IN FOCUS

A Vision for Democratizing Next-Generation Oncology Clinical Trials

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Summary: Revolutionary advancements in oncology have transformed lives, but the clinical trials ecosystem encounters challenges, including restricted access to innovative therapies and a lack of diversity in participant representation. A vision emerges for democratized, globally accessible oncology trials, necessitating collaboration among researchers, clinicians, patients, and policymakers to shift from converting complex, exclusive trials into a dynamic, inclusive force against cancer.

"We choose to go to the moon"
"If not us, who? If not now, when?"

John F. Kennedy

Groundbreaking research and innovative treatments in the field of oncology have transformed the cancer care and outlook for countless patients in the last five decades (1). Such discoveries as the cloning of the human genome and the National Cancer Act were instrumental in the rapid development of better weapons to fight this disease. However, the path from bench to bedside to the real world in oncology clinical trials has often been fraught with challenges, including limited access to experimental therapies, underrepresentation of diverse patient populations, and protracted trial timelines. The percentage of patients enrolled in oncology clinical trials varies significantly based on multiple factors including cancer type, trial eligibility criteria, institutional infrastructure, where the trial is conducted, socioeconomic factors, gender, and race as examples. It is estimated, that <3%–5% of clinical trial–eligible adult cancer patients in the United States and even less globally participate in therapeutic clinical trials (2). A primary reason for this low participate rate is that most patients are not even considered. To effect real change, patient recruitment must increase, and expansion of referral pathways and trial accessibility must improve globally.

Over this time period, the oncology landscape has evolved significantly with the integration of genomic information playing a pivotal role in the diagnosis, treatment, and understanding of cancer (3). Genomic data provides insights into the genetic underpinnings of various cancer types, enabling greater personalized and targeted treatment strategies. Genomics has become a major force in multiple facets in oncology, including therapeutics, diagnosis, prognosis, prediction and in a better understanding of inherited cancer risk (4). Genomic information has paved the way for precision medicine in oncology. Understanding the unique genetic alterations in a patient's tumor allows for tailored treatment plans that can increase the effectiveness of therapies and minimize potential side effects. Genomic data has led to the development of genomically targeted therapies or agents that arm the immune system. These therapies have shown remarkable success in certain cancer types with lung cancer leading as the poster child of precision oncology. The omics revolution beyond genomics, notably, has ushered in a new era of advanced discovery tools like spatial transcriptomics, phospho-proteomics, RNA-sequencing, and others. These tools hold particular significance, especially in the realm of nontargeted drugs and epigenetic agents.

The capacity and the potential for what amounts to a revolution in cancer care already exist, and the evidence grows every day of the beneficial impact on patients and on wider society. What is missing from the mix at present is a common consciousness among the multiple stakeholders in cancer care of the need to actively push for the revolution to take place. It will not happen of its own volition at a pace that matches the needs of patients. It depends on all stakeholders make deliberate and conscious efforts to create the conditions for it to happen across the wide range of necessary changes, and then to drive the process forward with the energy to confer a genuinely universal resonance and real action.

Navigating this genomic revolution mandates the dissolution of the now archaic norm where clinical care and research existed separately in their siloes. Today's cancer care calls for oncology physicians and valued clinical team members to not only be well-versed in traditional clinical practices but also gain that "genomic savvy" clinic-readiness in integrating clinical trials into their day-to-day practice.

To address these issues, a compelling vision for democratizing oncology clinical trials and the need to transform the oncology work force to one that is genomically savvy and adept in clinical trials has emerged. At its core, democratized clinical trials aim to make clinical research a part of routine cancer care globally (5). Efforts to improve clinical trial enrollment rates include increased patient education, advocacy, and an available and expansive portfolio of clinical trials. The impact and importance of the practice of clinical trial participation is nowhere clearer that in the pediatric oncology experience.

