



## EMR Embedded Trial Feasibility toolkit

### Definitions:

Clinician researcher: principal investigator of the trial and/or clinical subject matter expert.

Embedded trial team: data analyst (EMR builder and data expert) and project officer (facilitates and assists with trial design, feasibility, and regulatory activities)

### Background

Before a trial can be embedded into the electronic medical record (EMR), the feasibility of the trial should be assessed. This is to protect workflow efficiency, ensure effective resource allocation and mitigate risks such as failed implementation.

1. Embedded Trial Proposal Checklist (1) should first be used to vet trials that are broadly unsuitable for embedding, this checklist can be revisited as the feasibility assessment progresses.
2. The scale of embeddedness (2) helps define the level of EMR embedding required for the trial. This helps guide how to approach the rest of the feasibility assessment.
3. Next, a thorough review of the existing physical and electronic workflows (3) of both the clinician and participants need to be undertaken.

This assessment will ensure the trial is able to facilitate identification and enrolment of participants in line with the scale of embeddedness (1) and without onerously disrupting clinical workflows. Conducting this assessment also ensures the data required for the trial is already routinely collected in a timely, precise, and reliable way. Conducting a feasibility assessment is a considerable amount of work from both the clinician researcher, embedded trial project officer, and data analyst. Investing upfront in this process will save time and resources during trial conduct. This process should be undertaken at the same time as the trial design and protocol writing. The embedded trial team should contribute their embedded trial knowledge to the design and protocol, and with specialist data management plan production and any monitoring plans.

It can be useful to develop an electronic phenotype (4) for trial elements, for example the primary outcome or the trial population. This can be done shortly after or in conjunction with the data management plan.

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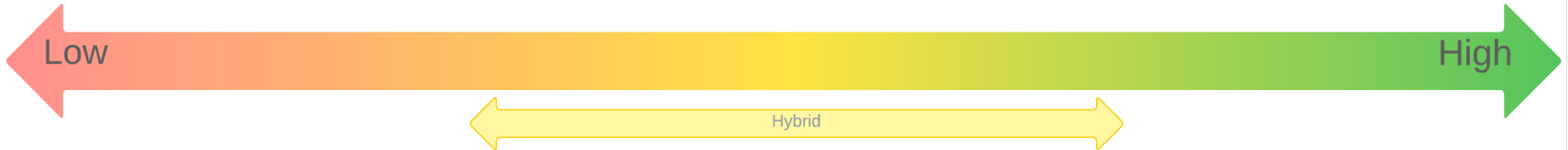


## 1. Embedded Trial Proposal Checklist

Trial Element	Proposal	Embedded Review
<b>Embedded Trial Design</b>		
<p>What are the treatment arms? Are they simple enough for a simple consent, and randomisation?            Are the treatment arms current standard of care? Do they need a CTN?            If blinded placebo, consider resourcing to support this.            What kind of consent would be appropriate?</p> <ul style="list-style-type: none"> <li>• Waiver of consent</li> <li>• Verbal consent</li> <li>• Simplified consent</li> </ul>		
<b>Patient Recruitment</b>		
<p>Study Design – Expected patient population adequate to meet planned sample size.</p>		
<p>Appropriate target population- how, where, when will patients be consented/enrolled/randomised?</p>		
<p>Eligibility Criteria- collected in Epic and simple enough for an embedded trial?</p>		
<b>Data Collection</b>		
<p>Are the outcome measures collected routinely in Epic at the correct timepoints?</p>		
<p>If yes, are most outcomes collected in discrete fields or free text?</p>		
<p>Are new Epic functions or fields required for this project to work?</p>		

