An Overview of Cancer Clinical Trial Matching Services

Summary
Clinical trial matching services facilitate patient enrollment in clinical trials by identifying potential trials for interested patients and their proxies (e.g., caregivers and providers), and in some cases by providing other support services such as educational materials or personnel who can answer questions or assist patients. While all services involve providing a list of trials to those using them, the actual goals of the services vary significantly, from largely fostering patient interest in clinical trials by showing them the breadth of trials open for their cancer, to full matching and enrollment assistance using detailed assessment of eligibility criteria, patient clinical data, and patient preferences. Below, we describe the attributes of services ranging from simple to more advanced.

Introduction
Clinical trials are pivotal to advancements in cancer treatment, but patient enrollment in these trials remains a challenge. Matching and enrollment can be driven either by healthcare providers or by the patient or their proxies (e.g., family members or caretakers). Studies show that the vast majority of cancer patients who have enrolled in a clinical trial (66 percent) became aware of the opportunity because they were approached by their physician or the staff from the clinical trial.¹ Six percent of patients found their trial through self-service matching services and a similar number found their trial through matching services provided by advocacy organizations.¹ This paper examines clinical trial matching services that either directly serve patients or are facilitated through patient advocacy groups. Services exist that are targeted toward providers and institutions as well, and a brief discussion of them can be found at the end of the paper.

While there are thousands of clinical trials underway in the U.S., a specific patient would only qualify for a small portion of them. This is because trial designers create eligibility criteria that individuals must meet to participate in clinical trials, which is critical for giving researchers confidence the trial results are due to the treatment and not an outside factor (confounding variable). At the broadest level, eligibility criteria include basic attributes that patients must possess to participate in a trial, such as a specific type and stage of cancer. These basic eligibility criteria are easy for patients to understand; however, by themselves they are not enough to fully characterize the types of patients sought for a given trial. Eligibility for a clinical trial is further determined by additional factors such as prior treatment history, presence of other diseases, overall...
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health and functionality, and whether the patient’s cancer has molecular markers that affect the cancer’s response to treatment. While these detailed inclusion/exclusion criteria are critical to helping researchers understand the impact of a treatment on a patient, they can be confusing for patients to navigate.

Clinical trial matching services identify trials that patients might be eligible for by comparing patient characteristics against the eligibility criteria of available trials. The degree of specificity of the matches varies significantly from service to service depending on the goal. For instance, services with a primary aim of fostering patient interest in trials typically require minimal information about the patient, like their diagnosis and zip code, to present a broad list of available trials that help patients understand the types of trials open for their cancer. These services focus on identifying clinical trials based on a consideration of the broadest eligibility criteria rather than more detailed inclusion/exclusion considerations.

Other services seek to help patients who are already interested in trials find a narrower list of potential trials that are most suitable for them. These services look beyond the basic eligibility criteria and examine the additional considerations for participation in a trial. Regardless of their intended goal, all services utilize either a web interface or a call center to connect with patients, although many services offer both options.

All clinical trial matching services have four key attributes, but differ significantly in either the quality, level of detail, presentation, or comprehensiveness of each attribute, as described below.

• **Patient Data** - Patients searching for available trials have unique clinical characteristics that may make them eligible for some trials and ineligible for others. Additionally, patients may have individual preferences, like how far they are willing to travel to take part in a trial and the type of intervention they are willing to undergo (e.g. surgery, infusion). Matching services vary by the type and amount of patient clinical and preference data used to screen for matching trials.

• **Clinical Trials Data** - All matching services must access one or more databases containing information about available trials, but these databases differ in their content.

• **Matching Process** - All services compare patient data with trial data to create a list of potential matches. However, they vary in how they help patients identify and prioritize trials that might be a good match.

• **User Experience** - Every service varies in how they engage patients and the degree to which they help patients understand search results and take next steps to enrollment.
Simple Services Foster Patient Interest and Awareness in Clinical Trials

