




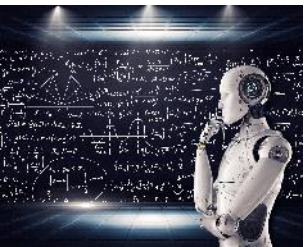

Clinical evidence for technological innovations

Alternative study designs

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Agenda

- Technology in healthcare
  - Current and future trends
  - Disruptive innovations
- Evidence in healthcare
  - Limitations with current best practices
- Evidence for technological healthcare innovations
  - A phased approach to technology evidence
  - Alternative study designs for generating clinical evidence

Technology-based innovations in healthcare

- "9 Health Technologies Every Executive Should Be Excited About in 2022"
  - Artificial intelligence
  - Blockchain
  - Voice search
  - Chatbots in healthcare
  - Virtual reality in healthcare
  - Advanced social media
  - Personalized mobile apps
  - Enhanced app/software partnerships
  - Video marketing

Source: https://healthcareweekly.com/health-technologies/

Technology-based interventions in healthcare

- Technological interventions can broadly be classified into three categories:
  - Assistive, therapeutic, and service delivery augmenting

- For example, a comprehensive framework for assistive and therapeutic intervention products:
  - ISO 9999:2016 Assistive products for persons with disability - Classification and terminology

Assistive innovations

- ***Assistive interventions*** support functional activity performance
  - E.g., wheelchairs, ramps, memory aids, or communication devices.

Sources: https://www.myhomehelper.co.uk/home/Features.aspx
https://www.which.co.uk/reviews/assistive-technology/article/memory-aids-for-the-elderly-a2FME7U7AKEI

How, et al. Evaluation of an intelligent wheelchair system for older adults with cognitive impairments. J NeuroEngineering Rehabil 10, 90 (2013).

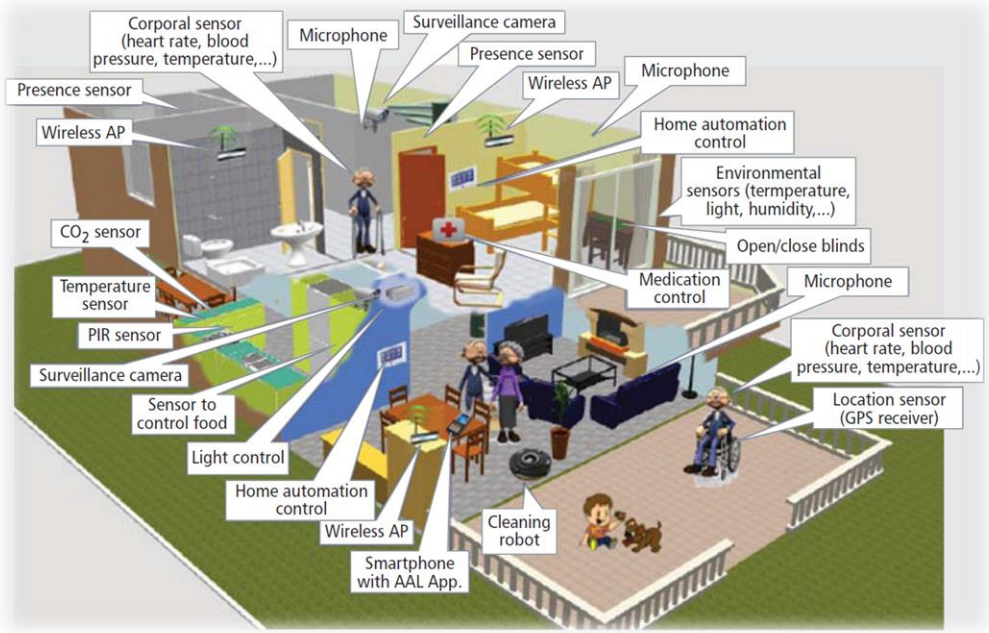
Therapeutic innovations

- ***Therapeutic interventions*** focus on restoring or improving functionality
  - E.g., robotic exoskeletons, virtual reality headsets and controllers, or gaming systems.

Sources: https://www.rimrehab.org/services/exoskeletons
https://www.digitalbodies.net/virtual-reality/vr-in-your-head-startups-offering-virtual-reality-exposure-therapy/

Service delivery innovations

- ***Service delivery*** interventions augment existing services or provide services not currently available to users
  - E.g., tele-rehabilitation systems, mobile applications, or ambient home monitoring systems.



https://cbphysiotherapy.in/blog/role-of-telerehabilitation-in-times-of-covid-19
https://medium.com/@aaujordanu/ambient-intelligence-33a8a9809725

