

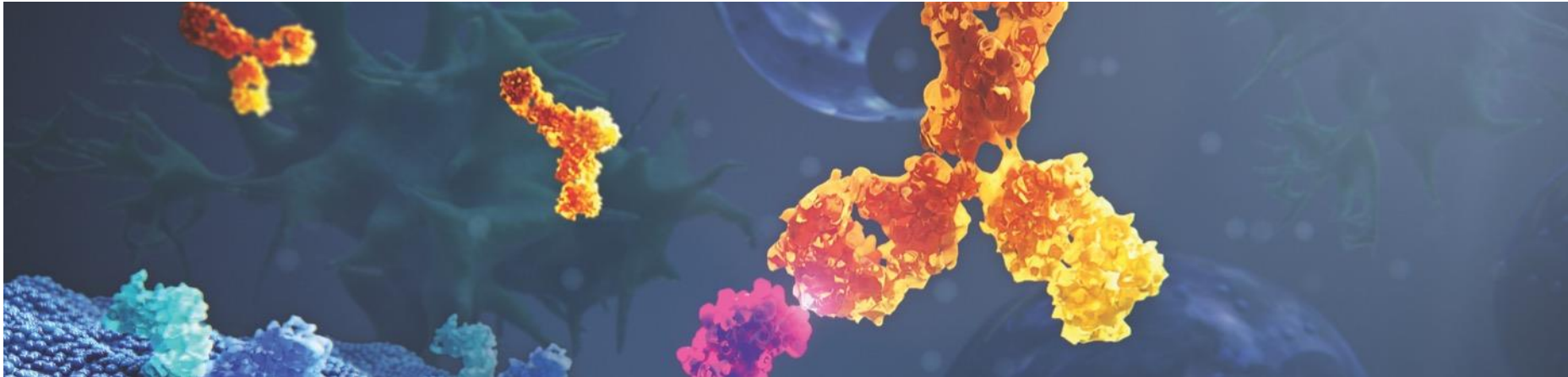
# Pragmatic Clinical Trials: Real World Evidence's Hidden Gem....

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# Outline

- Why the importance?
- What is PCTs
- How to reveal the gem
  - Use case: Registry based RCT – the DAPA MI study
  - Use case: Federated EHR platforms
- Outlook



# Why?

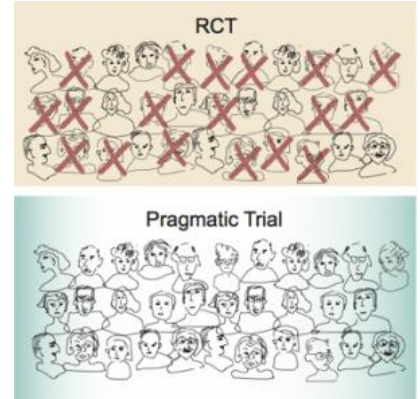
There is a **growing interest** in the collection of patient data beyond the traditional realm of randomised clinical trials (RCT)

The reasons for this are reasonably axiomatic. The costs for conducting RCTs have **steadily ballooned in recent years**, prompting pharma to turn to routinely-collected data as a means of creating more efficiency in their research

But while pharma companies continue to pump vast resources in the direction of RWE implementation, the field of pragmatic trials **remains comparatively disregarded**



Investigational sites estimate that over **70%** of data are duplicated between EHR and clinical trial systems<sup>2</sup>