When a patient is diagnosed with cancer, they face many decisions, including the selection of a preferred course of treatment. Clinical trials are an important treatment option, but frequently patients are unaware of them. The simplest services are designed to allow patients to explore trials as an option and typically require very little patient effort. Often by answering as few as three questions about the cancer type, age, and zip code, a patient can use simple services to identify a list of trials they may be eligible for. However, the list of trials identified by these services is typically quite long and the patient may not actually qualify for many of the trials identified because detailed inclusion/exclusion criteria were not part of the screening questions. The primary goal of these services, however, is not to provide a detailed trial match, but rather it is to provide a patient with an increased awareness of trials by providing sample trial opportunities that can help them consider more fully whether they would be interested in participating in a trial. Patients are typically encouraged to take the list of trials generated by the service to their provider, who can then further discuss trials as an option and more fully evaluate the patient for eligibility. Two notable examples of simple services include the National Library of Medicine’s clinicaltrials.gov (described below) and the National Cancer Institute’s (NCI’s) Contact Center.
**Case Study:** National Library of Medicine’s Clinicaltrials.gov ([https://clinicaltrials.gov/](https://clinicaltrials.gov/))

**Modality:** Web-based service

**Description:** Clinicaltrials.gov is a public, government-run resource that was originally designed as a resource for researchers, but has subsequently been employed to provide patients, health care professionals, and researchers with information about clinical studies on a range of medical conditions. The only information that cancer patients are required to provide to identify clinical trials is their diagnosis. The service leverages predictive text to help guide patients to the appropriate search term. Once a patient runs a search, he or she can narrow the search results using checkboxes on the results page. Using these functionalities, a patient can filter the search results based on the phase of the clinical trial and basic attributes that clinical trials are recruiting for, such as age and gender. Since clinicaltrials.gov was not originally designed for a public audience, the clinical trials descriptions often contain medical jargon and may not include details that are more important to a patient when selecting a trial to participate in. Additionally, patients often end up with a long list of trials that require further examination by medical professionals because the service only aims to provide an overview of existing clinical studies and does not seek to match patients based on detailed clinical criteria. To help patients with next steps, the service enables patients to quickly and easily download the results to share with providers or save for reference.

**Amount of Patient Data Required to Identify Matches:** Minimal – cancer patients only have to provide their diagnosis in order run a search for open trials.

**Features of Clinical Trials Database:** The service pulls clinical trial information directly from clinicaltrials.gov.

**Matching Process:** The service utilizes predictive text for the disease data field to help guide patients to the appropriate search term. After running an initial search, patients are also able to narrow the search by a limited number of parameters by utilizing a series of check boxes and data fields on the results page. However, as a basic service that aims to provide patients and their proxies with an overview of open trials, it does not have many features to actually identify the most appropriate trials.

**User Experience:** The service enables patients and their proxies to download the search results so they can share them with providers or reference them later. However, the search results do not contain patient education materials or help patients understand the clinical trials descriptions, which typically use medical or scientific terminology.

#-Predictive text provides a drop-down list suggested terms based on the words a user begins typing
**Advanced Functionality Allows More Tailored Matching**

Simple services like clinicaltrials.gov can be effective as a gateway for fostering patient interest, but the bare-bones features can produce an unsatisfactory user experience and result in a long list of clinical trials that patients and their proxies must sort through to determine eligibility. As a result, many organizations have developed more advanced services by capturing more patient data, developing more robust clinical trials databases, enhancing the matching process, or improving the user experience.

**Patient Data**

Compared to simple matching services, services with advanced functionality such as BreastCancerTrials.org (see below for more information) require patients to provide more detailed clinical and patient preference data (e.g., staging of cancer, prior treatment, laboratory results, number of miles the patient is willing to travel for a clinical trial). Some of this data requires patients to reference medical records and lab reports. While more cumbersome for patients to navigate, the trials identified by these services are more likely to be suitable for the patient for enrollment.

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**Figure 1:** Consideration of additional patient data further refines the clinical trials considered for a patient and makes a match more accurate. Data may include clinical characteristics like genetic mutations, but may also include patient preference data such as location of the trial or type of therapy.
Case Study: BreastCancerTrials.org ([https://www.breastcancertrials.org/bct_nation/home.seam](https://www.breastcancertrials.org/bct_nation/home.seam))

Modality: Web-based service

Description: BreastCancerTrials.org is a web-based service. Patients are required to complete an extensive clinical profile to assist with matching. To ensure that patients are entering accurate search parameters (e.g., comorbidities, mutation status), the service relies on the use of checkboxes, which eliminates the chance of users entering unrecognized terms. Based on the checkboxes that the patient selects, the service identifies additional relevant data fields to narrow the search (e.g., if the patient indicates they received chemotherapy, the service includes additional data fields and checkboxes for the type of chemotherapy the patient received). While their clinical trials database is based on breast cancer trials and information found in clinicaltrials.gov, the service also partners with trial sponsors to ensure that trial information in the BreastCancerTrials.org database is further updated on a regular basis to facilitate more accurate matching and patient information. Additionally, BreastCancerTrials.org also converts the medical terminology in clinical trial descriptions into patient-friendly language and the interface is easy to navigate, allowing patients to quickly see pertinent details, such as the distance from trial sites and anticipated treatment frequency.