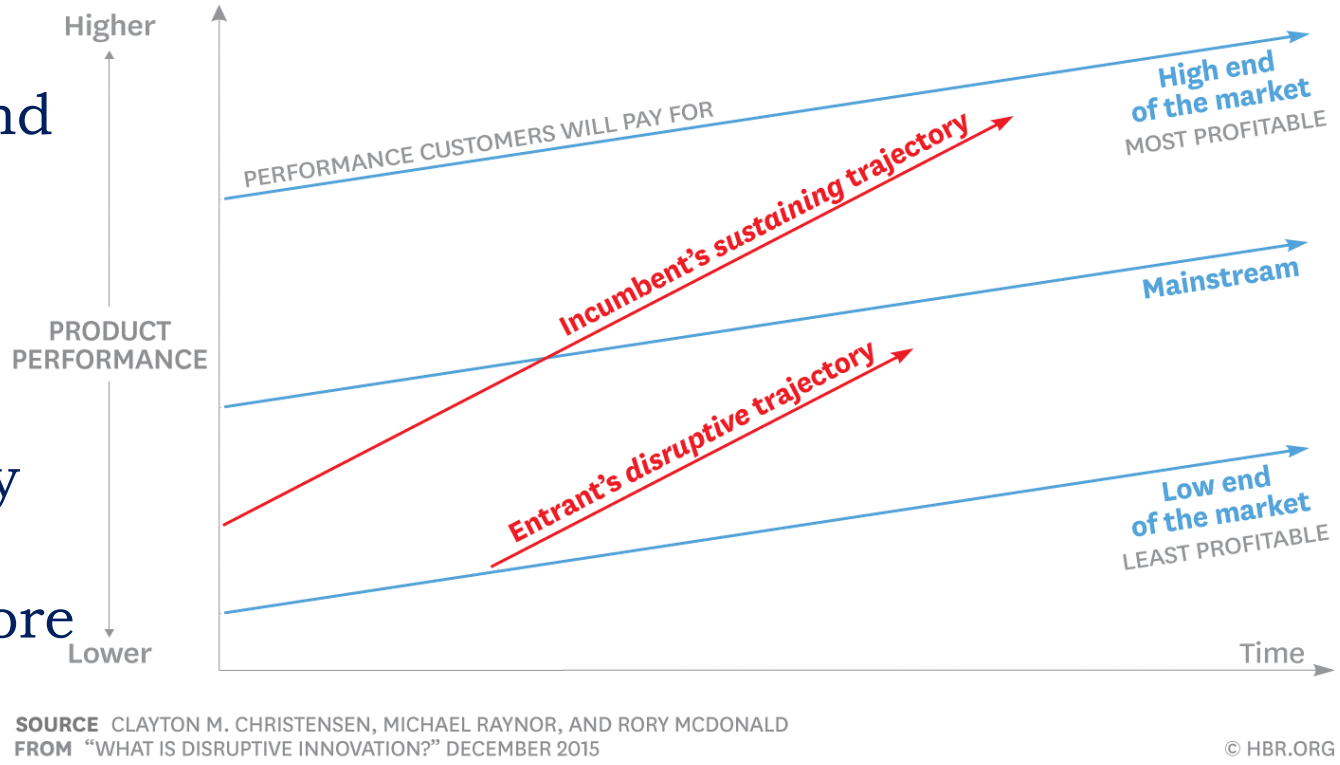
From research to market

- Technology-based interventions for healthcare are typically:
  - Complex
  - Target diverse users
  - Must function within variable environments

- Innovations challenge the current paradigm
  - Resistance to new technologies?
  - Require rigorous evidence, particularly in clinical applications

Disruptive innovations

- Disruption
  - "a process whereby a smaller company with fewer resources is able to successfully challenge established incumbent businesses"
- Incumbents
  - focus on improving products and services for most demanding customers
    - …and most profitable?
- Entrants
  - prove disruptive by successfully targeting overlooked segments
  - gain a foothold by delivering more suitable functionality



SOURCE CLAYTON M. CHRISTENSEN, MICHAEL RAYNOR, AND RORY MCDONALD
FROM "WHAT IS DISRUPTIVE INNOVATION?" DECEMBER 2015

© HBR.ORG

Source: Harvard Business Review, https://hbr.org/2015/12/what-is-disruptive-innovation

From development to disruption

- Many start-ups and technology developers/researchers want to build an evidence base for their products

