

Is ClinicalTrials.gov Breaking the Law?

By Harold Miller-Jacobs and Norman M. Goldfarb

The Food and Drug Modernization Act of 1997 called for "a registry of clinical trials... in a form that can be readily understood by members of the public." (§ 113(a)) Three years later, in 2000, ClinicalTrials.gov (<http://www.clinicaltrials.gov/>) was in operation. According to the developers:

"All stages of system development were guided by the needs of the primary intended audience, patients and other members of the public... To reach the broadest audience with the fewest barriers to access, we designed a Web-based system that would be easy even for a novice user to use and yet would have extensive functionality. The goal was to make it simple for users to formulate their queries and then obtain results that would guide them to further relevant, 'just-in-time' information. We involved patients and patient advocates in the early testing of the system, and we identified and then tested our site for accessibility using several readily available tools, also making sure that the system performs reasonably on a wide range of Web browsers."¹

Today, over six years later, ClinicalTrials.gov is, by far, the leading clinical trials registry. Over 29,000 people visit the website daily to learn about over 31,000 clinical trials.² However, has it achieved its goals for ease-of-use by the public? To find out, let's follow Roger, a hypothetical member of the public, as he seeks information at ClinicalTrials.gov.

A Trip though ClinicalTrials.gov

Roger has just returned from his doctor's office, where he learned he has diabetes. His doctor recommended lifestyle changes and discussed various treatments he could try to manage the disease. None of the treatments are a perfect solution, so she suggested that Roger consider participating in a clinical trial. They scheduled a follow-up appointment for next week to discuss the alternatives and make a plan.

Despite being agitated by the news and therefore not fully comprehending all the ramifications, Roger wants to learn more about clinical trials. He is not even sure what a clinical trial is all about. He opens his web browser and types in "clinical trials". He finds over 65 million results, but the first one sounds promising: ClinicalTrials.gov. He clicks on the link. The website does not have any visual focus so he is not sure where to start, but it appears to be a government service, so he continues looking.

He sees a search box in the middle of the page, enters "diabetes", and clicks on the "Search" button. A list of 919 trials appears. He doesn't know where to begin with all of these choices, nor is he familiar with the medical terminology. Roger wonders what the difference is between the links at the top of the page, e.g., "Home," "Search" and "Listings," and the buttons on the page, e.g., "Search-Within-Results" and "Query Details." He is looking at a list of trials, so he wonders if he is on the page where the "Listings" link goes. He clicks on that link and it takes him to another page, so he clicks on the back button and continues his search.

Roger wonders how to make any sense out of all this data and narrow it down to something manageable. He notices a button: "Map of locations"; maybe this will help, so he clicks on

it. The map shows 147 studies in California, the state where Roger lives. The map is color-coded, but there is no explanation of the colors. California is colored red; does that mean he's in more danger than in other states?

Roger clicks on the picture of California and finds the list of 147 studies. That's better than 919, but it's still too many. There is also no city information – California is a big state. "How is the list organized?"; he cannot figure that out. Not sure what he is doing, he clicks on the first study... a bewildering array of information! "Maybe this site is only for doctors. I can't make out what is being presented or even where to look."

Roger wants to know:

- What exactly is a clinical trial?
- Which ones would be suitable for me?
- Where do I go to participate?
- How long will it take?
- What are the costs, if any?
- What are the odds it will really help my diabetes?

Instead, he gets pages and pages of text that do not answer his questions.

He looks down the list for studies in San Jose, his hometown, but realizes that cities are not displayed. The first study does not offer any treatment, but he clicks on the link to see if the city information is inside. He scans down two or three pages of text and eventually finds a location nearby at Stanford University. Now he knows how to find study locations.

Returning to the list, Roger realizes that the 147 studies are not categorized in any way. It's going to take a long time to look through them all for studies in his geographical area, so he starts reviewing the list to find the ones that might offer the best treatment. It doesn't take Roger long to realize that there are studies for Type 1 diabetes, Type 2 diabetes, diabetes mellitus, adult onset diabetes, insulin-dependent diabetes, non-insulin-dependent diabetes, and probably more. He thinks he has Type 2 diabetes, but isn't sure what the other kinds are. He looks around for an explanation of the different types, but doesn't find any, so he returns to searching out clinical trials in his local area.