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Cancer Discov 2024;14:579–84

doi: 10.1158/2159-8290.CD-24-0017

Enrolling children in clinical trials has been central to pediatric cancer care; this culture has been successful, at least 60% of patients with pediatric cancer treated on a clinical trial (6). Today 80% of children diagnosed with cancer will be cured—a testament to the power of rigorous clinical trials, collaborative efforts, and the dedication of every stakeholder within the pediatric oncology community (6). Unremitting innovation through collaboration ensure that treatment approaches evolve to further improve outcomes while minimizing long-term side effects in survivors. Pediatric oncology clinical trials ecosystem imparts invaluable lessons as the entire community united to support children battling cancer. Even in pediatrics, we could do a lot better aiming toward a 100% cure. Advances in cancer treatments highlight the need for these seminal clinical trials of new therapies and treatment strategies to reflect the real-world clinical setting where the majority of persons with cancer receive their care (7).

In this article, we delve into this vision, examining the crucial factors that underpin its implementation and the potential it holds for advancing the field of oncology. If not us, who will bridge the gap between oncology clinical trials and the wider community? If not now, when will we bring the promising advances of precision medicine to the real world, where patients are waiting for hope and healing? It's our collective responsibility to turn the tide of progress into practical solutions, and the time to act is now. Together, we must strive to ensure that the benefits of cutting-edge research through clinical/translational trials reach those who in need, paving the way for a brighter future in the fight against this disease.

THE CURRENT LANDSCAPE

Oncology clinical trials are a cornerstone of cancer research, allowing us to evaluate new therapies, test innovative approaches, and develop deeper evidence-based treatments for various types of cancer (7). However, the traditional clinical trial model is broken and presents several challenges.

Access Inequities

Most of the clinical trials are offered in major cities, and niche centers in affluent areas and inaccessible to rural and minority populations. Historically, only a limited number of patients have been able to participate in clinical trials, leading to underrepresentation of certain demographic groups, such as racial, ethnic minorities or patients living in rural areas, older adults, veterans, adolescents, and young adults and those with comorbidities. This hampers the generalizability of trial results.

Timelines and Costs

Traditional clinical trials are time-consuming and costly, often taking years to complete. These extended timelines mean that promising treatments take longer to reach the patients who need them, and results are obsolete as the field moves quickly.

Data Sharing

Recent trends show a transformation of clinical data into a commodity, thereby adding to the already prevalent challenges with data sharing across stakeholders, be it institutions and health systems, sponsors, researchers. However, the progress that is hindered is difficult to quantify – how does one measure what could have been?

Multilevel Systemic Barriers

Several factors contribute to the low enrollment rates in oncology clinical trials, including various physician-related, societal, and patient-related factors. Clinical trials frequently impose strict eligibility criteria, excluding many patients based on factors such as age, prior treatments, and medical conditions. In addition, limited awareness of available clinical trials across clinical teams and patients as well as geographic disparities with little to no trial options in rural or underserved areas converge as missed opportunities for participation. Patient-centered factors that have emerged as barriers to access include concerns and misconceptions about clinical trials, leading to hesitancy in participation. Financial barriers and language & other cultural factors further lend their influence on patient understanding and willingness to consider clinical trials.

The high variability in referral patterns consistently emerges as a crucial factor, with physician recommendations significantly impacting patient enrollment. Variabilities in trial integration across clinical practice settings is often attributed to the administrative and regulatory burden and their associated time constraints. Furthermore, clinical trial education, design, and conduct are not typically integrated into the standard oncology curriculum. Oncology fellowship training even in major cancer centers across the United States relegates clinical trial readiness as an optional skill, rather than one that is central to everyday practice in any setting.

Although societies and guidance pathways, such as National Cancer Comprehensive Network algorithms, acknowledge clinical trials as an option for every line of therapy, there exists an unclear referral pathway for physicians and a lack of clear access pathways when clinicians and patients are looking for the next treatment options. Advancing this form of care requires better decision tools to select the best treatments for each patient, based on a better alignment of information among patients, physicians, and health care systems – including regulators, payers, and industry – to introduce clinical interventions that improve patient outcomes. Clinical trials and clinical cancer research must increasingly be more cooperative (bridging the academia–industry–community intersect) and deliver benefit—our patients both deserve and demand transformative rather than incremental change.

A VISION FOR CHANGE

The vision for democratizing oncology clinical trials encompasses several essential components:

Patient-Centric Approach

A fundamental shift toward patient-centered research ensures that patients (patient advocates and caregivers) play a more active role in clinical trial design and implementation. This includes greater patient involvement in decision-making, improving informed consent processes, and incorporating patient-reported outcomes into trial endpoints.

