

# DATA COLLECTION AND REUSE

**Patient Expert Group (PEG) meeting for paediatric patients**

Tim Friede

Department of Medical Statistics

University Medical Center Göttingen

## THAT'S ME ...



- ▷ My name is Tim
- ▷ At school I liked subjects like mathematics and physics but also history and geography
- ▷ I studied mathematics and learned more about statistics
- ▷ For some time I worked for a company that produces drugs. The company is called Novartis and is based in Switzerland
- ▷ Now I work at a university in Germany (where a lot of famous people worked in the past ...)



## PHRASING THE RESEARCH QUESTION: PICO(S)

<b>Patient, Population, or Problem</b>	How would I describe a group of patients similar to mine?
<b>Intervention, Prognostic Factor, or Exposure</b>	Which main intervention, prognostic factor, or exposure am I considering?
<b>Comparison or Intervention (if appropriate)</b>	What is the main alternative to compare with the intervention?
<b>Outcome you would like to measure or achieve</b>	What can I hope to accomplish, measure, improve or affect?

<http://hsl.mcmaster.libguides.com/content.php?pid=337527&sid=2763810>

▷ Study design: e.g. randomized controlled trial

# THE PARADIGMS TRIAL

- ▶ The doctors and scientists who ran the PARADIGMS trial wrote a report about it for one of the world's most famous journals in medicine, the so-called New England Journal of Medicine

*The NEW ENGLAND JOURNAL of MEDICINE*

ORIGINAL ARTICLE

## Trial of Fingolimod versus Interferon Beta-1a in Pediatric Multiple Sclerosis

Tanuja Chitnis, M.D., Douglas L. Arnold, M.D., Brenda Banwell, M.D.,  
Wolfgang Brück, M.D., Angelo Ghezzi, M.D., Gavin Giovannoni, M.D.,  
Benjamin Greenberg, M.D., Lauren Krupp, M.D., Kevin Rostásy, M.D.,  
Marc Tardieu, M.D., Emmanuelle Waubant, M.D., Jerry S. Wolinsky, M.D.,  
Amit Bar-Or, M.D., Tracy Stites, Ph.D., Yu Chen, M.Sc., Norman Putzki, M.D.,  
Martin Merschhemke, M.D., and Jutta Gärtner, M.D.,  
for the PARADIGMS Study Group\*

- ▶ You can read the article yourself, it can be found here  
<https://www.nejm.org/doi/pdf/10.1056/NEJMoa1800149>

## THE PARADIGMS TRIAL: PICOS

- ▷ **Population:** Patients 10 to 17 years of age with relapsing multiple sclerosis
- ▷ **Intervention:** Fingolimod (a new drug at the time)
- ▷ **Control:** Interferon Beta-1a (a drug that is around for longer already and was considered a standard treatment)
- ▷ **Outcome:** annualized relapse rate (number of relapses per year)
- ▷ **Study design:** randomized controlled trial



# THE STUDY PROTOCOL

- ▶ Good journals such as NEJM publish with the results of a clinical trial also the research plan, the so-called study protocol. It is typically found in the section “supplementary material”.
- ▶ For PARADIGMS the study protocol can be found here [https://www.nejm.org/doi/suppl/10.1056/NEJMoa1800149/suppl\\_file/nejmoa1800149\\_protocol.pdf](https://www.nejm.org/doi/suppl/10.1056/NEJMoa1800149/suppl_file/nejmoa1800149_protocol.pdf)
- ▶ The study protocol tells everyone helping with the study what to do when, in particular it details what needs to be measured and recorded and when. This is typically summarized in a table called “Assessment schedule”

# DATA COLLECTION IN CLINICAL TRIALS

- ▷ Assessment schedule from the PARADIGMS study protocol

**Table 6-1 Assessment schedule**

Phase	Pre-Randomization			Open-label Treatment Phase													
	Period	Screening	Baseline														
Visit No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14/ EOS	FU		
Study month	-45 days	-7 days	Day 1	½	1	2	3	6	9	12	15	18	21	24	+3 mo		
Informed consent	X																
Background, Demography	X																
Incl/exclusion criteria	X	X															
Medical history	X																
MS history/MS treatment	X																
Concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

- ▷ The table is too long to fit it onto this slide ...