## 2. Spectrum of Embeddedness Guide

### Scale of trial EMR embeddedness



- Uses an EMR feature individually but the trial exists largely outside of the EMR
- Reliance on eCRFs for data collection
- Use of paper consent forms, or other questionnaires for outcome measurement
- Using research staff to collect consent and randomise participants outside of routine clinical practice
- Trials utilising EMR research features to enroll and monitor participant safety without using outcome or demographic data directly exported from the EMR
- Randomisation or econsent hosted by a third party system that interface with the EMR
- Specific safety events can be collected utilising EMR adverse event research systems and/or EMR reports.
- Use of EMR or third party dashboards to monitor recruitment, quality, and/or safety
- Building new trial specific features into the EMR to capture trial data
- Most trial procedures conducted within in the EMR including identification, screening, enrollment, and participation end
- A clinician already seeing the participant as part of routine care able to conduct, document, and store consent in the EMR ( or a waiver of consent is used)
- Randomisation able to be performed with the EMR Cluster randomisation or sufficiently large simple randomisation will simplify this
- All data required for trial enrollment and analysis, including eligibility, demographics, and outcome data is reliability captured in the ERM as part of routine care. This data is able to be extracted for analysis
- Comparative effectiveness treatments both already approved and routinely used in the trial population



### 3. Electronic and Physical workflow assessment

#### Step 1: Co-design and consultation

Trial protocols need to be customised to the local site and EMR therefore engagement with stakeholders in the project design stage and maintaining this engagement throughout the life of the project is crucial for the success of an embedded trial.

Thorough consultation with clinical staff is essential for the design of embedded trials. The study team proposing the trial works closely with the embedded trials project team to ensure the trial eligibility, outcomes, consent, and randomisation workflows would work well as an embedded trial.

If the study team is from the proposed trial department (where recruitment is happening), the trial workflows should be discussed with other doctors and nurses working in the department to ensure the trials feasibility, not only as an embedded trial but within the clinical workflow. When the study team sits in a separate department from the trial department, consultation with representatives from the clinical department hosting the trial is even more prudent. All proposed workflows and data collection fields need to be reviewed with clinical investigators in the hosting department before builds and protocols are finalised. The on-the-ground team also need to be made aware of the trial before it's opening and encouraged to give feedback.

During the co-design process it is imperative for a member of the embedded trials team to shadow a member of the clinician team on the ground to understand the current physical participant and clinician workflow in the department and how the proposed trial workflow would sit within this. Understanding the physical workflow (how people move through the physical department/ward and interact with each other) enables the electronic workflow (how people interact with and use the electronic systems) to be fully realised. Throughout this document, we will refer to this relationship as the *electronic-clinical interaction* or *e-clinical interaction*.

#### Other clinical setting considerations:

- Trials embedded into routine care work best when clinicians can consent and enrol participants with minimal disruptions to their clinical care delivery. As the consent and enrolment process burden increases the clinician trial engagement and participation decreases.
- Research culture is also an important element, where clinicians who see research as a part of their clinical care are more likely to recruit than those who see research as an additional burden to their clinical care. Staffing capacity and workload will also decrease engagement as the capacity decreases with increased workload.
- Ideally if a waiver of consent or a verbal consent can be used with randomisation within EMR can be used this approach would optimise recruitment.
- GCP training will be required for investigators who are consenting or enrolling patients to the study. If consenting/enrolling staff are not already trained, then there needs to be an assessment of time and willingness for staff to receive training.
- Where an explicit consent and a multi-step randomisation are required, the ratio of potential participants numbers and recruiting clinicians should be evaluated.
- A larger or frequently changing pool of recruiting clinicians increases the trial administration burden and challenges in engagement and quality assurance. These issues should be balanced with high expected participant recruitment.

- A smaller or more consistent pool of recruiting clinicians will reduce trial burden and promote higher engagement and quality. The ratio of participants to each recruiting clinician will need to be assessed to ensure the clinicians aren't overburdened.

**Paediatric setting considerations:**

- Waivers of consents in paediatric populations require more justification than adult trials. Consumer consultation may assist in justifying this to regulatory bodies where suitable.
- Less drugs that are routinely used in the paediatric populations have Therapeutic Goods Association (TGA) approval. This may mean the added regulatory burden of a Clinical Trial Notification (CTN).
- When using the patient portal feature of an EMR the limitations of parental access need to be evaluated. This often requires producing identification and validation.

