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Lessons learned in the pandemic era and future challenges

10th International Conference for EBHC Teachers and Developers
10th Conference of the International Society for EBHC
Taormina, 25th - 28th October 2023

#EBHC2023

Impact of pragmatic trial design features on treatment effect estimates: the PragMeta project

Lars G. Hemkens
for the PragMeta team

GIMBE EVIDENCE FOR HEALTH

RC2NB Research Center for Clinical Neuroimmunology and Neuroscience Basel

PRAGMATIC EVIDENCE LAB RC2NB

University of Basel

University Hospital Basel

Background // Πρᾶγμα

- „Pragma“ (πρᾶγμα) is a term that was used in ancient Greek to describe actions, things done, matters.
- Clinical trials can focus on actions and decisions, then they have a pragmatic intent.
- Clinical trials can focus on mechanisms of decisions, then they have an explanatory intent.
- We need evidence that matters for making better decisions.
- But most clinical trials are not “pragmatic”.
  ➔ How useful is then their evidence for decision making?

Aims // Pragmatism and estimated effects

- Are effect estimates influenced by the pragmatism of a trial?
- If yes, which features of pragmatism, generalizability, and applicability are responsible?
- What is it that makes evidence more pragmatic?

Methods // PragMeta

- www.PragMeta.org
- Open database to catalyze meta-research on pragmatic trials
- >700 trials (10/2023)
- Filled by meta-research and shared data
- Structured by themes / topics (PragMeta modules)
- Download option for all available data
- Funded by Swiss National Science Foundation (SNSF; #320030_188675)

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Meta-research on pragmatic trials

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RESET FILTERS

SEARCH

Showing 1 to 10 of 48 entries

- PRECIS-2 ASSESSMENT
- PARTICIPANTS
- INTERVENTIONS
- CONTROL
- OUTCOME (MAIN)
- MODULE
  - PragAntitumor
  - PragCOVID
  - PragEpi
  - PragMS
  - PragQoL
  - PragSurgery

Carter A. (2014) Pragmatic intervention for increasing self-directed exercise behaviour and improving important health outcomes in people with multiple sclerosis: a randomised controlled trial

Module: PragMS *Registration Number: ISRCTN41541516* *Country: UK*

Assessed by PragMeta team

Participants Outpatients
Interventions Lifestyle
Control Usual Care
Outcome Other

Miller L. (2011) Evaluation of a home-based physiotherapy programme for those with moderate to severe multiple sclerosis: a randomized controlled pilot study

Module: PragMS *Registration Number: N/A* *Country: UK*

Assessed by PragMeta team

Participants Outpatients
Interventions Physiotherapy
Control Usual Care
Outcome Questionnaire Diagnostic

Hermens H. (2008) Clinical assessment of the HELLODOC tele-rehabilitation service

Module: PragMS *Registration Number: N/A* *Country: Italy, Spain, Belgium*

Carter A. (2014) Pragmatic intervention for increasing self-directed exercise behaviour and improving important health outcomes in people with multiple sclerosis: a randomised controlled trial

Trial details

Module	First Author	Publication Year	DOI
PragMS	Carter A.	2014	Https://Doi.Org/10.1177/1352458513519354

Publication Type	Trial Category	Trial Registration	Country Of Conduct	Trial Purpose
Findings	Index RCT	ISRCTN41541516	UK	Supportive Care

Funding	Protocol	Disease	Disease Type	Therapeutic Area
Public/Not-For-Profit	Published	Multiple Sclerosis	Chronic	Neurology

Participant Type	Age Category	Cluster Randomization	Blinding	Number Of Arms
Outpatients	Adult	No	None	2

N Randomized	Use Of Routinely Collected Data (RCD)	RCD Type
120	No	N/A

Comparisons

Intervention A type	Intervention A name	Intervention B type	Intervention B name
Lifestyle	Supervised Exercise Sessions	Usual Care	Usual Care Only

Assessed by PragMeta team

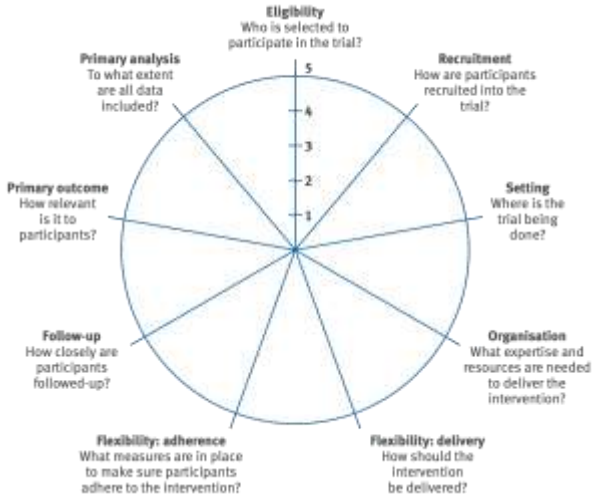
Outcome	Exercise behaviour
Outcome type	other
Outcome reported by	patient
Outcome hierachy	primary
Length of follow-up	9 months