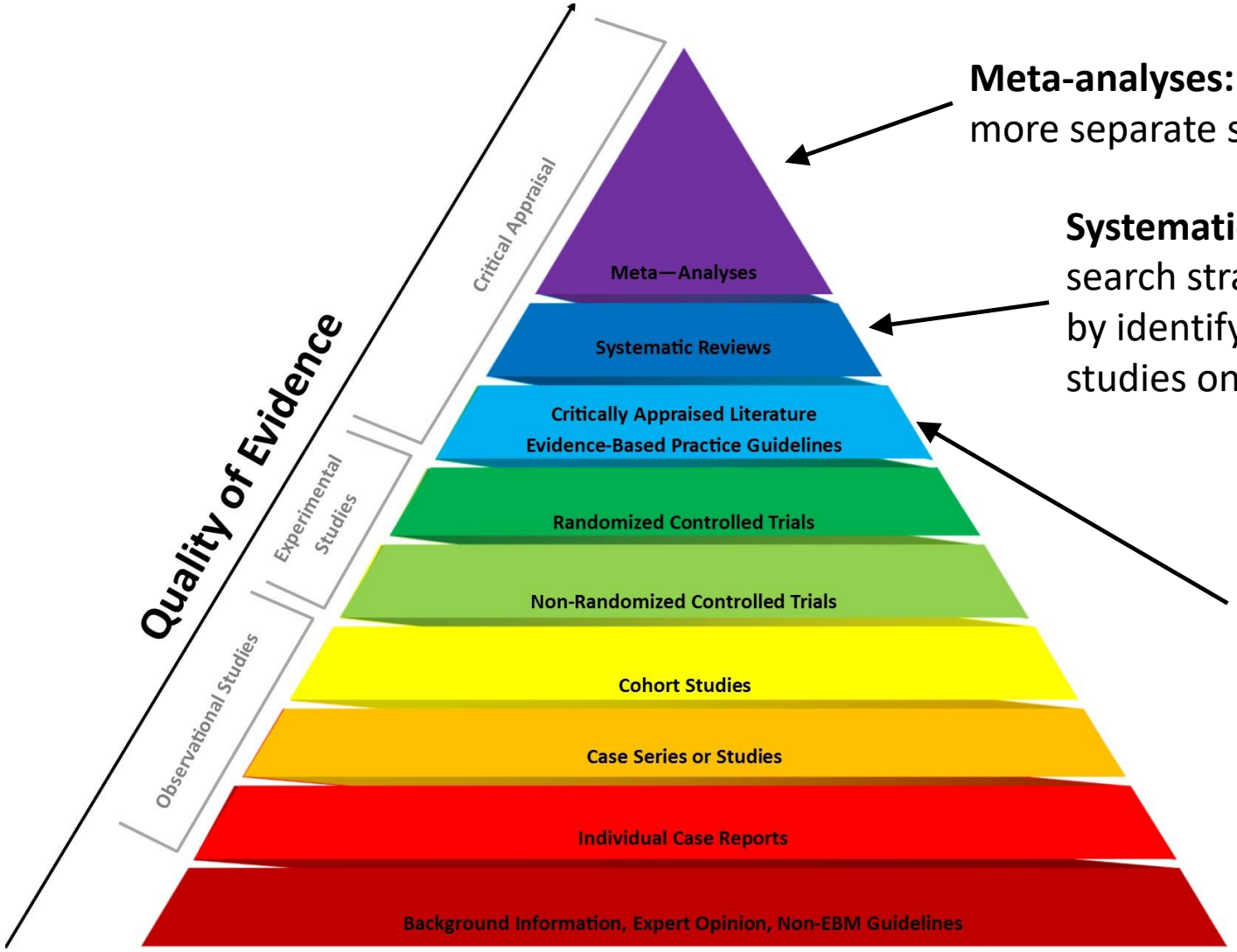
- Technological innovations within healthcare are held to a high standard
  - Clinical trial practices designed for pharmaceuticals
  - Most common are randomized controlled trials (RCTs)

- Such approaches are often unsuitable for technology-based interventions
  - Counterproductive to the goals of supporting people with disabilities and creating benefits for society.

Innovative healthcare technologies

What is evidence (of efficacy and effectiveness)?

Gold-standard sources of evidence



Meta-analyses: statistical combination of results from two or more separate studies

Systematic review: a detailed and comprehensive plan and search strategy derived a priori, with the goal of reducing bias by identifying, appraising, and synthesizing all relevant studies on a particular topic

Critically appraised literature: arms-length evaluation of existing studies
Evidence-based guidelines: systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances

Sources: Uman LS; 2011, Institute of Medicine; 1990

Randomized controlled trial (RCT)

- The current gold-standard approach for collecting and evaluating clinical evidence

- Key aspects of an RCT:
  - Randomization
  - Blinding
  - Control and intervention groups
  - Analysis of data
  - Reporting of results
    - E.g., Schulz et al. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMC Medicine 2010, 8:18

