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INTEGRATING HEALTH EQUITY STRATEGIES IN CLINICAL TRIALS DESIGN

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Health Policy in Action

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WHO WE ARE

Andrea Thoumi, MPP, MSc is the Area Lead, Community Health and Equity and Faculty Director, Health Equity. She brings 15 years of experience focused on reducing health inequities through health policy, health financing and community health. Her research focuses on mitigating systemic barriers that Latino/x/e communities experience and linking community-engaged research to policy changes in collaboration with interdisciplinary partners.

Sandra Yankah, PhD is a Postdoctoral Research Associate at the Duke-Margolis Center for Health Policy. Within this role, she lends her expertise to projects focused on health equity, health system improvement, and the exploration of bioethical implications at the nexus of health policy and biomedical innovation.

Trevan Locke, PhD is an Assistant Research Director at Duke-Margolis working on issues related to biomedical innovation. He oversees Duke-Margolis' involvement as a founding member of the Advancing Clinical Trials at the Point of Care Coalition and workstreams on evidence generation for Duke-Margolis' Real-World Evidence Collaborative.

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DUKE-MARGOLIS GOALS

Analyze and formulate health policy to further evidence-based, actionable, and effective solutions in three core focus areas:

Transform health care so that it is more accessible, affordable, equitable, and capable of delivering higher quality and value

Drive biomedical innovation to improve how drugs, devices, diagnostics, and medical services are developed, paid for, and used

Educate the next generation of health care leaders

Our Work


Focus Area:
Health Care Transformation
Focus Area:
Biomedical Innovation
Focus Area:
Education & Workforce Development
Cross-cutting Theme: 21st Century Public and Population Health
Cross-cutting Theme: Health Equity
Cross-cutting Theme: Global Health

KEY OBJECTIVES

1

Define the concepts of health equity, structural inequity, and trial representation

2

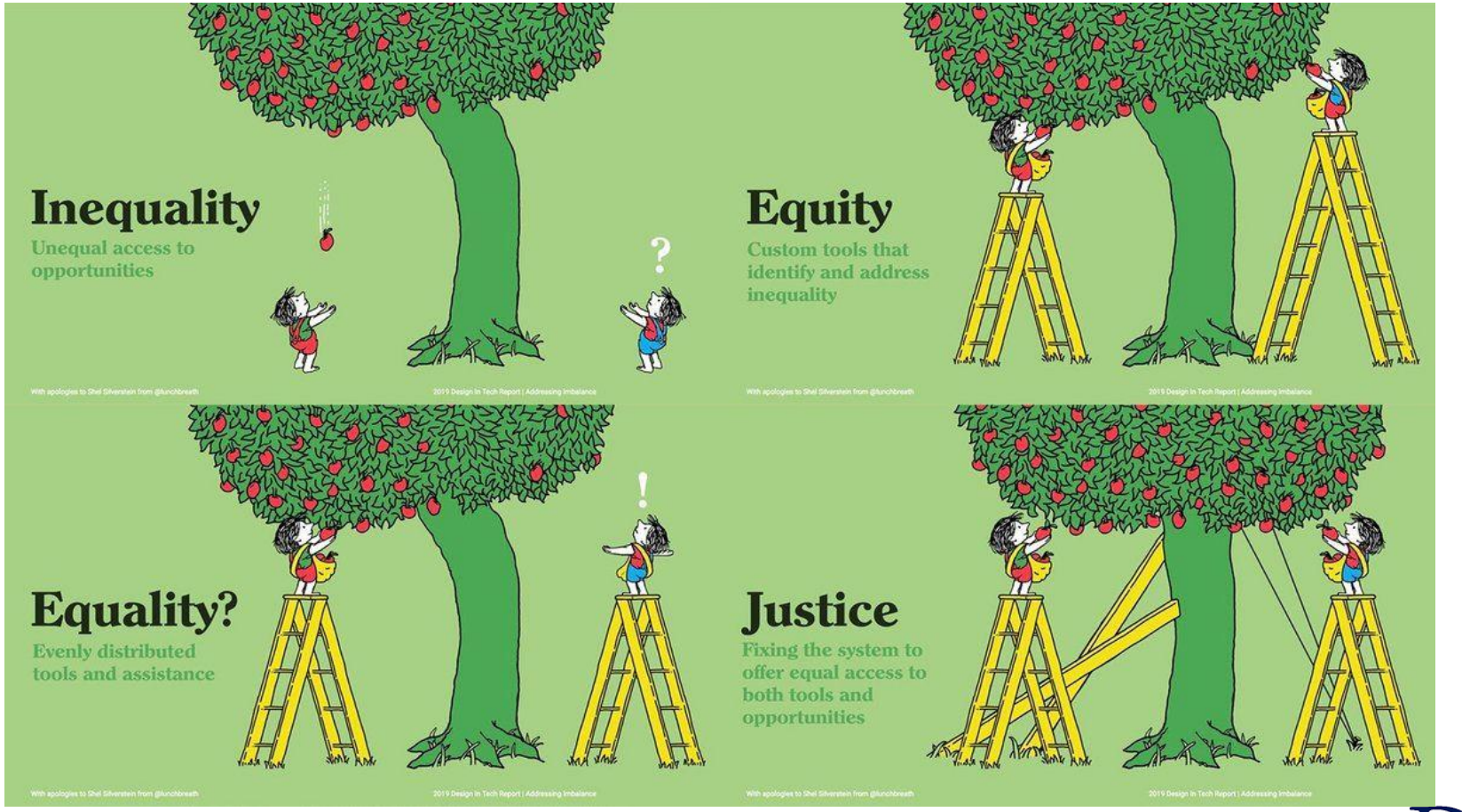
Examine the current clinical trial landscape, including individual and structural barriers to representation

