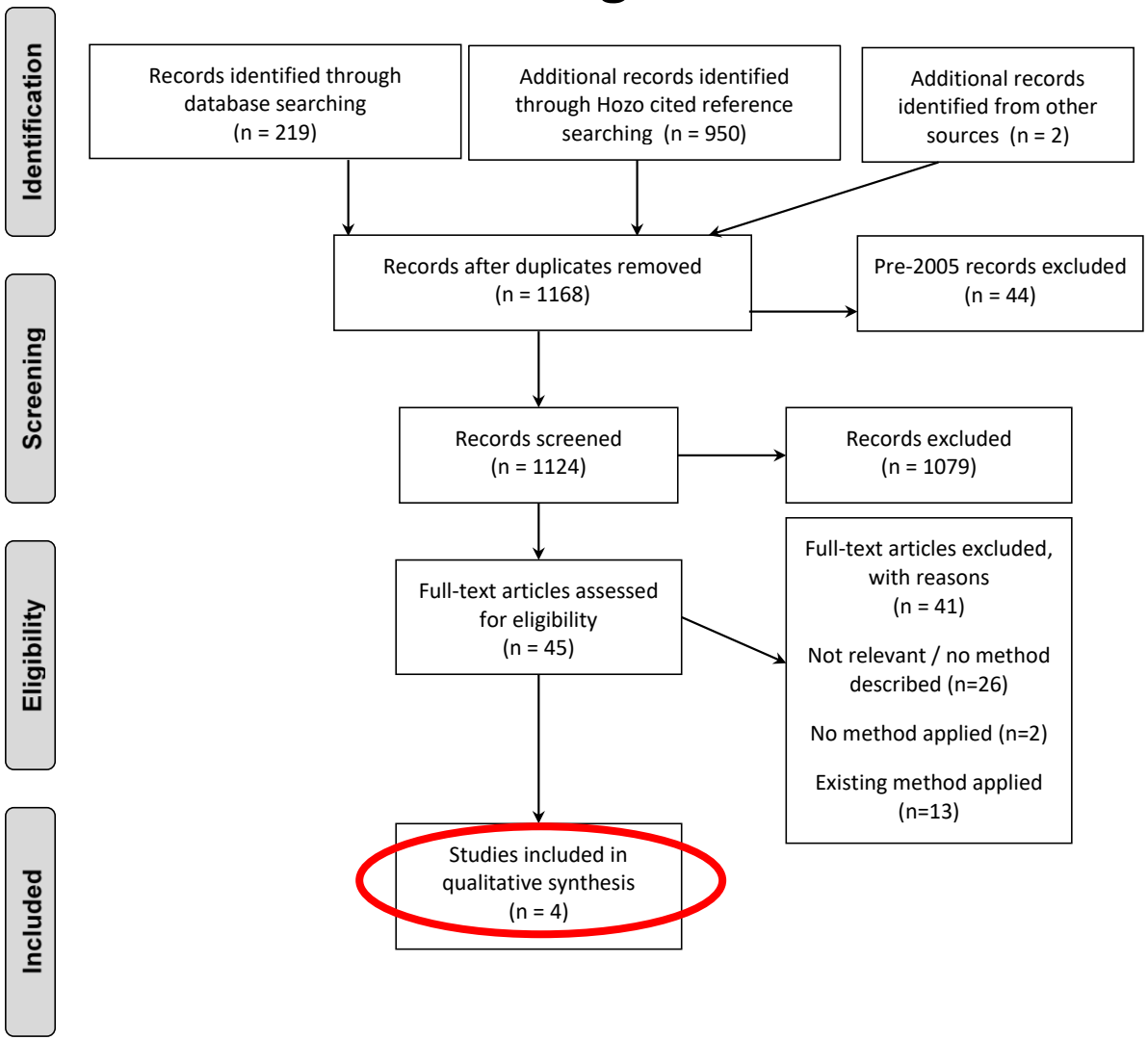
- Methods for determining mean where unreported
- Data sources (searched from 2005 to May 2016)
  - Searched EMBASE only
  - Full text from Journals@Ovid (OVFT), YourJournals@Ovid, PsycARTICLES Full Text, Books@Ovid or via inter-library loan
  - Grey literature – emails to CSMG topic experts
  - Cited reference searching of key paper:
  - Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med. Res. Methodol. 2005;5:13.

