

Use Case for Connecting Patients to Clinical Trials Using Electronic Health Records

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Scope:

This use case will define the stakeholders, preconditions, obstacles, post-conditions, and detailed perspectives and scenarios involved with more effectively connecting patients with the clinical trials for which they may qualify. This use case will describe the processes by which electronic health records (EHRs) and electronic health information exchanges (HIEs), such as the Nationwide Health Information Network (NHIN), will enable matching of patients to clinical trials based on the pre-screening criteria for the trials. Enabling better availability of clinical trial information to patients and physicians and more easily identifying patients who qualify for trials will benefit all parties involved, including patients, physicians, trial investigators, and clinical trial sponsors.

The scope of this use case will include the following:

- Determine the value-added outputs and services that can be provided to patients, physicians, trial investigators, and clinical trial sponsors based on improved matching of patients to clinical trials using electronic health records.
- Identifying the types of data necessary to match patients to trials and evaluate recruitment feasibility based on trial pre-screening criteria.
- The modeling of many interactions between the perspectives in this use case that occur as part of conducting normal business functions related to matching patients to trials and sponsor patient recruitment.
- In evaluating the perspectives of this use case, special consideration will be given to how the use of electronic health records can better connect patients to trials in the US, as well as other countries around the world. Initial implementations or pilot projects will likely focus on the US.

The scope of this use case will exclude the following:

- Trial sponsors targeting, identifying, and recruiting clinical trial investigators based on patient data from electronic health records.
- Requirements, design, and build of the technology necessary to determine whether patients meet clinical trial pre-screening criteria based on electronic patient health information.
- Phase I clinical trials will be excluded from the scope of this use case, because they often require healthy volunteers. This use case will focus on identifying patients for Phase II, III, and IV clinical trials.

Intent of this Use Case:

This use case document is meant to provoke thought and conversation about how electronic health records (EHRs) and emerging health information exchanges (HIEs) can be used to more easily connect patients to clinical trials. This document captures the thoughts and discussions of the Slipstream participants through a series of work group meetings, in which we aimed to describe future capabilities that could be built to pre-screen a patient for all registered clinical trials by comparing his/her electronic health record to the inclusion/exclusion criteria of all clinical trials.

This document is a starting point for evaluating future projects and does not intend to prescribe the way that future capabilities will be built or that policy and regulation will change over time. Please consider the many challenges to using EHR data to match patients to clinical trials, which are listed in the preconditions and obstacles sections, as you read the use case scenarios.

We hope that this document generates discussion and debate of how connecting patients to clinical trials can be included in the analysis, design, and implementation of national health information technology initiatives in the United States.

Data Element Requirements:

Authorized users involved in direct patient care will be able to see identified data in the patient's health record, according to the agreed privacy, security, and data access policies used in electronic medical record systems. Patient health data will be anonymized or pseudonymized prior to transmission from these source systems to third parties not directly involved in patient treatment so that it can serve secondary uses, such as matching patients to clinical trials. Once data is pseudonymized, a randomized data linker provides authorized entities the ability to re-identify the patient through the data provider. This should serve to protect the privacy and security of patient health information while allowing each of the scenarios in this use case to be carried out.

Several types of data elements will be required to evaluate whether patients meet the pre-screening criteria of clinical trials based on the data within the patients' electronic health records. To obtain the full value of this use case, all data elements must be stored and transmitted using emerging standards, as defined by the Healthcare Information Technology Standards Panel (HITSP) and international standards bodies.

The general categories of data elements required to support the processes defined in this use case are:

1. Patient Demographics
2. Patient Health History Data
 - a. Allergies
 - b. Family History
 - c. Personal Health History (e.g. smoking, alcohol, etc)
3. Clinical Practice Data
 - a. Visits
 - b. Diagnoses
4. Observation Data
 - a. Simple, vital observations (height, weight, etc)
 - b. Laboratory results
5. Procedure Data
6. Pharmacy Data
 - a. Prescription Order
 - b. Dispense
 - c. Administration

Executive Summary:

The Connecting Patients to Clinical Trials use case includes four scenarios that describe how electronic health records and health information exchanges can improve access to clinical trials for patients and physicians and enable faster patient accrual for trial investigators and sponsors. Each scenario is described briefly below. The full details of the scenarios are located in the Scenarios & Perspectives section of this document.

Direct to Patient Clinical Trial Matching Service:

In this scenario a patient provides consent for his/her electronic health record to be used to provide a personalized list of clinical trials for which the patient may qualify. The patient can also specify preferences for indications in which s/he is interested, the frequency with which s/he is contacted with matching trials, and the preferred method of contact (e.g. e-mail, phone, etc).

The patient's longitudinal electronic health record, which pulls data from many source systems, will be compared against structured inclusion and exclusion criteria for all registered clinical trials. The patient will be notified of the matching results, which will show a confidence interval indicating the likelihood that the patient will qualify for the trials.

The patient can then discuss the matching trials with his/her physician or a patient advocacy group to determine which trial is best for him/her. The matching list will provide contact information for the trial, so the patient can then set up a screening visit for the trial(s) of choice.

Site / Physician Service to Match Visiting Patients to Trials:

This scenario is meant to provide a physician office or investigator site a list of all clinical trials for which its patients match. The office or site will obtain the patient's consent to use his/her electronic health record to match him/her to all clinical trials for which s/he may qualify.

The office/site will identify the patients that it wants to match to clinical trials. The longitudinal electronic health records for these patients, which pull data from many source systems, will be compared against structured inclusion and exclusion criteria for all registered clinical trials. The office/site will be notified of the matching results for each patient, which will show a confidence interval indicating the likelihood that the patient will qualify for the trials. The matching list can be categorized for investigator sites to group all trials being run at that site separately from all other clinical trials.

The office/site can then discuss the matching clinical trials with the patient to determine which trials are right for the patient. The office/site can also provide the matching list to the patient. Investigator sites can also screen the patient for those matching trials that are being conducted at their site.

Clinical Trial Enrollment Feasibility Analysis Service:

Using longitudinal electronic health record data for large patient populations within the United States, clinical trial sponsors will be able to determine the patient populations that meet the pre-screening criteria of their trials. Sponsors will enter the pre-screening criteria in a structured format during the planning or execution of the trial to determine the feasibility of accruing patients.

Results can be stratified one or more cohort characteristics, including geography (e.g. by ZIP code, county, state, etc), race, gender, and other demographic distinctions, based on the preferences of the trial sponsor running the analysis. This may help the sponsor identify cohorts or geographies with the necessary patient populations and may be useful in identifying investigators for the trial.

Inform Investigator of Qualifying Patients:

This scenario provides a service to clinical trial investigators to find patients in a specified cohort, based on geography (e.g. by ZIP code, county, state, etc), race, gender, and other demographic distinctions, that potentially match the clinical trials being conducted at their site.

The investigator site will request the list of matching patients within a specified cohort. The longitudinal electronic health record for all patients will be compared against the cohort characteristics and the structured inclusion and exclusion criteria for all registered clinical trials being conducted at the investigator site. The site will be notified of the names of physicians that currently treat matching patients. The report will also show how many patients are treated by each physician, but no patient identifying information will be available to the investigator site.

Investigators must then contact physicians to determine whether the patient is interested in being screened for the matching clinical trials. Physicians will be able to specify their contact preferences for investigators. Once contacted, the physician office must contact the patient to determine interest in the trial(s). Interested patients will then be connected with the investigator for clinical trial screening.

Stakeholders:

The following list of stakeholders and their definitions are for discussion purposes within the context of the use case.

Figure 1 – Stakeholders for Connecting Patients to Clinical Trials

Stakeholder	Working Definition
Patients	Members of the public who require healthcare services from ambulatory, emergency department, and in-patient environments. If the patient is not capable of decision-making, a patient proxy may substitute for the patient in the use case processes.
Physicians	The treating physician(s) with direct patient interface in the delivery of care and prescribing of medications or treatments.
Investigators	Physicians recruited by trial sponsors to conduct clinical trials.
Study Coordinators	Also referred to as Site Coordinators or Research Nurses. Nurse or coordinator that drives the execution of the trial. These coordinators conduct initial screening and data analysis to match patients to trials for which they qualify.
Trial Sponsors	Companies or organizations that sponsor clinical trials of pharmaceuticals, biologicals, and/or medical devices.
Regulatory Agencies	Agencies, such as the Food & Drug Administration (FDA), that regulate the marketplace for pharmaceuticals and medical products and aim to protect the health and safety of the consuming public.
Other Healthcare Professionals	Health care providers, other than physicians, investigators, and study coordinators, with direct patient care responsibilities, including nurses, clinical supervisors, and their delegates.
Health care delivery organizations	Organizations, such as hospitals and physician practices, which manage the delivery of care.
Health Data Service Providers	A company or organization that collects, manages, and distributes patient health information. This category may include government payer organizations, non-government payer organizations, integrated delivery networks, data aggregators, or other organizations that supply, collect, or process health data.
Patient Advocacy Groups	Organizations set up to promote the cause of patients with a certain disease. Some of these organizations help patients find trials in a given disease or determine which available trial is right for the patient.