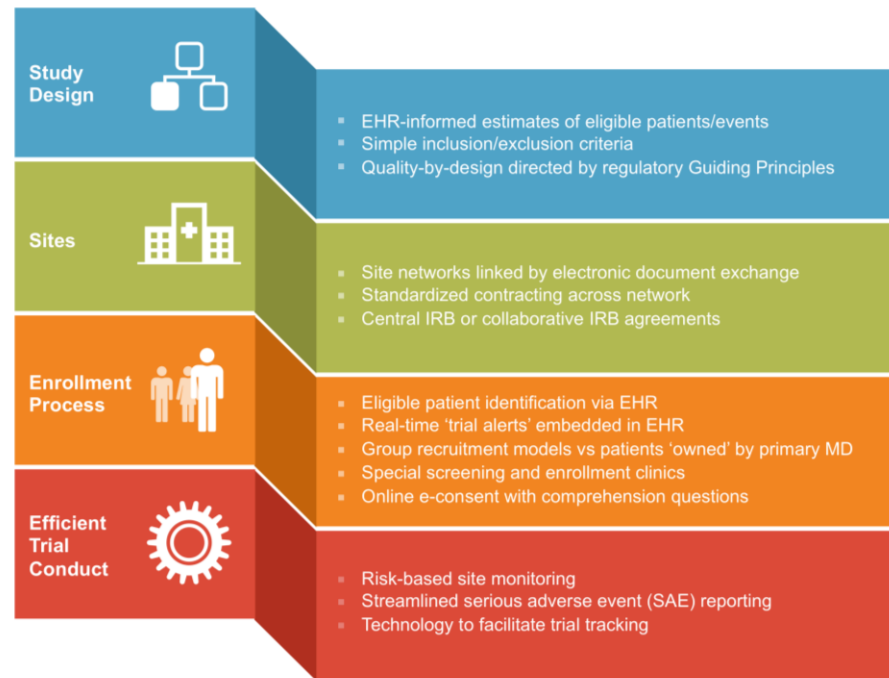
# What is PCTs?

Pragmatic clinical trials (PCT) are research investigations **embedded in health care settings** designed to increase the efficiency of research and its relevance to clinical practice.

**Costs can be reduced** by building RCTs upon existing registries and electronic health records (EHR), an approach that is **increasingly supported by health authorities**

**Aligning the protocol with medical practice** and using electronic data already recorded by sites likely creates higher willingness for recruitment and participation, should all other elements remain constant (e.g. investigator fees)

**Recruitment and follow-up can be simplified** by automatic provision of cohorts of patients who have already given consent for inclusion in disease registries



# The RCT-PCT continuum

- PCTs are not an abandonment of the scientific methods that have led to countless breakthroughs
- They don't take away from basic science or diminish the importance of traditional RCTs—we just need a balance.
- No clinical trial is completely explanatory or pragmatic. RCTs and PCTs exist on a continuum.



# Pragmatic Clinical Trials up until now

- **“Treatment strategy trials”**

- E.g. TASTE- for thrombus aspiration (UCR), DETOX2-AMI-supplemental oxygen (UCR)

- **Studies within approved indication**

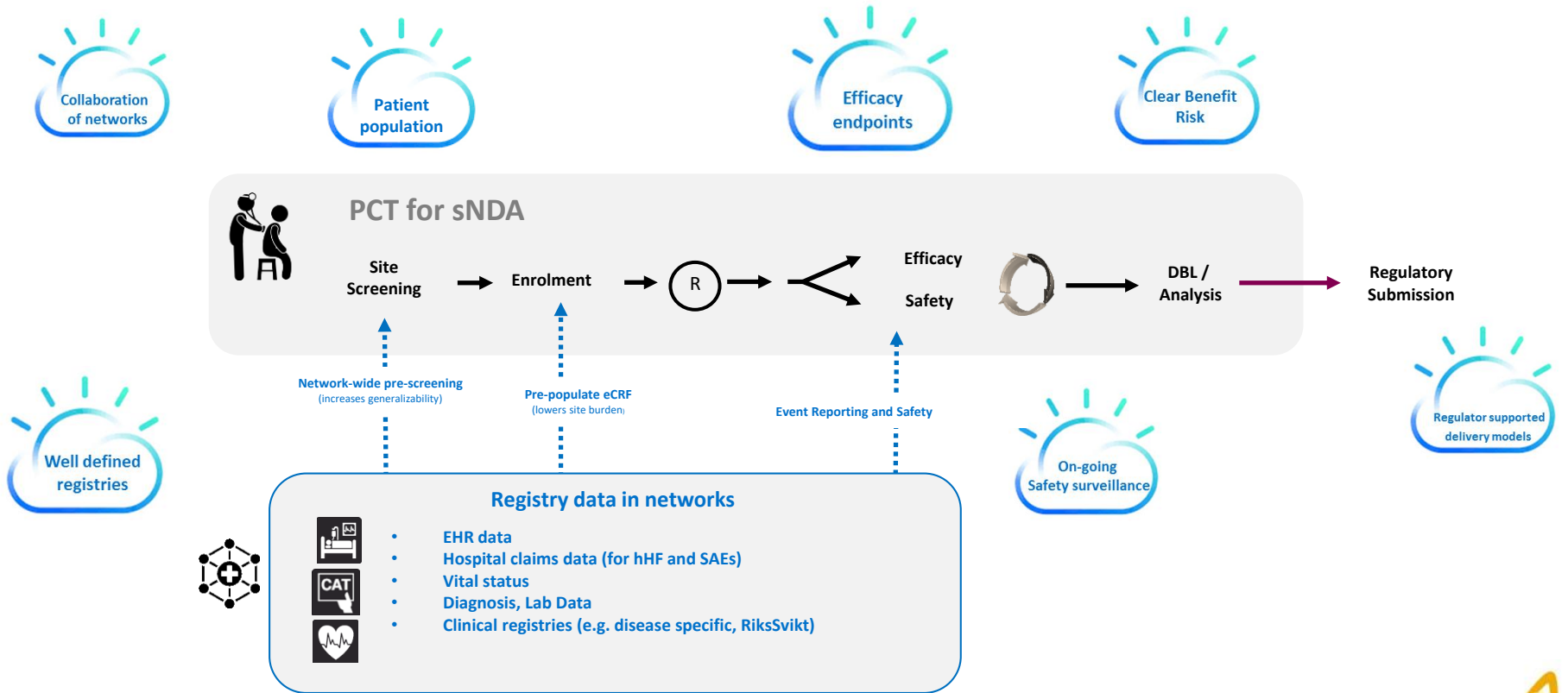
- E.g. VALIDATE-SWEDEHEART for bivalirudin (UCR), INVESTED-influenza vaccine (Harvard), ADAPTABLE-aspirin (DCRI)