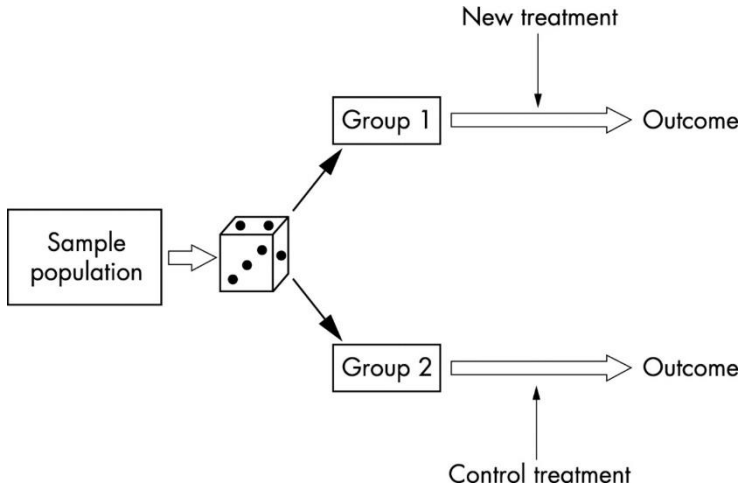
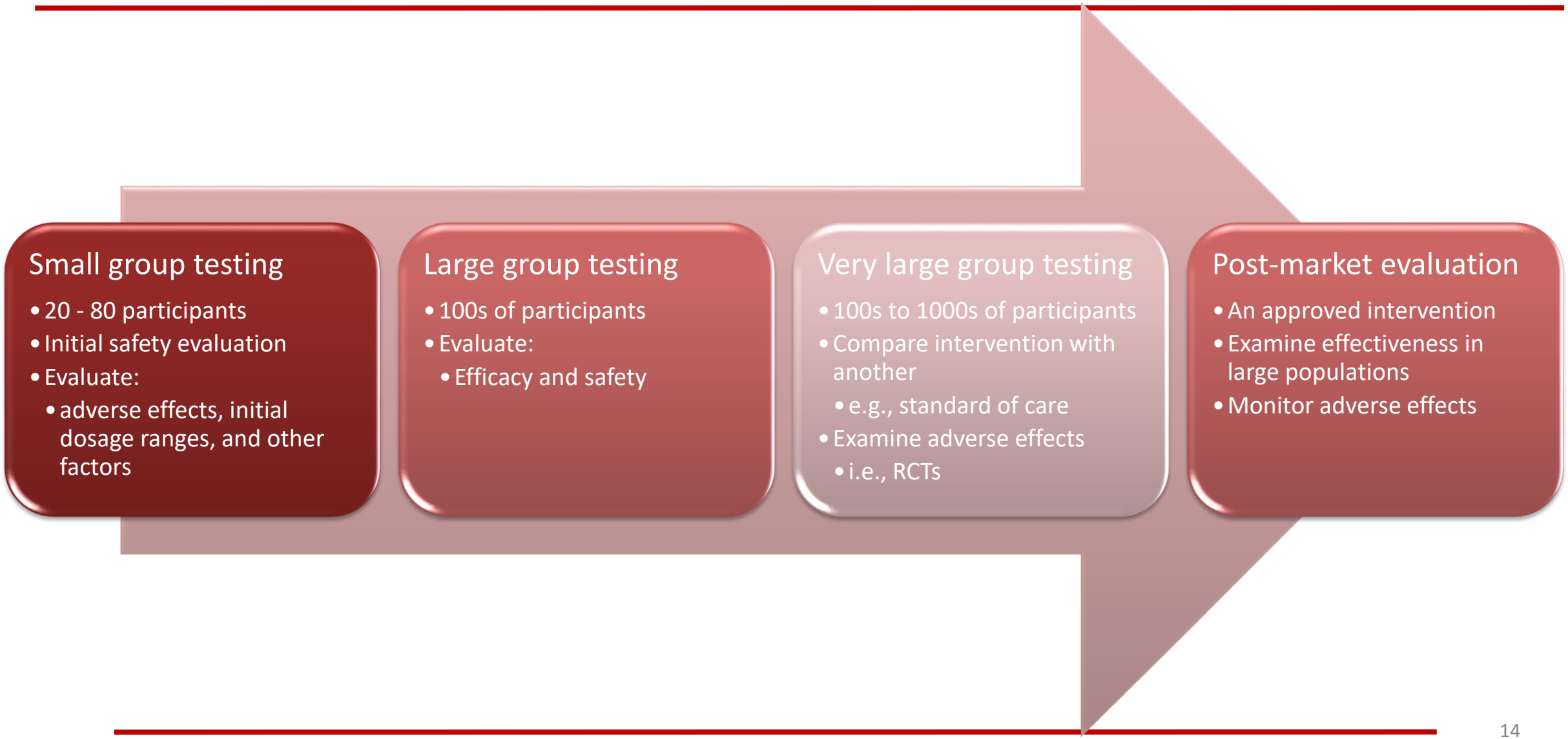


Image source: Kendall JM. Designing a research project: randomised controlled trials and their principles. Emergency Medicine Journal 2003;20:164-168.

Phases of clinical trials



Source: WHO. International clinical trials registry platform glossary. https://www.who.int/clinical-trials-registry-platform/about/glossary

RCT weaknesses and disadvantages

- Time
- Cost
- Ethics
  - Withholding treatment if intervention clearly benefits patients, particularly with “disruptive innovations”
- Conflict of interest
  - Due to the high cost and time, most RCTs are funded by various industries
    - E.g., pharmaceuticals

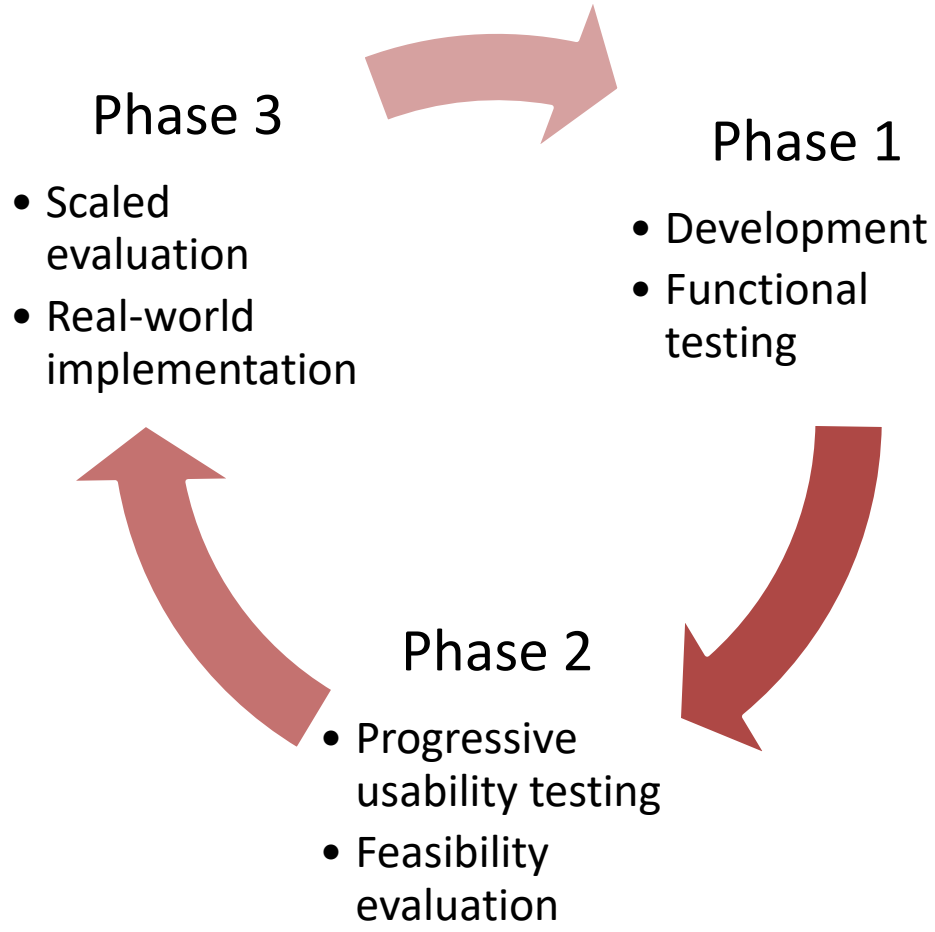
Why are RCTs challenging for innovations?