Roger wonders if he missed something in the search tool, so he returns to the home page and notices that, yes, he could have searched on "diabetes, san jose". He does the search and finds nine studies. He does the search again for "Palo Alto" and finds seven studies. He finds 36 in San Francisco. He remembers that Stanford is not actually in Palo Alto, and finds 22 studies there. He finds 18 in Monterrey, but then realizes that Monterrey is in Mexico; there are no studies in Monterey, California. There are eight in Los Gatos. He looks for a tool that searches within X miles of his zip code, but can't find one. He gets a map out of his car to find all the local cities and towns to search them individually.

Roger compiles a list of 15 studies that might be applicable to his condition, but he knows he may have missed some. Some may not even be in the ClinicalTrials.gov database, but he finds the idea of searching other clinical trial registries overwhelming.³

Roger wants to compare the studies. ClinicalTrials.gov enables him to check off studies that interest him, but he has to go back to the complete California list to find them all in one list. He realizes that he has written down the ClinicalTrials.gov study numbers, but those numbers are not displayed, so he scans the list for study names that look familiar. He finds 13 of the studies he is looking for. He finds the other two by repeating the searches he did before. He does the "diabetes, california" search again. His checkmarks are gone, so he scans the list again and finds all 15 of them.

Now that all 15 studies are in one place, Roger starts reviewing the descriptions. Some of the descriptions are very brief. Others provide more information, but it's Greek to him:

The main goals of the study are to evaluate the effect of [Drug 1] on endothelial-dependent vasodilation, as measured by flow mediated dilation (FMD), to evaluate the effect on endothelial-independent vasodilation, as measured by nitroglycerin (TNG) response, and to evaluate the effect on arterial stiffness, as measured by pulse wave analysis (PWA)....

The description of this study is unusual in that it describes what happens at each visit, for example:

Visit 2 (week 0): Participants will come in fasting. Interval medical history and medications will be reviewed. Vital signs will be obtained. PWA and FMD will be performed. The patient will then have fasting labs drawn which will include glucose, insulin, c-peptide, lipids, free fatty acids (FFA), CRP, TNF α , IL-6, ICAM, VCAM, endothelin 1, PAI-1 protein, PAI-1 activity, and FOX2. The patient will then have a mixed meal (time 0), and labs will again be drawn at 15, 30 minutes, 45 minutes, 60 minutes, 120 minutes, 180 minutes, and 240 minutes after the meal challenge measuring glucose, insulin, c-peptide, lipids, and FFA....

The problem is that he can't understand much of it. What are the eight "labs" to be "drawn"? He does an Internet search on the term "draw lab" and realizes they want to draw his blood eight times over six hours. That's going to be a long day.

Roger reads for a few minutes more and realizes he will never understand the study descriptions, much less whether they suit his needs. He prints out the study descriptions to bring to his next doctor visit. His doctor has always been very patient with him, answering all his questions, but what are the chances she is going to read through a thick computer printout?

ClinicalTrials.gov Usability Issues

If Roger's experience is at all representative, ClinicalTrials.gov is not readily understood by members of the public. It has problems in all four dimensions of usability:

- Content
- Navigation
- Interaction
- Presentation

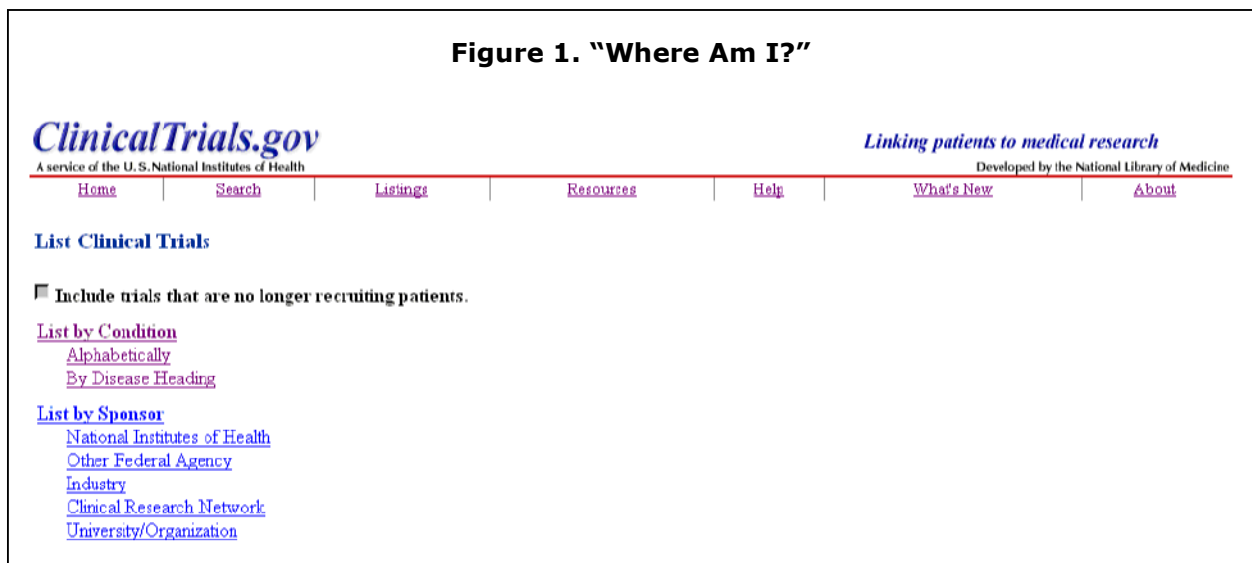
Content

The amount of information presented varies by study. Most of the text makes heavy use of medical and clinical research terminology that is incomprehensible to the general public. Leaving aside the words used, the complexity of the paragraphs and sentences in a sample of ten studies yields a reading level of grade 16.1 (fourth year of college).⁴ A reading level of grade seven or eight is generally advised for comprehension by the general public.⁵ ClinicalTrials.gov is often used by people in a difficult emotional state, which further impedes comprehension.

Navigation

The hyperlinks in websites enable users to move easily from one item to another, but that flexibility makes it easy for users to lose track of where they are on the website. It is not uncommon for users to never find their way back to an important page.

For example, in Figure 1, there is no clear indication that the user is on the "Listings" page. (The term "Listings" needs to be highlighted, enlarged or repeated in the title of the page.) In the absence of such indications, users may click almost randomly, becoming disoriented and frustrated. The emotional state of people coming to this website makes it imperative that the "Where am I?" answer be immediately obvious.



Study pages provide no indication as to how the user arrived at that page. The user may forget the series of searches he/she used to find that study.

Study pages include a link to Medline Plus, but without indicating that it includes a useful medical dictionary. There is no indication that Medline Plus is a completely different website, so users may not realize that they have left ClinicalTrials.gov.

Interaction

When ClinicalTrials.gov users are looking for clinical trials, they usually conduct multiple searches, modifying and refining them as they go. The ClinicalTrials.gov results page (Figure 2) does not allow users to modify previous searches. Users have to return to the Home page or the Search page to conduct a new search. Clicking on the "Back" button in the browser retains previous search terms; clicking on the "Home" or "Search" links deletes them. Users can search within their results, but they have to click on the "Search-Within-Results" button to go to a new page. Once a user has found a study, there is no way to bookmark it. Nor is there a way to save the searches previously performed so they can be repeated again at a future date or not repeated if they were unproductive.

There is no ability to sort listings by condition (disease), date posted, phase, eligible age group, or other criteria that help users narrow their search. There is no standardized lexicon of conditions, so users may have to conduct multiple searches or miss studies that use unfamiliar terminology. Because the maps only go down to the level of states, users may have to read through numerous inapplicable studies or conduct city-by-city searches.

