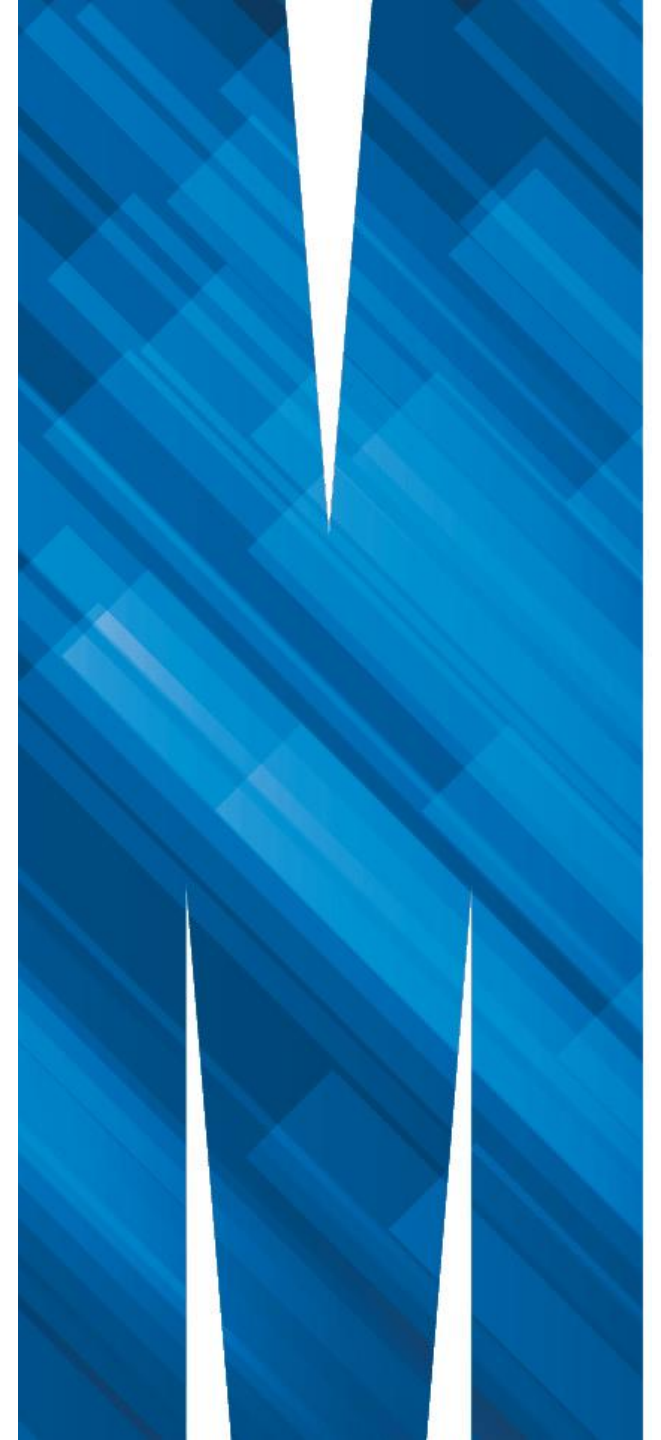


Meta-analysis methods used in systematic reviews of interrupted time series studies

ELIZABETH KOREVAAR

11th MAY 2021

MONASH UNIVERSITY
DEPARTMENT OF PUBLIC HEALTH AND PREVENTIVE MEDICINE



Systematic reviews

Used to inform health policy decision making

Natural disasters?

New laws?

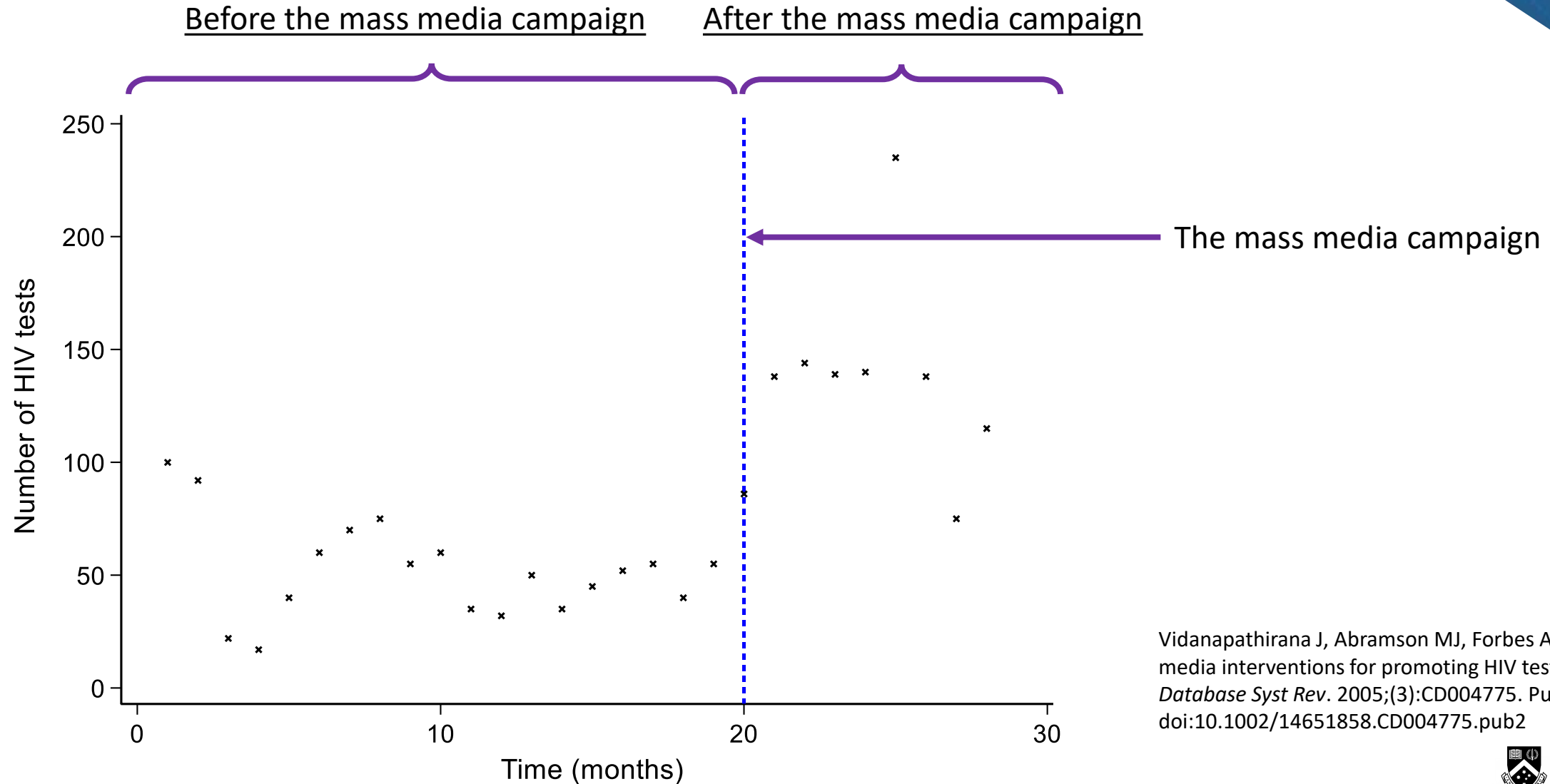
Organisational practice changes?

Financial crisis?

Media campaigns?

