D.R.I.V.E Initiative and Indianapolis Black Paper Summit

Fall 2022

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Introduction

Cancer is a leading cause of mortality in the United States. In 2021, 1,898,160 new cases and 608,570 deaths will occur in the United States. Increasing rates for cancer mortality in the United States occurred until 1991, but decreased through 2018 from its peak by 31%, with 3.2 million fewer cancer deaths in this period. However, these improvements are not equally applicable to all races, with significant differences in cancer mortality between Blacks and Whites. The 5-year relative survival rates for all cancers diagnosed between 2010-2016 were 68% (Whites) and 63%(Blacks), respectively. Disparities in cancer treatment, a major contributor to decreasing outcomes in cancer mortality can be related to the underrepresentation of Blacks and other racial minorities in clinical trials.[1]

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of the scientific community paid close attention to this disparity. CCTs are essential for cancer care, yet the evidence is scare when it comes to racial disparities in CCT participation. After adjusting for effects of socio-demographic, health status, and psychosocial variables, Kumar et all identified Black cancer survivors were

much less likely than White cancer survivors to be aware of CCTs, to express willingness to participate in CCTs, and to actually participate in CCTs. Furthermore, Black cancer survivors reported a lower level of trust in physicians and were less likely than White cancer survivors to believe that CCTs make a significant contribution to science.[2]

Participation of adult cancer patients in clinical trials in the U.S. is woefully low, additionally, the rate of the participation of patients belonging racial and ethnic minority communities is even lower.[3] A 2018 study showed that although Black and Hispanic patients accounted for 10% and 7% respectively, of cancer cases in 2018, only 6% and 2.6% of patients were enrolled in clinical trials listed on the ClinicalTrials.gov website.[4] A 2019 study revealed upward of 80% of enrollees in cancer clinical trials conducted between 2008 and 2018 were White compared with between 10% and 35% Asian and 0% and 10% Black and Hispanic patients.[4] Likewise, a 2021 study informed us that the ratio of observed expected trial enrollees remained high for Asian and non-Hispanic White patients but low for American Indian/Alaska Native, Black, and Hispanic patients.[5]

There are multiple barriers to patients from racial and ethnic minority communities going on clinical trials. First, clinician barriers include physician biases, poor communication, and limited number of minority oncologists. Second, narrow trial eligibility limits the number of patients of color participating in research studies. Third, patient barriers include lack of awareness, diminished access to cancer centers, social determinants of health, and distrust. Financial barriers such the inability to have laboratory and x-ray studies covered by health insurance plans are present, as well.[2]

Motivated by the inequalities in cancer mortality rates in the US which directly correlate to unequal access to clinical trails, a team of health care providers has drafted a five- step strategy to promote and improve DEIA in clinical trials for minorities has been

developed. This highly impactful initiative has been appropriately named D.R.I.V.E. and includes the following core elements:

D.R.I.V.E. is based on the following five steps:

- Appointing a clinical trial Diversity Officer
- Creating a RANK SCORE based on minority enrollment in clinical trails
- Individual diversity, equity, inclusion and access plan,
- Verification of clinical study's diversity, and
- Elevated training of minority investigators and research team members.

Diversity Officer

Indy Hematology Education, Inc. held a meeting with with global experts in \ Indianapolis, Indiana to gain consensus on these core elements.

The appointment of two disparate diversity officers: The Principal Diversity Officer will be an appointee of study sponsors which may be pharmaceutical companies, device manufacturers or cooperative groups. The role of the Principal diversity officer will be to ensure the promotion of DEI in clinical trials with institutional investigators and local clinics in effort to promote clinical trial participating among diverse populations. The second Institutional Diversity Officer will be appointed at the institution conducting clinical research. The Institutional Diversity Officer will ensure that research protocols adhere to DEI standards. The Institutional Diversity Officer will partner with other institutional faculty members to seek the enrollment of minority and underrepresented population in clinical trials. The ideal candidate would hold research credentials. Working in conjunction with the Principal Diversity Officer, the Institutional Diversity Officer will

work to promote the enrollment of underrepresented and diverse populations to clinical trials. Professionals serving in this capacity will posses a keen understanding of clinical research as be able to demonstrate cultural humility and awareness.

Diversity Officers will be put in place to create an infrastructure that logistically makes enrolling diverse populations on clinical trails easier. Likewise, officers will serve as a liaison between the study and the community for the purpose of utilizing training and education to build trust among the patients and cancer centers. Diversity Officers work alongside patient advisory groups to validate proposed strategies. Diversity Officers will assist in training clinical navigators and other intermediate providers in becoming instrumental in getting patients on to clinical trials by increasing trust and removing barriers.