## Step 2: Checklist during physical/ electronic workflow assessment

This checklist is a tool to help prompt the feasibility assessment of a EMR embedded trial. Once complete, this will also help guide the EMR build for the data analyst. Not all items will be relevant for every EMR embedded trial, this will depend on the intended scale of embeddedness.

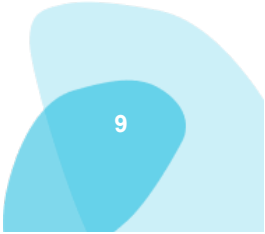
**Physical workflow:** How the clinician and the participant move through the physical environment. To assess the physical workflow at each trial phase, it is recommended that an embedded trial team member shadow a clinician as they move through the physical environment when interacting with potential participants. Depending on the clinical space (ward, outpatient clinic, emergency room etc), a nurse, clinician, or administrator may be best to guide the embedded trial team member through the physical environment potential participants move through.

Physical Workflow				
	Clinician		Participant	
<u>Trial Phase</u>	Notes		Notes	
Identification	Clinician interaction with participant to prompt EMR documentation		Setting where participant will be identified? Inpatient or outpatient?  Eligibility assessments complete?  Trial exposure via a poster? If applicable	
Consent	Trained clinical staff notified and able to consent (has EMR open at correct time has GCP training, and capacity to consent)  Suitable timing for clinician to consent		Participant approached at the appropriate time for consent (stage of treatment/ guardian presence etc)	

Physical Workflow		
	Clinician	Participant
Randomisation	Appropriately trained clinician in hospital/setting at the point of randomisation. How time sensitive is randomisation?	Participant in the required setting at time of meeting randomisation criteria? Still admitted
Treatment allocation	Clinical staff required onsite to prepare and administer drug (especially important if blinded)	Participant accessible for intervention start when randomisation criteria met?
Outcome measures	Clinician reviews the participant as part of routine care. Collecting routine measures, alignment with trial requirements? Consider baseline and outcome data requirements.	Participant outcomes measured when and where expected. Timing in line with routine care and protocol. Setting: hospital or linked service. Inpatient or outpatient visits
Safety monitoring	<p>Clinician able to fit time in workflow to review safety</p> <p>Clinician able to track and record adverse events</p>	Participant adverse events happen in the setting where they are observed, or are otherwise documented



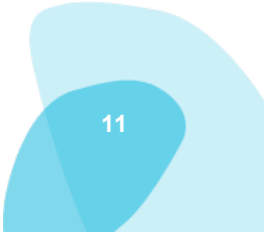
Physical Workflow	
Clinician	Participant
Participation End	Participant in expected setting at expected time (eg, inpatient, follow up outpatient visit etc)



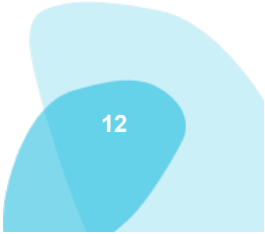
**Electronic workflow:** The physical workflow assessment will help inform the assumed electronic workflow. The embedded trials member should map out the electronic workflow based on the protocol and the physical workflow, and the clinical research should review this map.

Electronic Workflow			
Clinician		Participant	
Trial Phase	Notes	Notes	Notes
Identification	Interaction with EMR to see alert that a participant identified (review existing workflow), or to document a prompt for eligibility	Eligibility criteria collected in a timely consistent way  Eligibility criteria can be defined in an electronic phenotype  Trial exposure via EMR portal communication? If applicable	
Consent	Suitable timing for clinician to document consent in EMR	Participant able to review and sign econsent form. Access to phone/ computer/ internet connection	
Randomisation	Appropriately trained clinician logged into the EMR at the point of randomisation? Will they see the alert without	Participant eligibility for randomisation collected	