# DATA COLLECTION IN CLINICAL TRIALS

- ▶ **Clinical trials take often a long time to run ...**
- ▶ For instance, the PARADIGM trial
  - ▶ included 190 patients (over 3 years)
  - ▶ who were treated and followed (meaning data were collected) for up to 2 years each
  - ▶ The trial duration was between 4 to 5 years.
- ▶ **A lot of data are collected** (including for example blood samples and images depending on the disease)
- ▶ **Clinical trials are very expensive**



# HOW TO FIND RELEVANT STUDIES?

- ▶ Use the PICO(S) scheme to structure your question
- ▶ Studies currently running can be identified through **clinical trial registries**. The best known is <https://clinicaltrials.gov/>

## ClinicalTrials.gov

Find Studies ▾ Study Basics ▾ Submit Studies ▾ Data and API ▾ Policy ▾ About ▾

ClinicalTrials.gov is a place to learn about clinical studies from around the world.



The U.S. government does not review or approve the safety and science of all studies listed on this website. +

Read our full [disclaimer](#) for details.

Focus Your Search (all filters optional)

[Expert Search](#)

Condition/disease ⓘ

Other terms ⓘ

Search

## HOW TO FIND RELEVANT STUDIES? (CONT.)

- ▶ Use the PICO(S) scheme to structure your question
- ▶ **Results of completed studies can be found in literature databases**
  - ▶ Among the best known literature database in medicine is MEDLINE / PubMed (<https://pubmed.ncbi.nlm.nih.gov/> )

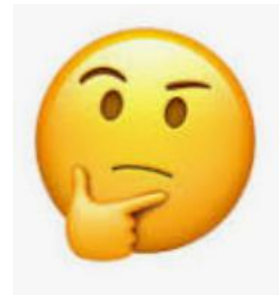


The screenshot shows the PubMed website interface. At the top left is the NIH logo and the text "National Library of Medicine" and "National Center for Biotechnology Information". At the top right is a "Log in" button. The main heading is "PubMed®". Below it is a search bar with a "Search" button. Under the search bar, it says "Advanced". At the bottom, there is a paragraph: "PubMed® comprises more than 37 million citations for biomedical literature from MEDLINE, life science journals, and online books. Citations may include links to full text content from PubMed Central and publisher web sites."

# REUSE OF DATA

- ▶ **For different reasons it makes sense to reuse data ...**


- ▶ Think of at least two reasons



- ▶ Available studies are identified in so-called **systematic reviews** searching literature databases and clinical trial registries.
- ▶ When several studies on one research question exists, their results are combined in so-called **meta-analyses**.
- ▶ Sometimes we do not reuse all the data from a trial but only one single group to reuse it in a new trial as control data. We call this **external controls** and meta-analysis techniques are used to combine the control group data from various trials.

# EXTERNAL CONTROLS IN PAEDIATRIC MS

- ▶ Is it useful to reuse data as external controls in paediatric MS? If yes, which data should be used and how?