- **Indication or label-changing trials** are next step

- Represent a novel ground presents new challenges
- Opportunity to use a more pragmatic design to reduce costs, improve generalisability and pace, while still having sufficient quality and acceptability to get label enhancement



# Requirements to conduct a Pragmatic Clinical Studies through registries to achieve a label change



# PCTs - How to reveal the gem





Use case: R-RCT DAPA-MI study

D169DC00001

DAPAMI

# “Pre-requisites” of a R-RCT for Registration Purposes

A green stamp with the word "APPROVED" in white, bold, capital letters, set against a background of faint, overlapping text and lines.

**APPROVED**

Seek a new indication for an approved drug

A white sign with the words "Safety first" in black, bold, lowercase letters, pinned to a dark background with a red pushpin.

**Safety first**

The approved drug has well-established safety profile and requires minimal additional safety monitoring outside of SoC

A document with the word "Guidelines" in a large, bold, black font, with a pen and a pencil resting on it.

**Guidelines**

The indication has established widely accepted diagnosis guideline



The primary endpoint is a hard endpoint



High-quality registries available



A flexible in-house data collection system compatible with registry

- **The DAPA-MI trial** is a pioneering Registry-based Randomized Controlled Trial (R-RCT) exploring the benefit of Farxiga (dapagliflozin) in patients without type-2 diabetes (T2D) following a recent, acute myocardial infarction (MI)
- DAPA-MI is a **first-of-its-kind, indication seeking R-RCT** that provides quicker access to data, reduces trial recruitment time and costs, and minimises patient and investigator burden.
  - R-RCTs are more efficient clinical trials – allowing for **immediate access to data**, lower per patient cost and streamlined delivery – enabled by **fewer trial visits and patient-centric digital solutions**
  - DAPA-MI combines “gold standard” RCT elements with innovative, real-world trial elements, and its unique trial design **could ultimately lead to a higher recruitment rate and lower overall costs** in comparison to conventional clinical trials

# DAPA-MI: An R-RCT for Registration Purposes

Evaluating dapagliflozin for prevention of heart failure and CV death following an acute myocardial infarction

6400 patients in only 2 countries

R

Dapagliflozin 10 mg once daily on top of SoC

Placebo once daily on top of SoC

Accelerating and expanding patient recruitment



SWEDEHEART



Use of quality registers from clinical routine through scientific leadership with UCR

Reduced patient and investigator burden



Streamlined trial design with automated data transfer from routine clinical practice

Remote patient monitoring



Patient app for information sharing and signalling of events

Advancing Drug Adherence



Use of SmartCap adherence monitoring technology

Innovative approaches enhance patient experience and drive 50% per patient cost reduction without impacting timelines