3

Discuss key lessons and starting points for meaningful change

KEY TERMS & CONCEPTS

DIFFERENT RESPONSES and INTERVENTIONS



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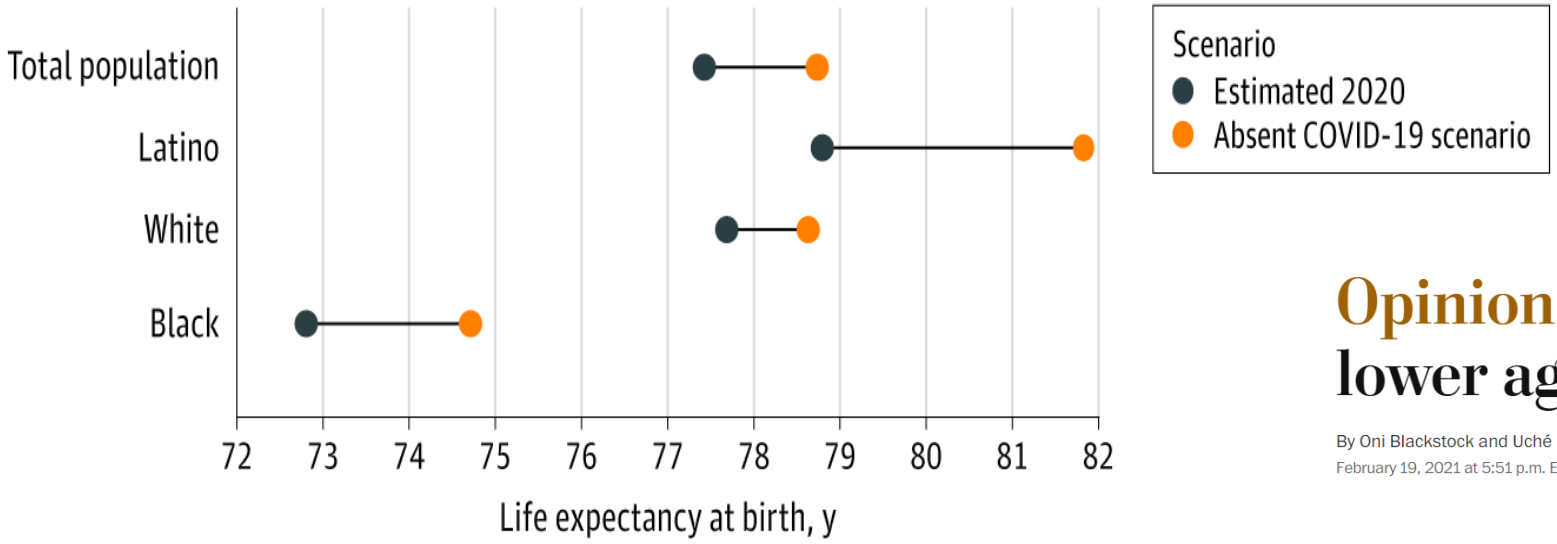
Eg: COVID-19 Vaccination Age Cut-Off: Equity or Equality