Preconditions:

Preconditions are the conditions that must be in place before the start of the use case. This includes, but is not limited to, the state of a stakeholder, data that must be available somewhere, or an action that must have occurred. This section also includes triggers for the initiation of the use case and discussions of important assumptions made about the use case during its development. A variety of preconditions are necessary for this use case, including:

Figure 2 – Preconditions for Connecting Patients to Clinical Trials

#	Precondition Description	Categories*	Scen. 1: Direct to Patient	Scen. 2: MD/Site Service	Scen. 3: Study Feasib.	Scen 4: Patient Locator
1	Established network and policy infrastructures to enable secure, consistent, appropriate, reliable, and accurate information exchange.	<ul style="list-style-type: none"> Data Exchange 	✓	✓	✓	✓
2	Systems must be able to exchange components of patient health data in a way that links all data from one patient together to make up the health record.	<ul style="list-style-type: none"> Identity Correlation Record Location 	✓	✓	✓	✓
3	Healthcare facilities' (i.e., hospitals, clinics, physician practices, laboratories, ancillary clinical facilities) ability to electronically collect, process, and transmit pertinent health data in a secure fashion using existing data exchange and vocabulary standards.	<ul style="list-style-type: none"> Data Content Security Data Translation 	✓	✓	✓	✓
4	All health information source systems must be connected to health information networks that can share the data necessary to make up the longitudinal health record of a patient.	<ul style="list-style-type: none"> Data Content Data Exchange 	✓	✓	✓	✓
5	Agreement about who can use identified, anonymized, and pseudonymized patient health information, under what circumstances they can use it, for what purpose they can use it, and whether or not patient consent is required for each type of data use required by this use case.	<ul style="list-style-type: none"> Data Usage Privacy 	✓	✓	✓	✓
6	Policies and agreements must be in place to govern access to patient health data, such that data available to one organization is available to equivalent organizations under the same terms and conditions.	<ul style="list-style-type: none"> Data Access Policy Alignment 	✓	✓	✓	✓

#	Precondition Description	Categories*	Scen. 1: Direct to Patient	Scen. 2: MD/Site Service	Scen. 3: Study Feasib.	Scen 4: Patient Locator
7	The policies, processes, and technology necessary to register and update clinical trial pre-screening criteria must make trial registration practical and feasible for trial sponsors.	<ul style="list-style-type: none"> Policy Alignment 	✓	✓	✓	✓
8	Physicians and healthcare professionals must be trained and must always enter necessary data to support this use case in a structured, standardized format.	<ul style="list-style-type: none"> Data Content 	✓	✓	✓	✓
9	Policy must be in place to designate who owns and is able to sell or authorize the sale of patient health data. Contractual terms and conditions must be agreed and well-defined to support the establishment of contracts to obtain patient health data from its owners/suppliers. Policies must consider both identified and anonymized data and indicate under what conditions patient consent is necessary to sell patient data.	<ul style="list-style-type: none"> Policy Alignment 	✓	✓	✓	✓
10	Standards must be defined to store protocol information in a standardized, structured, and machine-readable format. These standards must allow key elements of protocols to be searchable by queries in order to allow matching of protocol data to patient health data. <u>Note:</u> The current process to register and capture clinical trial information will likely need to change to accommodate this use case.	<ul style="list-style-type: none"> Data Content Data Translation Data Storage 	✓	✓	✓	✓
11	Technology must be available that can determine whether patients meet the complex pre-screening criteria of clinical trial protocols, based on the patient's electronic health record, with a level of accuracy that will minimize false-positive results. It is important to balance the benefit of informing the patient of trials against the negative impact that false-positive results have on patients and physicians.	<ul style="list-style-type: none"> Data Filtering 	✓	✓	✓	✓

#	Precondition Description	Categories*	Scen. 1: Direct to Patient	Scen. 2: MD/Site Service	Scen. 3: Study Feasib.	Scen 4: Patient Locator
12	Agreement from the pharmaceutical and medical products industries, regulators, and other stakeholders about who should build, maintain, and govern the system(s) necessary to conduct patient matching and notifications. Policies must be in place to ensure that there is no bias in reporting matching trial results based on external influences.	<ul style="list-style-type: none"> Policy Alignment Data Usage 	✓	✓	✓	✓
13	Determination of the minimum data set necessary to match patient health information with clinical trial pre-screening criteria.	<ul style="list-style-type: none"> Data Content 	✓	✓	✓	✓
14	Policies must be in place to clarify the liability of healthcare professionals that are provided information about clinical trials for which their patients may qualify. Healthcare professionals may not want to participate in clinical trial matching if it introduces additional liability. This includes protection from patients who are upset about false-positive matching results or poor results of the trial in which they enroll.	<ul style="list-style-type: none"> Policy Alignment 	✓	✓		✓
15	Technology and processes must be in place to prevent a patient or physician from being contacted multiple times about the same trial for which the patient matches. This includes steps to prevent contact for trials in which the patient is already enrolled, has explicitly said he/she does not want to participate, or has failed screening. The patient must also be able to indicate that he/she is no longer interested in receiving notification of trial matching and manage the frequency of notification of trial matching.	<ul style="list-style-type: none"> Data Content Data Filtering Data Access 	✓	✓		✓
16	Trial Sponsors must keep clinical trial pre-screening criteria and other trial registration information up-to-date at all times.	<ul style="list-style-type: none"> Data Content 	✓	✓		✓
17	Patient data from each of the required data element categories, listed in the Scope section, must be available in a normalized electronic format capable of being exchanged for each patient wishing to be matched to clinical trials.	<ul style="list-style-type: none"> Data Exchange 	✓	✓		

#	Precondition Description	Categories*	Scen. 1: Direct to Patient	Scen. 2: MD/Site Service	Scen. 3: Study Feasib.	Scen 4: Patient Locator
18	Agreement about whether and/or how a consumer's choice to restrict access to some or all of his/her electronic health information will be applied to patient matching for clinical trials using identified information.	<ul style="list-style-type: none"> Data Content Privacy 	✓	✓		
19	Patient data from each of the required data element categories, listed in the Scope section, must be available in a normalized electronic format capable of being exchanged for a sufficiently large population of patients to support study feasibility analysis and the location of patients for investigator sites.	<ul style="list-style-type: none"> Data Exchange Data Translation 			✓	✓
20	Agreement about whether and/or how a consumer's choice to restrict access to some or all of his/her electronic health information will be applied to aggregated, anonymized or pseudonymized data.	<ul style="list-style-type: none"> Data Content Privacy 			✓	✓
21	A consistent, agreed approach to anonymize and pseudonymize, including the following elements: <ul style="list-style-type: none"> list of patient data that must be removed to anonymize or pseudonymize ability to connect all data related to a patient or event to limit or prevent duplicates re-linking pseudonymized data by going back to the data provider 	<ul style="list-style-type: none"> Data Content Privacy 			✓	✓
22	Data from all provider systems, payer systems, laboratory systems, and other electronic data source systems that contribute patient data must be accessible in a manner that supports data analytics using algorithms and queries.	<ul style="list-style-type: none"> Record Location Data Storage 			✓	✓
23	Agreement about whether a patient's consent is required for the use of their anonymized electronic patient data for clinical trial recruitment feasibility analysis.	<ul style="list-style-type: none"> Data Usage Privacy 			✓	
24	Agreement whether a physician's consent is required to be contacted about his/her patients that match clinical trials being run by an investigator.	<ul style="list-style-type: none"> Policy Alignment 				✓

#	Precondition Description	Categories*	Scen. 1: Direct to Patient	Scen. 2: MD/Site Service	Scen. 3: Study Feasib.	Scen 4: Patient Locator
25	Policy must be in place to dictate what patient information trial investigators can provide to physicians to help the physicians identify which patients have been shown to match the investigator's trial.	<ul style="list-style-type: none"> Policy Alignment 				✓
26	Processes and technology must be in place to indicate which physician to contact regarding a patient's interest in a clinical trial (e.g. indication of the primary physician for the patient).	<ul style="list-style-type: none"> Data Content 				✓

* Categories are based on those used by the National Committee on Vital and Health Statistics (NCVHS) and the Office of the National Coordinator for Healthcare Information Technology (ONC) to evaluate requirements for the NHIN.

Obstacles:

In general, the absence of the prerequisites described in the previous section presents obstacles to implementation of the use case. Additional obstacles include an unwillingness to participate in activities due to perceived security and privacy concerns or to the lack of perceived value. These obstacles could affect several groups including:

1. Patients / Consumers: Must be adequately educated about the value of electronic health information and the security safeguards that are in place to protect their privacy and confidentiality, so that they will consent to sharing their data.
2. Health facilities: Some health facilities may lack resources to implement the technology to collect, process, and transmit the necessary health information electronically.
3. Physicians & Healthcare Professionals: Must be adequately educated about the uses of electronic health data and the value derived from data entry that impacts their workflow. Without this education and understanding of the value of data entry, these professionals may not enter all data necessary to support this use case.

Additional obstacles include:

Figure 3 – Obstacles to Connecting Patients to Clinical Trials

#	Obstacle Description	Categories*	Scen. 1: Direct to Patient	Scen. 2: MD/Site Service	Scen. 3: Study Feasib.	Scen 4: Patient Locator
1	Limited use of electronic medical record systems (EMRs) by physicians in small practices, who still rely primarily on paper records.	<ul style="list-style-type: none"> ▪ Data Content 	✓	✓	✓	✓
2	Inability of health information data providers to transform electronic data, using accepted standards, into filtered, normalized, and anonymized or pseudonymized form to enable data exchange. These organizations may require assistance with these capabilities to implement projects in the near- and mid-term.	<ul style="list-style-type: none"> ▪ Data Content ▪ Data Translation 	✓	✓	✓	✓
3	Limited access to connectivity capabilities for clinicians', laboratories', or healthcare delivery organizations' systems to securely share data across the Internet. This is more likely to be an obstacle for small physician practices than for larger, integrated healthcare delivery systems. The ability for trial sponsors to aid these organizations in system implementation is limited by Stark and anti-kickback legislation.	<ul style="list-style-type: none"> ▪ Data Exchange ▪ Policy Alignment 	✓	✓	✓	✓

#	Obstacle Description	Categories*	Scen. 1: Direct to Patient	Scen. 2: MD/Site Service	Scen. 3: Study Feasib.	Scen 4: Patient Locator
4	Incomplete data within the local EHR systems. Key elements necessary to support the matching of patients to trials may not be available in the near- to mid-term.	▪ Data Content	✓	✓	✓	✓
5	Unwillingness of healthcare delivery organizations to provide data management, including review of patient information to identify missing data elements necessary for matching patients to trials, manually enter data, and scan or manually enter historical information. This includes resistance of healthcare professionals to take on additional data entry that may affect their current workflow.	▪ Data Content	✓	✓	✓	✓
6	Unwillingness of current patient health information owners to share electronic patient health information outside of their organization. This reluctance could be driven by fear of liability based on the data provided, the desire to sell the data, or the lack of perceived value in sharing the data.	▪ Data Exchange	✓	✓	✓	✓
7	Limitations on the ability of pharmaceutical companies and third party organizations to access identified, anonymized, and pseudonymized patient health data. These limitations may mean that a third-party organization or government agency (e.g. FDA) will be required to maintain the capabilities necessary to match patients to clinical trials.	▪ Data Usage ▪ Policy Alignment	✓	✓	✓	✓
8	If regulators determine that the systems required to support this use case fall within GxP or Part 11 requirements, the necessary validation efforts for the patient matching system(s) would be an obstacle to implementation.	▪ Policy Alignment	✓	✓	✓	✓
9	Unwillingness of physicians to refer patients to other investigators that are running clinical trials. This will likely be driven by the fear of losing the patient to the other physician and the negative financial impact this would have on the physician's practice.	▪ Data Usage		✓		✓
10	Unwillingness of physicians to refer patients for clinical trials based on a lack of knowledge of the details of the clinical trial & alternative treatment options.	▪ Data Content		✓		✓

