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Pragmatic Clinical Trials: A crucial building block for health systems and treatment ?

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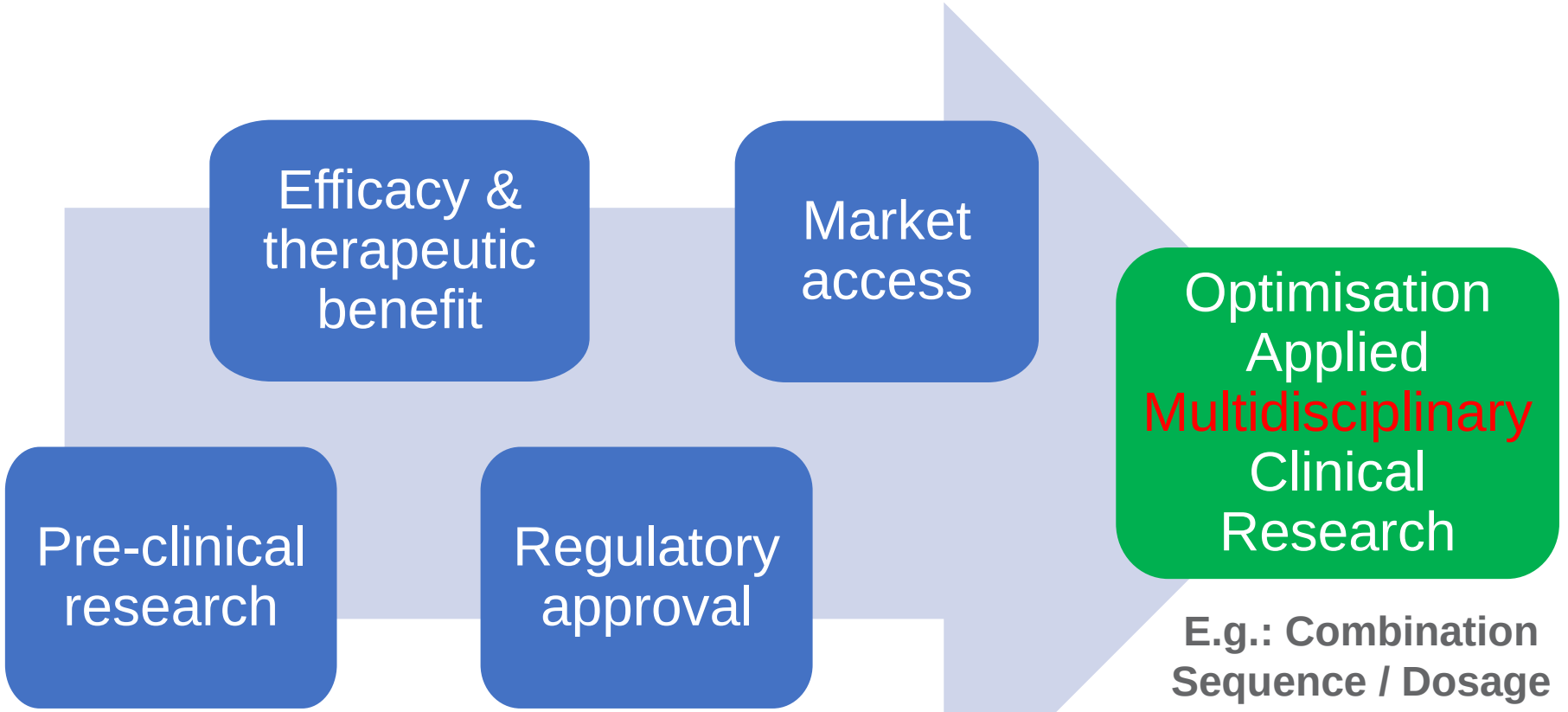
The work starts when a technology reaches the market.



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Original Research

Characteristics of clinical trials for haematological malignancies from 2015 to 2020: A systematic review

William Wesson [a], Vincent L. Galate [a], Douglas W. Sborov [b], Brian McClune [b], Aaron M. Goodman [c], Bishal Gyawali [d], Vinay Prasad [e], Saqib Abbasi [a], Ghulam Rehman Mohyuddin [b,*]

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Editorial Comment

Contemporary clinical trials in hematologic cancer: Have we forgotten where we came from?