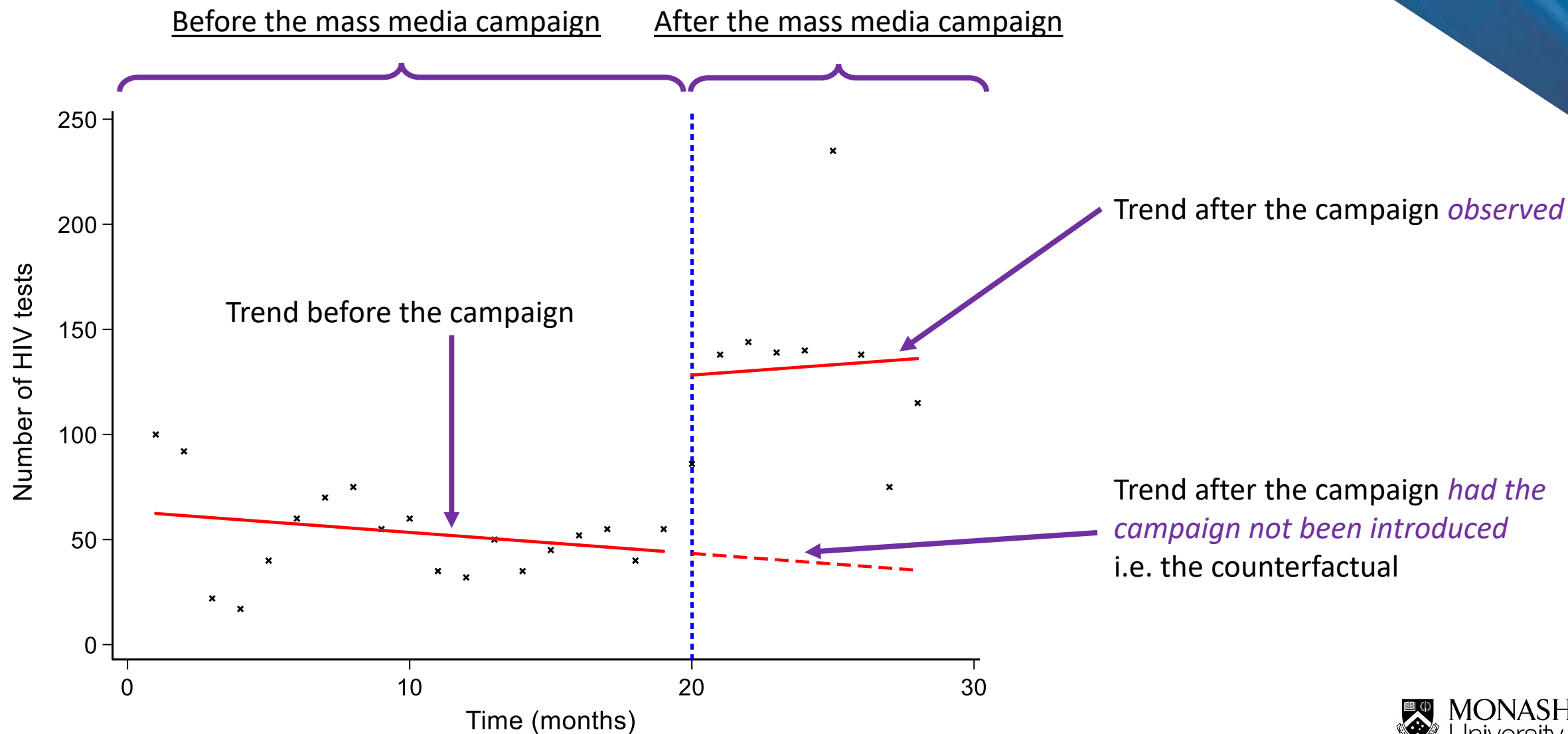
Social distancing policies?

INTERRUPTED TIME SERIES

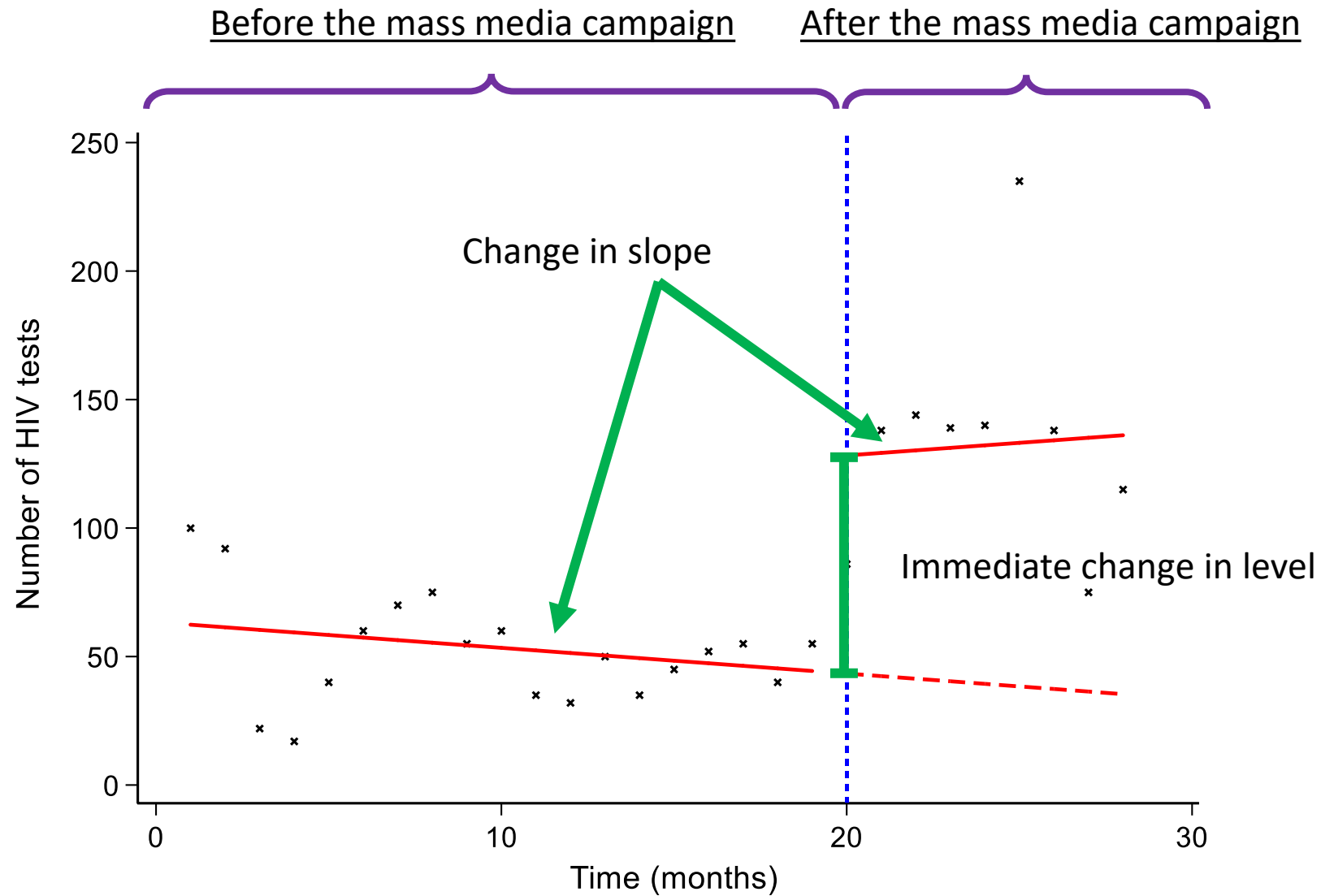


Vidanapathirana J, Abramson MJ, Forbes A, Fairley C. Mass media interventions for promoting HIV testing. *Cochrane Database Syst Rev.* 2005;(3):CD004775. Published 2005 Jul 20. doi:10.1002/14651858.CD004775.pub2

