PEER REVIEWED

Improving Health Literacy to Transform Clinical Trials

The healthcare industry struggles with resolving fundamental patient communication challenges. Approximately 50% of adults cannot read at a high school level and 88% of adults are not proficient in health literacy.[1] Health literacy is defined as "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions."[2] As a result, more than 80% of health information provided in the doctor's office is forgotten before patients or their parents get home, and more than 50% of the recalled information is remembered incorrectly.[3]

Paucity of knowledge, misunderstandings, and forgotten information have led to poor healthcare outcomes and the erosion of patients' trust in medicine. Traditional approaches to medical education clearly have not worked. A fresh approach is required, both to improve health outcomes and curb costs from poor communications resulting in reduced patient recruitment and retention, and avoidable delays. Within clinical trials alone, the numbers are staggering: every day that a trial is delayed, due to slower than expected patient recruitment or other issues, costs an additional $600,000 to $8 million.[4]

There is a global need to develop culturally sensitive, relatable medical education resources for patients, caregivers, and their families. This article will discuss successful strategies that have been employed to improve patient recruitment and retention in clinical trials.

Low patient recruitment and retention rates pose considerable challenges to the success of clinical studies and advancing medical science and healthcare practices. Worldwide, 90% of studies fail to enroll the target number of participants within the proposed time.[5] Slow recruitment can prolong the enrollment period, inflate costs, and possibly result in early trial termination. A 2013 analysis of listings posted on ClinicalTrials.gov found that 12% of studies were terminated early, and 57% of those studies were ended prematurely due to insufficient patient enrollment.[6] Dropout rates can reach 30% or higher in some studies, which may lead to biased results and impact the validity of the study findings.[7] Enrolling minorities can also be a challenge, and patients with minority racial/ethnic backgrounds are considerably underrepresented in clinical studies.[8,9]

Poor health literacy is a significant part of the problem recruiting and retaining participants for clinical studies. Nearly half of Americans have limited health literacy[10] and as a result are less informed about how to manage their condition, have poorer health, and are less likely to be involved in health promotion and disease prevention.[11,12,13] Exacerbating this issue, healthcare materials are often written at the tenth-grade level or higher, and yet the average reading level of U.S. adults is eighth grade.[12,13,14] Furthermore, even people who are highly health literate may have difficulty understanding health information presented to them while they are feeling stressed or anxious.

Providing Accessible Educational Materials

A lack of understanding of their health condition and of how participating in a clinical study could benefit them presents a significant hurdle to recruiting and retaining patients in clinical studies. One proven strategy to address this issue is to provide accessible patient educational materials at appropriate reading levels throughout the clinical trial process.[15,16,17,18,19] With access to clear information, patients can better understand their health, its management, and the benefits and risks of joining a clinical study.

Engaging patients with educational materials that are clear, easy to comprehend, and age appropriate equips them with the tools they need to make an educated choice about how to best manage their health.[12,20,21,22,23]

Supporting Informed Consent

Some patient materials, such as the Informed Consent document, can be particularly difficult to understand. The Informed Consent Form is not only a legal document confirming that the patient agrees to participate in the clinical study, but it also serves as a tool to educate them about the study purpose, procedures, and risks and benefits, thereby make an educated choice about whether participating in the study is right for them. Unfortunately, in many cases the Informed Consent document is too long and uses medical jargon, making it challenging for non-experts to read and understand, further reducing the number of people that can absorb and process the information.

The American Medical Association and the National Institutes of Health recommend that patient education materials are written at sixth to eighth grade reading levels or lower.[20,24] The reading level of a document can be assessed based on criteria such as sentence length, word count, syllable count, and use of familiar words.[21,22]

Health education materials should also reflect sensitivity to patients' social, emotional, and cultural needs. A patient may be overwhelmed by a new diagnosis or the sheer amount of information they need to process to decide whether to join a clinical study. Furthermore, the patient may prefer to digest information in a particular format, be it through direct discussion, learning online, watching videos, reading brochures, or listening to podcasts.[23, 25,26] Regardless of the way in which the patient best absorbs information, all materials should be presented in a straightforward way to encourage learning. Patients should also be given sufficient time to digest and review the materials on their own.

