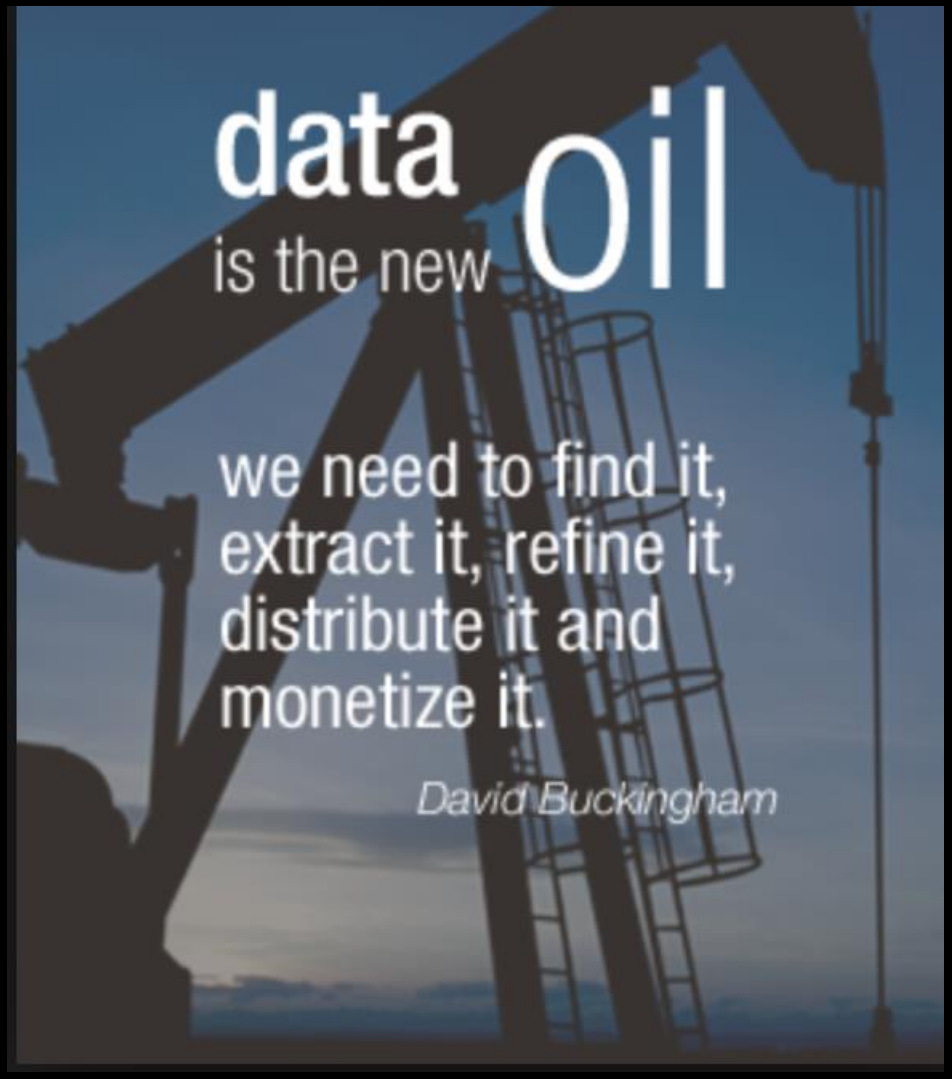
To valuable to waste:
the role of individual patient / participant / animal data meta-analyses

MaroeskaRovers
E-mail: Maroeska.Rovers@radboudumc.nl

Radboudumc


data
is the new oil
we need to find it,
extract it, refine it,
distribute it and
monetize it.
David Buckingham

Where are we now

- Doctors make life or death decisions on extremely limited information
- Only 30-40% of diagnosis and treatment decisions is evidence based

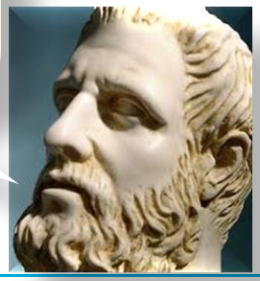
- Researchers and scientists draw broad conclusions from
  - small datasets,
  - a tiny slice of the population
  - over a short period of time


Cost Per Patient
$50,000
$45,000
$40,000
$35,000
$30,000
$25,000
$20,000
$15,000
$10,000
$5,000
$-
2008
2011
Phase I
Phase II
Phase III
Phase IV
IOM "Transforming Clinical Research" 2012

Wearables & IBM Watson

"It's far more important to know what person the disease has than what disease the person has."