The DAPA-MI study will promote patient health and quality of life after myocardial infarction through patient engagement



Active trial participant investigating a potentially life-saving medicine

Experiencing a role as co-investigator, supported by digital solutions

Prolonged follow-up by specialists in cardiology

Facilitated route of contact with health care professionals throughout study

Enhanced life-style change support that may improve prognosis and quality of life



# Use case: Federated EHR research platforms



# Setting the scene

Capabilities of new health data-collection/re-use technologies including EHRs will have a huge impact to support clinical research and trial execution over the next years

The foundation of this **federated EHR platform technology** is there, processes are in place and regulators are supportive. The technology is disruptive to the current Business Models by collaborating directly with HCOs



# What can the federated EHR technology do?

Global Hospital networks  
(US, Europe & beyond)

Sponsor interface

On-line Federated EHR central platform service provider

Provides a **new gateway to PCTs**. Capture data directly at source. Managed and controlled at site. Secure data transfer to through ICF at site, or pseudo anonymised mechanisms **at site** via central platform transfer. E.g. reducing SDV and site burden

Individual & clusters of hospitals

@site level

PROTOCOL FEASIBILITY

PATIENT RECRUITMENT

DATA CAPTURE AND EXCHANGE

New emerging services of data collection

**S1:** Enabling **protocol testing with real world data** in potential trial sites rather than with guestimates.

**S2:** Speeding up recruitment by making EHR data **searchable for investigators** and establishing a **unified communication path** between sponsors and sites.

**S3:** Facilitating **EHR data extraction** for applications used during trial execution (e.g. prefilling of CRFs and of SAE reporting).

**S4:** **emerging services:** allowing remote data analytics on large hospital sites. facilitate bi-lateral cooperation between pharma & hospitals to enable direct data access.

Services in place – were EHR data stays in site

Services in development – data transfer in a controlled environment



Local APP extension

sensors

AI/ML Free text integration

Genomics integration



# Additional value propositions: federated EHR platforms

## Protocol optimization/feasibility service

show that under optimal conditions this technology can significantly reduce current **+61 days feasibility** (industry standard turn around time per protocol) to less than 2-3 days (including multiple iterations of I/E criteria) using less resources

## Reducing amendments & time!

By assuming industry standard of 2.3 amendments per study, in which **1/3 relate to protocol description** or patient eligibility criteria, show cost saving 150 KUSD, BUT also to save time (median time is 65 days/amendment) multiplied by 2.3 amendments equals **four to five months of lost time**)

## Enhanced trial execution at site

Automatic transfer of EHR data to eCRF at site. Downstream, this technology provide a new vehicle for conducting pragmatic clinical trials e.g. EHR2EDC capability

## Gains for hospitals

overall faster clinical setup and initiation, speed up recruitment, reduced site burden, enhance quality, consolidated access to own EHR sources, and new research opportunities

Save feasibility time by

**2 months**

Feasibility turnaround in

**<2 days**

Reduction of amendment per study

**150 KUSD**

Reduction of Source Data Verification (SDV)