Figure 2. Search Results

The screenshot shows the ClinicalTrials.gov search results page. At the top, the logo 'ClinicalTrials.gov' is displayed in blue, with the tagline 'Linking patients to medical research' to its right. Below the logo, it states 'A service of the U.S. National Institutes of Health' and 'Developed by the National Library of Medicine'. A navigation bar contains links for Home, Search, Listing, Enrollments, Help, What's New, and About. The search results are for the query '(diabetes AND califomia) [ALL-FIELDS]'. There are three buttons: 'Search-Within-Results', 'Query Details', and 'Map of locations'. A checkbox is checked for 'Include trials that are no longer recruiting patients.' Below this, it says '154 studies were found. Here are studies 1 to 50.' with a 'Next 50' button. The first five studies are listed with checkboxes and their titles and conditions.

Study ID	Status	Title	Conditions
1.	<input type="checkbox"/> Recruiting	Exercise Training in Older Diabetic Women	Cardiovascular Diseases; Diabetes Mellitus, Type 2
2.	<input type="checkbox"/> Recruiting	Anti-CD3 mAb Treatment of Recent Onset Type 1 Diabetes	Type 1 Diabetes Mellitus
3.	<input type="checkbox"/> Recruiting	Cardiovascular Risk Disparities: Socio-Emotional Pathways	Hypertension; Cardiovascular Disease; Type 2 Diabetes
4.	<input type="checkbox"/> Recruiting	ORWH/SCOR on Sex and Gender Factors Affecting Women's Incontinence	Urinary Incontinence; Diabetes
5.	<input type="checkbox"/> Recruiting	Safety of Inhaled Insulin With Type 1 and Type 2 Diabetes.	Diabetes Type 1; Diabetes Type II; Non-Diabetic

Modern website design includes a search field on the results page. Advanced designs enable users to save previous searches so they can easily retrace their steps. Many retail websites include tools that enable users to find store locations within, say, ten miles of their home zip code, and then obtain driving directions. Some websites allow users to select several products or services and then make side-by-side comparisons.

Presentation

Study descriptions (Figure 3) are organized into standard sections – purpose, eligibility, etc., but there is no graphical design to highlight key areas and help the user’s eye find information of interest.

Some of the formatting is confusing and hard to read. For example, a small ruled table near the top presumably includes the most important information. Are users really most concerned about the study’s sponsor and who provided the information? The table’s left column is right-aligned and its left column is center-aligned. Consistent left alignment usually maximizes readability.

A second table includes one to three columns: “Condition,” “Intervention,” and “Phase.” The “Condition” column lists one or more conditions (plural). The optional “Intervention” column lists one or more interventions. If there are three conditions and three interventions, the table does not make it clear whether the first intervention applies to the first condition, or all interventions apply to all conditions. The optional Phase column sometimes includes more than one phase, without any explanation of how that is possible in one study. In addition, the phase name, e.g., “Phase IV,” is linked to an explanation of clinical trial phases, but that explanation does not mention Phase IV studies.

The website does not allow researchers to include graphical images that can help explain the text information presented.

A professional website design gives users an intuitive sense of how to move around and find the information they need. Features that may seem trivial, such as consistent capitalization, punctuation, and use of buttons vs. links, may be invisible to the typical user, but they help create this sense of feeling “at home.”

Figure 3. Study Description

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Linking patients to medical research
Developed by the National Library of Medicine

Help us improve -- [complete our brief survey](#)

[Home](#) | [Search](#) | [Listings](#) | [Resources](#) | [Help](#) | [What's New](#) | [About](#)

Diabetes Prevention Program in Schizophrenia [DPPS]

This study is currently recruiting patients.
Verified by Hamilton Health Sciences - McMaster University Medical Centre July 2005

Sponsors and Collaborators:	Hamilton Health Sciences - McMaster University Medical Centre Lawson Foundation Ontario Mental Health Foundation
Information provided by:	Hamilton Health Sciences - McMaster University Medical Centre
ClinicalTrials.gov Identifier:	NCT00182494

Purpose

Diabetes is 2-5 times more common in schizophrenia and it is a preventable; but the current diabetes prevention guidelines are not suitable for implementation in the severely mentally ill population. The principles of diabetes prevention are essentially dietary regulation, increased physical activity and adjunctive use of oral anti-diabetic drugs (metformin). In a modified diabetes prevention protocol suitable for use in mentally ill population, we packaged the original guide lines with an adventure and recreation program based on principles of experiential learning, cognitive restructuring and behaviour modification. In this proposed study, we plan to evaluate the feasibility of adopting the new protocol, and examine its effectiveness in preventing diabetes.