Systematic Review – Missing Mean



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Authors	Description	Statistics required
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Wan et al (2014)	Formulae provided	Lower and Upper Quartile, N
Bland (2015)	Formulae provided	Min, Max, Lower and Upper Quartile, Median,N
Kwon and Reis (2015)	Approximate Bayesian computation	Available summary statistics

Case Study – Early Supported Discharge after Stroke

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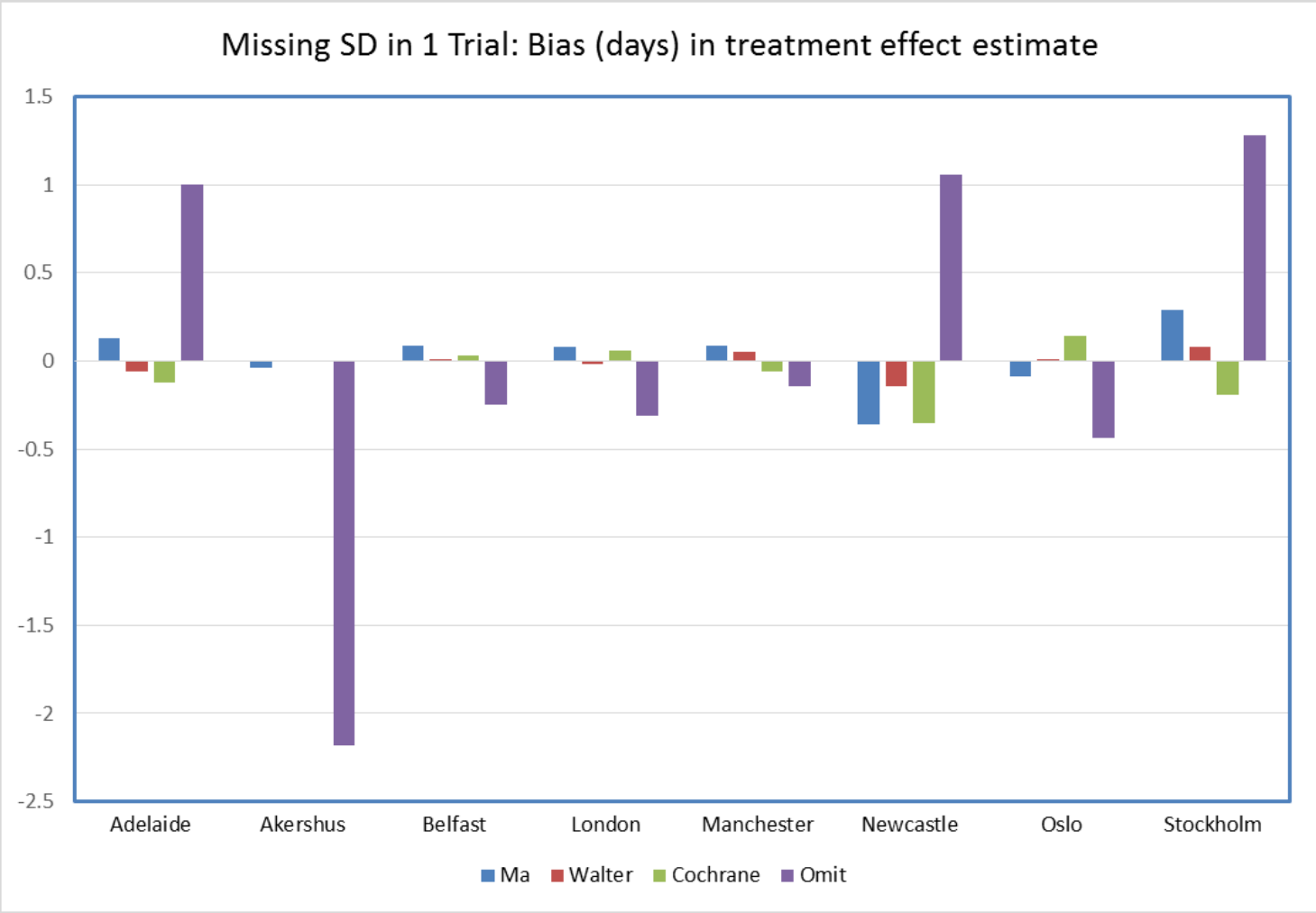
- Individual patient data from published Cochrane review
  - Fearon P, Langhorne P, Early Supported Discharge Trialists. Services for reducing duration of hospital care for acute stroke patients. Cochrane Database of Systematic Reviews 2012, Issue 9. Art. No.: CD000443. DOI: 10.1002/14651858.CD000443.pub3
- 8 trials
- Total of 1055 patients
- Key secondary outcome: hospital length of stay
- **Mean difference -9.4 days, 95% confidence interval (-16.3, -2.4)**

- Assessed how successful methods were in recovering unreported SD or mean under scenarios where these were missing from 1 or more trials
  - Any bias compared to true result?
  - Did they reflect the uncertainty (precision) in the true result confidence interval?

