How To Generate **Clinical Evidence** For **Digital Health Technologies (Part 1)**

Expert Insights from:

Prova Health

Roche

nature

“

Traditional research approaches are misaligned with the “**fail fast, fail often**” mantra espoused by technology start-ups.

This guide has been produced based on **two** important resources:

npj | Digital Medicine

www.nature.com/npjdigitalmed

PERSPECTIVE OPEN

Check for updates

Challenges for the evaluation of digital health solutions—A call for innovative evidence generation approaches

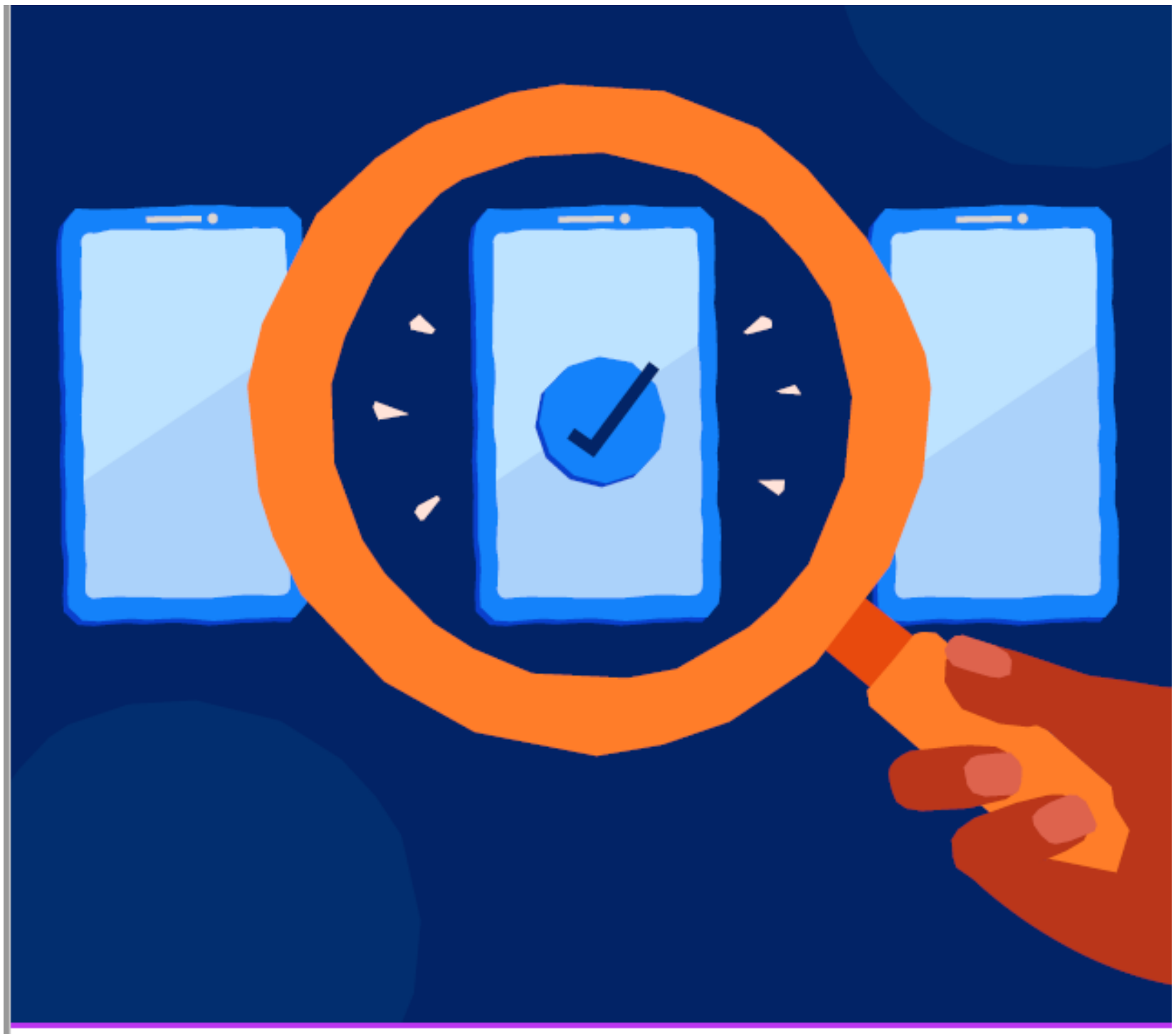
Chaohui Guo[1], Hutan Ashrafian[2], Saira Ghafur[2], Gianluca Fontana[2], Clarissa Gardner[2] and Matthew Prime[1]✉