Responsibilities of Diversity Officer

1. Prospectively develop an achievable, flexible and monitorable DEIA plan with accrual goals for diverse populations in cancer clinical research trials as required in NIH trials.
2. Establish an infrastructure to monitor and adjust recruitment efforts in a prospectively, including, when necessary, countries outside the United States to promote diversity goals, particularly in African countries where the infrastructure may not already exist.
3. Identifying impediments to meeting accrual goals at the micro-and macro-levels with the proposed solutions, including removal of exclusion criteria which disproportionately affect minorities but may not affect clinical trial results
4. Develop culturally appropriate study materials to promote minority accrual

5. Identify potential scientific questions and study design solutions for mankind and improve methods of prevention, diagnosis, and therapy in keeping with Greenberg
6. Advise the study sponsor(s) and, principal investigators and study steering committee on potential challenges and solutions

Qualifications of Diversity Office

1. Training in cancer research
2. Training in cultural awareness, sensitivity, appropriateness and diversity
3. An understanding of historical factors in precluding potential enrollment in clinical trials including, but not limited to, the Tuskegee syphilis study, Nuremberg code
4. Leadership

Training of Diversity Officer

Training programs must be developed, established, and funded by study sponsors for diversity officers at academic centers or organizations promoting the principles of DEIA in clinical research in the core areas of:

1. Clinical study design and statistics
2. Historical issues relating to diversity: slavery, racism, sexism, gender, and sexuality, with particular attention paid to understanding the Tuskegee syphilis study and the Nuremberg human experiments
3. Regulatory law and practice
4. Cultural sensitivity and awareness training

5. Understanding the interplay between safety and diversity and an understanding of the Greenberg report
6. Understanding the social construction including cultural factors and drivers in diverse communities
7. Understanding economic promoters and inhibitors of research participation in diverse communities
8. Leadership

Ranking

RANK SCOREs ranging from zero to five will be used to formally evaluate the quantity and quality of minority and underrepresented patient participation in clinical trials. RANK SCOREs are based on the achievement of minority participants representation relative to the epidemiology of disease. The D.R.I.V.E. is an informational tool used to evaluate DEIA efforts and provide a readily accessible measurement of the applicability of clinical data to all patient subgroups with the potential to force positive changes to promote DEIA and the health of mankind. RANK SCORE procedures are as follows:

1. Ranking should be reported by authors and required for all abstracts presented at major medical meetings and required for publication in peer-reviewed journals and favorably included in each journal impact factor assessment.[1]
2. Establish a reportable corporate ranking system for pharmaceutical companies based on the diversity of clinical data from the totality of studies from each company.

RANK SCORE stratification is as follows:

- RANK SCORE of 0 equates to less than 20% participation from underrepresented minorities
- RANK of 5 equates to greater than 80% participation from underrepresented minorities

RANK SCOREs will be used to determine qualifications for publication as well podium time at influential oncology society meetings. Professional society are charged with mandated with diversifying clinical trials and removing bias. For example, instruments such ASCO's Implicit Bias Training Tool will used to curve implicit bias and increase the number patients representing diverse populations being asked to go on clinical trials. Tools published by ASCO would be made public by ASCO resulting in cancer center volunteers will be equipped to reduce bias when enrolling patients on to clinical trials.

A five- year plan will be drafted resulting in professional societies being persuaded to include the RANK SCOREs as criteria for podium presentations and publication. FDA's longstanding recommendation regarding the inclusion of participants from historically underrepresented groups in clinical research will be used to promote clinical research DEIA strategies. Additionally, FDA's general strategies and tactics to enhance diversity in clinical trials shall be included as well.

The FDA diversity plan measures the sponsoring pharmaceutical company's tactics to be used to enroll participants in clinical trials. FDA's diversity plan is a dynamic document geared toward refining the sponsor's approach and tracking key metrics to determine if expectations were met or not.

Individual Plan

Clinicians, research scientists, and healthcare administrators alike should carry the mantle for DEIA in clinical trial participation. Specifically, principal investigators will be mandated to share their individual plan to sustain DEIA standards in clinical trial enrollment prior to funding and publication. It is important for professional societies to partnering with cancer centers in order to foster cultural humility and embrace equities in their mission statements. Mentorship is key tenet of creating a sense of urgency to pay attention to DEIA in method that is is not limited

to race and ethnicity but include gender identify, age, and sexual orientation.