Amount of Patient Data Required to Identify Matches: The service requires patients to provide many clinical data points, including lab and imaging results and treatment history. The exact amount of patient data required to conduct a search varies based on where the patient is in her treatment course (e.g., newly diagnosed but not yet started treatment, or currently on hormone treatment after surgery) and responses to questions (certain responses trigger additional questions).

Features of Clinical Trials Database: The service has a proprietary breast cancer-specific database that is based on data from clinicaltrials.gov that has been augmented with updated data from researchers. Clinical terminology in the database is translated into patient-friendly language.

Matching Process: The service leverages checkboxes and branching logic to ensure that patients are entering accurate and pertinent search parameters, increasing the likelihood the search will yield relevant trials.

User Experience: The service ensures that data entry is easy for patients through the use of checkboxes, patient-friendly language, and presentation of search results in an easy-to-navigate format.
Clinical Trials Data

Data about clinical trials, including which trials are open and descriptions of these trials (e.g., goals of the trial, eligibility criteria, contact information of the researchers) are located in databases. These databases are used by services to identify trials for patients. In the U.S., two publicly available governmental databases are widely used by services because they contain extensive listings of open trials – the National Library of Medicine’s clinicaltrials.gov and NCI’s Clinical Trials Reporting Program database.

Clinicaltrials.gov contains all federally and privately funded trials of an experimental nature for all medical conditions and was launched in 2000 by federal mandate. It is both a service for patients to find clinical trials (described above) and a clinical trials database that many other services use as a starting point for building proprietary databases. When the service was originally created, Congress only required clinical trial sponsors to register their studies with the National Library of Medicine. Since then, Congress has enacted additional legislation, including the 21st Century Cures Act, that increases the types of clinical studies that must be registered and the types of information that researchers must provide. As of August 2017, clinicaltrials.gov contained 44,258 actively recruiting studies in the U.S. and internationally. On the other hand, NCI’s Clinical Trials Reporting Program database contains cancer-specific studies that are either industry-sponsored trials conducted at NCI-designated cancer centers or NCI-sponsored trials. It contained 5,358 cancer studies in August 2017.

Many services utilize these public databases directly, particularly clinicaltrials.gov because it is the more extensive of the two. When services utilize NCI’s Clinical Trials Reporting Program database, it is often in conjunction with clinicaltrials.gov. However, the information in these databases are sometimes outdated or incomplete because researchers vary in how often they update the information. Additionally, because clinicaltrials.gov was originally created as a repository of clinical trials for research purposes, much of the information contained in it caters to the interests of researchers (e.g., researcher publications, primary and secondary outcomes) rather than the interests of patients who are trying to select a clinical trial. The descriptions of clinical trials, including inclusion/exclusion criteria, are also typically captured in narrative, unstructured format, which makes it difficult for patients to search and identify relevant trials that they are eligible for. As a result, when patients utilize services that rely directly on the clinicaltrials.gov or trials.cancer.gov databases, they may be frustrated by missing or inaccurate information if they further explore enrollment in the trial. Examples of common inaccuracies include trial sites being listed as open when they are not, incorrect indication of whether the trial is enrolling, contact information for site investigators, or eligibility criteria.
To increase the utility of search results, many services use information from these governmental databases as a starting point for creating their own proprietary databases in which information about the trials is augmented. There are a number of ways services augment information in their clinical trials databases. One way is to create a database specific to a type of cancer, which increases the likelihood that the trials identified are relevant to the patient’s cancer type. For example, BreastCancerTrials.org contains only open trials for breast cancer. Services like Antidote (described in more detail below) have augmented clinical trials information by querying trial sponsors directly to request additional information that is not available in the clinicaltrials.gov database. A few services are also working on structuring and standardizing otherwise free-text inclusion/exclusion criteria to make it easier for patients to filter out trials for which they are ineligible. Improving the information in clinical trials databases ensures that patients are receiving accurate and relevant information, which is critical for services whose goal is to fully enroll patients into a matching clinical trial. Such detail, however, is not as important for simpler matching services that aim only to show patients what a trial might look like or the breadth of options open for their cancer.
Matching Process
Improvements in the matching process itself can lead to greater confidence that the trials identified are relevant and appropriate for a patient. There are a number of ways services have leveraged technology and human resources to enhance the matching process. One way web-based services have leveraged technology to enhance the matching process is through the creation of robust algorithms to ensure that all iterations of a patient’s search term are searched. For example, if a patient or call center staff types in metastatic breast cancer, a robust search algorithm will search for all iterations of it (e.g., stage IV breast cancer, advanced breast cancer). Alternatively, some web-based services use predictive text or checkboxes to ensure that patients are entering the right search terms.