INTERRUPTED TIME SERIES

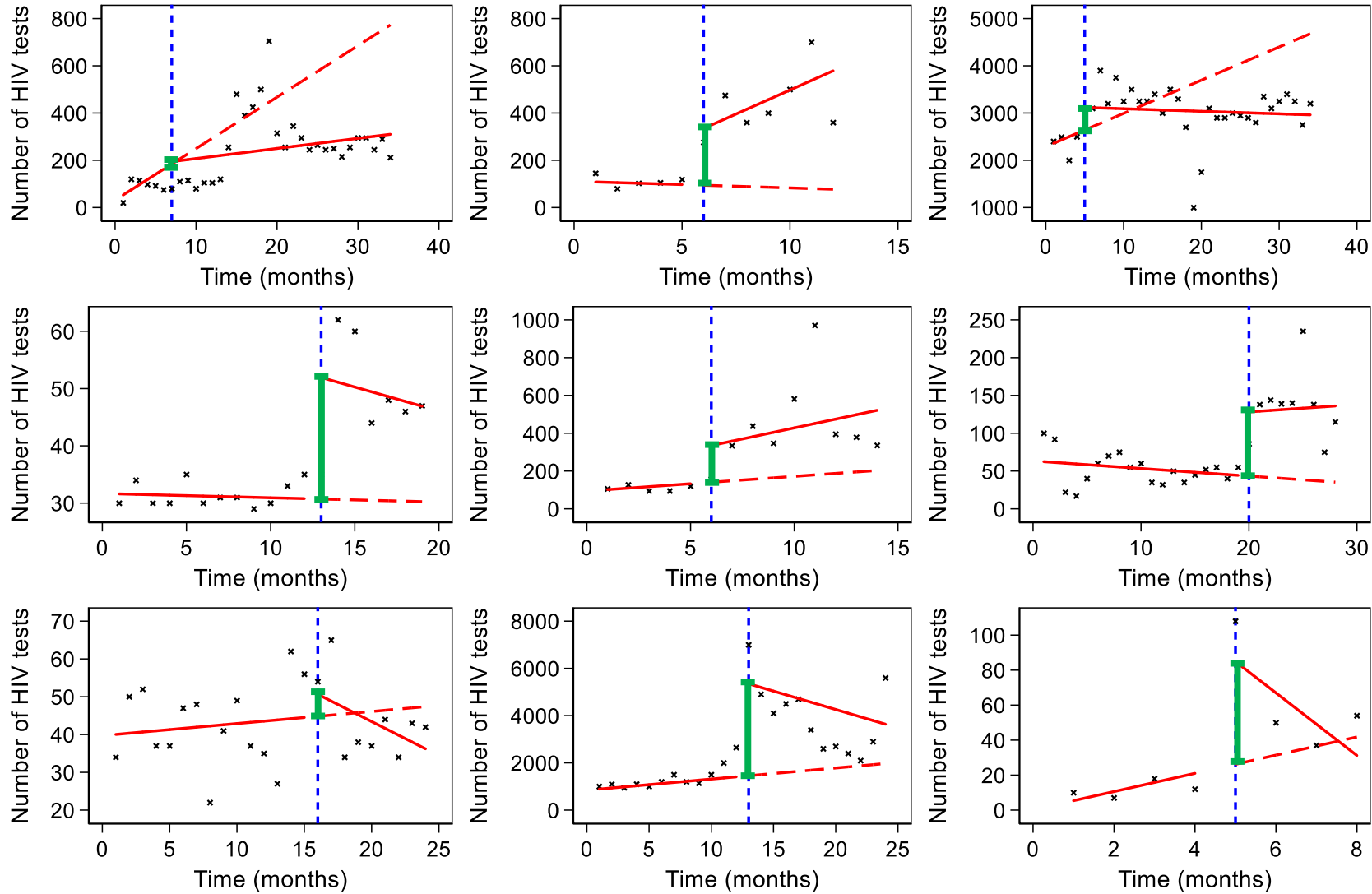


INTERRUPTED TIME SERIES



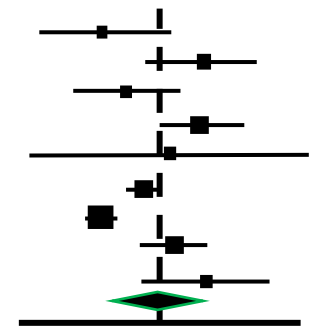
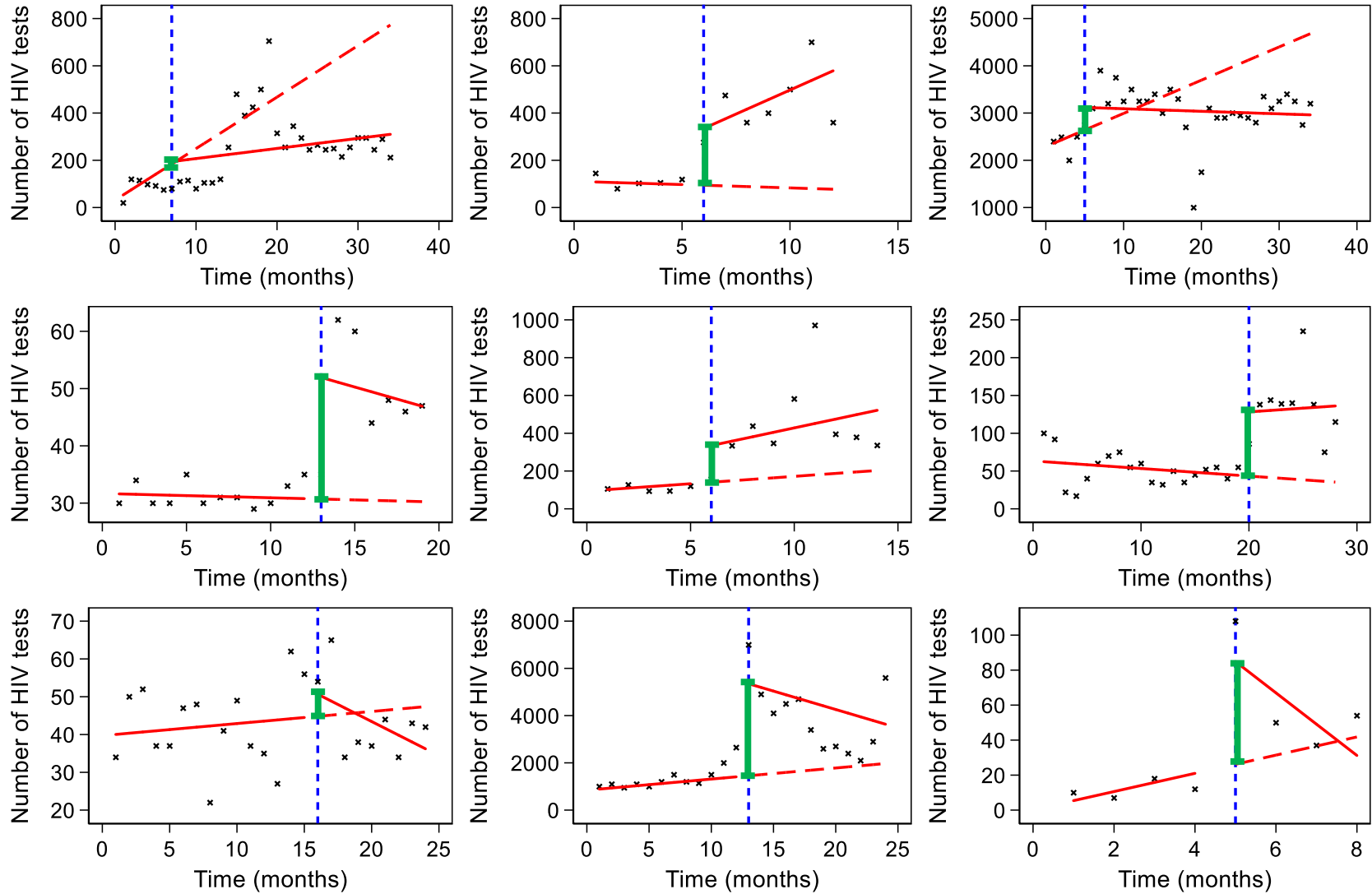
META-ANALYSIS OF ITS

9 different studies



META-ANALYSIS OF ITS

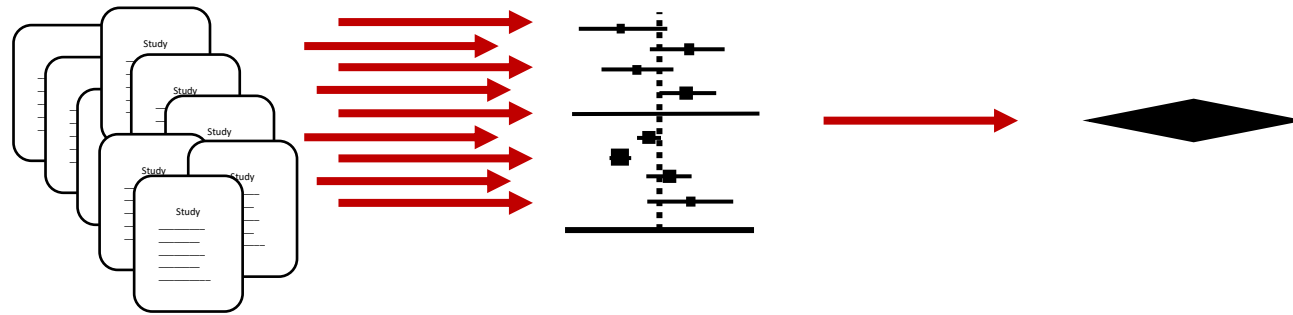
9 different studies



META-ANALYSIS

Statistical synthesis of evidence from multiple studies to produce a combined effect estimate