The individual diversity plan should be used as follows:

1. To understand and address unconscious bias and develop strategies to overcome these issues in the immediate environment, community, and practice.
2. Implement a cultural competency plan and remove communication barriers. Cultural competency is defined as healthcare providers' ability to function effectively in the context of cultural differences.
3. Self-education on the historical, structural, and systemic effects of racism, redlining, and economic factors preluding or preventing enrollment in clinical trials with their applicability to the community.
4. Develop a diverse workforce and research teams and enhance your organizational DEIA plans.

The overarching goal of the individual diversity plan is to address unrecognized bias and to develop a mindset to assisting overcoming the barriers preventing clinical trial participation among ethnic minorities and underrepresented populations.

Cancer centers, principal investigators and sponsoring pharmaceutical companies hold the responsibility of taking an account of the barriers associated to clinical trial participation.

Those barriers include but are not limited to the following.

- Poor social support
- Inherit mistrust
- Narrow eligibility requirements
- Cultural bias communication between patient and provider

- Regional cultural differences i.e. southern patients vs northern patients
- Immigrant populations
- Financial limitations to include travel, lodging, meals, dependent care, and time away from work

Institutions will be persuaded to hire and train clinical navigators and intermediate providers for the purpose of increasing clinical trial participation by remove barriers, fostering trust, calming fears, initiating dialogues, and sharing the benefits of participation. Likewise, professional societies will provide the oncology space with guidance on offering patients compensation for going on clinical trials. The D.R.I.V.E. initiative will push towards establishing a pathway by which ancillary expenses such as lodging, meals, dependent care would be covered for individuals deciding to go on clinical trials.

Verification

Principal Investigators will self-report the minority and ethnic composition of clinical studies. FDA and ASCO combined strategies will be shared with Principal Investigators to broaden tril specific controls such as easing eligibility criteria, reducing burdensome procedures, and enhancing data collection practices. These actions are thought make it more palatable for diverse populations go on to clinical trials. Principal investigator research methods will be examined against Project Equity standards. Project Equity is public health program sponsored by the FDA aimed to ensure that data submitted for approval of oncology medical products reflect the demographic representation of patients from the patients being targeted. The analysis includes race, ethnicity, sex, gender, and age. Project Equity fosters transparency promoting taking active steps during

the drug development process ensuring drug sponsors are fully innovating equity within their clinical development strategies. Likewise, Principal Investigators will be encouraged to utilize FDA structural practices to promote equity across scientific work thereby addressing structural barriers that may contribute to cancer health disparities. Cancer centers as well Principal Investigators will be asked to engage the FDA regarding strategies to enroll diverse populations on to clinical trials.

Preferential considerations will be granted to studies with minimal D.R.I.V.E. RANK SCORE of greater than three in regards to podium presentations at major medical meetings and publications in journals with a high impact factor. The D.R.I.V.E. seeks to have DEIA disclosures become an early factor in publication and podium presentation akin "conflict of interest" disclosure. This will result in principal investigator to strongly consider participation among ethnic minorities and underrepresented populations very early in the design phase of the clinical study. If DEIA participation metrics are not s representative of the relative to the epidemiology of disease adjustment may be made at that point in time.

Elevate

Medical and research diversity has been shown to improve the likelihood of achieving diversity goals in clinical research[1]. Scholarships, grants, and funding mechanisms should be established to training minority /diverse investigators practicing in minority communities. Training should include physicians, advanced providers, nurses, social workers, pharmacists, navigators, medical assistants, students, and other members of the clinical and research team, with enhanced funding and training of potential investigators in historical Black colleges and medical schools ensuring that various cultures and voices are included at the point of recruitment.

The funding sources for training could be from the establishment of a research diversity fund by PHARMA, philanthropy, and

government agencies. The requirement of diversity from regulatory agencies, journal editors-in-chief, major medical societies studying PIs, and study teams will further promote the elevate goal.

The D.R.I.V.E. initiative will help to create pathways for early careerist in clinical research fields representing ethnic minorities and underrepresented populations would be encouraged and compensated for further their research careers. Feedback from patients whom hold in high regards the benefits of clinical trial participation will be shared with research professionals as method of engagement, as well.

DISCUSSION and CONLUSION

The D.R.I.V.E initiative seeks to drive impactful changes in the global issues associated with DEIA in clinical trials. Each practical step has been outlined to illustrate and emphasize problems with the current system, while offering directives to achieve the DEIA goals of the medical field. IHE formally adopted the D.R.I.V.E. step during Indianapolis Black Paper Summit on Cancer Research Disparities held on September 9, 2022 in Indianapolis, Indiana.

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