The field of digital health, and its meaning, has evolved rapidly over the last 20 years. For this article we followed the most recent definition provided by FDA in 2020. Emerging solutions offers tremendous potential to positively transform the healthcare sector. Despite the growing number of applications, however, the evolution of methodologies to perform timely, cost-effective and robust evaluations have not kept pace. It remains an industry-wide challenge to provide credible evidence, therefore, hindering wider adoption. Conventional methodologies, such as clinical trials, have seldom been applied and more pragmatic approaches are needed. In response, several academic centers such as researchers from the Institute of Global Health Innovation at Imperial College London have initiated a digital health clinical simulation test bed to explore new approaches for evidence gathering relevant to solution type and maturity. The aim of this article is to: (1) Review current research approaches and discuss their limitations; (2) Discuss challenges faced by different stakeholders in undertaking evaluations; and (3) Call for new approaches to facilitate the safe and responsible growth of the digital health sector.

npj Digital Medicine (2020)3:110 ; https://doi.org/10.1038/s41746-020-00314-2

Resource 1:

This paper written by Guo et al published in the Nature Digital Medicine journal.



Generating evidence
for digital health solutions

Roche Information Solutions in collaboration with Prova Health

Resource 2:

The white paper written by Roche Information Solutions in collaboration with Prova Health.

WHAT IS EVIDENCE GENERATION?

Evidence generation is an umbrella term covering the entire range of activities that innovators may pursue in relation to the **development and validation** of digital health solutions.

There are three broad fields of activity.

Technical:

To validate a concept in the early stage.

Clinical:

To prove safety and treatment efficacy

Economic:

To show a positive economic impact

What Evidence is Required?

Evidence of safety & efficacy[1]

Clinical association

Demonstrate the digital health solution will solve a real problem.

Analytical performance

Verify the digital health solution performs its calculations accurately and reliably.

Clinical performance

Show the solution provides clinically relevant data when tested with its target population and in its target environment.

Who needs the evidence?

Regulators

Evidence of value

Clinical value

Show peer-reviewed evidence that your solution has a measurable impact on clinical outcomes.

Financial value

Conduct a HEOR[2] study (if your solution has a direct impact on patient care) or show enterprise benefit via a financial model.

Operational value

Demonstrate that your solution provides operational efficiencies, e.g., through improvements to clinical workflow.

Experience value

Conduct qualitative research to establish usability and acceptability.

Who needs the evidence?

Chief Medical Officer
Clinicians

Chief Financial Officer

Chief Information Officer

End users
(patients & clinicians)

Why is Evidence important in Digital Health?

Patient Safety

Foremost amongst all reason, evidence is needed to ensure the digital technology works as it should and **does not expose patients** to undue harm or risk.

Measuring Impact

Demonstrating and quantifying objectively the **positive clinical benefit** obtainable from using the digital health technology.

Regulatory requirements

Evidence generated from clinical studies serves as essential information required for the **necessary regulatory approval** (i.e. MHRA, FDA).