Digital Health and Telemedicine

Leveraging digital health technologies and telemedicine can extend the reach of clinical trials, enabling patients to participate from the comfort of their homes, while reducing the burden of travel and increasing the diversity of trial participants.

Global Collaboration

Fostering international collaboration in oncology clinical trials ensures that diverse patient populations have greater access to novel therapies and contributes to a more comprehensive database for patient safety and efficacy.

Data Sharing and Transparency

Open access to clinical trial data, protocols, and results promotes the advancement of research and prevents redundancy by allowing for collaboration and the reevaluation of findings. Initiatives like the World Health Organization's International Clinical Trials Registry Platform (ICTRP) aim to improve transparency and facilitate global access to clinical trial information.

Innovation in Trial Designs

Modernizing trial designs, such as adaptive designs, umbrella, basket, and pragmatic trials (7), enable more efficient testing of multiple treatments in parallel and tailoring therapies to individual patients, thereby reducing timelines and costs (8).

Real-World Evidence

Incorporating real-world evidence into clinical trials can enhance the generalizability of results and provide valuable insights into how treatments perform outside the controlled environment of clinical trials (7).

In summary, as we move away from a "one-size-fits-all approach" to personalized cancer care delivery, we need to adopt the same principle in our clinical trial design, particularly as tumor disease biology increasingly segments or stratifies patients into different clinical subgroups or cohorts. Our framework must be comprehensive but flexible, addressing relevant issues such as clinical trial access, the complex data challenges (both technical and ethical), the regulatory landscape, the cost-versus-value conundrum, the need for adequate infrastructures for precision oncology, and the views and experiences of patients. A fit for purpose clinical trials framework in the era of personalized medicine must above all be collaborative, bringing together all relevant stakeholders (health care professionals, patients, payers, policy makers, regulators, and researchers), in an added value partnership that strives to deliver optimal cost-effective care for patients with cancer.

THE IMPACT, PROMISE, AND IMPLEMENTATION BY INNOVATION IN TECHNOLOGY-DRIVEN SOLUTIONS

The democratization of oncology clinical trials holds immense promise for patients, researchers, and the field of oncology globally. We need to educate the importance of clinical trials and then implement it. We need to encourage the simplification of complex processes associated with clinical trials, making it easier for both patients, clinicians, and researchers to navigate the system. Streamlining bureaucracy and paperwork should be a top priority. We need to stress the importance of accelerating the entire clinical trial process, from patient recruitment to data analysis. Innovative trial designs, data-driven decision making, and streamlined regulatory processes could all be part of his approach. We need to think differently and challenging the status quo. We need to push for innovative trial designs, telemedicine solutions, and disruptive technologies that fundamentally change the way clinical trials are conducted and data is collected, encourage the use of cutting-edge technology in clinical trials, such as artificial intelligence (AI)-driven patient screening and matching algorithms, remote monitoring devices, and real-time data analysis (7).

AI

AI has the potential to play a transformative role in this process. AI can analyze patient data, medical records, and genomic profiles to identify eligible patients for specific clinical trials (9), streamlining the patient recruitment process and ensuring a broader and more diverse range of participants. AI can analyze the genomic data of cancer patients to identify specific biomarkers and alterations, allowing personalized treatment strategies with therapies tailored to their unique genetic profiles. AI can analyze historical clinical trial data to predict patient responses to different treatments, facilitating the selection of therapies and increasing trial efficiency. AI can assist the integration and analysis of electronic health records, enabling researchers to access comprehensive patient data (10), helping identify potential clinical trial candidates. AI-powered wearable devices and remote monitoring tools can collect data on patients participating in clinical trials, allowing continuous analysis. AI-driven telemedicine solutions can expand the reach of clinical trials, so patients can participate without frequent in-person visits. AI can review medical literature and identify relevant research papers and studies, aiding trial design (10), and AI can assist in the design of more efficient and patient-friendly clinical trial protocols. This may involve adaptive trial designs that can be adjusted in real-time based on emerging data. It can also standardize data from diverse locations, ease global collaboration among researchers by overcoming language barriers, mitigate biases in patient selection and data analysis, support ethical oversight and assist in ensuring patient data use remains secure and compliant with data protection regulations.

