PATIENT-CENTERED COMMUNICATION AND READABILITY OF LUNG CANCER BRIEF SUMMARIES ON CLINICALTRIALS.GOV: A QUANTITATIVE EVALUATION THREE YEARS AFTER PLAIN-LANGUAGE GUIDANCE

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ABSTRACT

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Doctor of Medical Humanities Dissertation by

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People diagnosed with cancer must process complex, unfamiliar medical information under significant emotional distress, which can impair comprehension and decision making. The ClinicalTrials.gov Brief Summary serves as a critical entry point for patients seeking to understand the purpose, design, and relevance of a clinical trial. Nevertheless, trial descriptions frequently contain technical terminology and complex sentence structures that limit their usefulness. To improve accessibility, the National Library of Medicine issued a Plain Language Checklist for Lay Brief Summaries on September 26, 2022, but limited empirical evaluation exists of whether this guidance produced measurable improvement.

This dissertation used a quantitative pre–post design to evaluate the checklist's impact across a representative sample of interventional lung cancer trials posted three years before and after issuance. The Plain Language Checklist Scoring Tool (PLCST) was developed to assess patient-centricity across focus, content, numbers, and structure, alongside validated readability metrics including Flesch–Kincaid Grade Level. The search identified 2,408 trial records. The Brief Summaries showed a mean Flesch–

Kincaid Grade Level of 19.66, corresponding to an advanced graduate school reading level, with no significant change after guidance. The mean PLCST score was only 3.93 of 11, and no summary met all criteria. Although exploratory patient-focused content improved modestly, this outcome reflected greater completeness rather than improved readability.

These findings suggest that the passive publication of plain-language guidance without enforcement, workflow integration, or accountability is insufficient to meaningfully change how investigators write Brief Summaries. The problem may not lie in the checklist itself but in the persistent challenge of clearly communicating complex medical information. This study establishes a benchmark for measuring future interventions and argues that treating communication as a core function of the clinical trial enterprise, rather than a compliance footnote, is essential to equitable patient access to research.

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INTRODUCTION

A cancer report can change the direction of a person's life in ways they never anticipated. One moment, you are moving through an ordinary day; the next, you are sitting across from a doctor, holding papers filled with unfamiliar words, numbers, and clinical terms that feel as though they belong to someone else's story. There is little time to take in what has happened or to make sense of it.[1]

People diagnosed with cancer are required to process complex and unfamiliar medical information under conditions of significant emotional distress, which can impair comprehension, recall, and decision making.[2] Once patients receive their diagnoses, they are often forced to learn an entirely new language: the lexicon of oncology. The gap between healthcare providers and patients is immense, with a significant difference between the knowledge they currently have and the knowledge they need to be active participants in their care and to fully participate in shared decision making. This burden exists for all cancer patients, regardless of their level of education or familiarity with cancer, as no two diagnoses are the same. However, other barriers to care can exacerbate this burden, which can include race, language, cultural competency, health literacy, socioeconomic health disparities, geographic isolation, medical mistrust, and structural healthcare system inequities.[3-5] Thus, patients increasingly turn to online resources, including clinical trial registries, during this moment of vulnerability to better understand their options.

Nevertheless, substantial evidence supports a persistent mismatch between the complexity of medical information and patients' ability to understand it, despite its public-facing intent. Research has demonstrated that patients may forget up to half or

more of the information communicated during clinical encounters, even when communication is clear and empathetic.[2] This limitation is not a lack of effort by clinicians or patients but the cognitive and emotional burden associated with receiving a serious diagnosis. In this context, health literacy is not solely determined by education level, as situational factors also highly influence it. As a result, even highly educated patients may struggle to interpret technical, jargon-heavy information. Within the context of the healthcare system and care continuum, these findings underscore the importance of presenting complex clinical information in clear, accessible, patient-centered language. These challenges can compound as patients and care partners seek additional information to understand their care options.

Patients are often diagnosed at later stages of disease and may progress rapidly through standard-of-care treatment options before being presented with additional therapies or clinical trial opportunities. While clinical trials have historically been viewed as a last option, oncology has increasingly recognized that they should be considered earlier in the treatment pathway. For example, the American Society for Clinical Oncology (ASCO) stated, “Improving patient access to cancer clinical trials is a fundamental ASCO priority because clinical cancer research is the essential link transforming biomedical discoveries into meaningful progress in cancer care and patient outcomes. Today’s standard of care emerged from yesterday’s clinical trials.”[6]

Nevertheless, only 7% of patients in the United States are estimated to ever participate in a cancer treatment trial.[7] One of the first steps in participating in a clinical trial is completing a search on a trial registry site to understand and evaluate trial opportunities either alone or in partnership with a healthcare provider. Hence, this

dissertation evaluates how clinical trial registries, specifically ClinicalTrials.gov, can be improved through plain language to improve accessibility to all patients.

All drugs entering the U.S. market require Food and Drug Administration (FDA) approval to ensure their safe and effective use in appropriate patient populations. A pivotal part of this process is interventional clinical trials that serve as the basis of the New Drug Application (NDA). The NDA includes data from a comprehensive collection of preclinical and clinical trials. As part of the FDA's modernization effort to increase transparency in drug development, the National Library of Medicine (NLM) created ClinicalTrials.gov, a clinical trial registry for consumer and investigator use. This registry intends to serve "individuals with serious or life-threatening diseases or conditions, to other members of the public, to health care providers, and to researchers."[8]

Today, over 582,144 trials are currently listed in the registry, with 65,458 trials open to enrollment.[9] Minor improvements to the registry have occurred since the launch in 2000. However, the ClinicalTrials.gov database underwent a major overhaul for the first time since its creation as part of the Modernization Process to enhance its website and the Protocol Registration and Results (PRS) system, which was considered largely complete by early 2026. At the time of the release of ClinicalTrials.gov in 2000, Donald A. B. Lindberg, M.D., Director of the NLM, the government entity in charge of the platform, stated, "If we are to continue making the giant strides in diagnosis, treatment, and cure of illness that marked the last century, we must have active participation in clinical trials by well-informed volunteers."[10]

The Modernization Project, a multi-year effort released in phases, offers a beta version and open public comment. The project aims to ensure access to clinical trial

information, with enhanced functionality for searching, viewing, and downloading it. It also offers additional support tools to sponsors and investigators to assist with their submission to the PRS system. Since the primary goal of ClinicalTrials.gov is accessibility to the lay public, the NLM issued expanded guidance for application to the "Brief Title" and "Brief Summary" sections of the PRS via the Plain Language Checklist for Lay Brief Summaries issued on September 26, 2022.[11] These two fields of the ClinicalTrials.gov database serve as the backbone for data extraction for most patient and clinician "trial finders," so they are of utmost importance for providing equitable access to clinical trials.

The Brief Summary field serves as a critical entry point for patients seeking to understand the purpose, design, and relevance of a clinical trial. Given its prominence and structured character limit, this field represents a key opportunity to present complex clinical information both accurately and accessibly. However, prior research and stakeholder commentary have suggested that trial descriptions frequently contain technical terminology, complex sentence structures, and insufficient contextual explanation, thereby potentially limiting their usefulness for patients and care partners.

Despite ClinicalTrials.gov's intention to serve as a publicly accessible resource, patients and care partners still struggle to navigate it. The introduction of the Brief Summary Checklist in September 2022 aimed to improve the readability and accessibility of the data field. However, limited empirical evaluation has assessed whether this effort has led to measurable improvements in lay language and patient-centered care. As a result, it remains unclear as to whether the issued policy and guidance have translated into meaningful changes in how clinical trial information is communicated to patients.

This gap represents a critical barrier to equitable access to clinical trials, informed decision making, and patient engagement in research.

This dissertation employs a quantitative analysis to evaluate the impact of the Plain Language Checklist for Lay Brief Summaries in a subset of oncology trials posted on ClinicalTrials.gov. The analysis's pre–post study design spans three years before and after the guidance's issuance. Specifically, the Plain Language Checklist Scoring Tool (PLCST) was developed using the Plain Language Checklist for Lay Brief Summaries and previously established patient-centric criteria to assess trial patient-centricity across four domains: focus, content, numbers, and structure. The PLCST helps assess sentence-structure metrics, readability metrics, plain-language usage, numerical communication, and the completeness of required information based on the checklist.[12] The aims of this study are threefold in nature: 1) to assess the changes in readability of the ClinicalTrials.gov Brief Summary before and after the implementation of the Plain Language Checklist, 2) to evaluate the quality of the content of the Brief Summary to determine the extent to which the content aligns with the principles of patient-centered communication, and 3) to understand whether the Brief Summary Plain Language Checklist has resulted in meaningful improvements in the usability of clinical trial summaries that may translate into future real-world improvements in clinical trial access.

This quantitative analysis assesses whether the Brief Summaries submitted after implementation of the Plain Language Checklist have demonstrated significantly improved readability, reflected by higher Flesch Reading Ease (FRE) scores and lower Flesch–Kincaid Grade Levels (FKGLs). The analysis also assesses whether sponsors have demonstrated greater alignment with patient-centered content criteria than pre-

checklist summaries by using the PLCST to assess adherence post-checklist issuance. Finally, an exploratory analysis aims to determine whether increased awareness of patient-focused drug development has improved the availability of clinical trial information most requested by patients for inclusion in the Brief Summary.

The health condition selected for this analysis is lung cancer, an inherently complex, heterogeneous, and rapidly expanding area of research with an abundance of clinical trials enrolling in the United States. Lung cancer is also an important area of research, as it is the second most common cancer in the United States, with an estimated incidence of over 238,000 new cases annually.[13] Lung cancers account for approximately 13% of all new cancer cases, and they remain the leading cause of cancer-related deaths in the United States. This year alone, over 125,000 Americans are estimated to die from lung cancer.[13]

Lung cancer is an aggressive disease that is often diagnosed in its later stages. The early signs and symptoms mimic those of other comorbidities and general illness, are often nonspecific, and may delay diagnosis. Overall, the relative five-year survival rate is 25%.[14] In this context, the intersection of clinical urgency, informational complexity, and patient vulnerability highlights the essential role of plain-language communication in enabling lung cancer patients to understand, evaluate, and meaningfully engage with clinical trial opportunities.

This dissertation is grounded in the interdisciplinary framework of Medical Humanities, which examines the human experience of illness through the lenses of communication, ethics, and narrative. At its core, Medical Humanities emphasizes that all aspects of healthcare must be as patient-centered as possible, even when involving

complex scientific concepts. While clinical trial registries such as ClinicalTrials.gov are often viewed as technical or regulatory tools, they also function as critical sites of patient engagement, where individuals encounter complex medical information during moments of vulnerability. The language used in these spaces shapes understanding of medical information, while also influencing decision making, agency, and access to care. Therefore, the language used in the Brief Summary is essential to the searchability of clinical trials and remains the backbone as the centralized public repository for all trial-matching and discovery tools.

This scholarly work reflects the fundamental principles of Medical Humanities by examining how communication within the clinical research landscape can either support or limit equitable access to care. While many barriers to care exist within the U.S. healthcare system, little has been done to bridge the gap, despite ongoing efforts of patient organizations and healthcare professionals. Within the oncology space, one of the most notable barriers is the lack of equitable access to clinical trials. For a drug to receive FDA approval, clinical trials must reflect the intended treatment population. Guidance finalized in 2024 requires all trials to have Diversity Action Plans and meet specific metrics to ensure the enrolled trial population is representative of the general population. This guidance also aims to enroll a sufficient number of U.S. patients: approximately 20% of the global population studied.[15]

Beyond these barriers, a recurring issue is that the trials are too complex for the public to understand. These trials can also be confusing for community oncologists and other healthcare professionals. Such trials often study new therapeutic agents with limited public information and data in therapeutic areas where technological advances often

surpass the average physician's ability to stay current on emerging agents not yet commercially available. Although patient advocacy groups and trial navigation teams have developed tools to support patients in this process, these resources fundamentally depend on the quality and clarity of the underlying data source: ClinicalTrials.gov. Therefore, trial sponsors must adhere to plain-language guidance offered by the Brief Summary Plain Language Checklist. This analysis provides an important benchmark for evaluating adherence to plain-language guidance and offers one of the first empirical assessments of whether policy-driven efforts have meaningfully improved the accessibility of clinical trial information for patients.

PERSPECTIVES ON PATIENT-FOCUSED DRUG DEVELOPMENT

Every two years, the Center for Information and Study on Clinical Research Participation (CISCRP) conducts the largest global assessment of public motivations and experiences with clinical research. This survey consistently demonstrates that substantial gaps remain in patient understanding of clinical trials, with many individuals reporting difficulty interpreting study information and identifying relevant trials. These findings show persistent barriers in the accessibility and clarity of clinical research communications.

Collectively, these efforts reflect growing recognition across stakeholders that traditional scientific and regulatory language may not meet the needs of prospective participants. However, the extent to which these patient-centered communication principles have been operationalized within publicly available trial registries, such as ClinicalTrials.gov, remains unclear. This gap underscores the need for systematic evaluation of readability and accessibility within these widely used resources.

In parallel, initiatives led by TransCelerate BioPharma have emphasized the importance of improving transparency and developing plain-language approaches to participant-facing materials, including efforts to standardize lay summaries and enhance the usability of clinical trial information. TransCelerate is a not-for-profit organization that was created to bring together a collaborative stakeholder group for the shared vision, “to improve the health of people around the world by accelerating and simplifying the research and development of innovative new therapies.”[16] Today, the organization has over 21 member companies and more than 25 ongoing initiatives to help provide a

framework to help researchers and industry find a practical approach to processes to eliminate inefficiencies in research and development, thereby enabling high-quality medicines to come to market faster. One of their core workstreams focuses on improving registry design and quality to increase access to clinical trials. TransCelerate believes that "clinical trial registries have the potential to be meaningful resources for patients, but limiting factors such as the lack of quality and scientific jargon found in registration data limit their use."[16] One of the major outputs of this workstream is the Clinical Trial Registration Tool.

This tool was created through a multi-step process that included speaking with patients to understand their preferences when looking for clinical trials. The result was an analytic framework to assess the quality of data fields, specifically ClinicalTrials.gov. Throughout "the process it became clear that the value of such registries is inherently dependent on the quality of the data it contains. Currently, many registry submissions include incomplete data fields, jargon, internal inconsistencies, and other quality issues, which limit their usefulness … and may present a barrier to patient access to meaningful clinical trial information."[16] Many of the outputs from the TransCelerate workstream are the foundation behind the premise of this dissertation, the need for clear, patient-friendly language in the Brief Summary to improve the accessibility of clinical trials to the public.

The first step in their workstream was a global survey to better understand patient preferences when accessing clinical trial registries such as ClinicalTrials.gov. The survey was conducted in February–March 2019 among 1,070 patients and caregivers, only 21.7% of whom had visited a clinical trial registry.[16] Of those who did visit a registry, the majority (51.3%) had visited ClinicalTrials.gov, followed by 38.8% visiting a

pharmaceutical company's website, 28.9% visiting the World Health Organization [WHO], and 23.7% visiting the EU Trial registry, and almost one-quarter (24.6%) unaware of which site they had accessed.[16] Survey participants were asked to rank order which data fields were most helpful in evaluating clinical trials for a series of nine options, with the following rank order results:[16]

1) condition or disease being studied in the trial,
2) a Brief Summary that provides a general overview of the clinical trial, written in plain language,
3) detailed information about the clinical trial drug being studied,
4) a short title describing the clinical trial, written in plain language,
5) criteria needed for participation, for example, inclusion/exclusion criteria,
6) health measurement(s) or observation(s) examined to determine the effect of the clinical trial drug,
7) the location where the trial will be conducted,
8) the chance of receiving the clinical trial drug if there is a placebo, and
9) information on who is funding the clinical trial.

These results clearly indicated that the Brief Summary (#2) and the Brief Title (#4) are critical pieces of information needed to determine whether a clinical trial may be a match for a patient's condition. As a result, these data fields were the primary focus of the analytic framework used for the quality assessment, as covered in detail in future chapters. TransCelerate's initial analysis of 346 studies selected from ClinicalTrials.gov demonstrated that in the Brief Title, while "most make mention of the condition in scope for the trial, many diligently exclude technical design study terms, and very few leverage

the term ‘participant’.”[16] For the Brief Summary, the study found that “most use complete sentences and roughly a quarter make no mention of the objective or purpose.”[16]

After the full analysis was complete, the researchers noted that of 346 studies, only 252 (73%) met all criteria expected for inclusion in submissions from the patient-preference perspective. Hence, room exists for improvement to better align with the needs of patients and care partners.[16] This foundational work led to their publication in *PLoS One*, “Patient Preferences When Searching for Clinical Trials and Adherence of Study Records to ClinicalTrials.gov Guidance in Key Registry Data Fields” and the creation of the open-sourced Clinical Trial Registration Tool.[12,16,17]

The TransCelerate Clinical Research Access Initiative envisioned creating the “registry of the future,” with a website concept designed to enable patients, their family members, healthcare professionals, researchers, and the public to search for clinical trial information when and where they need it. The team developed the tool through a structured approach that began by defining data quality from both regulatory and patient perspectives and by conducting a global patient survey to identify high-value data fields and preferences, which resulted in the focus on the Brief Title and Brief Summary. The Clinical Trial Registration Tool has been available since 2019 and allows users to proactively evaluate the quality of their ClinicalTrials.gov submissions before formally submitting to any registry. This downloadable tool is a macro-enabled, user-friendly file that analyzes and improves the Brief Title and Brief Summary data fields.

The Clinical Trial Registration Tool operationalizes patient preferences by allowing users to input text, along with automated and manual element assessments, while also evaluating readability using metrics such as FRE, the Flesch–Kincaid Reading

Age, and word counts. After completing the calculations, the program provides the sponsor with an assessment in two domains: "Your Brief Title/Summary Adherence Assessment" and "Your Brief Title/Summary Patient Focus Assessment" on a visual scale of 1–7. Beneath each rating is a list of rationales for the score, with areas for improvement provided for each assessed domain. By iteratively refining content, trial sponsors can improve the clarity, consistency, and patient relevance of trial descriptions. Images of the tool and an example of its application to a randomly selected Brief Title and Brief Summary can be found in the Appendix (Figures 34–37).

TransCelerate widely shared this tool with stakeholder groups and offered training and webinars to support its rollout. The work from this project was a clear example of how patient and care partner feedback could be used to create basic adjustments to critical pieces of the ClinicalTrials.gov data field to improve accessibility, searchability, and transparency between sponsors and the lay public. Additionally, the benefits were applicable to patients, sponsors, and regulators.[18]

Nevertheless, no known formal tracking or analysis was designed to show a substantial shift or change to the use of lay language in the Brief Title or Brief Summary following the tool's publication. Notably, this tool was available prior to the open-comment period for the "Request for Information (RFI): ClinicalTrials.gov Modernization" (December 30, 2019, to March 14, 2020) and made available for nearly two years before the rollout of the NLM Brief Summary Checklist in September 2022.[19]

The tool, either on its own or in support of the Brief Summary Checklist, advances the broader goal of enhancing access to clinical trials by ensuring that registry data are both compliant with regulatory standards and understandable to patients, thereby

improving engagement and facilitating more informed participation decisions. The tool can be accessed online at the TransCelerate webpage for Clinical Research Access Information Exchange Solutions.[17]

Yet another example that demonstrates the need to improve the language and accessibility of ClinicalTrials.gov comes from a focus group at the University of Michigan School of Medicine. This group convened a group of stakeholders that included input from patients, study teams, and community physicians to better understand how clinical trial information is developed and used within ClinicalTrials.gov and other related registrational platforms.[18] This work explored how the different audiences interacted with the trial data fields and sought to identify key gaps in usability and comprehension. The approach that the study team used combined real-world experience from the research teams who were directly responsible for drafting and posting content to ClinicalTrials.gov, as well as patients, care partners, and physicians who tried to search for and interpret the data.[18]

The focus group had

> … several participants [who] had previously been involved in research studies and clinical trials involving rare disease, chronic disease, cancer treatment, cardiac rehabilitation, diabetes, liver disease, and transplants. Even though several people had been previously involved in clinical trials, only four of twelve convened were aware of ClinicalTrials.gov before participating in the focus group, three of whom had previously used ClinicalTrials.gov to search for a trial for the purpose of enrollment. Almost all participants had previously searched for a clinical trial on sites other than ClinicalTrials.gov.[20]

The focus group comprised patients with chronic illnesses who were likely eligible for a clinical trial. Nevertheless, the results revealed that awareness of and

usability for ClinicalTrials.gov were limited, even among those with prior exposure to research. When working within the site, the participants in this group described the interactions as “imposing, overwhelming, confusing, dated, and bureaucratic,” which further demonstrated the deficiencies in a site intended for a lay audience.[20] These findings again highlight the fundamental mismatch between the intended users of the site, patient and care partners, and the current structure and presentation of clinical trial information.

Another central theme emerging from this focus group was the difficulty patients experience in understanding the trial content when reviewing core descriptive fields such as the Brief Title and Brief Study. The participants reported that the study records were “hard to distill down,” and it was “difficult to understand which study might be most suitable for a prospective participant.”[20] Even fields that were intended to specifically support patient comprehension were not effective at communicating in plain language. Outputs from the focus group reported, “Even though brief descriptions are supposed to be written in lay language, several participants did not understand the information.” Moreover, one participant “could not understand the trial after reading the Brief Summary,”[20] thereby identifying another critical limitation: the presence of a data field labeled as “Brief Summary” without proper guidance does not ensure accessibility unless it is written in patient-centered, plain language.

Patients and care partners also identified specific barriers related to terminology and content structure that directly inform how Brief Summaries should be written. Common clinical research terms such as “exclusion criteria, arm, and outcome measure” were cited as difficult to understand, thereby reinforcing the need to avoid or clearly

define technical language in patient-facing summaries, either in the content or in a glossary.[20] The participants also emphasized the importance of clarity around key decision-making information while noting that trial records often lacked "information that would be meaningful to a potential participant" and did not answer basic questions about the study. This point was also strongly emphasized in the TransCelerate report.[12,20] These findings suggest that effective Brief Summaries should prioritize purpose, relevance, and participation details over technical completeness.

The focus group findings were shared widely in the open letter to the "Public Comments Received in Response to RFI: ClinicalTrials.gov Modernization" docket.[20] The commentary strongly recommended a shift toward more patient-centered communication strategies that prioritize usability and comprehension. The authors noted that patients expressed a clear expectation that ClinicalTrials.gov "should share information in a manner that's easy for the public to understand," thereby emphasizing plain language as a core requirement rather than an optional enhancement.[20]

More broadly, the University of Michigan School of Medicine suggested that trial information should be presented in a "user-friendly platform with lay language, inviting interaction, and engaging questions."[20] This suggestion aligns with the premise that the Brief Summary, in conjunction with the Brief Title, should function as an accessible entry point into trial information that enables patients to quickly understand a study's purpose and relevance without requiring advanced health literacy. Collectively, the University of Michigan findings demonstrate that improving access to clinical trials depends on both the availability of information and on how that information is written and presented.

The focus group results provided unambiguous evidence that current ClinicalTrials.gov content, including summary-level descriptions, often fails to meet patient needs due to complexity, jargon, and poor usability. These insights directly support the need for structured, plain-language Brief Summaries that prioritize clarity, relevance, and patient understanding as essential components of a patient-centered clinical trial registry. The University of Michigan was one of several organizations that commented specifically on the utility of the Brief Summary during the open-comment period by pointing to the need for plain-language guidance as part of the ClinicalTrials.gov modernization project.

The open-comment period was to "obtain detailed and actionable input" by issuing an RFI, NOT-LM-20-003, on December 30, 2019, with comments due by March 14, 2020. According to the NLM, "The RFI's purpose was to solicit comments on the ClinicalTrials.gov website's functionality, information submission processes, and use of data standards."[19] The NLM received 268 responses, including anonymous responses, public commentary, patients, advocacy groups, regulators, research centers, academia, and industry. The comments received from the RFI demonstrate how the Modernization Project was the precipice for the creation and implementation of the Brief Summary Checklist.[19] A brief review of the open comments reveals repeated calls to action for the NLM to integrate patient-centered, plain language into the registry primarily through the Brief Title and Brief Summary. One anonymous suggestion was made as follows:[20]

> Communicat[ing] clinical trial information to the public in PLS format would require NLM to restructure how the clinical trial information of a study record on ClinicalTrials.gov is displayed. In order to successfully restructure the display of

> clinical trial information, it would require NLM to align ClinicalTrials.gov with current industry best practices for communicating aggregated results information on clinical trials in an easily digestible form for trial participants and the public who are unfamiliar with scientific terms and clinical research practices associated with the development of drugs, biologics, and medical devices for use in humans. This would require ClinicalTrials.gov to display clinical trial information using lay language in a lay summary format where the information is written, organized, and displayed in a manner understandable to someone with a health literacy level of a twelve-year-old. To elaborate on what a PLS format would look like, it would employ the use of infographics, pie charts, and tables to provide visuals in conveying complex information. …We feel this suggestion to display clinical trial information on ClinicalTrials.gov in PLS format, despite its unconventional method, is necessary and important to enhance information quality and content available to the public on ClinicalTrials.gov.

Dana Farber Cancer Institute, a leading academic and research-focused cancer center, echoed a similar sentiment:[20]

> The Brief Summary located in the Study Description section of the Registration module should be, as stated in the ClinicalTrials.gov Data Element Definitions, "written in a language intended for the lay public." It would be helpful if the NLM worked with experts in the field to develop guidance and tools to assist submitters in developing a brief summary that clearly communicates the purpose of the research. Examples of summaries would be helpful as well.

Furthermore, the Association of America Medical Colleges, a national organization representing academic medical centers, medical schools, and teaching hospitals, stated,

> Regarding the content itself, NLM should look for opportunities to display information in a more understandable way while still maintaining the scientific integrity of the site. For example, the Brief Summary section contained in each

> study record should, according to ClinicalTrials.gov element definitions, be written in language "intended for the lay public." Yet this section is often complex and full of technical jargon. We recommend that NLM work with experts in health literacy to create guidelines for researchers to ensure that this part of the study record fulfills its stated purpose.

Many pharmaceutical and biotech companies also offered robust feedback on the RFI. In a full circle moment, Sanofi, a global biopharmaceutical company with a focus on oncology and specialty care, suggested that the "use of small intelligent tools which can be embedded to PRS which will help enforcing required data into field; [the] 'Clinical Registration Tool' prepared by TransCelerate [can] enforce the elements required to be mentioned in [the] brief title and brief summary."[20] However, Sanofi was not the only organization to mention the TransCelerate Clinical Trial Registration Tool.

Harvard Multi-Regional Clinical Trials Center of Brigham and Women's Hospital, a research center that focuses on clinical trial transparency, ethics, and global research practices, also mentioned improvements for the Brief Summary, included below:[20]

> We note that there is great heterogeneity in how different sponsors complete the Brief Summary section and that it is often longer and more technical than is functionally useable. The current data element definitions note that the character limit for brief summaries is 5,000 words, which is longer than necessary to describe the purpose of the study. We believe that integrating health literacy principles would improve the understanding of visitors to the public site. We suggest NLM work with experts in the field to not only develop and adopt guidance, tools, and examples to assist submitters in developing a brief summary that clearly communicates the purpose of their search, but also to explore a means to assess various elements of health literacy automatically and provide real-time

> feedback to those entering the Brief Summary into the PRS database. We note the TransCelerate Clinical Trial Registration Tool is one such option.

Hence, academic institutions have recommended improving the Brief Summary in plain language while also providing a tool for study sponsors to develop this language in line with established guidance from the TransCelerate Working Group. Finally, coming full circle, TransCelerate provided a lengthy commentary in the RFI, as well as a proof of concept of what an ideal registry would look like based on feedback from their Patient Advisory Board. Recommendations from TransCelerate included the following:[20]

> Rather than simply presenting data, clinical trial registries should convey meaning through the use of straightforward language, consistent terms, and visuals where appropriate. Graphics and imagery should be used to represent more complex information or should be used alongside text to add further visual interest and make the user experience more approachable. Text-heavy pages and long paragraphs should be avoided, where possible, in favor of concise sections of information presented in a logical order. Information should be sequenced in order of priority based on patient preferences. To aid the evaluation of multiple sets of information (such as a handful of trial search results), functions which allow side-by-side comparisons can further enhance the utility of the information to the user according to his or her own priorities.

Additionally, as previously noted, shortly after the open-comment period TransCelerate published its findings in *PLoS One,* where they doubled down on plain language:

> [This] information is not written for the public. Registries and other sources of clinical trial information often contain a high volume of scientific, jargon-rich

> data that is difficult to digest and interpret. Data and information requiring a relatively high learning curve to understand renders it inaccessible for a variety of practical purposes, minimizing its value.[12]

TransCelerate also found that, in its analysis of 346 studies post-implementation of the Final Rule (FDAAA 801), no Brief Titles and only two Brief Summaries achieved the maximum assessment for focus on patient preferences, a rate of 0.6% across all studies reviewed.[12] It assessed that "the apparent absence of patient focus in brief summaries could be that sponsors consider trial registration in ClinicalTrials.gov solely as a legal requirement and not as an opportunity to engage with patients and raise interest for their trials."[12,20] It also noted that in its survey of clinical trial sponsors, fewer than one-third of companies reviewed the information posted on ClinicalTrials.gov to ensure relevance and understanding for a lay audience. The final recommendations were as follows:[20]

> Improvements of patient focus for brief titles and brief summaries could be achieved by either making the information items we have identified mandatory or by including them into the guidance documents for sponsors. However, the improvement of guidance needs to be complemented by making sponsors realize that ClinicalTrials.gov entries have the potential to much more adequately inform patients and the public about clinical trials. More patient-focused brief titles and brief summaries will allow for more informed decision making on clinical trial participation. The Clinical Research Access & Information Exchange Initiative has created a Clinical Trial Registration Tool that will help sponsors assess their data quality so they may produce more patient-focused, compliant clinical trial submissions.

While most of TransCelerate's recommendations are reflected in the NLM's Brief Summary Checklist, interestingly, its clinical trial tool is not among the resources provided in the "Learn More About Plain Language" section of the webpage. [21]

PATIENT NARRATIVES ON VALUE OF CLINICAL TRIALS

It is important to understand the role that a patient-centered approach to research plays from the standpoint of those most directly impacted. In this section, a brief review of several narrative perspectives is offered to reinforce the public discourse around the value of plain language in accessing clinical trials from the perspective of those involved in care.

Linnea, a long-term survivor of advanced ALK-positive lung cancer and prominent patient advocate, described the critical role of clinical trials in patient care, stating that "clinical trials are my lifeline." Here is part of Linnea's story:[22]

> Prior to my diagnosis, all I really knew about lung cancer was that the overall five-year survival rate was 16%. As a mother of three, I was determined that I would beat those odds. At stage IB, I was a candidate for surgery and adjuvant chemo, and I underwent both. Despite this aggressive approach, my cancer returned almost immediately. With few viable treatment options, we elected to take a watch-and-wait approach, and I remained treatment-free until June of 2008. My health again failing, a biopsy confirmed metastatic spread, and I was restaged to IV. One more line of therapy proved ineffective, and it looked as if I had run out of options. However, a sample from the biopsy for re-staging had been submitted for genetic testing: it came back positive for a rare ALK mutation found in only 4% of those with NSCLC. Better yet, there was a phase I clinical trial for an experimental therapy that targeted ALK mutations. The rest is personal history. I became the fourth person in the world with NSCLC to try this experimental therapy, and I was fortunate enough to have an amazing response. My good fortune—being in the right place at the right time with the right mutation—was newsworthy and garnered a mention on the ABC World News.

> As I enter my tenth year of surviving lung cancer, I am more aware than ever of the importance of lung cancer research. On May 20th, I had the lead in dose for what is now my third phase I clinical trial. Knock on wood, I think I'm responding to yet another experimental therapy. Thus far, the agents in the first two phase I trials I participated in have gone on to receive FDA approval and are now readily available therapies for NSCLC. With a whole lot of luck, this agent will do the same. It's an exciting possibility to consider; that even if advanced cancer can't be cured, perhaps it can be managed. Clinical trials are now my lifeline, cancer research my hope.

Faced with limited treatment options, Linnea was fortunate to work with her healthcare team to identify and enroll in an early-phase clinical trial offering a unique treatment not available on the commercial market. Early-phase trials are often small and conducted at limited centers. Another challenge is that, for many patients, timely identification of relevant trials is not optional but essential if they want to have every opportunity to treat their cancer. Linnea's experience emphasizes the need for clinical trial information to be accessible, interpretable, and actionable, as patients must often make rapid, risk-balanced decisions based on their understanding of available studies.

As a patient advocate, part of Linnea's mission is to ensure that patients can find and assess whether a clinical trial might be right for their treatment plan. In her TED Talk, "Patient, Parent Person, Research Subject," she describes some of the challenges that exist, with a specific focus on medical jargon and the need for patient-centric language:[23]

> My personal experience has transformed me from advocate to activist. Medical research is my lifeline, and I am both a huge fan and major proponent. However, I

think it is important to always keep a balanced perspective. As an activist, I now advise pharmaceutical and biotech companies on ways in which trials can be made more patient-centric or user-friendly. You can't just build it, I tell them—you must build it better.

The terminology of trials is problematic. Participants are referred to as volunteers. Healthy volunteers are compensated for participation because they wouldn't volunteer otherwise. But those of us who are desperately ill—emphasis on desperate—we pay to participate. Calling us volunteers is absurd. Clinical trial participation is not some extreme form of community service. None of us has chosen this circumstance; it chose us. There's an argument that compensating vulnerable populations constitutes inducement. Both language and concept are patronizing and exploitative. I am induced only by my imminent demise, and compensation would simply reduce my burden.

Recognize that words like compliant and non-compliant have no place in a healthy partnership. Participants and clinical trials are in a codependent relationship with investigators and sponsors, where power is not evenly distributed. Because of this uneven dynamic, I took a huge risk when I became non-compliant, as I could have been removed from the trial. Fortunately, I was not. Even better, almost two years ago, the sponsor changed the scanning schedule for all participants to the one I had requested.

We all understand that medical research cannot be advanced without clinical trials. Participants in first-in-human trials perform a necessary service to society. However, there remain many barriers to participation—from lack of access to precluding conditions. These need to be addressed if we wish to increase enrollment. My extended survival would never have been possible without medical research. I was in the right place at the right time with the right oncologists. I am exceedingly grateful for my good fortune.

Melissa is a long-term lung cancer survivor and a nationally recognized patient advocate who has lived with non-small-cell lung cancer for over two decades. She is

actively engaged in the lung cancer community through organizations such as LUNGevity, where she works to reduce the stigma surrounding lung cancer, discuss the role of biomarker testing, and improve patients' understanding of clinical research and treatment options. Below is part of her journey that highlights the value of clinical trial participation:[24]

> I've participated in five clinical trials and have had a wide range of trial experiences. I've traveled for treatment, received therapy locally, and even had my medication mailed directly to my doorstep. I've found that it is very important to be open and honest with the trial doctors providing my care and with my medical team. Following the strict protocols of every study is also important because the information they gather is crucial to lung cancer research and the development of new treatment options.
>
> I've always felt comfortable in any trial I decided to participate in because I trust my doctor. Communicating with and having confidence in your doctors and medical team is extremely important. I'm open to any trial he suggests because I'm confident in him. I'm of the mindset that I've tried everything else, so why not? And I feel that my participation impacts the progress toward making lung cancer manageable so that more patients can treat it as a chronic condition rather than a terminal illness. At least that's the goal right now.

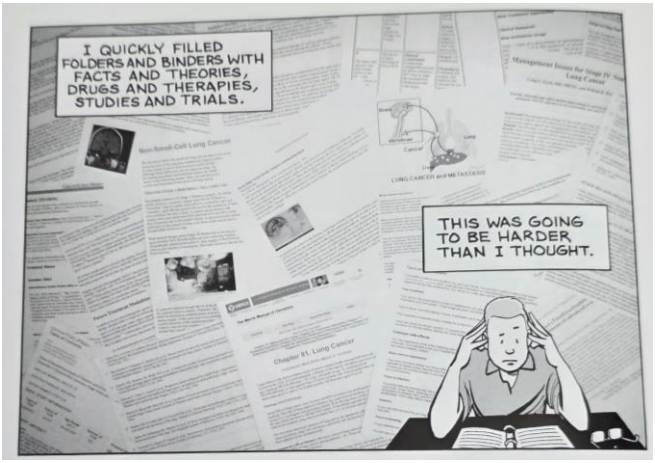
In his graphic memoir *Mom's Cancer*, Brian Fies illustrates the overwhelming experience of navigating his mother's diagnosis and treatment for metastatic lung cancer.[25] This graphic memoir poignantly captures the emotional and logistical challenges of caregiving. Through a series of illustrated vignettes, the memoir explores interactions with the healthcare system, treatment decisions, and the complexity of understanding cancer information. Figure 1 below depicts the moments after the doctor's visit and the

increasingly distressed state of attempting to keep up with the pace of medical information, as well as the shift from care partner to "researcher" as the panel progresses.[25]

Figure 1. Depiction of the Mismatch Between Patient Capacity and the Complexity of Cancer and Clinical Trial Information[25]

In Figure 2 below, the narrator describes rapidly accumulating "facts and theories, drugs and therapies, studies and trials," only to conclude: "this was going to be harder than I thought." This visual representation captures the cognitive burden associated with processing large volumes of complex medical information, reinforcing how even motivated and engaged individuals can become overwhelmed. The scene underscores a central challenge in cancer communication: the availability of information does not equate to understanding, particularly when content is dense, technical, and poorly structured for lay audiences.[25]

Figure 2. Illustration of Cognitive Overload From Complex Cancer Information and Clinical Research Materials[25]



Andrew Ciupek, Ph.D., is the Associate Director of Clinical Research at GO2 for Lung Cancer. This patient advocacy group has emphasized the critical role of clear communication in enabling patient understanding and engagement with clinical trials. Drawing on his experience supporting patients through trial navigation, Andrew describes informed consent materials as often "very jargony, very prescribed." Thus, patients often participate in clinical trials without fully understanding their options. Andrew notes, "To me, that's not informed. That's not empowered."[26] In a recent interview in collaboration with Patient Power, Andrew describes how working with a Patient Advocacy Nurse Navigator could assist in cutting through the jargon of ClinicalTrials.gov and help a patient prepare for discussing if a clinical trial might be right for a patient and the importance of communicating in language that patients and care partners clearly understand:[26]

> One of the things we do with clinical trials is we use the term informed consent. And I always say, you know, well, how do you make sure someone's really informed? Because I've talked to some patients, and they read through an

informed consent document for a clinical trial, which is very jargony, very prescribed. And they come away and they're like, "Well, my doctor told me this is a good decision, so I guess I'll sign it. And I'll do this. " And I'm like, "To me, that's not informed. That's not empowered." You trust your doctor and I think that's great and you should, but at the same time, I just know people would feel better if they said, "Yes, my doctor recommended it, but I also feel like I understand what I'm getting into." And it's not just, "Oh, I'm trusting my doctor because I can't understand it."