Updated Estimates of 2020 US Life Expectancy at Birth by Race and Ethnicity



Opinion | Black Americans should face lower age cutoffs to qualify for a vaccine

By Oni Blackstock and Uché Blackstock
February 19, 2021 at 5:51 p.m. EST

Figure Legend: Updated Estimates of 2020 US Life Expectancy at Birth by Race and Ethnicity Estimates for 2020 life expectancy were calculated using COVID-19 deaths reported to the National Center for Health Statistics. The absent COVID-19 scenario is assumed to be the mortality conditions of 2018.

Source: Andrasfay T, Goldman N. Association of the COVID-19 Pandemic With Estimated Life Expectancy by Race/Ethnicity in the United States, 2020. JAMA Netw Open. 2021;4(6):e2114520. doi:10.1001/jamanetworkopen.2021.14520

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SOCIAL DETERMINANTS OF HEALTH

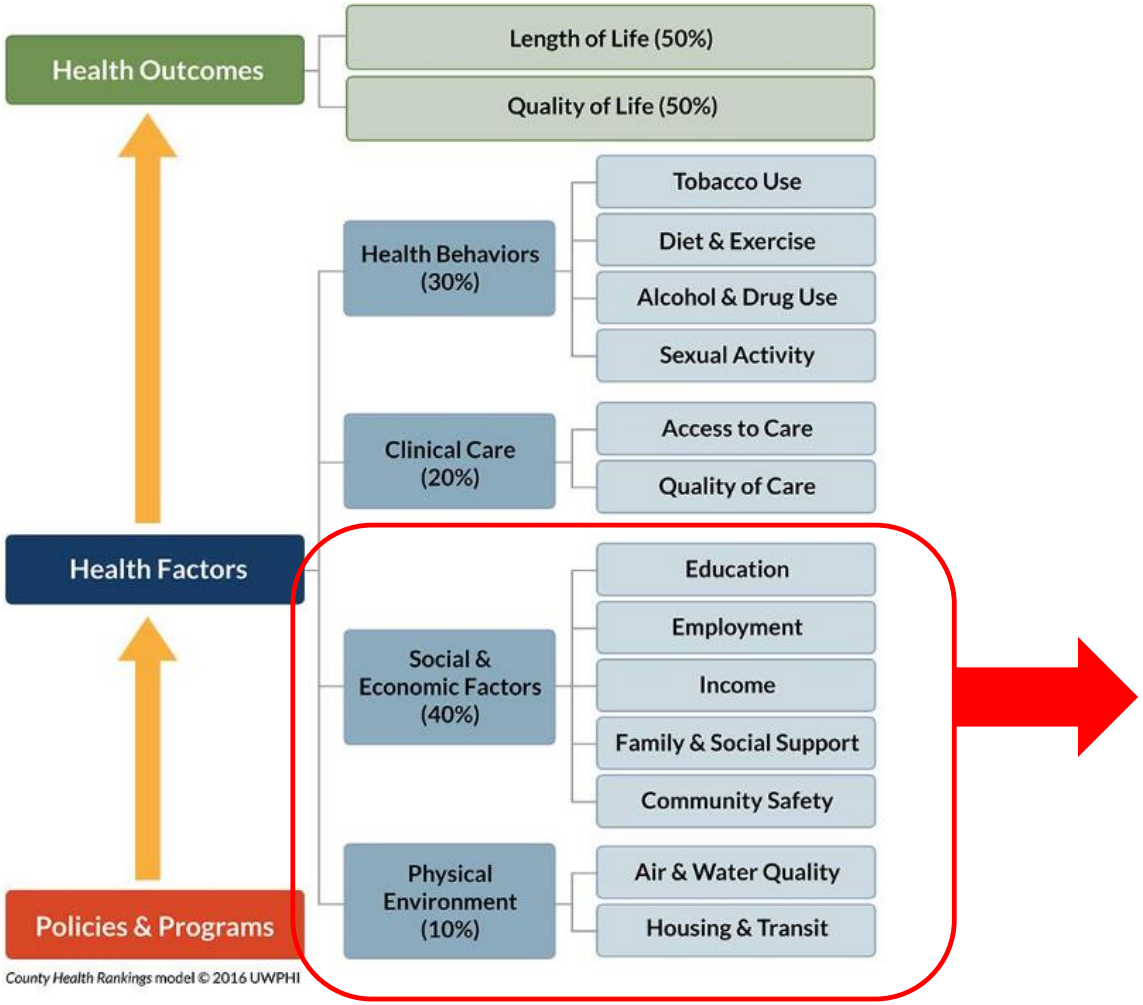

Figure 1

Social Determinants of Health

Economic Stability	Neighborhood and Physical Environment	Education	Food	Community and Social Context	Health Care System
Employment	Housing	Literacy	Hunger	Social integration	Health coverage
Income	Transportation	Language	Access to healthy options	Support systems	Provider availability
Expenses	Safety	Early childhood education		Community engagement	Provider linguistic and cultural competency
Debt	Parks	Vocational training		Discrimination	Quality of care
Medical bills	Playgrounds	Higher education		Stress	
Support	Walkability				
	Zip code / geography				

Health Outcomes
Mortality, Morbidity, Life Expectancy, Health Care Expenditures, Health Status, Functional Limitations