Case Study – Missing SD



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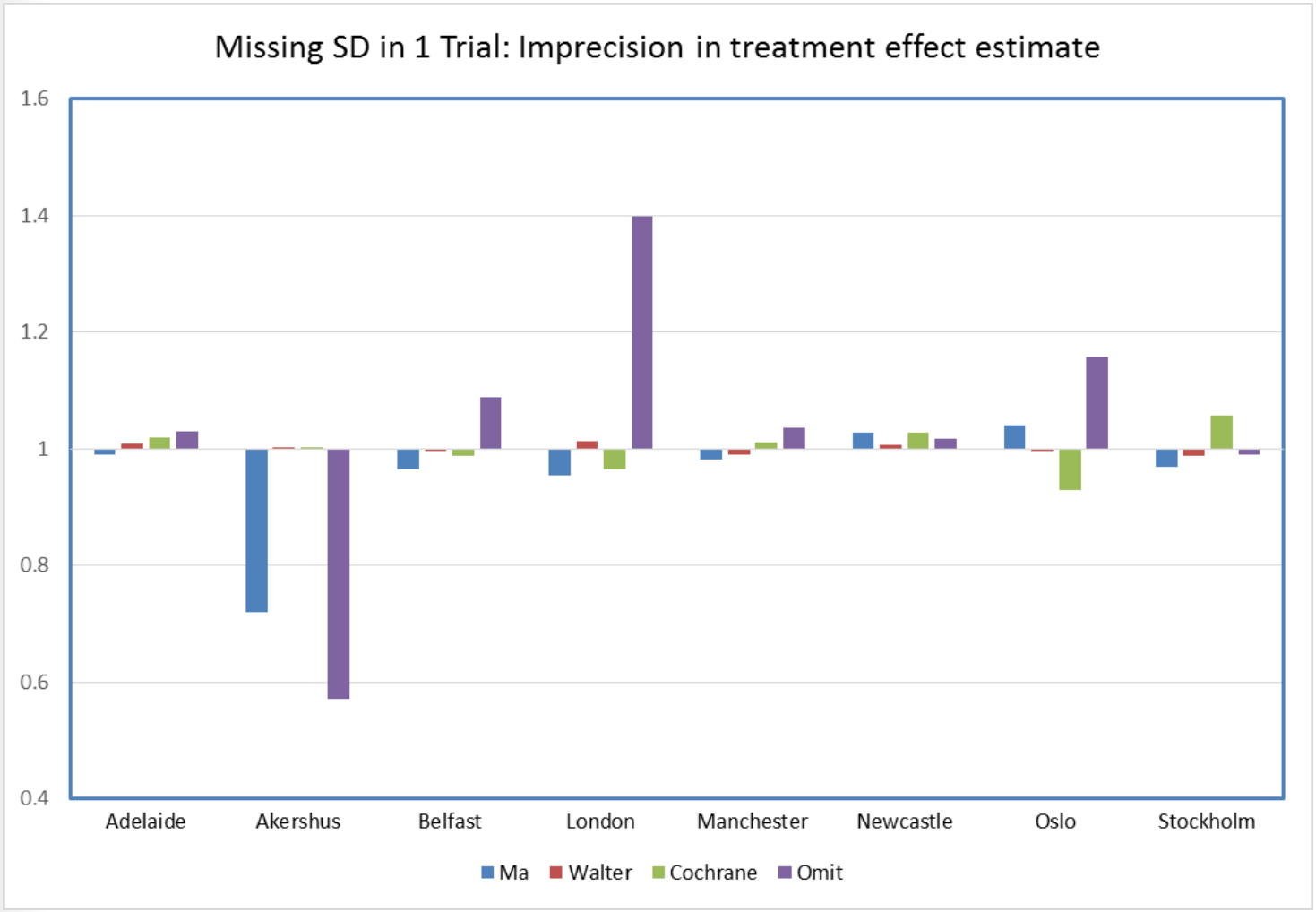
Case Study – Missing SD