Another term that gets thrown around a lot [is] shared decision making. But to me, real shared decision making is the patient understands what the doctor said to them and that they've truly said, "I felt like I made a mutual decision. We both got together." And I feel like you don't get that without really understanding. Not everyone gets that.

What does a patient navigator do?

I do this through what we call our LungMATCH program, and that's our GO2's one-on-one clinical trial and treatment navigation program. … But when you have a question about new treatment advances or you're trying to do a clinical trial search or trying to understand something that involves science, you can be referred to one of our LungMATCH navigators.

And there's a couple of people on the team like myself, we have different backgrounds in research or public health, and we act, like you said, as translators. Someone picks up and we say to them…they either want to understand what new treatment options might be available for them or they're looking to see what clinical trials are relevant to them. And so we find out what their journey has been so far, what their diagnosis is, what their doctor's been telling them.

And then we go through and we do clinical trial searches, we look for new treatments that have emerged, and then I just spend time with them on the phone and say, "Here's what the most recent research says about your condition, and these are some questions you might want to ask your doctor at the next

> appointment to be conversation starters. Here's what you might want to delve into." And then I work with them to make sure they feel comfortable with it when they ask those questions, they understand why that's an important question and what they're hoping to get from it. So they feel a little less, I think, overwhelmed.
>
> I've learned a lot of stuff about how to just talk about health in general, and it's been really empowering to me because I find it. ... I got into it because cancer's complex and it's hard for people to understand cancer biology, but I realized that honestly, anyone's looking for that when they go into the doctor, even just for regular care like I've been talking to my family about.
>
> I find that people want to feel empowered that they're making decisions about their health that they actually understand, and they're just looking for someone to have a very practical conversation, not necessarily a whole college lecture on health science or biology, just what does this mean for me, why is that drug I'm taking being prescribed for me, what does this mean? And I think it's been good for me because I've learned how different people think of different concepts, and just how people want to hear things. And that just comes with practice. And so I think I've learned as much from the people I've talked to as they have from me. I like to think of just how can we communicate better about health. And that's one thing I want to do is, as a health research community, how can we do a better job of making sure the average person just understands what we're doing and why. Because at the end of the day, it's health. It affects everyone.

Here, Andrew discusses some of the challenges patients encounter when trying to find a clinical trial or even just understanding basic information about their health condition. He also highlights that many patients seeking clinical trials are overwhelmed by complex scientific language and often need assistance from a trusted source to sort through the information. One such program is LungMATCH, which pairs patients with Oncology Nurse Navigators to help patients identify and understand clinical trials that

may be a match. This service is designed to help remove the burden of translating complex research into accessible, patient-centered language, thereby reinforcing the essential role of effective communication in meaningful participation and shared decision-making in clinical care. The role of navigation and support systems is further discussed in later chapters.

An excellent commentary from Fred Hutch Cancer Center's blog, titled "Say What? Medical Jargon Leaves Cancer Patients Feeling Lost in Translation," speaks to the challenges the institution faces in oncology care in describing the complex medical terminology associated with cancer care.[27] Dr. Bernardo Goulart is a lung cancer oncologist and researcher at the Fred Hutchinson Cancer Research Center and the University of Washington, who offered his insights into how he tries to improve communication with his patients. He speaks about the critical role of clear communication in oncology care by emphasizing that medical jargon can create significant barriers to patient understanding. He notes that while technical terms may be appropriate for clinical documentation, "If you're conveying a diagnosis to a patient, you need to use the proper word," reminding that clinicians must ensure patients can "understand, digest and engage in the decision-making process.[27] Here is a part of his commentary:[27]

> First and foremost, doctors—and oncologists in particular—have a professional obligation to provide patients with accurate medical information in a way that patients can properly digest it. Some doctors will talk to patients about the stage of their cancer without ever explaining what staging means. Or they will use euphemisms like "mass" or "tumor" without clarifying that it's cancerous. But he said that's not how it should be done.

> Words like “malignancy” and “neoplasm” are good for technical reports and progress notes, but if you’re conveying a diagnosis to a patient, you need to use the proper word, and that’s “cancer,” and if we’re using fluid terms around cancer like “mass” or “malignancy,” we have to make sure we complement that with clear information. It’s a cancerous tumor in your lung or your liver or whatever. The burden is on the physician … to make sure that patients understand, digest, and engage in the decision-making process.
>
> Even patients with higher education may have an impaired ability to process because they’re under huge emotional distress from the cancer diagnosis. Their ability to process is decreased. I use lay language across the board.

A key point Dr. Goulart makes in his narrative is that using lay language is important for all patients and care partners, regardless of literacy or education level. Even highly educated patients may have trouble understanding clinical information, particularly at the time of diagnosis, when emotional distress, fear, and uncertainty create a significant cognitive burden. Patients and care partners are often required to process complex and unfamiliar medical information while navigating “fear, uncertainty, and emotional upheaval,” which can impair comprehension and decision making.[1] As a result, the ability to understand clinical trial information is influenced by both literacy level and situational factors, which is why it is so important to present information in clear, plain language that can be readily interpreted, regardless of whether that communication is in a live conversation, on print or web resources, or is the language used in the Brief Summary on ClinicalTrials.gov.

DRUG REGULATION AND CREATION OF CLINICALTRIALS.GOV

The U.S. FDA regulates all medicines that enter the U.S. market by ensuring the safety, efficacy, and security of human drugs. It is one of the oldest consumer protection agencies in the United States; first managing agricultural products, and later, following the passage of the 1906 Pure Food and Drugs Act, modern regulatory monitoring began. The FDA has continued to evolve over the years, with several amendments to modernize the organization.

In 1933, Rexford Tugwell, the Assistant Secretary of Agriculture in the Roosevelt administration, insisted that the 1906 Food and Drugs Act be reviewed, as there were significant shortcomings within the power of the agency, which earned it the reputation of the "Chamber of Horrors" in the common press.[28] It took five years of legislative negotiations before the Federal Food, Drug, and Cosmetic (FDC) Act of 1938 was passed in Congress. One of the most important additions was the requirement that new drugs to be shown safe before marketing, which initiated a new system of drug regulation.[29]

The FDA continued to revise its policies to ensure the safe and effective use of medications, with occasional course corrections as new drug classes came to market. The next big shift in the agency, with consideration to this paper, was the Food and Drug Administration Modernization Act of 1997 (FDAMA; Public Law 105–115—NOV. 21, 1997), which was the most wide-ranging list of reforms since the FDC of 1938.[8] This legislation required the U.S. National Institutes of Health (NIH) to create a database of clinical trials under review by the FDA. As described by the NLM:

> Specifically, FDAMA 113 required that the registry include information about federally or privately funded clinical trials conducted under investigational new

> drug applications to test the effectiveness of experimental drugs for patients with serious or life-threatening diseases or conditions. The information in the registry was intended for a wide audience, including individuals with serious or life-threatening diseases or conditions, members of the public, health care providers, and researchers.[30]

Effectively, the FDAMA is responsible for the creation of ClinicalTrials.gov, which launched in 2000 and has been available to the public since. Within the first year after launch, the website had a total of 1,255 trials posted in 2000. More than 20 years later, this number has increased to 28,091 trials posted in 2025.[31] Several organizations began a critical evaluation of the website to request additional transparency about the work being done. Following a Ministerial Summit on Health Research in 2004, the World Health Assembly passed a resolution in 2005 that required "unambiguous identification of all interventional trials," as "the registration of all interventional trials is a scientific, ethical and moral responsibility."[31] This resolution led to the creation of a parallel clinical trial registry, the International Clinical Trials Registry Platform.

In 2005, the International Committee of Medical Journal Editors (ICJME) required that all sponsors and investigators make their clinical trials available in a public database, such as ClinicalTrials.gov, if they wanted their publication to appear in a medical journal. ICJME issued a report criticizing the following:

> Selective non-publication of the results of research distorts the published evidence base and is a threat to research integrity. In the case of clinical trials, non-publication of results means that information on the efficacy of new drugs or other medical interventions cannot be used. Falling short on "clinical trials

> transparency" in this way presents risks to human health, contributes to research wastage and means that clinical decisions are made without access to all the available evidence.[32]

The introduction of Title VIII of the Food and Drug Administration Amendments Act (FDAAA) of 2007 aimed to improve public transparency in clinical research, following several instances in which large pharmaceutical companies failed to adequately publish and disclose negative clinical trial results. One such case study is the 2004 FDA approval of Vytorin (ezetimibe/simvastatin), indicated for use as an adjunctive therapy to diet for the reduction of elevated total-C, LDL-C, Apo B, TG, and non-HDL-C, and to increase HDL-C in patients with primary (heterozygous familial and nonfamilial) hypercholesterolemia or mixed hyperlipidemia.[33]

Vytorin was approved based on short-term lipid-lowering and safety trials demonstrating reductions in low-density lipoprotein (LDL) cholesterol and bioequivalence data, without evidence from cardiovascular outcomes trials or atherosclerosis imaging studies.[34] At the time of approval, the FDA considered LDL lowering to be a sufficient surrogate endpoint for approval of cardiovascular therapies. Questions about the Vytorin approval were raised by the medical and research community following the publication of long-term results of the ENHANCE trial, four years after approval, in a 2008 *New England Journal of Medicine* article.[33,35]

The ENHANCE trial evaluated Vytorin (ezetimibe/simvastatin) compared to simvastatin alone in a large, randomized, controlled, phase-3 trial, with a primary endpoint that assessed the progression of atherosclerosis by measuring the change from baseline in mean carotid intima–media thickness (cIMT) measured by B-mode ultrasound

over 24 months, which served as a surrogate marker of atherosclerosis.[36] The results of this study showed that despite LDL lowering, there was no cIMT benefit. This outcome raised concerns in the research community about the use of surrogate endpoints, approval standards, and the delay in disclosing unfavorable or negative data.[36] It also raised broad questions about the approval of Vytorin without sufficient cardiovascular risk, myocardial infarction, stroke, or mortality endpoints. The FDA acknowledged in a statement that "delayed and partial data disclosure created public confusion while a full regulatory review was ongoing."[37] Laurent Hirsch, President and founding member of the International Society for Medical Publication Professionals, wrote a commentary, "Trial Registration and Results Disclosure: Impact of U.S. Legislation on Sponsors, Investigators, and Medical Journal Editors," which offered "that any attempt to interfere with disclosure of valid clinical trial results is a violation of public trust and ethical obligations to the study participants, and cannot be condoned."[38]

In summary, the ENHANCE trial demonstrated that reliance on surrogate endpoints and delayed disclosure can mislead clinicians and undermine patient trust. It became a case study that drove regulatory reform toward mandatory transparency and outcomes-based evidence via FDAAA Title VIII.

In the U.S. House of Representatives, Senator Charles Grassley from Iowa testified on February 13, 2007, prior to the passage of the legislation. He stated,

> Last month, Senator Christopher Dodd and I introduced two reform bills … to fix the safety shortcomings at the FDA. Our first bill would elevate and empower the office within the FDA that is responsible for monitoring FDA-approved drugs after they are on the market … the second bill … would expand an existing public database by mandating the registry of all clinical trials and the results of those

> trials. The American people assume that when clinical trials are conducted, the results—positive or negative—will be available. That assumption is often wrong. When unfavorable results are withheld, doctors and patients are left with an incomplete and misleading picture of a drug's safety and effectiveness. This reform is key to establishing greater transparency regarding clinical trials, the good ones, and the bad ones, and to hold drug makers and drug regulators accountable and to give doctors all the information they can to their patients. The FDA cannot protect the public if it does not have access to complete and accurate clinical trial information.[39]

The implementation of Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA 801) established the framework for ClinicalTrials.gov's expansion to include the PRS.[40] The creation of this web-based data entry system allows users to register a clinical study and submit results for clinical trials. The requirements of this legislation have been in effect since September 27, 2007, codified at section 402(j) of the Public Health Service (PHS) Act, and include conforming amendments to the Federal FDC Act.[40] The Final Rule for Clinical Trials Registration and Results Information Submission (42 CFR Part 11) clarifies and expands the regulatory requirements and procedures for submitting registration and results information for certain trials to ClinicalTrials.gov, in accordance with FDAAA 801.[41,42]

> This rule provides for the expanded registry and results data bank specified in Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) to help patients find trials for which they might be eligible, enhance the design of clinical trials and prevent duplication of unsuccessful or unsafe trials, improve the evidence base that informs clinical care, increase the efficiency of drug and device development processes, improve clinical research practice, and build public trust in clinical research. The requirements apply to the responsible

> party (meaning the sponsor or designated principal investigator) for certain clinical trials of drug products (including biological products) and device products that are regulated by the Food and Drug Administration (FDA) and for pediatric post-market surveillance of device products that are ordered by the FDA.[39]

In October 2008, NLM addressed the first step of implementation of FDAAA 801, modifying ClinicalTrials.gov by

> expanding the scope of required trials to include studies of devices and all diseases (only trials of drugs and biologics for serious or life-threatening diseases or conditions were required to be registered previously); and, increasing the information required to be registered (e.g., the primary and secondary outcome measures being studied).[43]

The second modification to the registry was the inclusion of basic trial results being publicly made available, with specificity around the data included in the summary data tables, including

> baseline characteristics, which are taken at the beginning of a trial and may include demographic and physiologic characteristics of the participants; participant flow to indicate the number of participants at each stage of the trial; and, outcomes data, including pre-specified primary and secondary outcomes, and relevant statistical analyses.[43]

At this time, the NLM also committed to reporting serious adverse events by including an option table for reporting them and other frequent adverse events observed during the trial.[43] This reporting step became mandatory by law on September 27, 2009.[40,44]

Tony Tse et al. from Lister Hill National Center for Biomedical Communications, NLM, reviewed these changes and clearly outlined how the results database intentions

had a far-reaching impact on multiple groups, including researchers, journal editors, institutional review boards, ethicists, patients, the general public, users of medical literature, and policymakers.[45] However, the authors noted,

> Results reporting in the database will commonly occur prior to journal publication. Unlike journal articles that have been peer reviewed by both scientific colleagues and editors, results submitted to ClinicalTrials.gov are not peer reviewed prior to posting, although minimal quality standards must be met. The public display of results in stand-alone tables needs to be self-explanatory and meaningful to a range of users. Results entries do not contain discussions or conclusions. However, as in writing a manuscript for a journal, an individual familiar with the study design and data analysis (e.g., a clinical investigator) will need to carefully consider ways to organize and annotate the results in order to optimize data presentation, especially for complex clinical study designs and results.[45]

Dr. Wood shared similar concerns in his *New England Journal of Medicine* Special Report:

> Creating a comprehensive clinical trials database is very challenging because of the wide variety of trial designs that must be registered. Because the submitted data will not be peer-reviewed and will not be interpreted, qualified, or explained, the results reported at ClinicalTrials.gov will complement rather than replace the thoughtful presentation and discussion of results characteristic of the best peer-reviewed publications.[46]

These critiques address the gap between communicating complex clinical trial data and accessibility to the lay public, with a need for both scientific manuscripts to better describe the data and Plain Language Summaries (PLSs) for the public. Moreover, publication of results data in ClinicalTrials.gov databases is not routinely considered

prior publication and does not violate most embargo policies of major congresses and ICJME member medical journals. Overall, Dr. Wood offered the following perspective:

> The dedication of patients who take the risks to participate in clinical research is dishonored when their data remain secret. Section 801 of the FDA Amendments Act will greatly expand the type and amount of information available on clinical trials. The use of these data and the enhanced public access to the FDA's database on clinical trials proposed in this article will greatly improve the ability of investigators and others to assess the full set of results for a given intervention, whether FDA-approved or not, eventually leading to more accurate systematic reviews, better clinical decision making, improved patient care, and improved research efficiency and safety.[46]

Today, while the overall guiding principles behind ClinicalTrials.gov are governed by FDAAA 801 and 42 CFR Part 11, other laws and policies also require the registration and reporting of clinical trials. The NIH Policy on Dissemination of NIH-funded Clinical Trial Information dictates that any clinical trial that is funded "in whole or in part by NIH of any intervention (includes drug, biological, and device products, as well as surgical procedures, and behavioral interventions)" requires registration and submission or results to ClinicalTrials.gov.[47] Similarly, studies funded by Patient-Centered Outcomes Research Institute (PCORI) require studies that show "comparative clinical effectiveness clinical trials and observational studies funded by PCORI" to register and submit summary results information to ClinicalTrials.gov[48] (PCORI) studies funded by the Department of Veterans Affairs (VA) have policies around registering, reporting, and updating all VA ORD-funded studies.[49] The policy states the following:

> The VHA Office of Research and Development (ORD) is committed to informing Veterans and the public about its research and maximizing the impact of the studies it supports. As a leader in the national clinical trials enterprise, ORD has been making clinical trial information available through public registries for more than 15 years. To achieve these goals, Principal Investigators (PIs) of ORD-funded clinical trials are responsible for registering their trials with and submitting summary results to the National Library of Medicine's (NLM) public registry, ClinicalTrials.gov, as a condition of funding. ClinicalTrials.gov provides patients, family members, health care professionals, and members of the public easy access to information on clinical trials for a wide range of diseases, conditions, and health problems.[50]

The WHO International Clinical Trials Registry Platform (ICTRP) is a global initiative to ensure that clinical trial information is prospectively registered and publicly accessible. Its mission is to "ensure that a complete view of research is accessible to all those involved in health care decision making; this will improve research transparency and will ultimately strengthen the validity and value of the scientific evidence base."[51] The WHO ICTRP defines the required trial information for the study to be fully registered with the WHO and all studies can be access via the search portal https://trialsearch.who.int.[52] Included in the ICTRP search portal are multiple registries including ClinicalTrials.gov, the ISRCTN Registry, the EU Clinical Trials Register, the Pan African Clinical Trials Registry, and more than 15 other primary registries that "meet the criteria for content, quality and validity, accessibility, unique identification, technical capacity and administration."[51,53-55] This platform was initially proposed in August 2005 and was launched in May 2006. It undergoes continual evaluation for needed updates.

In 2015, the WHO issued a report, "Rationale for WHO's New Position Calling for Prompt Reporting and Public Disclosure of Interventional Clinical Trial Results," which evaluated the current landscape of reporting and validated its April 14, 2015, declaration on the public disclosure of clinical trial results. The reports highlighted, "In a study that analyzed reporting from large clinical trials (over 500 participants) registered on ClinicalTrials.gov and completed by 2009, 23% had no results reported even after a median of 60 months following trial completion; unpublished trials included nearly 300,000 participants." Hence, policy change was not reflected in the real-world reporting on the ClinicalTrials.gov PRS system.[55,56] The WHO summarized the need for appropriate results reporting as follows:

> Not reporting clinical trial results is likely to lead to dissemination bias. This bias has the following major adverse consequences:[56]
>
> - It affects the understanding of the scientific state of the art,
> - It leads to inefficiencies in resource allocation for both research and development and the financing of health interventions,
> - It creates indirect costs for public and private entities, including patients themselves, who pay for suboptimal or harmful treatments,
> - It potentially distorts regulatory and public health decision making.

The ICMJE also took action in 2004 by creating the ICMJE Clinical Trials Registration Recommendations, which require registration of all interventional studies (e.g., drug, biological, and device products; surgical procedures; and behavioral treatments). However, it did not require results submission and instead "expects authors to meet results information submission requirements "of their funding and regulatory

agencies [and] encourages ... results reporting even when not required."[57] This policy also led many ICJME-recognized journals to no longer consider the publication of trials that were unregistered. Notably, while the WHO and the ICJME require the registration of all trials, regardless of phase, the FDAAA 801 excludes phase 1 drug trials and early feasibility device trials. In the United States, federal law requires all parties to register with and submit results to ClinicalTrials.gov.[58] Guidance from the FDA states the following:

> Transparency of clinical trial information is important to scientific advancement. Registering certain trials and posting summary results information permits the scientific community to build on the information made available. The public's participation in clinical trials makes it possible to further advance scientific progress. Posting clinical trial information on ClinicalTrials.gov honors volunteers who participate in research to advance medical science and enhances public trust by creating a transparent and robust public record of clinical trials and information about their results.[58]

The FDA provides requirements for certification of compliance via Form FDA 3674, which is a requirement for most Investigational New Drug Application (IND), NDA, Biologics License Application (BLA), Abbreviated NDA (ANDA), Premarket Approval Application (PMA), Humanitarian Device Exemption (HDE), and 510(k) submission, with only Investigational Device Exemption (IDE) being excluded form the Form FDA 3674 submission.[59] Among the requirements is a verbatim statement on Informed Consent about the inclusion of patient-level data, including adverse events reporting and results, as required by the Informed Consent Elements, 21 CFR 50.25(c).[60] The statement included in all Informed Consent Forms (ICFs) reads, "A description of

this clinical trial will be available on www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."[60,61] As of 2026, failure to comply with the FDA requirements may result in pre-notices of noncompliance, notices of noncompliance, corrective action, withholding of NIH grant funding, civil money penalties up to $15,000 a day with no cap, injunctions, criminal prosecution, and/or regulatory action.[62] The Final Rule became effective on January 18, 2017, and responsible parties have been required to comply since April 18, 2017.[63]

ClinicalTrials.gov allows the registration of clinical studies with human subjects that assess biomedical and/or health outcomes and that conform to the following:[64]

- Any applicable human subject or ethics review regulations (or equivalent);
- Any applicable regulations of the national or regional health authority (or equivalent).

Applicable drug clinical trial means a controlled clinical investigation, other than a phase 1 clinical investigation, of a drug product subject to section 505 of the Federal FDC Act (21 U.S.C. 355) or a biological product subject to section 351 of the PHS Act (42 U.S.C. 262), where "clinical investigation" has the meaning given in 21 CFR 312.3 and "phase 1" has the meaning given in 21 CFR 312.21.[65-68] A clinical trial of a combination product with a drug primary mode of action under 21 CFR part 3 is also an applicable drug clinical trial, provided that it meets all other criteria of the definition under this part.[69] The Final Rule provides additional clarity and is reinforced by 42 CFR 11.10, which states that applicable clinical trials include interventional trials that have

one or more arms with one or more pre-specified endpoints of FDA-regulated drugs and meet at least one of the following conditions:[70,71]

- The trial has one or more sites in the United States,
- The trial is conducted under an FDA investigational NDA or investigational device exemption, and
- The trial involves a drug, biologic, or device product manufactured in the United States or its territories and is exported for research.

FDAAA 801 is the law passed by Congress that created what we now consider the modern version of ClinicalTrials.gov. Title 42 is a statute in the United States Code (U.S.C.), the formal codification of federal law passed by Congress. Within 42 U.S.C. § 282, the PHS Act, ClinicalTrials.gov registration and results reporting are codified into law, including the regulatory authority, responsible parties, obligations, and legal requirements. This document grants the NIH and HHS legal authority to operate ClinicalTrials.gov. This next section reviews the statutes that define the content requirements for inclusion in the ClinicalTrials.gov registry and, importantly, includes the language that created the Brief Title, Brief Summary, and lay language requirements.[44]

(ii) Content (42 U.S. Code § 282)

The clinical trial information required to be submitted under this paragraph for an applicable clinical trial shall include—

(I) descriptive information, including—

(aa) a brief title, intended for the lay public;

(bb) a brief summary, intended for the lay public;

(cc) the primary purpose;

(dd) the study design;

(ee) for an applicable drug clinical trial, the study phase;

(ff) study type;

(gg) the primary disease or condition being studied, or the focus of the study;

(hh) the intervention name and intervention type;

(ii) the study start date;

(jj) the expected completion date;

(kk) the target number of subjects; and

(ll) outcomes, including primary and secondary outcome measures;

Title 42 addresses the use of in the Posting of Data requirements, which include lay language requirements:[44]

(B) Inclusion of results

The Secretary, acting through the Director of NIH, shall—

(i) expand the registry data bank to include the results of applicable clinical trials (referred to in this subsection as the ‘‘registry and results data bank’’);

(ii) (ii) ensure that such results are made publicly available through the Internet; (iii) post publicly a glossary for the lay public explaining technical terms related to the results of clinical trials; and

(iii) (iv) in consultation with experts on risk communication, provide information with the information included under subparagraph (C) in the registry and results data bank to help ensure that such information does not mislead the patients or the public.

Lay language guidance is also provided for Adverse Events:[44]

> (iv) Posting of other information in carrying out clause (iii), the Secretary shall, in consultation with experts in risk communication, post with the tables information to enhance patient understanding and to ensure such tables do not mislead patients or the lay public.

Finally, in the Expanded Registry and Results Data Bank, the required elements specify the use of lay language as follows:[44]

> The regulations under this subparagraph shall require, in addition to the elements described in subparagraph (C), information within each of the following categories:
>
> (I) A summary of the clinical trial and its results that is written in non-technical, understandable language for patients, if the Secretary determines that such types of summary can be included without being misleading or promotional.
>
> (II) A summary of the clinical trial and its results that is technical in nature, if the Secretary determines that such types of summary can be included without being misleading or promotional.
>
> (III) The full protocol or such information on the protocol for the trial as may be necessary to help evaluate the results of the trial.
>
> (IV) Such other categories as the Secretary determines appropriate.

This section continues with additional provisions that clarify what is “understandable language” for a lay audience:[44]

> The regulations under this subparagraph shall also establish—
>
> (I) a standard format for the submission of clinical trial information under this paragraph to the registry and results data bank;

> (II) additional information on clinical trials and results that is written in nontechnical, understandable language for patients;
>
> (III) considering the experience under the pilot quality control project described in paragraph (5)(C), procedures for quality control, including using representative samples, with respect to completeness and content of clinical trial information under this subsection, to help ensure that data elements are not false or misleading and are non-promotional;
>
> (IV) the appropriate timing and requirements for updates of clinical trial information, and whether and, if so, how such updates should be tracked;
>
> (V) a statement to accompany the entry for an applicable clinical trial when the primary and secondary outcome measures for such clinical trial are submitted under paragraph (4)(A) after the date specified for the submission of such information in paragraph (2)(C); and
>
> (VI) additions or modifications to the manner of reporting of the data elements established under subparagraph (C).

While FDAAA 801 took effect when it was passed in 2007, it was not until September 21, 2016, that the Federal Register Final Rule for 42 CFR was issued due to the complex nature of drafting federal regulations, which require a multi-state legal process and extensive review. The introduction of FDAAA801 was complex and controversial; the NIH–HHS sought extensive stakeholder input before implementation, and the entire process had to comply with the Administrative Procedure Act. The initial Notice of Proposed Rulemaking (NPRM) was made available for public comment from November 2014 to March 23, 2015.[72] This open-comment period received over 900 public comments, and as estimated by the HHS:

> About 60 percent were nearly identical in content, expressing support for clinical trial transparency efforts and the goals of the NPRM and provided specific perspectives on a number of the proposals. Another large subset of comments also expressed support for clinical trial transparency and the NPRM goals but did not comment on specific proposals. There were about 100 distinct comments that addressed specific NPRM proposals. As reflected below, all of the comments were reviewed and all points and perspectives were carefully considered.[73]

Major areas of controversy included whether phase 1 and feasibility trials needed to be included, posting of results for unapproved products, trade secrecy and intellectual property concerns, penalties and enforcement, and the potential burden on sponsors and academic investigators. It became a careful negotiation between balancing the need for transparency versus the overall regulatory burden. The full comments from this period can be found at www.regulations.gov by searching for Docket NIH–2011–0003.

The Final Rule discusses the comments submitted regarding the utility of the lay language and guidance. One area of commenting focused on a Brief Summary of the results, which is separate and different from the Brief Summary of the trial.[73] Regarding non-technical summaries specifically, commenters have noted that it may be difficult for members of the public to understand study results provided in a technical summary and that the provision of lay summaries would enhance public understanding of the results. Others have highlighted the difficulty of writing a simple summary that captures the nuances of complex research findings. They have noted that systematic reviews, which synthesize all available evidence, are better sources of information for the lay public than Brief Summaries of a single trial. One commenter suggested that the informed consent document could be required in lieu of a lay summary because it provides important basic

information in non-technical terms and has been reviewed by an independent party (i.e., an Institutional Review Board [IRB]).[73]

The response was as follows:

> Taking the public comments into consideration, and given concerns about the potential for harm to public health from the promotion of medical products for unapproved uses, the Secretary is declining at this time to require narrative results summaries until further research is conducted to determine whether and, if so, how summaries can be reliably and consistently produced without being promotional or misleading. Current approaches in the dissemination of trial summaries, such as the FDA's Drug Trials Snapshots, PCORI's summary reports, and industry efforts to return summary results to participants, may be informative and will be reviewed and considered as part of any further research.[73]

This decision removed any responsibility for trial sponsors to provide lay summaries of the results. However, it maintained the requirement for lay language in the Brief Title and the summary of the trial description. This decision also allowed sponsors to include additional information in their informed consent form since it does not provide any interpretation or analysis of the trial results and is presented to patients prior to clinical trial enrollment. The informed consent form is written in lay language and should fully characterize the trial's "purpose, procedures, risks, and potential benefits." This form may be posted on ClinicalTrials.gov if the sponsor requests publication.[73] The final rule did add clarity and specification to what is commonly referred to as the Brief Title and Brief Summary. They are included below, in full, from the final rule to allow the reader to have a complete understanding of the language, context, and rationale.[73]

A) Brief Title.

In § 11.10(b)(1) of the NPRM, Brief Title was defined as ‘‘a short title of the clinical trial written in language intended for the lay public, including any acronym or abbreviation used publicly to identify the clinical trial.’’ Section 402(j)(2)(A)(ii)(I)(aa) of the PHS Act specifically requires the submission of a brief title as part of the clinical trial information submitted at registration, but it does not define the term, other than to indicate that the title is ‘‘intended for the lay public.’’ As explained in the NPRM, we interpreted this requirement to mean that potential human subjects should be able to understand, from the Brief Title, the general purpose of the clinical trial and distinguish it from others listed in the data bank. Additionally, based on our experience to date with ClinicalTrials.gov, we recognized that acronyms are frequently used to refer to clinical trials (e.g., ‘‘ACCORD’’ for the Action to Control Cardiovascular Risk in Diabetes trial or ‘‘STAR*D’’ for the Sequenced Treatment Alternatives to Relieve Depression trial), and we believe that it is important for such acronyms to be included in the registry to enable users of the data bank to identify clinical trials that they may see referenced in other media (e.g., news reports, journal articles). As such, we considered an acronym used to identify a clinical trial to be part of the Brief Title (79 FR 69612). We received no comments on this description and therefore maintain the proposed description in the final rule. We note that a Brief Title intended for the lay public should include, where possible, information on the participants, condition being evaluated, and intervention(s) studied

(C) Brief Summary.

In § 11.10(b)(3) of the NPRM, Brief Summary was described as ‘‘a short description of the clinical trial, including a brief statement of the clinical trial’s hypothesis, written in language intended for the lay public.’’ As noted in the NPRM, section 402(j)(2)(A)(ii)(I)(bb) of the PHS Act expressly requires a ‘‘brief summary’’ to be submitted as clinical trial registration information, but it does not define the term other than to indicate that the Brief Summary is ‘‘intended for the lay public’’ (79 FR 69612). We received no comments on this description and therefore maintain the proposed description in the final rule.

At the time of the Final Rule, ClinicalTrials.gov was still largely viewed as a regulatory compliance system rather than a patient-facing health information resource, and there were no formal plain-language requirements. Today, it seems surprising that no comments were received about the content or writing of the Brief Summary. Given the landscape from 2014 to 2016, the primary focus of commenters was transparency, driven by concerns about data disclosures, trial results, and adverse event reporting. Sponsors and academia were concerned about costs, intellectual property, and the burden to their clinical staff members. Patient advocacy groups also participated in the open-comment period and raised similar concerns. It was not until several years later that a shift in the landscape emphasized shared decision making and patient-centered communication. Concerns were also raised about the inclusivity of clinical trials and the disparities observed when comparing enrolled populations in U.S. studies with real-world disease incidence.

A shift toward patient-centricity began around the time of the 21st Century Cures Act (2016), which strongly encouraged patient engagement in research, regulatory decision making, and policy.[74] This act established the model of patients as partners, supplanting the idea of patients as subjects by creating what is now referred to as Patient-Focused Drug Development. The first notable shift toward patient-centered communication within ClinicalTrials.gov began with NIH's launch of the ClinicalTrials.gov Modernization Initiative in 2019, which explicitly identified usability and the ability for the public to easily find and understand clinical trial information as a core strategic goal.[75] This emphasis on accessibility culminated in the release of the "Plain Language Checklist for Lay Brief Summaries" on September 26, 2022, and its

later expansion into a comprehensive “Plain Language Guide to Write a Brief Summary” on March 19, 2024.[21,76] These milestones reflected a transition from viewing ClinicalTrials.gov as a sponsor-facing submission system to recognizing it as a key public health communication resource for patients, care partners, and the broader community.

In summary, all clinical trials that fall under the purview of FDAAA 801 must be registered through the PRS, with relevant updates provided through the trial's completion and culminating in the submission of the results. The individual responsible for submission is defined as follows:[77]

- The sponsor of the clinical trial, as defined in 21 CFR 50.3; or
- The principal investigator (PI) of such clinical trial if so designated by a sponsor, grantee, contractor, or awardee, so long as the PI is responsible for conducting the trial, has access to and control over the data from the clinical trial, has the right to publish the results of the trial, and has the ability to meet all of the requirements for the submission of clinical trial information.

Notably, not all drug trials fall under the jurisdiction of the Public Health Act section 402(j), which dictates registration and submission requirements for ClinicalTrials.gov. A reminder of examples of trials that do not need registration includes the following:[78]

- Phase 1 trials of investigational drug products or biological products, including studies in which investigational drug products are used as research tools to explore biological phenomena or disease processes

- Small clinical trials to determine the feasibility of a device product or a clinical trial to test prototype devices, where the primary outcome measure relates to feasibility and not to health outcomes
- Trials that do not include drug, biological, or device products, such as behavioral interventions
- Noninterventional (observational) clinical research, such as cohort studies

While not required by law, the sponsor or responsible party may voluntarily submit their trial to the database. Justification for submission may include support for trial enrollment and public awareness, transparency within the research community, publication requirements, ethical responsibility, funding requirements, or other reasons not disclosed by investigators. Once submitted to the PRS system, the study may have to comply with the requirements of the PHS Act on a case-by-case basis.

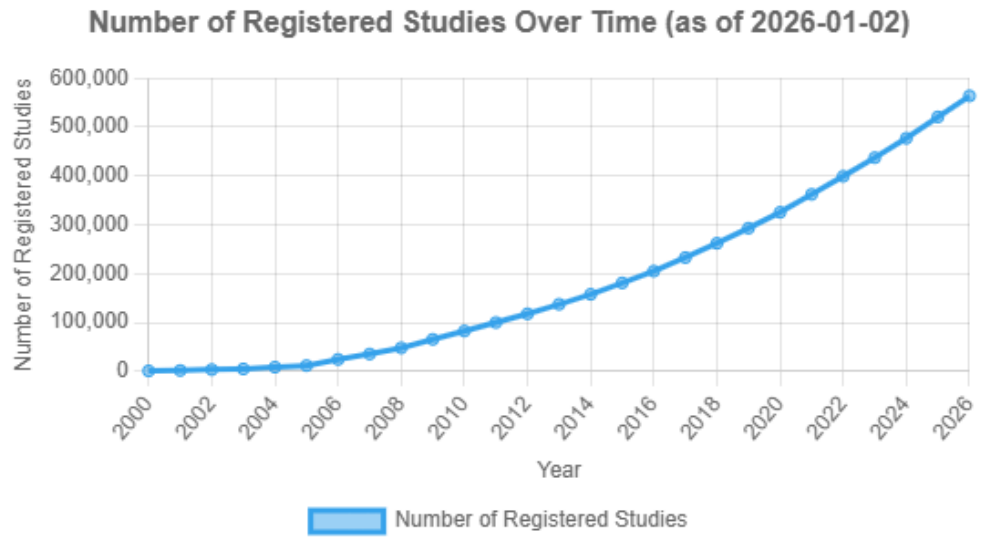
A historical estimate was presented by Anu Mathur, MS, CIP, from the University of Irvine Office of Research: "In 2015, 19,170 clinical trials were registered. 7,400 were applicable clinical trials. The remainder, 11,770 trials, can be considered voluntary or not fall under the rule. Of these, 526 were funded by NIH. This leaves an estimated 11,244 trials that do not fall under either the rule or the NIH policy."[77,79] Administrative burdens are associated with voluntarily registering a trial, primarily the need to maintain up-to-date trial data and ensure compliance with PRS reporting mandates, but the benefits outweigh the burden.

At the time of this writing, no legislation had been proposed that directly affected the NLM or the governance of ClinicalTrials.gov under the FDAAA Title VIII. It would be remiss not to remark on H.R. 3521 – Clinical Trial Modernization Act (119th

Congress, 2025), introduced into the U.S. House on May 20, 2025, by Rep. Raul Ruiz (D-CA-25), with Rep. August Pfluger (R-TX-13).[80] The goal of the act is to "modernize clinical trials and remove barriers for participation in clinical trials, and for other purposes" by reducing financial, logistical, and legal barriers, creating additional pathways for sponsor payments, and expanding access through decentralization to support inclusive research.[80] If approved, the downstream effect on ClinicalTrials.gov would be minimal but may require additional data fields, workflows, and registry fields to support decentralization, and potentially sponsor reimbursement disclosures.

Indeed, 2025 marked a banner year for the NLM as it celebrated 25 years of clinical research transparency following the launch of ClinicalTrials.gov in 2000. The NLM listed the 500,000th clinical trial in 2024, with listings in all 50 U.S. states and 226 countries and territories, and an average of 2 million monthly visitors in 2025.[82] To understand the scope of growth, Figure 3 below shows the year-over-year growth of registered studies. The next chapter discusses the Modernization Project of ClinicalTrials.gov that fostered this rapid growth.

Figure 3. Number of registered studies by year (as of January 2, 2026)[83]



Source: https://ClinicalTrials.gov

Note:
The International Committee of Medical Journal Editors (ICMJE) began requiring trial registration as a condition of publication in September 2005
The registration requirements of Food and Drug Administration Amendments Act of 2007 (FDAAA) began and were implemented on ClinicalTrials.gov in December 2007

MODERNIZATION PROJECT

ClinicalTrials.gov, a public clinical research registry and results database, is operated by the NLM, a component of the NIH. The original ClinicalTrials.gov website launched in 2000 and has seen substantial growth over the last 25 years, now the home to over half a million clinical trials, observational studies, and expanded access programs, with daily use by 113,000 visitors.[81] The modernization effort, initiated in 2019, is a multi-year initiative aimed at enhancing the user experience, accommodating growth, and improving efficiency. The NLM Board of Regents Public Services Working Group prepared annual summary reports on the ClinicalTrials.gov Modernization Effort from 2019 to 2024, with the final report scheduled for completion in Q4 2025. These reports outline the progress made in modernizing ClinicalTrials.gov, a public clinical research registry and results database operated by the NLM. A detailed outline of the Modernization Project over the five years appears in Figure 4 below.