Providing Ongoing Communications

Clinical studies can be an endurance test for patients. An important strategy for maintaining patient participation is to provide educational materials throughout the study. These can focus on what happens at each stage of the study and update patients on the study progress and results. Ongoing communication can help to build trust and promote patient awareness of their role in the study.

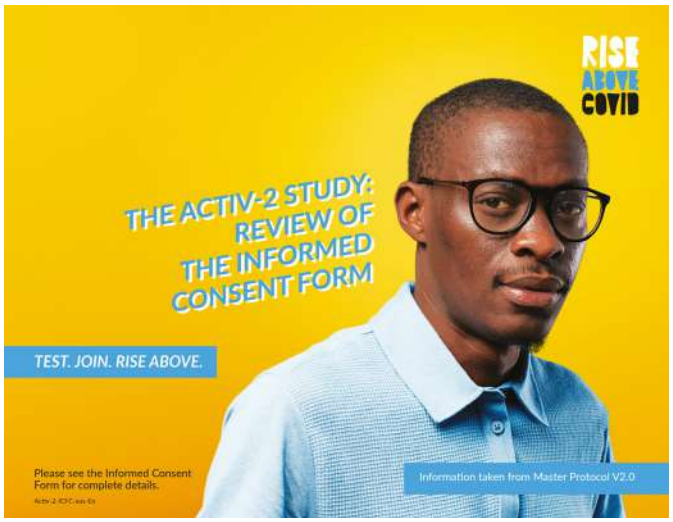
Following these recommendations will help to create effective patient education materials:

- Create age-appropriate materials that include visual aids, such as comic books and animation, to help reinforce the written word. Partner with youth advocates to make sure that the chosen messaging and format resonate with them.
- Develop content at the fifth and sixth grade reading level, ensuring that it is accessible to everyone.
- Prepare materials that combine visual and verbal elements, enabling readers to gain the requisite knowledge even if reading is difficult for them. Offer materials in a larger font for people who are visually impaired.
- Partner with patient advocacy groups and community advisory boards throughout the development process to ensure that all the information is clear, inclusive, and culturally sensitive.
- Develop a broad range of educational materials – both print and digital – to support clinical study recruitment and retention. These can include recruitment posters, booklets describing the medical condition, study brochures and welcome guides, informed consent/assent flip book discussion guides, videos describing the study and the informed consent/assent process, activity books, study passports so that children can track their progress through a study, and study schedule planners. Patient websites, podcasts and newsletters can also help to promote disease awareness, knowledge sharing, and create a sense of community among patients in a study.

Medical Education in Action

Enhancing Patient Recruitment

Recruiting patients who had tested positive for COVID-19 within the previous five days but did not require hospitalisation for an NIAID-sponsored Operation Warp Speed study of multiple drugs



for use as potential therapeutics was challenging. Not only did the sponsors need to recruit participants for a COVID-19 therapeutics study when the national focus was on vaccine campaigns, but trust in pharma was extremely polarised, especially amongst minority communities.

As COVID-19 was infecting Black and Hispanic people at 3.5 times the rate of other members of the public, it was imperative that the candidate therapeutics were shown to be safe and effective in those populations. To ensure that, needed to be appropriately represented in the study. Underscoring the urgency of this work, during the first six months of the pandemic, COVID-19 lowered the life expectancy of Black and Hispanic people by three years.

This was a massive study involving multiple government agencies, academia, and pharmaceutical companies and more than 200 clinical trial sites.

Community Advisory Boards were created so that key opinion leaders could partner with trusted members of the local communities, including barbers and hairstylists, to learn more about the barriers preventing people of color from enrolling in clinical studies. These relationships spurred grassroots outreach in the local neighborhoods and helped to overcome the prevalent mistrust of clinical trials.

The resulting multi-lingual medical education campaign, which prioritised recruiting a diverse patient population, included digital, print, licensed multi-media and custom educational resources. The campaign empowered patients to overcome their fear, take control of their lives and seek care for their COVID-19 infection by participating in clinical trials. It inspired hope and helped participants to transition from victim to victor as they played a critical role in developing new therapies.