- Within the context of technological innovations:
  1. Some interventions have obvious and observable benefits;
  2. Findings have limited generalizability to real-world contexts;
  3. Overreliance on group means and overlooking valuable individual responses or characteristics influencing outcomes;
  4. Heterogeneous populations are a reality;
  5. Lifelong use and effect are not considered;
  6. Cost and funding challenges; and
  7. Necessity for efficiency and expediency to align with rapid technology advances.

What can we change?

- Call for process changes during innovative technology development and evaluation:
  - Rapid intervention prototyping, engagement, and iterative testing with users and other stakeholders
  - Early deployment and scaled and replicated evaluation of interventions in real-world environments;
  - Active inclusion of ***heterogeneous*** user groups
    - E.g., people with disabilities, caregivers, policy makers, clinicians, researchers, businesses, and any other stakeholders

Technology-oriented development phase model



Study designs for technological innovations

A phased approach

Phase 1: Development and initial testing

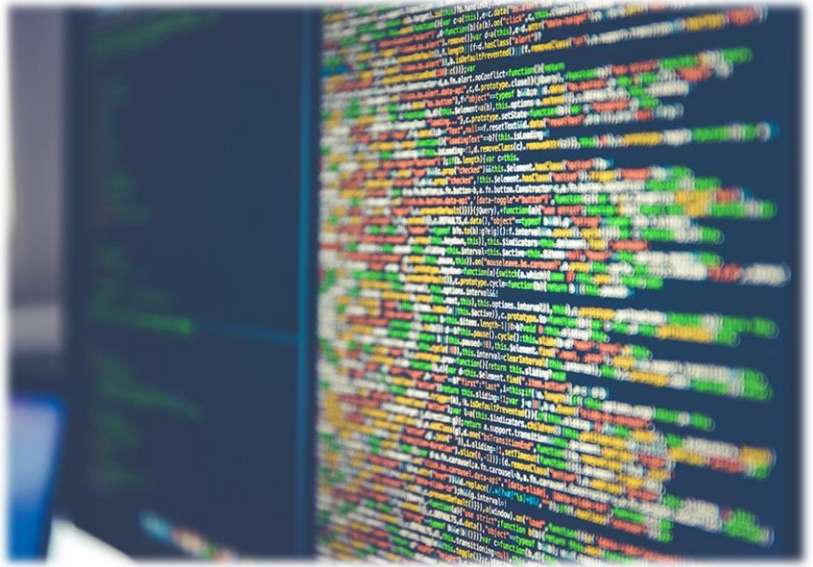
- Translation from idea to prototype
  - bridge technical and clinical processes
  - promote transdisciplinary working
  - create an integrated intervention
- Functional testing is key!
  - Possibly the largest derivation from standard clinical practice
  - Traditionally, this stage is more about device performance
    - Clinical outcomes, at least initially, are secondary outcomes
- Primary outcomes:
  - Developed and documented intervention and delivery process
  - User feedback to refine intervention, delivery and evaluation processes

Source: https://www.softwaretestinghelp.com/guide-to-functional-testing/

Study designs for Phase 1

- Technology experiments
  - Evaluating *innovation* against *technical* or *performance* requirements

- Identify functions the solution is expected to perform
  - Main components:
    - creation of input data based on the function's specifications
    - determination of output based on the function's specifications
    - execution of the test case
    - comparison of actual and expected outputs



Study designs for Phase 1 – continued

- Qualitative research:
  - Collecting and analyzing *non-numerical* data
  - Individuals' understanding of their social reality