Figure 4. ClinicalTrials.gov Modernization Project Overview by Year (2019–2025)[85]

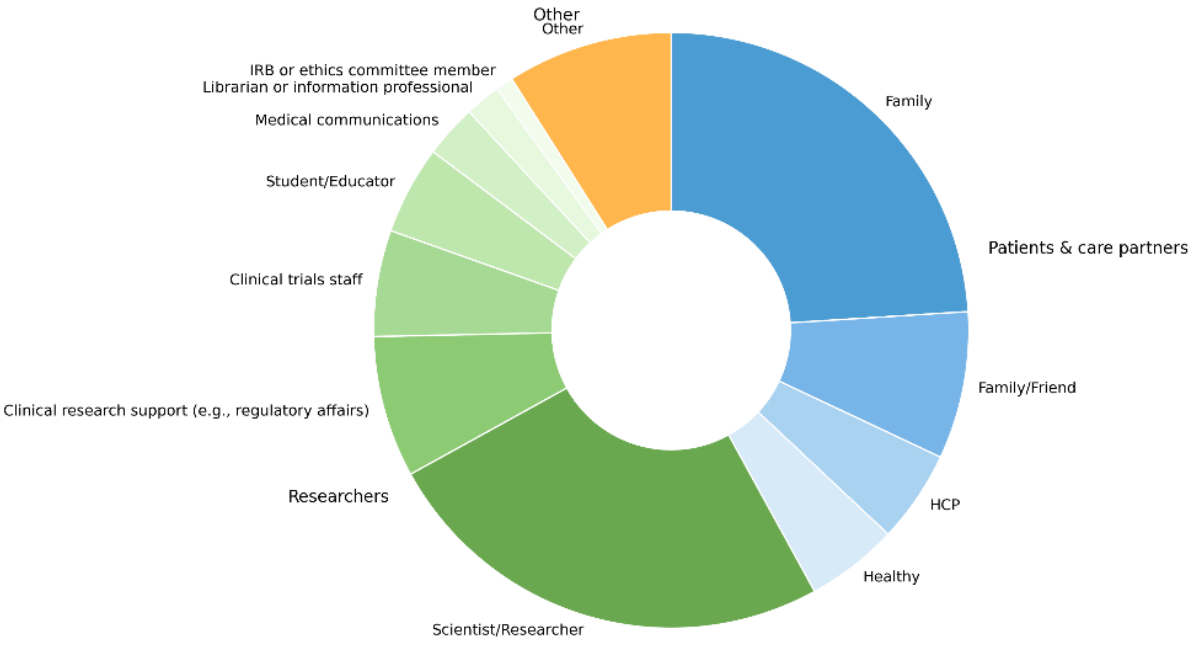
The modernized ClinicalTrials.gov became the primary site in June 2023. It reported detailed product releases, progress on strategic goals, input from the Working Group, public communications strategies, research supporting the effort, and plans through 2024. The Modernization of ClinicalTrials.gov was considered complete, as the classic website and application programming interface (API) were retired on June 25, 2024.[82]

In August 2019, the NLM launched a modernization initiative for the ClinicalTrials.gov website and the PRS. This initiative aimed to sustain ClinicalTrials.gov as a trusted public health resource, thereby ensuring its enduring value. The modernization strategy focused on stakeholder engagement, product development, and technical infrastructure enhancements.[83] This multi-year effort aimed to enhance user experience through an updated platform capable of accommodating growth and improving operational efficiency. The established Working Group supported the adoption of the three strategic goals that organize the desired outcomes, or effects, of the modernization effort: (1) clinical trial information is current, complete, and reliable; (2) anyone can easily find and use information about clinical trials; and (3) trial information, resources, and tools provide value to the research ecosystem.[83]

The NLM used a staged approach over five years for the modernization workstream, thereby allowing ample time to engage with stakeholders and conduct usability research. The project began with a "Request for Information: ClinicalTrials.gov Modernization" (Guide Notice Number: NOT-LM-20-003), which sought feedback on ClinicalTrials.gov's website functionality, information submission processes, and data standards usage.[84] The FDA hosted a webinar, "Learn About ClinicalTrials.gov

Modernization and How to Provide Input," on March 6, 2020, to increase reach and awareness among study sponsors, investigators, and clinical research coordinators.[85] The audience composition at the webinars can be seen in Figure 5 below.[86]

Figure 5. Audience Composition: Top-Level and Subcategory Breakdowns



Note: Researcher subcategories were proportionally normalized to 49% total (original sum was 51%); IRB/ethics used 1% placeholder scaled to ~0.96%.

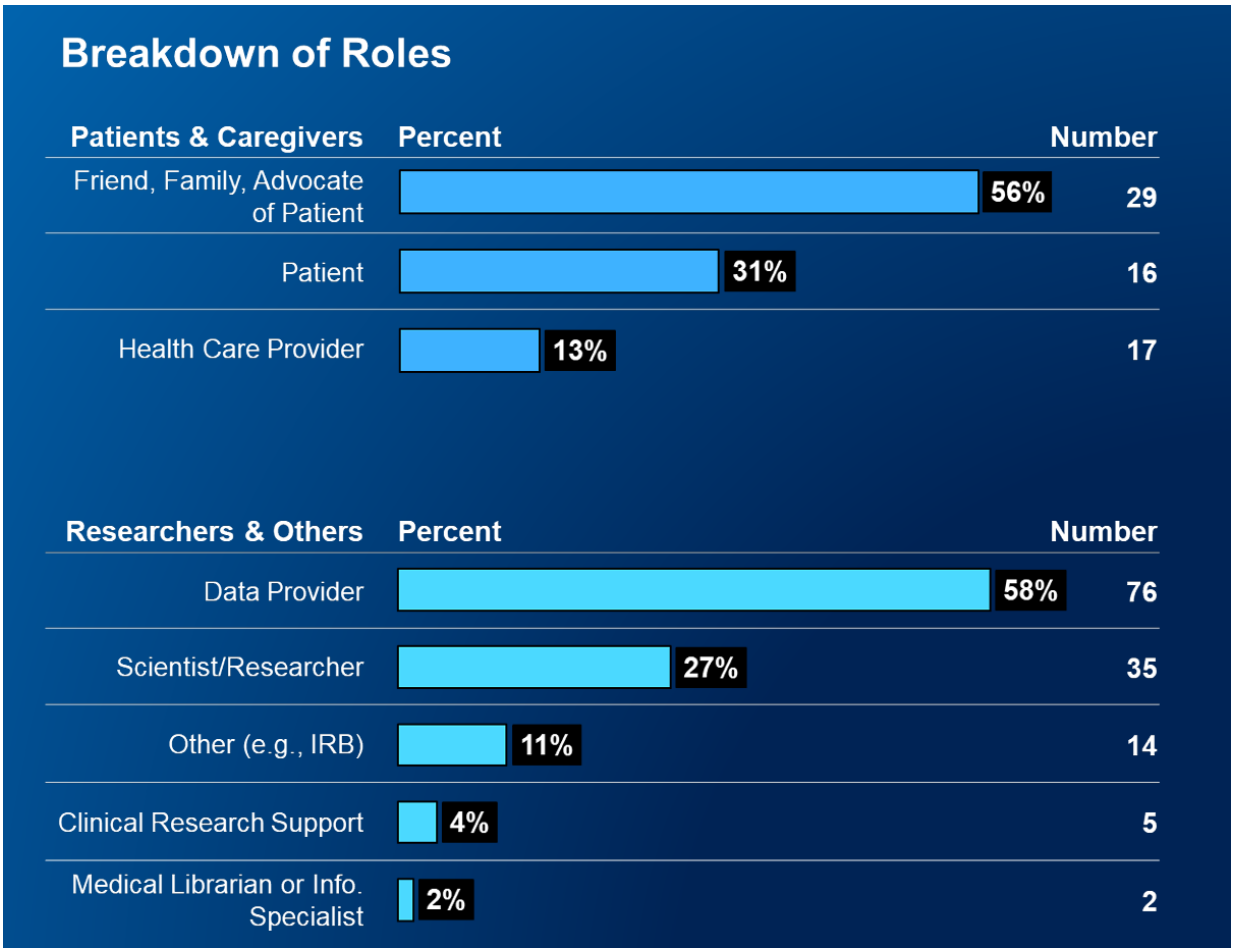
A justification for modernization was provided, with key themes including ensuring the registry remains a trusted public health resource, supporting growth and future needs, understanding usability feedback, accommodating technological changes,

and expanding data use cases (e.g., mobile integration). The NLM RFI was reviewed in depth, including steps for submission, follow-up, reviews, timelines, and discussing the core areas where feedback was being sought, specifically website functionality, information submission, and data standards. The comment period remained open for 75 days from December 30, 2019, to March 14, 2020, and comments were collected via a web-based form with three main topic areas and 11 specific sub-question prompts. The upload of attachments was also permitted.[87]

On April 20, 2020, 400 meeting attendees joined a public webinar to review the Modernization Project, with a focus on sharing responses to open comments and feedback from 12 listening sessions hosted by the NLM, which gathered input from 20 institutions and centers.[88] The open-comment period generated 268 responses, 49% who identified as researchers and others, 19% patients and caregivers, and 31% unknown.[88] The breakdown of roles is shown in

Figure 6 below.

Figure 6. Breakdown of Roles of Responders to RFI



Dr. Williams provided a high-level summary of comments by category type and theme and shared some highs and lows from the feedback, one of the highs being a direct quote:

> The ClinicalTrials.gov site provides an important public service, and it's invaluable to have the registry information freely available to the public. As the ClinicalTrials.gov platform continues to evolve, in both form and function, it will become even more widely used and beneficial to the patient, research, and funding communities. Thank you for your efforts on this project!

As part of the webinar, groups split up into a panel to give different user perspectives.[88] Alissa Gentile from Blood Cancer United (formerly The Leukemia and Lymphoma Society) joined the panel to represent the role of patient advocacy groups and how they use ClinicalTrials.gov to support patients who are considering a clinical trial. Her presentation focused on the complexity and overwhelming amount of content available on the registry and the rapidly changing landscape that makes it impossible to stay up to date on clinical trials. She approached the utility of ClinicalTrials.gov from two sides.

First, Alissa highlighted that their Clinical Trial Support Center, staffed by trained Oncology Nurse Navigators, uses the trial registry to assist patients in their search for trials. These navigators work one-on-one with a patient to gather information about their medical history, diagnosis, tumor profile, and treatment history and provide them with a "patient-friendly list of appropriate clinical trials to ultimately discuss with their health care team."[88] She noted that even with the list, patients often still had challenges reaching research nurses or PIs and emphasized the importance of up-to-date, location-based status in the registry.[88]

Alissa also detailed how Blood Cancer United has its own proprietary clinical trial finder Application Programming Interface (API), powered by CareBox, which is available to patients for conducting their own trial searches. It only requires a diagnosis and a zip code to begin. Through their software, they use most of the ClinicalTrials.gov search fields and discuss the importance of certain data fields (e.g., the Brief Title and Brief Summary), which allow the API to display patient-friendly language. Alissa emphasized, "The more accurate the information is on ClinicalTrials.gov, the less barriers for us nurses to have to go through that support and patient process to taking steps to be

considered for a clinical trial. And ultimately that patient would have more information."[89] At every touchpoint, the Clinical Trial Support Center websites prompt users to connect live with a navigator, as live support has the highest success rate. Alissa ended her presentation with a powerful message that emphasized the importance of accessibility of trials to patients:

> It's important to note that the goal of the Clinical Trial Support Center is not to enroll every patient into a trial, but to increase the opportunity for participation; facilitate informed decision-making about clinical trials; and really minimize those logistical barriers if the patient, in collaboration with their health care team, decides that a clinical trial is right for them. Ultimately, we want to educate, support, and empower those patients to be active participants and have some control over their treatment decisions.[89]

Another panelist was present, Seth Morgan, who represented the patient voice as a patient diagnosed with multiple sclerosis and as a board-certified physician by the American Academy of Neurology for 26 years. He described his personal experience as a physician being diagnosed with a complex, chronic disease, which explored how even with all the years of training he had, he struggled to personally understand what the diagnosis meant for him. He warned,

> You can also start grasping for anything, regardless of the scientific validity or the risk potential, and that's where the danger is."[89] He continued, "Access to research options and information is a very strong positive; it gives hope. It offers the possibility of a future and helping at least, if not finding the cure, or maybe finding it and starting on a medication, which will help you survive the situation that you're in.[89]

The final panelist to speak was Steven Woloshin, a consultant and researcher with the NIH, who shared his experience when trying to find a clinical trial and recent trial results for insomnia. He shared what his search experience was like, the challenge of using appropriate terms, the type of trials (i.e., interventional), and the effort required to sort through the 166 results presented as options. While his discussion focused mostly on the need to quickly identify studies with results and easily accessible data tables, he cited the Brief Summary as one of the most useful tools for quickly understanding the purpose of the study, thereby allowing him to quickly exclude trials that were irrelevant to his search. He added that while he had the benefit of a medical background, additional tools such as a layperson glossary would be a helpful addition to improve layperson accessibility, as well as linking to systematic literature reviews such as the Cochrane Library. In summary, this webinar did an outstanding job not only outlining the status and progress of the Modernization Project but also bringing the patient voice directly into the conversation, emphasizing the need for lay language and the importance of the Brief Summary to the patient community.

The next public webinar update was again presented by Dr. Rebecca Wiliams, Acting Director of ClinicalTrials.gov, on Feb 18, 2021. The objectives of the meeting were to provide a status update on the ClinicalTrials.gov modernization effort, explain the roadmap and phased approach, discuss findings from stakeholder engagement, and describe how users could volunteer to provide feedback. While much of the content was repetitive to prior open sessions, she presented the key themes from the public RFI, as outlined in Table 1 below.[88]

Table 1. Key Request for Information Response Themes[88]

Theme	Details
Search Options and Managing Search Results	• Make search more user friendly • Add more options to search • Improve tools for managing search results
Study Record Format and Content	• Standardize more content • More prominently display certain content; make more content available • Add features to make using content easier
Plain Language Information	• General health information and learning about study participation • Resources for using site features • Study record content

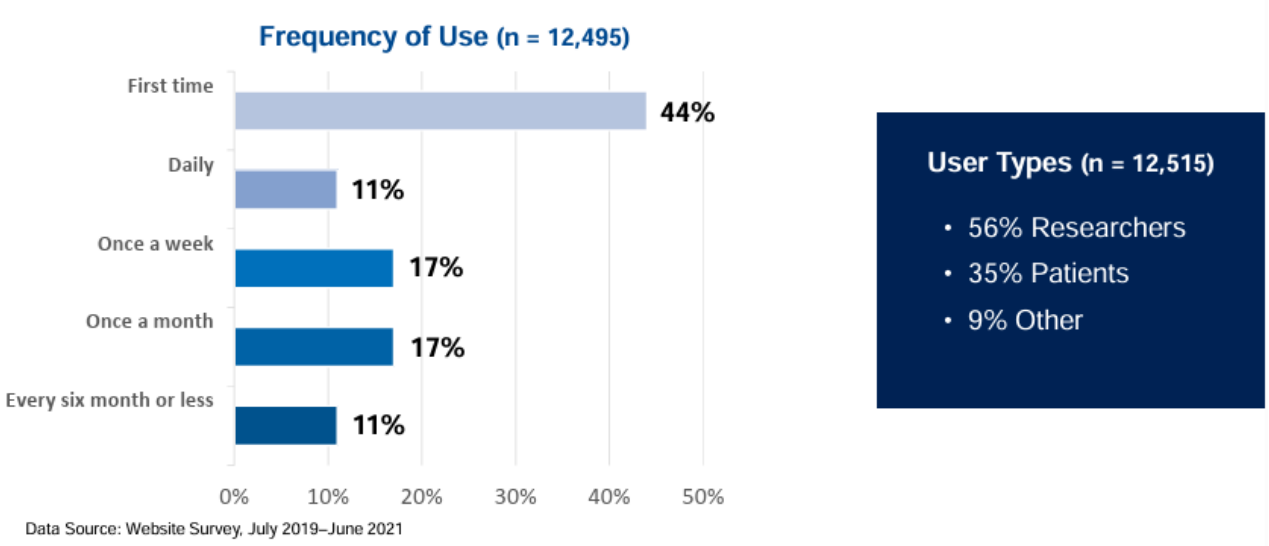
Dr. Williams stated that across all stakeholder groups, the need for plain language was a consistent theme. She explained that it is necessary to describe general information about the trial, the readability of study records, lay-friendly support materials, instructions for using the website, and guidance for data providers. The Brief Title and Brief Summary were highlighted as being two instances where lay language is currently in use. Dr. Williams said that "better guidance on how data providers can better meet that need" will be addressed in future updates, with a commitment to prioritized plan-language site content, give clear examples and expectations of PRS submissions, and acknowledged that patient, care partners, and advocacy groups were part of the key stakeholder feedback teams.[88]

During the ClinicalTrials.gov Modernization Beta Preview public webinar held on October 7, 2021, NLM provided background on the ClinicalTrials.gov modernization

effort, shared information on how users will be able to view and explore upcoming changes to ClinicalTrials.gov Beta and PRS Beta, communicated next steps, and answered questions from among the more than 450 attendees.[88,90] The webinar also reviewed the newly updated, modified search experience and layout, the reorganized study record page, and reviewed the plain language site content for new joiners of the webinar. At the time of the webinar, they anticipated the full beta would go live by the end of 2021, with the classic view concurrently available. An interesting new data point presented was a poll of *N* = 12,515 users of ClinicalTrials.gov to assess their frequency of use, as shown in

Figure 7 below.[91]

Figure 7. ClinicalTrials.gov Users and Frequency of Use[95]



This session also included a question-and-answer period in which one participant asked, “If more plain language is used on the site, will it change the requirement for how registration records need to be written?”[91] The direct response from Dr. Williams was as follows:

> Another great question. Initially, our plain language efforts have been focused on content that we, as the National Library of Medicine, provide. However, I will say that there is a need for data submitters to evaluate and improve certain data fields to better meet plain language expectations. There are two data items in our regulation: the Brief Title and the Brief Summary, which are explicitly required to be in plain language. This is certainly an area that we will be exploring in terms of how to provide additional guidance to data submitters in improving this content.[91]

The next public webinar was held on December 10, 2021, which attracted more than 300 live attendees and more than 700 recorded views.[92] During this ClinicalTrials.gov Modernization Update and Beta Website Demonstration, the NLM provided an update on the modernization effort and shared an overview and demonstration of the new ClinicalTrials.gov Beta website, which highlighted the changes that users would see, communicated next steps, and answered questions.[92] Attendees participated in an interactive poll to offer input regarding desired features for future ClinicalTrials.gov beta releases. The majority expressed preference for an advanced search function, with the next most requested feature being the option to download search results in additional formats. At this point, the beta site was live, with a launch date of December 8, 2021.[93]

On October 27, 2022, the NLM hosted a live webinar with Dr. Anna Fine, Acting Director, ClinicalTrials.gov, as the main presenter, which included an update on the progress of the ClinicalTrials.gov modernization effort, an overview of the ClinicalTrials.gov and PRS beta websites, and a question-and-answer session.[94] In this session, Christina Robinson, ClinicalTrials.gov beta product owner, spoke directly about the unique needs of patients when visiting the site. She acknowledged, “We know that the

majority of them come to ClinicalTrials.gov hoping to join a study." She detailed their needs to understand the trial information, decide whether to enroll, locate a study site, and identify the appropriate contact information. These factors were among the usability design considerations aimed at optimizing navigation through study details and location-based searches. They emphasized that plain language should reduce technical jargon, improve comprehension, and make the process less intimidating.[94]

The webinar also pointed to enhancements on the PRS side, including a plain-language glossary and a "help drawer" with plain-language descriptions for submitters. Finally, they acknowledged that the September 26, 2022, release of the Plain Language Checklist for Lay Brief Summaries (PDF) was added to the Support Materials under Data Element Definitions, Templates, and Checklists. They noted they did this early because "we were reviewing it for modernization and building these help features. We figured, why not put it out there in PRS now? And if you have feedback on that, we can make it even better before it's rolled out into the PRS Test and into the PRS Beta."[94] This idea was detailed in the annual report as follows: "ClinicalTrials.gov is considering the current landscape in determining how to best support data submitters in preparing all data elements required to be written in language for the lay public by FDAAA 801 and the Final Rule and may revisit this effort after modernization."[95]

The NLM hosted a Spring 2023 public meeting on April 25, 2023, to "share information about the modernized ClinicalTrials.gov website and PRS Beta, and provide an opportunity for users and stakeholders to ask questions and give feedback."[96] The targeted audience was described as follows:

> Sponsors and investigators who submit clinical trial information using the PRS. In addition, we hope to reach ClinicalTrials.gov public website users, including patients, families, health care providers, academics, industry representatives, members of nonprofit and advocacy organizations, staff of government agencies, and data researchers.[96]

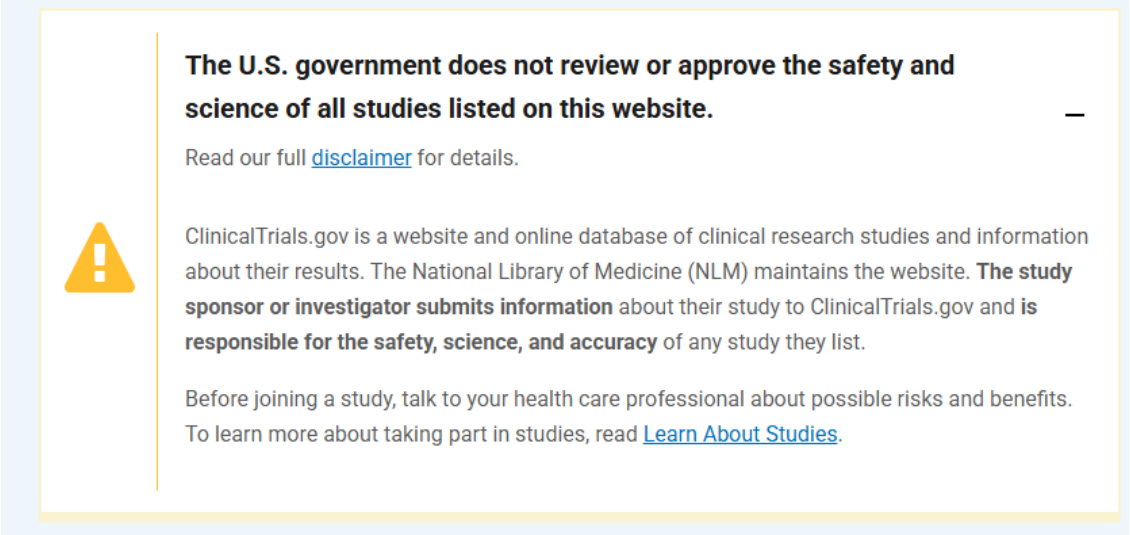
The nearly 500 attendees represented a wide range of perspectives, including those of academic, industry, and government data submitters; information specialists and librarians; regulatory and regulatory affairs staff; data researchers; and patients and their advocates."[97] During the webinar, the NLM shared an infographic that demonstrated the extensive reach the Modernization Project had since its initiation (see Figure 8 below).

Figure 8. ClinicalTrials.gov Modernization: Outreach and Engagement[102]

Attendees at this meeting were welcome to join one of two breakout rooms (i.e., the Modernization of ClinicalTrials.gov or PRS Beta) to listen to pre-recorded messages and participate in polling and chats about user feedback. The breakout room assigned to cover ClinicalTrials.gov provided an extensive overview of the plain-language support offered to patients on the new website. The first example highlighted was the new page "Learn About Studies."[98] This webpage provides general information regarding clinical research and the implications of participating in such studies. Additionally, it offers plain-language guidance for individuals submitting data through the PRS system. Developed and released last in 2022, this website was under review at the time of the webinar to identify further improvements. At the time of the webinar, it included a comprehensive checklist designed to help ensure lay summaries are clear and accessible. Today, this website has been revised to include only "Learn About Studies," with its content and structure expanded. The presenter also reviewed the template aligned with the checklist and strongly recommended that all submitters use the tool.

The last major plain-language improvement covered was the site disclaimer (see Figure 9 below),[99] which was described as "a big hurdle for us in terms of helping users understand, again, that we make the information available and it is a government website, but we are not, you know, responsible for the safety or the science related to those studies."[99,100] This banner was moved to the top of the page, where it remains today. The session concluded by reviewing, in detail, all the user interface improvements that made trials more visible, including clearly identifying the study status.

Figure 9. ClinicalTrials.gov User Warning[104]



Continuous feedback was also provided via the Spring 2023 NLM Office Hours, where 112 attendees participated in open feedback and question-and-answer sessions.[101] The stakeholder community praised the NLM for its accessibility, transparency, and communication of the overarching goals of the projects and integration of public feedback. Another session was held in the Fall to have office hours dedicated specifically for PRS Subject Matter experts, which gathered

> … 112 attendees, who were primarily librarians and information professionals, researchers, and data scientists but also included members of the public, representatives of federal agencies, and community-based organizations. The product owner gave an overview of the modernized ClinicalTrials.gov website along with future plans for continued development, and a panel of team members answered questions from the audience.[101]

On June 6, 2024, the NLM hosted the webinar “Modernized ClinicalTrials.gov Update,” intended for the general public, patients, patient advocates, data researchers,

data providers, and anyone who accesses and uses the information found on ClinicalTrials.gov.[106] The goals of the webinar were to share updates on the overall modernization effort, highlight features of the modernized website, and help users prepare for the retirement of the classic ClinicalTrials.gov.[107] Speakers outlined the rationale for modernization, progress to date, upcoming transitions, and new features designed to improve usability, accessibility, and transparency for diverse user groups. A central theme was balancing regulatory continuity with user-centered design to ensure that modernization did not impose new burdens on trial sponsors while improving the experience for patients, care partners, researchers, and data users.

However, during this webinar, the plans for updating the Brief Summary and title were not addressed. Questions from the community were about the availability of the classic site, the ability to download and transfer resources, the retirement of classic PRS, how to ensure their feedback was being reviewed, and whether there was a way to track the progress of submitted requests. Patient accessibility questions focused on issues such as how to determine how many study sites were in a trial/plan to be in a trial, whether a specific study site was actively recruiting (as opposed to the entire trial), and whether ClinicalTrials.gov could directly help them enroll in a trial. Overall, the session emphasized stakeholder engagement, iterative feedback, and a strong commitment to accessibility and mobile optimization.[106]

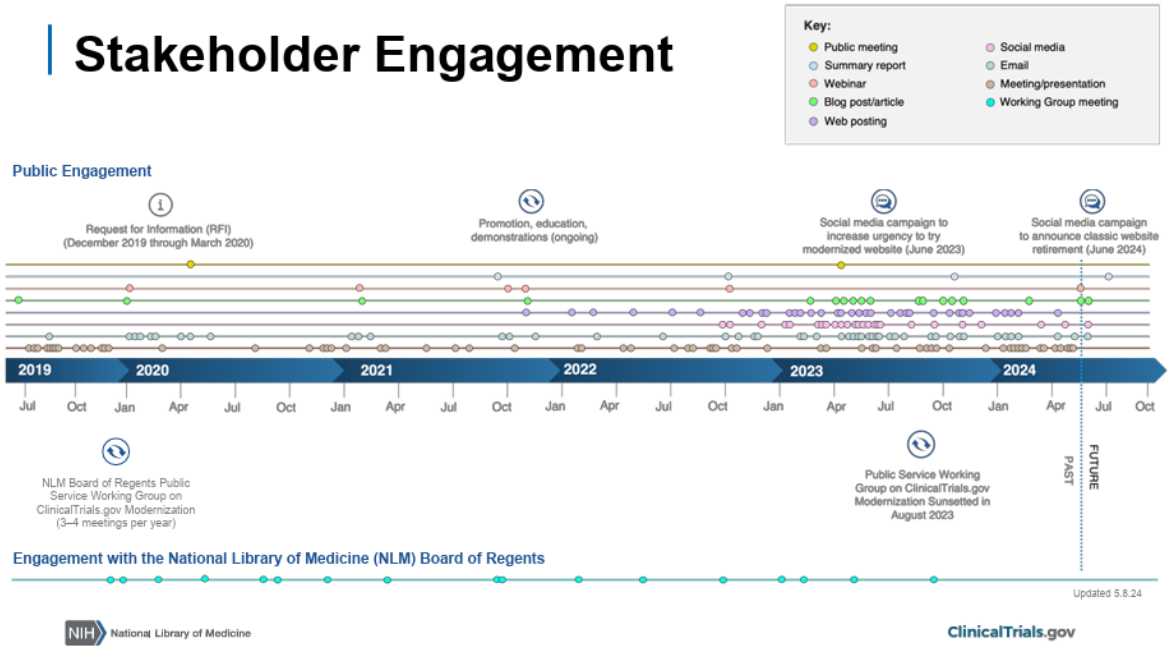
Following this webinar, a June 2024 NLM Technical Bulletin highlighted the addition of "plain language guidance and support materials" available on ClinicalTrials.gov.[108] On October 8, 2024, the NLM hosted another webinar, "Introduction to the Modernized Protocol Registration and Results System," to provide

updates on features of the modernized PRS website and any outstanding questions on the modernization of ClinicalTrials.gov.[109]

As demonstrated throughout this chapter, users have remained central to the ClinicalTrials.gov team's modernization approach. User feedback helps inform further development and improvements to the Modernized ClinicalTrials.gov and PRS system, while the NLM remains committed to a continuous feedback process even after the project's formal closeout. As seen in

Figure 10 below, stakeholder engagement was robust, with numerous public meetings, webinars, blog posts, web postings, social media campaigns, emails, and NLM office hours, thereby demonstrating diligence in gathering extensive user feedback.

Figure 10. Stakeholder Engagement[107]



The Modernization Project, spanning from 2019 to 2025, was a transformative initiative that moved the registry from a clunky platform mandated by policy to a modern, user-friendly data repository better aligned with the needs of today's researchers and patients. Through stakeholder engagement and iterative technical development, the NLM delivered on its three core goals: clinical trial information is current, complete, and reliable; anyone can easily find and use information about clinical trials; and trial information, resources, and tools provide value to the research ecosystem.[102] Key outcomes of the modernization included clearer navigation and plain-language support for patients and caregivers. They included the development of the "Plain Language Checklist for Lay Brief Summaries," enhanced search precision and data download capabilities for researchers, expanded transparency through integrated record history and APIs, and a scalable technical foundation that will support continued growth beyond the already 500,000 registered studies. Ultimately, the modernization strengthened ClinicalTrials.gov as both the central, trusted hub for global clinical research transparency and an accessible, plain-language resource that enables all patients, care partners, and members of the public to search for, understand, and use clinical trial information.

PRACTICAL APPLICATION: SEARCHING FOR TRIALS ON CLINICALTRIALS.GOV

ClinicalTrials.gov is the comprehensive database of all clinical trials that are available in the United States. The website itself has undergone several iterations to improve the user experience. In this dissertation, references to the Modernization Project refer to the most recent efforts to improve the website, initially announced by the NIH–NLM as part of its strategic plan for 2017 to 2027. As outlined in the "A Platform for Biomedical Discovery and Data-Powered Health," the NLM aims to

> … enrich its flagship clinical trial registry and repository, ClinicalTrials.gov, through improved front-end and back-end design. Enhancements to expand interoperability with data and information in other resources, such as individual-level data collected in the course of the trials supported by NIH, will be considered, along with improvements in operational efficiency in producing, curating, and ensuring long-term preservation of this resource.[103]

In August 2019, the NIH–NLM announced the first steps in the improvement processes with a goal to "deliver an improved user experience on an updated platform that will accommodate growth and enhance efficiency." At the time of the announcement, the NLM stated that ClinicalTrials.gov was the largest public clinical trial registry with over 300,000 trials listed, 145,000 unique daily users, and an estimated astounding 215 million page views each month.[104] After an extensive RFI from key stakeholders the core areas of improvement were narrowed to "several themes for modernizing ClinicalTrials.gov, including ways to improve the management of search results, study records, and plain language information for the website, as well as enhancements to

support structured and unstructured data, the quality control review process, and workflow management for information submission."[105] The modernization of ClinicalTrials.gov was driven by both policy mandates and usability concerns, including accessibility and health literacy issues identified in prior evaluations.

Studies have repeatedly found that experienced users had difficulty navigating the database and understanding key trial information, which limited ClinicalTrials.gov's potential to serve patients, care partners, and clinicians effectively.[106] A 2022 review of ClinicalTrials.gov led by the CISCRP evaluated the current compliance with plain language and clinical trial transparency on 30 ClinicalTrials.gov listings. Their assessment indicated the following:

> The components required by current regulation were largely present, but they lacked pieces of meaningful information and failed to disclose most information in accessible, plain, non-technical language. Overall, we noted gaps in plain language readability, clearly stated endpoint results, presentation of causally related safety data, and general usability. High-level summaries of the listings are not consistently interpretable without additional knowledge of the study or a detailed assessment by a trained clinical trial professional. This is due to the inconsistencies in information listed, and lack of high-level conclusions, even when data from the results is present.[106]

Although required elements may be present on ClinicalTrials.gov, many listings lack readable, meaningful content. Empirical research has demonstrated that lower health and computer literacy significantly impair users' ability to formulate queries and interpret clinical trial content on web-based search engines, further limiting equitable access to trial information.[107]

The NLM recognized that the multi-year Modernization Project would include interim feedback with continuous improvements made to the modernized site to address concerns raised by groups such as the CISCRP. It took approximately four years for the NLM to announce readiness for public access to the ClinicalTrials.gov Modernization Effort Beta release, first made available in December 2021. During this release, the goals were outlined: 1) introduce users to the new technology platforms and evaluate their real-world performance, 2) provide foundational features that will be expanded over time, 3) provide PRS users with improved functionality to manage their record portfolios and workflows, and 4) collect user input to inform future development activities.[107] The beta site was open to the public and key stakeholders for review, with several webinars, press releases, and learning sessions to help explain the improvements.

The NLM highlighted that this beta release would feature an improved site design optimized for desktop and mobile devices, with the key addition of information written in plain language. During this first phase, the NLM highlighted the release of a "redesigned home page and search feature, search results page with updated filter functionality, new study record design with improved record navigation and study location information displayed using a web-based mapping application, and informational content presented in plain language."[108] The addition of plain language was applied to the "Background, Learn About Studies, Study Record, and Resources" pages to better support a wide variety of users. The content was refined based on a full health literacy review "using the most up-to-date, evidence-based health literacy principles and feedback from focus group testing."[109]

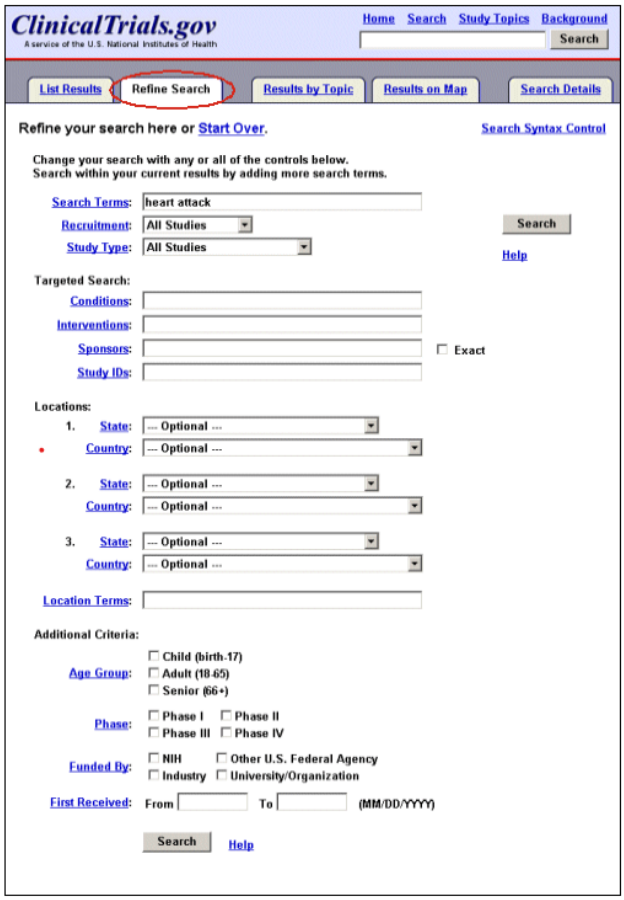
Another two years passed before the next major milestone, an announcement from the NLM that the new, modernized ClinicalTrials.gov website would be replacing the classic website in June 2023.[110] During this transition time, additional educational webinars detailed the changes in user interface that were explored in-depth in the previous Clinical Trial Modernization chapter of this dissertation. During the transition period, both the "classic" and "modernized" versions of the website were available to the public. However, visitors to ClinicalTrials.gov were on the modernized site as a standalone experience.

