Advancing Representative Enrollment in Clinical Trials

July 18, 2023

12:00pm-4:00pm ET

Duke | MARGOLIS CENTER *for* Health Policy

Welcome

Trevan Locke

Statement of Independence

The Robert J. Margolis, MD, Center for Health Policy is part of Duke University, and as such it honors the tradition of academic independence on the part of its faculty and scholars. Neither Duke nor the Margolis Center take partisan positions, but the individual members are free to speak their minds and express their opinions regarding important issues.

For more details on relevant institutional policies, please refer to the Duke Faculty Handbook, including the Code of Conduct and other policies and procedures. In addition, regarding positions on legislation and advocacy, Duke University policies are available at http://publicaffairs.duke.edu/government.

Remote Participation Instructions

Meeting Materials

- The meeting agenda and a brief background document are currently available on the Duke-Margolis website.
- A recording of the meeting and slides will be available on the Duke-Margolis website within a few business days.

Questions

- Please feel free to type your question into the Q&A box and we will use

your questions to inform the open discussion portions of the event.

Zoom Issues?

- Please send a Zoom message to Luke Durocher or email luke.durocher@duke.edu

Agenda

12:00pm ET	Welcome and Opening Remarks
12:10pm ET	Presentation
12:25pm ET	Session 1: Defining the Current Clinical Trial Landscape
1:25pm ET	Break
1:35pm ET	Session 2: Building Capacity for Representative Trials in Community Settings
2:35pm ET	Fireside Chat
2:55pm ET	Session 3: Defining the Role of Various Stakeholders in Improving Trial Representation
3:55pm ET	Closing Remarks & Next Steps
4:00pm ET	Adjournment

Why are we here?

- 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.

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

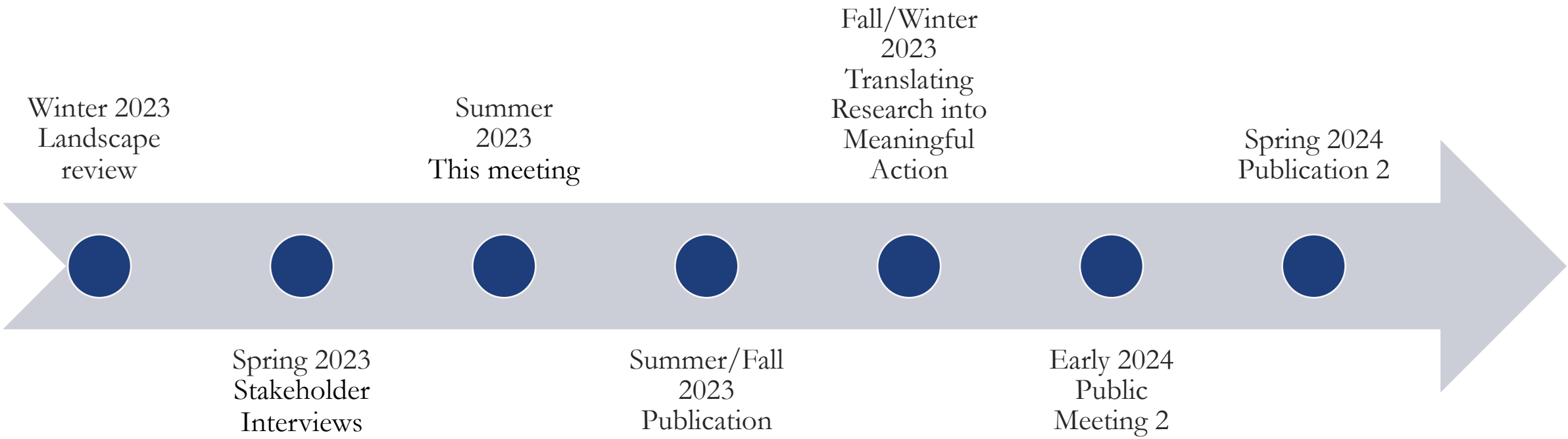
Trial Diversity Vs Representation

- 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 literature or the available data doesn't always reflect the actual disease burden due to disparities in care access that are a direct result of structural racism and discrimination

The Current Policy 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

Duke-Margolis and Trial Representation



Theme 1: Measurement Considerations for Assessing Trial Representativeness

- Prevalence rates, while a better baseline than census percentages, may not be wholly accurate representations of disease burden
- Race and ethnicity are flawed and often poorly collected variables that are surrogates for deeper demographic characteristics.
- There is a need for improved measurement of race and ethnicity data but also better measures of SDOH, SOGI, and other demographic measures to build a more holistic to representation
- With that in mind, stakeholders need to work toward widespread adoption and consistency in benchmarks used to evaluate representation and align representation metrics nationally and internationally

Theme 2: Barriers and Opportunities in Sustainable Community and Patient Engagement

- Historic and current health system and research practices that discourage trial participation
- Researchers and sponsors should establish ongoing relationships with organizations in the community to adequately gauge community needs and build sustainable research networks
- Trials sponsors and researchers can make more overt efforts to align funding and provide broader benefits for participants
- Sponsors and researchers should consider methods for providing sustainable benefits to the community, either in the form of knowledge or related programs and infrastructure

Theme 3: Modernizing Trial Processes through Pragmatic Design Approaches

- Pragmatic trials can be more flexible and accommodating to patients than traditional explanatory trials, especially when they take place in community settings
- Pragmatic trials can reduce the amount of resources patients need to participate in trials, and often leverage their existing trusted healthcare provider relationships for increased patient comfort with research

Theme 4: Importance of Instituting Formal Policies

- Regulatory agencies, funders, and research institutions can implement more overt rules and regulations to ensure that representation is not an afterthought in clinical trials
- Examples include:
  - Regulatory and funding requirements for applicants to submit a representative enrollment plan *before* conducting a study, including the new guidance from the FDA on diversity plans.
  - Research journal publication requirements around publishing metrics for representative enrollment.
  - Modifying existing funding structures to make it easier to provide compensation to community workers and patient-facing groups.

Point-of-Care trials and Representation

- Broader work by Duke-Margolis and collaborators centers around advancing point-of-care trials as one component of a modern clinical trial enterprise.
- Integrating clinical research into clinical care through point-of-care trials, may provide a means of solving some of the barriers resulting in low representation in clinical trials by providing increased access to clinical research where people receive care and increasing patient comfort with research in some cases.
- Throughout our conversations today you'll hear about point-of-care trials as we consider their potential role in addressing issues related to trial representation.
- This is a new approach to clinical research, and stakeholder input can shape future trial design. As clinical research evolves, it will be important to keep representation in mind.