- Quantitative research:
  - Descriptive studies
  - Correlational studies

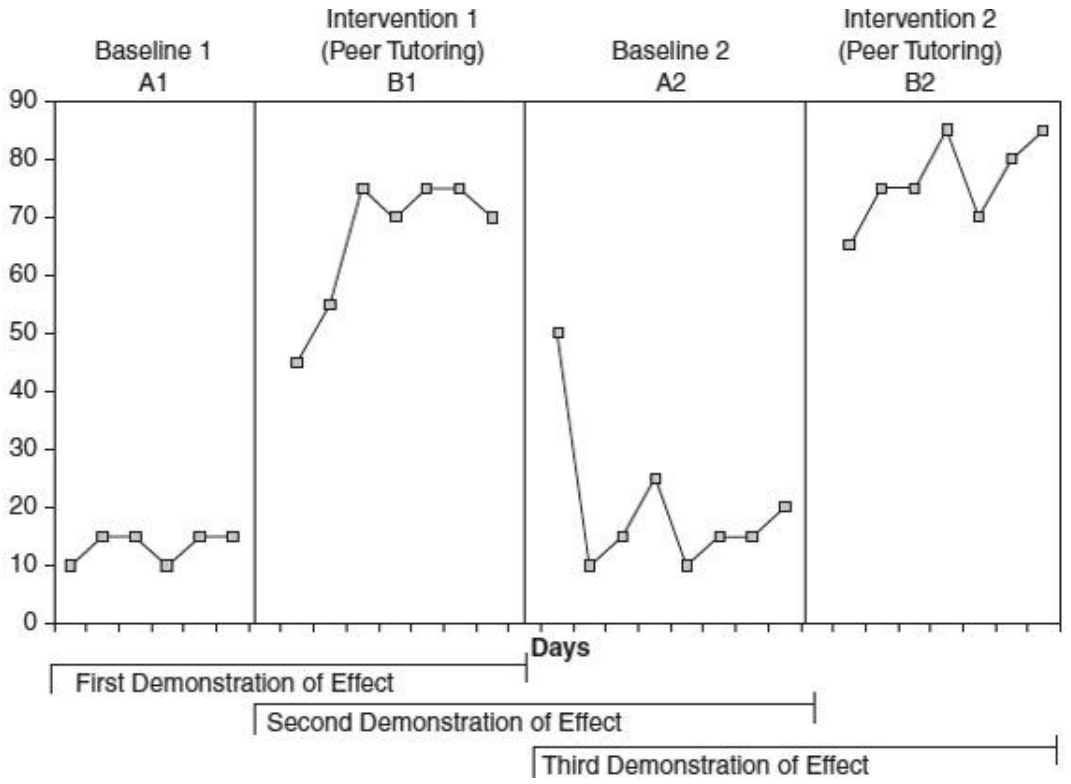
- Mixed-methods approaches
  - More than one method
  - Typically refers to combined qualitative and quantitative research

Study designs for Phase 1 – continued

- Single-subject research designs (SSRDs)
  - Serial observation of targeted behaviors within one user
    - before, during, and after application an intervention
  - Repeated measurement over a period of time
    - Differentiates SSRDs from case studies and many group designs
    - Facilitates the examination of client change in response to the intervention

Study designs for Phase 1 – continued

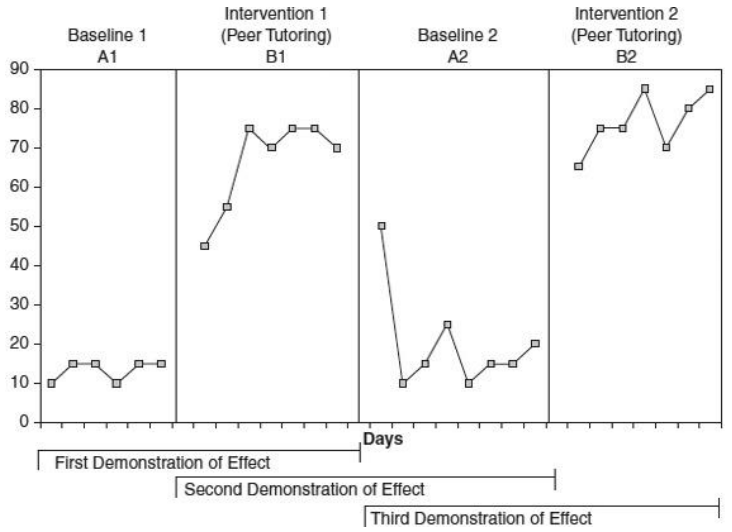
- SSRDs typically follow one of three structures:
  - Within-series design
    - Evaluation of data over time
      - E.g., intervention versus baseline
  - Between-series design
    - Comparison of two or more interventions
      - E.g., baseline vs. multiple interventions
  - Combined-series design
    - Both within- and between-series design



Coffee G. (2011) Single Subject Research Design. In: Goldstein S., Naglieri J.A. (eds) Encyclopedia of Child Behavior and Development

Study designs for Phase 1 – continued

- Data are traditionally been analyzed through visual inspection
  - This includes the assessment of level, trend, and variability.
- Certain nonparametric statistical tests may also be appropriate for SSRD data.
- For all SSRDs, internal validity is established by replication,
  - threats to internal validity can be reduced by:
    - repeated assessment,
    - continued assessment of client variability,
    - design flexibility, and
    - randomization.



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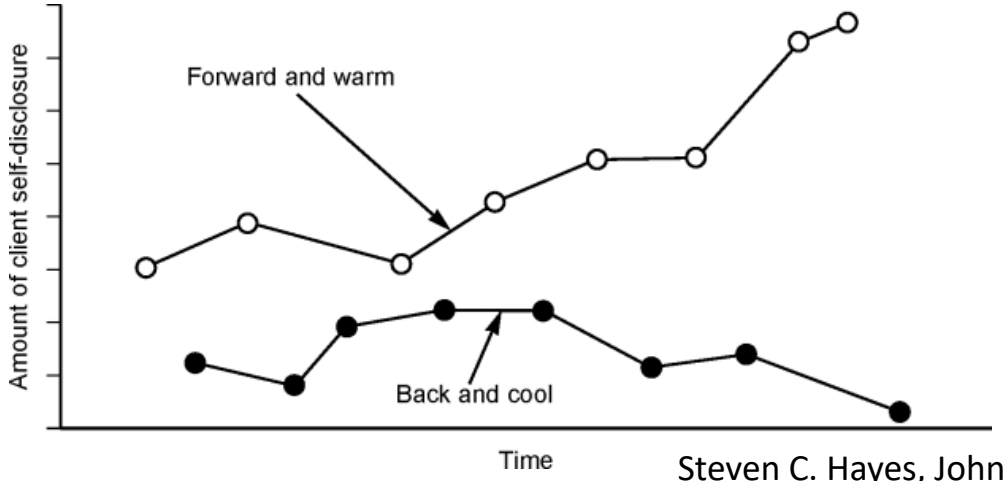
Phase 2: Usability and feasibility evaluation