Methods // Procedures and data workflow

- Collection of trials with identical PICO
- Spectrum of generalizability, applicability, and pragmatism
- Enrichment for pragmatic trials:
  - Self-labeled as “pragmatic”
  - Potential proxies of pragmatism (e.g., use of routine data)
  - Forward citation searching for systematic reviews
    → trials on same PICO

Methods // Assessment of Pragmatism

- PRagmatic Explanatory Continuum Indicator Summary tool (PRECIS-2)
- Degree of pragmatism (9 domains, overall score)
- Impact on treatment estimates of candidate determinants of pragmatism by, e.g.
  - regression analyses
  - ratio of odds ratios



https://www.precis-2.org/

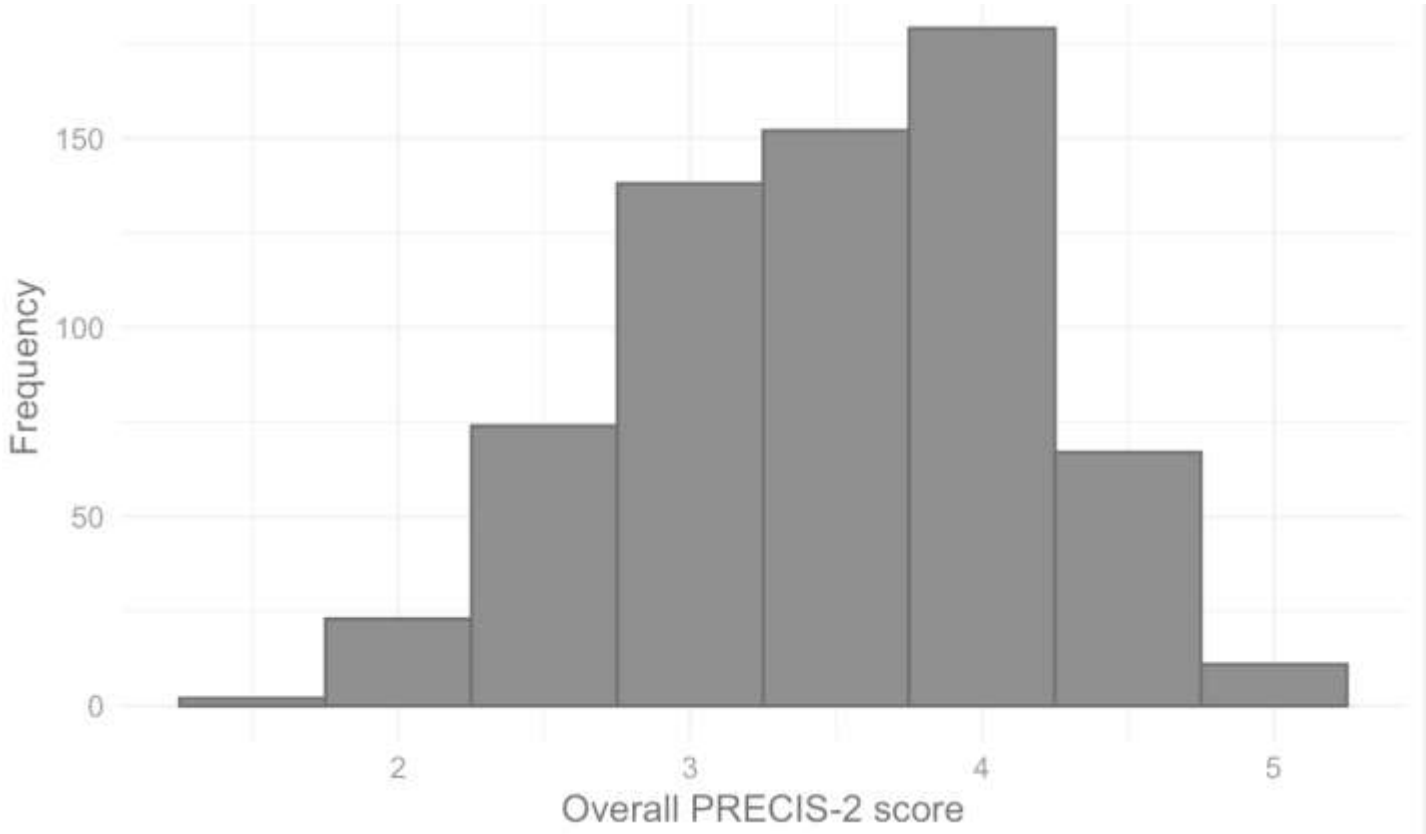
Results // PragMeta modules