At this point in the modernization process, the site had activated its "browse-by-map" feature, which allowed geospatial views of where trials are running, and its "browse-by-topic" feature, which allowed thematic and grouped browsing. The goal of both features was to enhance how search results were displayed and explored, beyond the plain tables in the classic view.[111] In the classic view, the search feature was a basic toolbox (see Figure 11 below).[112]

Figure 11. Basic Search Screen for "Heart Attack"[117]

The user could expand the search as an "Advanced Search" by clicking on the tab or link to offer the ability to "limit search based on recruitment status (i.e., open or closed to enrollment), study type (i.e., interventional, observational, or expanded access), and date ClinicalTrials.gov first received the study record. In addition, users could search for a specific study sponsor and search multiple locations at once (e.g., Washington, D.C., OR Virginia OR Maryland). The function of Advanced Search could also be applied to a search result by selecting the "Refine Search" tab (previously "Search Within Results") on the List Results page, and the user's original search term(s) would be retained (see Figure 12 below).[112]

Figure 12. Refine Search Page[117]

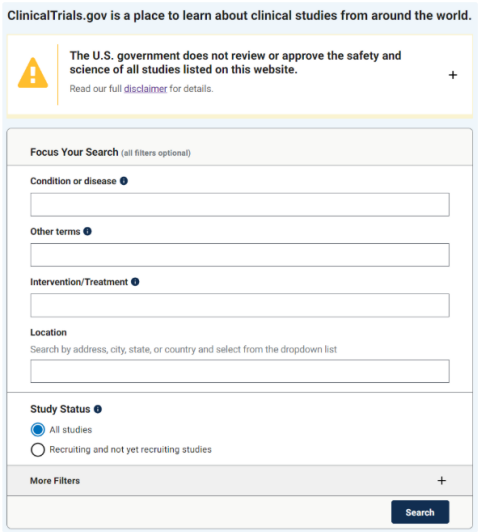


Interim releases have enhanced the ability to search, filter, and find trials by zip codes, link to PubMed, to improve usability, with one of the major beta releases made available on November 2, 2017.[113] These interim releases were all followed by a period of public commentary to allow for sufficient feedback on the usability of the registry. The current, modernized website features enhancements detailed by NLM as follows:

> A streamlined design with a color scheme and layout that is visually appealing, easy to read, and based on the U.S. Web Design System – consistent with other federal government websites. We've improved navigation with simple web components, such as left-side menus and expandable accordions, so you can quickly locate information. We have also added more plain language guidance and educational content. In addition, ClinicalTrials.gov has been optimized for mobile devices, so you can access this resource anytime from anywhere.[114,115]

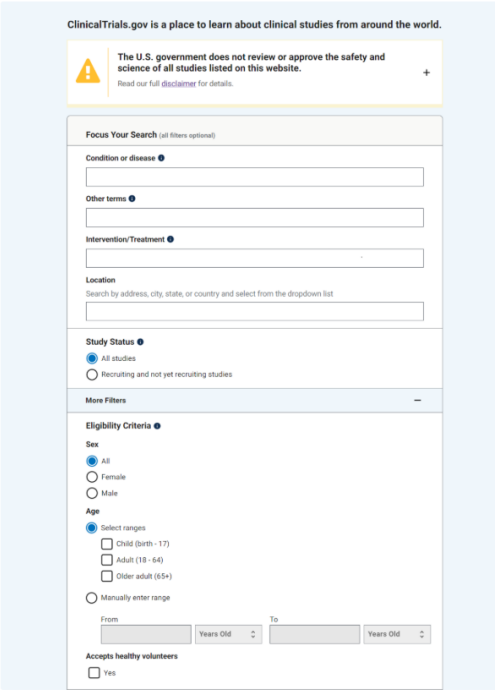
The updated search offered a sleek design with initial search options to help narrow users' searches from the start (see Figure 13 below).

Figure 13. Homepage Showing New "Search" Features[104]



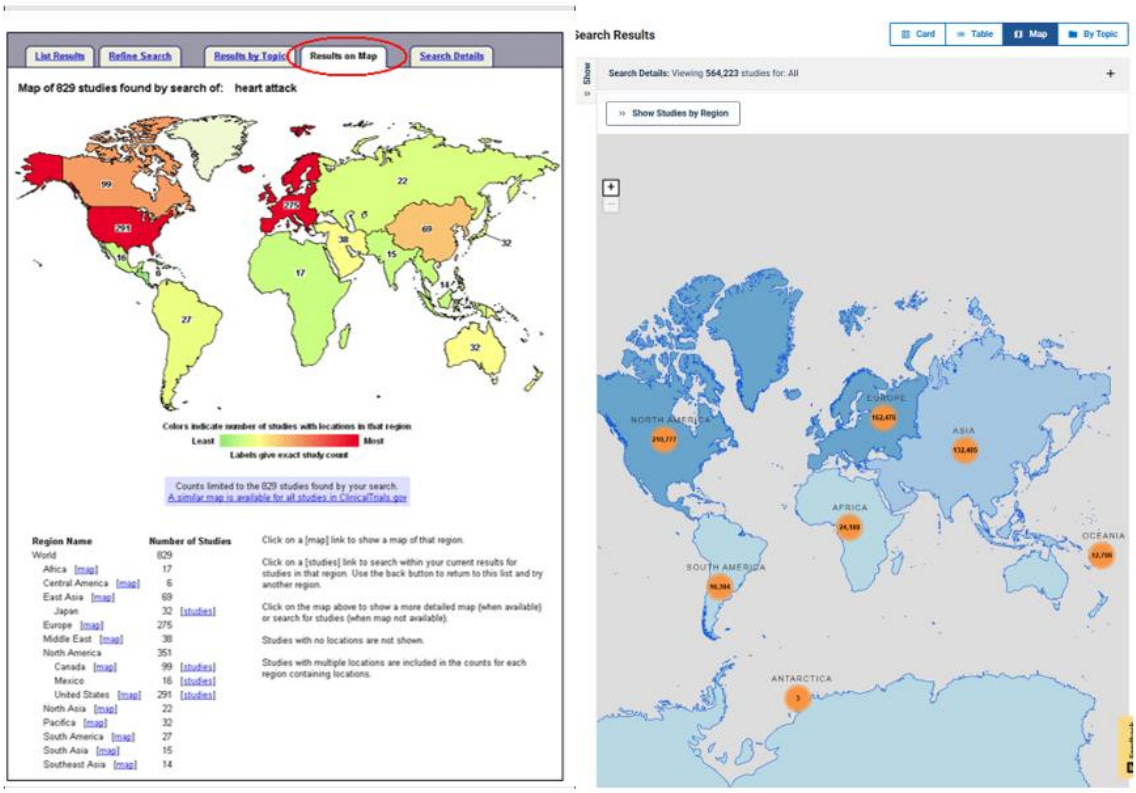
The NLM noted that, in addition to the new user interface views, the search used enhanced data capabilities, a cloud-based infrastructure, and an improved search engine that could process trial registries more quickly. The "advanced search" was again revised in name and structure and was now listed as "more filters," which included filters for sex, age, healthy volunteers, study phase, study type, study results, study documents, funder type, and date ranges (i.e., start, completion, posted, results, and last updates). Additional "more ways to search" options were also offered: title or title acronym, outcome measure, sponsor or collaborator, study ID, facility names, and FDAAA 801 violations (see Figure 14 below).[99]

Figure 14. Search Showing the "More Filters" Section[104]



Additionally, the search pages used a location-based API that was fully integrated into the site. They allowed the search results to be tailored to the user's current location using an IP address or a specified address or country. The classic site also featured the ability to search the study records page by study locations using the "Results on Map" tab. Shown side by side below are the classic and the modernized map in Figure 15 below.

Figure 15. Classic View Map of Study Locations for Original Search of "Heart Attack" (left) and Modern View (right)[104]



The NLM has made numerous other updates to the site, many of which have extended beyond the scope of this dissertation. The primary reason most clinicians and

patients visit ClinicalTrials.gov is to find a specific trial in which patients are eligible to enroll. However, how a trained or experienced user searches is vastly different from that of a new user. From the perspective of patients and care partners, the number of inexperienced users far outweighs that of repeat users. Some guides help inexperienced users understand how to get the most out of their search, but there is a learning curve.

The best way to search for a clinical trial is with assistance from a nurse navigator, a trained patient advocate, or other healthcare professionals. Patient navigation programs, structured services that guide individuals through care and trial decision pathways, are promising interventions for overcoming informational and logistical barriers to clinical trial participation. The general guidance given by ClinicalTrials.gov is to search for the following:

- Condition or disease (e.g., breast cancer or high blood pressure)
- Other terms (e.g., a treatment, NCT number, or investigator name)
- Intervention/Treatment (e.g., radiation therapy or a low-fat diet)
- Location (search by address, city, state, or country)
- Select a study status of recruiting or not yet recruiting studies

In the NSCLC example, consider what this basic search may look like for a newly diagnosed patient. Following the guidance above, if a user enters only “NSCLC” and “Recruiting or not yet recruiting,” it yields 1,757 studies globally, 583 of which are in the United States. If a user lives in New York City, the search is narrowed to 173 trial options with sites open within a pre-specified driving range. Of course, if someone lives in the middle of the country (e.g., Wichita, KS), it narrows down the availability of trial sites to just seven studies. Notably, some trials may enroll thousands of patients across hundreds

of sites, while others may be a single-site trial with limited openings. Physical access barriers also exist (e.g., geographic distance) that contribute to inequities in clinical trial participation; patients enrolled in cancer trials frequently travel substantial distances for study visits, which may disproportionately burden socioeconomically vulnerable groups.[116] For the intention of this example, assume a patient is willing to travel anywhere in the United States for treatment, thereby yielding 583 studies.

This user can take several approaches to these 583 trials. A knowledgeable user may next select the type of study. For most patients seeking active treatment, it would be an interventional trial, which would narrow the search to $N = 530$. Next, filtering by gender or age range may be useful, but given that this is for an NSCLC patient, these filters would be unhelpful. The next logical step would be to consider searching by phase. In this example, there are $n = 6$ in the early phase, $n = 275$ in phase 1, $n = 275$ in phase 2, $n = 78$ in phase 3, $n = 1$ in phase 4, and $n = 36$ not applicable (not that the total does not equal $N = 530$, since trials can be phase 1/2). It is challenging to use this as a filter because selecting a trial phase may depend on the line of therapy a patient is on, risk/benefit tolerance, disease aggressiveness, or other lifestyle factors.

Clinical trials have four phases. Phase 1 trials are the first studies of a new treatment in people and focus on safety and determining the best dose, usually in a small group. Phase 2 trials more closely examine whether the treatment works for a specific disease while continuing to monitor side effects. Phase 3 trials compare the new treatment with the current standard of care in larger groups of patients to confirm its effectiveness and identify less common side effects; successful results may support

regulatory approval. Phase 4 trials occur after approval and evaluate the treatment's long-term safety and real-world use.

Considering this description, one might assume that a phase 3 trial is best, but oncology experts know that in NSCLC, both phase 2 and 3 trials can lead to drug approvals. Because NSCLC is heterogeneous and biomarkers are nuanced, researchers often conduct smaller, single-arm studies to support drug approval through accelerated approval pathways. The next logical step might be to enter additional information about a condition or disease. For example, a patient may have an EGFR or KRAS mutation or no known biomarkers. A patient might be newly diagnosed or have received multiple lines of therapy. These additional terms can help narrow down a search but are highly dependent on how a sponsor writes the trial description in the Brief Title and Brief Summary, thereby highlighting the importance of these descriptors.

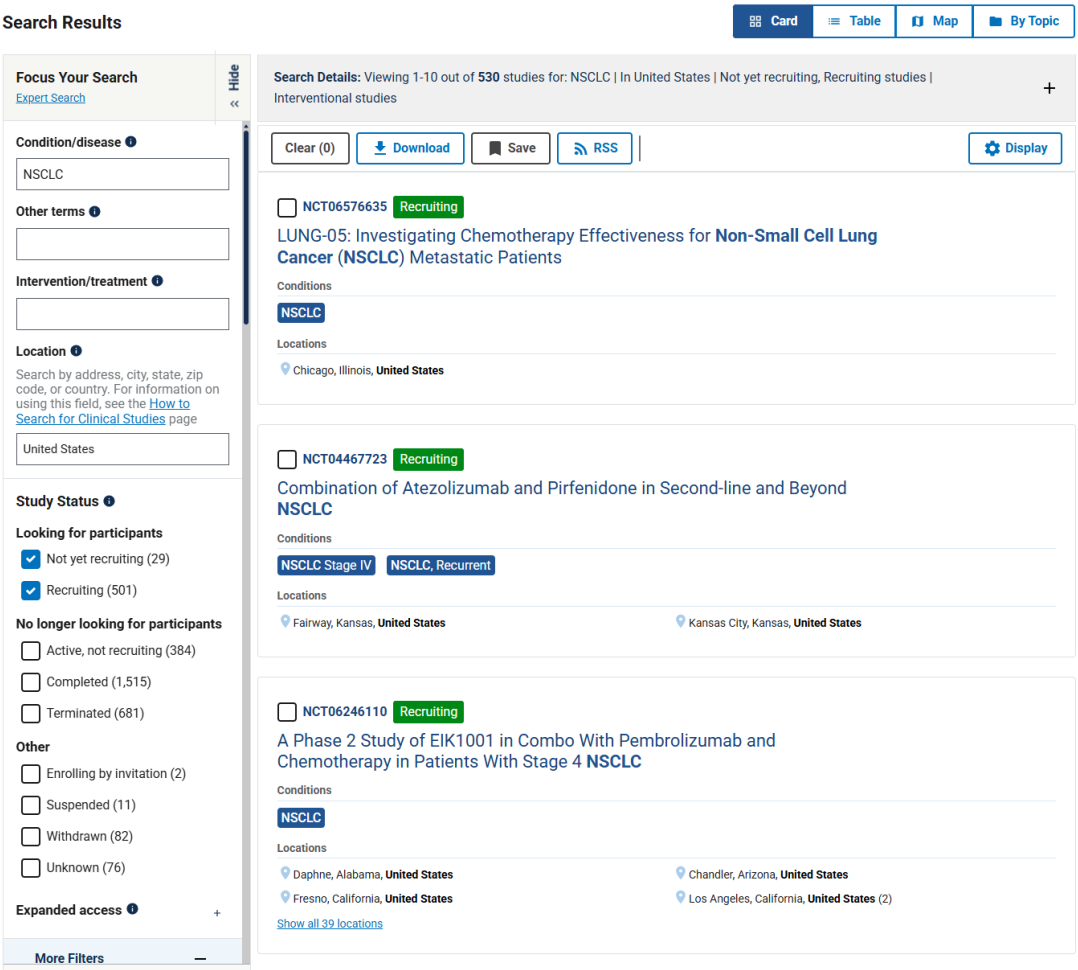
For example, when a user applies the term "newly diagnosed" to the 530 interventional trials, the search returns only six studies. An experienced user will immediately recognize that the "other term" used was inappropriate, given the few matches, whereas a new user might be deterred and stop searching. Simply changing the "other term" to "first line" increases the number of studies to $n = 109$, while using "frontline" yields $n = 4$ and "naïve" yields $n = 22$.

This change in the lexicon demonstrates that without knowing the technical language, or "jargon," searching the website is incredibly frustrating. An experienced/expert user using a Boolean search string using terms of clinical equivalence in "other terms" of "first-line OR naïve OR previously untreated OR frontline OR metastatic OR no prior systemic OR untreated OR first-line OR first line" yields the ideal

result of n = 367 studies. This same logic and example apply to many scenarios for each search term and show how technical language and Boolean logic significantly impact search outcomes, thereby posing challenges for inexperienced users.

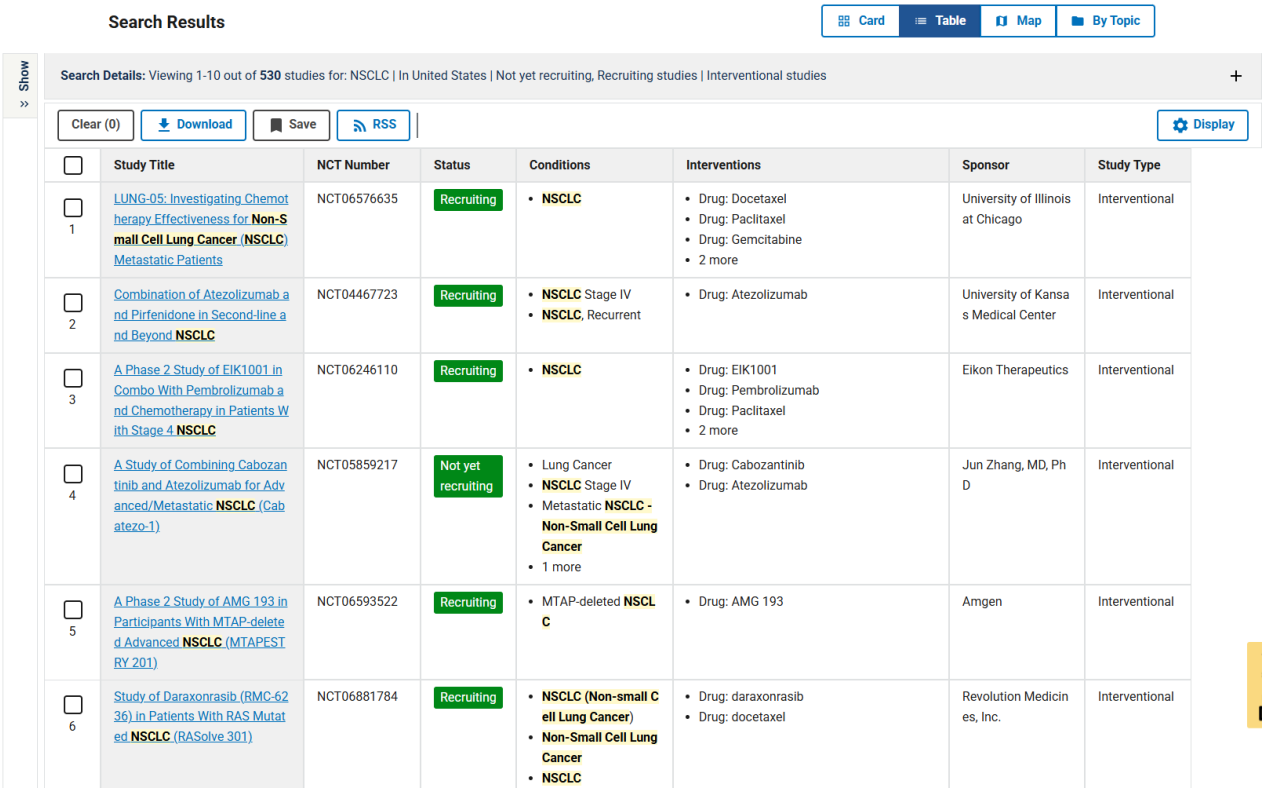
After the user narrows the search, ClinicalTrials.gov displays the results as a series of trials in "card view" (see Figure 16 below).

Figure 16. Trials in Card View[104]



What the user sees in this view are a few elements: the NCT trial identifier, the flagged green “recruiting” status, the Brief Title, the condition search term (and other applicable terms), and locations. Few options exist for how to start sorting through the trials on a case-by-case basis. The only options are to apply additional filters and narrow or change the display to sort by “relevance” or “newest first.” Experienced users often prefer the table view because it is faster, but inexperienced users may find it overwhelming (see Figure 17 below).

Figure 17. Trials in Table View[104]



ClinicalTrials.gov also allows users to view results by map or topic. They can customize the display in multiple ways, create accounts, and save or download selected

trials. After a user clicks into a trial, ClinicalTrials.gov displays the full trial page. At the top is a large disclosure that runs as a banner across all navigated pages. Next is Recruitment Status, Brief Title, NCT Number, Sponsor, Responsible Listing Party, and Last Updated. Next to each of these descriptors is an information button that explains the field in plain language (see Figure 18 below).

Figure 18. Display of a Clinical Trial Page[104]

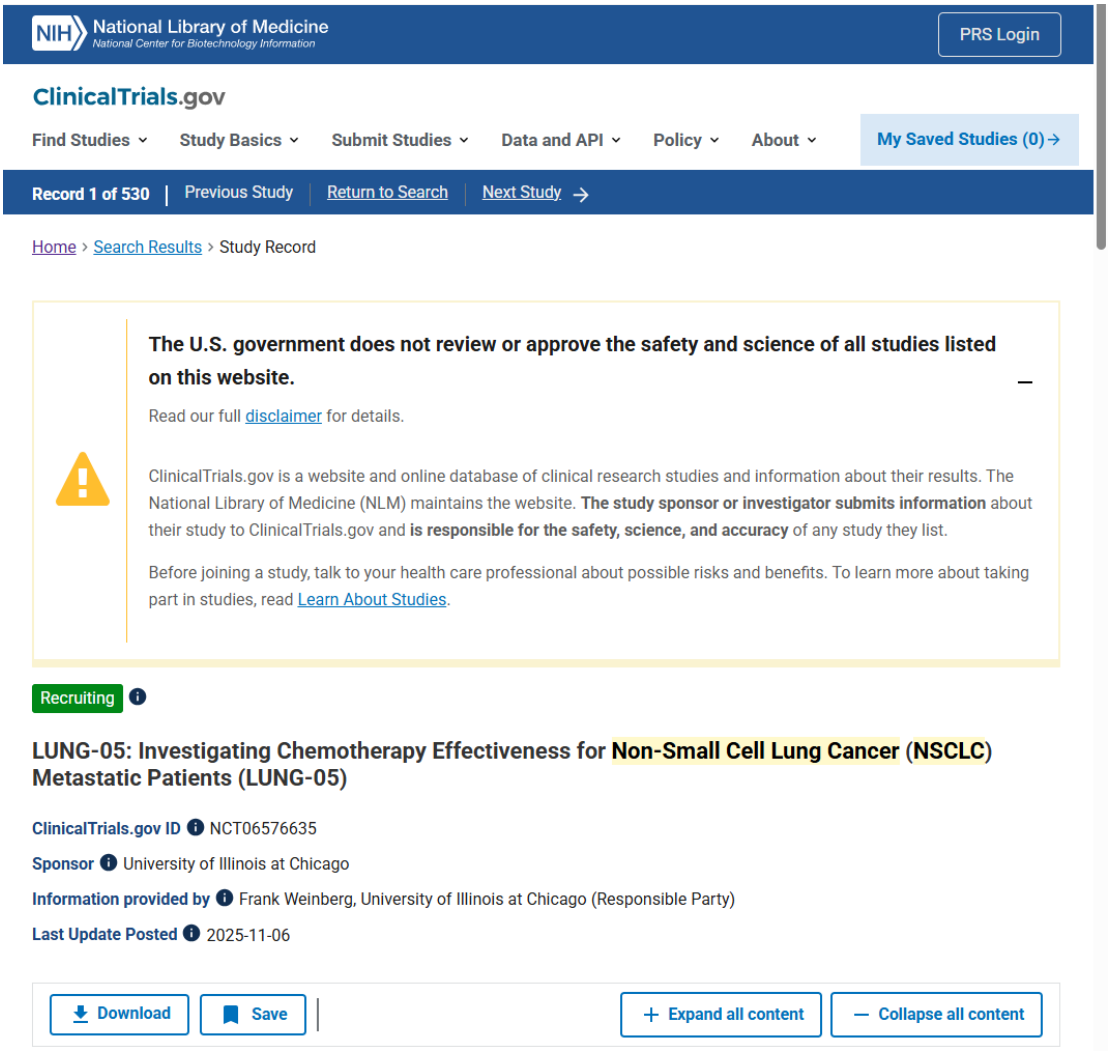
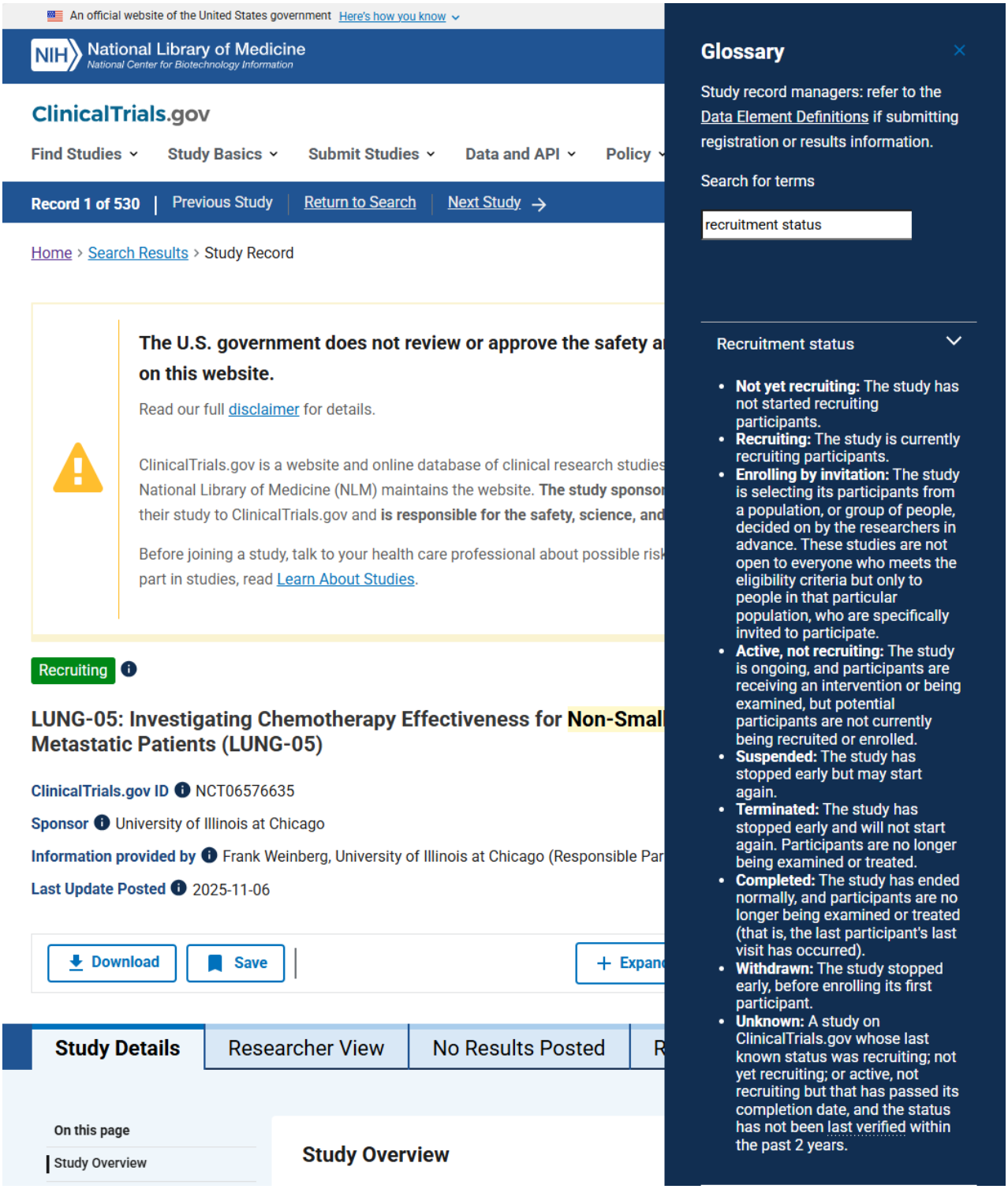
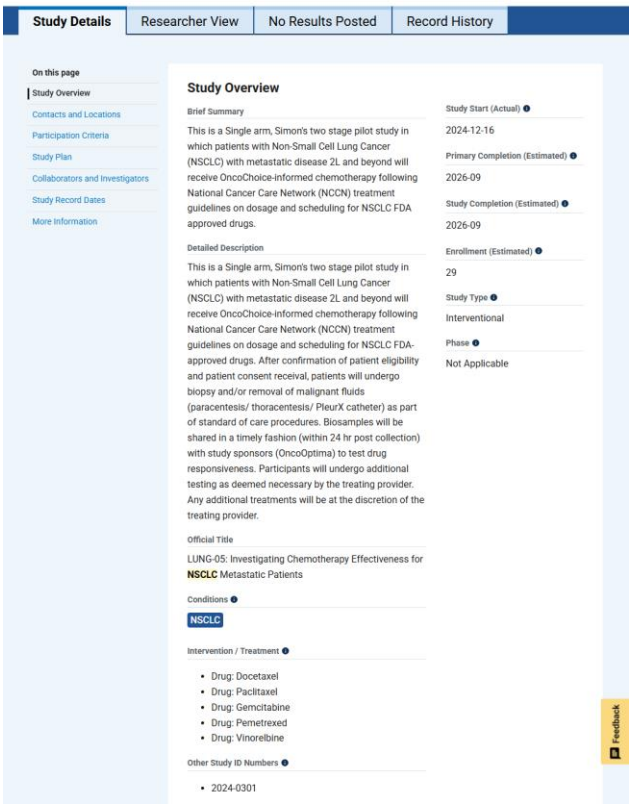


Figure 19. Glossary of Plain Language Showing the Definition of "Recruitment Status"[104]



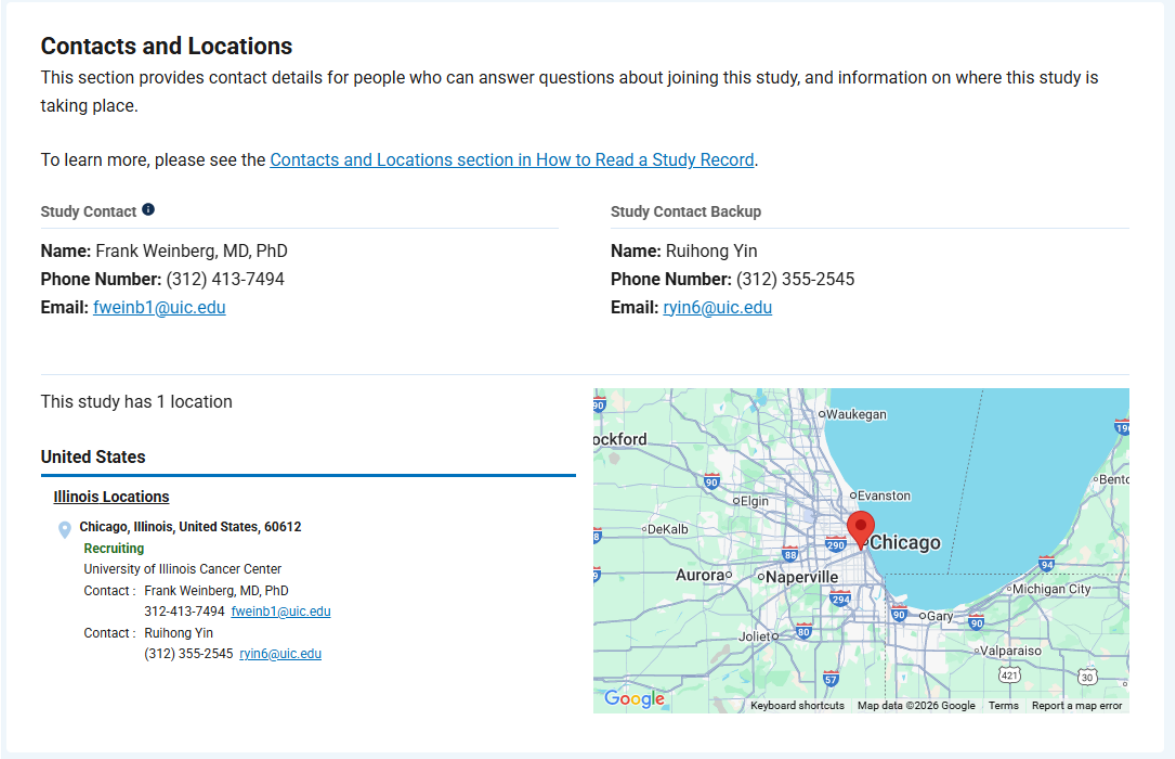
As users scroll through the trial page, they can review several sections. “Study Details” appears first and contains the information users most often rely on to determine whether a clinical trial may apply to their condition and treatment goals. This view shows the Brief Summary, Detailed Description, Official Title, Condition, Intervention/Treatment, Other Study ID Numbers, and, in the right column, Study Start, Primary Completion, Study Completion, Total Enrollment, Study Type, and Phase. What should be of note is the prominence of the Brief Summary section. It is the first description of the trial written in plain language, serves as the basis for search terms and filters, and has a specified/preferred template (see Figure 20 below).

Figure 20. Study Details View, Note the Brief Summary Under Study Overview[104]



The next section of the website provides contacts and locations, one of the most important enhancements of the modernized site, as it includes a contact number for more information (see Figure 21 below).

Figure 21. Contacts and Location[104]



The subsequent sections continue with the participation criteria, which list all eligibility criteria for the study, including the inclusion and exclusion criteria. These participation criteria are a key component of every clinical trial because they define exactly who is and is not eligible for a trial. These eligibility requirements include both inclusion criteria (i.e., the characteristics a participant must have, such as a specific cancer type, stage, biomarker, age range, or lab values) and exclusion criteria (i.e., factors that would prevent participation, such as certain medical conditions, prior treatments, or safety risks). Together, these criteria help researchers ensure that the study population is

medically appropriate for the treatment being tested, protect patient safety, and produce scientifically valid results that are meaningful for the specific group of patients the trial aims to help.

The study design section follows and explains how researchers structure a clinical trial, including whether the trial is interventional or observational, the phase, the number of participants, and the process used to assign participants to treatment groups, such as randomization. For example, in a typical interventional trial for NSCLC, the study design may specify that participants are randomly assigned to receive either a new therapy or the current standard of care (e.g., a randomized, controlled trial [RCT]). The design also indicates whether the study is blinded (i.e., the participants and/or researchers do not know which treatment is given), the primary purpose (e.g., the treatment or supportive care), the primary outcomes being measured (e.g., progression-free survival or response rate), and any secondary outcomes. Outlining the study design helps patients, clinicians, and researchers understand how reliable the results are likely to be and whether the approach fits a patient's goals and medical situations, since some patients might not want to enter a trial if they do not want to be randomized to a certain standard or care or placebo arm.

The last section of the trial listing is the collaborators and investigators, the study record dates, and more information. This webpage can be expanded to include supplemental information, such as full protocols, ICFs, trial records and amendments, and results. If you are unfamiliar with ClinicalTrials.gov and would like to see a brief instructional video, the NLM has one on its website. While ClinicalTrials.gov can be a substantial research tool, a steep learning curve remains in using the system effectively.

The Modernization Project has helped improve health literacy and accessibility by offering guidance on using plain language in the Brief Title and Brief Summary. However, numerous challenges remain between the point at which a patient becomes aware of an actual trial and the point of enrollment.

Patients can work directly with a Nurse Navigator to review ClinicalTrials.gov listings and interpret trial information in the context of their diagnosis, treatment history, and care goals. These healthcare professionals can employ strategies to overcome barriers to clinical trial participation by optimizing enrollment workflows and supporting patients as they navigate complex trial systems.[117] Most local health systems, all Commission on Cancer–accredited centers, and many patient advocacy groups provide navigation services to help patients review trial options and interpret clinical trial information.

Table 2. Key Differences Between Classic and Modernized ClinicalTrials.gov

Feature	Classic ClinicalTrials.gov	Modernized ClinicalTrials.gov
User Interface	Text-heavy, dated design	Modern, streamlined, mobile-friendly interface
Search Functionality	Basic keyword search	Advanced search with filters, facets, and autocomplete
Navigation	Limited intuitive navigation	Improved navigation with clear menus and breadcrumbs
Data Visualization	Minimal charts or graphics	Enhanced visualizations (graphs, summaries, trends)
Accessibility	Meets older accessibility standards	Updated to current WCAG standards for inclusivity
API and Data Access	Basic API with limited functionality	Expanded API with richer endpoints and documentation
Trial Record Layout	Dense text, less structured	Structured, user-friendly layout with collapsible sections
Mobile Optimization	Limited	Fully optimized for mobile and tablet use
Help and Support	Static help pages	Interactive help, tutorials, and contextual guidance
Plain Language Summaries	Not required or inconsistently provided	Integrated plain language summaries for lay audiences
Readability Standards	Technical jargon prevalent	Emphasis on readability (e.g., 8th-grade level for public-facing text)
Patient-Centric Content	Primarily researcher-focused	Includes patient-friendly explanations and a glossary of terms

THE CHECKLIST

The "Plain Language Checklist for Lay Brief Summaries" was published on the U.S. NLM ClinicalTrials.gov website on September 26, 2022, in the "*What's New"* announcement page.[15] This resource is self-described as "a checklist [that] identifies plain language best practices to help investigators write brief summaries that can be easily understood by the general public."[15] This checklist follows the main evidence-based plain language best practices for writing lay research summaries. The goal is a Brief Summary description that the lay public can easily understand and engage with."[15] The checklist encourages consistency and readability across clinical trials listings, which reduces confusion around eligibility for enrollment.

Over time, user-friendly summaries may improve equity in clinical trial participation by helping underserved populations engage with trial information that overly technical language may otherwise exclude. The checklist organizes its guidance into four core areas: focus, content, numbers, and structure, which later sections address in detail. The checklist concludes with the core recommendation to "Test the Summary." "The gold standard is to test the summary with people from your intended audience to ensure it is easy to understand. Or ask a peer in another field, a family member, or a friend to read and share feedback. This can help identify jargon and content that may be misinterpreted."[15] The checklist concludes with providing several references to plain language resources.

In oncology, where treatment options and eligibility criteria are complex, this simplification of medical jargon to plain language is increasingly important as the

therapeutic options rapidly expand. The emphasis on simplified information ensures that patients can quickly understand who can participate, what the study involves, and why it matters. This transparency fosters trust and supports informed decision making, thereby aligning with the goals of patient-centered care. When oncology patients and care partners can easily understand trial summaries, they can engage more effectively in discussions with clinicians about trial participation. The checklist's guidance enhances access and equity in cancer research by making opportunities more visible and understandable to the people who need them most.

One of the first professional organizations to issue a statement about the new resource was the American Medical Writers Association (AMWA), a group that promotes excellence in medical communication and provides educational resources to support that goal. In a topical feature, Schindler noted,

> Over the years, CT.gov moved further away from its initial intentions and became a website for pharma companies' transparency experts, competitive intelligence analysts, investors, and clinical trial aficionados. This development was a consequence of the technical operationalization of the transparency regulations without having the end user in mind.[118]

The introduction of this checklist has the potential to be a "revolutionary development" and a step toward gaining usability.[118]

The Modernization Project is part of an ongoing effort to improve the usability of ClinicalTrials.gov and enhance public accessibility. However, as Schindler highlighted, major gaps in accessibility remain, with the pain points being the Brief Title and Brief Summary. Schindler stated that despite improvement efforts, searches often provide the

user “with a paragraph of clinical trial gobbledygook and insider technical slang written for the fellow specialist.”[126] Despite these known deficiencies, no tool to date has been offered to help improve this gap by the NLM. While this checklist can help guide study managers and investigators, it cannot address potential knowledge gaps or a lack of core competency in writing for a patient/lay audience. Schindler concluded his commentary by offering this checklist to help medical writing professionals leverage their plan-language writing expertise to assist academic and industry partners.[126]

By the time this dissertation was published, ClinicalTrials.gov had removed the original “Plain Language Checklist for Lay Brief Summaries” and replaced it with the revised “Plain Language Guide to Write a Brief Summary,” published on May 15, 2025. The original “Plain Language Checklist for Lay Brief Summaries” served as a practical tool for improving how clinical research is communicated to lay audiences and provided specific metrics in a step-by-step flow across the four core areas. It helped the investigator/sponsor focus on clarity, brevity, and audience awareness to create summaries that patients can clearly understand. By encouraging the use of everyday language and avoiding jargon, the checklist reduced barriers that often prevent patients, especially those with limited health literacy, from engaging with clinical trial information.

This revised page moves away from a simplified compliance tool structured into four major areas toward an integrated, comprehensive instructional resource that expands on the older checklist. The updated page includes an expanded introduction section that provides study managers with additional contextual framing and an updated audience description. The updates to the page are due to iterative feedback received throughout the

modernization project and still reflect the core values and recommendations from the original checklist. The original checklist can be viewed in the Appendix (Figure 39).