This medical education program was quickly expanded from 10 clinical trial sites to 150. In eight months, it created 55 million social media impressions, 16 million search impressions, and more than 1 million website views. This resulted in a patient referral rate of 44% (three times greater than a chain pharmacy), a screen rate of 29% (20% greater than a CRO), and 64% of patients being randomised to enter the trial.

Facilitating Patient Screening

A Phase 3 randomised, double-blind, placebo-controlled study of the safety and efficacy of a new drug candidate to treat pulmonary arterial hypertension was expected to screen 385 patients at 191

sites in 26 countries. A screen fail rate of 33% was anticipated due to complex inclusion and exclusion criteria.

While most screen failures are due to inclusion/exclusion criteria, some aspects of site operations and training can also negatively impact conversion rates.

A series of site resources were developed to facilitate prescreening, explain the protocol, and train study investigators. These tools helped the sites better determine which patients were likely to qualify for the study before the formal screening process began. That step reduced the site burden during the actual screening process.

This multi-faceted educational program lowered the study screen fail rate by 9%, producing an estimated ROI of 9:1. Improving screening and enrollment processes can lead to reduced trial costs, shorter study timelines, and better study performance.

Improving Patient Retention

Retaining enrolled participants in a clinical trial is always important but when the study is of a rare disease with a very small patient population the future of the trial could depend upon it. When a patient drops out, their valuable clinical trial data are no longer usable. If several patients leave, regulatory authorities may stop the trial due to insufficient results or evidence.

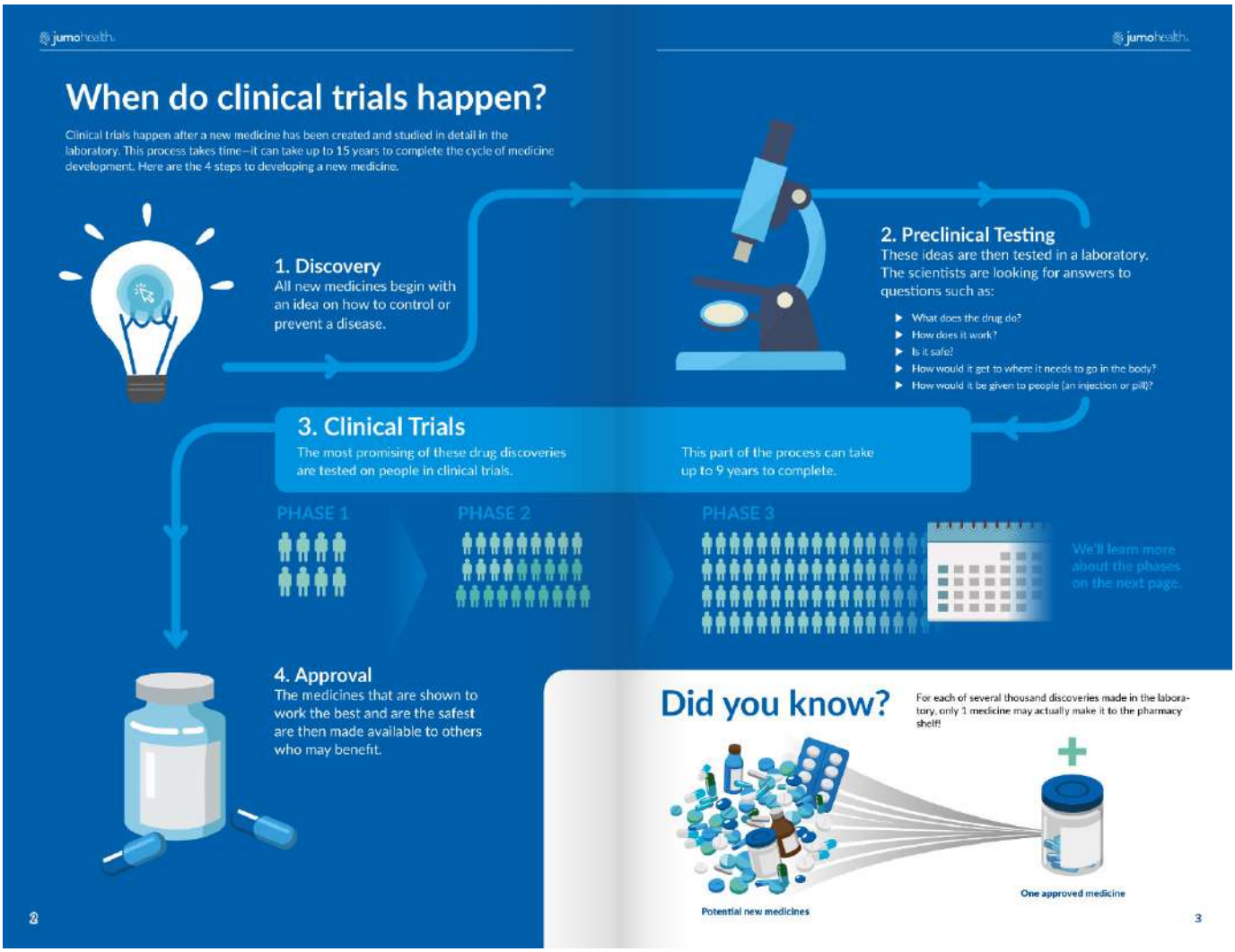
For a Phase 2a safety, tolerability, pharmacokinetic and pharmacodynamic study of participants with MELAS (mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes) syndrome, the goal was to enroll 20 patients and ultimately have 12 evaluable patients. The study involved a 29-day treatment period and 14-day follow up. A significant drop out rate was anticipated because the study involved quite an intensive schedule of protocol visits and procedures including neuroimaging, blood draws, patient-reported outcome assessments, and lifestyle restrictions.