Condition	Intervention	Phase
Diabetes Mellitus Schizophrenia	Behavior: Modified diabetes prevention protocol & Metformin	Phase IV

How to Design Usable Websites

Website designers may be subject matter experts, but, if they fail to take the user’s perspective into account, the site will probably come up short. The following simple process generates usable websites:⁶

- Determine the intended audience(s) and their capabilities.
- Generate a simple prototype (i.e., without software code).
- Test the prototype with actual users to ensure that it meets its goals.
- Refine the prototype; add graphics as needed and retest; repeat as necessary.
- Code the site and conduct final test.

For clinical trial registries, this process involves the following considerations:

Determine the audience

Clinical trial registries serve four audiences:

- The primary audience consists of potential research subjects and their relatives. Most of these users require lay terminology or handy definitions of medical and clinical research terms. Users are highly motivated, but may have to deal with other pressing issues. Many are first-time visitors to a clinical trial registry. Various subgroups have different requirements. For example, family members may want supplemental information such as "The Role of the Caregiver in Clinical Research." A significant subgroup has impaired eyesight and needs large text. Another subgroup has limited hand coordination and needs large buttons. Another significant subgroup is literate in a language other than English.
- The secondary audience consists of medical personnel (doctors, nurses, medical assistants, etc.) seeking information for their patients. These users are more comfortable with medical terminology. Physicians, in particular, are very hard-pressed for time. They may have dial-up Internet connections, or none at all in the office.
- The tertiary audience consists of researchers who want to determine if and how to list their studies in the registry. On the one hand, they may be competitors. On the other hand, if their listings are easy to read, the entire site becomes more usable.
- The quaternary audience consists of business competitors. To minimize competitive harm, information on the website should be limited to the extent allowed by regulations and guidelines.

Generate designs

Once the needs of the target audience are understood, a "user-centric" design process can begin. In user-centric design, design decisions are made from the primary user's perspective – not from the perspective of ease of development. The most common use scenarios are considered first. Checking the strengths and weaknesses of other sites can also be informative. The key is to generate designs without complex software coding, preferably on paper.⁷ The process involves mocking-up screenshots on paper and having the user work with them to navigate and make selections (i.e., point to the link he/she would press). Obviously, not all links can be prototyped, but key screens can be generated to test the main flow of the design. This technique identifies problems remarkably well. Design changes are much faster and easier prior to the more costly process of developing the software code.

Test designs

The simplest way to test a design is to sit with potential real-world users, one at a time. Ask them what they would like to accomplish. Then watch while they try to accomplish their goals, such as:

- Finding a clinical trial in their local area that may meet their needs.
- Understanding the information presented in the study description.
- Saving the information for review by their physician.

Ask them to think out loud while going through this process. The usability testing technique of probing (asking more in-depth questions), in particular when users pause or are confused, will produce valuable data for the next design iteration. Because clinical trial registries serve diverse populations, testing with diverse users is essential; different users will experience different problems. As the website goes through development, continue testing to identify new problems and opportunities that arise.

Conclusion

ClinicalTrials.gov, like many government web sites,⁸ falls short of its statutory mandate and original design goals. Given its popularity and the passage of over six years since its original launch, a major renovation is in order. To a greater or lesser extent, other clinical trial registries have similar shortcomings. Because these websites already exist, user testing is a relatively simple matter and a good place to collect initial data. Starting from scratch is probably not necessary. As illustrated above, incremental enhancements can significantly improve usability and help accomplish the registries' objectives. This process of understanding users, generating simple prototypes, and testing and retesting, can significantly improve the usability of clinical trial sites.

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