- **Two-stage approach**
- Effects calculated for each primary study
- Combined via meta-analysis

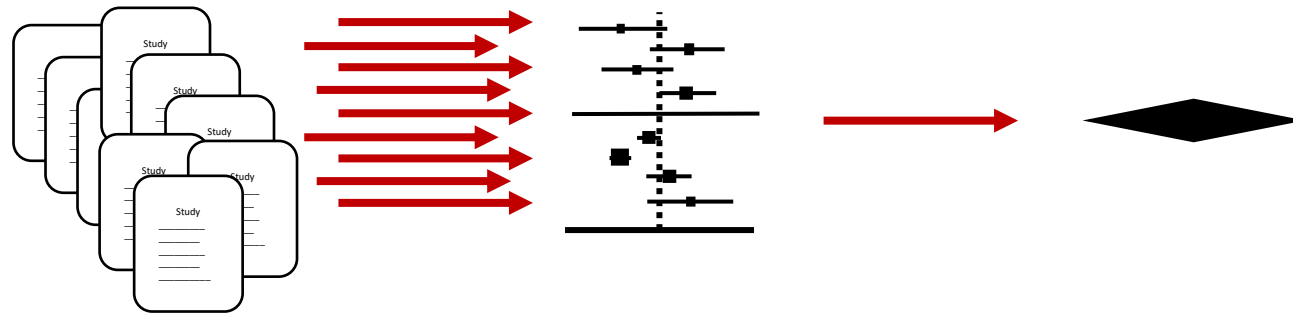


- **One-stage approach**

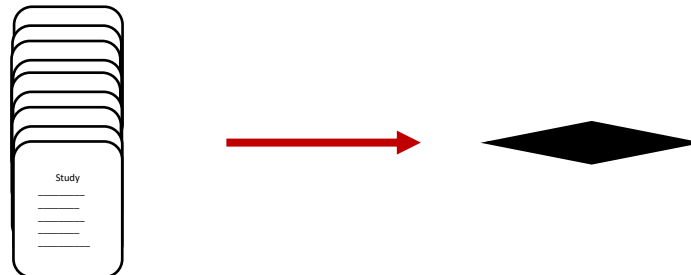
META-ANALYSIS

Statistical synthesis of evidence from multiple studies to produce a combined effect estimate

- **Two-stage approach**
- Effects calculated for each primary study
- Combined via meta-analysis



- **One-stage approach**
- Primary study data are analysed in one model, with an additional parameter to account for each study



A systematic review of methods to meta-analysis results of ITS studies

Objectives are to investigate:

1. Whether reviewers re-analyse primary ITS studies included in reviews, and if so, what re-analysis methods are used;
2. What meta-analysis methods are used;
3. What effect measures are used, and how completely the estimated combined effects are reported; and
4. What tools and domains are used to assess the risks of bias or methodological quality of the included ITS studies.

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Systematic review - Methods

Inclusion criteria

1. a review that included at least two ITS studies/series which met the review authors' definition of an ITS design; and
2. included at least one meta-analysis of ITS studies.