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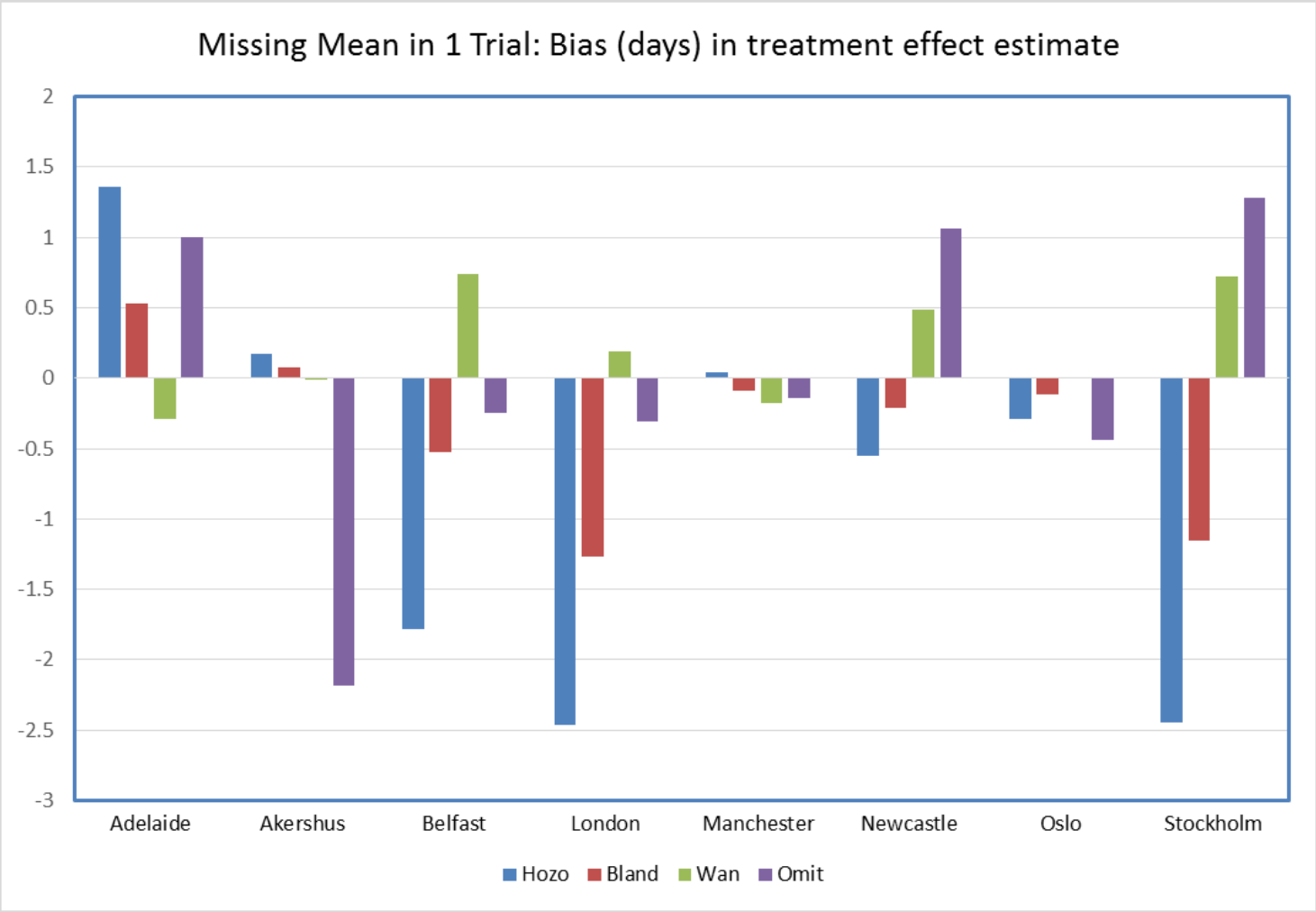
Case Study – Missing Mean