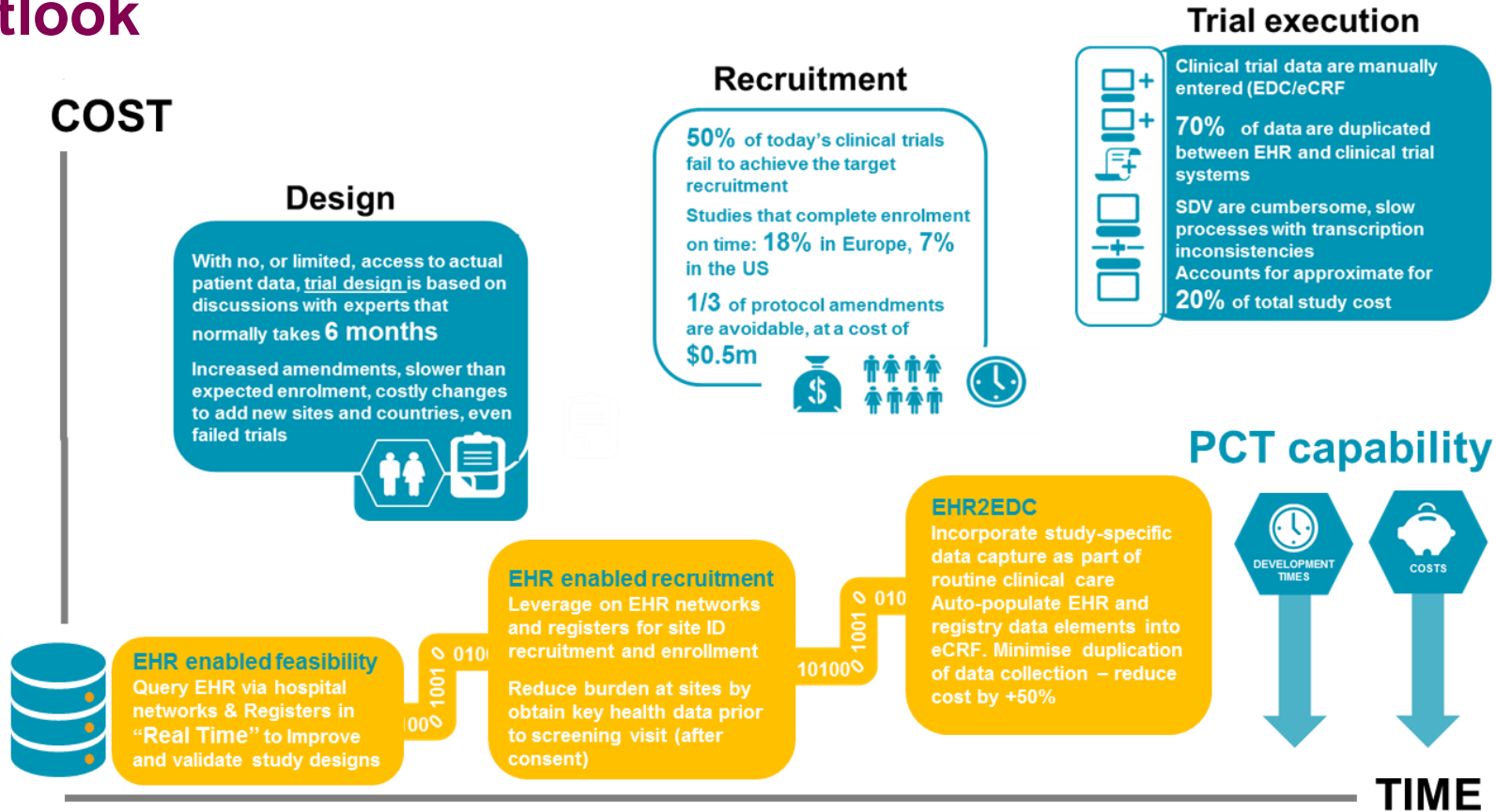
Reduce **feasibility saturation @site**.  
Data driven & real time feasibility  
replace questionnaires.....

# Views of regulatory agencies

- **What does regulators say?**
  - There is a high interest from both FDA and EMA in increased regulatory use of data generated in clinical practice (registries, networks, EHR)
- **Opinion:** Regulators recognize that there are many challenges:
  - Data quality and retention of patients
  - Implementation of reporting requirements for safety
  - Heterogeneity across countries/regions in global trials
- **Clear message:** **”Give us a concrete proposals to consider”**
  - Companies needs to take the first steps towards making pragmatic trials a reality and trigger further development and harmonization of registries to meet regulatory requirements



# Outlook



Federated EHR platform technology connecting RWD into the clinical trial process and provide gateway to Pragmatic Clinical Trials



# Vision for the future health care & pharma

*Tremendous opportunities for synergies between healthcare, payers, pharma and patients regarding the digitization of health data*



We will see radical progress in clinical outcomes, care pathways, quality of care, personalized medicine and new medicines faster to patients at lower cost. We are not limited to just conducting clinical trials....

To make it happen we need new collaboration models and governance mechanisms, trust and new technical platforms around trustworthy reuse of health data – **and it will revolutionize health care and new drug development**



# Thank You

Ask



# Thank You

Scaling up the technology reveal the gem provide new opportunities to collaborate!

This is a good example of a Nash equilibrium.....

***“Best results will come when everyone in the group do what is best for themselves, and the group“***

*(Governing dynamics - John Nash, Nobel Laureate in Economics, 1962)*

Ask