Another welcome addition to the page is the use of inclusive and person-centered language. Recommendations include using the term "participants" instead of "subjects" or "patients" and avoiding defining people by their health conditions or demographic characteristics. For example, using "people with lung cancer" instead of "lung cancer patients" or using "older adults" instead of "the elderly."[119-121] Another addition is the enhancement of grammar and style. New points added in the updated page include checking for spelling and grammar errors, using words instead of numerical symbols, and expanded guidance on the use of acronyms. The reference list has been expanded to provide a few additional resources, including the Centers for Disease Control's Inclusive Communication Principles and Preferred Terms, Just Plain Clear glossary (UnitedHealth Group), and the University of Michigan's Plain Language Medical Dictionary.[11] Finally, a template for writing a Brief Summary of the study is provided, along with a sample of a clinical trial and observational study summary. The template provided is as follows:

> The goal of this [study type: observational study or clinical trial] is to [primary purpose: e.g., learn if intervention or health behavior can treat, prevent, diagnose etc.] in [describe participant population/primary condition; could include any of the following: sex/gender, age groups, healthy volunteers]. The main question[s] it aims to answer [is/are]:
>
> - [primary hypothesis or outcome measure 1]?
> - [primary hypothesis or outcome measure 2]?

If there is a comparison group: Researchers will compare [arm information] to see if [insert effects].

Participants will [describe the main tasks participants will be asked to do, interventions they will be given and use bullets if there are more than two items].

This template provides a clear, structured framework that helps researchers organize complex study information into accessible plain language. Outlining the study's goal, population, key questions, and participant activities ensures patients receive the most relevant information first. In oncological research, this clarity can improve patient comprehension and engagement, which can make it easier for individuals to assess whether a clinical trial is appropriate for their condition and treatment goals. While this restructuring of the checklist into an expanded learning page is an improvement, it still does not eliminate the need for competency in creating patient-friendly plain-language materials.

What the checklist itself, in either its original or revised form, leaves unanswered is whether it worked. A well-designed resource, grounded in evidence-based plain language principles and refined through iterative feedback, is a reasonable thing to publish. Nevertheless, publishing a resource is different from changing the source data it was meant to improve. The checklist assumes that investigators and sponsors, once shown the best practices, will adopt them. However, this assumption has never been tested at scale against the Brief Summaries that patients encounter at ClinicalTrials.gov. Whether the September 2022 guidance shifted the readability, structure, or patient-centeredness of lung cancer trial summaries or whether it simply joined the extensive list of well-intentioned recommendations that the clinical research enterprise has

acknowledged and then largely set aside is an empirical question. Answering it requires moving from what the checklist recommends to what the data show. The following methodology explains how the analysis measured the checklist's impact by identifying the selected trials, defining the timeframe, developing a scoring tool to operationalize the checklist criteria, and comparing summaries written before and after the guidance was issued.

METHODOLOGY

This paper used a representative sample of the ClinicalTrials.gov study records as the basis of the analysis. Records were grouped into two predefined cohorts: trials first posted between September 25, 2019, and September 25, 2022 (pre-checklist), and trials first posted between September 26, 2022, and September 26, 2025 (post-checklist), from phase 1/2, phase 2, or phase 3 clinical trials. This study exported raw data from ClinicalTrials.gov. The selected dates provide a representative sample for comparing behavioral changes after implementation of the Final Rule (FDAAA801) with those after implementation of the Modernization Project's "Plain Language Checklist for Lay Brief Summaries," issued September 26, 2022. The analysis of records will focus on the Brief Summary.

The search was limited to interventional studies (excluding devices) in phases 1/2, 2, or 3, with the condition/disease primary field set to "lung cancer" and related search terms. Phases 1, 4, and n/a were excluded from study selection. The studies were retrieved based on the "first posted" date, regardless of their recruitment status at the time of posting or data extraction. No limitation was placed on the type of sponsor. The study included only records posted in English.

The author manually analyzed each study record and coded the presence or absence of predefined criteria in a Microsoft Excel file. Criteria were selected based on guidance in the Plain Language Checklist for the Brief Summary, suggested plain language and health literacy resources, and validated plain language tools. All items were weighted equally to avoid imposing subjective judgments regarding the relative

importance of individual plain-language elements, consistent with the exploratory nature of the analysis.

ClinicalTrials.gov offers limited guidance on what should be included in the Brief Title and currently defines it as "information on the participants, condition being evaluated, and intervention(s) studied." Moreover, it should be written for the lay public with limited technical terms and/or acronyms.[122] Additionally, prior to the checklist, the only requirements for the Brief Summary were the absence of bibliographic reference, complete sentences without formatting errors, study goal (i.e., hypothesis/purpose), statement about the availability of expanded access programs, and being within 5,000 characters.[131] This recommendation has now been expanded with the publication of the checklist. As such, the suggested criteria from Transcelerate[12] were applied to the Brief Title and Brief Summary for the selected time periods in an effort to establish a baseline for comparison to previously reported results, including the purpose of the study, the presence (or absence) of condition, study population, intervention described, route of administration, absence of technical terms, absence of unexplained abbreviation, and presence of any humanizing term (i.e., participant, patient, subject, and volunteer).

To evaluate the health literacy characteristics of ClinicalTrials.gov public text, this dissertation adopted a methodology modeled after prior research that combined large-scale data extraction with quantitative readability analysis. Wu et al. extracted all ClinicalTrials.gov trial descriptions and applied multiple surface and readability metrics to characterize the difficulty of comprehension relative to other health corpora.[123] Moreover, Baskin et al. conducted a targeted readability assessment of oncology Brief Summaries from ClinicalTrials.gov using standardized grade-level measures.[124] Mirza et

al. extended this approach by extracting ICFs for trials listed on ClinicalTrials.gov and correlating readability scores with participant dropout rates, thereby demonstrating a link between text complexity and trial outcomes.[125] Additional studies, including Karimi et al. and Khadraoui et al., have applied similar readability metrics to clinical trial consent documents in surgical and oncology settings, thereby further supporting the use of computational readability measures as markers of health literacy barriers in research documents.[126,127]

The criteria for the PLCST were created to assess the patient-centricity of trials based on the "Plain Language Checklist for Lay Brief Summaries," using the original four principal areas: focus, content, numbers, and structure. These criteria were compared with those established by the TransCelerate Working Group's assessment instruments for developing the PLCST, which evaluates sentence-structure metrics, readability metrics, plain-language usage, numerical communication, and completeness of required information.[12]

Data Extraction

This study employed a systematic review of clinical trials using the NLM's ClinicalTrials.gov registration and results database. The study examined a representative sample by narrowing the search to lung cancer clinical trials. Lung cancer provided a representative oncology indication due to its high volume of clinical trials, heterogeneity of interventions, and frequent use of complex terminology, which made it a rigorous test case for plain-language evaluation. The search was performed using the condition/disease heading and the Boolean search string of "lung neoplasm" OR "lung cancer" OR "non-small-cell lung cancer" OR "non-small-cell lung cancer" OR "NSCLC" OR "NSLC" OR

"small-cell lung cancer" OR "small cell lung cancer" OR "SLC" OR "SCLC." The search was refined by selecting "interventional studies" for study type, "phase 2" and "phase 3" for study phase, and selection for adult (18–64 years) and senior (65+ years) for age groups. The date range for "First Posted" was set from September 25, 2019, to September 26, 2025, to account for a period of three years prior to the publication of the Brief Summary Checklist (September 26, 2022) and three years post.

The search was executed on December 1, 2025. The results were exported in XLM format, converted to CSV for structured extractions, and imported to Microsoft Excel for manual abstraction and scoring. Data extracted included (1) the NCT number, (2) study title, (3) study status, (4) Brief Summary, (5) conditions, (6) interventions, (7) primary outcome measures, (8) sponsor, (9) collaborators, (10) phases, (11) enrollment, (12) funder type, (13) study type, (14) study design, (15), first posted, and (16) locations. The author screened all trials for inclusion in the study. Trials were excluded from analysis if they did not involve patients diagnosed with lung cancer or did not list medical therapy as an intervention. Phase 1 trials were excluded due to limited patient-facing relevance at first posting, while Phase 4 trials were excluded due to post-marketing differences in communication goals. Phase 1/2 dose escalation/dose expansion trials were allowed, as were trials enrolling multiple solid tumors if primary lung cancers were eligible for the trial. Trials with missing Brief Summaries were excluded from analysis. Brief Summaries containing protocol fragments or non-sentence artifacts were retained only if most of the text consisted of complete sentences intended for public display.

Limitations

The search was limited to English-language postings to ensure readability and align with plain language assessments. While this dissertation focused primarily on U.S.-based policy intervention through the NLM, this sample was not limited to only U.S. trial sites because ClinicalTrials.gov functions as the largest global registry. Moreover, U.S. policies often shape global trends in patient-centered medicine. Since this dissertation was focused only on trials posted within ClinicalTrials.gov, no additional trial search tools or registries were used, including the ICTRP, CenterWatch, Cochrane Central Register of Controlled Trials, Embase, NIH RePORTER, PubMed, Google Scholar, Patient Advocacy Tools, or any public or private search tools. As a result, trials registered solely outside the United States or published but not registered might have been missed. Additionally, trials were screened and evaluated by a single reviewer. While this approach ensured consistency, it might have introduced subjectivity into elements of coding that required human judgment. No inter-rater reliability statistics were calculated.

Ethical Approval

This study was considered exempt from IRB oversight, as it involved the analysis of publicly available, de-identified data from ClinicalTrials.gov. According to federal regulations [45 CFR 46.104(d)(4)], research involving publicly available datasets does not require IRB approval.[128]

Outcomes

The primary outcome was to assess the readability of the "Brief Summary" section available on ClinicalTrials.gov, using the PLCST to evaluate changes over a period of three years before and three years after the publication of formal NLM guidance

on the summary. The secondary outcome was to assess patient-preferred informational completeness of patient-focused content elements.

Data Analysis

Clinical trial data were downloaded in Extensible Markup Language format and imported into Excel with fields as previously noted. Data records were reviewed for completeness, and any study record that did not properly export was cross-checked against the official NCT listing. If trial data were available, they were manually imported. If the data export resulted in an error or an incomplete ClinicalTrials.gov listing, the study was removed from analysis. The Brief Title and Brief Summary were evaluated using a variety of readability metrics and binary assessments against predefined criteria.

Sentence-Structure and Readability Measures

All data extracted from ClinicalTrials.gov was placed in a Microsoft Excel File. After reviewing to ensure the trial fit the eligibility of this analysis, the text extracted for the Brief Summary was reviewed to ensure that no text was not in full sentences (e.g., titles, headings, subheadings, short captions, and bullet lists), embedded punctuation, and document design elements (e.g., gaps, white spaces, pictures and images, and text boxes) as a result of data export. ClinicalTrials.gov was used as the primary source of information if there were any doubts about the formatting.

Readability was scored using a validated readability software (i.e., Readable.com, Horsham, United Kingdom).[122,129-131] The Brief Title was assessed for word count, and the Brief Summary was assessed for: character count, word count, average sentence length, and average sentences per paragraph. The readability of each text was assessed

using three different indices: the FKGL, FRE, and Simple Measures of Gobbledygook (SMOG) Index. The FKGL was calculated as follows:

$$FKGL = 0.39\left(\frac{\text{total words}}{\text{total sentences}}\right) + 11.8\left(\frac{\text{total syllables}}{\text{total words}}\right) - 15.59$$

The FKGL is a widely used readability formula that estimates the U.S. grade level required to understand a written text. As previously described, the target reading level recommended in the Plain Language Checklist is a U.S. sixth- to eighth-grade level.

FRE is measured as follows:

$$FRE = 206.835 - 1.015\left(\frac{\text{total words}}{\text{total sentences}}\right) - 84.6\left(\frac{\text{total syllables}}{\text{total words}}\right)$$

The FRE scale ranks texts from 1 to 100 based on how easy they are to read, with 100 indicating the highest readability. A score of 70–79 corresponds to a school grade level of 8, while a score of 80–89 corresponds to a grade level of 6. Any score >69 was considered patient-friendly and aligned with the Plain Language Checklist guidance.

The SMOG Index was included for exploratory purposes, calculated as follows:

$$SMOG = 1.0430\sqrt{\text{Number of polysyllabic words} \times \frac{30}{\text{Number of sentences}}} + 3.1291$$

The SMOG index was included because, similar to the FKG, it provides a U.S. grade-level comprehension score and considers polysyllabic words, thereby increasing sensitivity to complex medical terminology. Thus, it is the most conservative of the three readability metrics. For each assessment, the average readability score for each index was calculated, and a binary score indicating whether it aligned with the guidance provided by the Plain Language Checklist was assigned.

Plain Language Checklist Scoring Tool

To systematically evaluate the readability of ClinicalTrials.gov Brief Summaries, a structured scoring tool was developed based on the ClinicalTrials.gov Plain Language Checklist for Brief Summaries that considered the intent of the original publication and the revised/updated version. The purpose of this tool was to operationalize checklist guidance into reproducible, measurable variables suitable for quantitative analysis while preserving transparency in scoring decisions. The PLCST assigns each trial a score on a scale of 0 to 11.

The PLCST integrates the Plain Language Checklist for Brief Summaries guidance with established readability metrics and the core informational elements identified in the original checklist: focus, content, numbers, and structure. Most of the guidance provided in the Plain Language Checklist for Brief Summaries can be reduced to a binary "yes" or "no" response that reflects whether the element is present in the Brief Summary. Met criteria that were indicated as a "yes" were coded as "1," while elements that were absent, ambiguous, or unverified were coded as "no and "0." The PLCST has a maximum value of 11 on a scale of 0–11. Criteria for the PLCST are listed in PLCST: Exploratory Analysis for Completeness of Patient-Preferred Information.

Additional exploratory analysis was conducted on five elements specified by Schindler et al., who identified data elements preferred by patients when searching for clinical trials.[12] Exploratory criteria are in PLCST: Exploratory Analysis for Completeness of Patient-Preferred Information. All abstraction was performed by a single reviewer (i.e., the author) using a predefined coding guide. The reviewer had over 20 years of oncology experience, with expertise in NSCLC, medical communications, plain-

language writing, and patient advocacy. A data field analysis guide and an example PLCST scorecard can be found in the Supplementary Data.

Table 3. Plain Language Checklist Scoring Tool (PLCST)

Criterion	Adherence Threshold / Definition
Brief Summary: average sentence length	≤15 words per sentence
Flesch–Kincaid Grade Level	≤8th-grade reading level
Explains the purpose of the study	Purpose or study objective clearly stated
Avoids medical jargon	No undefined medical jargon present
Avoids unexplained acronyms	Acronyms absent or clearly defined
Uses active voice	Text primarily written in active voice
Uses inclusive and person-centered language	Uses patient-centered terminology (e.g., "participants" instead of "subjects")
Uses words instead of numerical symbols	Uses written terms rather than symbols where appropriate
Uses both percentages and natural frequencies	Numerical percentages accompanied by natural frequencies
Avoids qualitative terms without context	Avoids unsupported terms such as "reduce" or "increase"
Uses consistent terminology	Consistent terminology maintained throughout the Brief Summary

Table 4. PLCST: Exploratory Analysis for Completeness of Patient-Preferred Information

Criterion	Adherence threshold / definition
Explains the purpose of the study	Purpose or study objective clearly stated
Condition listed	Disease or condition being studied clearly identified
Study population listed	Participant population or target patient group described
Intervention described	Study drug, treatment, or intervention identified
Route of administration listed	Route of administration described (e.g., oral, intravenous, subcutaneous)
Duration/frequency listed	Study duration, treatment schedule, or frequency described

Statistical Analysis

Baseline characteristics of included clinical trials were summarized using means and standard deviations (SD) or medians and interquartile ranges (IQR) for continuous variables and frequencies and percentages for categorical variables. Trial characteristics were compared between the pre-guidance and post-guidance cohorts using contingency tables. Fisher's exact test was used for binary and small-expected-cell-count categorical comparisons. Chi-square tests were used for larger multi-category comparisons when appropriate. Categorical variables included trial phase, sponsor type, recruitment status, geographic enrollment pattern, number of study locations, and intervention or mechanism-of-action categories.

Readability measures (i.e., the FKGL, FRE, SMOG Index, word count, character count, and average sentence length) were summarized overall and by guidance period. Pre- and post-guidance differences in continuous measures were evaluated using Welch's *t*-test because of unequal group sizes and potential unequal variances. Mann–Whitney U tests were also used as nonparametric sensitivity analyses for non-normally distributed or bounded variables.

The PLCST, exploratory patient-focused, and combined scores were summarized using means, medians, SDs, IQRs, and score distributions. Because these scores were discrete and bounded, pre- and post-guidance comparisons were evaluated using both Welch's *t*-tests for mean score differences and Mann–Whitney U tests as nonparametric sensitivity analyses. Individual PLCST and exploratory criteria were analyzed as binary variables and compared using Fisher's exact test. Subgroup analyses by geography, sponsor type, and trial phase were conducted using Welch's *t*-tests for two-group

comparisons and analysis of variance (ANOVA) for mean comparisons across multiple groups, with Mann–Whitney U or Kruskal–Wallis tests used as nonparametric sensitivity analyses, as appropriate. All tests were two-sided, and statistical significance was defined as $p < .05$. IBM SPSS Statistics, v. 31 (IBM Corp., Armonk, NY), was used for statistical analyses.

RESULTS

The search identified 2,408 clinical trial records that met the inclusion criteria, comprising 1,191 trials from the pre-guidance period and 1,217 from the post-guidance period. A total of 831 trials (34.5%) included at least one enrolling site in the United States, while 1,577 trials (65.5%) did not list a U.S. enrolling site. Phase 2 studies were the most common study type, accounting for 1,429 trials (59.3%), followed by phase 1/2 trials (514, 21.3%), phase 3 trials (407, 16.9%), and phase 2/3 trials (58, 2.4%). Among phase 2 studies, the most common funder category was Other (1,013, 70.9%), followed by Industry (326, 22.8%). In contrast, phase 3 studies were more frequently funded by Industry, with Industry listed for 273 trials (67.1%), compared with Other for 116 (28.5%). Industry funding was also common among phase 1/2 trials, accounting for 360 of 514 records (70.0%). The substantial number of phase 2 trials in this space is unsurprising, since the large unmet need and rapid therapeutic development in lung cancer can support extensive phase 2 investigation, including single-arm studies in select biomarker-defined populations.

The trials demonstrated broad geographic distribution, with study locations identified across at least 73 countries. The most frequently represented countries were China (1,107, 46.0%), the United States (831, 34.5%), Spain (335, 13.9%), South Korea (288, 12.0%), France (285, 11.8%), and Italy (263, 10.9%). Trials also varied by global region, with Asia represented in more than half of trials (1,369, 56.9%), followed by North America (880, 36.5%), Europe (552, 22.9%), Oceania (220, 9.1%), South America (165, 6.9%), and Africa (29, 1.2%). Because many studies were multinational, country

and regional categories were not mutually exclusive. Full study characteristics are shown in

Table 5 below.

Table 5. Study Characteristics

Characteristic	Pre-guidance, *n* (%)	Post-guidance, *n* (%)	*p*
N	**1,191**	**1,217**	
Type of clinical trial			.073
Phase 1/2	272 (22.8)	242 (19.9)	
Phase 2	711 (59.7)	718 (59.0)	
Phase 2/3	24 (2.0)	34 (2.8)	
Phase 3	184 (15.4)	223 (18.3)	
Sponsor type			.020
Industry	499 (41.9)	485 (39.9)	
Academic/medical center	492 (41.3)	515 (42.3)	
NIH/NCI	33 (2.8)	16 (1.3)	
Government/other federal	20 (1.7)	39 (3.2)	
Network/cooperative group	28 (2.4)	28 (2.3)	
Other/uncategorized	119 (10.0)	134 (11.0)	
Recruitment status			< .001
Actively recruiting	192 (16.1)	655 (53.8)	
Not yet recruiting	15 (1.3)	212 (17.4)	
Active, not recruiting	232 (19.5)	153 (12.6)	
Completed	200 (16.8)	30 (2.5)	
Terminated	153 (12.8)	32 (2.6)	
Withdrawn	61 (5.1)	34 (2.8)	
Suspended	4 (0.3)	5 (0.4)	
Enrolling by invitation	1 (0.1)	10 (0.8)	
Unknown	333 (28.0)	86 (7.1)	
Number of study locations			< .001
No locations listed	91 (7.6)	142 (11.7)	
Single-study location	510 (42.8)	575 (47.2)	
Multiple-study locations	590 (49.5)	500 (41.1)	
Location			< .001
United States only	243 (20.4)	183 (15.0)	
International only	640 (53.7)	704 (57.8)	
Located in United States and elsewhere	217 (18.2)	188 (15.4)	
No locations listed	91 (7.6)	142 (11.7)	

Character Count

All summaries analyzed were within the ClinicalTrials.gov-specified maximum of 5,000 characters, including spaces. The longest Brief Summary was 4,754 characters, and the shortest was 47 characters. Overall, the mean Brief Summary length was 549.4 characters (*SD* = 504.1), with a median length of 365 characters (IQR: 239–694). Most Brief Summaries were shorter than the allowable character limit: 1,533 summaries (63.7%) contained fewer than 500 characters, 2,088 (86.7%) contained fewer than 1,000 characters, and 2,278 (94.6%) contained fewer than 1,500 characters. Brief Summaries in the post-guidance period were longer than those in the pre-guidance period. The mean character count increased from 511.8 characters (*SD* = 472.4) before guidance to 586.1 characters (*SD* = 530.9) after guidance. This difference was statistically significant by Welch's *t*-test ($p < .001$) and Mann–Whitney U test ($p < .001$).

Figure 22. Brief Summary Character Count by Guidance Period

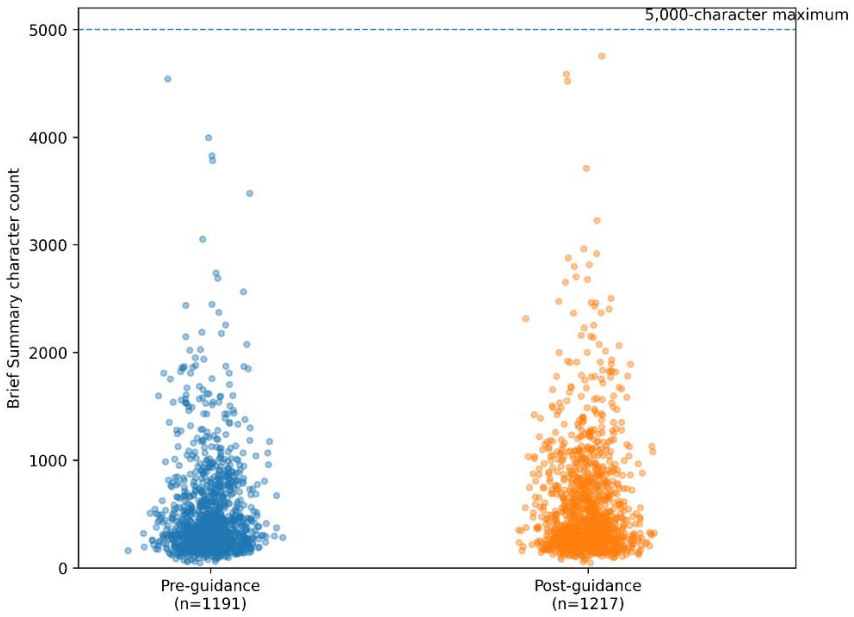


Table 6. Brief Summary Character Count Across All Studies

Measure	Overall
N	2,408
Mean character count	549.4
SD	504.1
Median	365
IQR	239–694
Shortest summary	47 characters
Longest summary	4,754 characters
Summaries >5,000 characters	0

The shortest Brief Summary had only 47 characters and seven words for NCT04444427, “Evaluation of GLR2007 for Advanced Solid Tumors.” The longest Brief Summary was 4,754 characters and 723 words from NCT06908993, a study titled “Tepotinib vs Standard Treatment in Patients With Advanced MET Exon 14 Mutated Non-Small-Cell Lung Cancer Previously Treated,” and for brevity, is not shown here.

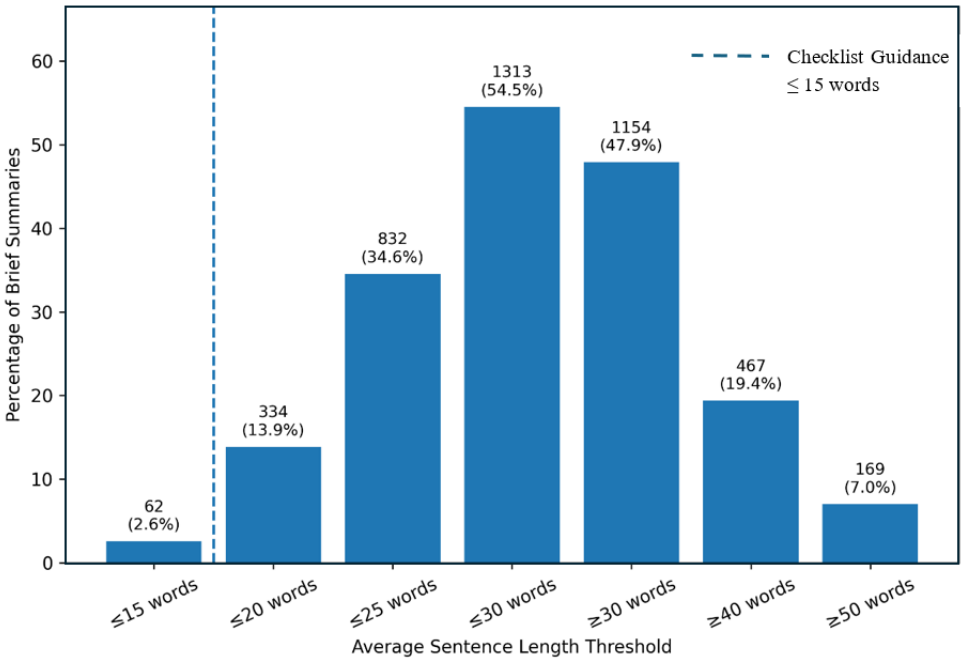
Length

The Plain Language Checklist Guidance recommends keeping sentences and paragraphs short. The goal is to use sentences with 15 words or fewer and paragraphs of three to five sentences or fewer. Across all 2,408 Brief Summaries, the mean average sentence length was 31.6 words (*SD* = 14.9), with a median of 29.0 words (IQR: 23.0–37.0). Summary-level average sentence length ranged from 6.5 words to 356 words. Only 62 of the 2,408 Brief Summaries (2.6%) met the recommended threshold of ≤15 words per sentence.

There was no meaningful improvement in average words per sentence between the pre- and post-guidance periods. The mean average sentence length was 32.2 words

(*SD* = 16.0) before guidance and 31.1 words (*SD* = 13.7) after guidance. This difference was not statistically significant. Similarly, the proportion of summaries meeting the ≤15-word threshold did not significantly differ before and after guidance (34, 2.9% vs. 28, 2.3%; p = .441). Although most summaries were short by total character count, their sentences remained longer than recommended.

Figure 23. Brief Summary Sentence-Length Thresholds



Readability

Readability was assessed using several metrics to determine whether the content of the Brief Summary met the guidance for accessibility at a sixth- to eighth-grade reading level. Text was analyzed for the FKGL, FRE, and SMOG Index. For the FKGL and SMOG Index (0 to no upper limit), higher scores indicate a higher required reading

level, while for FRE (0–100), lower scores indicate more difficult text. Guidance is recommended to be written at or below an eighth-grade reading level.

Overall, the results remained poor, with a mean FKGL across all studies of 19.66 (*SD* = 6.64) and a median of 18.93. This FKGL is equivalent to an advanced graduate, professional, or academic reading level, far beyond the literacy level of a substantial portion of the intended lay public audience. Only 13 of 2,408 Brief Summaries (0.5%) were written at or below an eighth-grade reading level. The mean FRE score was 10.45 (*SD* = 26.21), and only 13 summaries (0.5%) exceeded the patient-friendly threshold of 69. The mean SMOG score was 19.96 (*SD* = 4.36), and no summaries met the SMOG threshold of eighth-grade readability.

There was no statistically significant improvement in readability after publication of the Plain Language Checklist. A year-over-year view of the average grade level assessed by FKGL and SMOG Index stayed consistently high across all years, with no clear improvement, as shown in Figure 24, with the dotted line indicating the target maximum eighth-grade reading level. One-way ANOVA did not show statistically significant year-to-year differences for FKGL ($p = .349$). The mean FKGL was 19.68 (*SD* = 7.12) before guidance and 19.64 (*SD* = 6.14) after guidance, with no statistically significant difference. Similarly, FRE did not significantly differ between the pre-guidance and post-guidance periods (11.27 vs. 9.65; $p = .130$), nor did the SMOG Index score (19.91 vs. 20.01; $p = .576$), as shown in Table 7. The proportion of summaries meeting the FKGL ≤ 8 threshold remained very low in both periods (4/1,191, 0.3% before vs. 9/1,217, 0.7% after guidance; $p = .266$).

Figure 24. Year-Over-Year Readability Grade Level by First Posted Data (Sept–Sept)

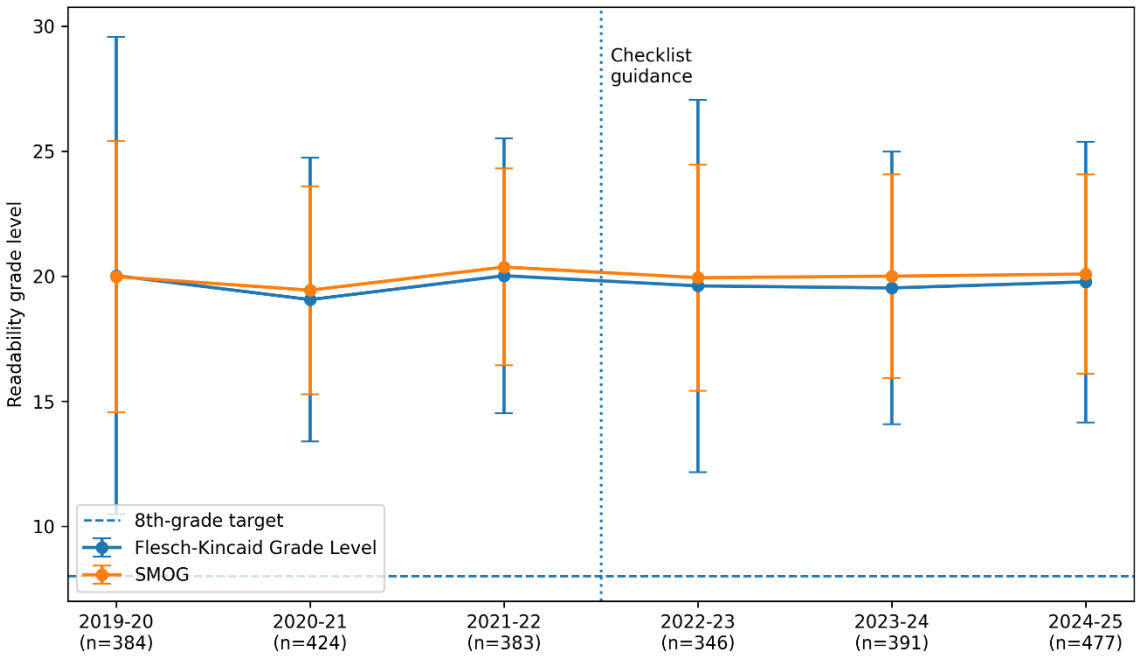


Table 7. Readability Summary of All Brief Summaries Pre- vs Post-Guidance

Measure	**Overall, *N* = 2,408**	**Pre-guidance, *n* = 1,191**	**Post-guidance, *n* = 1,217**	***p*-value**
FKGL, mean (***SD***)	19.66 (6.64)	19.68 (7.12)	19.64 (6.14)	.889
FRE, mean (***SD***)	10.45 (26.21)	11.27 (27.17)	9.65 (25.21)	.130
SMOG, mean (***SD***)	19.96 (4.36)	19.91 (4.56)	20.01 (4.16)	.576

Given the geographic distribution of trials, an analysis was conducted to determine whether readability differed between studies that enrolled at least one U.S. site and those that did not. A statistically significant difference was detected: studies enrolling in the United States had lower mean FKGL scores than studies with no U.S. sites (19.12; *SD* = 8.22 vs. 19.94; *SD* = 5.62; Welch's p = .010; see Table 8 below). Although this

difference was statistically significant, both groups remained far above the eighth-grade threshold recommended for patient-facing health information. Only 11 U.S.-enrolling studies (1.3%) and two studies without U.S. sites (0.1%) met the FKGL ≤ 8 criterion. No meaningful pre- vs post-guidance improvement was identified within either geography group.

Table 8. FKGL by U.S. Enrolling Sites vs. Non-U.S. Sites

Geography	*n*	Mean FKGL (*SD*)	Median FKGL (IQR)	FKGL ≤8, *n* (%)	*p*-value
U.S. sites	831	19.12 (8.22)	17.89 (14.44–22.90)	11 (1.3%)	
No U.S. sites	1,577	19.94 (5.62)	19.33 (16.05–22.98)	2 (0.1%)	
Comparison					.010

Readability also differed by study sponsor type. Sponsors were categorized as NIH/NCI, network or cooperative group, academic/medical center, government/other federal, industry, or other/uncategorized. The Other/uncategorized category included sponsors who could not clearly fit into a designated category, investigator-initiated research, or institutions that could not be clearly classified as an academic/medical center or oncology research network.

Readability differed significantly by sponsor type (ANOVA, $p < .001$). NIH–NCI-sponsored studies had the lowest mean FKGL score (13.52; $SD = 5.01$), followed by network or cooperative group studies (16.76; $SD = 5.02$). Other/uncategorized studies had a mean FKGL of 19.06 ($SD = 5.35$), academic/medical-center-sponsored studies had a mean FKGL of 19.30 ($SD = 5.02$), and government/other federal studies had a mean

FKGL of 19.40 (*SD* = 5.57). Industry-sponsored studies had the highest mean FKGL among major sponsor categories (20.67; *SD* = 8.16; see

Table 9 below).

Post hoc comparisons indicated that industry-sponsored summaries were significantly less readable than academic/medical center summaries. NIH/NCI-sponsored summaries were significantly more readable than academic/medical center, industry, government/other federal, and other/uncategorized summaries. Network or cooperative group summaries were significantly more readable than industry-sponsored summaries. However, the difference between the network/cooperative group and the academic/medical center summaries did not reach statistical significance in post hoc testing.

Table 9. FKGL by Sponsor Category

Sponsor category	*n*	Mean FKGL (*SD*)	Median FKGL (IQR)	FKGL ≤8, n (%)
NIH/NCI	49	13.52 (5.01)	12.50 (9.36–16.76)	4 (8.2%)
Network/cooperative group	54	16.76 (5.02)	15.79 (13.27–18.85)	0 (0.0%)
Other/uncategorized	317	19.06 (5.35)	18.53 (15.73–21.46)	3 (0.9%)
Academic/medical center	945	19.30 (5.02)	18.72 (15.69–22.39)	1 (0.1%)
Government/other federal	59	19.40 (5.57)	18.16 (15.80–21.87)	0 (0.0%)
Industry	984	20.67 (8.16)	19.93 (15.61–24.07)	5 (0.5%)

Active Voice

The Plain Language Checklist Guidance recommends that sentences be written in active voice, in which the subject performs the action of the verb. Overall, approximately two-thirds of the Brief Summaries used active voice. A total of 1,577 summaries (65.5%) met the active-voice criterion, including 798 pre-guidance summaries (67.0%) and 779 post-guidance summaries (64.0%). Although the proportion of summaries using active

voice decreased slightly after the guidance was implemented, the difference was not statistically significant (p = .123).

Medical Jargon and Consistent Terminology

One step to improve readability is to remove complex and difficult words from the vocabulary, including words that may be considered jargon or medical terminology. While it may not always be possible to remove jargon completely from the Brief Summary, the 5,000-character limit allows space to provide definitions when possible. The Plain Language Checklist recommends replacing complex terms, avoiding jargon, and, if jargon is necessary, defining essential jargon using common words. Several sources are available to investigators to help replace complex medical terms with lay language, including the NIH Glossary of Common Terms, the NCI Dictionary of Cancer Terms, and the NCCN® Informed Consent Language Database. While measuring the extent of replacement of complex terms was outside the scope of this work, the analysis evaluated whether Brief Summaries avoided jargon or provided sufficient plain-language explanations of technical terms.

Only 154 of 2,408 Brief Summaries (6.4%) were identified as avoiding jargon or providing sufficient plain-language explanation for technical language. Most summaries did not meet this criterion (2,254, 93.6%). Jargon avoidance differed significantly between the pre-guidance and post-guidance periods, with 92 pre-guidance summaries (7.7%) and 62 post-guidance summaries (5.1%) meeting this criterion (p = .010). This finding suggests that jargon remained highly prevalent after guidance and may have become slightly less likely to be avoided in the post-guidance period.

Consistent terminology was defined as using language that remains constant within the Brief Summary. The guidance gives the example of using “researchers” consistently instead of alternating with “investigator.” For this analysis, terminology variation was evaluated using predefined term groupings, including researcher/investigator/study doctor/trial doctor; participant/patient/subject/volunteer; treatment/therapy/intervention/study drug; study/trial/research study/clinical trial; side effect/adverse event/reaction; cancer/tumor/malignancy/disease; medicine/drug/agent/product; receive/administered/given; placebo/inactive treatment/sugar pill; and spread/metastasized/advanced disease.

Overall, 2,334 of 2,408 Brief Summaries (96.9%) used consistent terminology, while 74 (3.1%) did not. A total of 1,167 pre-guidance summaries (98.0%) and 1,167 post-guidance summaries (95.9%) used consistent terminology ($p = .003$). Although terminology inconsistency was uncommon overall, it was significantly more frequent in the post-guidance period. A proxy analysis of terminology variation showed that the most common areas of inconsistency involved cancer-related terms, study/trial descriptors, treatment-related terms, and labels for enrolled individuals. For example, 579 summaries (24.0%) used two or more terms from the cancer/tumor/malignancy/disease group, and 450 summaries (18.7%) used two or more terms from the study/trial/research-study group. In the post-guidance period, Brief Summaries were more likely to use multiple labels for enrolled individuals, such as “patient,” “participant,” and “subject” (3.8% vs. 9.9%, $p < .001$), and were also more likely to mix study/trial terminology (13.9% vs. 23.4%, $p < .001$), as shown in Table 10 below.

Table 10. Terminology Groups Using More Than Two Terms: Pre- and Post-Guidance

Concept group with ≥2 terms used	**Pre-guidance, *n* (%)**	**Post-guidance, *n* (%)**	***p*-value**
Patient/participant/subject/volunteer	45 (3.8%)	121 (9.9%)	<.001
Study/trial/research study/clinical trial	141 (11.8%)	213 (17.5%)	<.001
Treatment/therapy/intervention/study drug	186 (15.6%)	205 (16.8%)	.439
Cancer/tumor/malignancy/disease	312 (26.2%)	315 (25.9%)	.889
Spread/metastasized/advanced disease	225 (18.9%)	258 (21.2%)	.169
Receive/administered/given	43 (3.6%)	66 (5.4%)	.039

These findings suggest that although most Brief Summaries met the binary consistent-terminology criterion, terminology variation persisted across several concept areas and increased after the checklist's publication. In particular, the continued use of “subject,” as well as shifting among “patient,” “participant,” and “subject,” may reflect an effort to balance regulatory language with patient-centered phrasing. However, this variation may also conflict with the plain-language goal of using consistent terminology throughout the Brief Summary.