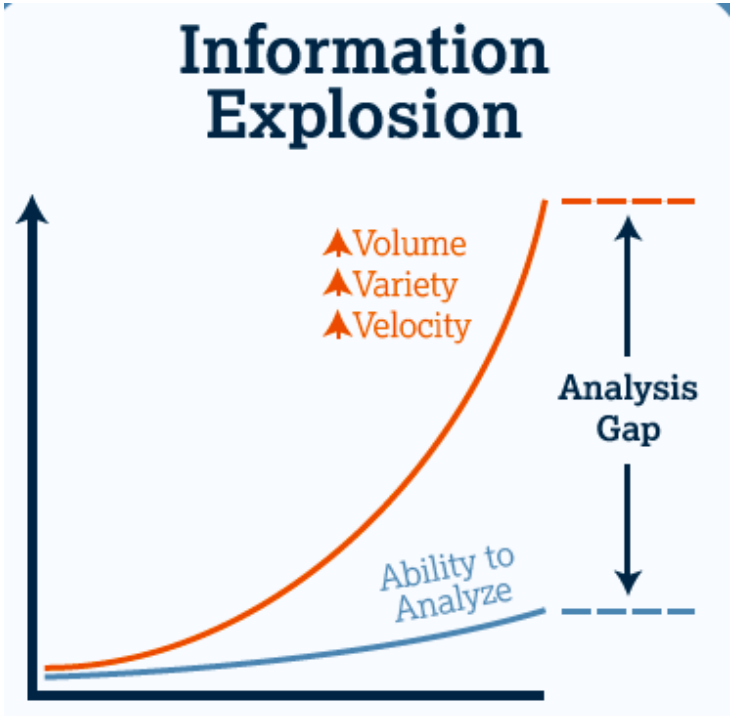
Hippocrates, 400 B.C



Animal studies

The challenges…..

- Heterogeneity of data
- Inconsistency or incompleteness
- Privacy (icloud, insurance etc.)
- Ecosystem
- Translation
- Validity
- …..?



→ What can we learn from Individual Patient / Participant / Animal Data meta-analyses

What is an IPD meta-analysis?

- Involves the central collection, checking and analysis of individual participant data

Enhancing the QUAlity and Transparency Of health Research

EQUATOR resources in Portuguese | Spanish

Search for reporting guidelines

Use your browser's Back button to return to your search results

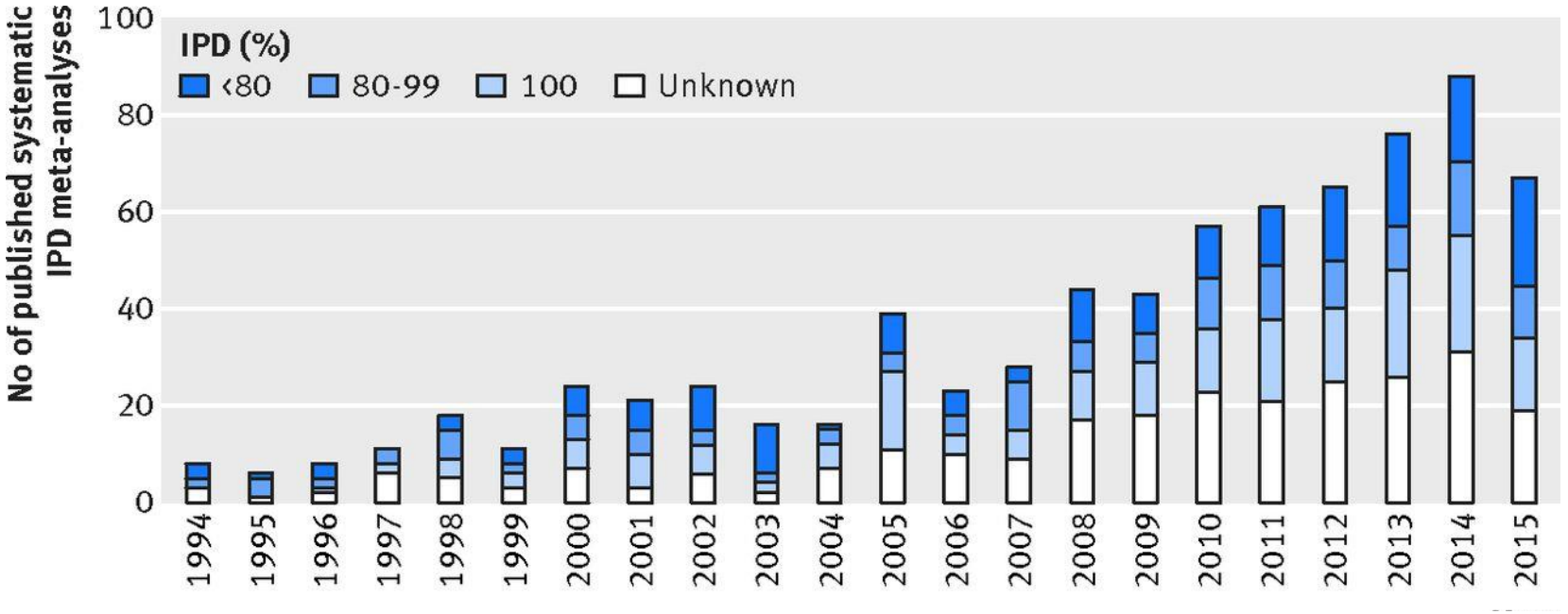
Preferred Reporting Items for Systematic Review and Meta-Analyses of individual participant data: the PRISMA-IPD Statement