Facilitate Procurement

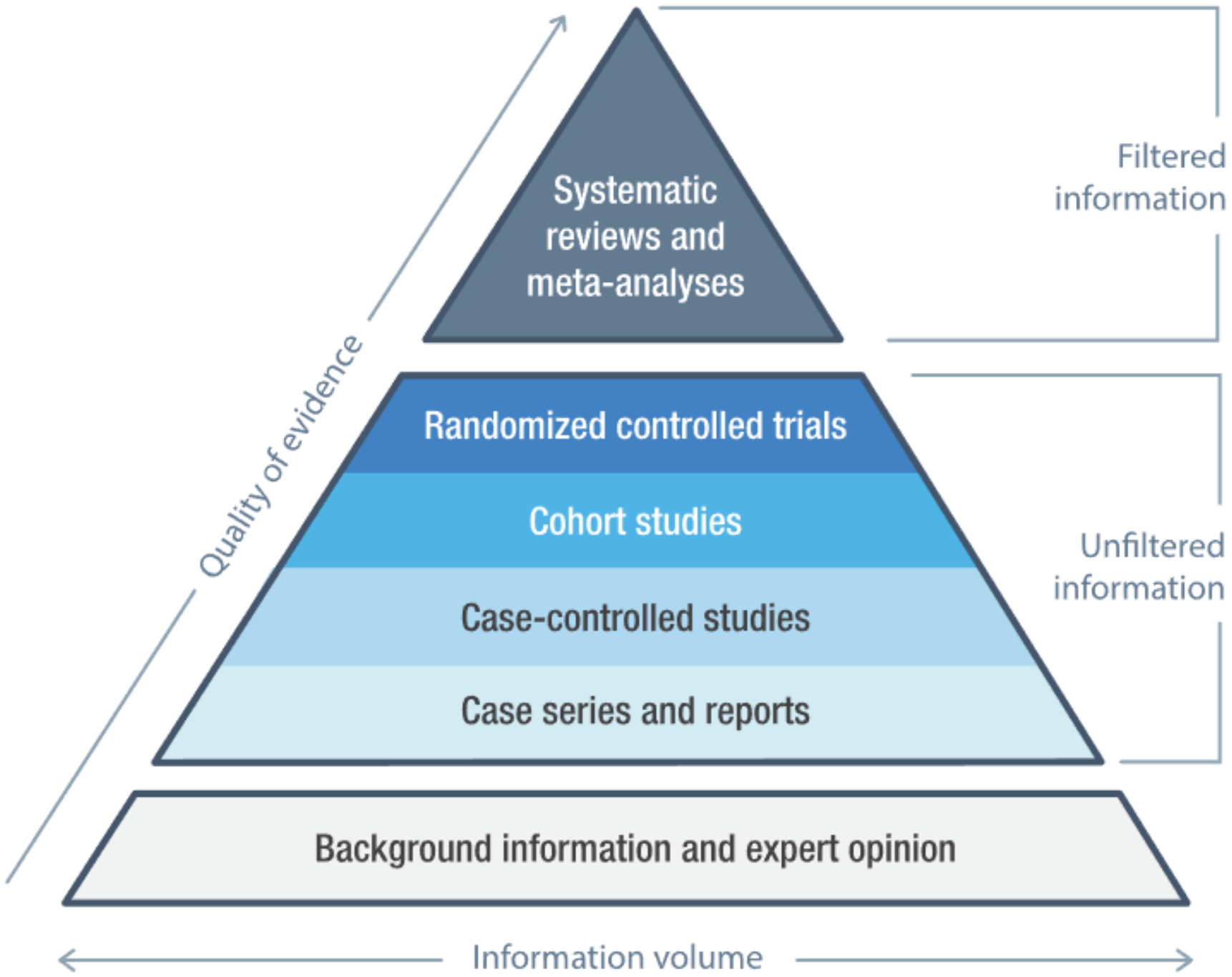
Economic Evaluation and Cost Benefit Analysis generated from these studies serve to provider payors with crucial information whether a solution is **financially viable**.

Having said all that,

There are **significant challenges to evidence generation** for digital health technologies.

Let's explore this.

Let us first talk about the **various grades** of **clinical evidence**.



Traditionally, clinicians are taught to appraise evidence **based on the study design** and the **quality of the individual study**.

Challenge #1
Study Design

Traditional methods to develop more robust evidence are incongruent with the **agile approach** taken in software development.

For example, the mismatch between the length of **Randomised Control Trials** (RCT) and the typical development and update cycle of software.

To illustrate, RCTs takes an average duration of **5.5 years** from enrolment to publication. This presents **a clear risk for app/AI obsolescence** occurring before study completion.

Challenge #2
Limited Resources

Small Medium Enterprises (SME) typically prioritize and allocate their research and development budget to **product development**.

Well designed and executed studies require **skilled researchers**, often via **collaboration with academia**, adding further complexity.

It has been estimated that the timescale for producing a research proposal and receiving ethical approval for a pilot or trial study can take **as long as 6 months to 3 years**.

This just means **burning the financial runway** of a HealthTech company that they simply do not have for a function they do not often understand.

Challenge #3
Unclear Reimbursement

Evidence generation **can be very expensive**.

Considering that in most markets reimbursement pathways **that reward good evidence** do not exist, there is often too little incentive for manufacturers to make this investment.

This is unlike for **pharmaceutical companies** where there are clear reimbursement pathways for medicine with strong evidence base.

Reimbursement pathways should be established for digital health solutions, with clearly defined evidentiary requirements.