Acronym Use

Guidance for the Brief Summary recommends that sponsors write out the full names of acronyms on first use and provide the acronym in parentheses. Oncology is full of acronyms, especially in lung cancer, where many trials are biomarker-driven. To account for this, certain acronyms were excluded from analysis, including NSCLC, SCLC, KRAS, NTRK, EGFR, PDL1, PD-L1, PD1, PD-1, ALK, ROS1, BRAF, MET, RET, HER2, ERBB2, TMB, MSI, MSI-H, dMMR, MMR, DNA, RNA, CT, MRI, PET, PET-CT, RECIST, ECOG, FDA, NCCN, NIH, NCI, and IV, with the full exclusion list included in the Supplementary Data.

Across all 2,408 Brief Summaries, 1,914 summaries (79.5%) met the criterion for avoiding unexplained acronyms, while 494 summaries (20.5%) did not. No difference was found between the pre-guidance and post-guidance periods. A total of 947 pre-guidance summaries (79.5%) and 967 post-guidance summaries (79.5%) met the criterion for avoiding unexplained acronyms (p = 1.000, Fisher's exact test). These findings suggest that acronym handling did not meaningfully change after publication of the Plain Language Checklist.

Table 11. Pre- vs Post-Guidance Acronym Findings

Measure	**Pre-guidance, *n* = 1,191**	**Post-guidance, *n* = 1,217**	***p*-value**
Avoided unexplained acronyms	947 (79.5%)	967 (79.5%)	1.000
Did not avoid unexplained acronyms	244 (20.5%)	250 (20.5%)	

Clinical Trial Naming Conventions and Abbreviations

One area not addressed in the Plain Language Checklist Guidance concerns trial naming conventions. It has become common to name your trial something aspirational or "catchy" that aligns with the disease states, uses part of a biomarker in the name, or is a trial series that uses part of a generic or branded drug name. Ten (0.4%) trials were identified as having titles that used aspirational or positive language. Examples included RESCUE, ACHIEVE, BOOST, UNLOCK, BRIGHT, INSIGHT, and PROPHET. However, some of these titles were taken from abbreviations from the title of the study (i.e., INSIGHT: Randomized Phase III Trial **IN**corporating Pathologic Complete Re**S**ponse in Part**I**cipants With Early Sta**G**e Non Small Cell Lung Cancer to Optimize

Immunot**H**erapy in The Adjuvan**T** Setting [INSIGHT] and RESCUE: **RESt**oring lympho**C**ytes **U**sing NKTR-255 After chemoradioth**E**rapy in Solid Tumors [RESCUE]), while other were randomly assigned. Nine trials were identified with names that use wordplay on a biomarker, gene, or target: KRYSTAL (n = 2), ALKOVE, CodeBreaK, MTAPESTRY, and IZABRIGHT.

Numbers

The Plain Language Checklist Guidance outlines several considerations when including numbers in the Brief Summary and recommends including only essential numbers closely related to the study's purpose. If numbers are used, the guidance recommends providing context and meaning, such as whether the number is "better" or "worse," and, when possible, using words and numbers together. These broader measurements were not included in the analysis because they were difficult to define consistently. Three numeric recommendations were included in the PLCST: using percentages alongside natural frequencies, using words rather than numeric symbols, and avoiding qualitative terms such as "reduce" or "increase."

Overall, 539 of 2,408 Brief Summaries (22.4%) used words instead of numeric symbols, with no significant difference between the pre-guidance and post-guidance periods (275, 23.1% vs. 264, 21.7%; p = .434). Symbols remained common, particularly slashes used in ratios or regimen descriptions, plus signs used in combination regimens, percent signs, and greater-than or less-than symbols used in eligibility thresholds. A total of 155 Brief Summaries (6.4%) included at least one percentage symbol or percentage-related term, with no significant difference before and after guidance (77, 6.5% vs. 78, 6.4%; p = 1.000). Only one Brief Summary (0.04%) paired a percentage with a natural

frequency. However, the percentages used in Brief Summaries were often not patient-facing probability statements. Instead, they commonly appeared as biomarker thresholds (e.g., PD-L1 expression or TPS cutoffs), response or survival endpoints, safety rates, or background epidemiologic information. Hence, the checklist recommendation to pair percentages with natural frequencies may be less directly applicable to many Brief Summaries unless the summary is presenting risk, benefit, probability, or frequency information.

Avoidance of qualitative terms was met by 904 summaries (37.5%) and did not differ significantly before and after guidance (450, 37.8% vs. 454, 37.3%; $p = .833$). The results are shown in

Table 12 and 13 below.

Table 12. Changes in Pre- and Post-Guidance Adherence to Number-Related Criteria

Criterion	Pre-guidance, *n* (%)	Post-guidance, *n* (%)	Total, *n* (%)	*p*-value
Uses words instead of numeric symbols	275/1,191 (23.1%)	264/1,217 (21.7%)	539/2,408 (22.4%)	.434
Uses both percentages and natural frequencies	1/1,191 (0.1%)	0/1,217 (0.0%)	1/2,408 (0.04%)	.495
Avoids qualitative terms	450/1,191 (37.8%)	454/1,217 (37.3%)	904/2,408 (37.5%)	.833

Table 13. Types of Percentages That Appear in Brief Summaries

Percentage context	Summaries, *n*	% of summaries with percentages, *n* = 155	% of all summaries, *N* = 2,408
Efficacy, endpoints, response, survival, recurrence, or disease-control rates	136	87.7%	5.6%
Tumor component, biomarker, mutation, or expression thresholds	120	77.4%	5.0%
PD-L1/TPS eligibility thresholds	65	41.9%	2.7%
Safety, toxicity, adverse events, or grade ≥3 event rates	96	61.9%	4.0%
Epidemiology/background prevalence	60	38.7%	2.5%

Purpose of the Study

Brief Summaries should state the study purpose: the "why" of the research, including why researchers are conducting the study and, when appropriate, any benefits of participation. The analysis evaluated this criterion under both the PLCST and the exploratory patient-focused criteria, as they clarify why researchers are conducting the study and help patients understand the trial's relevance. Although this criterion contributed to both scores, the combined score counted it only once to avoid double-counting.

Overall, 1,576 of 2,408 Brief Summaries (65.4%) stated the purpose of the study, while 832 summaries (34.6%) did not. The proportion of summaries stating a purpose increased modestly after guidance, from 754 pre-guidance summaries (63.3%) to 822 post-guidance summaries (67.5%). This difference was statistically significant ($p = .032$). No meaningful difference was identified by geography; purpose was stated in 546 U.S.-enrolling studies (65.7%) and 1,030 studies with no U.S. sites (65.3%; $p = .857$).

Purpose statements differed by sponsor type ($p < .001$). Industry-sponsored trials were most likely to state the study's purpose, with 742 of 984 studies (75.4%) including a clear purpose statement. Government/other federal studies included a purpose statement

in 36 of 59 summaries (61.0%), academic/medical center studies in 562 of 945 summaries (59.5%), other/uncategorized studies in 184 of 317 summaries (58.0%), NIH/NCI-sponsored studies in 28 of 49 summaries (57.1%), and network/cooperative group studies in 24 of 54 summaries (44.4%), as shown in

Table 14 below.

Table 14. Purpose Stated by Sponsor Type

Sponsor category	***n***	**Purpose stated, *n* (%)**
Industry	984	742 (75.4%)
Government/other federal	59	36 (61.0%)
Academic/medical center	945	562 (59.5%)
Other/uncategorized	317	184 (58.0%)
NIH/NCI	49	28 (57.1%)
Network/cooperative group	54	24 (44.4%)

When a purpose was stated, it usually appeared early in the Brief Summary. Among summaries coded as stating a purpose, 1,109 (70.4%) included purpose-related language in the first sentence, 1,278 (81.1%) within the first two sentences, and 1,388 (88.1%) in the first paragraph. Common purpose-related terms included evaluate, assess, objective, determine, purpose, compare, goal, and aim. The most common opening phrase was “The purpose of this study is…,” which appeared at the beginning of 141 summaries, followed by “The goal of this clinical trial is…,” which appeared at the beginning of 57 summaries.

Summaries that did not state a purpose were not simply shorter versions of otherwise complete summaries. Among the 25 shortest Brief Summaries, only 5 (20.0%) stated a purpose. In contrast, among Brief Summaries longer than 250 words, 88 of 104

(84.6%) stated a purpose. These findings suggest that brevity often resulted in the omission of suggested content rather than in successful plain-language communication (see Table 15 below).

Table 15. Brief Summary Including a Purpose Statement by Word Count

Brief Summary word count	***n***	**Purpose stated, *n* (%)**
≤25 words	210	89 (42.4%)
26–50 words	918	627 (68.3%)
51–75 words	395	272 (68.9%)
76–100 words	247	161 (65.2%)
101–150 words	324	204 (63.0%)
151–250 words	210	135 (64.3%)
>250 words	104	88 (84.6%)

Benefit-Oriented Language

Benefit-oriented language was evaluated as an exploratory patient-focused measure because the Plain Language Checklist recommends explaining the purpose or "why" of the research, including possible benefits. Because clinical trials should not imply guaranteed outcomes or benefit, this variable was interpreted conservatively as the presence of language describing possible benefit, improvement, quality of life, disease control, tumor shrinkage, delayed progression or recurrence, prolonged survival, or reduced toxicity. General statements about "efficacy and safety" alone were not counted as patient benefit language.

Overall, 978 of 2,408 Brief Summaries (40.6%) included benefit-oriented language. There was no significant difference between the pre-guidance and post-guidance periods, although benefit-oriented language was slightly more common after guidance (465, 39.0% vs. 513, 42.2%; $p = .125$). The most common forms of benefit-

oriented language involved prolonged or extended survival or life (347, 14.4%), improvement or better outcomes (315, 13.1%), disease or tumor control, reduction, shrinkage, delayed progression, or prevention of recurrence (296, 12.3%), reduced toxicity or fewer side effects (291, 12.1%), direct use of benefit-related terms (281, 11.7%), and quality of life (93, 3.9%).

Benefit-oriented language differed significantly across trial phases and sponsor types. Phase 1/2 trials were most likely to include benefit-oriented language (266, 51.8%), followed by phase 2/3 trials (25, 43.1%), phase 3 trials (158, 38.8%), and phase 2 trials (529, 37.0%; $p < .001$). Benefit-oriented language also differed by sponsor type ($p < .001$). NIH–NCI-sponsored studies were most likely to include benefit-oriented language (44, 89.8%), followed by network/cooperative group studies (33, 61.1%). Industry-sponsored studies were least likely to include benefit-oriented language (352, 35.8%).

Inclusive and Person-Centered Language

Inclusive and person-centered language was evaluated against the recommendation to use respectful, person-centered terms (e.g., “participants” rather than “subjects” or “patients”) and to avoid language that defines people by their disease. This analysis was also informed by broader oncology communication guidance emphasizing sensitive, respectful, and inclusive language. For this strict criterion, summaries were coded as meeting the criterion if they used preferred referent language such as “participants,” “people with,” “persons with,” “individuals with,” “adults with,” or “older adults,” and did not use terms such as “subjects,” “patients,” or disease-first constructions.

Overall, 389 of 2,408 Brief Summaries (16.2%) met the strict PLCST criterion for inclusive and person-centered language. This criterion did not significantly improve after guidance, with 191 pre-guidance summaries (16.0%) and 198 post-guidance summaries (16.3%) meeting the criterion (p = .912). U.S.-enrolling studies were more likely to meet the criteria than studies with no U.S. site (277, 33.3% vs 112, 7.1%; p < .001).

Use of strict patient-centered language also differed significantly by sponsor type (p < .001). Industry-sponsored and NIH/NCI-sponsored studies were most likely to meet the criterion, with 301 of 984 industry-sponsored studies (30.6%) and 15 of 49 NIH/NCI-sponsored studies (30.6%) using strict patient-centered language. They were followed by other/uncategorized studies (22, 6.9%), network/cooperative group studies (three, 5.6%), academic/medical center studies (46, 4.9%), and government/other federal studies (two, 3.4%; Table 17).

Table 16. Inclusive and Person-Centered Language Pre- and Post-Guidance

Guidance period	**Met criterion, n (%)**	**Did not meet criterion, *n* (%)**	***p*-value**
Pre-guidance, ***n*** = 1,191	191 (16.0%)	1,000 (84.0%)	
Post-guidance, ***n*** = 1,217	198 (16.3%)	1,019 (83.7%)	
Total, ***N*** = 2,408	389 (16.2%)	2,019 (83.8%)	.912

Table 17. Inclusive and Person-Centered Language by Sponsor

Sponsor category	***n***	**Met criterion, *n* (%)**
Industry	984	301 (30.6%)
NIH/NCI	49	15 (30.6%)
Other/uncategorized	317	22 (6.9%)
Network/cooperative group	54	3 (5.6%)
Academic/medical center	945	46 (4.9%)
Government/other federal	59	2 (3.4%)

A descriptive language analysis showed that “patient(s)” remained the dominant referent term, appearing in 1,418 summaries (58.9%). Use of “participant(s)” increased significantly after guidance, from 193 pre-guidance summaries (16.2%) to 268 post-guidance summaries (22.0%; $p < .001$). The term “subject(s)” appeared in 203 summaries (8.4%) and did not significantly differ before and after guidance (94, 7.9% vs. 109, 9.0%; $p = .379$).

Person-first and disease-first phrasing were also examined descriptively. Phrases such as “patients with lung cancer,” “patients with NSCLC,” or “patients with non-small-cell lung cancer” appeared in 97 summaries (4.0%) and did not significantly differ before and after guidance (39, 3.3% vs. 58, 4.8%; $p = .078$). Preferred person-centered phrasing (e.g., “people with lung cancer” or “people with NSCLC”) was rare, appearing in only seven summaries (0.3%). Disease-first phrasing remained more common: “lung cancer patients” appeared in 214 summaries (8.9%), and “NSCLC patients” or “non-small-cell lung cancer patients” appeared in 172 summaries (7.1%). Neither disease-first phrase category differed significantly before and after guidance. These findings suggest that while the use of “participant(s)” increased after guidance, “patient(s)” remained the dominant term, and strictly person-centered referent language remained uncommon.

Table 18. Common Phrases Used to Describe Person-First Compared to Disease-First

Phrase type	Total, *n* (%)	Pre-guidance, *n* (%)	Post-guidance, *n* (%)	*p*-value
Patients with lung cancer / NSCLC / SCLC	97 (4.0%)	39 (3.3%)	58 (4.8%)	.078
Lung cancer patients	214 (8.9%)	97 (8.1%)	117 (9.6%)	.223
Patients with NSCLC / non-small-cell lung cancer	71 (2.9%)	30 (2.5%)	41 (3.4%)	.230
NSCLC / non-small-cell lung cancer patients	172 (7.1%)	76 (6.4%)	96 (7.9%)	.155
People with lung cancer / NSCLC	7 (0.3%)	3 (0.3%)	4 (0.3%)	1.000
Subjects with lung cancer / NSCLC	4 (0.2%)	3 (0.3%)	1 (0.1%)	.369

Plain Language Checklist Scoring Tool (PLCST)

In 2,408 Brief Summaries, the PLCST score was 3.93 (*SD* = 1.05), representing 35.7% of the maximum possible score of 11. No Brief Summary met all 11 PLCST criteria. Scores ranged from 0 to 8, with the most common score being 4 (967 summaries, 40.2%). Only 147 summaries (6.1%) scored 6 or higher (Figure 25). PLCST scores did not significantly improve after publication of the Plain Language Checklist. The mean PLCST score was 3.96 (*SD* = 1.03) in the pre-guidance period and 3.90 (*SD* = 1.06) in the post-guidance period. The difference was not significant.

Individual PLCST criteria showed mixed patterns. Purpose statements increased significantly after guidance, from 754 summaries (63.3%) to 822 summaries (67.5%; p = .032). Jargon avoidance decreased after guidance, from 92 summaries (7.7%) to 62 summaries (5.1%; p = .010), and consistent terminology also decreased, from 1,167 summaries (98.0%) to 1,167 summaries (95.9%; p = .003). No significant improvement was observed for sentence length, FKGL, unexplained acronyms, active voice, numeric-symbol use, qualitative terms, or use of percentages with natural frequencies (see Figure 26).

Together, these findings suggest that the checklist was not associated with meaningful improvement in overall plain-language checklist adherence or readability. Although purpose statements improved modestly after guidance, most checklist criteria did not improve, and several language-related criteria either remained unchanged or performed worse in the post-guidance period.

Figure 25. Distribution of PLCST Scores for All Trials

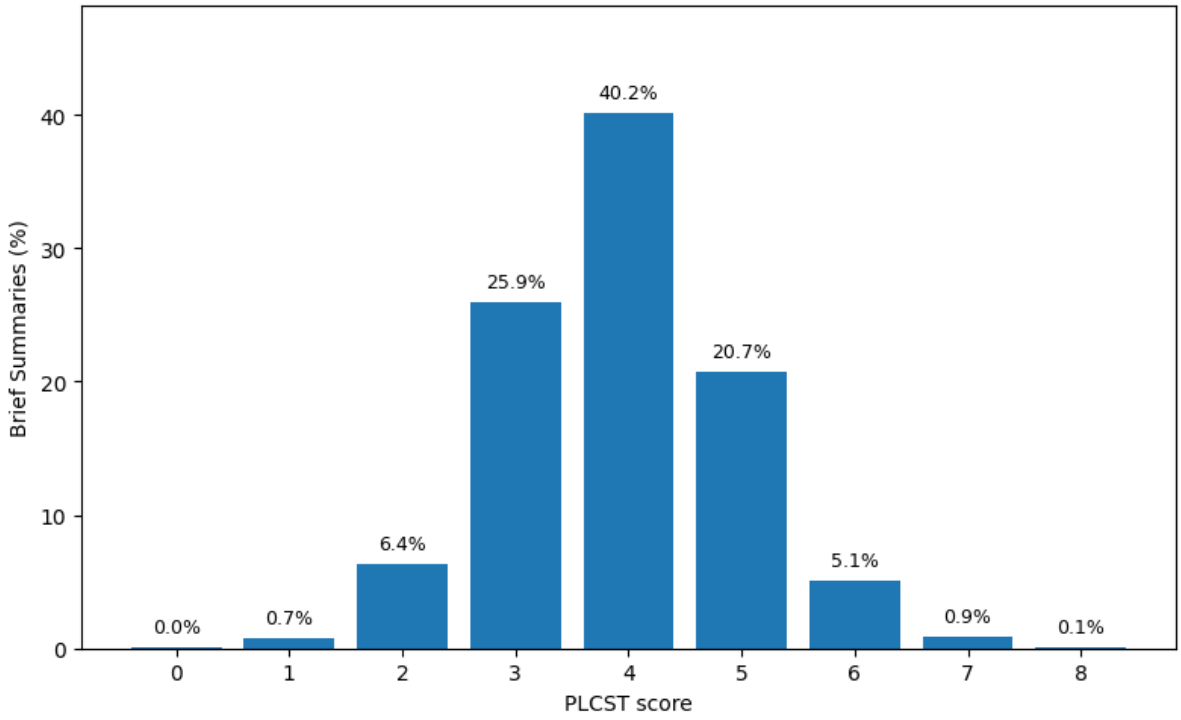


Figure 26. PLCST Criteria Met, Pre- and Post- Guidance

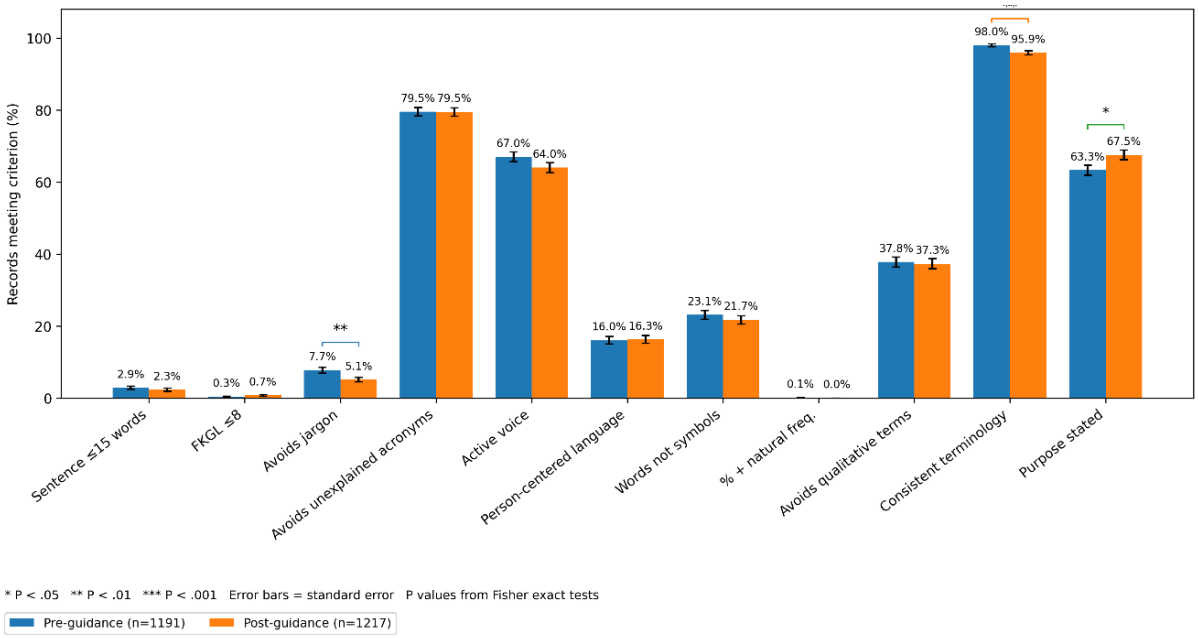


Table 19. PLCST Criterion Pre- and Post-Guidance

Criterion	Pre-guidance *n* (%) [95% CI]	Post-guidance *n* (%) [95% CI]	P
Average sentence length ≤15 words	34 (2.9) [2.0, 4.0]	28 (2.3) [1.6, 3.3]	.441
FKGL ≤8	4 (0.3) [0.1, 0.9]	9 (0.7) [0.4, 1.4]	.266
Avoids jargon	92 (7.7) [6.3, 9.4]	62 (5.1) [4.0, 6.5]	.010
Avoids unexplained acronyms	947 (79.5) [77.1, 81.7]	967 (79.5) [77.1, 81.6]	1.000
Uses active voice	798 (67.0) [64.3, 69.6]	779 (64.0) [61.3, 66.7]	.123
Inclusive/person-centered language	191 (16.0) [14.1, 18.2]	198 (16.3) [14.3, 18.4]	.912
Uses words instead of numeric symbols	275 (23.1) [20.8, 25.6]	264 (21.7) [19.5, 24.1]	.434
Uses percentages + natural frequencies	1 (0.1) [0.0, 0.5]	0 (0.0) [0.0, 0.3]	.495
Avoids qualitative terms	450 (37.8) [35.1, 40.6]	454 (37.3) [34.6, 40.1]	.833
Uses consistent terminology	1,167 (98.0) [97.0, 98.6]	1,167 (95.9) [94.6, 96.9]	.003
States purpose of study	754 (63.3) [60.5, 66.0]	822 (67.5) [64.9, 70.1]	.032

Additional subgroup analyses were conducted to evaluate whether PLCST scores differed by geographic enrollment pattern, trial phase, or sponsor type. Mean PLCST scores were slightly higher among U.S.-enrolling studies than studies with no U.S. site (4.20; *SD* = 1.13 vs. 3.79; *SD* = 0.97; Welch's $p < .001$; Mann–Whitney U $p < .001$), although the absolute difference was modest. PLCST scores did not differ significantly by trial phase (ANOVA, $p = .116$; Kruskal–Wallis, $p = .093$), with mean scores ranging from 3.86 (*SD* = 0.98) for phase 2/3 trials to 4.04 (*SD* = 0.99) for phase 3 trials.

PLCST scores differed significantly by sponsor type (ANOVA $p < .001$; Kruskal–Wallis $p < .001$). NIH/NCI-sponsored summaries had the highest mean PLCST score (4.82; *SD* = 0.88), followed by network/cooperative group summaries (4.11; *SD* = 1.02), industry-sponsored summaries (3.98; *SD* = 1.01), academic/medical center summaries (3.89; *SD* = 1.04), government/other federal summaries (3.86; *SD* = 1.01), and other/uncategorized sponsors (3.73; *SD* = 1.13). These findings should be interpreted cautiously because even the highest-scoring sponsor categories met fewer than half of the possible PLCST criteria on average, and all sponsor groups continued to perform poorly on key readability-related measures such as FKGL, sentence length, and jargon avoidance.

Table 20. PLCST Score by Sponsor Type

Sponsor type	*n*	Mean PLCST (*SD*)	Median (IQR)
NIH/NCI	49	4.82 (0.88)	5 (4–5)
Network/cooperative group	54	4.11 (1.02)	4 (4–4)
Industry	984	3.98 (1.01)	4 (3–5)
Academic/medical center	945	3.89 (1.04)	4 (3–5)
Government/other federal	59	3.86 (1.01)	4 (3–5)
Other/uncategorized	317	3.73 (1.13)	4 (3–4)

Among industry-sponsored studies, company-level analyses were evaluated descriptively because sample sizes varied by sponsor. The most frequent industry sponsors were AstraZeneca (*n* = 50), Merck (*n* = 34), Hoffmann–La Roche (*n* = 27), Bristol-Myers Squibb (*n* = 21), Chia Tai Tianqing Pharmaceutical Group (*n* = 20), Akeso (*n* = 19), Amgen (*n* = 17), Jiangsu HengRui Medicine (*n* = 17), and Novartis Pharmaceuticals (*n* = 16). Selected large pharmaceutical sponsors had moderate PLCST scores, but FKGL scores remained high across companies. For example, AstraZeneca had a mean PLCST score of 3.94 and a mean FKGL of 22.85; Merck Sharp & Dohme LLC had a mean PLCST score of 4.18 and a mean FKGL of 20.65; and Bristol-Myers Squibb had a mean PLCST score of 4.19 and a mean FKGL of 20.85. These findings suggest that company-sponsored summaries may meet selected checklist criteria without necessarily achieving patient-facing readability.

Table 21. PLCST for Industry Sponsors With Trials Enrolling in the US

Sponsor	*n*	Pre *n*	Post *n*	Mean PLCST	Pre-mean PLCST	Post-mean PLCST	Mean FKGL
AstraZeneca	50	28	22	4.44	4.32	4.59	22.85
Merck	34	15	19	4.65	4.60	4.68	20.65
Hoffmann–La Roche	27	21	6	4.48	4.29	5.17	26.76
Bristol-Myers Squibb	21	8	13	4.90	5.25	4.69	20.85
Chia Tai Tianqing	20	11	9	3.50	3.55	3.44	23.40
Akeso	19	10	9	3.84	4.00	3.67	18.50
Amgen	17	6	11	4.12	4.17	4.09	21.81
Jiangsu HengRui	17	14	3	3.47	3.50	3.33	20.06
Novartis Pharmaceuticals	16	15	1	4.25	4.20	5.00	23.48
Daiichi Sankyo	13	7	6	4.00	3.86	4.17	24.02
GlaxoSmithKline	11	5	6	5.00	4.40	5.50	19.62
AbbVie	9	2	7	4.33	4.00	4.43	14.29
BioNTech SE	7	0	7	4.14	—	4.14	22.19

Exploratory Analysis Using Patient-Focused Criteria

Across 2,408 Brief Summaries, the mean exploratory patient-focused score was 3.70 (*SD* = 1.09) out of 6, representing 61.7% of the maximum possible score. The median score was 4 (IQR: 3–4). Only 117 summaries (4.9%) included all six exploratory elements, while the largest proportion scored 4 of 6 (911 summaries, 37.8%). Score distribution was as follows: 14 summaries (0.6%) scored 0, 39 (1.6%) scored 1, 240 (10.0%) scored 2, 691 (28.7%) scored 3, 911 (37.8%) scored 4, 396 (16.4%) scored 5, and 117 (4.9%) scored 6 (Figure 27).

Exploratory scores improved modestly after guidance. The mean score increased from 3.61 (*SD* = 1.08) before guidance to 3.79 (*SD* = 1.10) after guidance, representing

an increase from 60.2% to 63.2% of the maximum score. This difference was statistically significant by Welch's *t*-test ($p < .001$) and Mann–Whitney U test ($p < .001$). At the criterion level, three criteria improved significantly after guidance.

The proportion of summaries stating the purpose of the study increased from 754 pre-guidance summaries (63.3%) to 822 post-guidance summaries (67.5%; $p = .032$). The proportion describing the condition increased from 1,091 summaries (91.6%) to 1,146 summaries (94.2%; $p = .017$). The proportion describing study duration increased from 252 summaries (21.2%) to 321 summaries (26.4%; $p = .003$). In contrast, there was no significant change in whether summaries described the study population, intervention, or route of administration. Route of administration and study duration were the least frequently included criteria overall, appearing in only 401 (16.7%) and 573 (23.8%) summaries, respectively (see

Figure 28 below).

Exploratory patient-focused scores did not differ significantly by geography. U.S.-enrolling studies had a mean exploratory score of 3.71 (*SD* = 1.06), compared with 3.70 (*SD* = 1.11) for studies with no U.S. site (Welch's $p = .892$; Mann–Whitney U $p = .651$). Exploratory patient-focused scores differed significantly by sponsor type. NIH/NCI-sponsored studies had the highest mean exploratory score (4.31; *SD* = 1.36), followed by network/cooperative group studies (3.89; *SD* = 1.13), other/uncategorized sponsors (3.82; *SD* = 1.19), government/other federal sponsors (3.73; *SD* = 1.01), industry sponsors (3.68; *SD* = 1.07), and academic/medical center sponsors (3.64; *SD* = 1.06). Differences by sponsor type were statistically significant by ANOVA ($p < .001$) and Kruskal–Wallis testing ($p = .004$).

Exploratory scores did not differ significantly by trial phase. Mean scores were similar across Phase 1/2 trials (3.70; *SD* = 1.11), Phase 2 trials (3.68; *SD* = 1.08), Phase 2/3 trials (3.69; *SD* = 1.26), and Phase 3 trials (3.80; *SD* = 1.09; ANOVA $p = .268$; Kruskal–Wallis $p = .131$). These findings suggest that informational completeness improved modestly after guidance, particularly for descriptions of purpose, condition, and study duration. However, practical participation details (e.g., route of administration and study duration) remained uncommon.

Figure 27. Distribution of Exploratory Patient-Focused Criteria Scores

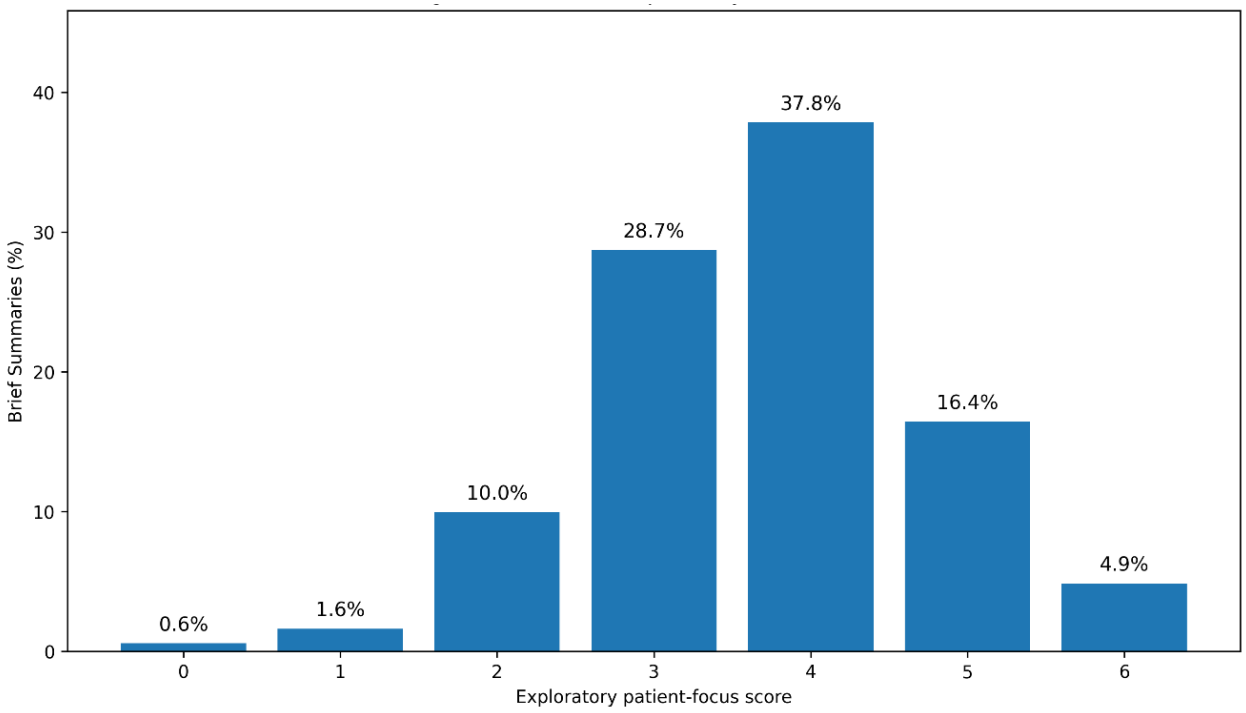
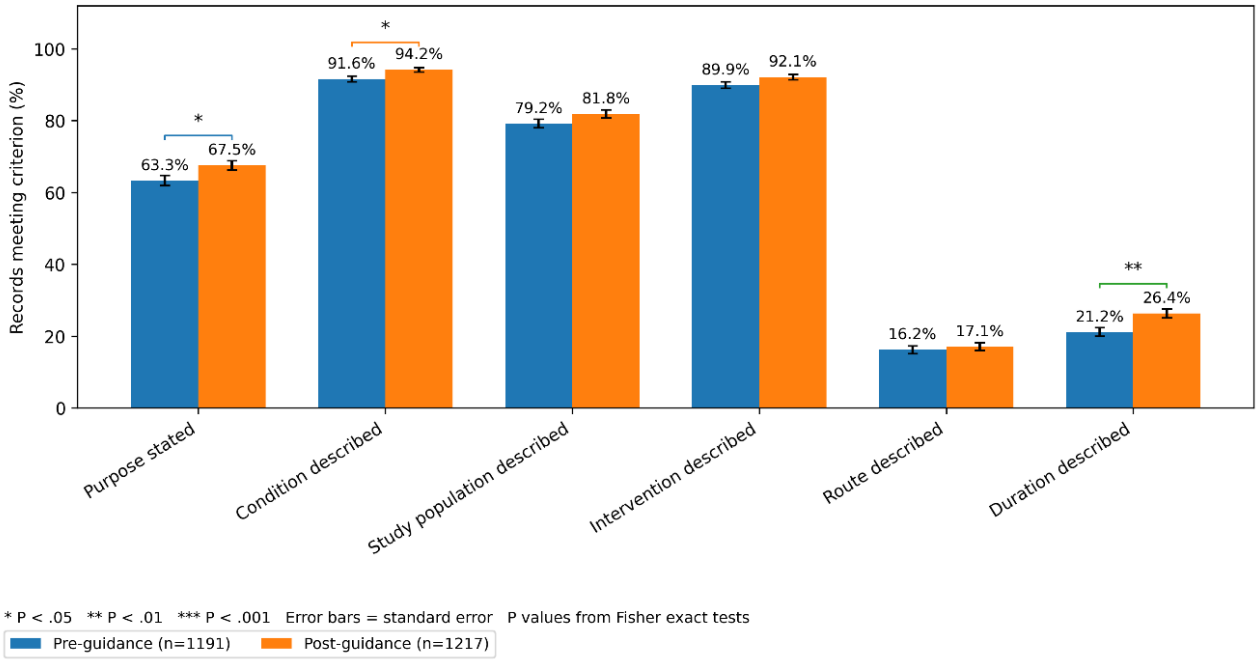

Brief Summaries (%)
40
30
20
10
0
0.6%
1.6%
10.0%
28.7%
37.8%
16.4%
4.9%
0
1
2
3
4
5
6
Exploratory patient-focus score

Figure 28. Exploratory Patient-Focused Criteria Met Pre- and Post-Guidance

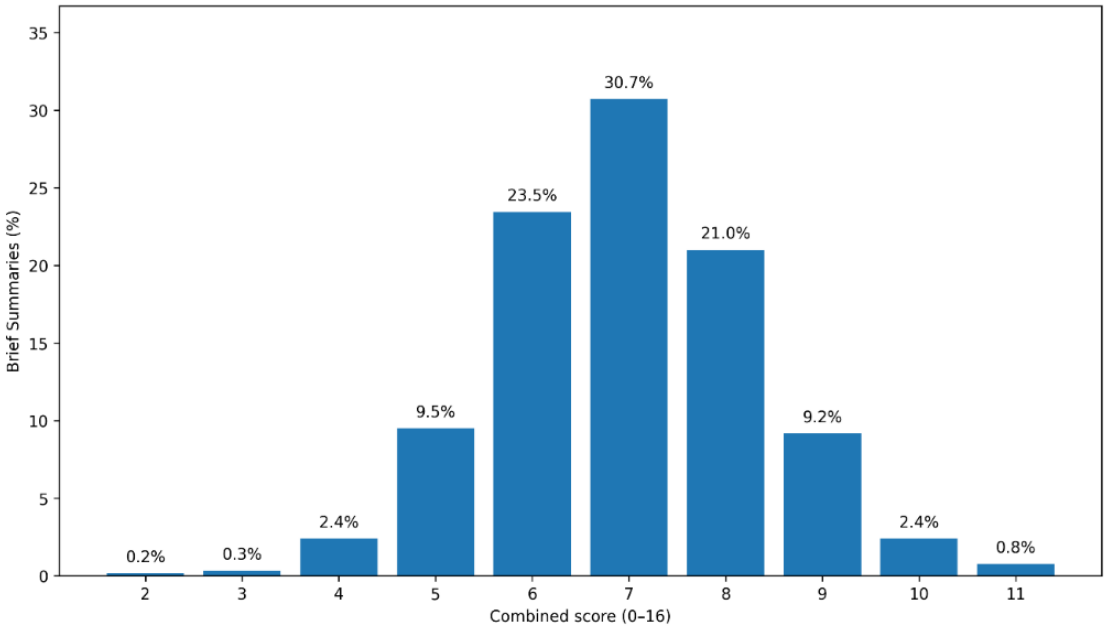


Combined Scoring

In the final analysis, the combined score integrated the PLCST and exploratory patient-focused measures, with the purpose-of-study criterion counted only once. The maximum possible combined score was 16. Across 2,408 Brief Summaries, the mean combined score was 6.98 (*SD* = 1.36), representing 43.6% of the maximum possible score. The median score was 7 (IQR: 6–8), and scores ranged from 2 to 11. No Brief Summary reached the maximum possible combined score (see

Figure 29 below).