Patient educational materials were developed for pre-consent, screening, and enrollment, explaining the study, outlining the appointment schedule, and setting appropriate expectations. Most importantly, these new resources, which promoted ongoing compliance and retention, were produced using a variety of media that were visually engaging, easily understandable, relatable, and empowering to this small patient population.

As a result, patient retention rates exceeded the sponsor's expectations by 40% and delivered an estimated ROI of 4:1. The educational resources helped to keep participants in the trial and the study on track, which ensured better data quality and integrity, and saved time, money, and other resources.

Conclusion

Having a limited understanding of medical concepts or poor health literacy increases stress, confusion, and anxiety amongst patients, their caregivers and family members. Those combined factors make it hard for patients to make informed decisions regarding possible treatments and clinical trial participation. That can lead to sponsors



having difficulty recruiting and retaining patients in clinical trials. It may also result in poor patient compliance with medical staff instructions during the trial.

The solution to all these problems is medical education. But that new information must be delivered in the right format using a combination of text and visual elements – which are age-appropriate, culturally sensitive, and relatable so they easily understood. The medium selected is also important and can range from comic books and animation to virtual reality experiences and patient interviews, depending on the audience's age and experience.

Partnering with patient advocacy groups and community and youth organisations when developing these materials helps to ensure that the messaging resonates and is authentic.

An increasing emphasis on improving health literacy will raise the public's level of healthcare knowledge and understanding, which will not only benefit society today but also future generations.