Case Study: Antidote (https://www.antidote.me/)

Modality: Web-based service

Description: Antidote has a range of technology solutions that serve both researchers and patients. Antidote Match is their patient-facing platform through which patients find potential trial matches. Their trial matching engine uses structured eligibility criteria (using industry standard and custom-designed ontologies), proprietary algorithms, and machine learning to explore a patient’s eligibility for every trial. Patients can answer a handful of questions about their health, and the Antidote Match engine will traverse thousands of clinical trials to provide matching studies in their neighborhood.

With each additional question that a patient answers, Antidote Match narrows the list of matching trials. Antidote aims to ask patients fewer than ten questions to avoid being cumbersome to patients. The descriptions of clinical trials are presented in a visually friendly way and also include key functionalities for following up, including allowing patients to email themselves with the trial information, including site-specific contact information.

Amount of Patient Data Required to Identify Matches: While only four data points (cancer type, patient location, age, sex) are required to conduct a search, the service asks for additional cancer-specific questions (usually up to 10) to refine search results.

Features of Clinical Trials Search Tool: Antidote pulls data from clinicaltrials.gov, structures this data using medical ontologies, then runs it through proprietary algorithms to generate questions to match patients to trials.

Matching Process: The search engine dynamically generates simple health questions to narrow a patient’s trial results list to only relevant trials.

User Experience: The service ensures that data entry is easy for patients with a conversational flow, and turns key medical terminology into patient-friendly language. Trial descriptions are presented in an easy to navigate format.
Another way to enhance the matching process is by leveraging human resources in lieu of technology to help patients prioritize results after a search has been conducted and aid in patient decision making. For example, Smart Patients (described below) ranks trials based on other patients’ perceptions of the trial and experience of being on the trial. Services like the American Cancer Society’s Clinical Trials Matching Service (described below) and the Leukemia and Lymphoma Society’s (LLS) Clinical Trials Support Center (described in user experience section below) use registered nurses, specially trained in hematologic malignancies to respond to callers requesting help with identifying the most relevant trials. Leveraging a human connection to help patients sort through concerns about trials increases patients’ understanding about available options and helps patients prepare for a consultation with their treating physician about available options.

**Case Study:** American Cancer Society’s Clinical Trial Matching Service  (note this service has been discontinued)  

**Modality:** Telephone-based service

**Description:** The service is a help line for patients wanting to learn more about their cancer and treatment options, including clinical trials. Their staff gather necessary clinical information about the patient over the phone, including diagnosis, age, location, performance status, and common genetic mutations. After collecting this information through an informal conversation with the patient, staff use eviti’s TrialCheck to search clinical trials and identify potential matches. Before sharing the results with patients, staff evaluate matched trials to identify the most relevant and appropriate matches which are sent to the patient separately after the call.

**Amount of Patient Data Required to Identify Matches:** Moderate

**Features of Clinical Trials Database:** The service uses eviti’s TrialCheck database that pulls data from clinicaltrials.gov and trials.cancer.gov.

**Matching Process:** After running an initial search for clinical trials through their database, the service’s clinical trials specialists selects a subset of the search results deemed to be the most relevant trials which are sent to patients after the call.
User Experience

To improve the likelihood that patients will utilize the service to search for trials and make use of the search results, some services dedicate resources to ensuring the user-friendliness of the search process and/or search results. One way web-based services improve the search process is by enhancing the data entry process for patients. For example, services such as Antidote translate medical terminology into patient-friendly
language. Other services, like BreastCancerTrials, focus on improving the user interface of search results by designing the list of trials so that patients can quickly see the pertinent details of each trial identified, including how often they have to receive treatment on a trial, the number of sites that are recruiting, and whether travel is required. Another approach used by services is the inclusion of patient education materials, like FAQs, glossaries, articles, or videos in the search results. Other services leverage human interaction to enhance user experience (see Leukemia and Lymphoma Society case study below).