 *Therapeutic Advances in Neurological Disorders*

*Meta-analysis*

## Improving pediatric multiple sclerosis interventional phase III study design: a meta-analysis

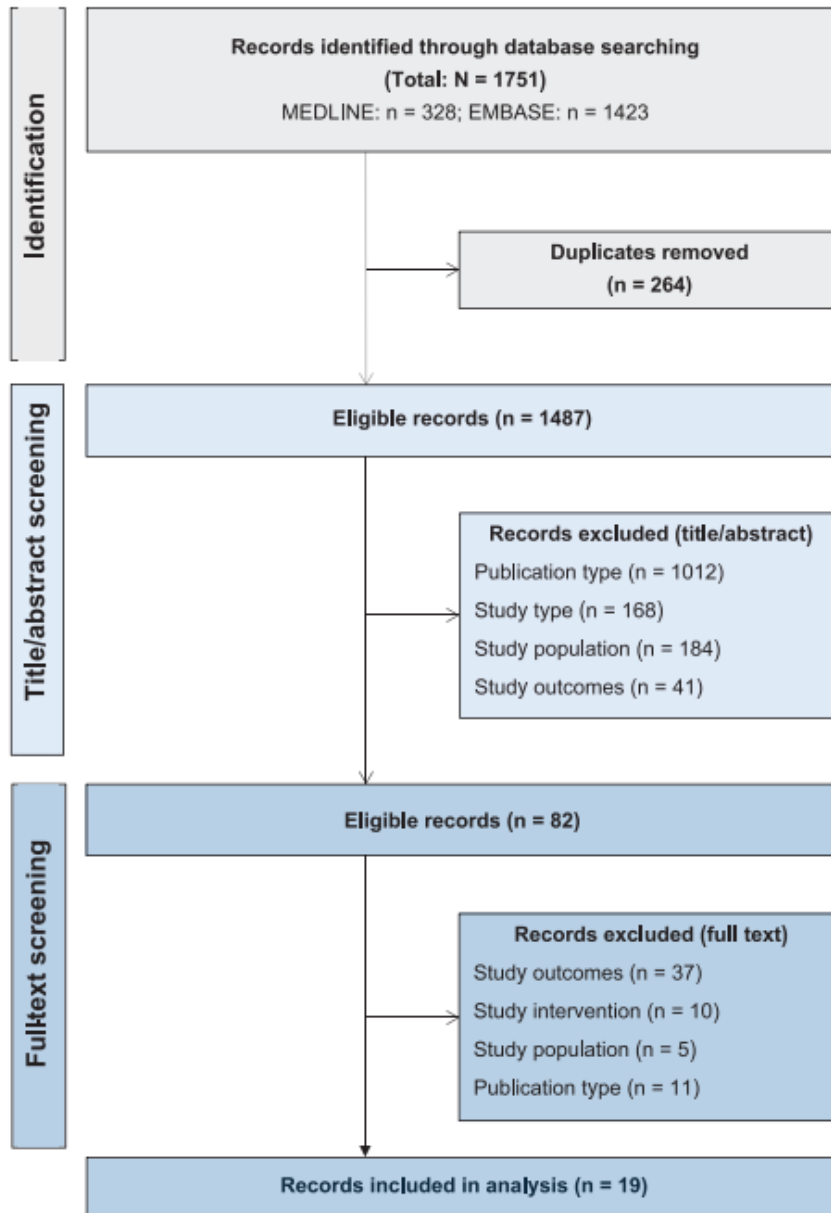
Jennifer S. Graves, Marius Thomas , Jun Li, Anuja R. Shah, Alexandra Goodyear, Markus R. Lange, Heinz Schmidli, Dieter A. Häring, Tim Friede  and Jutta Gärtner