Reporting guideline provided for? (i.e. exactly what the authors state in the paper)	Reporting systematic reviews and meta-analyses of individual participant data (IPD).
Full bibliographic reference	Stewart LA, Clarke M, Rovers M, Riley RD, Simmonds M, Stewart G, Tierney JF; PRISMA-IPD Development Group. Preferred Reporting Items for Systematic Review and Meta-Analyses of individual participant data: the PRISMA-IPD Statement. JAMA. 2015;313(16):1657-1665.
Language	English

Reporting guidelines for main study types

Randomised trials	CONSORT	Extensions
Observational studies	STROBE	Extensions
Systematic reviews	PRISMA	Extensions
Case reports	CARE	Extensions
Qualitative research	SRQR	COREQ
Diagnostic / prognostic studies	STARD	TRIPOD
Quality improvement studies	SQUIRE	

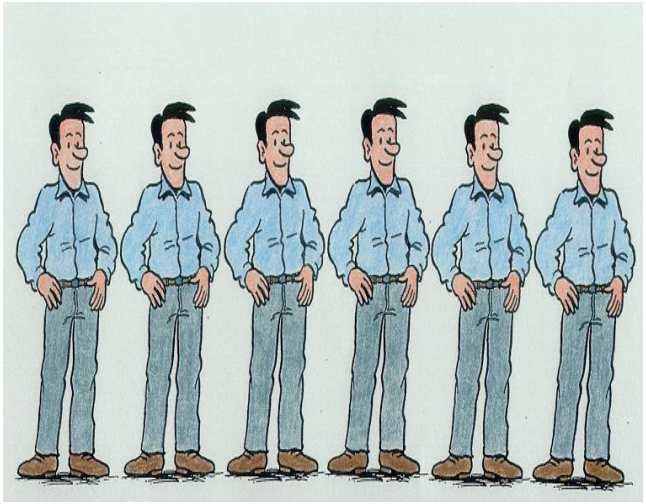
Number individual participant data (IPD) meta-analyses published to August 2015 and proportion of IPD provided.



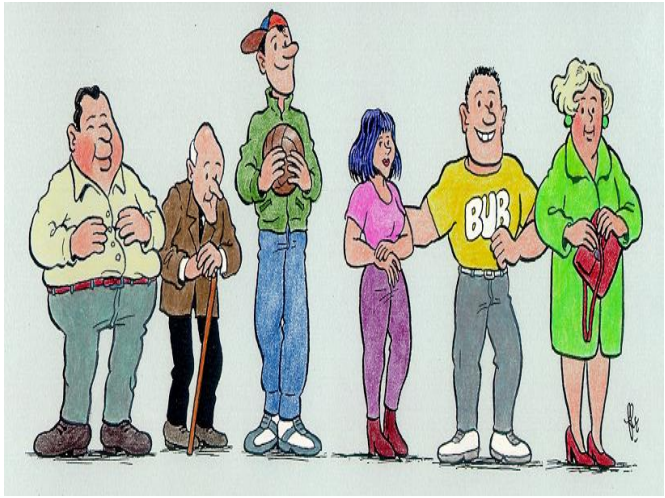
Sarah J Nevitt et al. BMJ 2017;357:bmj.j1390

Why IPD?