Defining Point-of-Care-Trials

- Operational approach to data collection that integrates clinical research into routine care
  - Key clinical trial operations (patient screening, consent, randomization, and data collection) are incorporated into routine care through electronic health records platforms
  - Trial conduct is completed in usual care conditions without significant differentiation for patients; and research and clinical care delivery workflows are integrated
- Point-of-care trials have the potential to simplify trial conduct, lower costs, and improve generalizability by increasing access to clinical research for real-world populations while eliminating the need for large-scale, single-use trial infrastructure

Acknowledging and addressing systemic issues

- While these trial approaches may improve the representativeness of clinical trial cohorts, meaningful, sustainable change may be difficult in a clinical trials enterprise that is heavily impacted by and helps maintain larger structural and societal problems
- Avoiding "recruitmentology" tactics is important in not further exploiting research subjects and narrowing the gap in comfort levels between different groups that may participate in clinical trials
- Systemic barriers such as a lack of insurance, transportation, resources, etc. as well as limited bilingual or bicultural clinical personnel to staff and lead clinical trials, will continue to be a concern for trial participation and may impact retention
- Creating longstanding and sustainable partnerships across sectors and stakeholders has proven difficult due to misalignment of funding and power structures

Session 1: Defining the Current Clinical Trial Landscape

Moderator: Trevan Locke, Duke-Margolis
Jen Miller, Yale School of Medicine
Lola Fashoyin-Aje, Oncology Center for Excellence, FDA
Sneha Dave, Generation Patient

Measuring Clinical Trial Representativeness

Jennifer E. Miller, PhD

- Associate Professor, Yale School of Medicine
- Founding President, Bioethics International
- Director, Good Pharma Scorecard
- @millerbioethics Jennifer.e.miller@yale.edu

Duke Margolis Center for Health Policy, July 18, 2023

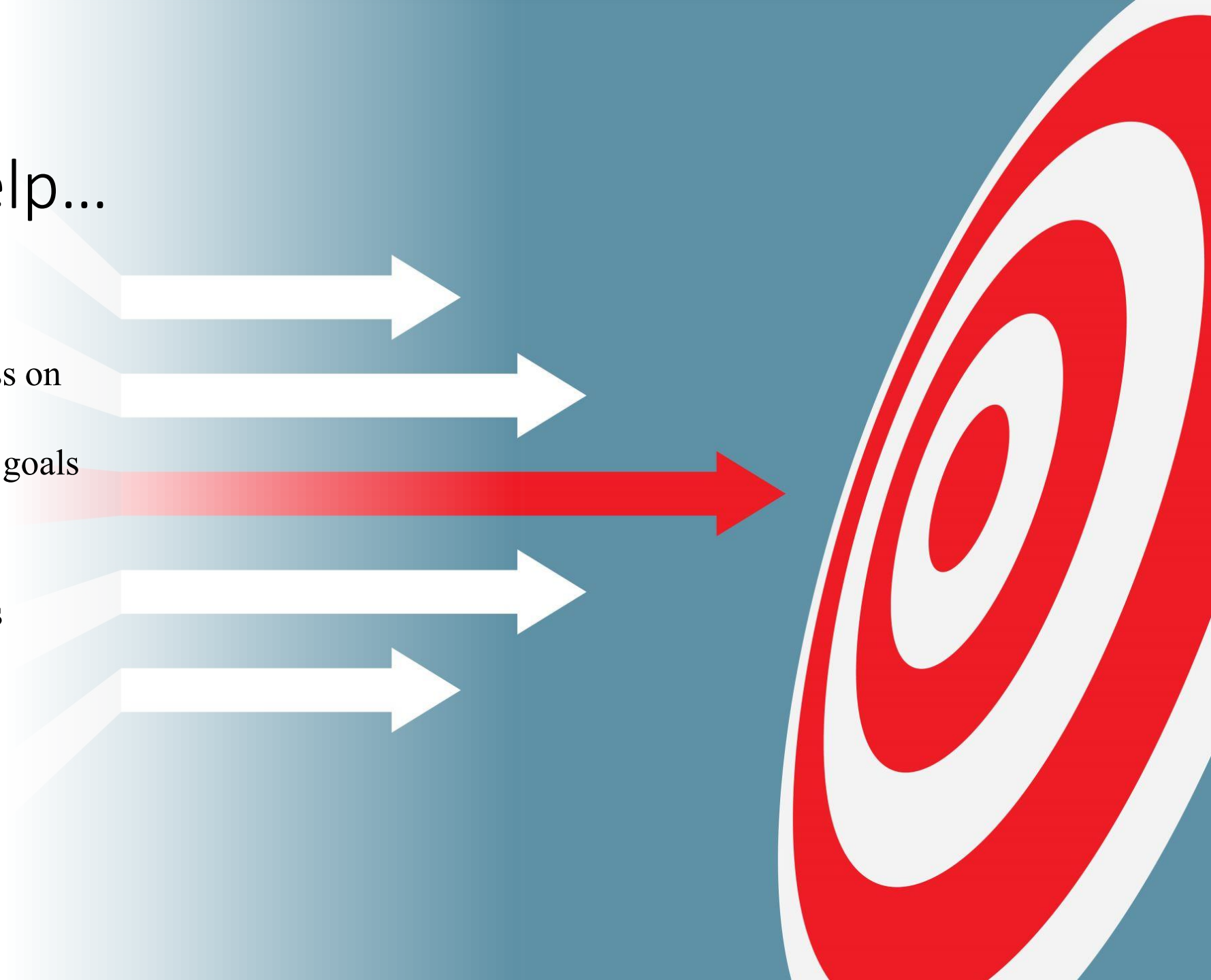
Yale School of Medicine

What is the Good Pharma Scorecard (GPS)?

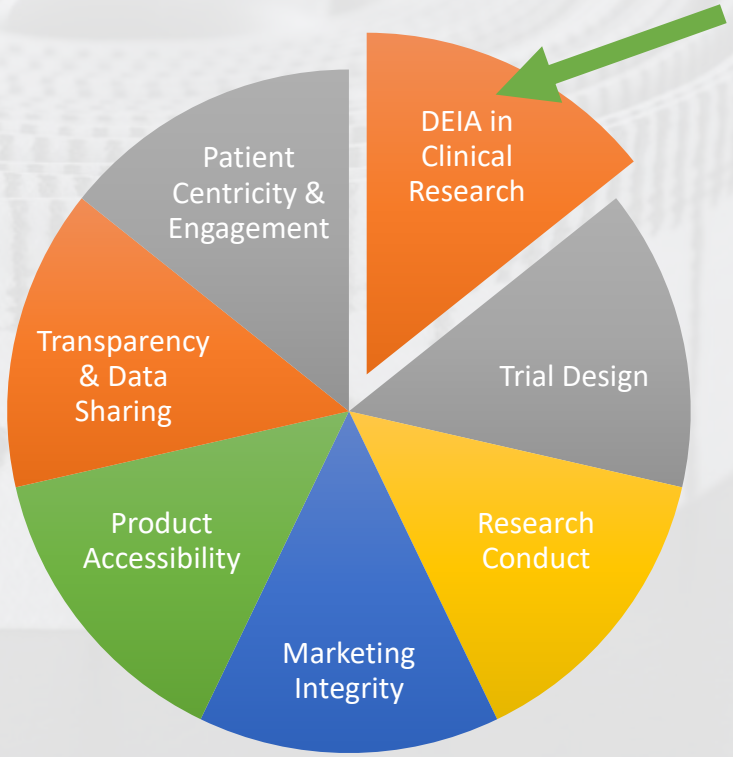
- An index that rates + ranks bio-pharmaceutical companies on their bioethics + social responsibility performance
- Housed at Bioethics International, a nonprofit founded in 2005
- Supported by investigators at Stanford University + Yale School of Medicine
- Disseminated in partnership w Scientific American

Scorecards help…

- Educate + raise awareness on issues
- Set + communicate clear goals
- Track progress on goals
- Recognize best practices
- Catalyze better behaviors



GPS Areas of Focus



Studies show a lack of diversity in clinical trials

- We tend to test new medicines & vaccines in patients who are healthier, younger and more likely to identify as white and male than real world US patients with targeted conditions.