Post-conditions:

Post-conditions are the conditions that will be a result or output of the use case. This includes, but is not limited to, the state of a stakeholder upon conclusion of the use case, data that were created or are available at the conclusion of the use case, and actions that may serve as pre-conditions for other use cases. The post-conditions for this use case include:

Figure 4 – Post-Conditions for Connecting Patients to Clinical Trials

#	Post-Condition Description	Categories*	Scen. 1: Direct to Patient	Scen. 2: MD/Site Service	Scen. 3: Study Feasib.	Scen 4: Patient Locator
1	Patient health data sources will be able to electronically exchange the data elements necessary to match patients to clinical trials and conduct trial recruitment feasibility analysis.	<ul style="list-style-type: none"> Data Exchange Data Content 	✓	✓	✓	✓
2	Data provided will support the privacy and security of patient health information.	<ul style="list-style-type: none"> Privacy Security 	✓	✓	✓	✓
3	Clinical trial sponsor companies will have the capability to register their trials in a structured format, including pre-screening criteria and contact information to get more details about the trial.	<ul style="list-style-type: none"> Data Content 	✓	✓	✓	✓
4	Controls will be in place to prevent redundant notifications to patients, physicians, and investigators. This includes capabilities to indicate that a patient is already enrolled in a trial, a patient has previously failed screening for a trial, a patient has indicated that s/he is not interested in a trial, or that a physician has already been notified about a patient that matches a trial.	<ul style="list-style-type: none"> Data Usage 	✓	✓	✓	✓
5	The technology used to match patients to clinical trials will provide as much protection as possible against false-positive and false-negative matching results.	<ul style="list-style-type: none"> Data Quality 	✓	✓	✓	✓
6	Patients will have control over their consent to use their electronic health information for the purposes of clinical trial matching.	<ul style="list-style-type: none"> Privacy 	✓	✓	✓	✓
7	The technology used to match patients to clinical trials will show all data sources and data elements that were not available or were missing at the time the match was completed.	<ul style="list-style-type: none"> Data Content Data Quality 	✓	✓	✓	✓

#	Post-Condition Description	Categories*	Scen. 1: Direct to Patient	Scen. 2: MD/Site Service	Scen. 3: Study Feasib.	Scen 4: Patient Locator
8	An authorized party can send an email or mail notification to a patient when s/he has consented and is matched to one or more clinical trials.	▪ Data Usage	✓			
9	Patients will be able to specify their preferences for receiving notifications about clinical trials for which they may qualify.	▪ Data Usage	✓			
10	Reports will be available to show a patient all clinical trials for which he or she meets the pre-screening criteria, along with contact information to get trial enrollment details.	▪ Data Content	✓			
11	Reports indicating clinical trials for which a patient matches the pre-screening criteria will indicate the confidence interval (using a percentage) of the match.	▪ Data Content	✓	✓		✓
12	Investigator sites or physicians can request and receive a report of the clinical trials for which their patients qualify. This report will be categorized to separate trials that the site/physician is conducting from all other qualifying clinical trials.	▪ Data Content		✓		
13	Clinical trial sponsor companies will be able to conduct recruitment feasibility analyses for trial protocols or more general trial profiles based on available patient health data.	▪ Data Content			✓	
14	An authorized party can notify an investigator participating in a clinical trial of all physicians that are treating patients in a specified cohort or geography that meet the pre-screening criteria for the clinical trials being run at the investigator's site.	▪ Data Content				✓
15	Investigator sites will provide as much information about the patient that matches their trial as is allowed by policy. This will allow the physician office to easily identify the patient to which the investigator site is referring.	▪ Data Content ▪ Identity Correlation				✓

* Categories are based on those used by the National Committee on Vital and Health Statistics (NCVHS) and the Office of the National Coordinator for Healthcare Information Technology (ONC) to evaluate requirements for the NHIN.

Perspectives & Scenarios:

Each scenario will be represented using visual diagrams that depict a combination of all events used in the scenario flow, an outline that defines each step of the scenario in greater detail, and a visual diagram that shows the steps in the process from the perspective of each stakeholder group.

The list of scenarios for evaluation in this use case is:

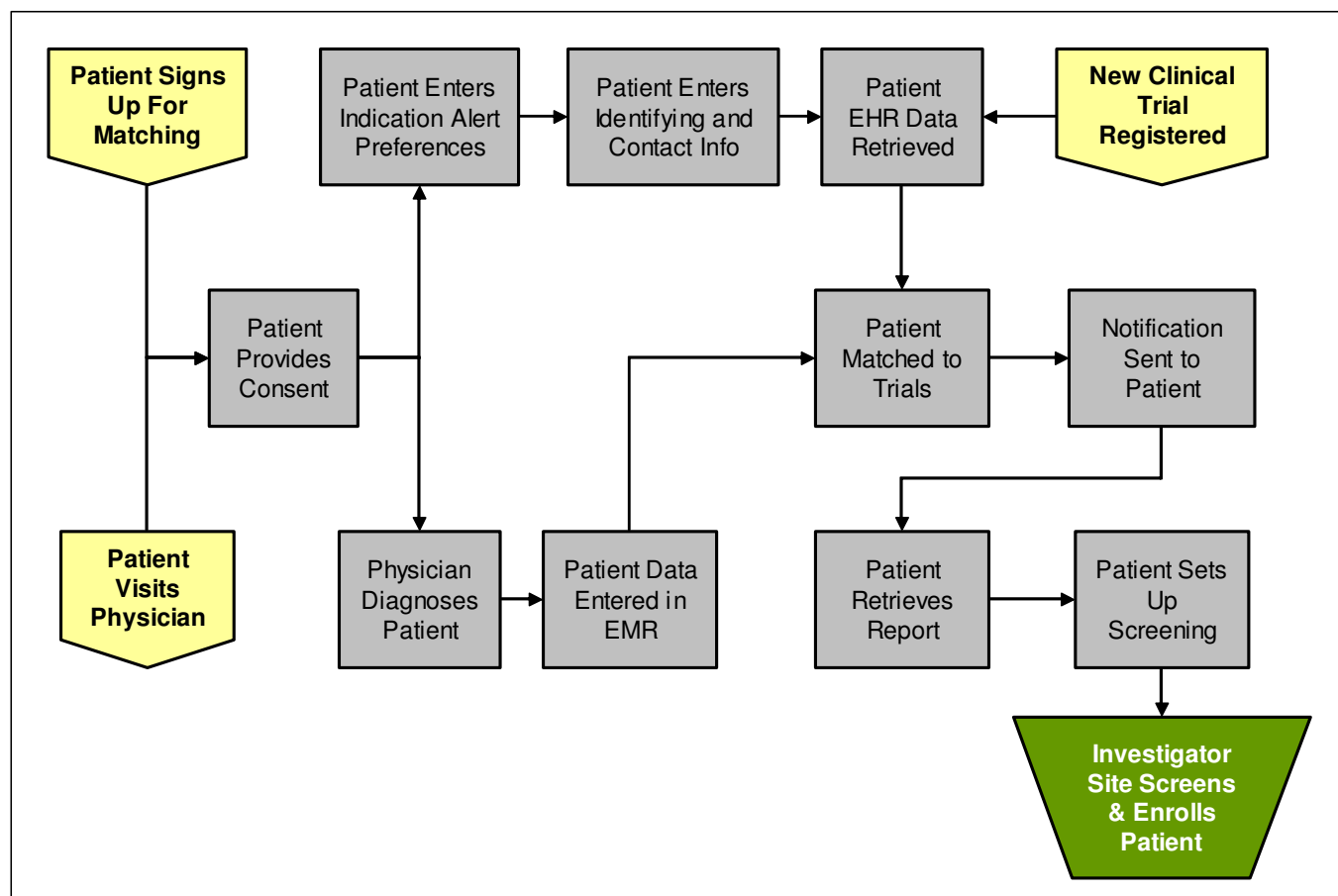
1. Direct to Patient Clinical Trial Matching Service
2. Site / Physician Service to Match Visiting Patients to Trials
3. Clinical Trial Enrollment Feasibility Analysis Service
4. Inform Investigator of Qualifying Patients

The processes used to match patients to clinical trials will be considered for patients based in the US and other countries around the world. Different scenarios may be defined for the US and other countries. Preliminary efforts will focus on US patient matching.

Scenario 1: Direct to Patient Clinical Trial Matching Service

The following diagram represents the process of matching patients to clinical trials and notifying patients of the resulting matches. The sections below the diagram describe the sequence of events in more detail. The final diagram in this section shows the process from the perspective of each stakeholder group.

Figure 5 – Direct to Patient Clinical Trial Matching Process



Process Flow:

1. Trial Sponsor Companies Register Clinical Trials

- a. Sponsor companies enter structured pre-screening criteria in the public domain.
- b. Sponsor companies enter contact information for enrollment in the study in the public domain. This information will vary by trial and sponsor.

Patient Provides Consent and Other Information

- c. Patient or patient proxy provides consent to share the patient's health information for the purpose of clinical trial matching. This consent may be granted electronically when specifying other matching service preferences or may be indicated during a visit to a physician or healthcare provider.
- d. Optional: Patient or patient proxy provides indications for which s/he would like matching trial lists & alerts of new trials. This may be particularly useful for trials in indications that may not show up in the patient's health record, such as baldness and other "lifestyle" indications.
- e. Patient or patient proxy provides key identification and contact information for patient.

2. Patient Visits a Physician or Provider

- a. Physician or provider observes and diagnoses the patient.
- b. Diagnosis and other patient information from the visit are entered into an EMR system.

