AI-Driven Patient Charting for Rapid, Efficient, Effective Cohort Sizing and Patient Inclusion

Bryan Allinson, director of partnerships at Deep 6 AI

Dan Fort, PhD, MPH, biomedical research informatics leader and associate professor for the Ochsner Center for Outcomes Research

Oncology clinical trials have led to the development of new therapies and treatments that help patients with cancer to live longer, healthier lives. As a result, the volume of clinical trials is expanding dramatically. According to the Association of Clinical Research Professionals, over the past 20 years, the number of investigational treatments targeting cancer has nearly quadrupled from 421 to 1489.[1] Further, there are over 11930 active oncology interventional clinical trials underway including 5500 with a biopharmaceutical company as a sponsor.

Due to an increasing number of eligibility criteria, laboratory tests, and complicated trial designs, oncology clinical trials are becoming more complex. Additionally, screening and treatment durations are much longer in phase 2 and 3 oncology clinical trials compared to other drug trials. Oncology clinical trials generate a much higher volume of data, particularly in terms of phase 2 protocols, compared to other drug trials. Compared to trials involving other drugs, phase 2 and 3 trials of oncologic agents have more protocol deviations and generate more substantial protocol amendments.[1] As a result, clinical research teams are stretched thin, and trial durations for oncology drugs are 30% to 40% longer than needed for other drug trials.[1]

For the biopharmaceutical company sponsoring the development of an oncology drug for approval, multiple factors contribute to increased volume and complexity of trials. First, a complete molecular profile is now often necessary to understand the underlying cancer biology.[2] This includes immune, DNA and RNA, proteomic, and/or other biomarker screening. Second, therapy should be matched to the biology of the tumor, including combinations of drugs to target the multiple drivers that are present in most metastatic cancers. Third, trials are designed to accelerate drug development and regulatory approval while lessening adverse effects. Fourth, innovative trial designs—including platform studies and umbrella, basket, multi-arm, and adaptive trials—have the common goal of using novel methods and master protocols to answer many questions simultaneously in a single trial.[3] These decisions are designed to enhance outcomes for the corporate sponsor but often lead to increased complexity for the oncology research site.

To meet the increasing demand of numerous and more complicated oncology clinical trials, physician investigators and research teams at the study site increasingly are using electronic systems to support the conduct of clinical research. Critical questions for research staff to answer involve where and how much to invest organizational resources to support eligibility screening by clinical research teams for higher volumes and increased complexity of studies. If too little is invested in patient screening, then too many ineligible patients are enrolled, and research teams waste precious time with screen failures. If too much time is invested in screening patients, then the cost of running the trial can drain precious resources from the cancer center.

To address these issues, Ochsner Health in New Orleans, Louisiana, is employing a new type of artificial intelligence (AI) and natural language processing to enhance its ability to screen patients for studies and reduce the personnel cost of screening.

In 2020, Ochsner Health formed a partnership with Deep 6 AI, an artificial intelligence and natural language processing software company that focuses on AI-supported charting solutions that include sizing and characterization of cohorts, recommending cohorts for specific patients, and developing business intelligence tools.

(Continued on page 28)

Where treatment and profitability meet.

Don't get caught in the margins. Recover more revenue in six months or less with OCI's proprietary Oncology Revenue Recovery (ORR™) technology. Let us help you substantially improve your profitability while you focus on your patients.

We offer complete Revenue Cycle Management

- Revenue Cycle Audits
- Billing System Optimization
- Financial Counseling, Prior Authorization, Coding and Billing

Oncology Convergence

oncologyconvergence.com

(Continued on page 26)

In this article, Bryan Allinson, director of partnerships at Deep 6 AI in Pasadena, California, interviews Dan Fort, PhD, MPH, a biomedical research informatics leader and associate professor for the Ochsner Center for Outcomes Research, part of Ochsner Health, about challenges related to oncology clinical trials. Before joining Deep 6 AI, Allinson served as senior director for AdventHealth, in Orlando, Florida, where he led oncology clinical research operations. Previously, Allinson served as executive director for the University of Texas, leading statewide clinical and translational research partnerships, and as a director at Geisinger Health System, focused on data, device, and biopharmaceutical innovation.