Case Study: The Leukemia and Lymphoma Society's Clinical Trial Support Center (CTSC) (https://www.lls.org/treatment/types-of-treatment/clinical-trials)

Modality: Telephone-based service

Description: The service is a help line for patients to learn more about treatment options, including clinical trials. If a patient is interested in clinical trials, clinical trial nurse specialists collect clinical information about the patient and run a search through clinicaltrials.gov and internal database resources. Nurse specialists help patients understand the clinical trials appearing on this final list to prepare them for a consultation with their treating physician. After the initial call, nurse specialists follow up with patients to help address barriers to enrollment and make necessary referrals to financial assistance, transportation, trial coordinators, or providers.

Amount of Patient Data Required to Identify Matches: Moderate

Features of Clinical Trials Database: The initial search is performed by staff using clinicaltrials.gov. The data from clinicaltrials.gov is supplemented by the service’s own internal databases.

Matching Process: Hematology trained clinical trial support nurses collect information from patients over the phone and answer or clarify issues in real time. Nurses then provide patients with a carefully constructed list of trials that match their preferences and qualifications, utilizing clinicaltrials.gov and internal databases. The trial list provided is an objective and comprehensive compilation of all trials that match patients’ preferences and qualifications. While the nurses may explain the treatment modality utilized in particular trials of interest, the patient is advised to bring the list to their physician for further consultation.

User Experience: The service leverages hematology nurse specialists to help patients through their entire decision making and trial entry process. An ongoing relationship is formed where patients are able to connect directly with ‘their’ nurse through phone or email. Nurses may also reach out to trial sites, connect with the patient’s healthcare provider team, and are available to family members who want to know more about the disease or available trials. The nurse specialists connect with patients or others on behalf of patients on average more than a dozen times after the initial call.
Services that are Tailored to Providers and Institutions
As discussed in the introduction, the services previously described are largely tailored towards patients and their proxies; however, there are other services designed to help providers and institutions directly recruit patients for trials. These services usually interact directly with the institution’s electronic health record (EHR) to obtain detailed clinical information about patients, and compare these against open trials within a database. Databases can be proprietary or public and contain either trials only open at the institution or all open trials regardless of location. Examples of these services include Mendel.ai (described below) and IBM’s Watson for Clinical Trial Matching. Both utilize artificial intelligence to sift through structured and unstructured patient clinical data held within the EHR and clinical trial databases to determine whether a patient is a good match for a trial.

Case Study: Mendel.ai (https://mendel.ai/)

Modality: Web-based service

Description: Mendel.ai is one example of a clinical trial matching solution that leverages AI to help providers and institutions implement evidence-based treatment, including referrals to clinical trials. It reads structured and unstructured data from clinicaltrials.gov and patients’ EHRs to determine eligibility. If a patient is eligible for a clinical trial, it alerts the provider at point-of-care or through a regularly scheduled batch report. In determining eligibility, Mendel.ai casts a wide net to ensure that patients are not ruled out based on unclear eligibility criteria or criteria that can be easily changed (e.g., A1c level). As a result, providers are notified of clinical trials that patients are eligible for, but they can also see trials where patients could be eligible with further treatment or clarification.

Amount of Patient Data Required to Identify Matches: High

Features of Clinical Trials Database: Pulls directly from clinicaltrials.gov

Matching Process: This service leverages artificial intelligence (AI) to analyze clinical information from the electronic health record (EHR) and trial information from clinicaltrials.gov to identify clinical trial matches for patients.

User Experience: N/A – this service is not intended for use by patients but rather by providers/institutions.

Conclusion
Clinical trial matching services vary in their primary goals. Simpler services seek to introduce patients and their proxies to the breadth of trials open for a particular cancer and foster further interest. More advanced solutions seek to help patients identify and enroll in trials that they are more likely to be eligible for and interested in. Depending on their goals, services vary across four key attributes that include the amount of patient
data required, the information contained in their clinical trials database, the degree to which they help patients. Advanced technology solutions are not required to provide matching services – some organizations leverage human resources to accomplish the same tasks as technology (e.g., collect accurate patient information, provide patients with a list of relevant trials).

Bibliography