3. Patient Data Matched to Trial Criteria

- a. Patient's health data and indication preferences are communicated through a health information network. The source of the patient data may be the patient's PHR, the physician office or provider organization EMR system, or another health information data source. Data from all source systems will create the longitudinal electronic health record for the patient, which will be used for trial matching.
- b. Patient's requested indications and his/her health information are compared to the indication and pre-screening criteria of all registered clinical trials.
- c. Notification is sent directly to the patient informing him/her how to securely retrieve the list of matching trials and the contact information for enrollment in each study. Another alert will be sent to the patient each time a new clinical trial is registered and shows the patient as a match.

4. Patient Selects a Trial and Sets Up Screening

- a. Patient or a patient proxy retrieves the list of clinical trials for which he/she may qualify and the contact information to get screened for each clinical trial.

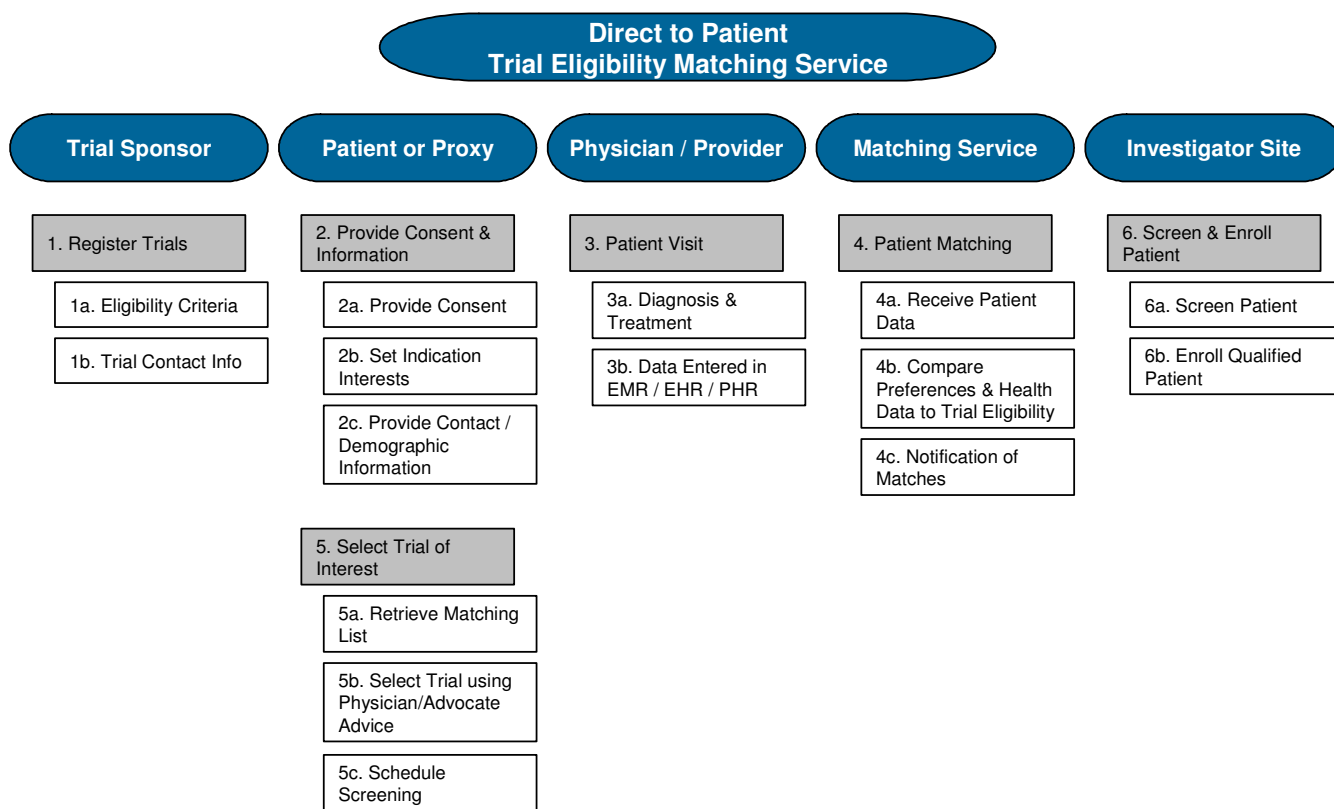
- b. Patient or proxy selects a trial of interest from the matching list. This may involve discussions with the patient's physician or an advocacy group in the particular condition, which can provide additional help in determining the best trial for the patient to pursue.
- c. Patient or patient proxy uses contact information to set up an appointment for trial screening.

5. Patient Screening & Enrollment

- a. Patient visits investigator office for screening.
- b. If qualified, patient is enrolled in trial. If not, patient repeats the steps above to get screened for a different trial.

Stakeholder Perspectives:

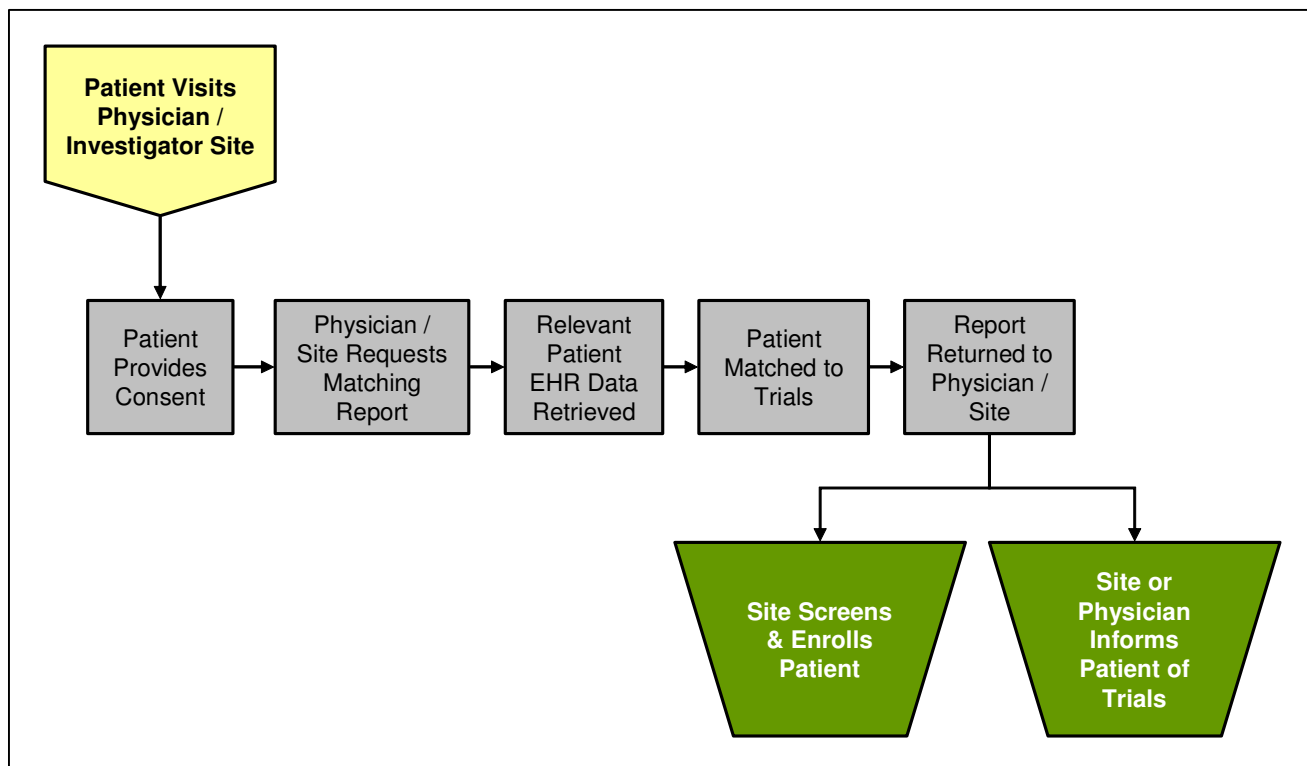
Figure 6 – Stakeholder Perspectives – Direct to Patient Clinical Trial Matching



Scenario 2: Site / Physician Service to Match Visiting Patients to Trials

The following diagram represents the process of matching patients to trials for investigator sites and physician offices that those patients visit. The sections below the diagram describe the sequence of events in more detail. The final diagram in this section shows the process from the perspective of each stakeholder group.

Figure 7 – Investigator Site Service to Match Visiting Patients to Trials



Process Flow:

1. Trial Sponsor Companies Register Clinical Trials
 - a. Sponsor companies enter structured pre-screening criteria in the public domain.
 - b. Sponsor companies enter contact information for enrollment in the study in the public domain. This information will vary by trial and sponsor.
2. Trial Site or Physician Requests Report to Match Visiting Patients to Trials
 - a. Trial site or physician office obtains consent from patient or patient proxy to use the patient's electronic health information for the purpose of clinical trial matching.