- **PragCOVID**: COVID-19 trials self-labeled as pragmatic (37 trials)
- **PragMS**: Pragmatic trials in Multiple Sclerosis (48 trials)
- **PragQoL**: Comparing trials with patient-reported outcomes (pain, fatigue, and quality of life) to objective clinical outcomes (52 trials)
- **PragEpi**: PRECIS-2 in SRs/meta-analyses (citing and assessing) (185 trials)
- **PragSurgery**: PRECIS-2 assessment in surgery (388 trials) [shared/linked]
- **PragAntitumor**: PRECIS-2 assessment in antitumor treatments (31 trials) [shared/linked]
- **PragRCD**: PRECIS-2 assessment of trials using routinely collect data (547 trials)
  → *ongoing*

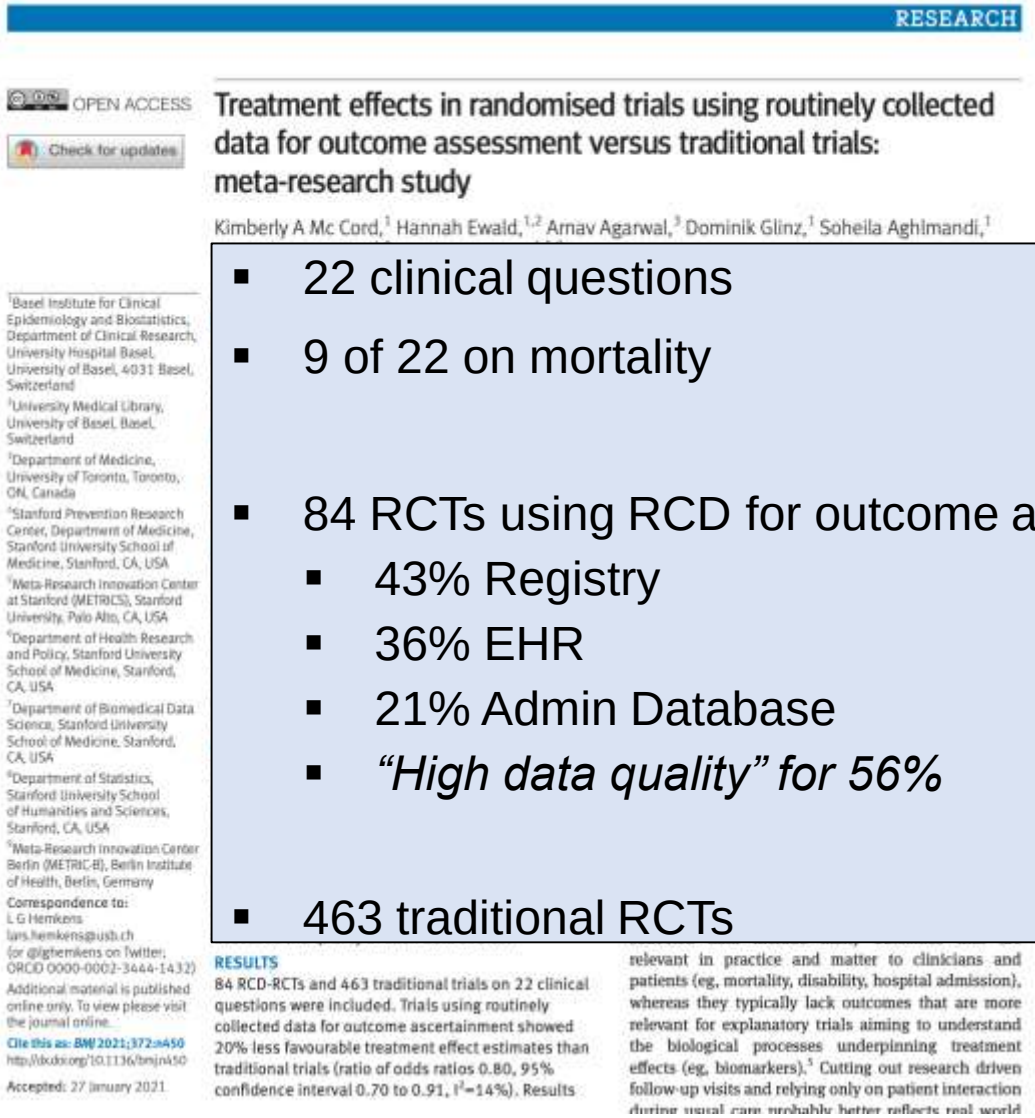
https://osf.io/6zn4y/
https://doi.org/10.1001/jamanetworkopen.2021.1449
https://doi.org/10.1136/bmj.n450