Systematic review - Methods

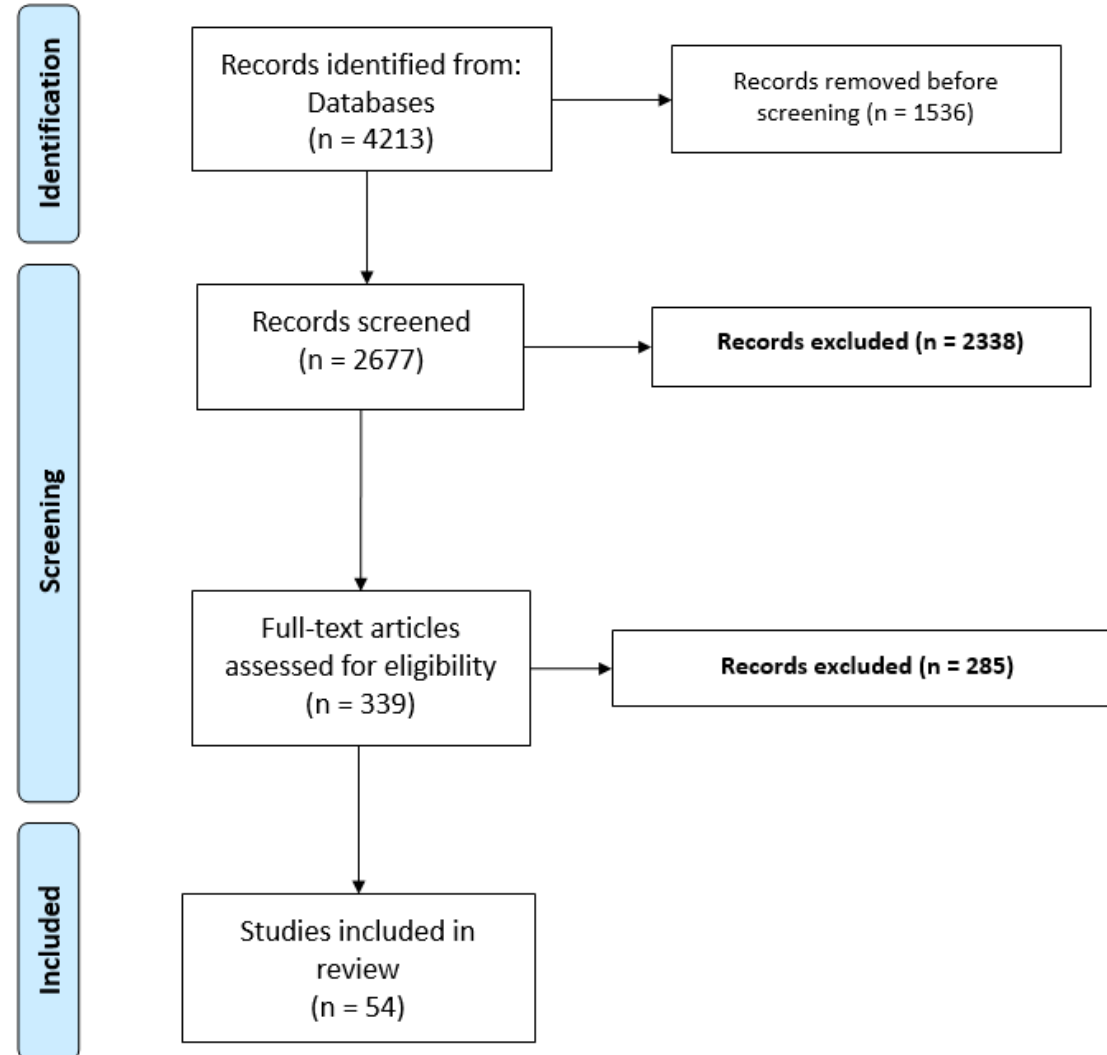
Data extraction

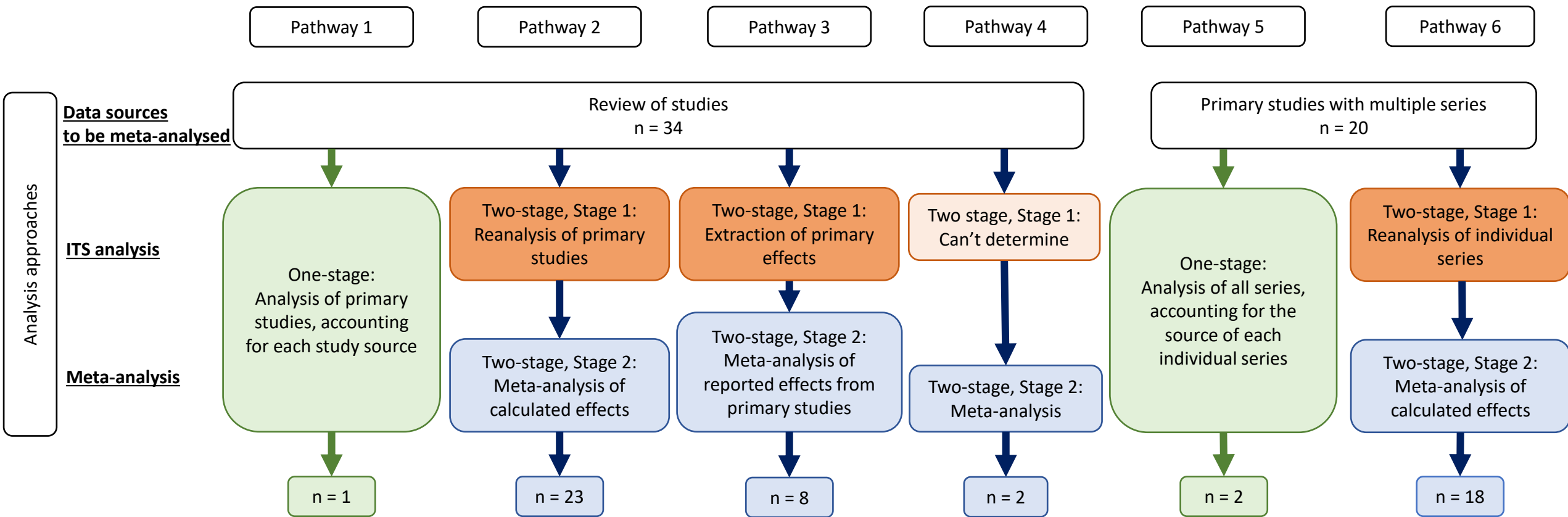
| Domain | Items |
|--|---|
| Review characteristics | Author, journal, discipline, PICO elements |
| Outcome and studies included | Type of outcome Number of ITS studies |
| Methods for combining ITS results | One-stage, two-stage meta-analysis Re-analysis of primary studies Accounting for autocorrelation etc |
| Results/Estimates | Type of effect measures Level change, slope change, combination of level and slope (counterfactual) Completeness of reporting (e.g. combined effect estimate confidence interval, measure of heterogeneity) |
| Risk of bias and/or assessment of study quality | Assessment of primary study risk of bias / methodological quality; Tool or domains used for assessment |

Systematic review - Results



PRISMA 2009 Flow Diagram





Analysis approaches

Data sources to be meta-analysed

ITS analysis

Meta-analysis

Pathway 1 Pathway 2 Pathway 3 Pathway 4 Pathway 5 Pathway 6

Review of studies
n = 34

Primary studies with multiple series
n = 20

One-stage:
Analysis of primary studies, accounting for each study source

Two-stage, Stage 1:
Reanalysis of primary studies

Two-stage, Stage 1:
Extraction of primary effects

Two stage, Stage 1:
Can't determine

One-stage:
Analysis of all series, accounting for the source of each individual series