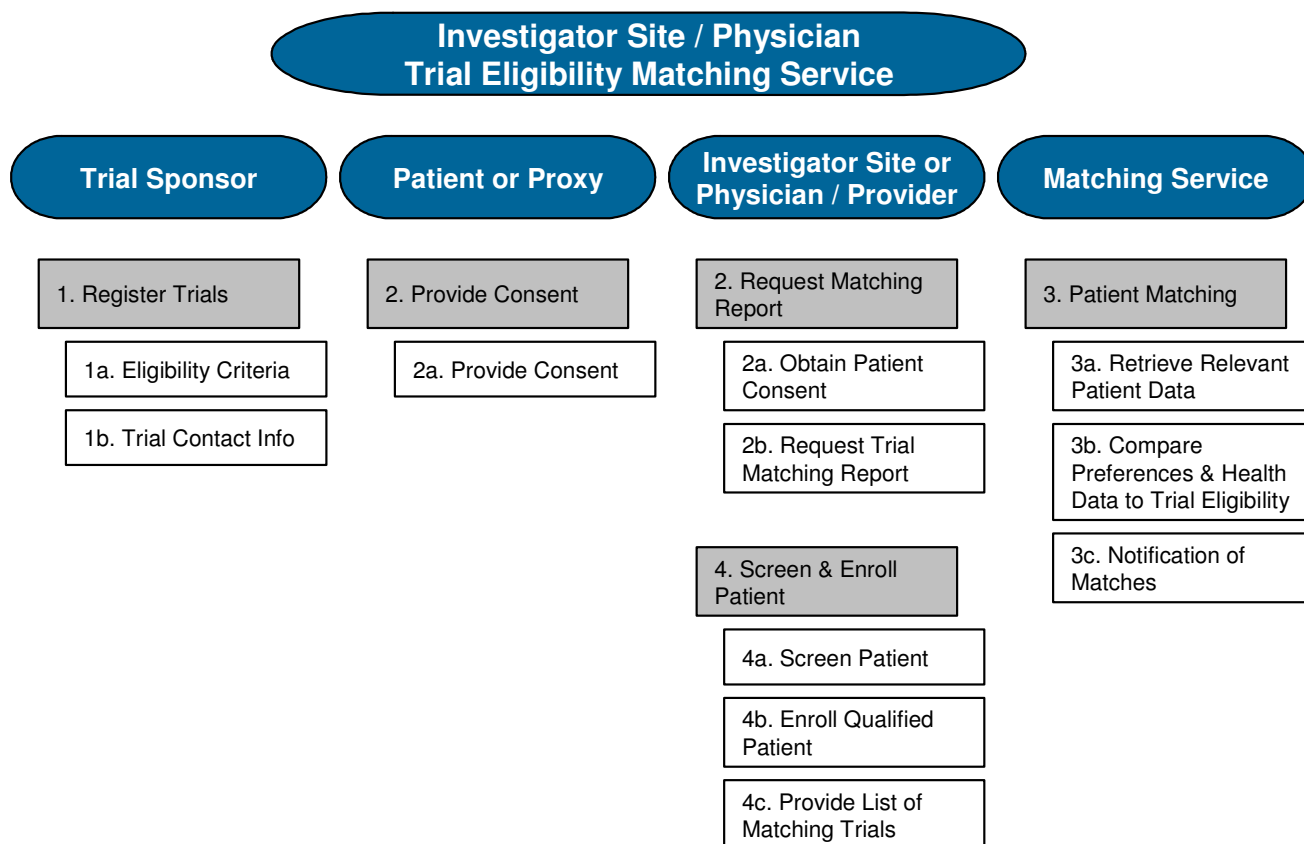
- b. Trial sites can select the clinical trials that are being run at their site from the registered trial list. This will allow the matching report to designate any matches to the site's trials separately from all other clinical trials.
- c. Trial site or physician office requests a report to identify all clinical trials for which the visiting patient(s) qualify. This step may occur before, during, or after a patient visit.

3. Patient is Matched to Trials

- a. Relevant information from the patient's longitudinal electronic health record is retrieved through a health information network. The source of the patient data may be the patient's PHR, the physician office or provider organization EMR system, or another health information data source. Data from all sources systems will create the longitudinal electronic health record for the patient, which will be used for trial matching.
- b. Patient's health information is compared to the pre-screening criteria of all registered clinical trials.
- c. Notification is returned to the trial site or physician office allowing them to use a secure site to retrieve the list of all trials for which the patient(s) qualify. If specified in the request, the matching list will return a yes/no answer for trials being run at the requesting trial site. The report will also include all other matching clinical trials.

4. Investigator Enrolls Patient or Informs Patient of Available Trials

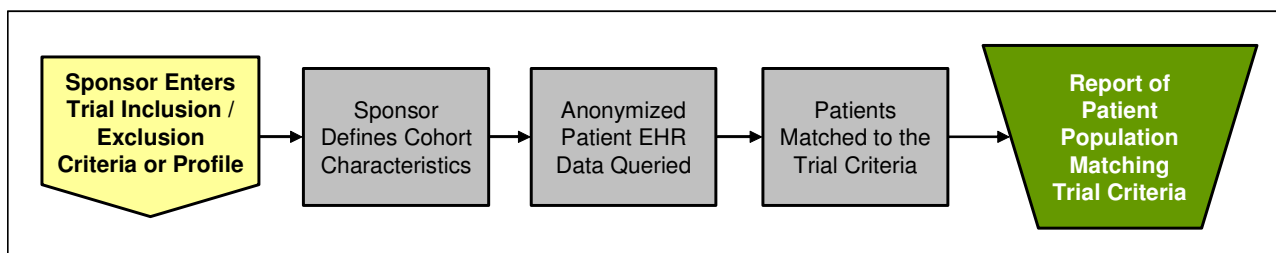
- a. If the matching report returns trials that the requesting investigator site is running, the investigator site screens the patient.
- b. If the patient qualifies for the trial, the investigator site enrolls the patient.
- c. If the report only returns trials being run by other investigators or the patient does not meet the requirements for the investigator's trial, the list of all matching clinical trials should be provided to the patient.

Stakeholder Perspectives:**Figure 8 – Stakeholder Perspectives – Investigator Site / Physician Service to Match Patients to Trials**

Scenario 3: Clinical Trial Enrollment Feasibility Analysis Service

The following diagram represents the process of determining the feasibility of successfully accruing patients for a clinical trial based on its pre-screening criteria. The sections below the diagram describe the sequence of events in more detail. The final diagram in this section shows the process from the perspective of each stakeholder group.

Figure 9 – Clinical Trial Enrollment Feasibility Analysis Service

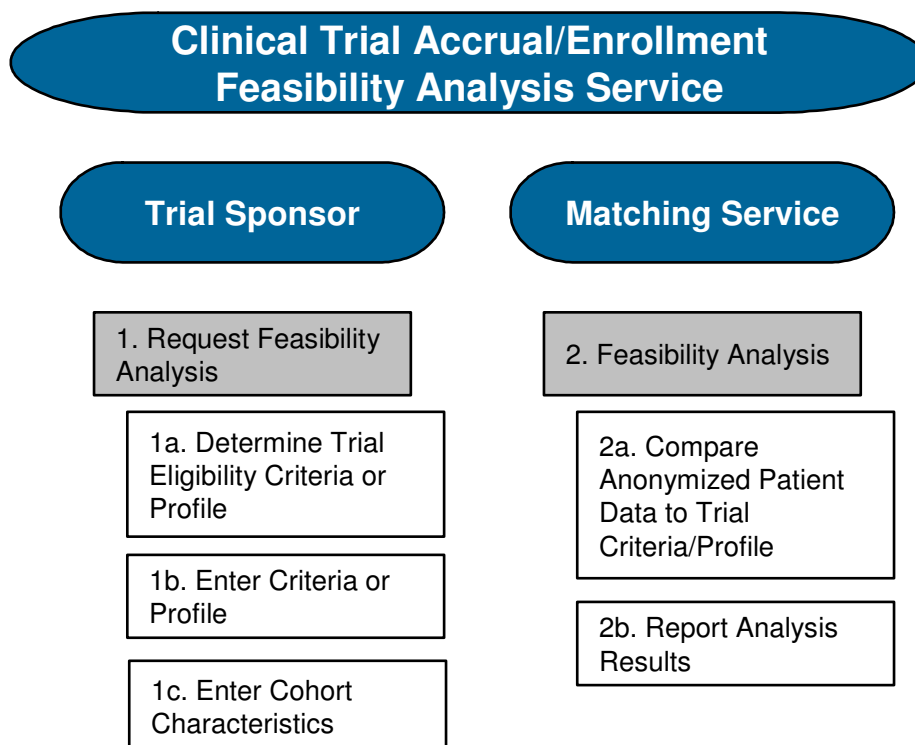


Process Flow:

1. Trial Sponsor Decides to Analyze Enrollment Feasibility
 - a. Trial sponsor creates a protocol or general trial profile with pre-screening criteria.
 - b. Trial sponsor enters detailed, structured pre-screening criteria or trial profile in matching service.
 - c. Trial sponsor enters preference for how the matching population is reported. This designation may include one or more cohort characteristics, including geography (e.g. by ZIP code, county, state, etc), race, gender, and other demographic distinctions.
2. Determine and Report the Number of Matching Patients
 - a. The matching service compares all available anonymized patient health information to the study's pre-screening criteria or profile.
 - b. The matching service provides a report of the number of patients matching the criteria by specified cohort characteristics. No information about the identity of patients is provided to the trial sponsor.

Stakeholder Perspectives:

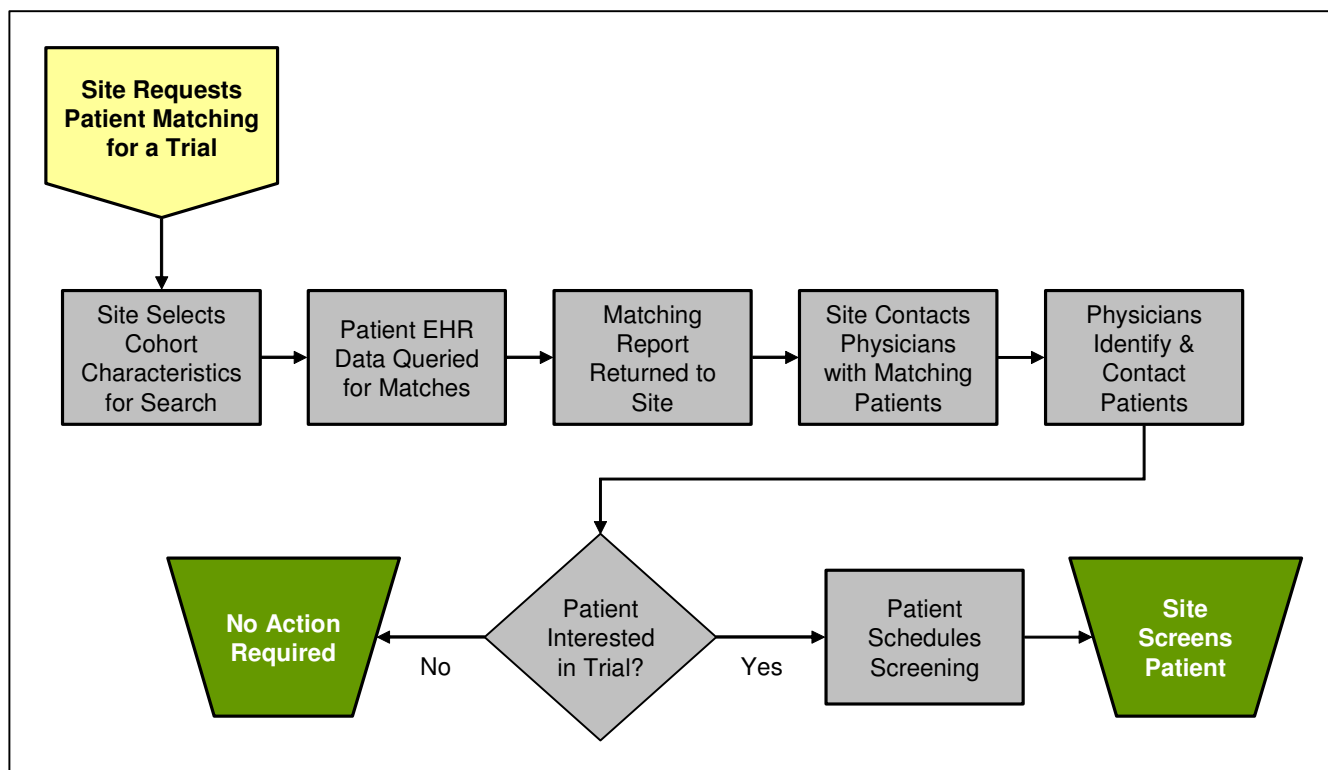
Figure 10 – Stakeholder Perspectives – Clinical Trial Enrollment Feasibility Analysis Service