Source: *Kaiser Family Foundation, 2018*

KFF

Source: *National Academy of Medicine. Social Determinants of Health 101 for Health Care: Five Plus Five*

DETERMINANTS OF HEALTH THAT RESULT IN INEQUITABLE TRIAL ACCESS

- Access to health care based on **documentation status** with effects on individuals and households with mixed immigration status
- Overrepresentation in **low-wage jobs** requiring multiple jobs making it challenging to participate in trials that not provide fair compensation
- Residence in geographic areas with **lower bandwidth access**, access to a **computer, pharmacies** or **grocery stores**
- Varying degrees of **health literacy**
- Experiences of **discrimination** in the health system and other sectors leading to warranted **mistrust and low trustworthiness** of health systems
- Insufficient **language equity** or payment systems that support language equity

STRUCTURAL INEQUITIES

"Health inequity arises from root causes that could be organized in two clusters:

1. Intrapersonal, interpersonal, institutional, and systemic mechanisms (also referred to as **structural inequities**) organize the **distribution of power and resources differentially** across lines of race, gender, class, sexual orientation, gender expression, and other dimensions of individual and group identity.
2. The **unequal allocation of power and resources**—including goods, services, and societal attention—which manifests itself in unequal social, economic, and environmental conditions, also called the determinants of health."