First Results + Limitations

- Trials with same PICO question seem to have similar pragmatism acc. PRECIS-2
- Included topics are often free of very non-pragmatic evidence
- Broader spectrum needed



Outlook and Challenge:
Pragmatism of Real World Evidence



RESEARCH

OPEN ACCESS

Check for updates

Treatment effects in randomised trials using routinely collected data for outcome assessment versus traditional trials: meta-research study

Kimberly A Mc Cord,[1] Hannah Ewald,[1,2] Arnav Agarwal,[3] Dominik Glinz,[1] Soheila Aghlmandi,[1]

[1]Basel Institute for Clinical Epidemiology and Biostatistics, Department of Clinical Research, University Hospital Basel, University of Basel, 4031 Basel, Switzerland
[2]University Medical Library, University of Basel, Basel, Switzerland
[3]Department of Medicine, University of Toronto, Toronto, ON, Canada
[4]Stanford Prevention Research Center, Department of Medicine, Stanford University School of Medicine, Stanford, CA, USA
[5]Meta-Research Innovation Center at Stanford (METRICS), Stanford University, Palo Alto, CA, USA
[6]Department of Health Research and Policy, Stanford University School of Medicine, Stanford, CA, USA
[7]Department of Biomedical Data Science, Stanford University School of Medicine, Stanford, CA, USA
[8]Department of Statistics, Stanford University School of Humanities and Sciences, Stanford, CA, USA
[9]Meta-Research Innovation Center Berlin (METRIC-B), Berlin Institute of Health, Berlin, Germany

Correspondence to:
L G Hemkens
lars.hemkens@usb.ch
(or @lghemkens on Twitter;
ORCID 0000-0002-3444-1432)

Additional material is published online only. To view please visit the journal online.

Cite this as: BMJ 2021;372:n450
http://dx.doi.org/10.1136/bmj.n450

Accepted: 27 January 2021

- 22 clinical questions
- 9 of 22 on mortality
- 84 RCTs using RCD for outcome assessment
  - 43% Registry
  - 36% EHR
  - 21% Admin Database
  - *"High data quality" for 56%*
- 463 traditional RCTs