ORIGINAL CONTRIBUTION

Participation in Cancer Clinical Trials

Race-, Sex-, and Age-Based Disparities

Vivek H. Murthy, MD, MBA
Harlan M. Krumholz, MD, SM
Cary P. Gross, MD

TEN YEARS HAVE PASSED SINCE Congress responded to concerns about unequal access to clinical trials and enacted the National Institutes of Health (NIH) Revitalization Act, which encouraged representation of women and minority patients in NIH-sponsored research.[1] Ensuring broad access to research studies has subsequently been an important aim of national research policy. The National Cancer Institute (NCI) has addressed concerns about enhancing heterogeneity of trial populations through multiple mechanisms, including the creation of Minority Community Clinical Oncology Programs, the development of focused initiatives in partnership with the Centers for Disease Control and Prevention and academic medical centers, and emphasis on trials that focus specifically on the elderly.[2,3] Moreover, while the NCI budget has grown from approximately $2 billion in 1993 to approximately $4 billion in 2002,[4] and the number of trial participants has increased, it is not clear if minorities, women, and the elderly have shared in this growth.[3]

Investigations of race- and sex-based disparities in cancer trial participation have yielded conflicting results. A study of black and Hispanic participation between 1991 and 1994 concluded that these groups were represented in cancer trial populations in equal proportion to the cancer disease burden in these groups.[5] This report was confirmed by a subsequent analysis of enrollment by the Southwestern Oncology Group that compared the proportion of blacks and Hispanics enrolled in trials for 13 cancer types with their share of the US cancer population between 1993 and 1996.[3] Nota-

Context Despite the importance of diversity of cancer trial participants with regard to race, ethnicity, age, and sex, there is little recent information about the representation of these groups in clinical trials.

Objective To characterize the representation of racial and ethnic minorities, the elderly, and women in cancer trials sponsored by the National Cancer Institute.

Design, Setting, and Patients Cross-sectional population-based analysis of all participants in therapeutic nonsurgical National Cancer Institute Clinical Trial Cooperative Group breast, colorectal, lung, and prostate cancer clinical trials in 2000 through 2002. In a separate analysis, the ethnic distribution of patients enrolled in 2000 through 2002 was compared with those enrolled in 1996 through 1998, using logistic regression models to estimate the relative risk ratio of enrollment for racial and ethnic minorities to that of white patients during these time periods.

Main Outcome Measure Enrollment fraction, defined as the number of trial enrollees divided by the estimated US cancer cases in each race and age subgroup.

Results Cancer research participation varied significantly across racial/ethnic and age groups. Compared with a 1.8% enrollment fraction among white patients, lower enrollment fractions were noted in Hispanic (1.3%; odds ratio [OR] vs whites, 0.72; 95% confidence interval [CI], 0.68–0.77; $P<.001$) and black (1.3%; OR, 0.71; 95% CI, 0.68–0.74; $P<.001$) patients. There was a strong relationship between age and enrollment fraction, with trial participants 30 to 64 years of age representing 3.0% of incident cancer patients in that age group, in comparison to 1.3% of 65- to 74-year-old patients and 0.5% of patients 75 years of age and older. This inverse relationship between age and trial enrollment fraction was consistent across racial and ethnic groups. Although the total number of trial participants increased during our study period, the representation of racial and ethnic minorities decreased. In comparison to whites, after adjusting for age, cancer type, and sex, patients enrolled in 2000 through 2002 were 24% less likely to be black (adjusted relative risk ratio, 0.76; 95% CI, 0.65–0.89; $P<.001$). Men were more likely than women to enroll in colorectal cancer trials (enrollment fractions: 2.1% vs 1.6%, respectively; OR, 1.30; 95% CI, 1.24–1.35; $P<.001$) and lung cancer trials (enrollment fractions: 0.9% vs 0.7%, respectively; OR, 1.23; 95% CI, 1.16–1.31; $P<.001$).

Conclusions Enrollment in cancer trials is low for all patient groups. Racial and ethnic minorities, women, and the elderly were less likely to enroll in cooperative group cancer trials than were whites, men, and younger patients, respectively. The proportion of trial participants who are black has declined in recent years.

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See also Patient Page.

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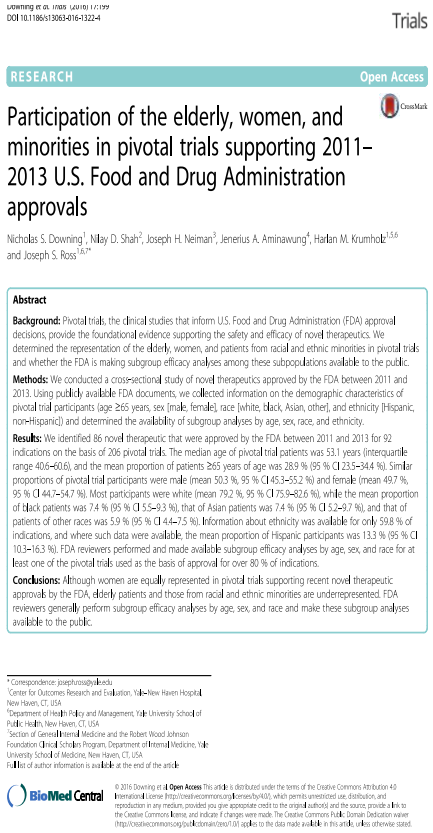

Downing et al. Trials (2016) 17:169
DOI 10.1186/s13063-016-1322-4

Trials

RESEARCH Open Access

Participation of the elderly, women, and minorities in pivotal trials supporting 2011–2013 U.S. Food and Drug Administration approvals

Nicholas S. Downing[1], Nilay D. Shah[2], Joseph H. Neiman[3], Jenerius A. Aminawung[4], Harlan M. Krumholz[1,5,6] and Joseph S. Ross[1,6,7*]

Abstract

Background: Pivotal trials, the clinical studies that inform U.S. Food and Drug Administration (FDA) approval decisions, provide the foundational evidence supporting the safety and efficacy of novel therapeutics. We determined the representation of the elderly, women, and patients from racial and ethnic minorities in pivotal trials and whether the FDA is making subgroup efficacy analyses among these subpopulations available to the public.

Methods: We conducted a cross-sectional study of novel therapeutics approved by the FDA between 2011 and 2013. Using publicly available FDA documents, we collected information on the demographic characteristics of pivotal trial participants (age ≥65 years, sex [male, female], race [white, black, Asian, other], and ethnicity [Hispanic, non-Hispanic]) and determined the availability of subgroup analyses by age, sex, race, and ethnicity.