In his role at Ochsner Health, Dr Fort facilitates oncology physicians and investigators with access to research resources, including biostatistics and data analytics, collection, and extraction. He uses Epic (Epic Systems), Ochsner Health's electronic health record (EHR) system, to precisely size potential cohorts for research studies, especially when these studies have numerous and complex inclusion and exclusion criteria. Dr Fort has 55 articles that have been published in such journals as *The New England Journal of Medicine*; *The American Journal of the Medical Sciences*; *American Journal of Transplantation*; *Applied Clinical Informatics Journal*; *Cancer Immunology, Immunotherapy*; *Cancers*; *Clinical Imaging*; *Frontiers in Oncology*; *Journal of the American Informatics Association*; and *Value in Health*.

Allinson. Can you tell us about the role of artificial intelligence in the development of new cancer therapeutics?

Dr Fort. Obviously, AI applications are rapidly evolving, and [they] have already proved instrumental in [the] targeted development of novel therapeutics and parsing the complex interactions of the relationships between germline and tumor genetics. But in my world, the number 1 impact of AI in clinical trials has been the ability to automatically parse and evaluate evidence in unstructured text. Subtle diagnoses, [those] of exclusion, suspicions, and differential diagnoses—particularly when monitoring patients for either first line treatment failure or recurrence—can frequently only be detected in text. Additionally, the results of certain classes of procedures, namely radiology and pathology, exist only as notes and are often the earliest sign of a patient reaching qualification for targeted oncology trials. Application of AI to these inclusion and exclusion criteria has saved countless hours of manual chart review.

Allinson. How can AI tools be applied to EHRs to precisely characterize a cancer cohort based on the inclusion and exclusion criteria?

Dr. Fort. Recruiting eligible participants for clinical trials is a significant bottleneck in the development of new medical interventions. Hospitals and practices often struggle to efficiently identify suitable candidates within their patient populations. This challenge can lead to delays in trial initiation, increased costs, and, sometimes, the inability to conduct a trial due to inadequate participant recruitment.

Identifying the right patients for a particular trial requires a comprehensive understanding of complex eligibility criteria, frequently requiring expert research personnel to accomplish. These criteria can involve factors such as medical history, age, gender, previous treatments, and specific health conditions all outside the targeted characteristics of the cancer itself. Manual screening of patient records to match these criteria is laborious, time-consuming, and prone to human error.

At Ochsner Health, my teams support clinical research operations primarily by assessing feasibility even before we make the decision to open a [clinical] trial. We start by evaluating historic availability of patients in the system as a whole, then the recruiting hospital location, the recruiting specialty department, and finally the recruiting specialty department with a scheduled appointment in the next 2 weeks. If recruitment can be met based on scheduled appointments, then our research coordinators merely need to meet the patients in the waiting room. Part of the feasibility assessment is not simply a number but a strategy to meet that number. One crucial additional insight is to assess feasibility using the same tools we would use for real patient identification. Often, it does not matter how many qualifying patients we *have*, but how many we can actually *find*. Once a trial is activated, the same queries and reports we used for the feasibility assessment turn into a feed of potential patients for prospective screening, evaluation, and, hopefully, trial recruitment.

AI and natural language processing provide us with an opportunity to read unstructured data with the same understanding and context as a trained researcher.

I should also mention that the traditional way researchers find patients for clinical trials is by either searching structured data ([eg], diagnosis codes, dates) or doing keyword searches. Then staff manually review the patients' chart files to make sure they match all of the trial's inclusion and exclusion criteria. Often, these searches are performed by other departments ([eg], the IT [information technology] team) and can take weeks or months to receive. These types of searches generate large lists that research teams must review and validate to find the small number of patients they can enroll. This tedious and time-consuming process is one of the key contributors to study recruitment delays.

One reason for this scattershot approach is because study eligibility criteria [do] not correspond to available information in the EHR, called *structured data*. In other words, structured data are what can be presented and evident as a data point of the EHR.

The biggest issue with cohort sizing is that structured EHR data only represent a small portion (10%) of all the available data in health care. The remaining information is in the form of unstructured data, such as free-form clinical notes, imaging, biopsies, [laboratory] results, pathology reports, or patient-reported outcomes. The challenge here is that unstructured data are largely inaccessible to research teams without writing complicated and time-consuming record queries. Harnessing the value of unstructured data sources

to match eligibility criteria lies in their diversity and disparate locations and the ability to parse and understand free form text as well as changes in systems and data standards over time. Until recently, there have been many attempts to overcome these roadblocks with little success.

However, AI and natural language processing provide us with an opportunity to read unstructured data with the same understanding and context as a trained researcher.

Allinson. Can you describe some tangible benefits of using AI-assisting charting to access unstructured data?