– *National Academy of Medicine, Communities in Action*

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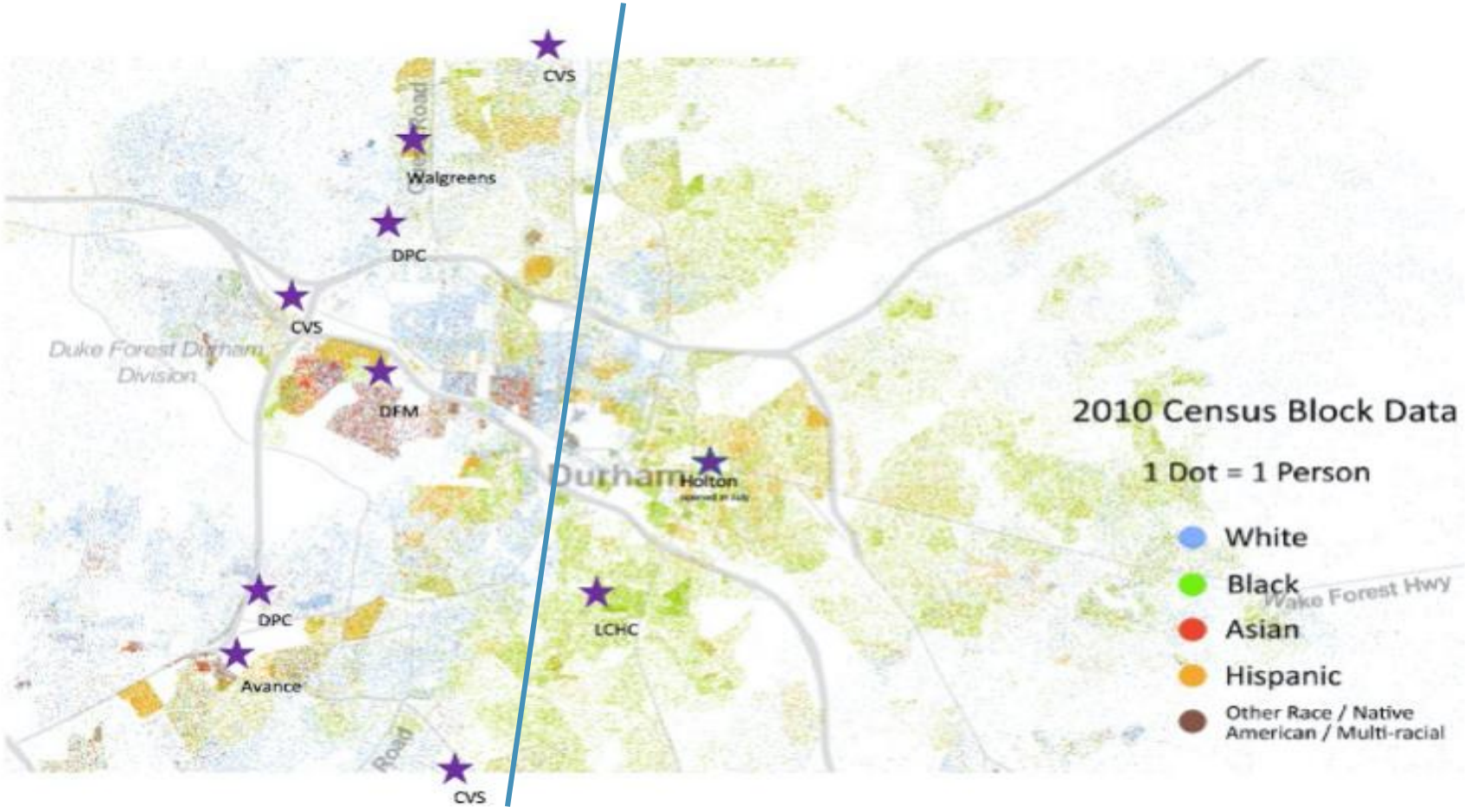
INACCESSIBLE TESTING SITES

- Geographic distribution of COVID testing sites in Durham, NC in July 2020



INACCESSIBLE CLINICAL TRIALS

The phrase term "hard-to-reach" places onus on communities rather than on decision-makers, providers, and researchers to make trials equitable and accessible.

The clinical research infrastructure has the responsibility to create accessible opportunities for all populations to receive resources and services.

COMMUNITY ENGAGEMENT IN CLINICAL TRIALS

- Embedding community health workers with bicultural and community expertise in clinical trials
- Community-informed co-development process to ensure community voices are included in research direction and trust-building