Overall result from single typical trial



Searching for many subgroups



How to solve this problem?

- Clinical **AND** methodological knowledge warranted to solve this

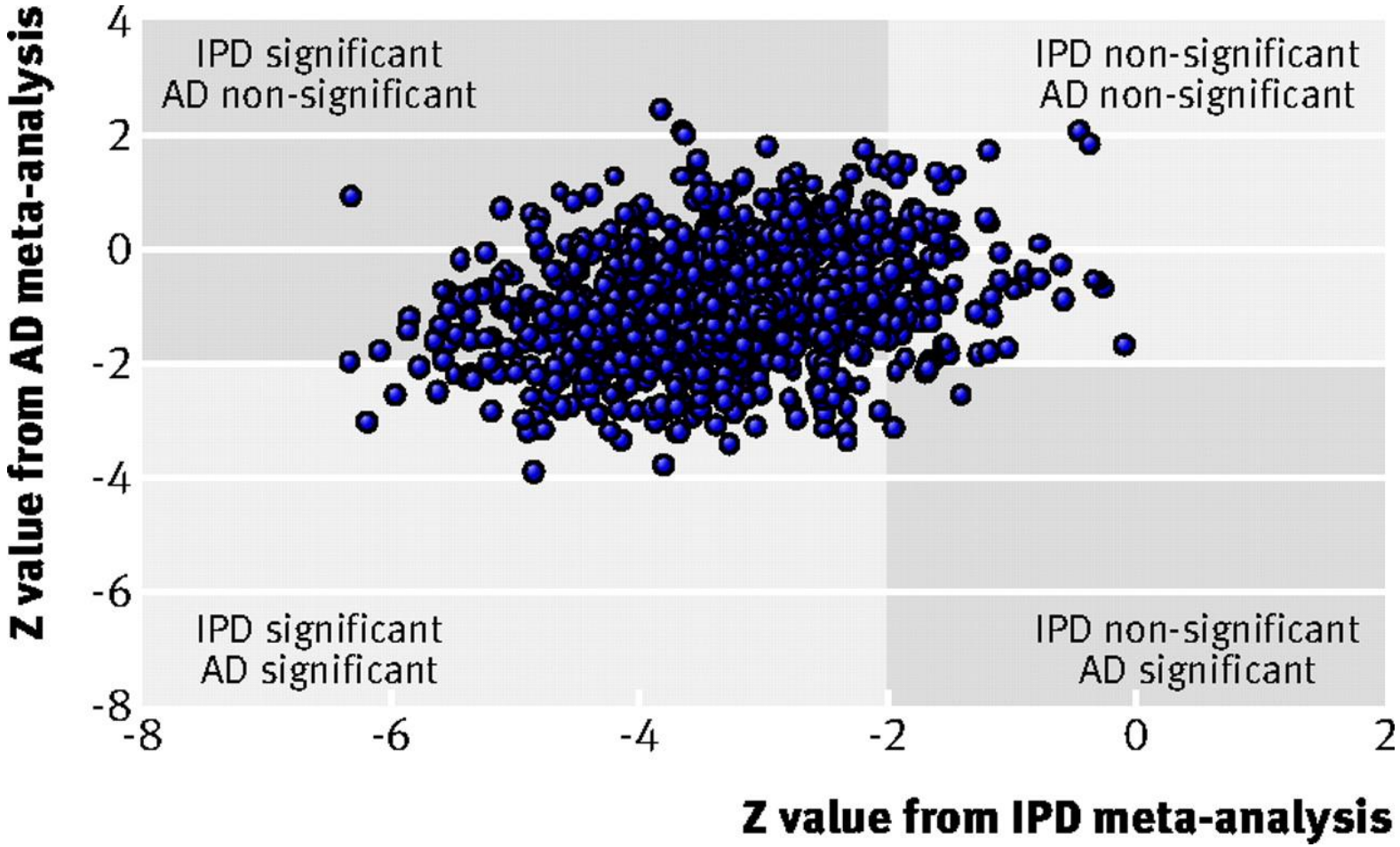
- Individual Patient Data (IPD) meta-analyses
  → Unique opportunity to identify subgroups that benefit more or less from an intervention

Why IPD meta-analysis?