Decentralized Trials

Decentralized oncology clinical trials or decentralizing elements of oncology trials represent a transformative approach to conducting cancer research by leveraging technology to enhance patient participation and streamline study processes (7). Unlike traditional trials that often require patients to travel to centralized locations, decentralized trials prioritize patient centricity by allowing individuals to participate from the comfort of their homes. This approach utilizes telemedicine, wearable devices, and remote monitoring tools to collect real-time data, promoting continuous and comprehensive patient insights (7). By decentralizing the trial infrastructure, participants can contribute to oncology research without

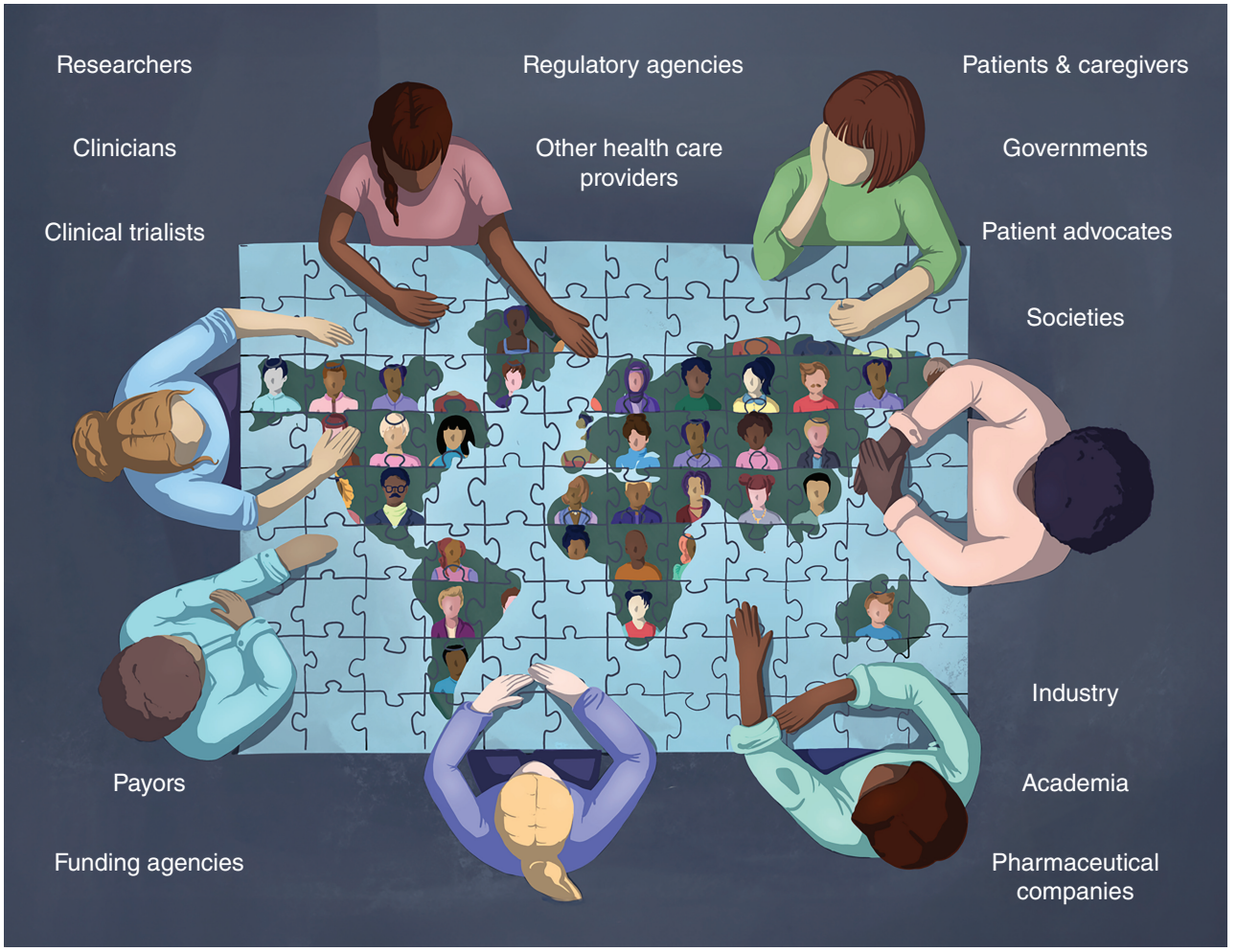

Figure 1. A vision for democratizing next generation oncology clinical trials: bench to bedside to the world. The necessity of multifaceted collaboration spanning industry, government, academia, patients, patient advocates, societies, community oncology, and regulatory bodies is crucial to enhance the effectiveness of the global clinical trials ecosystem and solve this big jigsaw puzzle. This collaboration is imperative not only in specific regions but worldwide, ensuring patient-centered success on a global scale.

the burden of extensive travel, thereby potentially increasing overall recruitment and retention rates. This innovative model not only enhances the efficiency of clinical trials but also facilitates a more diverse and representative participant pool, ultimately accelerating the development of new cancer treatments and improving the overall landscape of oncology research.

Global Accessibility/Collaboration and Standardization

International collaboration extends the reach of clinical trials, enabling a more diverse and representative patient population to participate (Fig. 1). We need to be supportive of efforts to ensure that clinical trials are accessible to people worldwide and promote the use of technology to bridge geographic gaps and provide equal opportunities for patients from different regions to participate in trials with a global perspective, collaborating with experts from around the world on the projects. We need to advocate for standardized global protocols and data formats to ensure seamless collaboration among international researchers and institutions (11). Throughout history, big pharmaceutical companies have advocated for the global expansion of clinical trials, engaging low- and middle-income nations. Although the primary motives behind this initiative are to enhance participant recruitment, cut down operational expenses, and hasten the overall completion of studies, this may be a strategic approach aimed at