Challenge #4
Digital Health Literacy

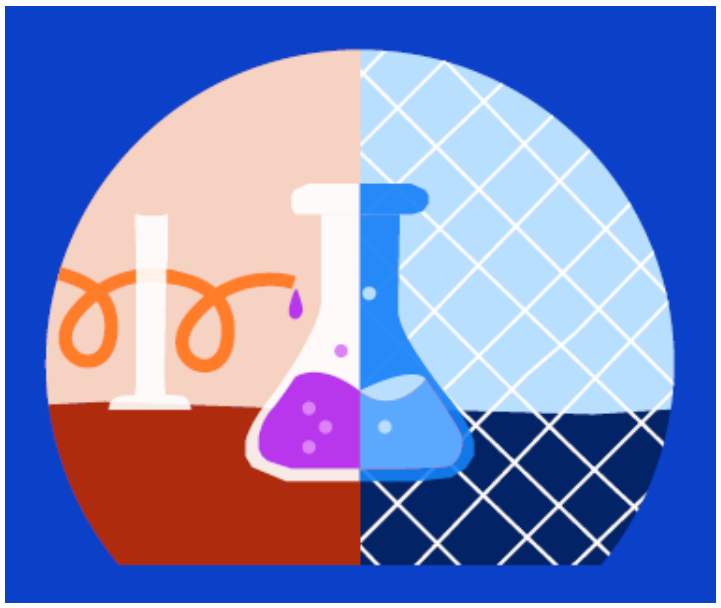
Poor digital health literacy among both **patients** and **healthcare professionals** is a significant hurdle to improved evidence generation and the wider adoption of digital health solutions.

Therefore, Innovators face significant challenges to overcome this paradox in digital health:

> **“No evidence, No implementation. No implementation, No evidence.”**

To address these challenges, there have been **3 new study designs** that have been proposed.

While **relatively new**, each of them may be suitable if conducted under the **right environment** for the **right indication**.



Clinical Simulation

Simulation methods are emerging as **promising evaluation tools** for digital health solutions.

High-fidelity, synthetic patient cases may be used to replicate real-world healthcare settings.

Synthetic patient data can also be generated from Real World Data (RWD) using models designed to **minimize privacy issues**.

Simulation also allows **inclusion of high-risk patient profiles** and direct observation of scenarios that may be impossible in the real world.

Example:

Researchers from the **Institute of Global Health Innovation** (IGHI) evaluated the impact of a digital solution on the conduction of **cancer multidisciplinary team (MDT) meetings.**

56 healthcare professionals who were regular participants at lung cancer tumour boards, were recruited to take 10 simulated MDT sessions.

High-fidelity (Very realistic) mock patient cases were developed by the study team and clinical experts.

Participants discussed up to 10 patient cases, using a standard UK approach to conduct MDTs (paper handout and PACS system) in the control condition, compared with the **NAVIFY Tumour Board solution**.

Pros:

- **Good balance** between the **strength of evidence** (e.g., “near-live" clinical scenarios) whilst remaining **cost-effective and timely** for fast version updates.
- **Scalability** and **flexibility** in design of studies (e.g. different scenarios, various types of participants).
- **Feasibility in being implemented** as remote and/or distributed.

Cons:

- **High fidelity** is a prerequisite for generating valid and effective evidence.
- Clinical simulation results itself alone probably are **not adequate for approval application** from Health authorities, particularly for higher-risk group of digital solutions that would need to be approved as SaMD.

Real World Data

REAL-WORLD DATA (RWD)

“**data** relating to patient health status and/or the delivery of health care routinely collected from a variety of sources."

REAL-WORLD EVIDENCE (RWE)

“the **clinical evidence** about the usage and potential benefits or risks of a medical product derived from analysis of RWD."

The **digitization of healthcare** has produced the ability to **generate vast amounts of RWD** during routine clinical practice, through out the patient's everyday life.

These data may be analysed to gain meaningful insights forming RWE.

Advancements in AI and ML are increasing our capacity to analyse RWD and may yield insights not previously within our reach.

In digital health, **RWE is often more useful than evidence derived from RCTs**, giving a more accurate understanding of the effectiveness of a solution in a clinical setting.

Limitations

Whilst studies using RWE are useful to demonstrate the overall effectiveness of a solution, they are **not useful for identifying the impact** that specific features or variables have on this effectiveness.

Determining this would be better served by an RCT.