- Major improvement in subgroup analysis
  - *Greater power*
  - *All measured subgroups available*
  - *Recoding into identical subgroups might be possible*

- But also:
  - *Time to event analyses*
  - *Other multivariate analyses*

Comparison of treatment effect across two groups of patients when individual participant data (IPD) or aggregate data (AD) are used



Richard D Riley et al. BMJ 2010;340:bmj.c221

Benefits of IPDMA

- Improved quality
- Improved outcome data
- Improved analysis quality
- Improved trial identification, interpretation and dissemination via collaborative approach

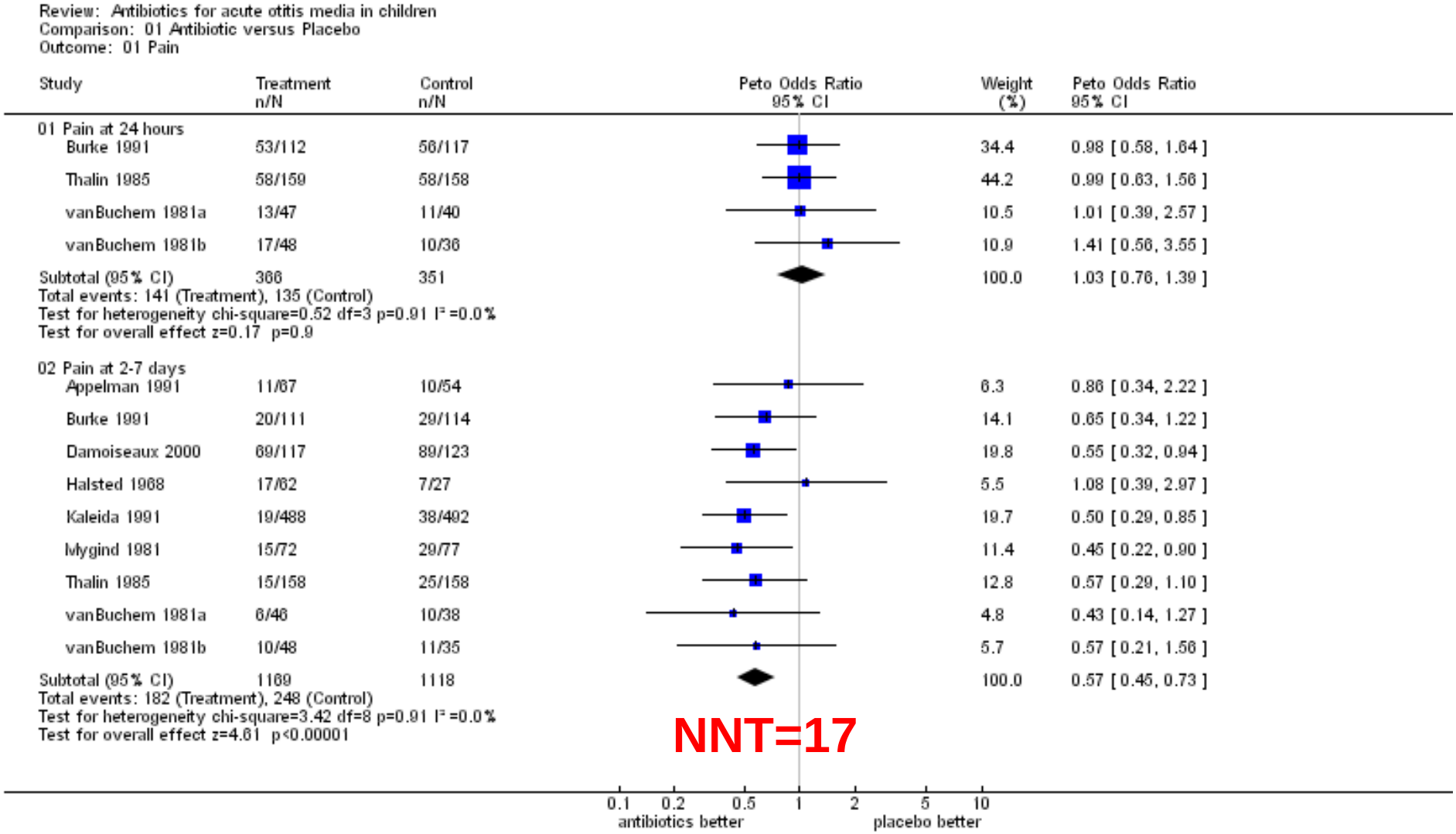
- Collaboration can lead directly to new trials and studies

- Results may lead to better guidelines

- Improve methods for RCTs, IPD and other meta-analyses
  - Use IPD as resource for research into bias, analysis methods, e.g. how to impute missings, combine randomised and non-randomised studies