Dr. Fort. The use of AI and natural language processing results in a dramatic increase in precision ([ie], reducing the number of patients identified as eligible for the study and finding patients who are not possible to find with structured data alone). This reduces the amount of effort required while simultaneously increasing the number of patients identified. And for phase 1 trials for which our targeted enrollment may be as low as a single patient, the ability to rapidly eliminate patients who do not qualify—even if it turns out we have no patients for the trial—is still a win.

For example, for a single lung cancer study using AI to match patients, 1 patient was matched, and that same patient was approved for enrollment. If the research team had used traditional manual screening methods, maybe 292 patients would have been matched, but still only the same 1 patient approved.

Leveraging AI-assisted charting optimizes resource allocation by focusing efforts on patients likely to meet the trial criteria and reducing reliance on human chart reviewers, saving both time and resources.

In another example for gynecologic cancer, AI matched 64 patients, and 62 were approved. If the operations teams had used manual screening,…834 patients would have been matched to the study criteria, and only 40 would have been approved. This example shows both a reduction in false positives from 794 to 2 and a reduction in false negatives from 22 to zero.

Expanding further, cancer treatment is moving toward more targeted therapies. Researchers are identifying cancer molecular pathways and targets, and it's becoming possible to treat the target tumor regardless of the organ of origin. More targeted therapies may change, which may benefit patients and treatment of cancers… since a given treatment may only impact very specific biomarkers and genetic profiles.

Platform-type studies aiming to open and close cohorts quickly based on surrogate end points can help explore these targeted therapies more efficiently. These study designs often include multiple substudies examining the investigational treatment's effect on different populations and targets. Such study designs challenge sponsors, contract research organizations, and research sites to manage incoming data and make and disseminate decisions. It can be a challenge for the institutional review board as well—balancing the need for a complete and timely review. All of this work takes time and drains resources. So, it is critically important to select only the best trials for which the site can actually enroll.

To expand on this, there are 4 ways to leverage AI for accessing unstructured data. First, this technology can be used to confidently size the cohort. Protocol eligibility criteria are often complex and specific, especially in oncology studies. Clinical research teams need to demonstrate to the sponsor that they precisely understand how many patients they have in their system who are eligible for a study. The study may have dozens of individual inclusion and exclusion criteria, and it is nearly impossible for a human being to evaluate all of those variables from disparate data sources simultaneously. With AI, complex and numerous data can be processed simultaneously with minimal human effort.

Second, AI can help confirm potential participants. Clinical research teams use chart reviews to meticulously evaluate patient records against these criteria, ensuring that only suitable candidates are considered for enrollment. Staff carefully examine patients' medical records to determine whether they meet the eligibility criteria of the study. AI can create a virtual chart to compare eligibility criteria as independent variables and specific patient data as the dependent variables. Through the visual display, clinical research teams can confirm eligibility in a matter of seconds.

Third, this technology can screen and enroll participants. Based on the AI-assisted virtual chart review, research teams can identify patients who meet the initial eligibility criteria and flag them for further evaluation. These candidates are then formally screened for study enrollment. Because the AI has already confirmed patient eligibility, the result is a highly precise cohort with a low false-positive rate in a short amount of time with only minimal burden on research teams. By contrast, without AI-assisted virtual charting, the result is a low-precision cohort with a high false-positive rate, high operational burden, and longer time spent.

And lastly, AI can help maximize enrollment by identifying remote and unknown patients. AI-assisted virtual charting can find patients who are in the organization's system but have not yet visited the physician's clinic. Since the AI is searching the organization's entire EHR, these patients are positively confirmed for eligibility. Research teams can then reach out to their providers to see if they are interested in study participation.

Allinson. Can you describe the advantages of using AI-assisted patient charting for eligibility criteria?

Dr. Fort. There are 4 main advantages of using AI here. The first is efficiency and accuracy. AI-assisted charting enables clinical research teams, including study coordinators, to efficiently screen many patient records. What takes a person 1 hour to do, AI can do in seconds. Also, AI gives better results, ensuring a thorough evaluation for trial eligibility with enhanced accuracy.

The second is streamlined patient recruitment with high precision. AI can review an unlimited number of eligibility criteria simultaneously to avoid limitations of human screening, resulting in dramatically fewer false positives.

The third is the ability to recall a patient from anywhere in the system and at any time. AI can quickly identify suitable candidates through guided chart reviews. AI evaluates candidates currently on the schedule to be seen at the site location, candidates on the schedule at clinics elsewhere in the organization (even geographically distant locations), and candidates not on the schedule. Without AI, clinical research teams are only drawing from candidates on the schedule.