Results: We identified 86 novel therapeutic that were approved by the FDA between 2011 and 2013 for 92 indications on the basis of 206 pivotal trials. The median age of pivotal trial patients was 53.1 years (interquartile range 40.6–60.6), and the mean proportion of patients ≥65 years of age was 28.9 % (95 % CI 23.5–34.4 %). Similar proportions of pivotal trial participants were male (mean 50.3 %, 95 % CI 45.3–55.2 %) and female (mean 49.7 %, 95 % CI 44.7–54.7 %). Most participants were white (mean 79.2 %, 95 % CI 75.9–82.6 %), while the mean proportion of black patients was 7.4 % (95 % CI 5.5–9.3 %), that of Asian patients was 7.4 % (95 % CI 5.2–9.7 %), and that of patients of other races was 5.9 % (95 % CI 4.4–7.5 %). Information about ethnicity was available for only 59.8 % of indications, and where such data were available, the mean proportion of Hispanic participants was 13.3 % (95 % CI 10.2–16.3 %). FDA reviewers performed and made available subgroup efficacy analyses by age, sex, and race for at least one of the pivotal trials used as the basis of approval for over 80 % of indications.

Conclusions: Although women are equally represented in pivotal trials supporting recent novel therapeutic approvals by the FDA, elderly patients and those from racial and ethnic minorities are underrepresented. FDA reviewers generally perform subgroup efficacy analyses by age, sex, and race and make these subgroup analyses available to the public.

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JAMA Network Open.

Original Investigation | Health Policy

Reporting of Study Participant Demographic Characteristics and Demographic Representation in Premarketing and Postmarketing Studies of Novel Cancer Therapeutics

Jarvee Varma, BA; Joshua D. Wallach, PhD, MS; Jennifer E. Miller, PhD; Dominic Schnabel, MPH; Joshua J. Skydel, BS; Audrey D. Zhang, MD; Michaela A. Dinan, PhD; Joseph S. Ross, MD, MHS; Cary P. Gross, MD

Abstract

IMPORTANCE Adequate representation of demographic subgroups in premarketing and postmarketing clinical studies is necessary for understanding the safety and efficacy associated with novel cancer therapeutics.

OBJECTIVE To characterize and compare the reporting of demographic data and the representation of individuals by sex, age, and race in premarketing and postmarketing studies used by the Food and Drug Administration (FDA) to evaluate novel cancer therapeutics.

DESIGN, SETTING, AND PARTICIPANTS In this cross-sectional study, premarketing and postmarketing studies for novel cancer therapeutics approved by the FDA from 2012 through 2016 were identified. Study demographic information was abstracted from publicly available sources, and US cancer population demographic data was abstracted from US Cancer Statistics. Analyses were conducted from February 25 through September 21, 2020.

MAIN OUTCOMES AND MEASURES The percentages of trials reporting sex, age, and race/ethnicity were calculated, and participation to prevalence ratios (PPRs) were calculated by dividing the percentage of study participants in each demographic group by the percentage of the US cancer population in each group. PPRs were constructed for premarketing and postmarketing studies and by cancer type. Underrepresentation was defined as PPR less than 0.8.

RESULTS From 2012 through 2016, the FDA approved 45 cancer therapeutics. The study sample included 77 premarketing studies and 56 postmarketing studies. Postmarketing studies, compared with premarketing studies, were less likely to report patient sex (42 studies reporting [75.0%] vs 77 studies reporting [100%]; $P < .001$) and race (27 studies reporting [48.2%] vs 62 studies reporting [80.5%]; $P < .001$). Women were adequately represented in premarketing studies (mean [SD] PPR, 0.91; 95% CI, 0.90-0.91) and postmarketing studies (mean PPR, 1.00; 95% CI, 1.00-1.01). Although older adults and Black patients were underrepresented in premarketing studies (older adults: mean PPR, 0.73; 95% CI, 0.72-0.74; Black patients: mean PPR, 0.32; 95% CI, 0.31-0.32), these groups continued to be underrepresented in postmarketing studies (older adults: mean PPR, 0.75; 95% CI, 0.75-0.76; Black patients: mean PPR, 0.21; 95% CI, 0.21-0.21).

CONCLUSIONS AND RELEVANCE This study found that older adults and Black patients were underrepresented in premarketing studies of novel cancer therapeutics to a similar degree that they were underrepresented in premarketing studies. These findings suggest that postmarketing studies are not associated with improvements to gaps in demographic representation present at the time of FDA approval.

Key Points

Question Are the demographic characteristics of patients enrolled in premarketing and postmarketing studies used by the US Food and Drug Administration (FDA) to evaluate the safety and efficacy of novel cancer therapeutics clearly reported and representative of the US cancer population?

Findings In this cross-sectional study of 77 premarketing studies and 56 postmarketing studies for FDA-approved cancer therapeutics, there was inconsistent reporting of demographic data and underrepresentation of older adults and Black patients in premarketing and postmarketing studies of cancer therapeutics.

Meaning Premarketing and postmarketing studies used by the FDA to evaluate novel cancer therapeutics may not adequately represent the US cancer population.

+ Invited Commentary
+ Supplemental content

Author affiliations and article information are listed at the end of this article.

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Research

JAMA Oncology | Original Investigation

Disparity of Race Reporting and Representation in Clinical Trials Leading to Cancer Drug Approvals From 2008 to 2018

Jonathan M. Loree, MD; Seerat Anand, MBBS; Arvind Dasari, MD; Joseph M. Unger, PhD; Anirudh Gothwal, Lee M. Ellis, MD; Gauri Varadhachary, MD; Scott Kopetz, MD; Michael J. Overman, MD; Kanwal Raghav, MD

Supplemental content

IMPORTANCE Representative racial/ethnic participation in research, especially in clinical trials that establish standards of care, is necessary to minimize disparities in outcomes and to uphold societal equity in health care.

OBJECTIVE To evaluate the frequency of race reporting and proportional race representation in trials supporting US Food and Drug Administration (FDA) oncology drug approvals.

DESIGN, SETTING, AND PARTICIPANTS Database study of all reported trials supporting FDA oncology drug approvals granted between July 2008 and June 2018. Primary reports of trials were obtained from PubMed and ClinicalTrials.gov. Food and Drug Administration approvals were identified using the FDA archives. The US population-based cancer estimates by race were calculated using National Cancer Institute–Surveillance, Epidemiology, and End Results and US Census databases.

MAIN OUTCOMES AND MEASURES Primary outcomes were the proportion of trials reporting race and the proportion of patients by race participating in trials. Secondary outcomes included race subgroup analyses reporting and gaps between race proportion in trials and the US population. Descriptive statistics, Fisher exact, and χ^2 tests were used to analyze the data. Proportions and odds ratios (OR) with 95% CIs were reported.