An example: antibiotics for AOM

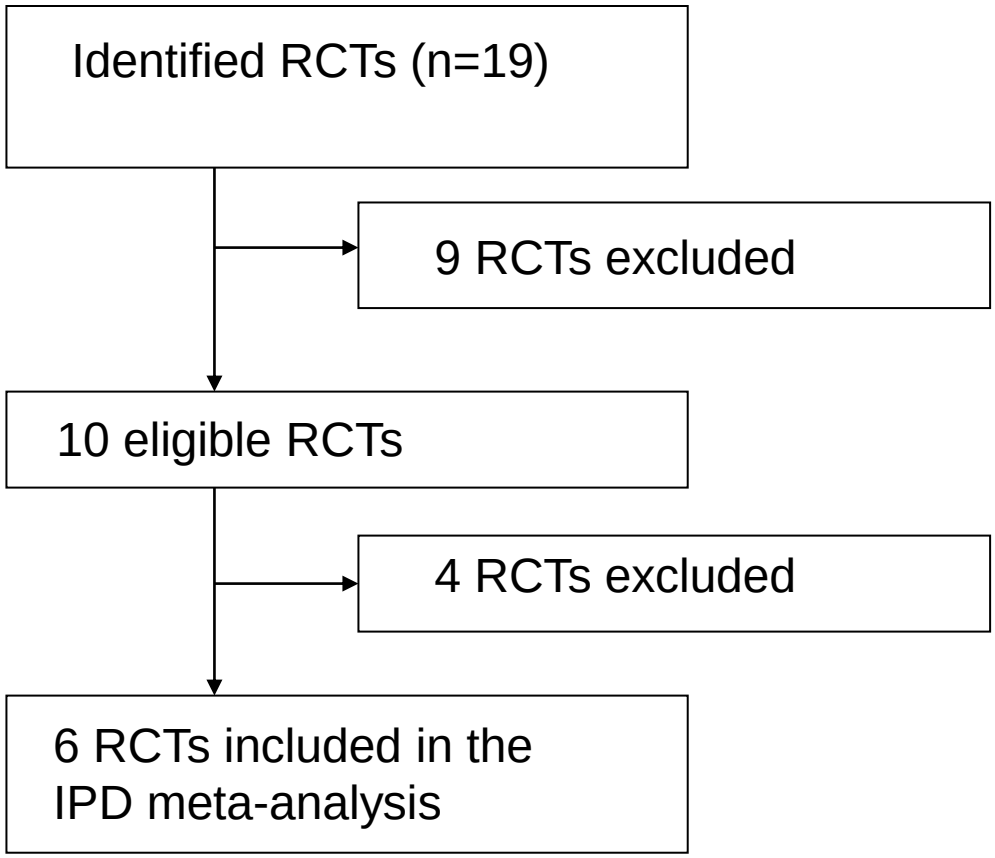
Evidence: Cochrane review



Method

- Systematic literature search for randomised trials on effectiveness antibiotics
- Ask investigators for raw data
- Recode and analyse individual data
- Identify children which benefit more or less from treatment with *antibiotics*

Results

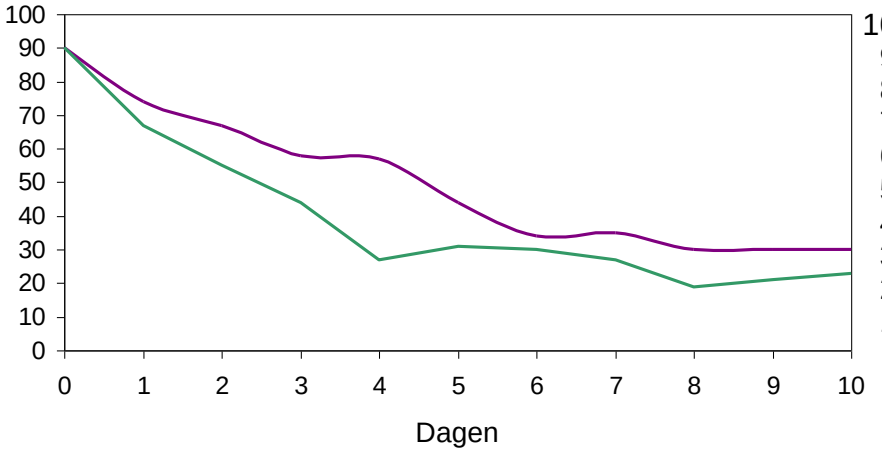

Identified RCTs (n=19)
9 RCTs excluded
10 eligible RCTs
4 RCTs excluded
6 RCTs included in the IPD meta-analysis