Two-stage, Stage 1:
Reanalysis of individual series

Two-stage, Stage 2:
Meta-analysis of calculated effects

Two-stage, Stage 2:
Meta-analysis of reported effects from primary studies

Two-stage, Stage 2:
Meta-analysis

Two-stage, Stage 2:
Meta-analysis of calculated effects

n = 1

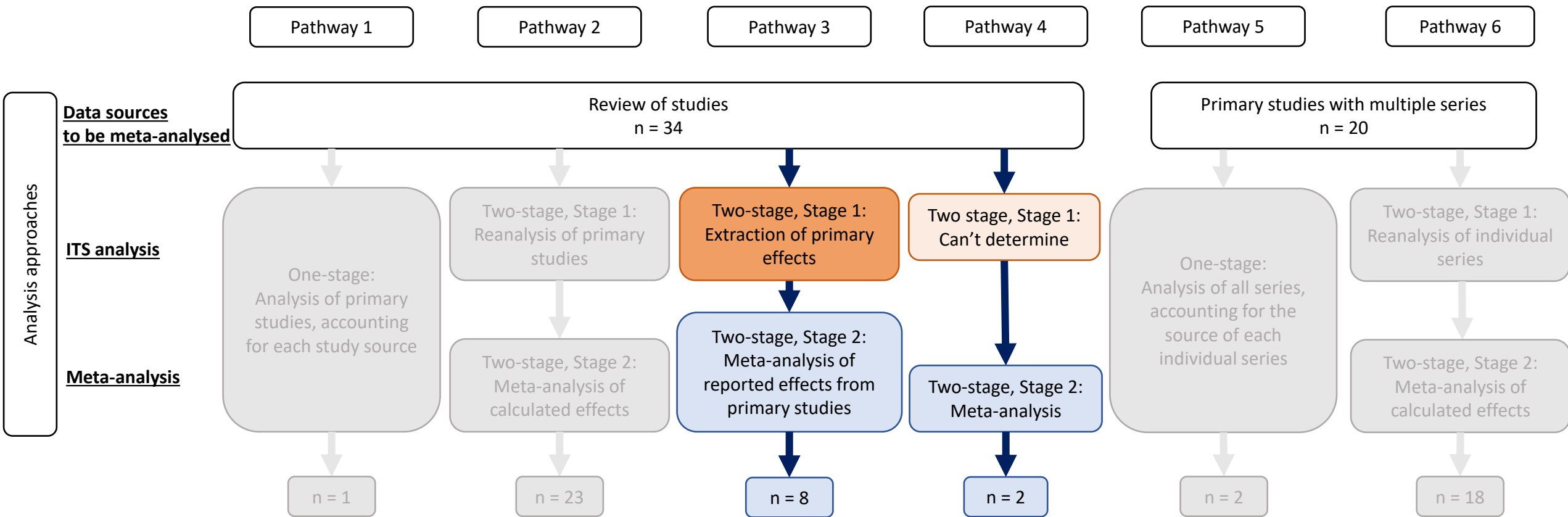
n = 23

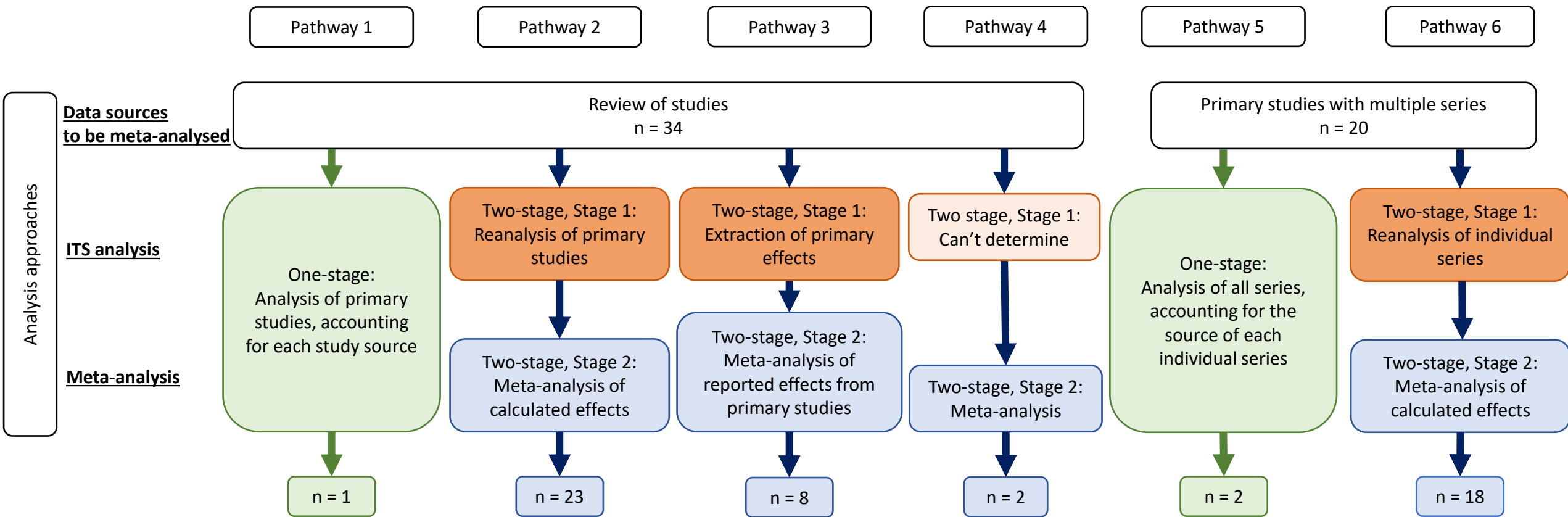
n = 8

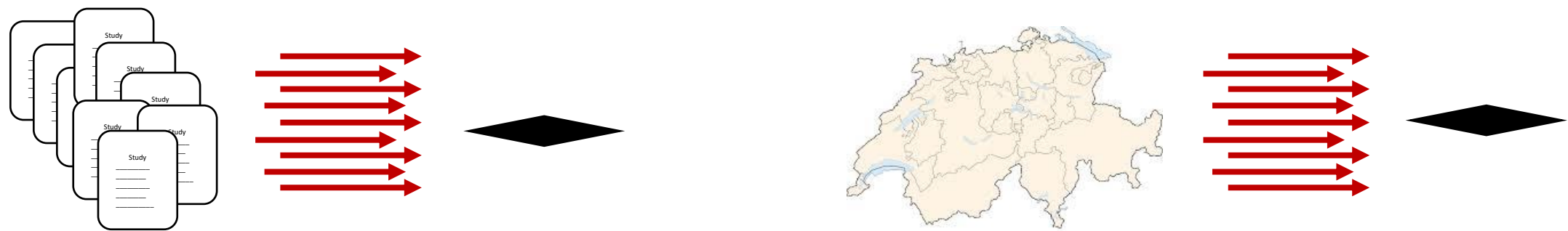
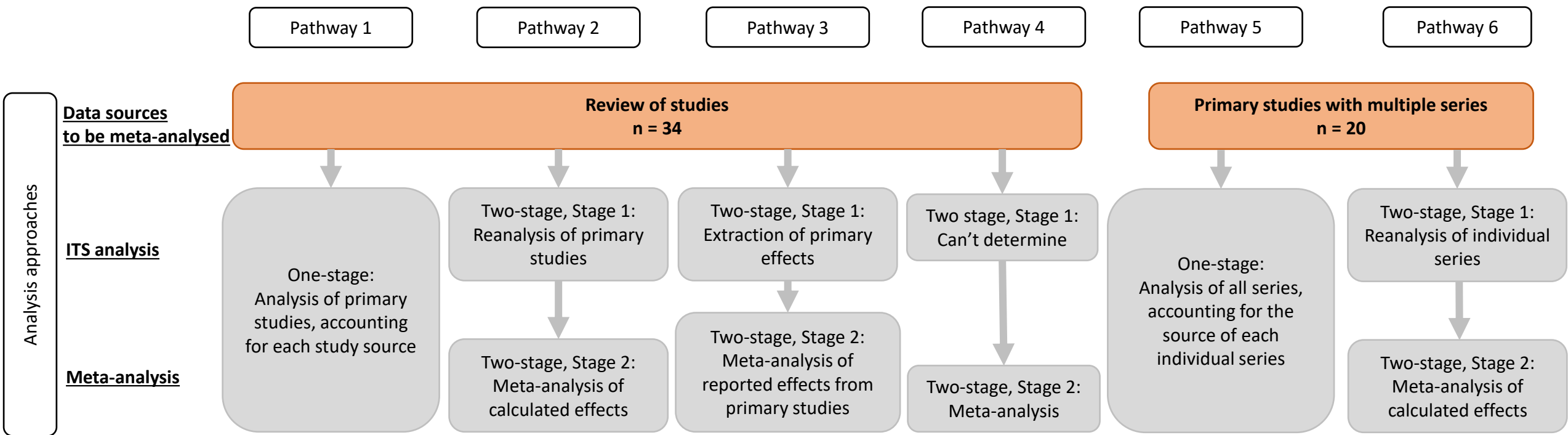
n = 2

n = 2

n = 18







Analysis approaches

Data sources to be meta-analysed

ITS analysis

Meta-analysis

Pathway 1

Pathway 2

Pathway 3

Pathway 4

Pathway 5

Pathway 6

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Number of ITS *studies* combined in meta-analysis
Median 5 studies, IQR: 3 – 7.5

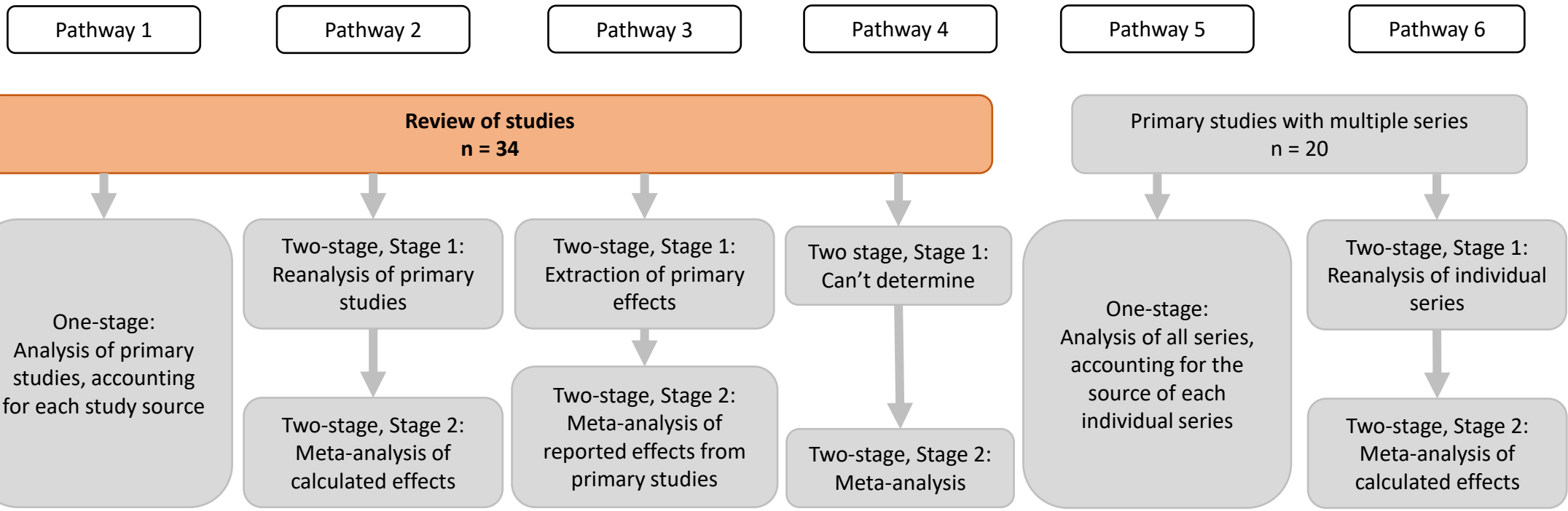
Number of ITS *series* combined in a meta-analysis
Median 12 series, IQR: 6 – 26