The fourth is cost savings. Leveraging AI-assisted charting optimizes resource allocation by focusing efforts on patients likely to meet the trial criteria and reducing reliance on human chart reviewers, saving both time and resources.

Allinson. Your research focus is informatics. How does AI relate to informatics for oncology teams?

Dr. Fort. The traditional funder of research informatics is the National Library of Medicine. In the same way that library science is a set of skills to rapidly identify appropriate sources of information, informatics can be understood as a set of skills to rapidly identify and use appropriate analytic methods. AI is not a single technique but an umbrella term that describes techniques starting somewhere on the fuzzy boundary between multivariate regression and machine learning, stretching through neural-network and deep-learning models and the current frontier of large language models. For oncology teams or any clinical research team, for that matter, AI can seem intimidating, because the term obscures what is actually being used and proposed. Having a partner to explain what and why a technique is used and how it can be evaluated can make all the difference.

Allinson. ACCC's membership includes medical oncology, radiation oncology, pathology, laboratory medicine, radiology, palliative care, pharmacy, hospice, primary care, administrators, genomics vendors, and others. Each of these stakeholders provides input into oncology clinical trials of new therapies. Can you discuss AI from their perspective?

Dr. Fort. It's common to have different specialists or health care professionals as part of the cancer care treatment team. So a multidisciplinary approach to clinical trials is just a natural extension of this.

By way of background, having different professionals and disciplines work together is an approach that is used in many hospitals and clinics before, during, and after cancer treatment. Some have had specialized additional training that focused on a specific type(s) of cancer treatment, a particular area of the human body, comorbid health problems, and overall coordination of care factoring in all those variables. Clinical trials are increasingly being looked at as a care option, and they are also known as *research as care*. So identifying a team or teams of diverse health professionals to support clinical trials is completely consistent with this approach.

Allinson. When selecting an AI partner, what criteria do you look for?

Dr. Fort. First, we look at the AI performance. We look at how good the technology is, how fast it can deliver results for our team, and key performance indicators such as false positives and false negatives. Second, we look at the network. We wanted to pick a partner that had significant experience, especially in oncology studies. Finally, not everyone is experienced in AI software, especially in our research teams. So we need to ensure that any partner has a strong operational customer success team. The people making the decisions on which partner to pursue are almost never the day-to-day users, so access to responsive trainers for new users has been crucial to our success. OI

References

1. Clinical trial complexity levels show unrelenting increase. Association of Clinical Research Professionals blog. May 5, 2021. Accessed March 21, 2024. https://www.acrpnet.org/2021/05/clinical-trial-complexity-levels-show-unrelenting-increase/

2. Sicklick JK, Kato S, Okamura R, et al. Molecular profiling of cancer patients enables personalized combination therapy: the I-PREDICT study. Nat Med. 2019;25(5):744-750. doi:10.1038/s41591-019-0407-5

3. Fountzilas E, Tsimberidou, AM, Vo HH, Kurzrock R. Clinical trial design in the era of precision medicine. Genome Med. 2022;14(1):101. doi:10.1186/s13073-022-01102-1

Additional Resources

Adashek JJ, Subbiah V, Kurzrock R. From tissue-agnostic to N-of-one therapies: (R)evolution of the precision paradigm. Trends Cancer. 2021;7(1):15-28. doi:10.1016/j.trecan.2020.08.009

Barlow C. Oncology research: clinical trial management systems, electronic medical record, and artificial intelligence. Semin Oncol Nurs. 2020;36(2):151005. doi:10.1016/j.soncn.2020.151005

Bhatt DL, Mehta C. Adaptive designs for clinical trials. N Engl J Med. 2016;375(1):65-74. doi:10.1056/NEJMra1510061

Carrell DS, Schoen RE, Leffler DA, et al. Challenges in adapting existing clinical natural language processing systems to multiple, diverse health care settings. J Am Med Inform Assoc. 2017;24(5):986-991. doi:10.1093/jamia/ocx039

Dagogo-Jack I, Manoogian A, Jessop N, et al. Integrated radiology, pathology, and pharmacy program to accelerate access to osimertinib. JCO Oncol Pract. 2023;19(9):786-792. doi:10.1200/OP.23.00031