facilitating the development and regulatory approval processes for novel anticancer agents to open up clinical trials and funding to many less resourced areas. Given the frequent scarcity or absence of government-based funding, partnerships with pharmaceutical companies and contributions from philanthropic sources emerge as crucial pillars in underpinning the progress of international academic trials. Currently, many developing nations offer only a limited number of drugs listed in the WHO list. This exclusion results in the omission of most precision medicines, leading to significant inequities in modern drug access. Within economically challenged nations,

participating in global clinical trials can offer timely access to modern and new investigational agents that would otherwise be inaccessible. This engagement allows health care practitioners in these regions to cultivate expertise in drug development, establish new infrastructures, and provide training to study team members. The cumulative effect of these activities holds the promise of contributing to an overall improvement in global health.

BUILDING AN OMIC-SAVVY WORKFORCE THROUGH MENTORSHIP

Advancing the frontier of cancer research depends on the rejuvenation of its workforce and the cultivation of a new cadre of clinical investigators inspired by a passion to seek breakthroughs and a determination to dismantle the barriers that confound our understanding of this formidable adversary. Health care professionals, including oncologists, nurses, genetic counselors, and researchers and biostatisticians, must receive specialized training and continuous education and professional development. Effective care in the genomic era requires seamless collaboration among health care professionals.

This oncology workforce must be not only well-versed in traditional clinical practices but also be "genomic savvy." (12). In the pursuit of unlocking the full potential of genomics and all the "omics" beyond genomics, it is imperative to champion a workforce that reflects this. The promise inherent in genomics and all the 'omics technology can only be fully realized when we actively seek, nurture, and retain talents from backgrounds traditionally underrepresented in the genomics domain. Such a workforce can provide optimized patient care (12), and can provide patients with valuable information about hereditary cancer risks. It can contribute to the discovery of novel genetic markers, pathways, and potential therapeutic targets. It can design and conduct clinical trials that incorporate genomics, allowing for the evaluation of new therapies in a more targeted and efficient manner. It can interpret complex genomic data, ensuring that the insights derived are reliable and clinically relevant.