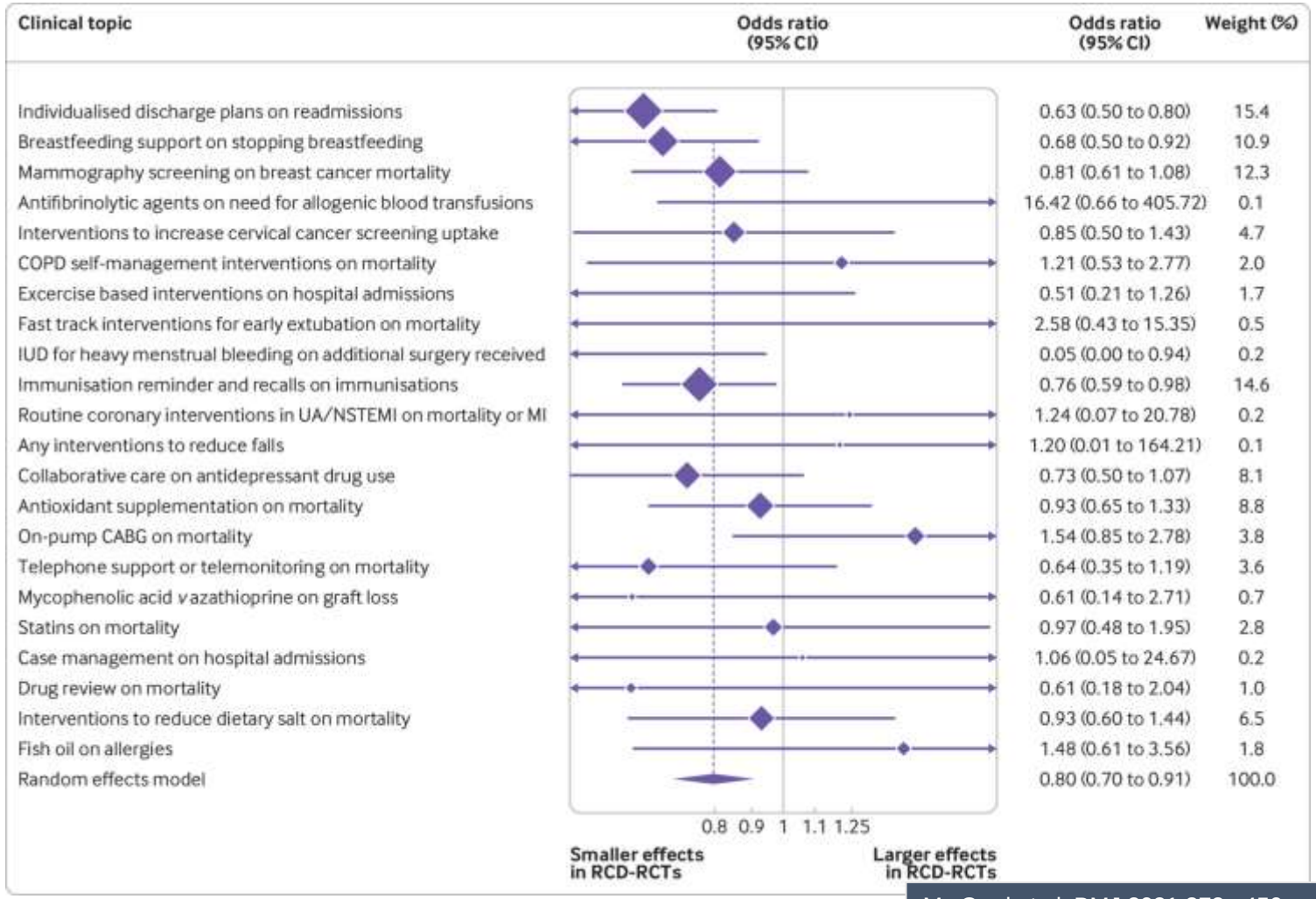
RESULTS

84 RCD-RCTs and 463 traditional trials on 22 clinical questions were included. Trials using routinely collected data for outcome ascertainment showed 20% less favourable treatment effect estimates than traditional trials (ratio of odds ratios 0.80, 95% confidence interval 0.70 to 0.91, I^2=14%). Results

relevant in practice and matter to clinicians and patients (eg, mortality, disability, hospital admission), whereas they typically lack outcomes that are more relevant for explanatory trials aiming to understand the biological processes underpinning treatment effects (eg, biomarkers).[5] Cutting out research driven follow-up visits and relying only on patient interaction

Mc Cord et al. BMJ 2021;372:n450
URL: https://www.bmj.com/content/372/bmj.n450

RCD-RCTs find 20% smaller benefits than traditional RCTs



Conclusions

Meta-research needs a broader focus

- Extensive work on biases and internal validity
- Limited work on pragmatism (applicability, generalizability, indirectness).
- PragMeta is the first large scale project to catalyze meta-research on pragmatism

Join the mission and connect

- We welcome support and collaboration
- Share ideas and suggestions

Lars G. Hemkens MD MPH

Lead Pragmatic Trials and Real World Evidence
RC2NB - Research Center for Clinical Neuroimmunology and Neuroscience Basel
University of Basel and University Hospital Basel | Basel | Switzerland

ORCiD: 0000-0002-3444-1432

Lars.Hemkens@usb.ch

@LGHemkens

PragMeta
pragmeta.org

PRAGMATIC EVIDENCE LAB | RC2NB

www.pragmatic-evidence.org

Special Thanks

PragMeta @ RC2NB (U Basel):
P Janiaud
J Hirt
C Axfors
P Düblin
T Woelfle
K Dembowska
TVT Ngyuen
A Sison

Collaborators:
R Dal-Ré (U Madrid)
H Ewald (U Basel)
G Gartlehner (U Krems)
S Goodman (U Stanford)
C Granziera (U Basel)
A Howie (U Ontario)
JPA Ioannidis (U Stanford)
L Kappos (U Basel)
T Mathes (U Goettingen)
J Meerpohl (U Freiburg)
D Moher (U Ottawa)
F Naudet (U Rennes / INSERM)
TV Pereira (U Leicester)
S Treweek (U Aberdeen)
M Zwarenstein (U Ontario / ICES)
PRECIS-2 group
NB Robinson (Weill Cornell Medicine)
R Saesen (EORTC)
M Taljaard (U Ottawa)
B Thombs (U McGill)
D Strech (QUEST)

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