Manju Sengar [a], Christopher M. Booth [b,c,*]

original reports

Low-Dose Immunotherapy in Head and Neck Cancer: A Randomized Study

Vijay Maruti Patil, MBBS, MD, DM[1]; Vanita Noronha, MBBS, MD, DM[1]; Nandini Menon, MBBS, MD, DNB[1]; Rahul Rai, MBBS, MD[1]; Atanu Bhattacharjee, PhD[2]; Ajay Singh, MBBS, MD, DM[1]; Kavita Nawale, PDCR[1]; Shweta Jogdhankar, MSc[1]; Rupali Tambe, BCom[1]; Sachin Dhumal, BHMS[1]; Riddhi Sawant, PDCR[1]; Mitali Alone, MSc[1]; Devanshi Karla, MSc[1]; Zoya Peelay, MSc[1]; Shruti Pathak, MSc[1]; Arun Balaji, MASLP[3]; Suman Kumar, MBBS, DNB[4]; Nilendu Purandare, MBBS, DNB[5]; Archi Agarwal, MBBS, DNB[5]; Ameya Puranik, MBBS, DNB[5]; Abhishek Mahajan, MBBS, DNB[4]; Amit Janu, MBBS, DNB[4]; Gunjesh Kumar Singh, MBBS, MD, DM[1]; Neha Mittal, MBBS, MD[6]; Subhash Yadav, MBBS, MD[6]; Shripad Banavali, MBBS, MD[1]; and Kumar Prabhash, MBBS, MD, DM[1]

editorials

Cost Savings and Increased Access With Ultra-Low-Dose Immunotherapy

Aaron P. Mitchell, MD, MPH[1]; and Daniel A. Goldstein, MD[2,3,4,5]

The Wild West of Checkpoint Inhibitor Development

Julia A. Beaver, M.D., and Richard Pazdur, M.D.

Over the past 7 years, the Food and Drug Administration (FDA) has approved seven antibodies directed against the programmed death 1 (PD-1) or programmed death ligand (PD-L1) pathway and more than 85 oncology indications for this class of checkpoint inhibitor drugs. More than 2000 clinical trials are evaluating at least 33 anti–PD-1 or anti–PD-L1 antibodies.[1] Although these products have simil identical, mechanisms o safety profiles, and clinic ity, no studies have direc pared them. And altho development of immun

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Analysis

Replacing RCTs with real world data for regulatory decision making: a self-fulfilling prophecy?

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Cite this as: *BMJ* 2023;380:e073100

Article | Related content | Metrics | Responses | Peer review

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SPECIALTY SECTION
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Project Optimus, an FDA initiative: Considerations for cancer drug development internationally, from an academic perspective

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ANALYSIS

Check for updates

New drugs: where did we go wrong and what can we do better?

More than half of new drugs entering the German healthcare system have not been shown to add benefit. **Beate Wieseler** and colleagues argue that international drug development processes and policies are responsible and must be reformed

Beate Wieseler *head of department of drug assessment*, Natalie McGauran *researcher*, Thomas Kaiser *head of department of drug assessment*

Institute for Quality and Efficiency in Health Care, Cologne, Germany

Project Pragmatica

Advancing evidence generation for approved oncology medical products

Pragmatica-Lung study : Ramucirumab Plus Pembrolizumab vs Usual Care for Treatment of Stage IV or Recurrent Non-Small Cell Lung Cancer Following Immunotherapy