RESULTS Among 230 trials with a total of 112 293 participants, 145 (63.0%) reported on at least 1 race, 18 (7.8%) documented the 4 major races in the United States (white, Asian, black, and Hispanic), and 58 (25.2%) reported race subgroup analyses. Reporting on white, Asian, black, and Hispanic races was included in 144 (62.6%), 110 (47.8%), 88 (38.2%), and 23 (10.0%) trials, respectively. Between July 2008 and June 2013 vs July 2013 and June 2018, the number of trials reporting race (45 [56.6%] vs 100 [67.1%]; OR, 1.63; 95% CI, 0.93-2.87; $P = .09$) and race subgroup analysis (13 [16.1%] vs 45 [30.2%]; OR, 2.26; 95% CI, 1.16-4.67; $P = .03$) changed minimally and varied across races. Whites, Asians, blacks, and Hispanics represented 76.3%, 18.3%, 3.1% and 6.1% of trial participants, respectively, and the proportion for each race enrolled over time changed nominally (blacks, 3.6% vs 2.9% and Hispanics, 5.3% vs 6.7%) from July 2008 to June 2013 vs July 2013 to June 2018. Compared with their proportion of US cancer incidence, blacks (22% of expected) and Hispanics (44% of expected) were underrepresented compared with whites (98% of expected) and Asians (438% of expected).

CONCLUSIONS AND RELEVANCE Race and race subgroup analysis reporting occurs infrequently, and black and Hispanic races are consistently underrepresented compared with their burden of cancer incidence in landmark trials that led to FDA oncology drug approvals. Enhanced minority engagement is needed in trials to ensure the validity of results and reliable benefits to all.

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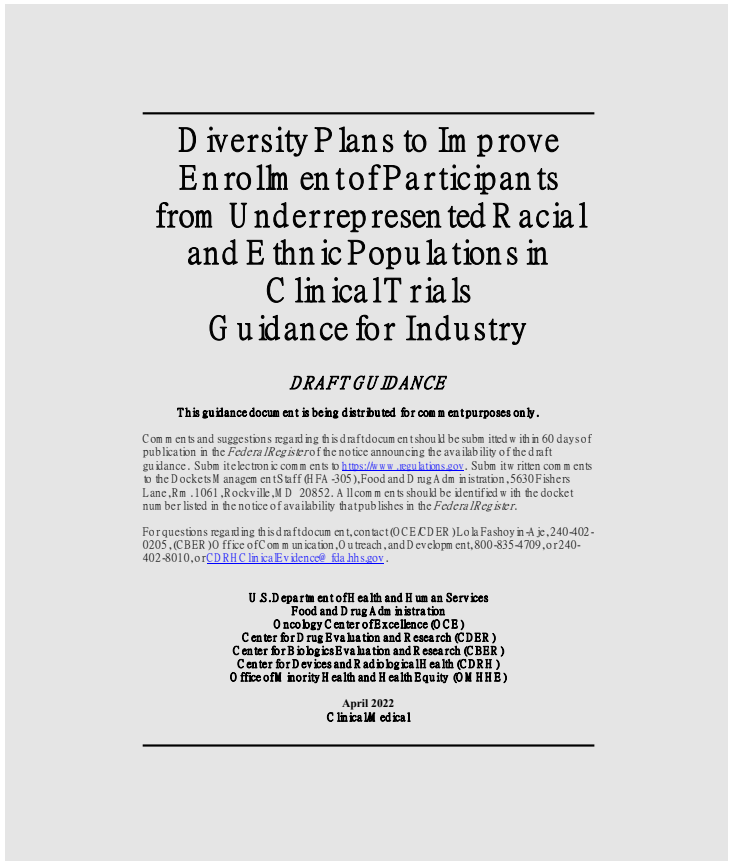
Policy efforts to improve diversity span decades, w limited impact



Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials
Guidance for Industry

DRAFT GUIDANCE

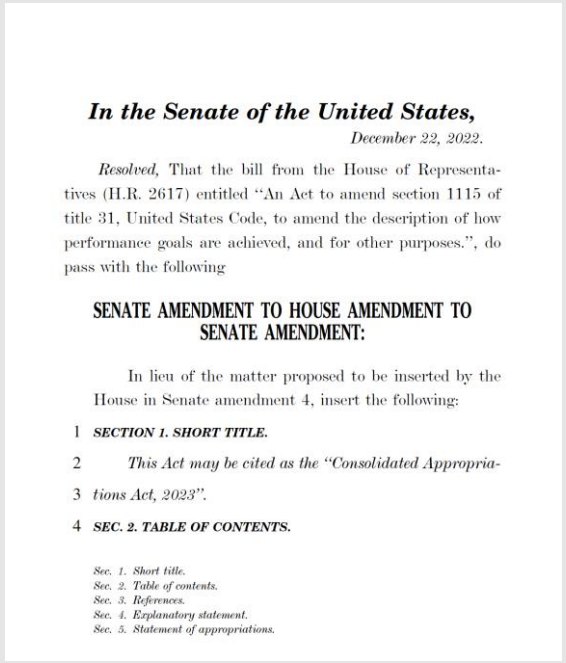
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (OCE/CDER) Lola Fashoyin-Aje, 240-402-0205, (CBER) Office of Communication, Outreach, and Development, 800-835-4709, or 240-402-8010, or CDRHClinicalEvidence@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Office of Minority Health and Health Equity (OMHHE)

April 2022
Clinical Medical



In the Senate of the United States,

December 22, 2022.

Resolved, That the bill from the House of Representatives (H.R. 2617) entitled "An Act to amend section 1115 of title 31, United States Code, to amend the description of how performance goals are achieved, and for other purposes.", do pass with the following

SENATE AMENDMENT TO HOUSE AMENDMENT TO SENATE AMENDMENT:

In lieu of the matter proposed to be inserted by the House in Senate amendment 4, insert the following:

SECTION 1. SHORT TITLE.

This Act may be cited as the "Consolidated Appropriations Act, 2023".

SEC. 2. TABLE OF CONTENTS.

Sec. 1. Short title.
Sec. 2. Table of contents.
Sec. 3. References.
Sec. 4. Explanatory statement.
Sec. 5. Statement of appropriations.

- 1983, FDA "Guideline for the Study of Drugs Likely to be Used in the Elderly," finalized in 1989, (65+)
- 1993, ICH E7 guidelines state, "It is important…to seek patients in the older age range, 75+…" in trials
- 1993, FDA "Guideline for the Study and Evaluation of Gender Differences in the Clinical Evaluation of Drugs"
- 1993, rev. 2017, NIH Revitalization Act, directs NIH to ensure inclusion of minority groups + women in trials
- 1998, FDA publishes Final Rule on "Investigational New Drug Applications and New Drug Applications" amending regulations for new drug applications (NDA's) "to clearly define in the NDA format + content regulations the requirement to present effectiveness and safety data for important demographic subgroups, specifically gender, age, + racial subgroups." 21 CFR Parts 312 + 314
- 2013, CDER revised Good Review Practices advising IND reviewers to discourage needless trial exclusions
- 2001, rev. 2017, NIH Policy & Guidelines: The Inclusion of Women and Minorities as Subjects in Clinical Research
- 2020, FDA, Enhancing the Diversity of Clinical Trial Populations: Eligibility Criteria, Enrollment Practices +Trial Designs: Industry Guidance
- 4/2022, FDA draft guidance, "Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Subgroups in Clinical Trials," recommending medical product sponsors develop + submit a "Race and Ethnicity Diversity Plan" to FDA early in clinical development
- 12/29/22, President Biden signed the Food and Drug Omnibus Reform Act (FDORA), requiring sponsors to submit "diversity action plans" to the FDA, outlining trial enrollment goals by age, sex, race, ethnicity, geographic location + socioeconomic status, with rationales, and plans for meeting enrollment goals