Figure 29. Percentage Distribution of Combined Scores



Combined scores were slightly higher after Plain Language Checklist Guidance, but the difference was small and not statistically significant after recalculating PLCST with the corrected strict patient-centered language criterion. The mean combined score was 6.94 (*SD* = 1.35) before guidance and 7.02 (*SD* = 1.36) after guidance, corresponding to an increase from 43.4% to 43.9% of the maximum possible score. This difference was not statistically significant (see

Figure 30 below). There was also no statistical change year-over-year (see Figure 31 below).

Figure 30. Combined Score by Guidance Period

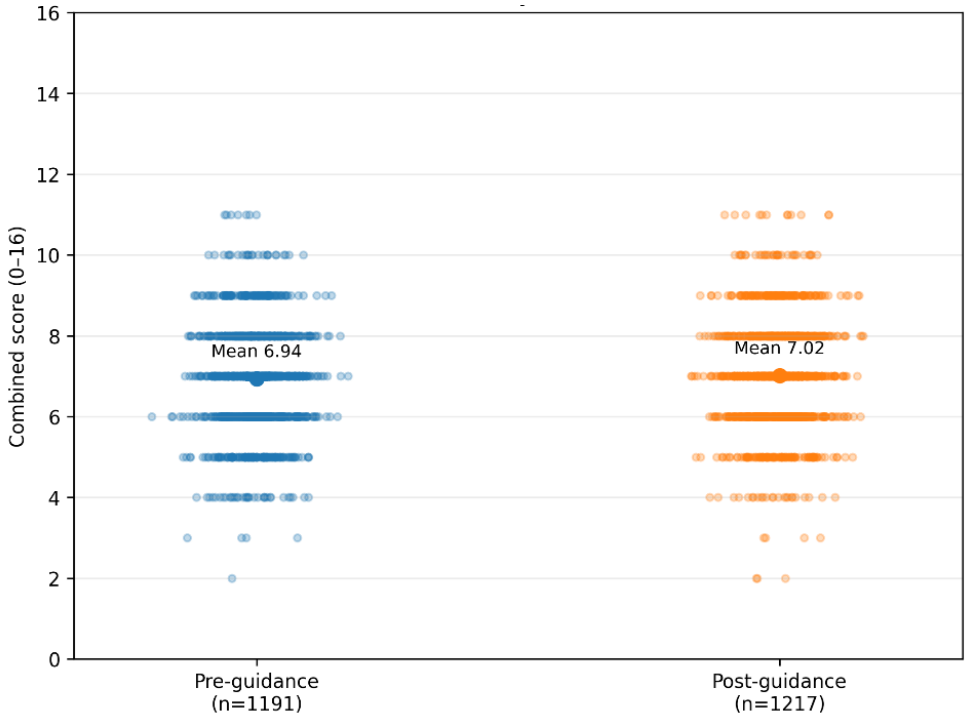
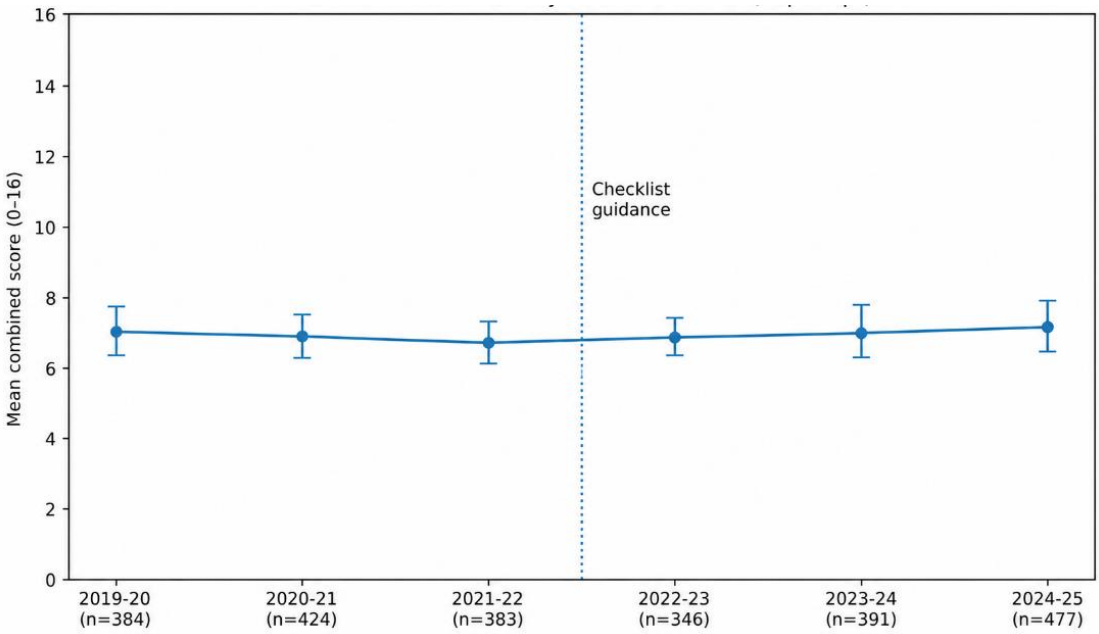


Figure 31. Year-Over-Year Analysis of Combined Scores by Posting Date



Combined scores differed modestly by geography and sponsor type, but not by trial phase. Overall, U.S.-enrolling studies had higher combined scores than studies with no U.S. sites (7.25; *SD* = 1.49 vs. 6.84; *SD* = 1.27; Welch's $p < .001$; Mann–Whitney U $p < .001$). This difference was present in both the pre-guidance and post-guidance periods. In the pre-guidance period, U.S.-enrolling studies had a mean combined score of 7.20 (*SD* = 1.41), compared with 6.78 (*SD* = 1.29) for studies with no U.S. site ($p < .001$). In the post-guidance period, U.S.-enrolling studies had a mean combined score of 7.31 (*SD* = 1.58), compared with 6.89 (*SD* = 1.24) for studies with no U.S. site ($p < .001$).

Combined scores did not differ significantly by trial phase. Mean scores were similar for phase 1/2 trials (6.96; *SD* = 1.42), phase 2 trials (6.95; *SD* = 1.34), phase 2/3 trials (6.98; *SD* = 1.41), and phase 3 trials (7.10; *SD* = 1.36; ANOVA $p = .265$; Kruskal–Wallis $p = .214$). Combined scores differed significantly by sponsor type (ANOVA, $p < .001$; Kruskal–Wallis, $p < .001$). NIH–NCI-sponsored studies had the highest mean combined score (8.55; *SD* = 1.46), followed by network/cooperative group studies (7.56; *SD* = 1.24), government/other federal studies (6.98; *SD* = 1.33), other/uncategorized studies (6.96; *SD* = 1.34), academic/medical center studies (6.94; *SD* = 1.27), and industry-sponsored studies (6.91; *SD* = 1.40).

The combined score was strongly correlated with both the PLCST score (Spearman's $r = 0.689$, $p < .001$) and the exploratory patient-focused score (Spearman's $r = 0.706$, $p < .001$). It was only weakly correlated with FKGL (Spearman's $r = –0.072$, $p < .001$), word count (Spearman's $r = 0.375$, $p < .001$), and character count (Spearman's $r = 0.371$, $p < .001$). Although these correlations were statistically significant in the full sample, the FKGL association was small. These findings suggest that the combined score

captures checklist adherence and patient-focused content but does not meaningfully capture text readability as measured by grade-level formulas.

Figure 32. Year-Over-Year Scores and Readability by First Posted Date (Sept–Sept)

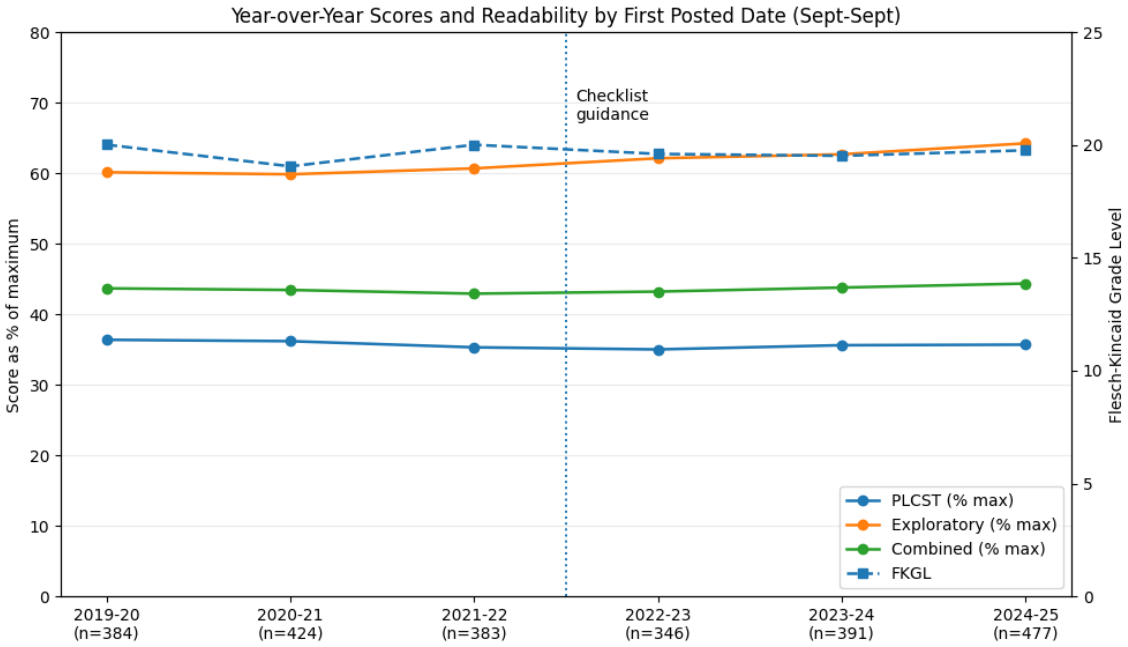
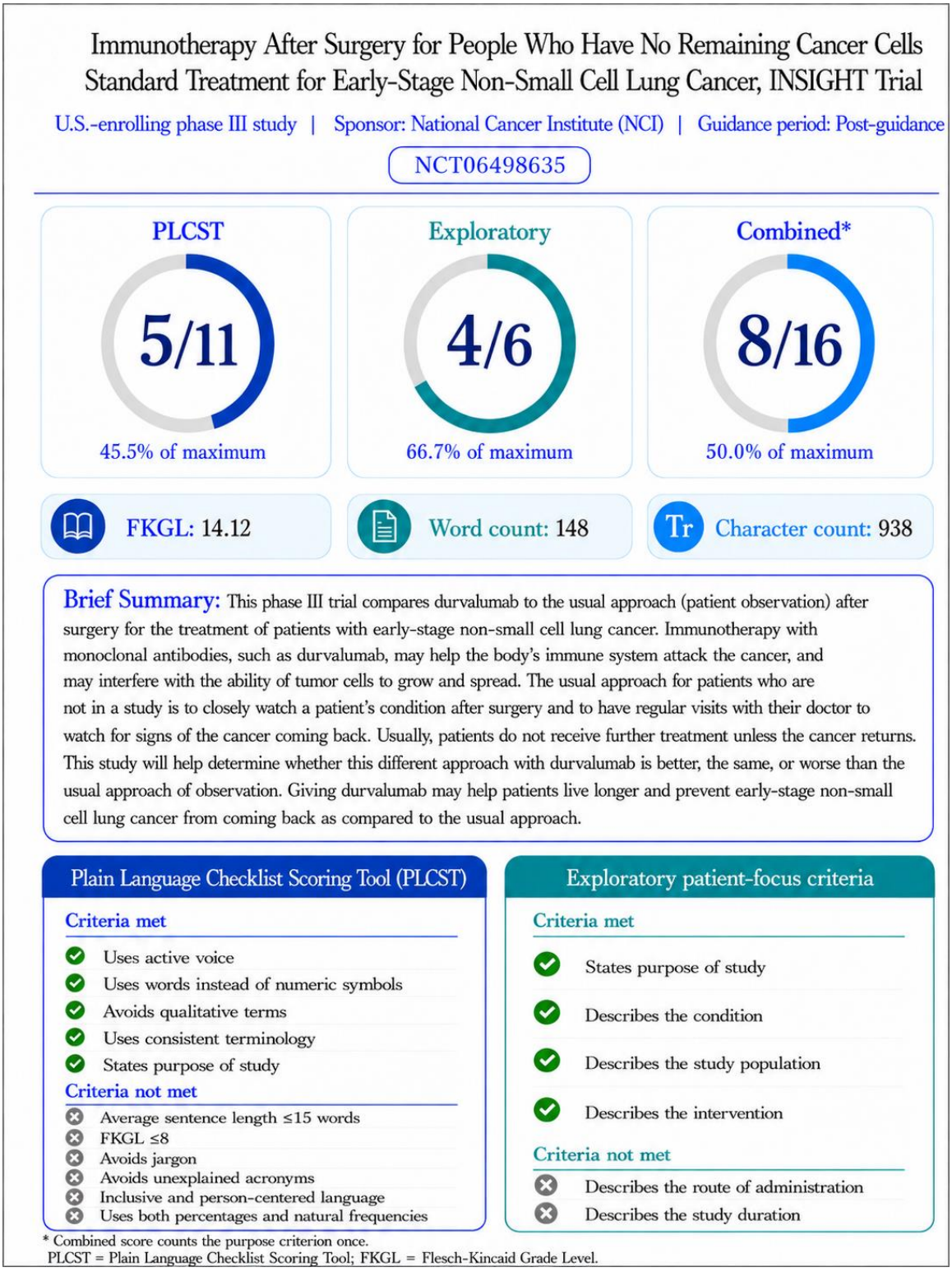


Table 22. Score Summaries

Score	Overall mean (*SD*)	Overall median (IQR)	Pre-guidance mean (*SD*)	Post-guidance mean (*SD*)	*p*-value
PLCST, max 11	3.93 (1.05)	4 (3–5)	3.96 (1.03)	3.90 (1.06)	.204
Exploratory, max 6	3.70 (1.09)	4 (3–4)	3.61 (1.08)	3.79 (1.10)	<.001
Combined, max 16	6.98 (1.36)	7 (6–8)	6.94 (1.35)	7.02 (1.36)	.144
FKGL	19.66 (6.64)	18.93 (15.44–22.95)	19.68 (7.12)	19.64 (6.14)	.889

Figure 33. Visual Representation of Individual Trial Score Card



DISCUSSION

Patients diagnosed with cancer rarely have the luxury of time when making healthcare decisions. Mostly diagnosed in the later stages of disease, patients are rushed through the diagnosis process, searching, sometimes hoping to find a biomarker that will allow them to receive a targeted therapy for their specific type of cancer. Some patients "get lucky" with a prognostically favorable diagnosis, some qualify for a clinical trial testing a promising new therapy, and others may only be eligible for the standard of care. Patients often receive a first line of therapy, followed by a period of remission, followed by the recurrence of cancer, a cycle that repeats itself until a patient starts salvage therapy, palliative care, and eventually hospice.

Clinical trials can be a lifeline for many patients seeking the best chance of improving their survival. This manuscript began by sharing the stories of patients who participated in clinical trials, adding years of disease remission to their lives due to new therapies. Linnea was willing to be among the first patients to receive a new therapy targeting her biomarker, which at the time showed unprecedented efficacy. Moreover, Melissa participated in not one but five clinical trials, all in an effort to find a cure for her lung cancer. The patient advocacy and healthcare communities are aligned: clinical trials are not just a last option; they are a first option. Nevertheless, only 6–8% of U.S. patients with lung cancer participate in clinical trials year-over-year.[132]

If a patient is interested in participating in a clinical trial, the gateway for that information is ClinicalTrials.gov. Regardless of how a patient chooses to search for trials (e.g., ClinicalTrials.gov, Google, third-party trial finders, or academic trial finders), the information patients receive is only as good as the information sponsors enter into the

system. Specifically, the Brief Title and the Brief Summary are the key data fields intended to provide the lay public with a plain-language description of the trial. The Plain Language Checklist for Brief Summaries, issued in September of 2022, was intended to help researchers improve the readability of the most important data field.

After extensive analysis, the central finding is that three years after the publication of the Plain Language Checklist for Brief Summaries, the Brief Summaries of interventional lung cancer trials on ClinicalTrials.gov showed no meaningful improvement in readability or overall plain-language adherence. The summaries showed an FKGL of 19.66, written at the level of an advanced graduate student or professional, with no statistically significant change between the pre- and post-guidance periods. The PLCST, developed specifically for this analysis of the checklist criteria's impact, yielded a mean adherence score of 3.93 out of 11, representing only 35.7% of the possible score.

No Brief Summary in the dataset of 2,408 trials met all the criteria. Brief Summaries remained challenging to understand, with a lot of medical jargon and complexity in a data field meant to provide simplicity that complements other complex data fields, such as inclusion and exclusion criteria. While the exploratory patient-focused content showed modest improvement, evaluation of the full data set attributes this change more to content “completeness” than to improvements in readability or usability. These findings suggest that the passive publication of plain-language guidance, without enforcement, workflow integration, or accountability, is insufficient to effect meaningful changes in how investigators write ClinicalTrials.gov Brief Summaries.

These findings do not diminish the need to emphasize the use of plain language in Brief Summaries. The Plain Language Checklist was issued after extensive feedback

solicited by the NLM. The guidance is well-designed, grounded in established plain-language principles, and consistent with the TransCelerate framework that patient advocacy groups and industry stakeholders have been calling for since the 2020 RFI comment period.

The problem may not lie in the checklist itself or in its being voluntary; it may simply be the nuances of clearly communicating complex medical information. The sections that follow interpret the data to explain why this gap persists, who bears responsibility for closing it, and what a more effective approach may look like. The goal is to connect the findings of this research to the broader ecosystem in which patients search for trials, the potential role of artificial intelligence (AI) in mediating that search, and the human navigation infrastructure that currently compensates for the lack of accessibility of patient-friendly clinical trial information.

Limits of Voluntary Guidance: PLCST Findings

The PLCST can tell us more about the data than what is just statistically significant. A mean PLCST score of 3.93 out of 11 across 2,408 lung cancer trial Brief Summaries is well off target from the expectations. There is a persistent, measurable gap between what federal law requires of ClinicalTrials.gov: a Brief Summary intended for the lay public versus what patients and care partners encounter when they open a trial record and try to understand whether a study may be right for them. This gap did not close after the checklist was issued. The mean score before guidance was 3.96; after guidance, it was 3.90. The difference was not only statistically insignificant but also showed no improvement. Understanding why requires looking beyond the composite score to the individual PLCST criteria because the pattern of what moved and what did

not reveal something important about how sponsors are responding to voluntary guidance.

Although data analysis often emphasizes improvement, the most useful lessons sometimes come from understanding what worsened. One of the worst-performing criteria was jargon. Jargon avoidance declined significantly after checklist publication, from 7.7% of summaries pre-guidance to 5.1% post-guidance ($p = .010$). In the three years following the NLM's guidance to replace complex terms with common, everyday words, fewer Brief Summaries met that standard than before the guidance existed.

One interpretation is not that sponsors became less conscientious but that the types of trials posted increased in technical complexity, with more biomarker-driven trials, more combination regimens, different routes of administration, and more global submissions from sponsors less familiar with U.S. plain-language norms. When controlled for geography, U.S.-enrolling studies performed better on jargon avoidance than studies with no U.S. site, although performance was still poor in both groups: 91 of 831 U.S.-enrolling summaries (11.0%) met the jargon-avoidance criterion compared with 63 of 1,577 summaries with no U.S. site (4.0%; $p < .001$). Hence, U.S. enrollment may be associated with greater adherence to plain-language expectations. However, even among U.S.-enrolling trials, nine in ten summaries still failed to avoid or explain jargon.

The ability to write a patient-friendly Brief Summary was in no way limited by the maximum character count of 5,000. In fact, the average use of characters used only 11.0% of the allotted character space, with a median of just 7.3% of space used. Short summaries were not necessarily plain-language summaries. Some of the shortest summaries consisted of a single technical sentence or fragment, reducing word count

without improving patient-centeredness or explanatory value. In contrast, longer summaries were modestly more readable, which may seem counterintuitive but may reflect that longer summaries had more space to provide context, background, and explanatory framing rather than language pulled directly from a clinical trial protocol. Therefore, improvements in patient-centered communication may require clearer expectations regarding the full use of this data field to fully understand the trial purpose, intervention, and participation. Plenty of room remains to provide definitions, expand on acronyms, and explain expectations throughout the clinical trial.

The use of consistent terminology showed a similar pattern, declining from 98.0% pre-guidance to 95.9% post-guidance ($p = .003$). While this change appears minor, the proxy analysis revealed something more meaningful. The post-guidance period saw a significant increase in sponsors using multiple terms for enrolled individuals, with "patient," "participant," and "subject" appearing within the same summary and greater mixing of study and trial terminology. This inconsistency is precisely the kind that creates cognitive burden for lay readers, who may wonder whether patients, participants, and subjects refer to the same people or distinct groups. The fact that this inconsistency increased after guidance suggests that some sponsors may have attempted to incorporate preferred terms such as "participant" without fully replacing older language, which resulted in summaries that are internally inconsistent rather than coherently patient-centered. Moreover, it feels like the best writing practice to use varied terms to reduce redundancy within a block of text, but in the case of the Brief Summary, repetition of language serves as a reinforcement tool.

Despite many shortfalls, improvements were noted in the exploratory criteria between the pre- and post-guidance postings. The use of purpose statements increased significantly, from 63.3% to 67.5% of summaries ($p = .032$). Condition description improved modestly (91.6% to 94.2%, $p = .017$). Study duration increased from 21.2% to 26.4% ($p = .003$). Use of "participant(s)" rose from 16.2% to 22.0% ($p < .001$). Purpose statements, condition descriptions, and preferred terms are among the easiest checklist criteria to implement since they only require adding a sentence or swapping a word. They do not require restructuring a document, simplifying technical medical language, or fundamentally reconsidering how scientific information is communicated to a lay audience. It is also unclear why these three criteria improved, but not the intervention or the route of administration.

The criteria that did not improve, especially those that can directly impact readability, sentence length, FKGL, jargon avoidance, and acronym use without definitions, are precisely the ones that require the most substantive change in how sponsors write the Brief Summary. Mean FKGL remained at 19.66, unchanged ($p = .889$). Only 62 summaries (2.6%) met the sentence length guideline of 15 words or fewer. The FKGL metric, while widely used and appropriate as a standardized comparison point for ease of reading by grade level, is structurally disadvantaged in oncology. Drug names (e.g., pembrolizumab, atezolizumab, trastuzumab deruxtecan, osimertinib, and biomarker designations) are polysyllabic by scientific necessity, not by choice. Every additional syllable in a drug name adds to the formula's grade-level estimate regardless of whether a lay reader would find that term more comprehensible than a shorter word. Moreover, while many of the drugs listed in the clinical trials also have trade names, the generic

names, or even their research designations, are the appropriate and acceptable names to use in a trial registry. The SMOG Index, which this analysis also calculated, is somewhat more robust for health literacy contexts but shares the same vulnerability in disease areas defined by molecular terms, complex medical terms, and drug names, and showed no improvement in readability, returning essentially the same grade level as the FKGL.

The patterns observed in this analysis are not dissimilar to those previously reported. However, it was hoped that a shift toward patient-centricity and the availability of the Brief Summary Checklist, along with several evidence-based examples of the importance of accessibility, would have resulted in more meaningful change. Schindler et al.'s (2020) analysis, conducted before the checklist's creation, found that Brief Summaries averaged only 50.4% of the maximum patient-focused score across a representative sample of 346 trials.[12] The authors concluded that the lack of patient focus might be attributed to sponsors continuing to treat ClinicalTrials.gov as a registration tool with structural requirements rather than an opportunity to meaningfully engage with the patient community.[12]

While the Schindler et al. study was a randomized analysis across trials of multiple disease states, additional data are available in other fields for comparison. Lung cancer was selected as a focus for several reasons, including its complexity, the availability of sufficient trials to power a three-year analysis, and the authors' preference for and experience with the disease. For example, Baskin et al.'s 2025 analysis of 17,175 urologic oncology Brief Summaries across six cancer types found a mean FKGL of 18.7, strikingly similar to the 19.66 found in this study. The authors concluded that despite

modest post-2017 improvement in readability trends, summaries continued to require graduate-level reading comprehension.

Stepping outside the lens of oncology, Eddington conducted a similar analysis to evaluate the impact of the guidance over a one-year period following the publication of the Checklist.[133] The data extraction yielded 3,347 study results, which were narrowed to phase 3 and phase 4 trials for rheumatoid arthritis, knee replacement, and conjunctivitis, resulting in a dataset of 62 studies.[133] While a specific overall FKGL was not reported in the thesis, the dataset contained zero studies with a readability level of sixth to seventh grade, three studies with an eighth- to 12th-grade reading level, and most studies (n = 45) assessed at a college-graduate reading level. Taken together, these findings suggest that poor readability of ClinicalTrials.gov Brief Summaries is a registry-wide problem, not a feature of any disease area or the complexity of oncology drug development.

What the quantitative data cannot fully answer is why voluntary guidance leaves this gap intact. Eddington's (2024) qualitative analysis of 62 Brief Summaries in the first year after the checklist offered the first useful explanatory framework. It concluded that the checklist is difficult to find on the ClinicalTrials.gov website, is not linked from the submission workflow, is not reviewed or scored during the registration process, and investigators submitting large grant packages treat the Brief Summary as a low-priority document because it carries no consequences for funding or approval.[133] These structural conditions, not sponsor indifference, may explain why three years of voluntary guidance have produced marginal change. The question this dissertation now raises is not whether the checklist was a reasonable intervention but whether guidance alone can change

patient-facing communication without visibility, workflow integration, real-time review, and accountability.

Compliance by Sponsor Type and the FKGL Paradox

The subgroup analysis by sponsor type produced one of the more interesting findings in this dataset because it revealed how different kinds of institutions approach the Brief Summary in ways that reflect their underlying relationship to the clinical trials as a whole and potentially by guidance either publicly or privately mandated by their organizations. NIH–NCI-sponsored summaries had the highest mean PLCST score (4.82 of 11) and the highest combined score (8.55 of 16). Network and cooperative group summaries followed. Industry-sponsored summaries ranked third on PLCST, ahead of academic and medical center summaries, which ranked lowest.

When considering the order of the PLCST scores, one might assume that industry sponsors are more attentive to plain-language guidance than academic investigators, who were numerically the least compliant with the PLCST. When the FKGL was examined alongside PLCST, industry-sponsored summaries had consistently high FKGL scores (i.e., complicated readability) despite their moderate PLCST performance. AstraZeneca, the most frequently appearing industry sponsor in this dataset with 50 trials, had a mean PLCST of 4.44 and a mean FKGL of 22.85. Bristol-Myers Squibb had a mean PLCST of 4.90 and a mean FKGL of 20.85.

In each case, higher structural compliance on the checklist did not translate into more readable text. The summaries were more formally organized, more likely to state a purpose, to use consistent terminology, to avoid qualitative terms, and to use person-centered referent language. However, they remained written at a level requiring many

years of graduate-level education to understand. Baskin et al., similarly, found that industry-sponsored urologic oncology Brief Summaries were the least readable by sponsor type, with a mean FKGL of 19.1 compared with 18.1 for academic sponsors and 16.0 for government sponsors, reinforcing a broader pattern in which industry-sponsored summaries appear especially likely to maintain protocol-driven, technical language without improved readability.[124]

The above findings align with what may be considered the FKGL paradox of industry compliance: industry sponsors are most likely to have regulatory or clinical affairs teams, medical writers, and a formal submission review process, which results in summaries that score relatively well on checklist structural criteria while remaining among the least readable by grade-level measures. Industry sponsors satisfy the checklist's formal requirements (e.g., adding purpose statements, using preferred patient-centric language, and using consistent vocabulary) without addressing the underlying problem of technical complexity. A well-structured summary written in scientific language at a "22nd-grade reading level" is not plain language and not accessible to the lay public. Given the industry's propensity to adhere to guidance once directed, it is far more likely that they are following a corporate template and not the actual Plain Language Checklist. If that were the case, there would be a noticeable improvement and far better adherence to additional elements outside of FKGL, which may remain an unattainable metric for oncology trials.

NIH–NCI-sponsored summaries present a different picture. Their higher scores on PLCST reflect institutional alignment rather than checklist awareness alone. The NIH–NCI, as a sponsor, operates within a framework that has long emphasized public

communication and health literacy as organizational values rather than mere regulatory requirements. The higher PLCST and exploratory scores for NIH–NCI-sponsored summaries, along with their higher rates of benefit-oriented language (89.8%), suggest that the communication philosophy underlying these submissions is not solely based upon structural compliance.

Baskin et al. found a parallel pattern in which government-sponsored urologic oncology summaries had a mean FKGL of 16.0, meaningfully better than both academic and industry summaries, though still well above the sixth- to eighth-grade target.[124] The NIH–NCI-sponsored summaries, being the most patient-centric, were unsurprising given their plain-language efforts and broad support for patient accessibility, which they have continuously evaluated and supported by providing researchers with tools to improve these efforts.[124] At American Association of Cancer Research Annual Meeting (AACR 2026), the NCI chaired a panel, "Modernizing Clinical Trial Communication: NCI's AI-Enabled Toolkit for Research Protocols and Participant Materials" which broadly highlighted AI as a potential intervention to "leverage large language models to automate time-intensive document workflows, including informed consent generation, lay language trial summaries, and Spanish language translation, while maintaining regulatory compliance and scientific rigor."[134]

Academic and medical center sponsors present the most concerning findings of this analysis. They represent the largest sponsor category in this dataset (945 trials, 39.2%) and had the lowest mean PLCST score (3.89) and among the lowest combined scores (6.94). Academic investigators are, by training and professional identity, writers of scientific purpose, direct and to the point. The norms of scientific writing that dictate

journal publications, grant applications, and clinical documentation are antithetical to plain-language communication. Academic investigators may be the least likely to recognize that the language they use fluently every day is inaccessible to the patients they seek to enroll. Eddington observed that experts struggle to "unsee" their expertise and "might have difficulty thinking and writing as if they were members of the lay public."[133] The gap between expert and lay reader is hardest to bridge when the writer has spent a career inside the language and lexicon they are asked to simplify.

ClinicalTrials.gov serves multiple audiences, not only patients. Researchers, regulators, sponsors, and clinicians all interact with the registry. Within the clinician category, the community oncologist considering whether to refer a patient to a trial is different from the academic investigator who designed it. A community physician in a non-academic practice may be reading a Brief Summary in a disease area outside their primary expertise and may be unaware of the therapeutic agent, mechanism of action, or even the basic rationale that informs the study design. Plain-language communication can be just as useful in this situation for physicians or nurse navigators who often assist patients in finding clinical trials. Providing plain language from the start ensures that the healthcare provider is not acting as an intermediary translator of medical information. The case for accessible Brief Summaries is, at its core, the ability to serve as an access point for the full range of users.

The plain-language problem does not begin or end with the registry; it runs through the entire clinical trial ecosystem. After a patient is identified as a potential good fit for a clinical trial, the next conversation typically involves reviewing the informed consent form. Healthcare communication experts also criticize the informed consent

process because informed consent materials consistently exceed recommended reading levels. Zai et al.'s (2024) analysis of 5,239 consent forms posted to ClinicalTrials.gov found that forms persistently exceeded the recommended eighth-grade reading level across nearly two decades of submissions.[135] Khadraoui et al.'s (2025) analysis of gynecologic oncology trial consent forms found a mean reading level of 13th grade and found no significant difference between NCI and industry-sponsored trials (13.3 vs. 13.6).[127]

The sponsor advantage, as visible in Brief Summary PLCST scores, interestingly does not extend to consent forms. Patient-facing brochures, enrollment materials, and sponsor websites show similar patterns in published research. Improving the Brief Summary is a necessary first step in making clinical trial information accessible. However, it is one component of a larger plain-language reform that the clinical research enterprise has yet to undertake at scale, without delving into the lay summaries of published data and trial results.

What U.S.-Enrolling Trial Patterns Reveal About Policy Culture

When this dissertation was designed, one methodological question was whether to limit the included studies to only U.S.-enrolling trials or to include all trials posted to ClinicalTrials.gov. The rationale for limiting it to the United States only was to help eliminate any translation bias and, in acknowledgment that NLM's Plain Language Checklist Guidance would have the greatest visibility among U.S.-based sponsors, investigators, and institutions, as evidenced by the U.S.-heavy commenters during the RFI. Additionally, limiting U.S.-only may have reduced some uncertainty related to international trial practices, including variation in regulatory requirements, sponsor

workflows, translation practices, and expectations for public-facing trial communication. However, limiting the analysis to U.S.-enrolling studies would have also excluded a substantial portion of the ClinicalTrials.gov lung cancer trial landscape. Many trials listed on the platform are multinational or international, so patients, clinicians, researchers, advocacy organizations, and third-party trial-finding tools may encounter these records regardless of where the trial is enrolling. For this reason, the primary analysis included all eligible English-language Brief Summaries posted to ClinicalTrials.gov, while U.S.-enrolling studies were evaluated as a subgroup.

U.S.-enrolling studies, defined as trials with at least one site in the United States, had higher mean PLCST scores (4.20 vs . 3.79), higher combined scores (7.25 vs. 6.84), and were significantly more likely to use inclusive and person-centered language (33.3% vs. 7.1%) than studies with no U.S. enrollment sites. All aforementioned differences were statistically significant in both the pre- and post-guidance periods, thereby suggesting that factors outside the guidance were likely to contribute to these findings.

One potential reason for this may be that U.S.-enrolling trials are disproportionately subject to a regulatory environment that produced the checklist in the first place. The NLM Plain Language Checklist is a U.S.-based guidance document, issued by a U.S. federal agency and subsequently disseminated through U.S.-facing channels. Sponsors who register trials with U.S. sites are more likely to have clinical and regulatory affairs teams familiar with FDA and NIH expectations, to use medical writers trained in U.S. plain-language standards, and to have encountered the checklist through ClinicalTrials.gov submission workflows or professional development in the U.S. clinical research community. One of the most outspoken groups advocating plain language

communication is TransCelerate, whose members represent a substantial proportion of global pharmaceutical companies. Given their industry support, 89% had at least one trial in this data sample and accounted for approximately 34% of industry-sponsored, U.S.-enrolling studies.

ClinicalTrials.gov is a global database. As of 2026, trials from 226 countries and territories were registered on the platform.[136] The overall trends currently reported by the NLM show that 28% of trials are U.S.-only, 57% non-U.S., and 4% both U.S. and non-U.S., while this lung oncology data set trended slightly differently, with 17.8% U.S.-only, 56% non-U.S., and 16.7% both U.S. and non-U.S. Both data sets had approximately 10% of trials with missing data.[136] The 1,577 non-U.S.-enrolling trials in this dataset (65.5%, which includes missing/no sites listed) represent a substantial portion of the global lung cancer trial landscape, and their lower PLCST scores suggest that the plain-language deficiencies are considerable. Only 7.1% of non-U.S.-enrolling summaries met the criterion for inclusive and person-centered referent language, compared to 33.3% of U.S.-enrolling summaries. The analysis defined person-centered language by how the Brief Summary describes people, including whether it refers to them as participants, patients, subjects, or by their disease. Notably, this criterion was strictly defined by the Plain Language Checklist (i.e., “patient” is a non-preferred term), which could have contributed to the observed differences, as the word “patient” should have been avoided and may be counterintuitive in other cultures or languages.

Clinical trials that enroll globally present a particular complexity from a U.S.-centric lens. Non-U.S. sites often enroll quickly and efficiently, in part because patients outside the United States may not have access to standard-of-care therapies that would

otherwise make them ineligible and in part because the healthcare infrastructure in some regions creates concentrated patient populations at research centers. Additionally, while there are variations by country and region, investigators can be incentivized to enroll patients and often have a much smoother contracting and start-up process, thereby allowing them to accrue sites more quickly than their U.S. counterparts. With this consideration, the registry intended to serve the lay public is increasingly populated with trial records written by sponsors whose primary audiences, regulatory relationships, and language norms are not those of the U.S. patients ClinicalTrials.gov was designed to reach.

Language sits at the intersection of these concerns. A Brief Summary that is inaccessible to a patient from an underserved community, whether because of its grade level, its jargon, or its failure to state why the trial is being conducted, creates an additional barrier to accessing trials in an already complicated system. Patient advocacy organizations, including Blood Cancer United (formerly LLS), Cancer Support Community, ACS CAN, ASCO, and LUNGevity, have all called for recruitment materials to be written in grade-appropriate language, translated for non-English-speaking populations, and designed for the full range of patients who might benefit from trial participation. These recommendations reflect recognition that the clinical trial enterprise depends on public trust and public participation, both of which require clear, accessible communication, starting with ClinicalTrials.gov.

The geography finding does not lend itself to a simple fix. Requiring NLM-standard plain-language Brief Summaries to have compliance from all sponsors globally would require either international harmonization of registry standards or a tiered

enforcement approach that applies different standards to U.S.-regulated versus non-U.S.-regulated submissions. Neither is straightforward. Nevertheless, the data reveal that the current approach of applying a voluntary U.S.-facing Plain Language Checklist to a global registry is not creating meaningful change in how we share information with the public.

How Patients Search for Trials in the Digital Age

ClinicalTrials.gov is rarely the first information resource that a patient encounters when searching for educational materials or even specifically for a clinical trial. No two patient journeys are ever the same, but a cancer diagnosis always comes as a surprise. Sometimes it is a patient with fatigue, a nagging cough, and just a little chest pain that they cannot seem to shake. They wait months to see a pulmonologist or eventually end up at their local emergency room. Suddenly, a patient who has never smoked a day in their life receives a stage IV lung cancer diagnosis. Appointments follow, treatment discussions occur, and then the search for options begins. Stacks of pamphlets from the doctor's office and a quick Google search, which is now being overtaken by AI-assisted searches, or even directly to ChatGPT and Claude for answers. A patient will eventually stumble across the concept of clinical trials, hopefully through Patient Advocacy or an educational website. They may even find a search tool designed specifically for patients. However, at the end of the day, all roads will lead to ClinicalTrials.gov.

The landscape of trial-finding tools has grown over the past decade, driven by patient advocacy organizations, technology companies, and increasingly, AI platforms. These tools share a common architecture: they pull data from the ClinicalTrials.gov application programming interface, present it through a simplified patient-facing

interface, and return matched results based on answers to plain-language questions about diagnosis, treatment history, and location that act as filters for the complex inclusion and exclusion criteria that determine eligibility for a trial. What a patient sees in these interfaces, the name of the trial, a description of its purpose, who can join, and the location, derives entirely from the Brief Summary and Brief Title fields.