Analysis approaches

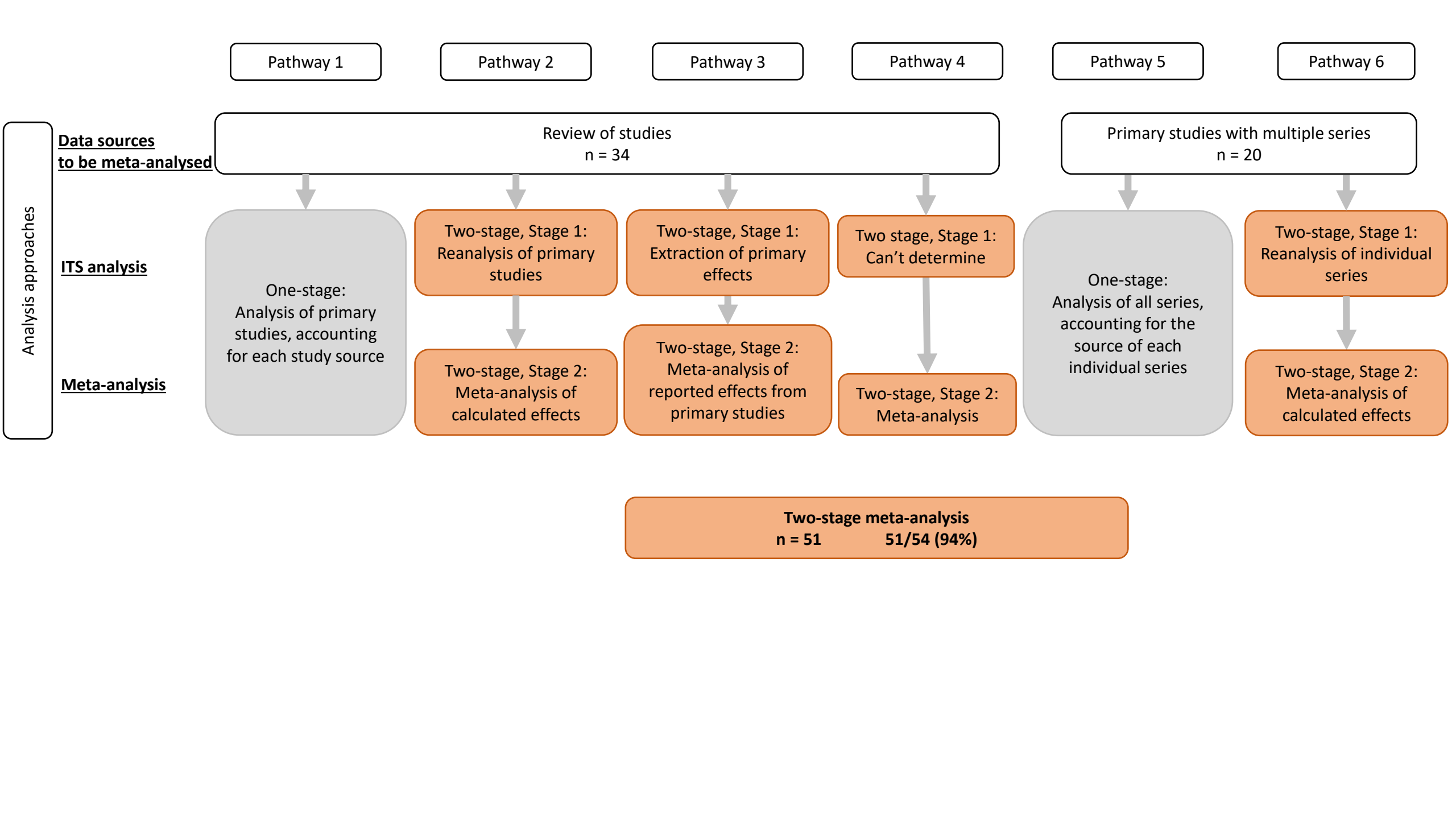
Data sources to be meta-analysed

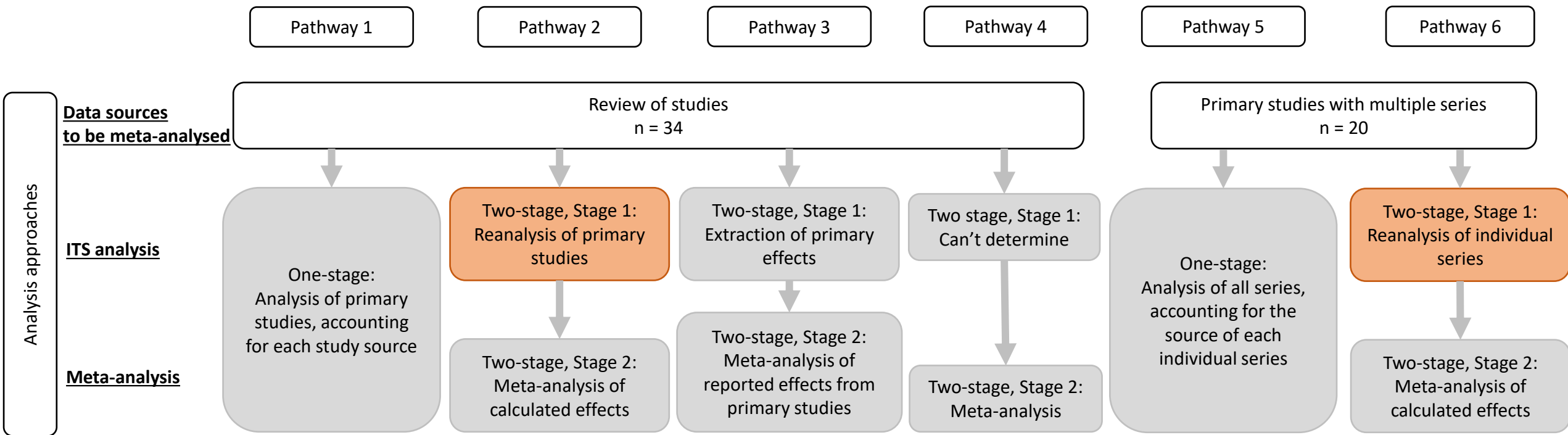
ITS analysis

Meta-analysis

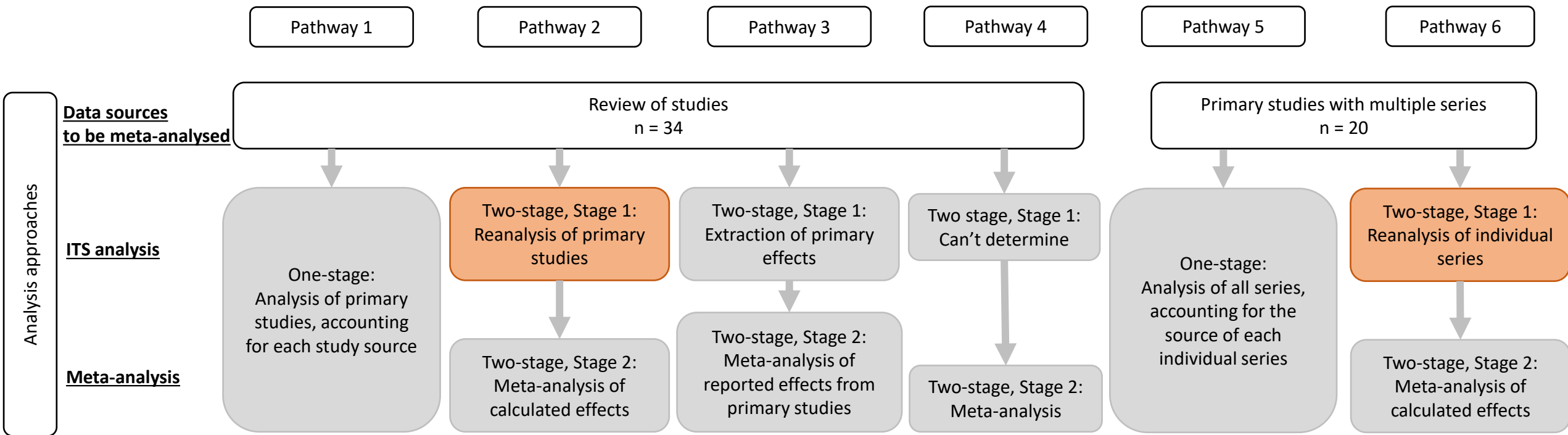


Provide a definition of ITS: 22/34 (65%)
Combined ITS with other designs: 15/34 (44%)
Assessed Risk of bias: 33/34 (97%)





41/51 (80%) reviews perform their own analysis of the raw ITS data
 The most commonly reported reason for re-analysis was to analyse as a time series



Segmented time series regression: 35/41 (87%)
 22% used ARIMA
 25% could not determine IF or HOW autocorrelation was adjusted for

Can't determine: 2/41 (5%)