Scenario 4: Inform Investigator of Qualifying Patients

The following diagram represents the process of notifying an investigator site of patients in a specified geography or cohort that qualify for the clinical trial(s) being conducted at that site. The sections below the diagram describe the sequence of events in more detail. The final diagram in this section shows the process from the perspective of each stakeholder group.

Figure 11 – Inform Investigator of Qualifying Patients



Process Flow:

1. Trial Sponsor Companies Register Clinical Trials
 - a. Sponsor companies enter structured pre-screening criteria in the public domain.
 - b. Sponsor companies enter contact information for enrollment in the study in the public domain. This information will vary by trial and sponsor.
2. Investigator Site Requests Report of Matching Patients
 - a. Investigator site designates trials it is conducting by choosing from the registered list.
 - b. Investigator selects the cohort characteristics to use when searching for matching patients. This designation may include one or more characteristics, including geography (e.g. by ZIP code, county, state, etc), race, gender, and other demographic distinctions.

- c. Investigator site can select whether it would like to be informed when new patients are identified that may qualify for their trials. This is a separate trigger for alerting the site of qualifying patients.

3. Patients are Matched to the Selected Trials

- a. Comparison is run using relevant health information of all patients that consented to trial matching against the structured protocol pre-screening criteria for the selected trials.
- b. A report is generated based on all patients matching its trials and the selected cohort characteristics. The report provides the names of physicians that currently treat the matching patients and the number of patients treated by each physician. The report does not identify the patients to the investigator site.

4. Investigator Contacts Physicians with Matching Patients

- a. Investigator site retrieves the report of physicians treating patients that qualify for the selected trials.
- b. Investigator site contacts these physicians to determine the patients' interest in being screened for and participating in the relevant trial(s). Physicians may need to provide consent to be contacted directly by investigators about their patients.

5. Physician Identifies and Contacts Patient

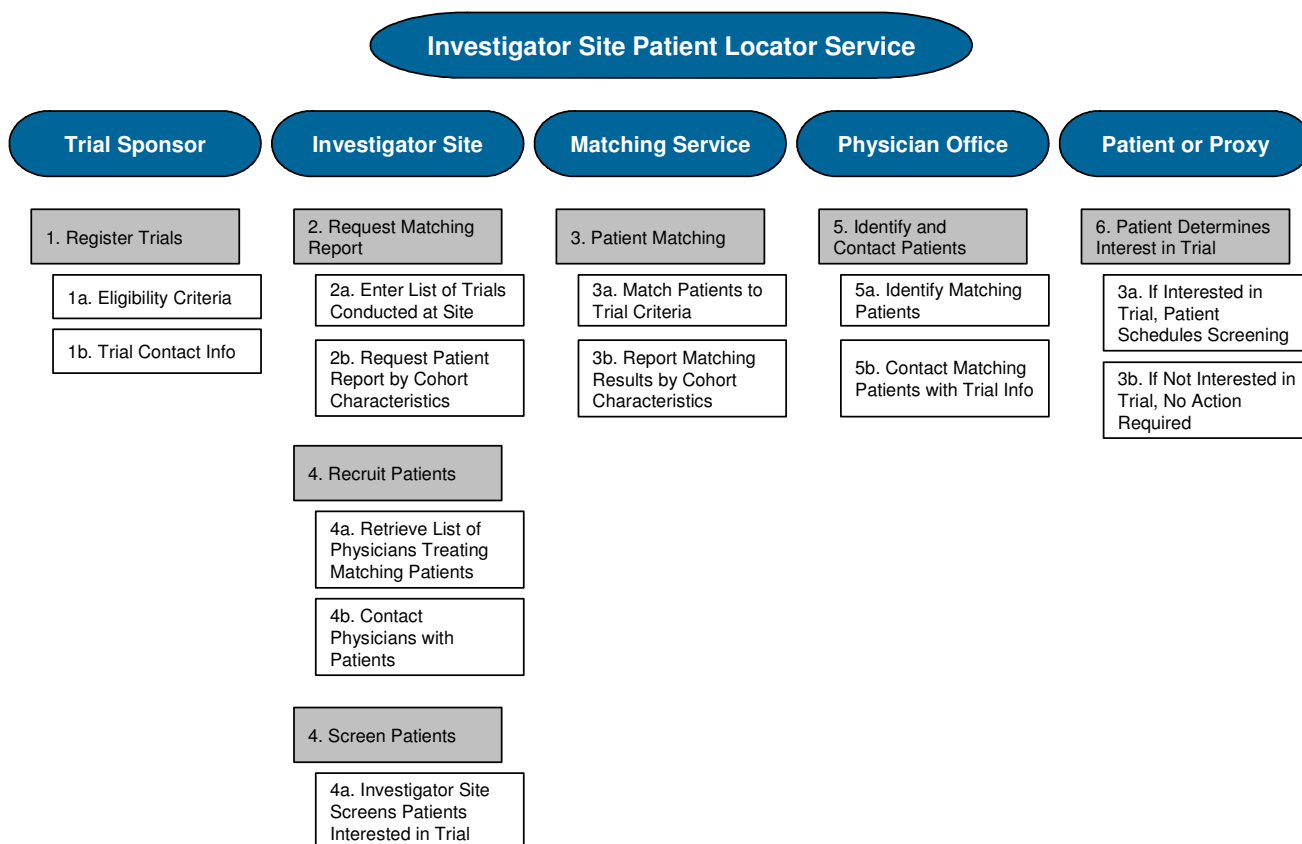
- a. Physician office identifies the particular patient(s) that qualify for the investigator's trial. Policy decisions and technology capabilities will determine how much information can be provided by the investigator site or the matching service to enable the physician office to identify the matching patient(s).
- b. Physician office contacts the patient(s) to determine interest in participating in the trial(s). The physician may consult the patient on the appropriateness of the trial and, if the patient is interested, the physician office will provide the patient the contact information for trial screening.

6. Patient Determines Interest in Trial

- a. If the patient is interested in the trial, he or she contacts the investigator site to schedule screening. The determination of interest in the trial may involve discussions with the patient's physician or an advocacy group in the particular condition, which can provide additional help in determining the best trial for the patient to pursue.
- b. If the patient is not interested in the trial, he or she does not need to take any action.

7. Investigator Site Screens Patient

- a. The investigator site screens patients that are interested in the trial(s) to verify that they meet the screening criteria and will be fit subjects for the trial.

Stakeholder Perspectives:**Figure 12 – Stakeholder Perspectives – Inform Investigator of Matching Patients**

Value Propositions:

This section will outline the value propositions related to the four scenarios identified in this use case. Each way in which the use case provides value to one or more stakeholder group(s) is outlined in this section along with a description of how the new processes and technology from these scenarios will enhance today's capabilities to connect patients to clinical trials. Key metrics will be identified that could be used to quantify the value derived by the stakeholders.

This section will include:

- Explanation of the benefit and value created for each stakeholder group by the scenarios described in this Connecting Patients to Clinical Trials use case.
- Key metrics that may be useful in quantifying the value of the use case.
- Some assumptions and challenges that may limit the value obtained by stakeholders.

This section will not include:

- Quantification of the key metrics for each benefit to stakeholders.
- Recommendations for business models by which stakeholders can contribute to the development and implementation of the scenarios described by this use case.
- Identification of proof of concept projects to demonstrate the value of the use case scenarios or how to overcome the preconditions and obstacles to achieve the value of the scenarios.

Value Propositions Matrix:

The table on the following page shows each of the value propositions, which stakeholders receive value, and which use case scenarios are involved in creating the value.

The value propositions are shown in the second column. The remaining columns to the right show whether each stakeholder group receives the stated value. Each cell will contain numbers that indicate which of the four use case scenarios provide the value to each stakeholder group.