- Progressively refined intervention prototypes are:
  - iteratively evaluated in small-scale studies with users
  - ideally in real-world contexts

- Primary outcomes:
  - Comprehensive understanding of users, intervention, delivery, and use contexts
  - Evidence supporting usability and feasibility
  - User feedback on how to improve intervention, delivery and processes

Phase 2: Single subject-research designs

- Randomized controlled N-of-1 trials
  - Consider the previous SSRD, with an ABAB design
    - A = baseline/no intervention; B = intervention phase
    - Can we randomize? For example, AABBAB?
- Alternating interventions designs
  - Rapid alternation (i.e., ABABABABAB), far fewer within-phase measures

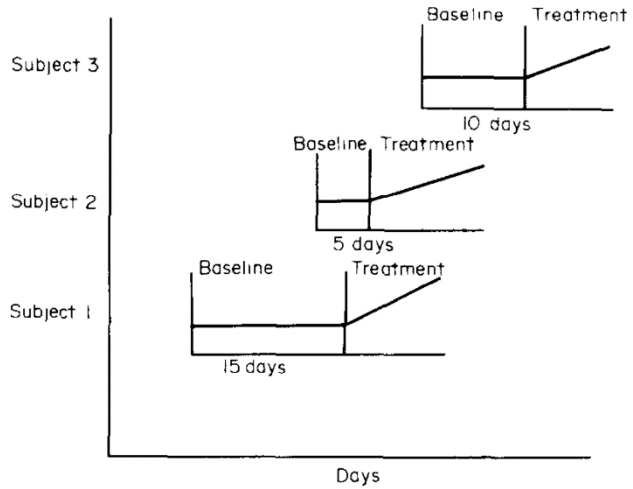


Steven C. Hayes, John T. Blackledge, in Comprehensive Clinical Psychology, 1998

Lillie, et al. (2011). The n-of-1 clinical trial: the ultimate strategy for individualizing medicine?. *Personalized medicine*, *8*(2), 161–173.

Phase 2: Single subject-research designs

- Multiple baseline design
  - Non-concurrent design
    - Apply treatment to several individuals at delayed intervals

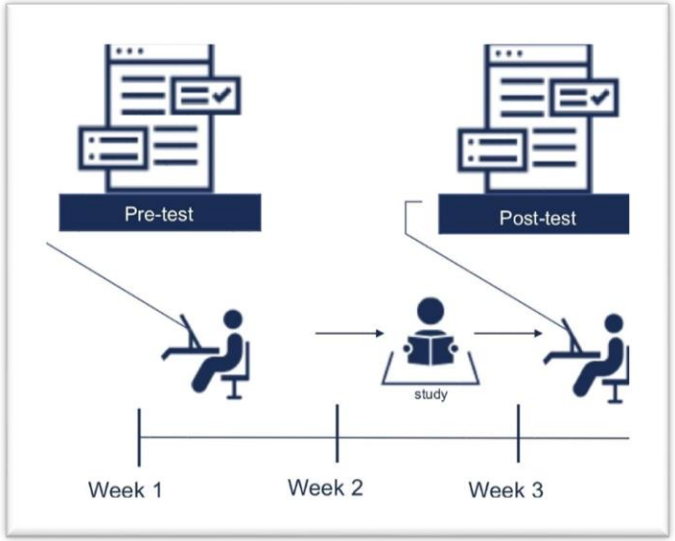


  - Concurrent design
    - All participants undergo treatment simultaneously

Watson et al, The non-concurrent multiple baseline across-individuals design: An extension of the traditional multiple baseline design, J. Behav Ther and Exp Psych, 12 (3), 1981