Diversity in Clinical Research: A public health and social just imperative

Original research

Diversity in clinical research: public health and social justice imperatives

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ABSTRACT

It is well established that demographic representation in clinical research is important for understanding the safety and effectiveness of novel therapeutics and vaccines in diverse patient populations. In recent years, the National Institutes of Health and Food and Drug Administration have issued guidelines and recommendations for the inclusion of women, older adults, and racial and ethnic minorities in research. However, these guidelines fail to provide an adequate explanation of why racial and ethnic representation in clinical research is important. This article aims to both provide the missing arguments for why adequate representation of racial and ethnic minorities in clinical research is essential and to articulate a number of recommendations for improving diversity going forward.

Appropriate racial and ethnic representation and fair inclusion help (1) increase the generalisability of clinical trial results, (2) equitably distribute any benefits of clinical research and (3) enable trust in the research enterprise.

Although black, Latinx and Indigenous patients have been disproportionately affected by the COVID-19 pandemic, evidence suggests racial and ethnic minorities may be under-represented in COVID-19 clinical trials.[1 2] In fact, in the USA, racial and ethnic minorities are under-represented in clinical trials for most therapeutics and vaccines.[3–5] Clinical trial participants are more often male and tend to be whiter, younger and healthier than real-world patients, raising concerns about the safety and effectiveness of novel therapeutics and vaccines for under-represented populations.[6–8]

The National Institutes of Health (NIH) and the Food and Drug Administration (FDA) have made strides to improve demographic representation in research since at least the 1980s. The NIH Revitalization Act of 1993, for example, directed the NIH to establish guidelines for the inclusion of women and racial and ethnic minorities in clinical research.[9] Additionally, the statute required NIH-sponsored clinical research to address the inclusion of historically under-represented demographic groups in proposed research and in phase 3 clinical trials. Recently, the FDA published detailed guidance for research sponsors, as part of the FDA Reauthorization Act of 2017 mandate, on how to better enrol diverse study participants.[10] The guidance makes recommendations, such as broadening protocol eligibility criteria and avoiding unnecessary exclusion criteria in research, to better understand the safety and efficacy of novel therapeutics in a diverse patient population.

While helpful, these efforts, like many, fail to answer a fundamental question: why is racial and ethnic representation in clinical research important? Given that demographic representation in research advances understandings of safety, efficacy and effectiveness for novel therapeutics in the population expected to use them, demographic representation is important if there is reason to believe that there will be a differential response to a therapeutic by sex, age, race or ethnicity. It is well established that there can be differential responses to therapeutics between women and men and between older and younger adults due to differences in pharmacokinetics/pharmacodynamics and drug toxicity by sex and age.[11–13] Yet, in failing to explain why race, a social construct, is grouped with sex and age, biological attributes, we worry that guidance to improve representation of racial and ethnic minorities in clinical research may unintentionally endorse a biological basis for race and ethnicity. Here, we provide the missing arguments for why racial and ethnic representation in clinical research is essential. We then articulate a number of recommendations for improving the enrolment of racial and ethnic minorities in clinical research going forward.

ARGUMENTS

Clinical characteristics and responses to novel therapeutics can differ by race and ethnicity. However, the underlying causes of any differences are driven by social determinants and structural racism, not inherent genetic differences.[14] Racial and ethnic minorities are, for example, over-represented in poverty due to structural inequities, which results in disparities in access to quality education, healthy foods, a clean and safe environment, income and wealth, among other factors that contribute to a healthy life.[15 16] This manifests in a disproportionate rate of comorbid conditions and concomitant medication use, both of which can alter the safety profile of a therapeutic.[17 18] Therefore, failing to adequately include patients identifying as racial and ethnic minorities in research, can potentially limit understandings around the benefits, risks and harms of novel therapeutics for excluded and under-represented patients groups.

While race is not a biological construct, it is worth noting that evolutionary history or ancestry may be biologic constructs of value. However, ancestry is not a proxy for race and should not be used as such. Genetics research has illuminated how humans cannot be divided into biologically distinct categories and that there is more variation within racial groups than between racial groups.[19 20] Although there may be some genetic

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Goals of Increasing Diversity in Clinical Trials.		
Goal	**Key Challenges**	**Implications**
Building trust in medical research and institutions	Distrust of medical and scientific professions can be an important obstacle to receiving effective medical care.	The effect on public trust of the design and conduct of clinical trials can be as important to public health as trials' results. Investments should be made in elucidating how clinical trial practices affect public trust.
Promoting fairness for potential participants and their communities	Opportunities to participate in trials are limited. Preferences, resources, and trust all affect willingness to participate in trials. Health systems' capacities to conduct trials vary among communities.	Overcoming unjust barriers to participation for disenfranchised groups will require affirmative outreach and recruitment actions. Grading trials on inclusive outreach and recruitment practices, rather than solely enrollment demographics, may better reflect recruitment equity. Investing in trial capacity in marginalized communities may benefit such communities broadly by improving adoption of innovations.
Generating biomedical knowledge	Sample sizes are often too small to permit assessment of treatment efficacy within particular subgroups. Clinically significant differences in treatment efficacy between groups that are underrepresented and those that are overrepresented in trials may not be common. Efforts to diversify trials address only some of the barriers to efficient patient recruitment.	Investigators should acknowledge that more inclusive trials may not show whether a treatment is effective for certain patient subgroups or meaningfully shift estimates of the treatment's efficacy. Shifting the focus of trials to diseases that disproportionately affect marginalized groups may more effectively generate knowledge benefiting these groups. Future meta-research could clarify the importance and detectability of heterogeneous treatment effects.

Schwartz, et al, NEJM, 2023;388(14):1252-1254

Yale School of Medicine

Abstract

- **Objective** To develop a measure for adequate diversity and fair inclusion of women, older adults (65 years and older), and racially and ethnically minoritized patients in pivotal trials and use it to score, rate/rank the performance of trials, therapeutics and sponsor
- **Design** Retrospective cross sectional study.
- **Population** Sponsors of novel oncology therapeutics approved by the US FDA in 2012 - 2017.

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Metrics, baseline scores, and a tool to improve sponsor performance on clinical trial diversity: retrospective cross sectional study

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► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjmed-2022-000395).

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ABSTRACT

OBJECTIVE To develop a measure for fair inclusion in pivotal trials by assessing transparency and representation of enrolled women, older adults (aged 65 years and older), and racially and ethnically minoritized patients.

DESIGN Retrospective cross sectional study.