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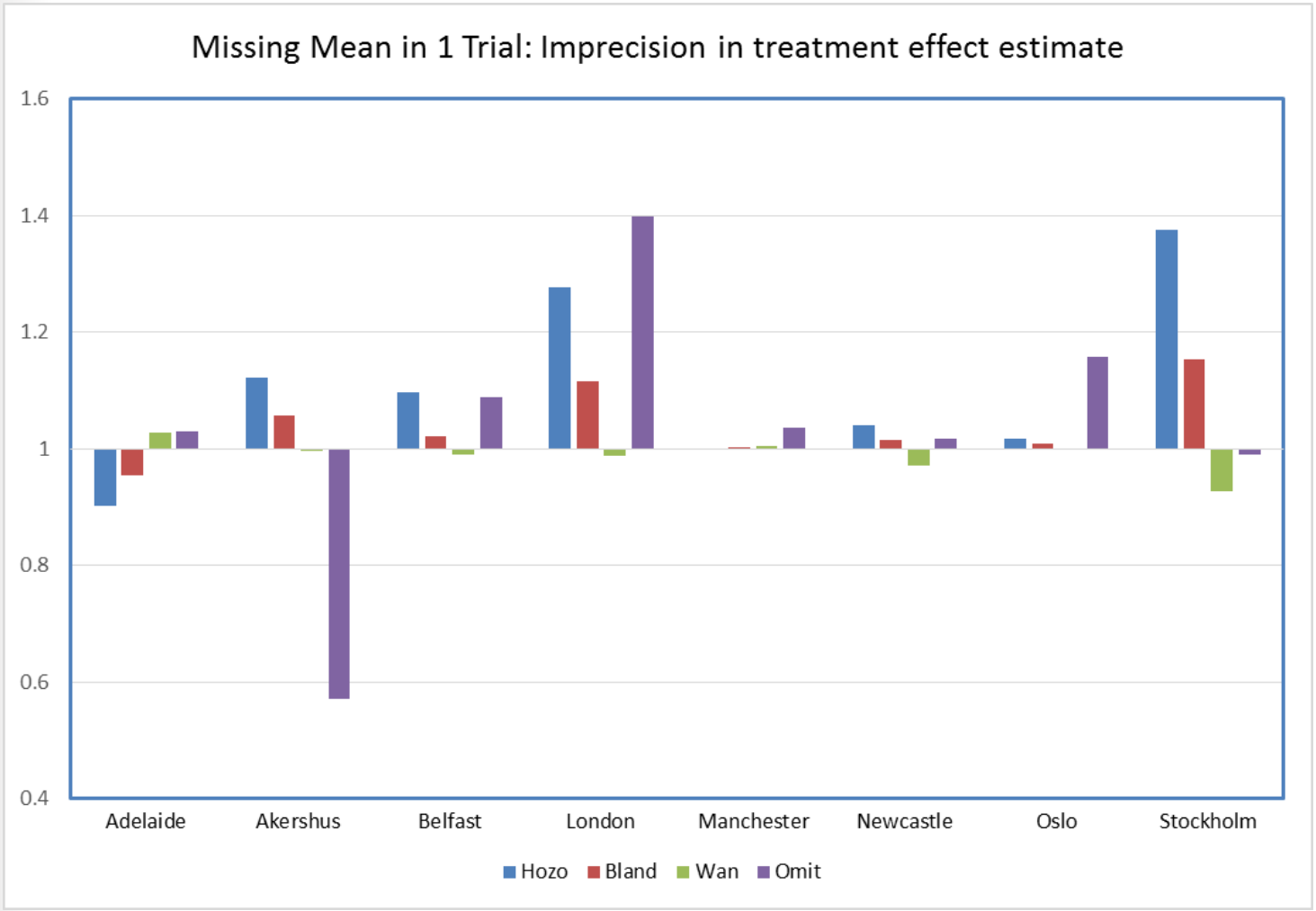
Case Study – Missing Mean



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Conclusions

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- Unreported mean and SD lead to trials being omitted from meta-analysis
- Numerous recent methods published
  - 15 for unreported SD (since 2002)
  - 5 for mean (since 2005)
- For SD
  - Method of Walter and Yao (2007) performed best
  - But needs minimum, maximum to be reported
  - Cochrane handbook method also performed well if upper, lower quartiles reported
- For mean
  - Wan (2014) method got closest to true value
  - Practically useful as includes values often reported

Polling Question 3

Final Thoughts

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- Sometimes meta-analysis based on mean / SD not appropriate
  - Other methods (e.g. ratio of mean/ratio of geometric mean) do not depend on these
- No one method should be recommended
  - Need range of approaches in case the statistics required by “best” method not available
- Continue to promote high quality reporting of trials to address issue
  - But these methods always needed for historical studies

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Questions and Comments?

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