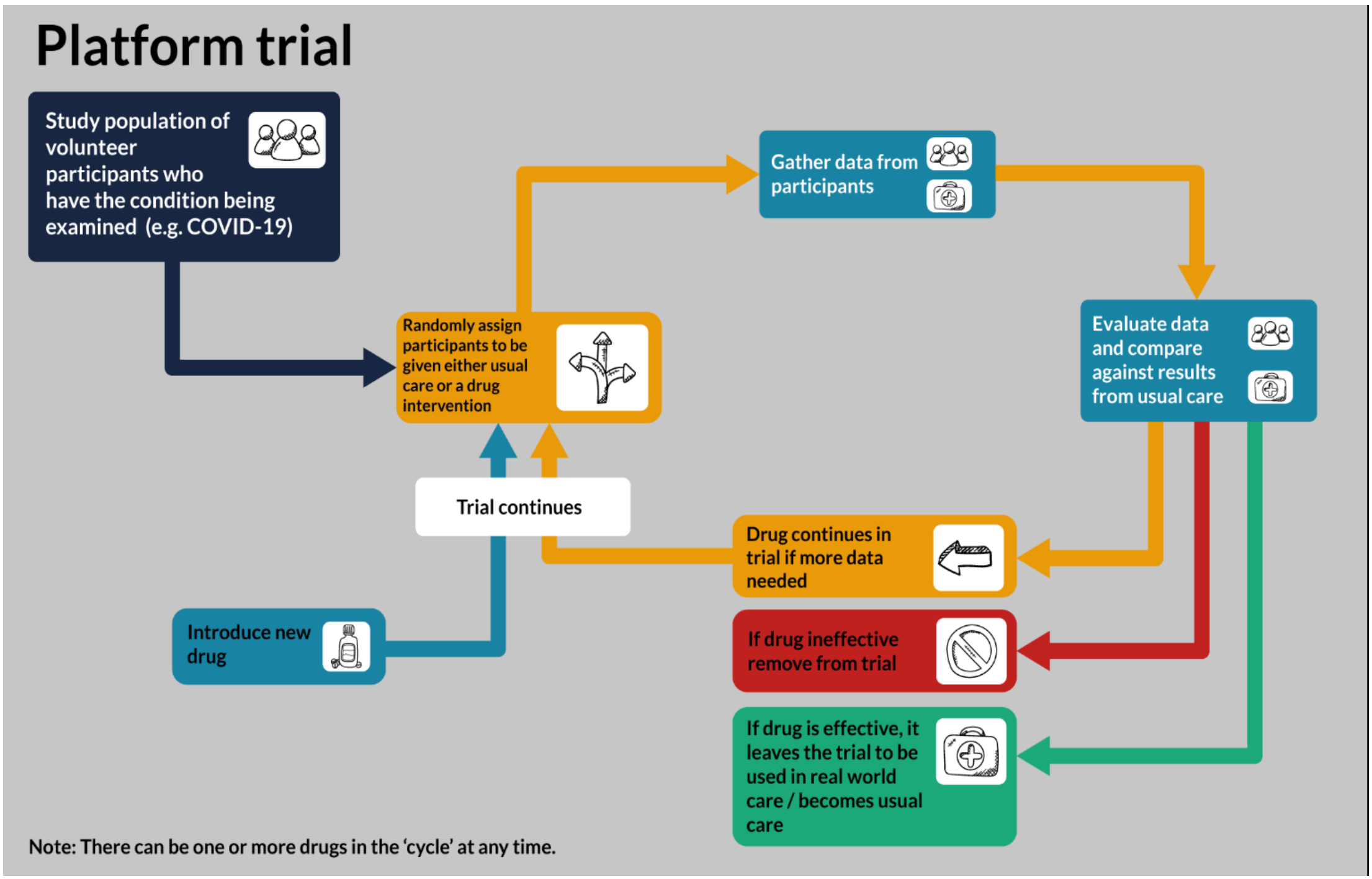
Generating RWE also **relies heavily on the availability of data**, which is often not sufficient. Currently there are no widely established standards for study design and best practice for studies using RWE, **limiting wider confidence** in these methods.

Platform Trials

Platform trials (PTs) are a **novel study type** which may be useful for the evaluation of quickly-evolving digital health solutions, as these trials are designed to be **adaptive**, allowing for interventions to be **modified**, or changed completely, **over time**.

The key features of platform trials are their scope and adaptability. They are designed to evaluate multiple therapies simultaneously.

“Rather than test drugs one at a time, you test them all at the same time.”



PTs are an **adaptive type of RCTs**, which may be described as **"multi-arm"** or **"disease focused"** (rather than "intervention-focused") as they allow for the efficient study of various interventions or versions, **against a constant control**, to determine the best intervention for a disease.

Image reference: https://www.phctrials.ox.ac.uk/platform-trials-an-explainer

Platform Trials can be used to **trial MULTIPLE digital health technologies** that serve to treat ONE particular condition such as depression or anxiety.

As such, they can continue indefinitely, **adding new arms to test new therapies**, discontinuing existing ones as soon as it becomes clear the drug is ineffective or harmful, and substituting the control arm for a new standard-of-care, if the evidence favours such a move.

Key limitations include the **complexity** of setting up platform trials, requirement of **academic** partners and collaboration between **multiple industry providers**.

Hope you all found this helpful!

This is part of a series to help HealthTech founders access better resources for their projects.

Just our small way of trying to help!