POPULATION Sponsors of novel oncology therapeutics that were approved by the US Food and Drug Administration over 1 January 2012 to 31 December 2017.

DATA SOURCES Trial data from Drugs@FDA, ClinicalTrials.gov, and corresponding publications; cancer incidence demographics from US Cancer Statistics and the American Cancer Society.

MAIN OUTCOME MEASURES Transparency measures assess whether trials publicly report participant sex, age, and racial and ethnic identity. Representation measures assess whether trial participant demographics represent more than 80% of the US patient population for studied conditions, calculated by dividing the percentage of study participants in each demographic subgroup by the percentage of the US cancer population with the studied condition per group. Composite fair inclusion measures assess average transparency and representation scores, overall and for each demographic group. Results are reported at the trial, product, and sponsor levels.

RESULTS Between 1 January 2012 and 31 December 2017, the FDA approved 59 novel cancer therapeutics, submitted by 25 sponsors (all industry companies) on the basis of 64 pivotal trials. All 25 sponsors (100%) reported participant sex, 10 (40%) reported age, and six (24%) reported race and ethnicity. Although 14 (56%) sponsors had adequate representation of women in trials, only six (24%) adequately represented older adults, and four (16%) adequately represented racially and ethnically minoritized patients (black, Asian, Hispanic or Latinx). On overall fair inclusion, one sponsor scored 100% and the median sponsor score was 81% (interquartile range 75-87%). More than half of sponsors (13 (56%) of 25) fairly included women, 20% (n=5) fairly included older adults, and 4% (n=1) fairly included racially and ethnically minoritized patients in trials. 80% of product had pivotal trials that fairly included women, 24% fairly included older adults, and 5% fairly included racially and ethnically minoritized patients.

CONCLUSIONS This novel approach evaluates trials, products, and sponsors on their fair inclusion of demographic groups in research. For oncology trials, substantial room was noted for improved inclusion of older adults and patients who identify as black or Latinx and transparency around the number of participants identifying as Native Hawaiian, Pacific Islander, American Indian, and Alaska Native. These measures can be used by sponsors, ethics committees, among others, to set and evaluate trial diversity goals to help spur progress toward greater research equity in the US.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Women, older adults, and racially and ethnically minoritized patients are often under-represented in clinical research even though adequate representation is important for equitably assessing the safety and efficacy of novel therapeutics in the patients who ultimately use them.

⇒ Despite policy efforts to improve diversity, poor inclusion in trials persists, suggesting additional strategies are needed.

⇒ Development of accountability measures and publicly rating and ranking sponsors might be an effective reform strategy for improving diversity and fair inclusion in research.

WHAT THIS STUDY ADDS

⇒ This paper develops baseline quality measures for fair inclusion and diversity in clinical research that capture the transparency of participant demographics and representation of women, older adults, and racially and ethnically minoritized patients.

⇒ Applying the measures to score and rank novel oncology therapeutics FDA approved from 2012 through 2017, along with their sponsors and trials, we found that while a few sponsors have done well, most have substantial room for improvement on their inclusion of older adults and racially and ethnically minoritized patients, and to a lesser extent women.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ The fair inclusion score we developed and tested on oncology pivotal trials provides a useful, feasible method of assessing critical indices of equity in clinical trials.

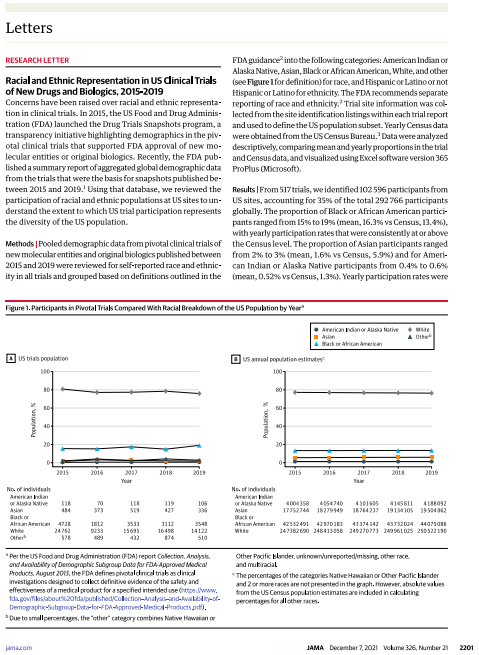
⇒ The fair inclusion measure can be used to track and catalyze progress across the research ecosystem on clinical trial diversity, a key public health and social justice goal.

Introduction

Demographic representation in clinical research is important for equitably assessing the safety and efficacy of novel therapeutics in the patients who will use them. However, women, older adults, and some racial and ethnic groups are often under-represented in research, particularly in cancer trials.[1–4] This under-representation can challenge clinicians,

Conceptualizing Adequate Representation: 2 Approaches

- "Country-population approach"



Letters

RESEARCH LETTER

Racial and Ethnic Representation in US Clinical Trials of New Drugs and Biologics, 2015-2019

Concerns have been raised over racial and ethnic representation in clinical trials. In 2015, the US Food and Drug Administration (FDA) launched the Drug Trials Snapshots program, a transparency initiative highlighting demographics in the pivotal clinical trials that supported FDA approval of new molecular entities or original biologics. Recently, the FDA published a summary report of aggregated global demographic data from the trials that were the basis for snapshots published between 2015 and 2019.[1] Using that database, we reviewed the participation of racial and ethnic populations at US sites to understand the extent to which US trial participation represents the diversity of the US population.

Methods | Pooled demographic data from pivotal clinical trials of new molecular entities and original biologics published between 2015 and 2019 were reviewed for self-reported race and ethnicity in all trials and grouped based on definitions outlined in the FDA guidance[2] into the following categories: American Indian or Alaska Native, Asian, Black or African American, White, and other (see **Figure 1** for definition) for race, and Hispanic or Latino or not Hispanic or Latino for ethnicity. The FDA recommends separate reporting of race and ethnicity.[3] Trial site information was collected from the site identification listings within each trial report and used to define the US population subset. Yearly Census data were obtained from the US Census Bureau.[3] Data were analyzed descriptively, comparing mean and yearly proportions in the trial and Census data, and visualized using Excel software version 365 ProPlus (Microsoft).

Results | From 517 trials, we identified 102 596 participants from US sites, accounting for 35% of the total 292 766 participants globally. The proportion of Black or African American participants ranged from 15% to 19% (mean, 16.3% vs Census, 13.4%), with yearly participation rates that were consistently at or above the Census level. The proportion of Asian participants ranged from 2% to 3% (mean, 1.6% vs Census, 5.9%) and for American Indian or Alaska Native participants from 0.4% to 0.6% (mean, 0.52% vs Census, 1.3%). Yearly participation rates were

Figure 1. Participants in Pivotal Trials Compared With Racial Breakdown of the US Population by Year[a]

No. of individuals	2015	2016	2017	2018	2019
American Indian or Alaska Native	118	70	118	119	106
Asian	484	373	519	427	336
Black or African American	4728	1812	3533	3112	3548
White	24762	9233	15695	16498	14122
Other[b]	578	489	432	874	510

No. of individuals	2015	2016	2017	2018	2019
American Indian or Alaska Native	4004358	4064740	4101605	4145811	4188092
Asian	17752744	18279949	18744237	19134105	19504862
Black or African American	42532491	42970183	43174142	43732024	44075086
White	247382690	248413598	249270773	249961025	250521180

[a] Per the US Food and Drug Administration (FDA) report *Collection, Analysis, and Availability of Demographic Subgroup Data for FDA-Approved Medical Products, August 2013*, the FDA defines pivotal clinical trials as clinical investigations designed to collect definitive evidence of the safety and effectiveness of a medical product for a specified intended use (https://www.fda.gov/files/about%20fda/published/Collection-Analysis-and-Availability-of-Demographic-Subgroup-Data-for-FDA-Approved-Medical-Products.pdf).