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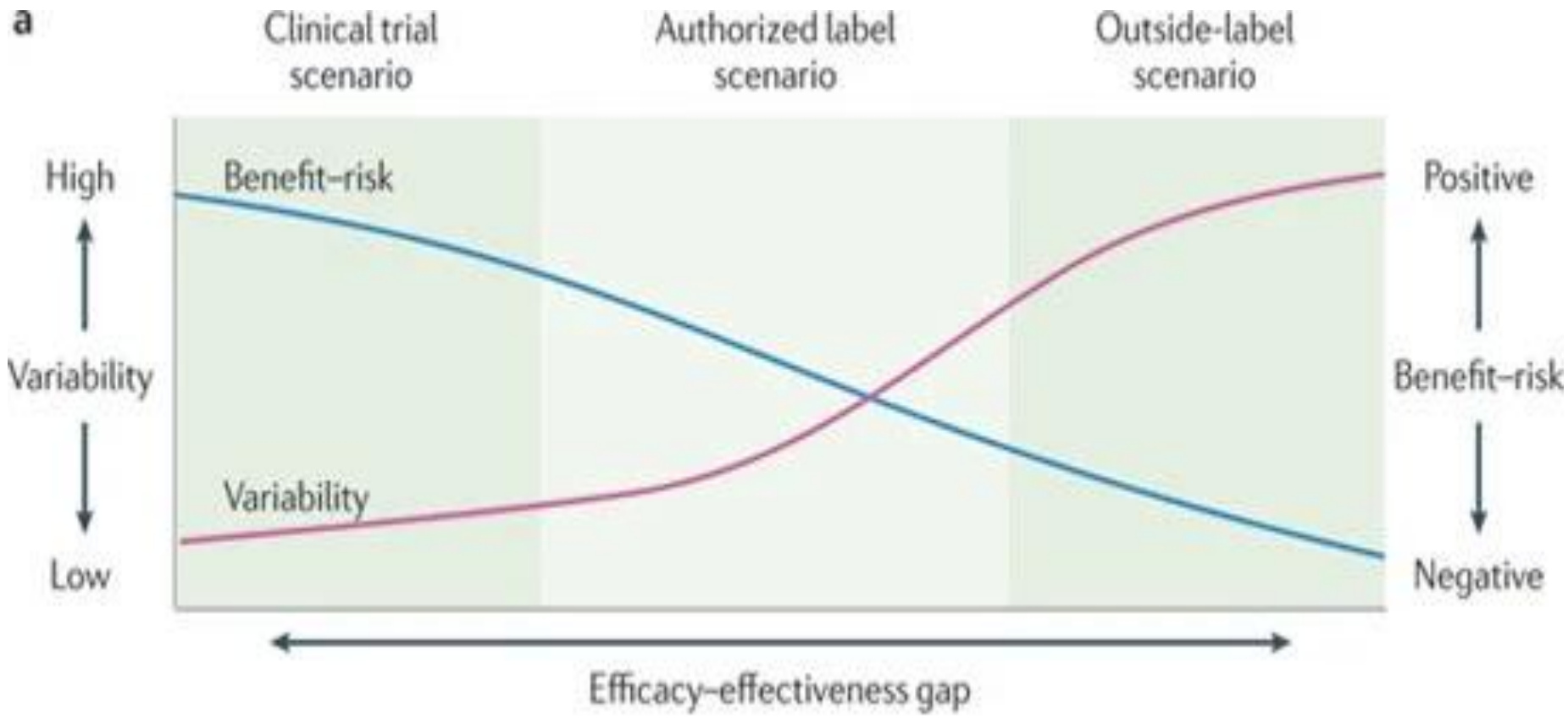
Pragmatic Clinical Trials (PCT)

What is it all about?

The efficacy-effectiveness gap



Treatment efficacy > Treatment effectiveness

>99% of trials <1% of trials

Eichler et al. *Nat Rev Drug Discov* (2011)
Chalkidou et al. *Trials* (2012)

Complementarity of clinical trials
The continuum drug development- access

Explanatory Clinical Trials

- Strict eligibility
- Additional procedures and processes as compared to standard
- Conducted at specific institution, organized for the complexity
- Extensive data collection and curation
- Endpoints targeting scientific knowledge and understanding of disease / intervention processes

Limited to poor external validity: the obtained estimates may not be representative of effects in the day-to-day practice. This includes both effectiveness and safety.

Pragmatic Clinical Trials

- Wide inclusion criteria
- Procedures as per standard practice
- Conducted in extended networks including community hospitals
- Limited data collection relevant to decision makers
- End-points directed to answer clinically relevant questions based on patient centric end-points

Good external validity: provides information on the applicability of therapeuticinterventions

The value of pragmatic trials

Pragmatic trials are especially valuable to:

- **Patients**, by painting a more realistic picture of a treatment's benefits and harms for the average patient
- **Clinicians**, by guiding clinical decision-making
- **Payers**, by informing reimbursement-related decision-making

Pragmatic trials combine the methodological strengths of RCTs with the inclusiveness of studies that analyze real-world data