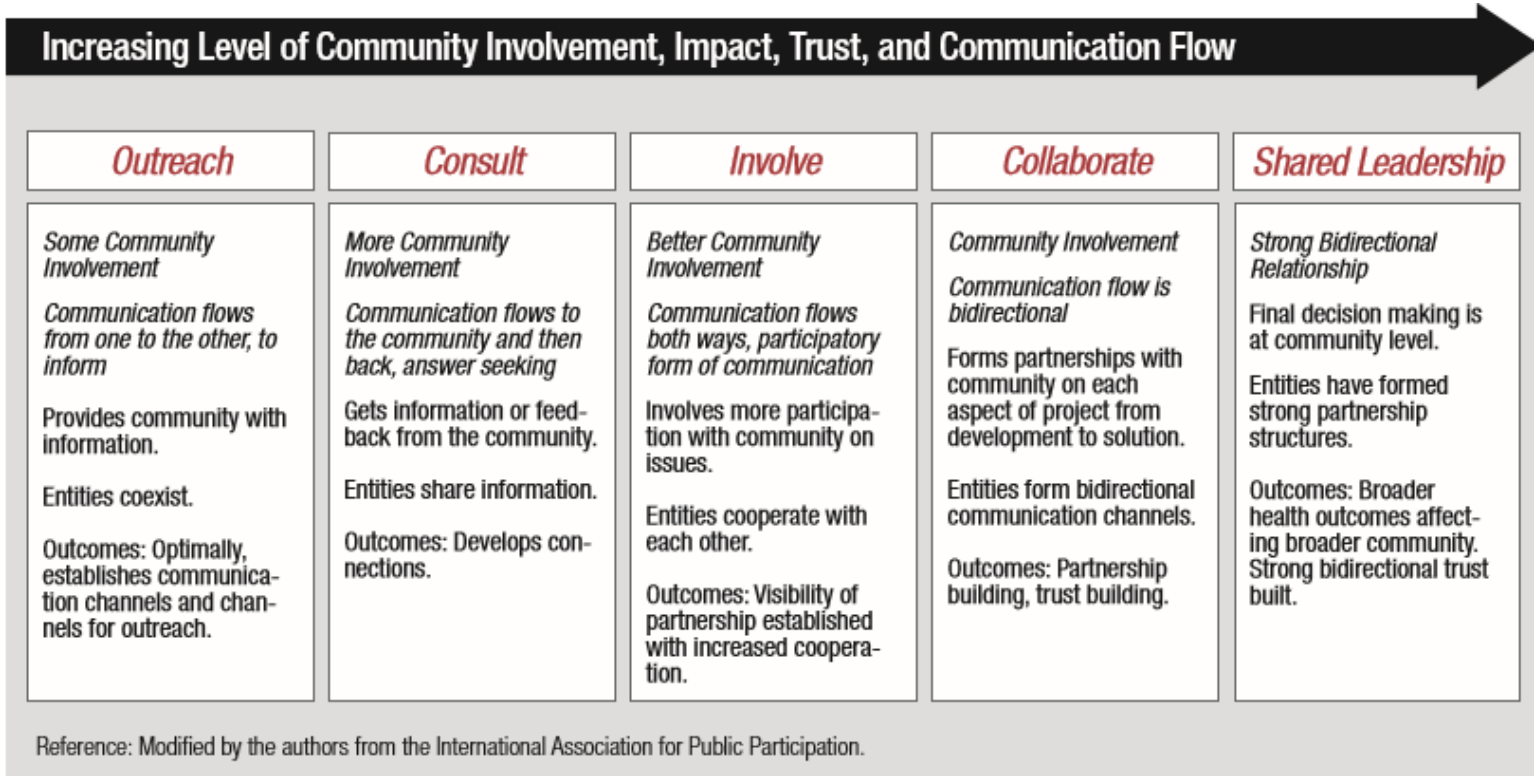


Image source: https://www.atsdr.cdc.gov/communityengagement/pce_what.html

Source: Gabriela Plasencia, Kamaria Kaalund, Andrea Thoumi, "Training Latinx Community Health Workers as Clinical Research and Health Care System Navigators", *American Journal of Public Health* 113, no. 11 (November 1, 2023): pp. 1157-1159.https://doi.org/10.2105/AJPH.2023.307418

IMPORTANCE OF COMMUNITY ENGAGEMENT AND TRUST BUILDING

- Community engagement is integral to **acknowledging** and **intervening** on systemic and structural contributors to poor trial representation
- Community engagement needs to be approached as **genuine relationships** with ongoing communication, opportunities for shared leadership, meaningful efforts to engage with community members outside of trial activities, and sustainable investment in community priorities
- To sustain these efforts, the creation of **incentives** that encourage community relationships are also needed

Clinical Trial Landscape

Overview and Level Setting

PRE-TESTING

Pre-Clinical Evaluations

Approved Protocol

Further Testing

CLINICAL RESEARCH

PHASE 1	PHASE 2	PHASE 3
		
Researchers test the safety, dosage and method of the treatment. These trials are not always specific to a type of cancer.	Based on Phase 1 trial findings, the drug or treatment is tested to see whether it is effective against a certain type of cancer.	Randomized* testing to compare new treatment with current standard of care. May become the new standard of care.
NUMBER OF PATIENTS		
15–20	100+	1000+
LENGTH		
Several Months	Months–2 Years	1–4 Years
PURPOSE		
Safety and Dosage	Efficacy, Side Effects	Assess Effectiveness

DATA ANALYSIS

Biostatistical Analysis

Determine Medically Compelling & Statistically Significant Results

FOLLOW UP

New Therapy Development

Medical Authorities

Continue Testing

Link: https://brasddp.com/clinical-trials/

Randomized Trial Approach Continuum

Explanatory Trials

Pragmatic Trials

Traditional Trials

Usually in specialized **centers; locations m**ay limit diverse patient participations