REFERENCES

1. https://www.washingtonpost.com/news/answer-sheet/wp/2016/11/01/hiding-in-plain-sight-the-adult-literacy-crisis/
2. Ratzan and Parker. National Library of Medicine Current Bibliographies in Medicine: Health Literacy. 2000. https://www.researchgate.net/publication/230877250_National_Library_of_Medicine_Current_Bibliographies_in_Medicine_Health_Literacy
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC539473/#:~:text=40%2D80%25%20of%20medical%20information,that%20is%20remembered%20is%20incorrect.
4. http://www.pharmafile.com/news/511225/clinical-trials-and-their-patients-rising-costs-and-how-stem-loss
5. Institute of Medicine. Transforming Clinical Research in the United States: Challenges and Opportunities: Workshop Summary. 2010. Washington, DC: The National Academies Press. https://doi.org/10.17226/12900.
6. Williams RJ, Tse T, DiPiazza K, Zarin DA. (2015) Terminated Trials in the ClinicalTrials.gov Results Database: Evaluation of Availability of Primary Outcome Data and Reasons for Termination. PLoS ONE 10(5): e0127242. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0127242
7. National Research Council. The Prevention and Treatment of Missing Data in Clinical Trials. Washington, DC: The National Academies Press. 2010. https://doi.org/10.17226/12955
8. Society for Women's Health Research and FDA Office of Women's Health. Dialogues on Diversifying Clinical Trials: Successful Strategies for Engaging Women and Minorities in Clinical Trials. September 22–23, 2011. Washington, DC.
9. Clark et al. Increasing Diversity in Clinical Trials: Overcoming Critical Barriers. Curr Probl Cardiol, May 2019. Pages 148-172.
10. Kutner M et al. National Center for Education Statistics. The Health Literacy of America's Adults. Results from the 2003 National Assessment of Adult Literacy. September 2006.
11. DeWalt et al. Literacy and Health Outcomes: A Systematic Review of the Literature. J Gen Intern Med 2004;19:1228–1239.
12. Institute of Medicine. Health Literacy: A Prescription to End Confusion. Washington, DC. 2004. The National Academies Press. https://doi.org/10.17226/10883
13. Kirsch et al. National Center for Education Statistics. Adult Literacy in America: A First Look at the Findings of the National Adult Literacy Survey. April 2002.
14. Hadden et al. Improving Readability of Informed Consents for Research at an Academic Medical Institution. J Clin Transl Sci. 2017 Dec;1(6):361-365. https://doi.org/10.1017/cts.2017.312.
15. Chhatre et al. Patient-centered Recruitment and Retention for a Randomized Controlled Study. Trials. (2018) 19:205. https://doi.org/10.1186/s13063-018-2578-7
16. Huang et al. Clinical Trials Recruitment Planning: A Proposed Framework from the Clinical Trials Transformation Initiative. Contemporary Clinical Trials. 66 (2018) 74-79.
17. Greenberg et al. Parents' Perceived Obstacles to Pediatric Clinical Trial Participation: Findings from the Clinical Trials Transformation Initiative. Contemporary Clinical Trials Communications. Volume 9, March 2018, Pages 33–39. https://www.sciencedirect.com/science/article/pii/S2451865417301564?via%3Dihub#!
18. Caldwell PHY, Hamilton S, Tan A, Craig JC (2010) Strategies for Increasing Recruitment to Randomised Controlled Trials: Systematic Review. PloS Med 7(11): e1000368. https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1000368.
19. Sacristan et al. Patient Involvement in Clinical Research: Why, When, and How. Patient Preference and Adherence. 27 April 2016. http://dx.doi.org/10.2147/PPA.S104259
20. NIH U.S. National Library of Medicine. MedlinePlus. Health Literacy. https://medlineplus.gov/healthliteracy.html
21. CDC. Simply Put: A Guide for Creating Easy-to-understand Materials. April 2009. https://www.cdc.gov/healthliteracy/pdf/simply_put.pdf.
22. Program for Readability In Science & Medicine (PRISM) Readability Toolkit. https://www.kpwashingtonresearch.org/about-us/capabilities/research-communications/prism
23. Harris and Kelly. Patient Education in Clinical Trials and Throughout the Product Lifecycle. Medical Writing. Volume 25 Number 4. December 2016.
24. Weiss. Health Literacy: A Manual for Clinicians. American Medical Association, American Medical Foundation, Chicago, 2003.
25. NIH U.S. National Library of Medicine. MedlinePlus. Choosing Effective Patient Education Materials. https://medlineplus.gov/ency/patientinstructions/000455.htm
26. Guise et al. Using Health Literacy and Learning Style Preferences to Optimize the Delivery of Health Information. Journal of Health Communication, 17:122–140, 2012. https://pubmed.ncbi.nlm.nih.gov/23030566/

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