Participant Diversity in Stroke-Related Medical Device Trials: Historical Context and Ongoing Challenges

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ABSTRACT

Despite an acknowledgement of the ethical and clinical importance of recruiting diverse populations into clinical trials, there is a continued under enrollment of patients with diverse demographic characteristics within the field of Neurology and more specifically, in stroke-related device trials. Efforts on the part of the United States Congress, the National Institutes of Health, the Food and Drug Administration, and the Centers for Medicare and Medicaid Services over the last several decades have attempted to increase trial participant diversity with varying success. This historical context provides an important lens for analyzing diversity proposals and their bearing on device trials in the field of stroke neurology. Despite economic and logistical challenges, recruitment of appropriately diverse clinical trial populations through policy change and community engagement is critical to continuing to advance health equity goals.

INTRODUCTION

- There is an **ethical and clinical need for recruiting diverse populations** into clinical trials, but we continue to see under enrollment of patients with diverse demographic characteristics in many studies [1] .
- When clinical trial populations are not representative of disease populations, it limits our ability to draw conclusions about the safety and effectiveness of a therapy for patient populations.
  - This lack of representation can also impact **research innovation** and result in **economic costs** for the healthcare system (Table 1) [2].

Table 1: Considerations for trial diversity efforts

Theme	Challenge	Example
Generalizability	Lack of participant diversity within a trial can limit how applicable the results are to other groups [2].	Early genetic studies of warfarin were performed largely in populations of European descent which resulted in dosing structures that could not be adequately generalized to US populations of African and Asian descent (who carried different genetic variants) [2].
Innovation	Studies aimed specifically at exploring variation within populations can lead to clinically significant and previously unknown findings [2].	A study intentionally designed to explore variation in cardiovascular risk factors, disease, and care by demographic group (i.e., race, gender, location) resulted in the discovery of a key player in cholesterol homeostasis [2].
Economic costs	Improved trial diversity could help reduce costs associated with health disparities [2].	The Future Elderly Model, an economic model designed to estimate the potential benefit of reducing disparities in chronic disease, estimates that eliminating all life expectancy disparities for diabetes, heart disease, and hypertension has a societal value of roughly $11 trillion [2]. More inclusive clinical trials could help mitigate those outcome disparities.

METHODS

- **Literature review** conducted to explore current trends in representation within neurologic clinical trials.
- **Policy analysis** used to examine historical policies that have impacted clinical trial diversity.
  - Policies from the United States Congress, the NIH, the FDA, and the CMS explored for intended impact and challenges encountered.
- **CDC's Policy Analytical Framework** was used as a guide to identify the problem (current state of diversity in neurologic trials, current trial approval processes), analyze historical policies, and recommend directions for future policy development (Figure 1) [32].

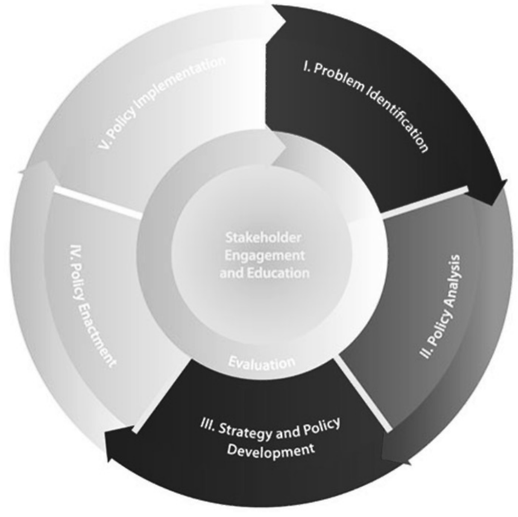

Figure 1: Policy Analytical Framework (Domains I, II, III of CDC's Policy Process)

RESULTS

- Major clinical trials in neurology have not enrolled appropriately diverse patient populations.
  - Research in many subspecialties (e.g., dementia, stroke) have revealed **underrepresentation** of several populations [4-10].
- Global neurovascular device market:
  - Represents a small percentage of the overall medical device market share but is **growing at a faster rate** than other sectors [11,12].
- Policies from Congress, the NIH, the FDA, and the CMS have had **varying success** in determining appropriate diversity requirements for trials, monitoring enrollment diversity, and linking funding and regulatory approval to clinical trial diversity requirements [2].
- **Ongoing challenges** to trial diversity efforts:
  - Balance between trial size/duration and cost, potential for justifiable exclusion of groups, lack of clear definitions for certain demographic categories, relative lack of diversity data for medical device trials [22-27].
- **Proposed efforts** to increase diverse enrollment:
  - Financial incentives (e.g., direct grants, tax credits), expanded requirements for post-approval studies/screening logs/clinical databases, community engagement [1,9,28-31].

LIMITATIONS

- The relative lack of data on diversity and the implementation of diversity efforts for medical device trials specifically required us to rely on and extrapolate from the available data for medication trials.
- This project is a review of available literature and texts, future developments or publications could affect the relevancy of these findings.

CONCLUSIONS

- Diversity in clinical trials is undoubtedly important:
  - Allows for the discovery of **clinical variation** and identification of the **best therapy** for each group of patients.
- Adoption of diversity requirements that are **too restrictive** can lead to trials that are never completed (deemed too time-consuming or too costly by sponsors).
- Trial sponsors should aim to optimize the inclusivity and generalizability of the results of a study during its design.
- Directions for **future policy development**:
  - Continued focus on actions of the federal agencies that approve and provide coverage for new therapies
  - Increased attention to site selection and community engagement
  - Further consideration of patient eligibility characteristics
  - Expanded device-specific diversity data
- **Goal**: to promote the enrollment of appropriately diverse patient populations and the generation of an evidence base for stroke-related devices that is applicable to all patients seen in clinical practice.

REFERENCES

DISCLOSURES

No outside funding was obtained for this project. Dr. John Carroll holds active consulting relationships with Abbott Vascular and ReCross Cardio. Dr. Nicole Gonzales holds a position as Associate Editor for Diversity, Equity, and Inclusion for *Neurology*. Dr. Karen Orjuela holds a position as Digital Editor for *Stroke* and has received research compensation from Abbott Laboratories and Bristol Myers Squibb Foundation .

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