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Trial and routine care visits are separate; data from visits may not be shared (e.g. via EHRs)

Accommodates more **complex endpoints** and **detailed data collection**

Hybrid Decentralized Trials

Study visits may occur outside of specialized centers through telehealth, routine care, or remote site visit, but **often do not fully integrate workflows**

Potential to reach patients and providers who might not engage in traditional research

---

Typically feature **centralized administration**

Ability to **leverage virtual components** (e.g. wearables and web portals)

Partially Embedded Trials

May take place where patients receive routine care

Integrates some elements of research into health care delivery

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Potential to reach patients and providers closer to the point of care

---

Aligns more closely with clinical workflows

Additional patient follow-up, (e.g., lab visits) may be needed

Point-of-Care Trials

Occurs where patients receive routine care

Integrates with EHR systems for enrollment, randomization, and data collection

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Reaches patients at the point-of-care, providing **virtually indistinguishable** patient experience between research and care

---

Fully integrated care and research workflows focused on **streamlined data collection**

ACT@POC

Coalition for Advancing Clinical Trials at the Point of Care

More Complex Protocols, Less Integrated Into Care → **Simplified Protocols, More Integrated Into Care**

**Adapted from* CTTI Recommendations to Sponsors for Planning Decentralized Trials

CURRENT CHALLENGES

Many clinical trials are affected by structural and systemic complexities that can result in failure to address important research questions quickly, equitably, and efficiently

There is a growing impetus to reimagine trial conduct to improve trial representation while not compromising vital research standards

Without adequate trial representation, it is difficult to generate generalizable clinical research findings

Representative trials are good science and contribute to 1) the development of clinically meaningful medical products and 2) patient acceptability of new products upon approval

TRIAL DIVERSITY VS REPRESENTATION

- Our goal is not diversity targets for the sake of diversity targets, but rather ensuring that clinical trials are truly representative of the real-world disease burden. This encompasses race and ethnicity, but also geography, age, socioeconomic status, SDOH, and SOGI.
- An **equitable** clinical research infrastructure would be comprised of clinical trials and studies that accurately match the demographics of the disease burden under study
- It is important to acknowledge that the disease burden as quantified in the research literature and available data doesn't always reflect the actual disease burden due to disparities in care access that are a direct result of social and structural inequities

Defining the Problem

- Overall, non-Hispanic, white patients are overrepresented in clinical trials: according to 2020 FDA data, 75% of trial participants were white
- 2022 National Academies report showed little progress in enrolling underrepresented racial and ethnic patient populations
- Likewise, there are continued challenges in geographic, socioeconomic, age, and gender representation in clinical research
- One model suggests that if just 1% of health disparities were improved by better representation in clinical trials, this would lead to $40 billion in gains for diabetes and $60 billion for heart disease
    - The economic costs of clinical trial underrepresentation come from reduced life expectancy, shortened disability-free lives, and fewer years working among populations that are not proportionally represented in clinical trials

Point-of-care trials and Representativeness

- Integrating clinical research into clinical care through point-of-care trials, may provide a means to address some of the barriers resulting in both low representation and inadequate power to detect subgroup effects in clinical trials, by providing increased access to clinical research where people receive care, lowering infrastructure costs to conduct trials, and enabling larger trial sizes
- Point-of-care trials have the potential to simplify trial conduct and increase evidence on particular subgroups, by increasing access to clinical research for real-world populations while eliminating the need for large-scale, single-use trial infrastructure
- Infrastructure is improving to engage people in clinical research where they receive their usual care – with a growing number of countries undertaking efforts to improve point of care participation in clinical trials

The Current Landscape

- The federal government as well as private research foundations have set standards and requirements for encouraging representativeness in clinical trials. Under new FDA reform legislation (Public law No 117-328) passed by Congress in 2022, FDA will require drug sponsors to submit diversity action plans for their trials.
- In 2020, Congress passed the Clinical Trial Treatment Act, which requires all state Medicaid programs to cover routine costs associated with qualifying clinical trials. This act went into effect beginning in 2022.
- In 2022, the National Academies released a report titled: Improving Representation in Clinical Trials and Research: Building Research Equity for Women and Underrepresented Groups
- In 2023, CTTI released recommendations for improving diversity in clinical trials and a corresponding maturity model
- Trial sponsors, payers, academic journals, and other stakeholders have engaged in voluntary efforts to increase trial representation