OPTIMIZING THE CLINICAL TRIALS ECOSYSTEM: THE IMPERATIVE OF MULTIFACETED COLLABORATION

Collaboration across industry, government, academia, patients, patient advocates, societies, community oncology, and regulatory bodies is imperative for enhancing the effectiveness of the clinical trials ecosystem (Fig. 1). Strategic partnerships should be nurtured between industry, government agencies, and academic institutions to facilitate the sharing of resources, expertise, and infrastructure crucial for successful clinical trial execution. Involving patients and advocates throughout the entire process, from trial design to execution, ensures trials are attuned to real patient needs. Clear communication channels between regulatory bodies, industry stakeholders and academic and community sites streamline processes and ensure compliance. Standardized data-sharing practices, education, training initiatives, and community engagement are essential for fostering a collaborative environment. Embracing innovative technologies, creating incentives for industry participation, and promoting adaptive trial designs contribute to a more streamlined and efficient clinical trials ecosystem. Similarly, global collaboration, ethical considerations, and strategies to improve patient recruitment and posttrial access are crucial for success. The unprecedented and unconventional collaboration observed in the development of COVID-19 vaccines serves as a model, showcasing the power of collective action in addressing global health crises (7). Applying a similar all-hands-on-deck approach to cancer, another global health crisis, necessitates rethinking and improving the clinical trials ecosystem. By collectively addressing these aspects, the clinical trials ecosystem can become more patient-centered, efficient, and successful.

CONCLUSION

The need to transform the clinical trials landscape is now—leveraging cutting-edge technology, collaboration, and streamlined processes accelerates the translation of groundbreaking scientific discoveries into effective treatments. We should be dedicated to fostering a dynamic ecosystem that ensures the efficient and ethical execution of clinical trials, bringing hope, healing, and progress to patients worldwide. By pursuing this we can aspire to create a future where the pace of clinical trials matches the breathtaking progress in basic science, ultimately transforming health care and improving the lives of individuals around the world.

The urgency for persons and families affected by cancer is underscored by the hope that comes with progress against this disease. Yet, the journey from the lab bench to the real-world bedside within the United States and across the world remains a complex and often sluggish process. Now is the moment to tap the synergy of collaboration, innovation, and community engagement to translate cutting-edge research into accessible, effective treatments. It is up to us to drive this transformation. In the spirit of John F. Kennedy's vision to go to the moon, we choose to advance precision medicine clinical trials in oncology from the bench to the bedside and, ultimately, to the real world. We do this not because it is easy, but because it is a beacon of hope for those battling cancer, a testament to the relentless pursuit of knowledge, and a testament to our commitment to a healthier and brighter future for all. If not us, who will champion this cause? If not now, when will we seize this opportunity to make a difference in the world of oncology clinical trials and precision medicine?

Democratizing oncology clinical trials drives global access to emerging treatment options while increased the efficiency and timeline of drug development. Partnering across stakeholders, including researchers, clinicians, patients, and policymakers (Fig. 1) brings us closer to this vision of oncology clinical trials as a dynamic, inclusive force for change in the fight against cancer.

Authors' Disclosures

V. Subbiah reports research funding for clinical trials paid to institution from Abbvie, Agensys, Alfasigma, Altum, Amgen, Bayer, BERG Health, Blueprint Medicine, Boston Biomedical, Boston Pharmaceuticals, D3 Bio, Dragonfly Therapeutics, Exelixis, Fujifilm, GlaxoSmithKline, Idera Pharmaceuticals, Incyte, Inhibrix, Eli Lilly/Loxo Oncology, MedImmune, NanoCarrier, Novartis, PharmaMar, Pfizer, Relay Therapeutics, Roche/Genentech, Takeda, Turning Point Therapeutics, and Vegenics; consulting/advisory role (paid to institution) from Abbvie,

Astex Pharmaceuticals, AstraZeneca, Bayer, Genmab, Incyte, Lilly/Loxo Oncology, Novartis, Obsidian Therapeutics, Pfizer, Pheon Therapeutics, Regeneron, Relay Therapeutics, Roche; and other consulting/advisory role, CME from Helsinn Healthcare, Jazz Pharmaceuticals, Incyte, Loxo Oncology /Lilly, Novartis, Relay Therapeutics, Daiichi Sankyo, Illumina, Bayer, Medscape, OncLive, Clinical Care Communications, PERS, and Med learning group. No other disclosures were reported.

Acknowledgments

The author would like to thank Ms. Emma Vidal, Draw Impacts for the figure originally commissioned for this article.

Published first April 4, 2024.

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