Figure 13 – Value Proposition Matrix by Stakeholder and Use Case Scenario

#	Value Proposition	Stakeholders Receiving Value						
		Patients / Public	Physician Offices	Investigators / Sites / Study Coordinators	Clinical Trial Sponsor	Regulatory Agencies	Patient Advocacy Groups	Payers
1	Reduced Time/Effort for Patients to Find Clinical Trials For Which They Qualify	1, 2, 4					1, 2, 4	
2	Reduced False-positive Trial Screenings	1, 2, 4	1, 2, 4	1, 2, 4	1, 2, 4		1, 2, 4	
3	Increased Awareness of Clinical Trials As Treatment Options	1, 2, 4	1, 2, 4	1, 2, 4	1, 2, 4	1, 2, 4	1, 2, 4	1, 2, 4
4	Reduced Duration and Cost for Patient Accrual in Clinical Trials	1, 2, 3, 4	1, 2, 4	1, 2, 3, 4	1, 2, 3, 4	1, 2, 4	1, 2, 4	1, 2, 3, 4
5	Eliminate the Need to Manual Match Patients to Trials		1, 2	1, 2, 4				
6	Better Knowledge of How Many & Which Patients Participate in Clinical Trials	1, 2, 4	1, 2, 4	1, 2, 4	1, 2, 4	1, 2, 4	1, 2, 4	
7	Reduce Costs for Organizations that Currently Maintain Clinical Trial Registries and Matching Databases				1, 2, 4	1, 2, 4	1, 2, 4	
8	Increase Number of Trials in Indications with Unmet Patient Needs	3		3	3		3	3

Value Proposition Definitions and Key Metrics

The following subsections describe the potential value that can be provided to each stakeholder group through the four scenarios defined in this use case. Each subsection provides a description of the value proposition that explains how it improves on the current processes and systems used for connecting patients to clinical trials. It then lists one or more key metrics that can be used to quantify the value of the scenarios and compare them to today's benchmark metrics for clinical trials.

1. Reduced Time/Effort for Patients to Find Clinical Trials For Which They Qualify:

The process by which a patient finds a clinical trial today is time consuming and requires a lot of effort by the patient, a proxy or family member on behalf of the patient, the patient's doctor, or a patient advocacy group. There are many websites available today that list clinical trial information, but it can be time-consuming for patients to search through all of the available information to figure out which trials may be right for them.

Providing patients with a service that uses their electronic health records to automatically screen them against all registered clinical trials and provide a list of matching trials with a confidence interval indicated for the match has the following benefits:

- Comprehensive & Transparent Information Source:
 - i. Many of today's trial registry websites do not contain all available clinical trials and many doctors today are only aware of a limited set of clinical trials. The matching service would contain all registered clinical trials. Patients would, therefore, be assured that they received a matching list that took all clinical trials into account.
 - ii. Many of today's trial registry websites require patients to search for trials using free-text searches. The matching service would increase accuracy of searches by automatically matching structured information in the patient's health record to structured clinical trial pre-screening criteria, which will improve the accuracy of matching results.
- Active Trial Information Source:
 - i. Matching service automatically does the work to determine which trials the patient may qualify for based on the electronic health record.
 - ii. Matching service alerts the patient about newly registered clinical trials that match the patient's preferences and health record.
 - iii. This is much better than today's passive information sources, such as websites with trial registries, and will save the patient time and effort in finding clinical trials and determining whether they may qualify for the trials.
- Patients Control Information Flow:
 - i. Patients can enter their contact preferences using the matching service's online access system. They can specify the contact information to use to receive

information about matching trials and can specify how often they would like to be contacted with updates.

- ii. Patients can specify categories of trials that interest them to receive updates when new clinical trials are available in that category. This may allow patients that are interested in “lifestyle” indications, such as baldness, to learn about new clinical trials without the need for research.

The key metrics that may be useful in quantifying the time and effort savings for patients using the matching service described in this use case are:

- Average amount of time and effort patients spend searching for clinical trials today.
 - i. This may include the amount of time they spend talking to advocacy groups, talking to their doctors, and using trial registry and advocacy websites.
 - ii. This can be compared with the time and effort necessary to sign up for the matching service and receive the first trial matching report.
- Percentage of patients that would use matching service.
 - i. Determine percentage of patients that would consent to the use of their electronic data for clinical trial matching.
 - ii. Determine percentage that would sign up for the matching service, as opposed to using current mechanisms (doctor, advocacy group, website searches).
- Accuracy of today’s clinical trial searches.
 - i. Measure the accuracy of current searches of trial registry websites.
 - ii. May measure percentage of searches that give results that match the patient’s intention. May also measure percentage of searches that yield trials for which the patient may qualify.

2. *Reduced False-positive Trial Screenings:*

Many patients fail screening for clinical trials today, because they do not know whether they meet the inclusion and exclusion criteria for the trials. Patients get screened for a trial only to find out that some factor of their health prevents them from participating. Furthermore, patient screening for clinical trials takes up the patient's and investigator site's time and costs money, so failed screenings have negative impact on everyone involved.

Today's web-based searches to find information about clinical trials do not take into account all aspects of the patient's longitudinal health record. The clinical trial matching service described in this use case could reduce false-positive screenings by using patient EHRs to provide a list of potential clinical trials for which the patient may qualify. The matching service will supply a confidence interval for each matching trial that indicates the likelihood that the patient will pass screening based on the information available in or missing from the patient's EHR. These capabilities should reduce the percentage of false-positive clinical trial screening visits.

This reduction in false-positives will have the following benefits:

- Patient Expectations:
 - i. Patients will be given a clear indication of the likelihood that they will qualify for a clinical trial based on their electronic health record. This should set better expectations with the patient.
- More Efficient Use of Time:
 - i. Patients can reduce the amount of time they spend being screened for trials for which they clearly do not qualify.
 - ii. Physicians and healthcare professionals at investigator sites that are involved in screening patients for trials can spend less time screening patients that clearly do not meet the trial's criteria. They can spend their time screening patients that are more likely to qualify.
 - iii. Investigator sites can use the matching service to check patients that set up screening appointments and confirm the likelihood that the patient matches their clinical trial. This should allow them to avoid visits for patients that very clearly do not qualify for the trial based on pre-screening with the patient's EHR.
- More Efficient Spending for Trial Screenings:
 - i. Trial sponsor payments to investigators for patient screening will be more efficiently used to screen patients with higher likelihood of qualifying for the trial.
 - ii. A smaller percentage of false-positive trial screening visits should make cost of these visits more efficient for health insurance companies.
 - iii. Patients will reduce or eliminate the amount they spend on co-payments for false-positive clinical trial screening visits.

- iv. Patients will reduce out of pocket travel related costs spent on trips to distant investigator sites.

In describing these benefits of reduced false-positive screenings, it is important to note that we have assumed that all of the “kinks” have been worked out in the algorithms used to match patient EHRs to structured trial pre-screening criteria. We have assumed that the matching algorithms are able to produce a list of trials with a reasonably accurate confidence interval. There will certainly be a period of time when the matching algorithms are being developed when false-positive screenings may be increased, because patients will receive longer lists of matching trials that may over or under represent the likelihood of the patient qualifying. During this development period for the matching algorithms, the time, effort, and cost-savings benefits described above may be reduced.

One mechanism that may be employed to minimize the impact of false-positives during this development period for the matching service is online, electronic questionnaires that patients are asked to fill out before setting up their screening appointments. Asking patients several key questions related to key inclusion or exclusion criteria for the trial (e.g. pregnancy, smoking history, etc) could help minimize the impact of false-positive results from the matching service.

It is also important to note that the trial matching service and confidence intervals in trial matches will not necessarily reduce the pure number of false-positive screening visits. Ideally, the matching service will increase awareness and interest in clinical trials and, in turn, increase the total number of screening visits for trials. Even if the matching service reduces the percentage of false-positive screenings, the increase in total screening visits may mean that there is still a larger quantity of false-positive screenings.

The key metrics that may be useful in quantifying the time and cost savings for patients and physicians and the improvement in patient expectations about qualifying for trials are:

- Patient Expectations:
 - i. Percentage of patients that do not pass pre-screening today. (i.e. screen-fail rate).
 - ii. Percentage of screen-fails that could have been screened out using EHR-enabled matching.
- Time Savings – Investigators & Healthcare Professionals (HCPs):
 - i. Amount of time spent on average by investigator and other healthcare professionals (HCPs) at the site for each screening.
 - ii. Combine average time spent with screen-fail rate to determine average time spent by investigators/HCPs on failed screenings today.
 - iii. Time savings for investigators/HCPs based on percentage of failed screenings that could be avoided with EHR matching.
- Time Savings – Patients:
 - i. Use the same three metrics as Investigators & HCPs (see above), but for patients.

- Cost Savings:
 - i. Average cost of time spent by investigators/HCPs on failed screenings (use time metrics above).
 - ii. Average cost of screening visits to insurance companies. Combine with screen-fail rate to determine how much failed screenings cost.
 - iii. Average co-payment for patient for screening visits. Each avoided screen-fail saves patient this co-payment or allows them to use it on a trial for which he/she will more likely qualify.

3. Increased Awareness of Clinical Trials As Treatment Options:

The ability to provide patients, physician offices, and investigator sites listings of clinical trials for which a patient matches will greatly improve the awareness of clinical trials as treatment options for the patient. In today's world, patients rely on sources such as their physician, their friends and family, websites, advertisements, and advocacy groups to get information about clinical trials available for their conditions. Each of these sources has different information about which clinical trials are available and appropriate for the patient, but there is currently no single source of information that includes all clinical trials and tailors the information to a specific patient's health.

The matching service described in this use case can provide this information to patients, physician offices, and investigator sites to increase the overall knowledge of the available clinical trials and provide the patient with more options for treatment. The benefits of these clinical trial matching services are:

- More informed treatment decisions:
 - i. Physicians will be better able to determine all available treatment options for the patient, including clinical trials. This should lead to more informed treatment decisions.
 - ii. Patients will be empowered with unbiased, personalized trial matching lists to better participate in their treatment decisions when speaking with their physician.
 - iii. Matching service will enable patients and physicians to learn more about clinical trials by including sponsor-provided contact information to learn more about the trial. This additional information could be a link to a website, a phone number to call for more information, or a listing of trial investigator contact information.
- Increase physician awareness of clinical trials:
 - i. Physicians will be aware of more clinical trials for various conditions, because they will be able to see information about all clinical trials for which their patients qualify.
- Provide lower cost treatment options:
 - i. Many clinical trials provide treatments at no cost to patients. Increasing understanding of all available clinical trials will provide lower cost treatment options for patients.
 - ii. If patients participate in clinical trials and treatment is funded by trial sponsors, this may reduce the cost of treatment for that patient's insurance company.
- Added control of clinical trial information for regulators:
 - i. Regulatory agencies will be able to control the quality and content of the clinical trial information supplied through the matching service to ensure it is unbiased, complete, secure, protects privacy, and meets all applicable regulations.