Results: effects antibiotics

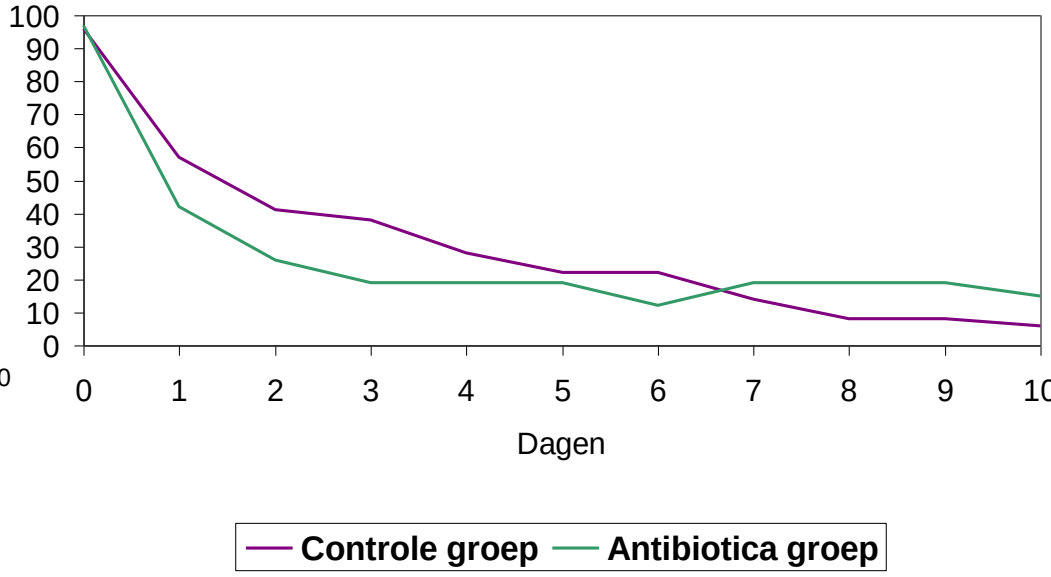
	RD	NNT
< 2 years + bilateral AOM	25%	4
< 2 years + unilateral AOM	5%	20
≥ 2 years + bilateral AOM	12%	9
≥ 2 years + unilateral AOM	4%	25