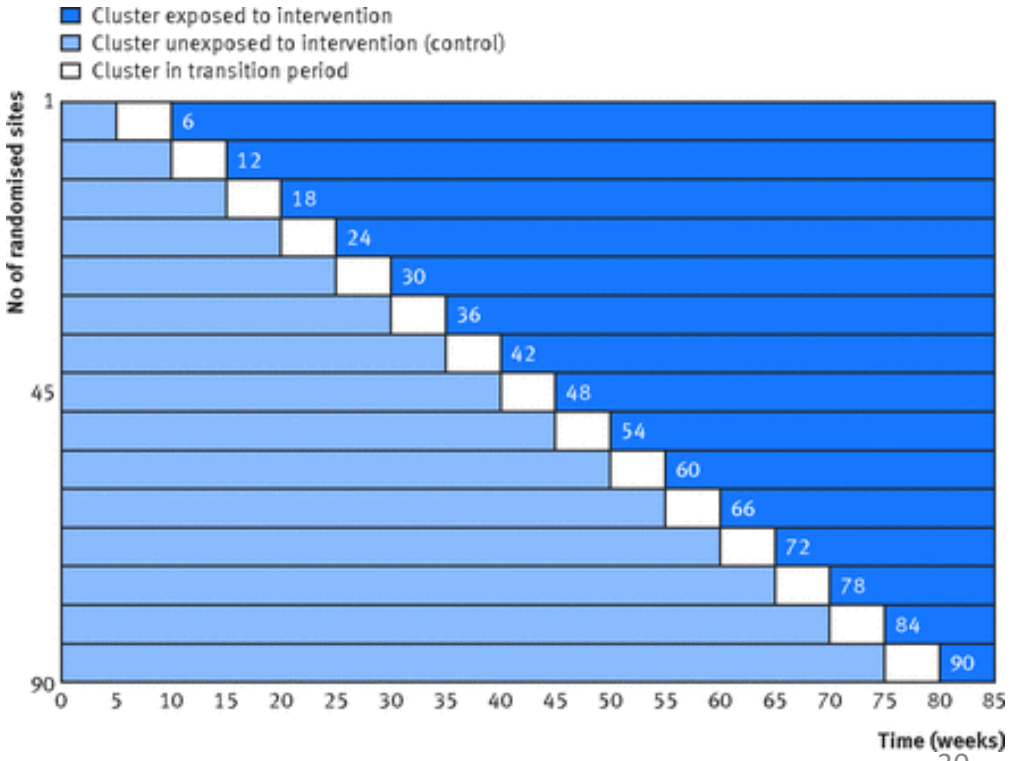
Phase 2: Group-based designs

- Interrupted time series design
  - A series of measurements over long periods of time
  - Time series is interrupted by an intervention
    - Series includes baseline, intervention, and follow-up phases.
  - Effect of intervention can be statistically understood by changes in data
- One-group pre- post-test
  - Participants serve as their own controls
    - i.e., no control group
  - Variable of interest is formally assessed:
    - before (pre-intervention) and
    - after (post-intervention)



Phase 2: Group-based designs

- Non-equivalent pretest-posttest control group designs.
  - Control and intervention group are naturally occurring
  - Size of groups is, as a result, not the same
- Stepped wedge trial designs
  - Sequentially provide intervention over time to all groups.
  - Germane when withholding an intervention is potentially unethical or when simultaneously providing the intervention to all participants is not possible.



Hemming K, Haines T P, Chilton P J, Girling A J, Lilford R J. The stepped wedge cluster randomised trial: rationale, design, analysis, and reporting BMJ 2015

Phase 3: Scaled evaluation and implementation

- The intervention is deployed and evaluated with users:
  - in real-world contexts
  - with clinicians who typically deliver the intervention
  - with caregivers (and other stakeholders) who support use

- Progressively scaled and replicated
  - E.g., with different user populations, clinician characteristics, care contexts, geographic locations, researchers not originally involved in intervention development

- Primary outcomes
  - Evidence for short- and long-term use, effectiveness, adoption/abandonment, functional, social, and economic outcomes
  - Cumulative evidence on impact of intervention
  - User feedback for iterative refinement

Study designs for Phase 3

- Tracker trials
  - Useful when developments or variants frequently occur
  - Provide “early warnings” of issues with trials or innovations
  - Do not require stability
    - Rather, allow comparison at each stage of change

- Benefits:
  - Track changes in interventions over time *without* having to wait for the intervention to be fully developed
  - allow comparison of the new intervention to the standard of care
  - flexible protocols with no predetermined sample size or duration and interim analyses

Lilford, et al. (2000). Trials and fast changing technologies: the case for tracker studies. BMJ (Clinical research ed.), 320(7226), 43–46.

Study designs for Phase 3

- Pragmatic trials
  - examine intervention effectiveness under real-world, usual conditions.
    - explanatory trials aim to test whether an intervention works under optimal situations
  - produce results that can be generalized and applied in routine practice settings
    - most results from exploratory trials fail to be broadly generalizable
  - In practice, most trials have both pragmatic and explanatory aspects

Patsopoulos N. A. (2011). A pragmatic view on pragmatic trials. Dialogues in clinical neuroscience, 13(2), 217–224.

Pragmatic versus explanatory trials – summary

Explanatory	Pragmatic
Strict eligibility criteria	No inclusion or exclusion criteria
Strict experimental intervention	No practitioner guidelines on the experimental intervention
Highly experienced experimental practitioner	Intervention is applied by all practitioners, thus covering the full spectrum of clinical settings
Flexibility of the comparison intervention	Best alternative treatments are used for comparison with no restrictions
Highly experienced comparison practitioner	Comparative treatment is applied by all practitioners, covering the full spectrum of clinical settings
Rigid follow-up	No formal follow-up sections
Specific clinical outcomes	Clinical meaningful outcome that does not require extensive training to assess
Strict participant compliance	No required compliance
Strict practitioner adherence	No required practitioner's compliance
Analyze primary outcomes	Analyze all participant data

Patsopoulos N. A. (2011). A pragmatic view on pragmatic trials. Dialogues in clinical neuroscience, 13(2), 217–224.

Discussion and conclusion

- Any clinical intervention will necessarily require evidence!
- RCTs are currently the gold-standard
  - not *necessarily* the most appropriate or effective method of generating clinical evidence
- Technological healthcare innovations will never "disrupt" if RCTs are required
  - Many "new" study designs are emerging as appropriate methods of generating ***high quality*** evidence!

Thank you!

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