It is important to consider that physicians may not want to be responsible as the source of clinical trial information for their patients. Therefore, the only way to fully ensure that patients know about all possible clinical trials is to provide matching reports directly to patients. Ideally, the patient will receive the matching trial list and the physician will also review the matching trial list when determining the best treatment option for the patient.

The key metrics that may be useful in quantifying increased awareness of clinical trials as treatment options are:

- More informed treatment decisions:
 - i. Current percentage of trials of which patients, physicians, and advocacy groups are aware and for which the patient may qualify.
 - ii. Percentage of patients, physicians, and advocacy groups that are aware of current clinical trial registries and clinical trial information sources.
 - iii. Track inquiries about trials. Seeking more info and asking how to get screened. Measure before and after number of inquiries with pharma.
 - iv. Current percentage of patients participating in clinical trials compared to the percentage after this use case is implemented. Survey to find out how patients found out about clinical trials in which they enrolled.
- Increase physician awareness of clinical trials:
 - i. Percentage of trials of which physicians are aware and for which the patient may qualify.
 - ii. Once matching service is available, survey the percentage of physicians that find out about clinical trials for first time through the patient matching service.
- Provide lower cost treatment options:
 - i. Determine the average price of leading treatment options in various conditions, estimate how many patients would select a clinical trial instead, and estimate cost savings to patient and insurance company.

4. *Reduced Duration and Cost for Patient Accrual in Clinical Trials:*

Long durations for patient accrual in clinical trials today cause costly delays for trial sponsors. Patient recruitment expenses add to the large cost of developing drugs and each day that the trial is delayed is another day that the new treatment is not approved for use by the patients that need it.

The matching service described in this use case can provide better information to patients, physician offices, and investigator sites to speed the identification of clinical trial candidates. The matching service can also be used by clinical trial sponsors to determine the feasibility of accruing enough patients before beginning studies. These clinical trial matching services lead to the following benefits:

- Shorter Patient Accrual Times
 - i. Providing patients and physicians with listings of clinical trials for which the patient may match could lead to more interest in clinical trials as treatment options, which in turn could lead to more patients enrolling in clinical trials. Ideally this can shorten patient accrual time for some trials.
 - ii. Providing investigators with information about physicians who are currently treating patients that match their trial's pre-screening criteria could help the investigator recruit patients more quickly. This may reduce the duration of patient accrual for the investigator's trials.
 - iii. Reducing patient accrual times may lead to shorter overall clinical trial timelines, thus improving the chances of getting the investigational drug approved faster and into the hands of patients sooner.
- Reduce Costs of Patient Accrual
 - i. Reducing the duration of patient accrual means that investigators and their staff will need to spend less time during patient accrual, leading to reduced cost of this phase of the trial.
 - ii. If patient accrual for the trial is sufficiently driven by patients learning of the trial through the clinical trial matching service, investigators and sponsors may need to spend less on advertising the clinical trials, thus reducing the cost of the patient accrual phase.
 - iii. The ability of trial sponsors to determine how many patients with various cohort characteristics (including geography) meet the pre-screening criteria for their trials could allow them to accrue patients using fewer investigator sites, thus reducing site startup costs.
- Avoid Delays Due to Trial Design
 - i. Clinical trial sponsors can conduct more statistically powerful patient accrual feasibility analyses with larger sample size of data. These studies can be used to determine whether the clinical trial's design, including the pre-screening criteria, will provide enough patients to conduct the trial.

- ii. Adjusting clinical trial design before patient accrual begins can allow sponsors and investigators to avoid costly delays that occur when they need to adjust the trial protocol during the trial.
- iii. Trial sponsors will be able to determine whether patient accrual within the trial's current design will be possible and cancel trials earlier if recruitment will be infeasible.

When considering the value added by the service for investigators to locate patients meeting their clinical trials, one must consider that investigators may need to provide an incentive to physicians to refer their patients for the trial. Some physicians may be unwilling to refer their patients for the trial because they feel that they will lose the patient to the investigator, which would be financially detrimental. One place where this obstacle may not be a problem is within large institutions that conduct clinical research. When patients are seen by a physician within the investigator's own institution, this service would enable the investigator to find matching patients within their own organization.

For clinical trial feasibility analyses, it is important to consider that the analysis will only give the number of matching patients with the specified cohort characteristics. There may be socio-economic and other factors that would prevent or dissuade these patients from participating in the clinical trial. Actual yield of patients for the trial will differ from feasibility analysis results.

The key metrics that may be useful in quantifying the benefits of reduced time and cost of clinical trial patient accrual are:

- Shorter Patient Accrual Times
 - i. Current average patient accrual duration by phase, type of trial, therapeutic area, and other factors
- Reduce Costs of Patient Accrual
 - i. Current average patient accrual cost by phase, type of trial, therapeutic area, and other factors
 - ii. Number of enrolled patients per site. Estimate impact of matching service to determine reduction in number of sites.
 - iii. Current average number of sites used for clinical trials and current average marketing spend by a site to recruit patients. Estimate total cost savings if marketing reduced at each site and fewer sites necessary.
- Avoid Delays Due to Trial Design
 - i. Current cost of anonymized patient data used by companies to conduct feasibility analyses for protocols
 - ii. Determine cost of clinical trials whose design leads to slow recruitment or trial cancellation. Determine cost that could be saved by avoiding the start of recruitment for these trials.

5. Eliminate the Need to Manual Match Patients to Trials:

Healthcare professionals working at investigator sites and some physician offices today spend time manually comparing patient charts to clinical trial pre-screening criteria to determine for which trials the patient may qualify. This same manual matching is also done by some patient advocacy groups today. This is a very time-consuming process for these healthcare professionals.

The matching service described in this use case could eliminate the need for this manual matching by providing automated matching based on the patient's electronic health record. This would save time for these healthcare professionals and allow them to refocus their time on other aspects of patient care.

The key metrics that may be useful in quantifying the time savings for these healthcare professionals are:

- Time and effort of current patient matching process by healthcare professionals in physician offices
- Time and effort of current patient matching process by healthcare professionals in investigator sites
- Time and effort of current patient matching process by patient advocacy groups

6. Better Knowledge of How Many & Which Patients Participate in Clinical Trials:

In order to prevent trial matching notifications for clinical trials in which a patient is already enrolled, it will be necessary to track which patients are enrolled in which clinical trials. If this information can be anonymized and aggregated, it may provide the ability to know how many patients in a particular cohort are participating in a given one trial or a group of trials. This would enable better utilization of patient populations.

One challenge to tracking in which clinical trial a patient is enrolled is that some trials are blinded. The matching service capability must maintain security of information about trials that are blinded. If, however, the challenges to tracking the enrollment of patients clinical trials, the information can enable better use of patient populations and additional research about the willingness of patients to enroll in clinical trials.

7. *Reduce Costs for Organizations that Currently Maintain Clinical Trial Registries and Matching Databases:*

The matching service described in this use case would contain registered information about all clinical trials and would provide personalized listings of clinical trials for which a patient matches the pre-screening criteria. Furthermore, trial sponsors would be able to provide contact information for patients to get more information about each clinical trial.

Having one source of clinical trial registration and matching information would eliminate the need for many of today's duplicative clinical trial registry and matching websites. These organizations could reduce the expense of building and maintaining their databases. These current data sources include:

- Patient advocacy groups that have clinical trial and patient matching databases.
- States that have built or are considering building their own trial registries.
- Existing websites containing clinical trial registries and matching services.

We recognize that there are some organizations that currently make money by providing these registries and matching services to patients. The concept of this use case is to create a single source of information and a robust capability to match patients to clinical trials using longitudinal electronic health records. In order to do so, there must be one "source of the truth" for clinical trials. Some regulation would likely be necessary to define this single source and the conditions under which it is built and operated.

8. *Increase Number of Trials in Indications with Unmet Patient Needs:*

Today's available patient information for patient accrual feasibility analyses of clinical trials may not be sufficient to identify patient populations for some indications. Access to longitudinal electronic health records from large patient populations may allow researchers to identify new areas of unmet medical need that have a large enough patient population to conduct clinical trials.

This improved feasibility analysis service may allow clinical researchers to conduct clinical trials that currently would not be pursued due to a lack of available data to show that the necessary patient population exists. This improvement could lead to an increased number of clinical trials and marketed drugs for certain diseases. Trial sponsors may be able to identify new areas of unmet medical need and increase development efforts for these areas with confidence in the size of the patient population.

Glossary of Terms

The following table provides definitions for terms that are used throughout this use case document.

Figure 14 – Glossary of Terms

Term	Working Definition
Anonymized Data	Data that has been rendered non-attributable to a specific individual by removing identifying information.
Pseudonymized Data	Data that has been manipulated so that real-world identifiers for the specific individual have been removed, and an alternative identifier added. Such identifier may, or may not, be used consistently across multiple data sets. Such identifier may, or may not, be reversible to permit the identification of the patient.
Electronic Health Record (EHR)	All electronic information related to the health of one patient/consumer that exists. This information may be located in many different source systems in different organizations and geographies.
Electronic Medical Record (EMR)	All electronic information related to the health of one patient/consumer that exists within the systems of one organization/entity. This information may reside in more than one system, but those systems must all reside within one organization.
Personal Health Record (PHR)	Electronic health information that a patient/consumer has collected from one or more sources for the purpose of understanding his/her health status and sharing it with his/her physician(s).
Nationwide Health Information Network (NHIN)	A nationwide health information network is not a single entity, but a system of systems. It is envisioned that such a network would provide for the secure exchange of health information for many uses, in multiple ways, and by a number of different health information network providers. A nationwide health information network can also address needs relative to security services, privacy protections, and methods to identify (or de-identify) individuals who are the subject of the health information exchanged.
Health information exchanges (HIEs)	Networks that have been established to exchange health information among several healthcare organizations.
Interoperability	The ability to exchange and use information (usually in a large heterogeneous network made up of several local networks).

Term	Working Definition
Longitudinal health record	The accumulation of all health-related information about an individual from many clinical encounters over a long period of time. This information may be contained in many different healthcare provider locations.
Clinical Trial Sponsor	A company, institution, or organization that initiates, manages, and/or finances a clinical trial.
Patient Proxy	A person designated to make decisions on behalf of a patient who is not capable of making them on his/her own. One example of a proxy is a parent who makes decisions on behalf of their minor child.