Dhingra K. Oncology 2020: a drug development and approval paradigm. Ann Oncol. 2015;26(11):2347-2350. doi:10.1093/annonc/mdv353

Dickson D, Johnson J, Bergan R, Owens R, Subbiah V, Kurzrock R. Snapshot: trial types in precision medicine. Cell. 2020;181(1):208-208.e1. doi:10.1016/j.cell.2020.02.032

Edgcomb JB, Zima B. Machine learning, natural language processing, and the electronic health record: innovations in mental health services research. Psychiatr Serv. 2019;70(4):346-349. doi:10.1176/appi.ps.201800401

Freidlin B, Korn EL. RE: Impact of a biomarker-based strategy on oncology drug development: a meta-analysis of clinical trials leading to FDA approval. J Natl Cancer Inst. 2016;108(3):djv430. doi:10.1093/jnci/djv430

Health professionals associated with cancer care. American Cancer Society. May 5, 2021. Accessed March 21, 2024. https://www.cancer.org/cancer/managing-cancer/finding-care/health-professionals-associated-with-cancer-care.html

Korach ZT, Yang J, Rossetti SC, et al. Mining clinical phrases from nursing notes to discover risk factors of patient deterioration. Int J Med Inform. 2020;135:104053. doi:10.1016/j.ijmedinf.2019.104053

Le Tourneau C, Delord JP, Gonçalves A, et al; SHIVA Investigators. Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial. Lancet Oncol. 2015;16(13):1324-1334. doi:10.1016/S1470-2045(15)00188-6

Liu R, Rizzo S, Whipple S, et al. Evaluating eligibility criteria of oncology trials using real-world data and AI. Nature. 2021;592(7855):629-633. doi:10.1038/s41586-021-03430-5

Mapes D. Cancer clinical trials exclude patient eligibility. Hutch News Stories. August 11, 2021. Accessed March 21, 2024. https://www.fredhutch.org/en/news/center-news/2021/08/cancer-clinical-trials-exclude-patients-eligibility-criteria.html

Minutes not months. Deep 6 AI. Accessed March 21, 2024. https://deep6.ai/download-unstructured-data-white-paper/

Pyle S. 4 unique challenges of oncology trials. Advarra Research Library. June 20, 2023. Accessed March 21, 2024. https://www.advarra.com/blog/4-unique-challenges-of-oncology-trials/

Roberts C, Torgerson DJ. Understanding controlled trials: baseline imbalance in randomised controlled trials. BMJ. 1999;319(7203):185. doi:10.1136/bmj.319.7203.185

Rodon J, Soria JC, Berger R, et al. Genomic and transcriptomic profiling expands precision cancer medicine: the WINTHER trial. Nat Med. 2019;25(5):751-758. doi:10.1038/s41591-019-0424-4

Sicklick JK, Kato S, Okamura R, et al. Molecular profiling of cancer patients enables personalized combination therapy: the I-PREDICT study. Nat Med. 2019;25(5):744-750. doi:10.1038/s41591-019-0407-5

Sheikhalishahi S, Miotto R, Dudley JT, Lavelli A, Rinaldi F, Osmani V. Natural language processing of clinical notes on chronic diseases: systematic review. JMIR Med Inform. 2019;7(2):e12239. doi:10.2196/12239

Sicklick JK, Kato S, Okamura R, et al. Molecular profiling of advanced malignancies guides first-line N-of-1 treatments in the I-PREDICT treatment-naïve study. Genome Med. 2021;13(1):155. doi:10.1186/s13073-021-00969-w

Tsimberidou AM, Iskander NG, Hong DS, et al. Personalized medicine in a phase I clinical trials program: the MD Anderson Cancer Center initiative. Clin Cancer Res. 2012;18(22):6373-6383. doi:10.1158/1078-0432.CCR-12-1627

Tam CS, Gullick J, Saavedra A, et al. Combining structured and unstructured data in EMRs to create clinically-defined EMR-derived cohorts. BMC Med Info Dec Mak. 2021;21(1):91. Published 2021 Mar 8. doi:10.1186/s12911-021-01441-w

Vamathevan J, Clark D, Czodrowski P, et al. Applications of machine learning in drug discovery and development. *Nat Rev Drug Discov*. 2019;18(6):463-477. doi:10.1038/s41573-019-0024-5

Warner JL, Sethi TK, Rivera DR, et al. Trends in FDA cancer registration trial design over time, 1969-2020. *J Clin Oncol*. 2020;38(15). doi:10.1200/JCO.2020.38.15_suppl.2060