Results: Children with pain/fever

< 2 years with bilateral AOM



≥ 2 years with unilateral AOM

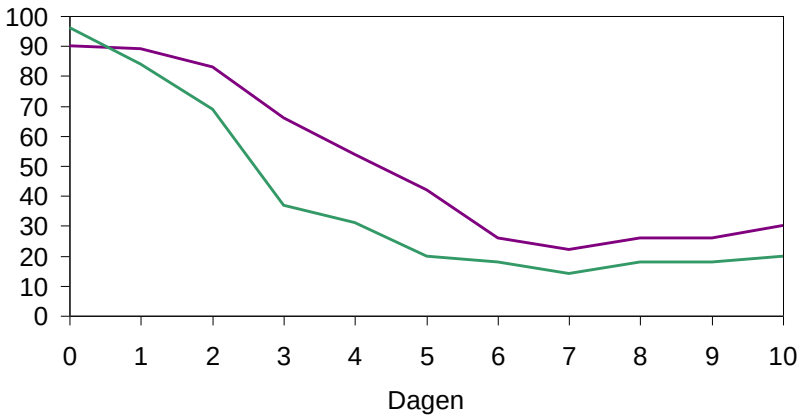


Results: pain and/or fever

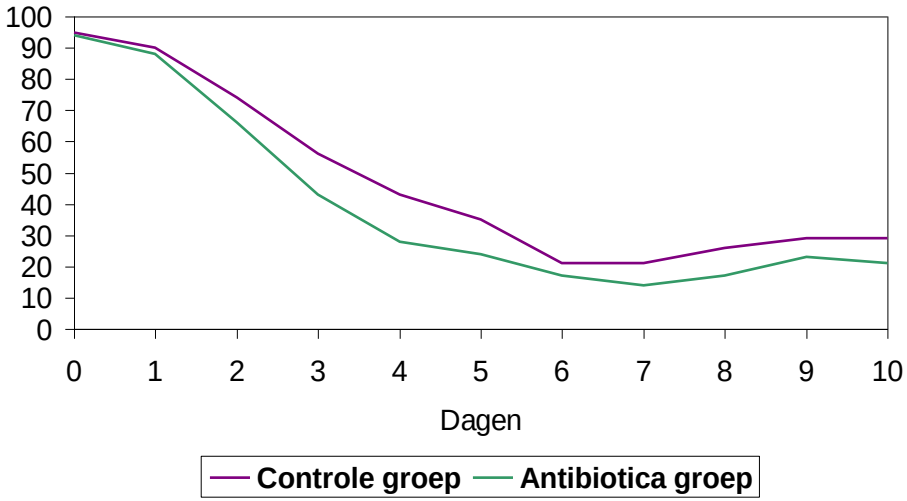
	RD	NNT
Otorrhea		
yes	36%	3
no	14%	8

Children with pain and/or fever

AOM with otorrhea

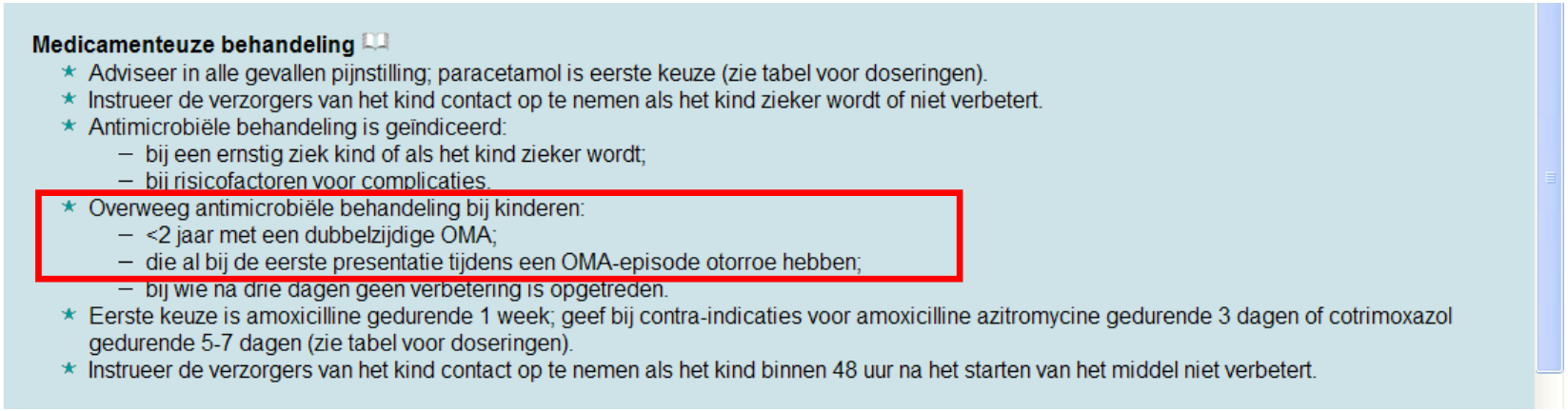


AOM without otorrhea



Guidelines

- Dutch, NHG guideline:



Medicamenteuze behandeling

- Adviseer in alle gevallen pijnstilling; paracetamol is eerste keuze (zie tabel voor doseringen).
- Instrueer de verzorgers van het kind contact op te nemen als het kind zieker wordt of niet verbetert.
- Antimicrobiële behandeling is geïndiceerd:
  - bij een ernstig ziek kind of als het kind zieker wordt;
  - bij risicofactoren voor complicaties.
- Overweeg antimicrobiële behandeling bij kinderen:
  - <2 jaar met een dubbelzijdige OMA;
  - die al bij de eerste presentatie tijdens een OMA-episode otorroe hebben;
  - bij wie na drie dagen geen verbetering is opgetreden.
- Eerste keuze is amoxicilline gedurende 1 week; geef bij contra-indicaties voor amoxicilline azitromycine gedurende 3 dagen of cotrimoxazol gedurende 5-7 dagen (zie tabel voor doseringen).
- Instrueer de verzorgers van het kind contact op te nemen als het kind binnen 48 uur na het starten van het middel niet verbetert.

- Guidelines in other countries:
  - Revised according to our findings in the UK, Sweden, USA, France, Denmark and Norway

Conclusions

- Individual participant data (IPD) meta-analyses are resource demanding, time consuming, and methodologically challenging, but when conducted well, provide more detailed and potentially more reliable results
- We have to ensure that procedures to access IPD do not become over-burdensome, over-costly, and prohibitive