Electronic Workflow		
	Clinician	Participant
	disrupting clinician workflows?	accurately, timely, and discreetly to prompt alert
Treatment allocation	<p>Study status automatically updated in EMR, so clinical staff aware of enrolment</p> <p>Allocation entered into EMR if relevant</p>	
Outcome measures	Clinical staff able to collect outcome measures in the EMR in line with the phenotype. Is the data required already routinely collected to an acceptable standard?	Participant data/outcomes measured in the EMR as expected in electronic phenotype (timing, definition, measure/scale)
Safety monitoring	Clinician able to review and monitor adverse events within EMR or a dashboard	Adverse events and safety monitoring phenotype well defined



Electronic Workflow		
	Clinician	Participant
	<p>Clinician alerted of significant safety issues immediately in EMR</p> <p>Clinician able to track and record adverse events</p>	
Participation End	<p>Study status updated in EMR</p> <p>Data in EMR ready for extraction for analysis. Staff expertise to extract and use.</p>	<p>Results shared with participant at trial end (EMR portal use or mail out?)</p>



### Step 3: Conduct retrospective data review and/or prospective observational study

Trial population assessment at RCH evolved from using previous studies/ literature to using retrospective data to make more informed trial design choices. To help guide realistic expectations around recruitment numbers, retrospective data from the target population provides the best insights. Reviewing deidentified data from the target population allows the overall feasible trial population to be assessed and allows the reliability of the desired baseline and outcome data to be scrutinised. The appropriate ethical approval must be sought for this review if not covered under an existing approval.

#### Retrospective data review

- Does the current document process allow the EMR to accurately identify potential participants? Can the clinical EMR documentation be improved?
- Review the number of patients with a particular condition, or on a specific care path. Suitable setting and population size for a trial?
- Use this data to inform an electronic phenotype of the trial population, and the conditions or outcomes
- Ability to review current standard practice (what treatments are given, in what ratio 80:20 vs. 50:50 between two treatments, is this practice changing over time?).
- How are the outcomes measured and defined, how are they collected in EMR (discrete field, single place or multiple, timely)?
- Is the data trending in a particular direction. For example, is the potential study population decreasing over time e.g. due to another intervention

#### When to conduct a prospective observational study?

When EMR improvements were made to allow the EMR documentation of clinicians to better adherence to clinical practice guidelines, a prospective study can be used to evaluate the new use.

#### Using routine data in research

These data review extracts can be used to develop a data dictionary for your data. Data dictionaries are an essential element of your data management for a research study or trial.

These should list all the data elements required from the protocol and then map how they are extracted from the EMR (table type), the format of the data extracted and any possible values (category values or ranges where applicable).

When reviewing the data needed for your research, you should thoroughly securitise the reliability and consistency of data point collection in the EMR. You need to ensure that you can define what a lack of a result means in your data. Does the absence of result mean a condition isn't present or is the data missing (a negative result only indicates a condition isn't present). Developing an electronic phenotype (section 4) can assist in defining this missingness.

#### 4. Use knowledge to design trial and embed the trial in EMR

If you want to apply your findings into a clinical trial embedded into your EMR you will need to engage with experts in the EMR system at your institution at the project design and ideation stage to ensure it is feasible and that the resources available are adequate to implement this design

These personnel would also be best positioned to advise on the best EMR features to use to help with recruitment, randomisation, treatment allocation, safety and quality data monitoring and extracts. Codesign with clinical staff continues to be paramount when designing and implementing these features.

Some examples of EMR features used in the embedded trials implemented at RCH include.

- Our Practice Advisory (OPA) alerts that prompt consent and randomisation procedures. These are programmed using criteria which align with eligibility and patient location criteria. These can be active or passive. These can be monitored via reports in Epic. Acting as an EMR screening log.
- OPAs can also be used to remove ineligible patients before they can be randomised for safety reasons.
- OPAs can prompt the correct treatment allocation after randomisation.
- Research Activity in EMR can log the time and dates of status change and automatically removes patients from the trial once the prespecified timepoint is reached.
- Extract custom data extracts of required trial data.