*Ther Adv Neurol Disord*

2022, Vol. 15: 1–13

DOI: 10.1177/  
17562864211070449

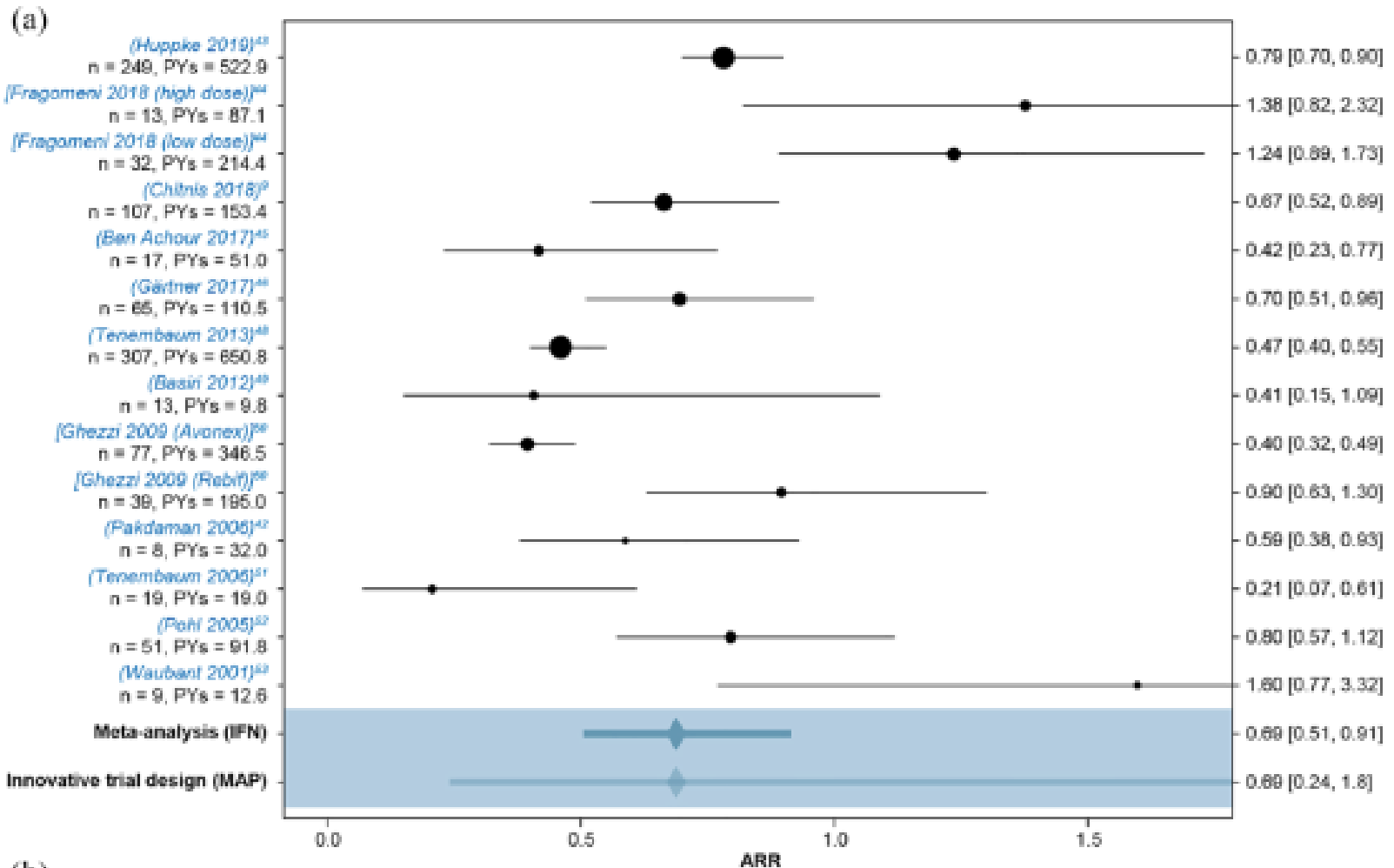
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- ▷ Studies identified in a **systematic review** by Jennifer Graves and colleagues

**Figure 1.** PRISMA diagram for study selection.  
PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

# ▶ Meta-analysis of annualized relapse rates when treated with IFN by Jennifer Graves and colleagues



(b)

## SOME SUMMARY POINTS

- ▶ Phrasing research questions: PICO(S) can be very useful
- ▶ The study protocol tells everyone helping with a study what to do when
- ▶ Data collection in a clinical trial can be a lot of work, in particular with many patients and long treatment / follow-up periods
- ▶ Reuse of data makes a lot of sense
- ▶ Relevant data can be identified through systematic reviews
- ▶ When combining data across trials we use special statistical techniques called meta-analysis