Analysis approaches

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n = 8

n = 2

Only 50% mentioned autocorrelation

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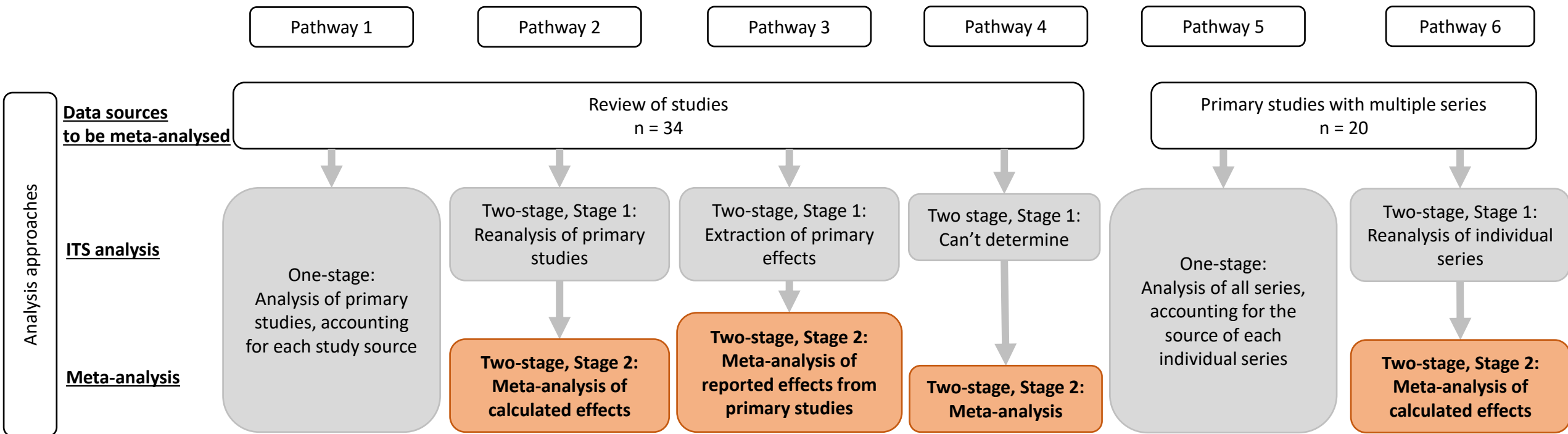
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Immediate level change: 42/51 (82%)
Slope change: 10/51 (19%)



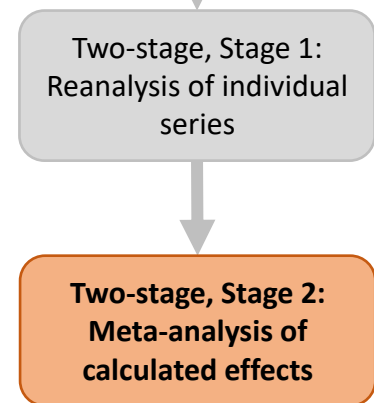
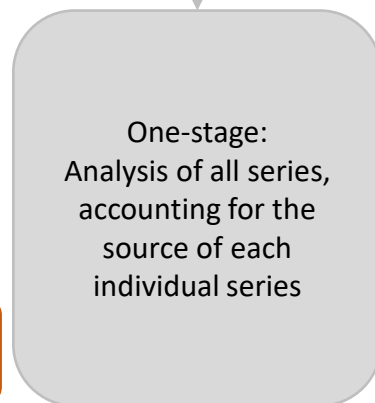
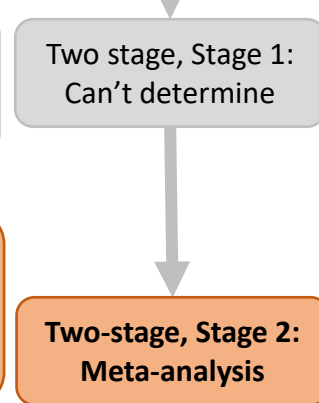
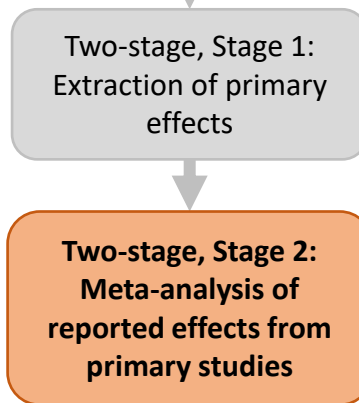
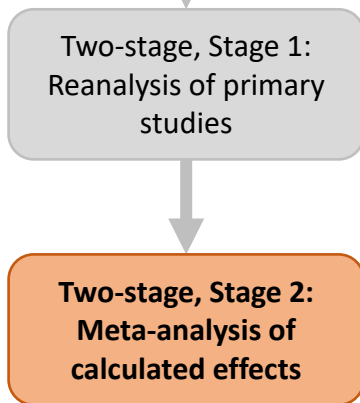
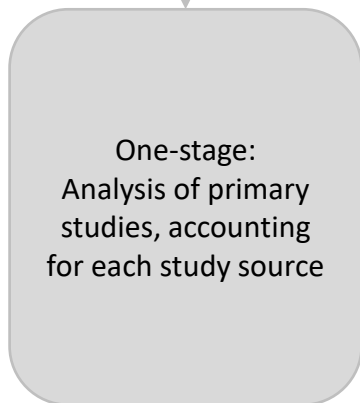
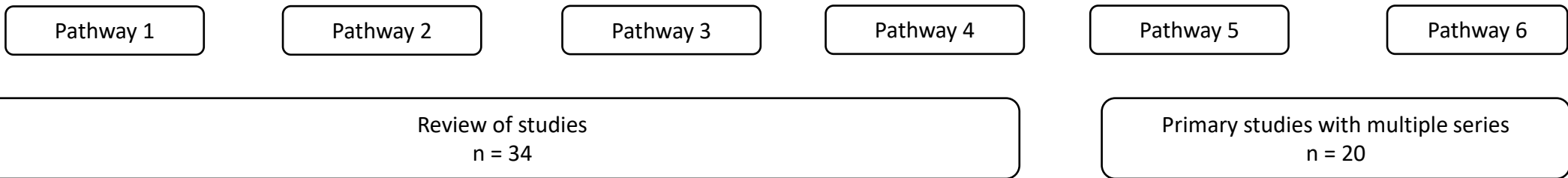
| Meta-analysis method | |
|---|-------------|
| Random effects: | 35/51 (69%) |
| Can't determine: | 2/51 (4%) |
| Heterogeneity variance estimator | |
| Dersimonian and Laird: | 19/51 (37%) |
| Can't determine: | 14/51 (27%) |
| Confidence interval method | |
| Wald type | 18/51 (35%) |
| Can't determine | 15/51 (29%) |

Analysis approaches

Data sources to be meta-analysed

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Meta-analysis



49/82 (60%) report a measure of heterogeneity

Analysis approaches

Data sources to be meta-analysed

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Meta-analysis

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n = 3
All meta-analysed immediate level change only
Only one mentioned autocorrelation

Systematic review - Discussion

- ITS studies ARE being meta-analysed!
 - Most often using two-stage meta-analysis approaches
 - Reporting of included study designs must be improved
 - Reporting of the statistical methods used to analyse the primary ITS studies must be improved
 - Regardless of whether the analysis was performed by the review authors or if they extracted the effect estimates from the primary studies
 - Reporting of the meta-analysis methods should be improved

Systematic review - Discussion

- Strengths
 - We followed a pre-specified a systematic review protocol
 - Searched several disciplines (public health, economics, psychology and education)
 - Detailed data extraction completed on all studies retrieved by our search
- Limitations
 - Reporting of definition of ITS studies
 - Identifying if ITS studies are included in the meta-analyses
 - We only captured the information reported in the reviews

Systematic review - Conclusions

- There is a necessity for improved reporting on the design and analysis characteristics of ITS studies that are included in meta-analyses.
- The meta-analysis methods used to combine results from the included studies should also be reported fully, including the effect estimator, methods of calculating confidence intervals and levels of between-study heterogeneity.

Thank-you!

Supervisors:

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Andrew Forbes

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Simon Turner

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Other thanks:

Methods in evidence synthesis group

Biostatistics group

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Questions?