Starting Points for Change

OUR AIMS

- Encourage coordination and accountability to reduce redundant and conflicting endeavors that hinder overall progress
- Illuminate existing obstacles and areas ripe for improvement.
- Spotlight systemic equity barriers and encourage the integration of clinical trials across diverse healthcare settings and contexts

Achieving Representativeness Requires Continued Focus and Accountability Across Stakeholders

- All stakeholders have a role in achieving measurable progress in achieving clinical trial diversity – toward the goal of reducing health disparities
- Clinical leaders and regulators, in individual countries and international organizations, can help set expectations and achieve measurable progress toward representative trials informed by patient and community needs

Source: https://mrctcenter.org/diversity-in-clinical-research/guidance/action-for-change/

Starting Points for Driving Action and Accountability

Stakeholder	Roles and Potential Actions
Regulators	• Require diversity action plans for all submitted trials • Assess content of plans for thoroughness and thoughtfulness and produce additional resources to drive creation of high quality plans • Continue providing general public directed educational resources on clinical research and related topics that are culturally and linguistically considerate
Industry	• Support sustainable clinical research ecosystems in a broad range of local and community sites and settings • Develop and adhere to high quality diversity action plans, leveraging post-market research to address any gaps
NIH and non-industry funders	• Requiring and enforcing a plan (e.g., through current or future funding penalties) for enrollment in a sponsor's grant submission that is aligned with the demographics and disease burden of the condition. • Prerequisite of funding to develop enrollment plans early, how sponsor will engage with communities throughout each phase of the trial, and how they will enroll patients most impacted by that disease

Starting Points for Driving Action and Accountability

Stakeholder	Roles and Potential Actions
Policy and Research oriented Non-profits	• Conduct research and establish best practices towards data collection and evaluation of ongoing efforts • Continue engaging the broader stakeholder community and communicate findings in easily digestible formats
Journals	• Create a score or metric that can report out how well published trials meet representation expectations • Require authors disclose the anticipated representativeness of the study sample and deviations in final trial populations
Health systems/ providers	• Support the development of a diverse workforce trained in clinical research principles • Support sustainable clinical research ecosystems throughout catchment areas leveraging academic center expertise where appropriate • Create systems that make potential trial participants aware of opportunities to participate in research and actively ask for participation
IRBs	• Include representativeness expectations as part of IRB review • Consider incorporation of or collaboration with community based review to ensure resources are put towards areas that matter to local communities

Key Takeaways

1. Addressing the complex equity involves confronting **structural racism** within the healthcare system and promoting **robust community engagement**. These factors are pivotal for achieving inclusive clinical trials.
2. By bringing together stakeholder across the clinical trial enterprise we have the ability to **harness collective expertise and resources** to tackle the systemic barriers and disparities that hinder representative enrollment.
3. To ensure accountability, we propose strategic investments and coordinated efforts within a **policy framework**

Open Questions

- **Can we develop better, more consistent measures of clinical trial diversity?**
- **How do we scale successful community engagement strategies?**
- **How do we drive organizational and collective accountability for improving representation?**
- **How can we leverage policy reform to drive change?**

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Duke-Margolis Resources

- Advancing Representativeness in Clinical Trials
  Event: https://healthpolicy.duke.edu/events/advancing-representative-enrollment-clinical-trials

- Gabriela Plasencia, Kamaria Kaalund, Andrea Thoumi, “Training Latinx Community Health Workers as Clinical Research and Health Care System Navigators”, *American Journal of Public Health* 113, no. 11 (November 1, 2023): pp. 1157-1159. https://doi.org/10.2105/AJPH.2023.307418

- Kaalund K, Phillips EJ, Farrar B, Perreira K, Taylor M, Wellman M, Dave G, Kibbe W, Cohen-Wolkowiez M, Thoumi A. Opportunities to Enhance Health Equity by Integrating Community Health Workers into Payment and Care Delivery Reforms. Washington, DC: Duke-Margolis Center for Health Policy, UNC CHER, DCRI; 2023

THANK YOU!

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