→ Sources of robust and actionable real-world evidence

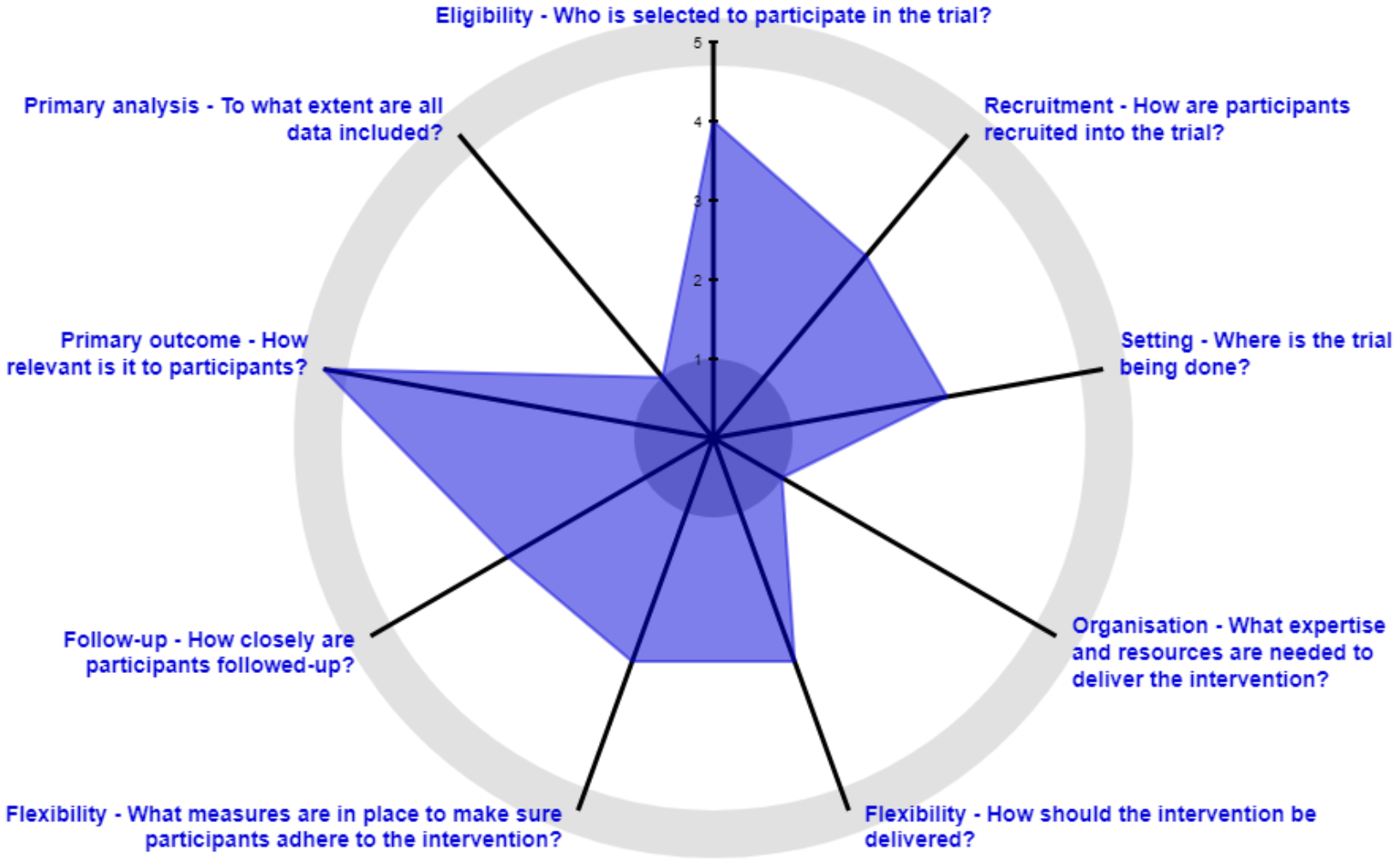
Simon et al. *N Engl J Med* (2020)
Neyt et al. *J Comp Eff Res* (2016)
Zuidgeest et al. *J Clin Epidemiol* (2017)

How can you recognize a pragmatic trial?

PRECIS-2 wheel

More pragmatic

More explanatory



Loudon et al. *BMJ* (2015)

Articulations for forward thinking

- Improve the understanding of PCTs
- Discuss The value and benefits of PCTs for the different stakeholders
- Understand how can PCTs help addressing the gap efficacy –effectiveness
- Identify how can PCTs subscribe to the evolving health care systems
- Alert policy makers on the need to take PCTs into account in the evolving regulatory and legal landscape
- Address the challenges to run PCTs.