All EMR infrastructure built for the purposes of a clinical trials should be tested rigorously before being moved to the production environment for use.

Other electronic features of embedded trials

- Monitoring of safety and quality data in a PowerBI dashboard
- Documentation and storage of e-consent and randomisation in other systems. Able to pipe information between EMR and these systems for ease of use.

Plans should be included in the data management plan on how these tools will be monitored for ongoing relevance and efficiency. This is in addition to how the tools are used to monitor the trial (quality and safety monitoring).

## 5. Electronic Phenotyping guidance

Conduct feasibility assessment first, although you will have need to ensure your protocol data can be collected in the EMR and what that looks like already. Retrospective/ prospective data will be required to thoroughly develop an electronic phenotype. If the data required is not currently collected, then the protocol needs to be re-considered or a plan to update the EMR to collect the data point will be needed.

An electronic phenotype allows the translation between clinical definitions and trial data required into the EMR space and international standards. The use of standard definitions ensures reliability and reproducibility of research (1).

Electronic phenotype describes how the required clinical and research data are defined with the EMR. This includes but is not limited to:

- ICD, OMOP and other codes used in the EMR to classify diseases or terms
- How, where, and who captures the data. Is this in a discrete or free-text field?

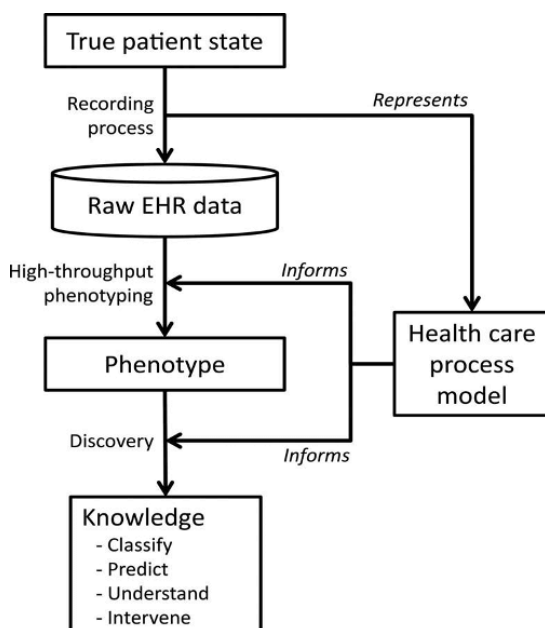
Uses for electronic phenotype include (1):

- Identification of patient groups for recruitment identification or describing cohorts for health service research
- Gathering baseline characteristics including demographics and clinical attributes
- Defining primary and secondary outcomes
- Collating information for safety monitoring

The definition of an electronic phenotype allows for comprehensive data quality and accuracy review.

Figure 1: Electronic phenotype process.

<https://rethinkingclinicaltrials.org/chapters/conduct/electronic-health-records-based-phenotyping/electronic-health-records-based-phenotyping-introduction/>



An example of an electronic phenotype is the below definition of paediatric febrile neutropenia in the EMR.

Resource <https://phekb.org/phenotype/febrile-neutropenia-pediatric>

## References

1. Richesson RL, Hammond WE, Nahm M, Wixted D, Simon GE, Robinson JG, Bauck AE, Cifelli D, Smerek MM, Dickerson J, Laws RL, Madigan RA, Rusincovitch SA, Kluchar C, Califf RM. Electronic health records based phenotyping in next-generation clinical trials: a perspective from the NIH Health Care Systems Collaboratory. *J Am Med Inform Assoc.* 2013 Dec;20(e2):e226-31. doi: 10.1136/amiajnl-2013-001926. Epub 2013 Aug 16. PMID: 23956018; PMCID: PMC3861929.