In the lung cancer space, GO2 for Lung Cancer's LungMATCH program represents the gold standard for matching patients with clinical trials: one-on-one navigators are trained clinical research professionals who conduct the search alongside the patient, translating and contextualizing what the registry contains based on the patient's medical history and their treatment preferences. Navigators act as translators who determine where the patient is on their journey, identify relevant trials, and help them prepare questions for their next clinical appointment. Another example of support is LUNGevity's trial finder, which offers a similar patient-facing experience with guided search questions tailored to lung cancer patients and direct access to clinical trial navigators provided via CareBox.

In the absence of a clinical trial navigator, whether provided at the site of care or by an advocacy organization, a patient-facing clinical trial finder is the next-best access point for patients seeking self-service. The growth of AI has both simplified and added complexity to the process of searching for clinical trials. These "patient-friendly" interfaces do not replace ClinicalTrials.gov; they simply build an interpretive layer on top of it. A multitude of vendors provide this service, including CareBox Health, TrialX, EmergingMed, SparkCures, Antidote, and myTomorrows. These user interfaces all attempt to convert complex registry records into navigable outputs by matching patient

characteristics to eligibility criteria, identifying biomarkers and key medical history, prior treatment, location, and sometimes offering a general number to call for live navigation. While the front end of the system simplifies the search, the output remains the same: often a redirect to ClinicalTrials.gov, where the first two pieces of information the person sees are the Brief Title and the Brief Summary.

The vendor landscape is also partially fragmented because trial access is a multidimensional problem. However, at the core, these trial finders are for-profit companies selling a technology that ultimately receives funding from non-profits or the sponsors of the trial, rather than fixing the problem at the source, many sponsors would rather pay for an added technology. Other distinctions exist as well: some tools emphasize AI-based eligibility parsing and electronic health record (EHR) integration, while others rely on patient-entered questionnaires, advocacy partnerships, or navigator-supported matching. Disease-specific platforms such as SparkCures illustrate the value of combining trial matching with education and community-based support provided via their Advocacy partner, the International Myeloma Foundation. Broader tools such as Antidote, TrialX, CareBox Health, and EmergingMed demonstrate that trial-finding infrastructure increasingly depends on transforming registry data into more patient-facing formats. However, these downstream tools remain dependent on the quality, completeness, and clarity of the source records in ClinicalTrials.gov.

One vendor, ResearchLinQ, offers a patient-friendly search screen and, when returning trial results, shows the Brief Title and the Brief Summary, rewritten to be below an eighth-grade level, completely powered by AI. While the lay summary may oversimplify a study, it provides patients with an accessible starting point for a

conversation with their healthcare provider, who is ultimately responsible for understanding a trial's criteria.

The advocacy community has been explicit about its dependence on ClinicalTrials.gov for the Brief Summary and has repeatedly requested that the burden of translating complex medical terminology not be placed on patients, care partners, navigators, or even prescribers when the sponsors themselves can create it. When the underlying Brief Summary is inaccessible, the patient-facing output is limited by the source's quality. A tool that must translate a graduate-level summary performs interpretive work before a patient can even understand whether the trial is relevant to them. This interpretive work is currently performed by navigators, advocacy organizations, and, increasingly, AI. However, none of these solutions substitutes for a Brief Summary that communicates clearly in the first place.

The emerging frontier is AI-assisted matching that draws not just on registry data but on the patient's own medical record. HealthTree Foundation, a nonprofit focused on blood cancers, launched an AI-powered personalized clinical trial finder in March 2025. HealthTree has built one of the most technologically advanced platforms for patients, which offers education and support through its programs. At the core of its work is CureHub, a patient-facing, disease-specific platform that combines medical-record aggregation, patient-entered data, education, research participation, treatment option support, and clinical trial matching. Within this ecosystem, patients can opt in to share their EHR data, which is then used by an algorithm and live medical review to create a patient registry record. The system loads the medical record into a dashboard where

patients can track their disease status, access diagnosis-specific education, and explore clinical trials.

Once linked to a patient's EHR, any new medical information will be fed into the system. If the medical record flags for "progression," meaning that a patient will need to seek a new therapy, the AI algorithm pulls new educational materials for potential treatment and will automatically search ClinicalTrials.gov for potential trial options. Once a patient is ready to explore clinical trials, they are offered a custom page that grades the trials (e.g., A+, A, and A–) based on how well their medical history matches the trial's criteria. They are also given a patient-friendly view of the trial, their matching criteria, study info, and live navigators. Notably, even as the best-case scenario of what "good" looks like from a Patient Advocacy perspective, this clinical trial dashboard still relies on the Brief Summary as part of the data pull. However, future enhancements are planned to ensure that this information is available in plain language.

This development is genuinely promising and is being modeled in other Advocacy Organizations and within healthcare systems. EHR-linked matching can close gaps that no amount of plain-language Brief Summary writing can address, specifically, the gap between what patients know about their own medical history and what eligibility criteria require. Nevertheless, it introduces a new dependency, the accuracy and completeness of the underlying trial record. If the Brief Summary misstates the purpose of the study or if the eligibility criteria contain inconsistent terminology, the AI matching engine inherits those errors and amplifies them. A patient who is incorrectly screened in or out of a trial due to errant source data may make an enrollment decision based on false information.

For a patient with limited treatment options and a rapidly progressing disease, a missed match or a false match is unacceptable. This issue comprises the core argument for plain-language improvement in the era of AI-assisted trial finding. The tools are becoming more sophisticated, but the data sources have not kept pace, even though AI-assisted tools are available to sponsors.

Can AI Solve the Plain Language Problem?

The application of AI to clinical trial matching represents one of the most significant developments in patient access to research in the past decade. AI systems can already process eligibility criteria that would take a human navigator hours to review, identify matches across hundreds of open trials simultaneously, abstract information from unstructured clinical notes, and present results in plain language regardless of how the underlying registry record was written. A 2020 evaluation of an AI clinical trial matching system in Australian lung cancer patients found that the system could assess more than 7,000 patient attributes against 12,000 individual eligibility criteria in under 16 seconds per patient, with high agreement with clinician consensus.[139]

For a patient with advanced lung cancer navigating a complex biomarker-driven landscape, where eligibility may turn on whether their EGFR mutation is an exon 19 deletion versus an exon 20 insertion or whether their PD-L1 TPS exceeds a specific threshold, AI matching that draws on actual pathology reports and NGS testing results is meaningfully superior to any keyword search a patient could conduct on their own. The commercial ecosystem has organized itself around exactly this premise, and its growth is itself evidence of the problem this dissertation measures. An abundance of vendors has emerged specifically because ClinicalTrials.gov data is structured for regulatory

compliance rather than patient comprehension. These platforms are, at their most basic, translation services built on top of a registry that was supposed to communicate directly with patients.

SparkCures, whose partnerships include the International Myeloma Foundation and multiple academic cancer centers, describes ClinicalTrials.gov content as "confusing and overwhelming" and frames its core value proposition as ensuring that patients "shouldn't have to become a medical expert" to find a trial. TrialX explicitly identifies medical jargon as a barrier to participation and offers AI-generated summaries that translate complex eligibility criteria into patient-friendly language, with multilingual engagement capabilities designed to address the global usability gaps highlighted by this study's geographic findings. CareBox Health, which powers the clinical trial-matching service used by LUNGevity, among others, offers guided questionnaire-based matching that reduces the search burden by abstracting away the complexity of the underlying registry data. EmergingMed similarly combines algorithmic matching with human navigation support, recognizing that no technology alone fully closes the gap between what the registry says and what a patient needs to understand.

Even with these capabilities, AI cannot simplify information that was never written, a reminder that one in three Brief Summaries did not include a purpose statement. Across the clinical trial finder vendor landscape, performance is measured in time savings, matching accuracy, and engagement metrics. Almost no platforms report readability improvements, patient comprehension outcomes, or trial enrollment conversion rates specifically tied to language accessibility. The same gap exists in regulatory guidance: the NLM checklist measures compliance with plain-language

criteria rather than patient comprehension. This dissertation attempted to measure compliance with a checklist rooted in patient-centricity but was unable to assess the degree to which trial communication meets patients where they are.

Moreover, potential problems can arise from improperly trained AI systems. There is a risk of garbage amplification or circular logic if the content is unclear. Hallucinations in large language models have remained widely reported, and potential future monetization of AI systems may limit widespread adoption due to costs.

Additionally, no level of AI can close some of the gaps in health equity. The populations least served by the current ClinicalTrials.gov system are patients in rural areas, patients who are not digitally literate, patients whose primary language is not English, and patients who lack access to academic medical centers where AI matching tools are most often deployed. All of these are the same populations least likely to benefit from AI integration.

The final consideration is trust. The 2025 CISCRP Perceptions and Insights Study found that while three in four respondents were comfortable with AI analyzing data collected during a clinical study, data accuracy was the top concern among those who were not comfortable, cited by 75% of that group.[106] Most patients surveyed (57%) said it was particularly important for pharmaceutical companies to clearly disclose how AI is used in clinical research.[106] These findings are not an argument against AI in the trial-finding ecosystem but an argument for transparency, accuracy, and trust.

What Meaningful Improvement May Look Like

The temptation at this point in the analysis is to conclude with a straightforward policy recommendation: mandate plain-language compliance, enforce the checklist, and attach consequences to non-adherence. That argument has surface appeal, and this study's data, which show no meaningful improvement three years after voluntary guidance was issued, suggests that voluntary guidance alone is insufficient. Nevertheless, the honest version of this argument is more complex. Hence, the Medical Humanities framework that grounds this dissertation demands that complexity be honored rather than resolved by policy revision.

The first complication is that the Brief Summary may not be the place where plain-language investment yields the highest return. This study documented that 65% of the trial ecosystem patients encounter is written at a graduate- or professional-level reading level. However, patients encounter inaccessible language at every point in the clinical trial journey when they search the registry, read materials on sponsor websites, review eligibility criteria in a trial finder interface, and most consequentially, receive and are asked to sign an informed consent form. Research examining the readability of oncology clinical trial consent forms has found mean reading levels at the 13th-grade level, regardless of sponsor type or disease site. Fixing the Brief Summary without addressing the consent process, the sponsor-facing educational materials, and the clinical encounter itself would be meaningful but incomplete.

The second complication is the question of enforcement. The regulatory architecture governing ClinicalTrials.gov is built around disclosure requirements rather than communication quality standards. Building an enforcement architecture around

readability metrics would require either automated quality gates in the PRS submission system or human review of submitted summaries at a scale the NLM does not currently have the infrastructure to support. It is unlikely that either of these approaches will be adopted. The more practical near-term path is to make plain-language compliance easier rather than mandatory through automated feedback tools embedded in the submission workflow, required training for investigators, and the formal recognition of resources (e.g., the TransCelerate Clinical Trial Registration Tool) that are not currently linked from NLM's own guidance pages.

What this study reveals, more than any specific checklist failure, is the indispensable role of human navigation in bridging the gap between what the clinical research enterprise produces and what patients need. Navigation programs exist because the system, as designed, does not reach patients where they are. As previously stated, real shared decision making requires that patients understand what they are agreeing to, not merely that they trust their physician enough to sign a consent form. The navigator is the human layer that makes that understanding possible when the written record does not. When the LLS's Clinical Trial Support Center achieved a 30% clinical trial entry rate among patients they supported with live navigation (compared to a national average of ~7%), the difference was not attributable to better written summaries; it was attributable to human beings spending time with patients, explaining their options, translating the language of research into the language of lived experience.

It is important to consider that navigation is expensive, unevenly distributed, and dependent on philanthropic and organizational resources that not every patient community has access to. The clearer and more accessible the underlying documents are,

the less translational work the navigator or physicians must do, and the more of their time can be devoted to the relational and decision-support functions that no document can replace. The structural intervention with the greatest potential to change clinical trial access at scale is integrating trial eligibility into the clinical encounter itself. Current practice treats clinical trial discussion as something that happens when standard-of-care options are exhausted, the last conversation rather than the first one.

ASCO has stated explicitly that clinical trial participation should be considered earlier in the treatment pathway. The barrier is not patient reluctance; the literature consistently shows that patients who are offered trials and given genuine information about them are willing to consider them. The barrier is that trials are invisible at the point of care. A community oncologist seeing a newly diagnosed patient with stage III NSCLC in a 20-minute appointment does not have time to search ClinicalTrials.gov. They need the trial to surface in their workflow, alongside the treatment options they are already considering.

EHR-integrated matching, which uses the patient's clinical data to identify eligible trials in real time, is the most promising approach to achieving this. When a physician enters a diagnosis, a biomarker result, and a treatment history, the system should return a curated list of trials for which the patient may be eligible, not as a separate task requiring a separate search, but as a natural output of the clinical documentation workflow. Several institutions and platforms are developing this capability. Scaling it to community practice, where most cancer care occurs, is the biggest challenge.

AI will accelerate progress on multiple fronts simultaneously. It will make EHR-integrated matching faster and more accurate. It will reduce the translational burden on navigators by pre-processing complex eligibility criteria into plain-language summaries. It will enable personalized patient materials, summaries tailored to a specific patient's diagnosis, treatment history, and literacy level, that no standardized Brief Summary field could produce. The direction of progress is clear: toward a system in which the registry serves as infrastructure for more sophisticated patient-facing communication rather than as the communication itself.

What this study can contribute to that trajectory is a benchmark. The PLCST score of 3.93 of 11, representing 35.7% adherence to plain-language criteria, with no statistically significant improvement over three years of voluntary guidance, establishes the baseline before meaningful investment in plain-language improvement occurred. Future researchers can replicate this analysis in two years, five years, or a decade while asking whether the trajectory has changed and, if so, what changed it. Future policymakers, patient advocates, and sponsors can use this instrument to evaluate specific interventions: automated submission feedback, required training, enforcement mechanisms, and navigator-informed template development.

This conversation starts from a simple premise that this dissertation has tried to document in data: patients are not failing to access clinical trials because they lack motivation, intelligence, or trust; they are failing to access them because the system was not designed with them in mind. The Brief Summary was supposed to be different. The law said it should be intended for the lay public, but the data show it is still not truly accessible. Changing it requires more than a checklist; it requires commitment from

sponsors, regulators, advocacy organizations, and the institutions that conduct research to treat communication as a core function of the clinical trial enterprise, not a compliance footnote.

CONCLUSION

When a person is diagnosed with lung cancer, the clock starts immediately. They are asked to absorb an unfamiliar vocabulary, weigh options they did not know existed days earlier, and decide quickly, often while frightened and unwell. For many, a clinical trial represents the best, and sometimes the only, path to additional time. The stories that opened this dissertation, Linnea's and Melissa's among them, are reminders that behind every trial record is a person trying to understand whether that study might be the thing that lets them stay. ClinicalTrials.gov is the gateway to that decision, and the Brief Summary is the first thing they read. This dissertation asked a simple question about that first encounter: three years after the NLM issued plain-language guidance, has the Brief Summary become any easier for a patient to understand?

The answer, across 2,408 interventional lung cancer trials, is that the Brief Summaries were written at a mean FKGL of 19.66. This graduate-level reading demand is far beyond what the intended lay audience can be expected to navigate, with no statistically significant change after the guidance was issued. The PLCST, developed specifically for this work, found a mean adherence of just 3.93 of 11 criteria, only 35.7% of what the checklist itself calls for, and not a single summary in the entire dataset met all of them. The handful of criteria that improved, most notably the inclusion of a purpose statement, were the ones requiring the least effort: adding a sentence, swapping a word. The criteria that would have made the text genuinely readable, shorter sentences, less jargon, a lower grade level, did not move at all, and in the case of jargon avoidance, measurably worsened. What looked at first like progress in patient-focused content turned out, on closer inspection, to be greater completeness rather than greater clarity.

These findings support a single conclusion, issuing well-designed guidance is not the same as changing behavior. The Plain Language Checklist was not a flawed document. However, NLM published the checklist as part of a workflow that never required anyone to use it. Users may have difficulty locating it on the site, and the submission process does not require sponsors to apply it or score records against it during registration. A Brief Summary carries no consequences for funding, approval, or publication, so, for many sponsors, it remains a low-priority field completed out of obligation rather than written for the person on the other side of the screen. Voluntary guidance without visibility, integration, and accountability changes does not result in meaningful change, as this empirical research has demonstrated.

The subgroup patterns deepen rather than soften this conclusion. Industry sponsors, with their regulatory teams and medical writers, have produced summaries that met the checklist's structural elements yet ranked among the least readable of any group, a paradox in which formal compliance and genuine accessibility move in opposite directions. Academic and medical-center sponsors, the largest group in the dataset, scored the lowest, thereby reflecting how difficult it is for experts to unsee their own expertise and write as members of the public. U.S.-enrolling trials performed somewhat better on overall checklist adherence and readability than trials with no U.S. site, consistent with their closer proximity to the U.S. regulatory culture that produced the guidance. Nonetheless, even among U.S.-enrolling summaries, the great majority failed to meet basic plain-language standards.

Moreover, on the one criterion meant to capture respectful, person-centered language, U.S. and non-U.S. summaries performed almost identically and poorly alike, a

reminder that proximity to the guidance did not translate into the kind of voice and agency that patient-centered communication is supposed to convey. The problem, in other words, is not confined to any one sponsor type or any one geography. It is a registry-wide condition, echoed in the readability literature across cancer types and disease areas, and it extends well beyond the Brief Summary into ICFs and the broader body of patient-facing trial materials.

The findings from this study do not diminish the utility of plain language. The emergence of an entire commercial and nonprofit ecosystem of trial-finding tools, navigators, and AI-assisted matching platforms is itself evidence of the gap this dissertation measures. These tools exist because the source records do not speak to patients directly, and so an interpretive layer, human or algorithmic, has been built to translate them.

Nevertheless, translation is not a substitute for clarity at the source. As AI systems increasingly draw on the patient's own medical record to match them to trials, the accuracy of the underlying Brief Summary matters more, not less. A matching engine inherits and amplifies any errors, omissions, or inconsistencies present in the registry record. For a patient with a rapidly progressing disease and few options, a missed match or a false match can mean the difference between fewer or more months of life.

This dissertation reflects the central commitment of the Medical Humanities: how we communicate within the clinical research enterprise is not a clerical detail but a determinant of who can participate in it. A Brief Summary written above a patient's reach is a barrier as real as any eligibility criterion, with the crucial difference that it excludes people not by design but by neglect. Treating the Brief Summary as a compliance

footnote, rather than as a genuine act of communication, is a choice the clinical trial system continues to make by default. The path forward will require what voluntary guidance alone could not deliver: visibility into the submission workflow, real-time review, accountability for the responsible party, and recognition that clear communication is a core function of running a trial rather than an afterthought. Until this shift occurs, the promise of ClinicalTrials.gov as a public resource will remain unfulfilled, and the patients it was built to serve will continue to depend on others to tell them what it says.

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APPENDIX

Figure 34. TransCelerate Brief Title Scoring Tool Template

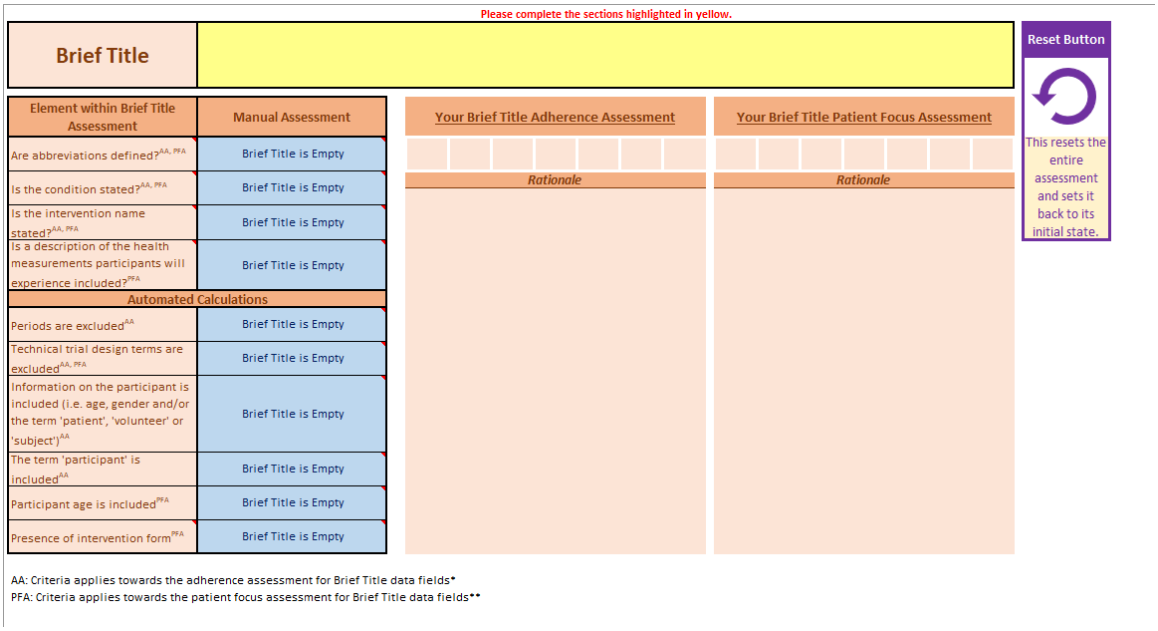

Figure 35. TransCelerate Brief Summary Scoring Tool Template

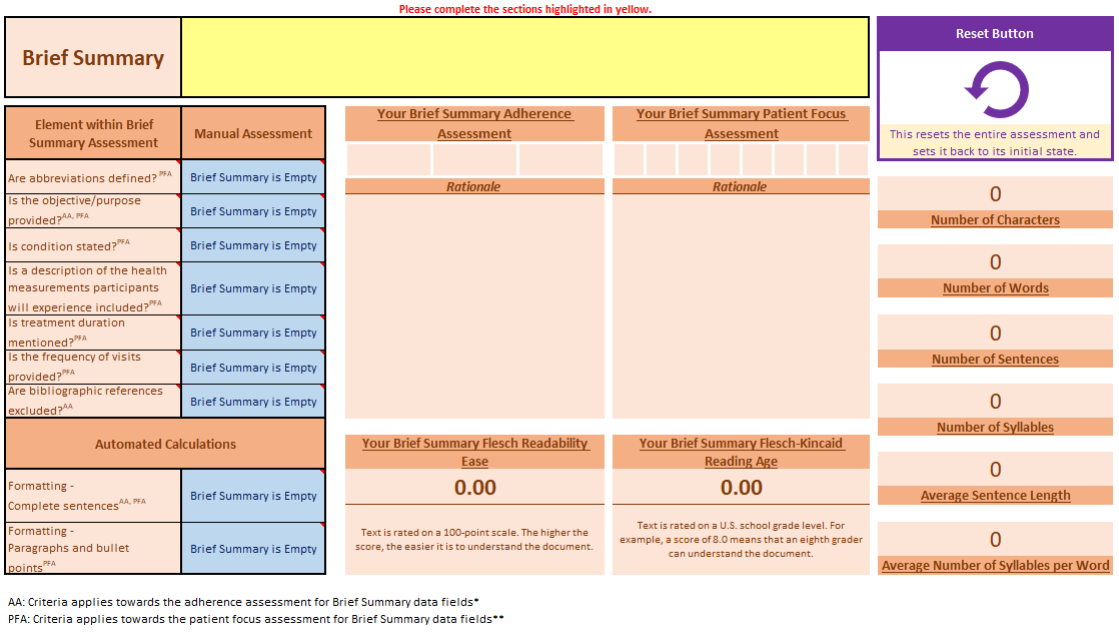

Figure 36. TransCelerate Brief Title Scoring Tool Template With Example Trial

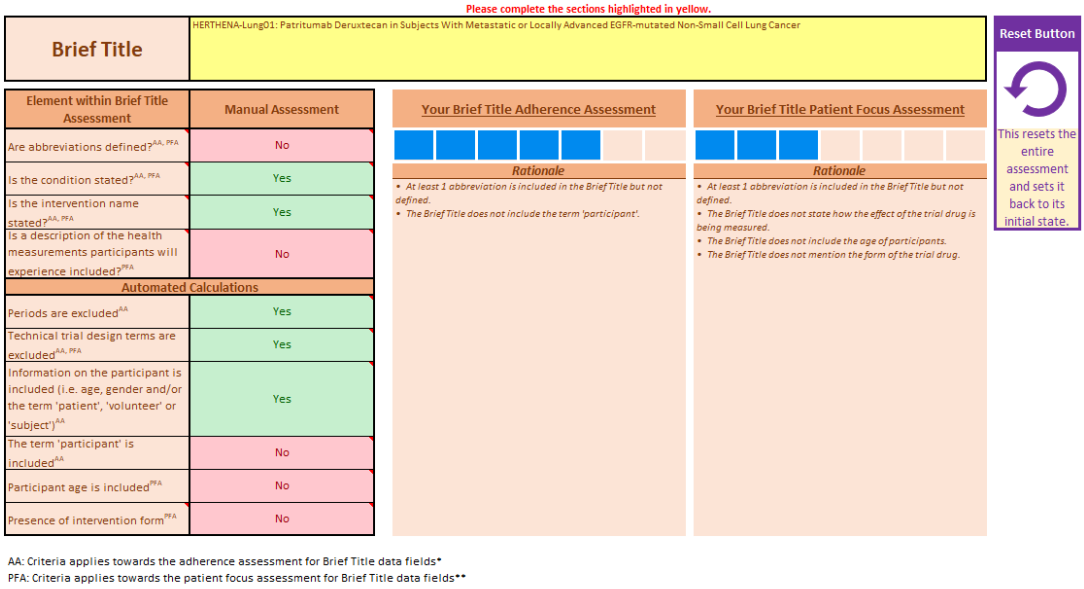

Figure 37. TransCelerate Brief Summary Scoring Tool Template With Example Trial

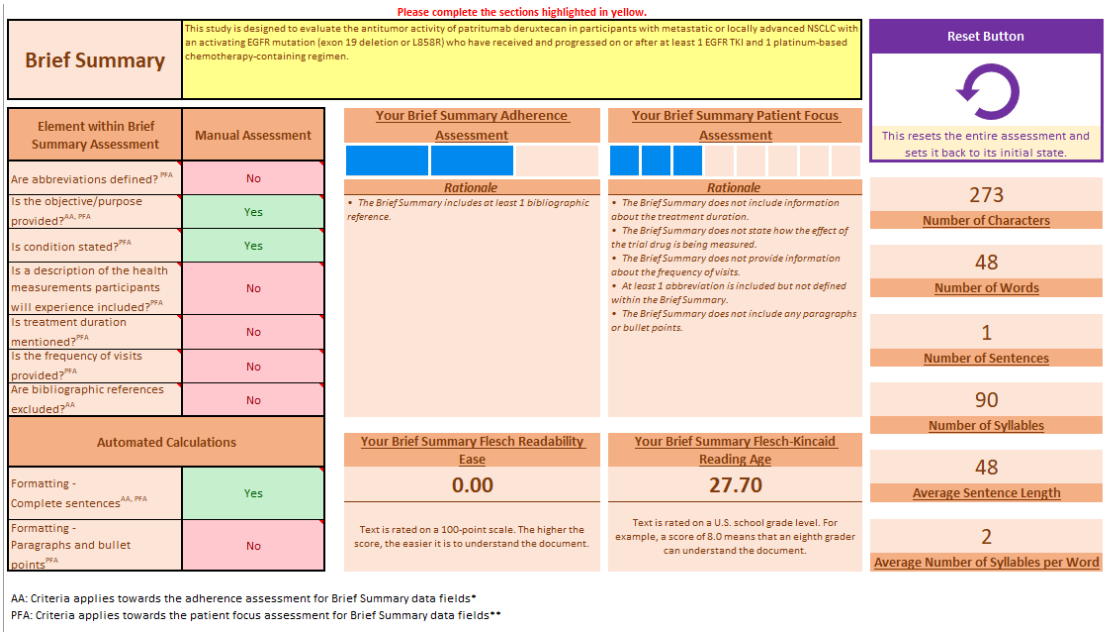

Figure 38. Total Number of Study Records Posted Per Year on ClinicalTrials.gov and Timeline of Related Major Events[82]

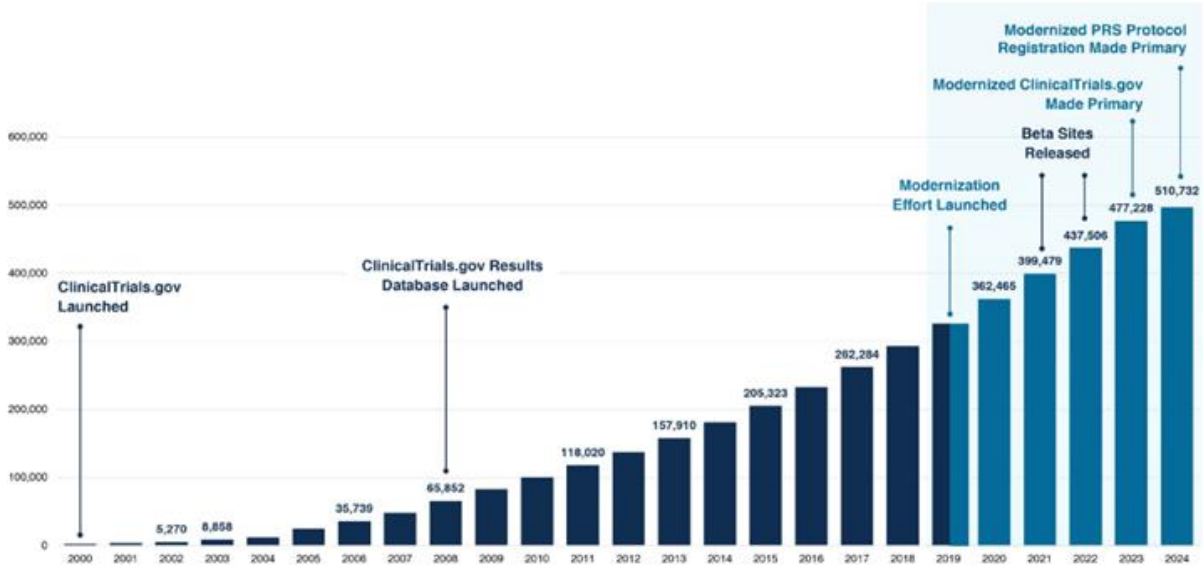

Figure 39. Original Plain Language Checklist for Lay Brief Summaries Posted September 26, 2022

Plain Language Checklist for Lay Brief Summaries

Study managers can use this checklist to write a "brief summary description" that follows the main evidence-based plain language best practices for writing lay research summaries. The goal is a brief description that the general public can easily understand and engage with.

Focus

Know your intended audience and make the purpose of your research clear to your readers:

- ☐ Think about your audience. Keep them in mind as you write the summary: their age, gender, ethnicity, health conditions, reading level, and cultural beliefs. What background knowledge do they have and what questions might they have?
- ☐ Explain the purpose or "why" of the research, including possible benefits.
- ☐ Identify the information that is most relevant and include only that "need to know" information. "Need to know" information includes "who" can take part and "how" the research will happen. Omit "nice to know" information, such as previous research or background information.

Content

Make your words easier to understand by saying what you mean and nothing more:

- ☐ Replace complex terms with common, everyday words. For example:
  - Effective = works well
  - Utilize = use
- ☐ Define essential jargon using common words. For example, "a placebo is a look-alike substance that contains no active drug".
- ☐ Write out the full name for acronyms on first use.
- ☐ Write sentences in active voice, in which the subject performs the action: "The researcher read the chart" instead of "The chart was read".
- ☐ Use consistent terms rather than varying them. If you choose "researchers" stick with it throughout the summary, instead of using both "researchers" and "investigators".
- ☐ Keep sentences and paragraphs short. Aim for sentences of 15 words or less, and paragraphs of 3-5 sentences or less.
- ☐ Aim for a 6th-8th grade reading level.

Numbers

Make numbers easier to understand by including only essential numbers and giving them meaning:

- ☐ Include only essential numbers that are highly related to the purpose or that will help readers take action. Eliminate background information, such as prevalence data.
- ☐ If you must include numbers, frame numbers by giving them context. Give numbers meaning by using words such as "high" or "low" and "better" or "worse".
- ☐ Use words and numbers to give a complete understanding. For example, pair "about half" with "17 out of 40".
- ☐ Give both percentages and use natural frequencies: 7 out of 10 participants (70%).
- ☐ Avoid qualitative terms such as "reduce" or "increase". Try "lower" or "raise".

Structure

Structure your summary so readers can easily find what they need:

- ☐ Place the content in this order:
  1. Most important information – the core message or what patients **need** to know to take action
  2. Supporting information
  3. Background information, if required to understand the research – history or data. Remove background information if not required.
- ☐ Stick to 1 main message supported by 3 to 5 points that tie directly to the purpose.
- ☐ Delete extra words that muddy sentences, such as "In order to...".
- ☐ Use bullets for lists of items. Limit bulleted lists to 2-7 items.

Test the summary

The gold standard is to test the summary with people from your intended audience to ensure it is easy to understand.

Or, ask a peer in another field, a family member, or a friend to read and share feedback. This can help identify jargon and content that may be misinterpreted.

Resources

- Health Literacy Online at https://health.gov/healthliteracyonline/
- CDC Health Literacy Resources at https://www.cdc.gov/healthliteracy/learn/resources.html
- Plain Language Action and Information Network at https://www.plainlanguage.gov/
- CDC's Everyday Words for Public Health Communication at https://www.cdc.gov/other/pdf/everydaywordsforpublichealthcommunication.pdf
- Health Research for Action's Plain Language Word List https://multco.us/file/46697/download

SUPPLEMENTARY DATA

Table 23. Intervention Class

Intervention class	Pre-guidance, n (%)	Post-guidance, n (%)
Chemotherapy	56 (4.7)	71 (5.8)
Targeted therapy	186 (15.6)	161 (13.2)
Immunotherapy/checkpoint	108 (9.1)	91 (7.5)
Chemo + targeted	84 (7.1)	78 (6.4)
Chemo + immunotherapy	159 (13.4)	180 (14.8)
Immunotherapy + targeted	69 (5.8)	36 (3.0)
Chemo + immunotherapy + targeted	85 (7.1)	93 (7.6)
ADC	39 (3.3)	77 (6.3)
CAR-T/cell therapy	75 (6.3)	96 (7.9)
Radiation	194 (16.3)	214 (17.6)
Vaccine/other immunotherapy	7 (0.6)	4 (0.3)
Other/unclassified	129 (10.8)	116 (9.5)

Table 24. Molecular Targets of Trials

Mechanism/target	Pre-guidance, n (%)	Post-guidance, n (%)
PD-1/PD-L1	557 (46.8)	518 (42.6)
EGFR	227 (19.1)	253 (20.8)
VEGF	168 (14.1)	136 (11.2)
ALK	63 (5.3)	71 (5.8)
MET	69 (5.8)	74 (6.1)
KRAS	38 (3.2)	50 (4.1)
HER2/HER3	52 (4.4)	49 (4.0)
CTLA-4	38 (3.2)	36 (3.0)
ROS1	32 (2.7)	32 (2.6)
TROP2	10 (0.8)	34 (2.8)
BRAF/MEK	19 (1.6)	15 (1.2)
RET	20 (1.7)	11 (0.9)
PARP	26 (2.2)	8 (0.7)
NTRK	6 (0.5)	5 (0.4)

ABBREVIATIONS

Abbreviation	Definition
ACS CAN	American Cancer Society Cancer Action Network
AI	Artificial Intelligence
ALK	Anaplastic Lymphoma Kinase
ANDA	Abbreviated New Drug Application
ANOVA	Analysis of Variance
API	Application Programming Interface
ASCO	American Society of Clinical Oncology
BLA	Biologics License Application
CFR	Code of Federal Regulations
cIMT	Carotid Intima–Media Thickness
CISCRP	Center for Information and Study on Clinical Research Participation
CSC	Cancer Support Community
CTSC	Clinical Trial Support Center (Leukemia & Lymphoma Society)
EGFR	Epidermal Growth Factor Receptor
EHR	Electronic Health Record
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FDAMA	Food and Drug Administration Modernization Act of 1997
FD&C Act (FDC)	Federal Food, Drug, and Cosmetic Act of 1938
FKGL	Flesch–Kincaid Grade Level

Abbreviation	Definition
FR	Federal Register
FRE	Flesch Reading Ease
GO2	GO2 for Lung Cancer
HDE	Humanitarian Device Exemption
HHS	Department of Health and Human Services
ICMJE	International Committee of Medical Journal Editors
ICTRP	International Clinical Trials Registry Platform (WHO)
IDE	Investigational Device Exemption
IND	Investigational New Drug Application
IQR	Interquartile Range
IRB	Institutional Review Board
IV	Intravenous
KRAS	Kirsten Rat Sarcoma viral oncogene
LLS	Leukemia & Lymphoma Society
MET	Mesenchymal–Epithelial Transition factor
MSI	Microsatellite Instability
NCI	National Cancer Institute
NCT	National Clinical Trial (ClinicalTrials.gov registry identifier)
NDA	New Drug Application
NIH	National Institutes of Health
NLM	National Library of Medicine
NPRM	Notice of Proposed Rulemaking

Abbreviation	Definition
NSCLC	Non-Small-Cell Lung Cancer
NTRK	Neurotrophic Tyrosine Receptor Kinase
ORD	Office of Research and Development (VHA)
ORR	Objective Response Rate
PCORI	Patient-Centered Outcomes Research Institute
PD-1	Programmed Cell Death Protein-1
PD-L1	Programmed Cell Death Ligand-1
PHS Act	Public Health Service Act
PhRMA	Pharmaceutical Research and Manufacturers of America
PI	Principal Investigator
PLCST	Plain Language Checklist Scoring Tool
PLS	Plain Language Summaries
PMA	Premarket Approval Application
PRS	Protocol Registration and Results System
RCT	Randomized Controlled Trial
RECIST	Response Evaluation Criteria in Solid Tumors
RET	Rearranged during Transfection
RFI	Request for Information
ROS1	ROS Proto-Oncogene 1
SCLC	Small-Cell Lung Cancer
SD	Standard Deviation
SMOG	Simple Measure of Gobbledygook (Index)

Abbreviation	Definition
SPSS	Statistical Package for the Social Sciences (IBM SPSS Statistics)
TPS	Tumor Proportion Score
UMLS	Unified Medical Language System
VA	Department of Veterans Affairs
VHA	Veterans Health Administration
WHO	World Health Organization

VITA

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Educational Institutions:

School	Place	Degree	Date
Drew University	Madison, NJ	Bachelor of Arts	2006
Drew University	Madison, NJ	Master of Medical Humanities	2017
Drew University	Madison, NJ	Doctor of Medical Humanities	2026