[b] Due to small percentages, the "other" category combines Native Hawaiian or Other Pacific Islander, unknown/unreported/missing, other race, and multiracial.

[c] The percentages of the categories Native Hawaiian or Other Pacific Islander and 2 or more races are not presented in the graph. However, absolute values from the US Census population estimates are included in calculating percentages for all other races.

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- "Condition-based approach"

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Participation of Women and Sex Analyses in Late-Phase Clinical Trials of New Molecular Entity Drugs and Biologics Approved by the FDA in 2007–2009

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Abstract

Background: Biological sex differences may contribute to differential treatment outcomes for therapeutic products. This study tracks women's participation in late-phase clinical trials (LPCTs), where efficacy and safety of drugs and biologics are evaluated, of new molecular entity (NME) drugs and biologics approved by the U.S. Food and Drug Administration (FDA) in 2007–2009. Furthermore, presentations of sex-based analyses were assessed from the FDA reviews.
Methods: New drug applications (NDAs) and biologics license applications (BLAs) were accessed from the U.S. FDA database and evaluated for women's participation in LPCTs. Sex-based analyses for efficacy and safety contained in FDA reviews were surveyed. Ratios for women's LPCT participation (PROPORTION OF STUDY SUBJECTS) to their proportion in the disease population were calculated for each approved therapeutic product and grouped into therapeutic categories.
Results: Sex-specific ($n=5$) and pediatric ($n=3$) drug applications were excluded. Women's participation in LPCTs was 39%, 48%, and 42% in NDAs ($n=50$) and 49%, 62%, and 58% in BLAs ($n=11$) for 2007, 2008, and 2009, respectively. Sixty-four percent of NDAs and 91% of BLAs had participation to proportion ratios of ≥0.80. Seventy-four percent of NDA reviews and 64% of BLA reviews included safety and efficacy sex analysis. Ninety-six percent of NDA reviews and 100% of BLA reviews included efficacy sex analysis.
Conclusion: Women's participation in LPCTs averaged 43% for NDAs and 57% for BLAs in 2007–2009 and varied widely by indication. As a comparison, the 2001 U.S. Government Accountability Office (GAO) reported 52% of women's participation for drug clinical trials in1998–2000 and an FDA study reported 45% for BLAs approved from 1995 to 1999. This study showed that sex-analysis of both safety and efficacy in NDA has increased to 74% since the GAO report of 72%, while those for BLAs increased to 64% from 37% reported for therapeutic biologics approved in 1995–1999. Knowledge of disease prevalence and participation in clinical trials provides an understanding of recruitment and retention patterns of patients in these trials.

Introduction

THE PARTICIPATION OF both women and men in clinical trials is of paramount importance in determining potentially different treatment outcomes between sexes for medical products. Systemic exposure (pharmacokinetic, PK) differences between women and men may result from absorption, distribution, metabolism, and excretion differences and could cause dissimilar safety or efficacy responses.[1] These sex differences in PK of a drug may be due to physiological and hormonal differences between men and women. Pharmacodynamic (PD) differences, independent of PK, have also been reported to result in response differences between men and women. For example, in men and women with similar plasma concentrations of quinidine, a higher QTc interval prolongation can be seen in women compared with men,[2] and women tend to have a longer QTc interval compared with men at baseline.[3,4] Higher fracture risk has been reported for women as compared with men during long-term use of hypoglycemic drugs of the thiazolidinedione class.[5] A diabetes outcome progression trial showed that men's fracture risks were approximately 4% for rosiglitazone, 3.4% for metformin, and

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Measures. Components, parameters + outcomes

Component	Parameter	Outcome measure
Transparency (n=7)	Sex	Sex of participants reported
	Age	% Older adult participants reported (>64)
	Race	% Alaskan Native /American Indian participants reported
		% Asian participants reported
		% Black participants reported
		% Native Hawaiian / Pacific Islander participants reported
	Ethnicity	% Latino participants reported
Representation (n=5)	Sex	PPR for female participants[+]
	Age	PPR for older adults (>64)[+]
	Race	PPR for Black participants[+]
		PPR for Asian participants[+]
	Ethnicity	PPR for Latino participants[+]

Transparency: Whether trials publicly report participant sex, age, and racial and ethnic identity

Representation: Whether trial participant demographics represent 80-120% of the US patient population for studied conditions

Fair inclusion: A composite measure of transparency + representation scores

Methods. Sample + data sources

Sample. Novel drugs + biologics FDA approved for oncologic indications, 2012-17

Data sources (n=7)	Measures		
	Transparency	**Representation**	**Cancer Incidence**
Drugs@FDA, approval packages		X	
ClinicalTrials.gov	X	X	
Publications, indexed on ClinicalTrials.gov	X	X	
FDA Snapshots		X	
Product labels		X	
2016 US Cancer Statistics dataset: Cancer registry data from National Program of Cancer Registries + National Cancer Institute's Surveillance, Epidemiology + End Results [SEER]		X	X
American Cancer Society, Cancer Facts + Figures		X	X

Sample characteristics, novel oncology therapeutics FDA approved 2012-17

Sample Characteristics	No. (%)
Product Type	**59**
Drug	39 (66)
Biologic	20 (34)
Sponsors	**25**
Approval year	
2012	11 (19)
2013	8 (14)
2014	8 (14)
2015	14 (24)
2016	4 (7)
2017	14 (24)
Approval pathway	
Priority review	46 (78)
Accelerated approval	28 (47)
Fast track	30 (51)
Breakthrough	27 (46)
Orphan drug status	45 (76)
Broad oncological indication	**16**
Leukemia	10 (17)
Lung cancer	6 (10)
Breast cancer	6 (10)
Multiple myeloma	6 (10)
Non-Hodgkin’s lymphoma	6 (10)
Melanoma	5 (8)
Colorectal cancer	3 (5)
Ovarian cancer	3 (5)
Other*	13 (22)
Pivotal trials, total analyzed (median, per product)	**64 (1)**
Trial participants, total analyzed (median per trial [IQR]	**29,959 (326 [138-668])**

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- **Figure.** Proportion of trials, products, and companies receiving a 100% score on transparency, representation, and fair inclusion measures for women, older adults, and racially and ethnically minoritized patients participating in clinical trials for novel oncology therapeutics approved by the US Food and Drug Administration during 2012-17.

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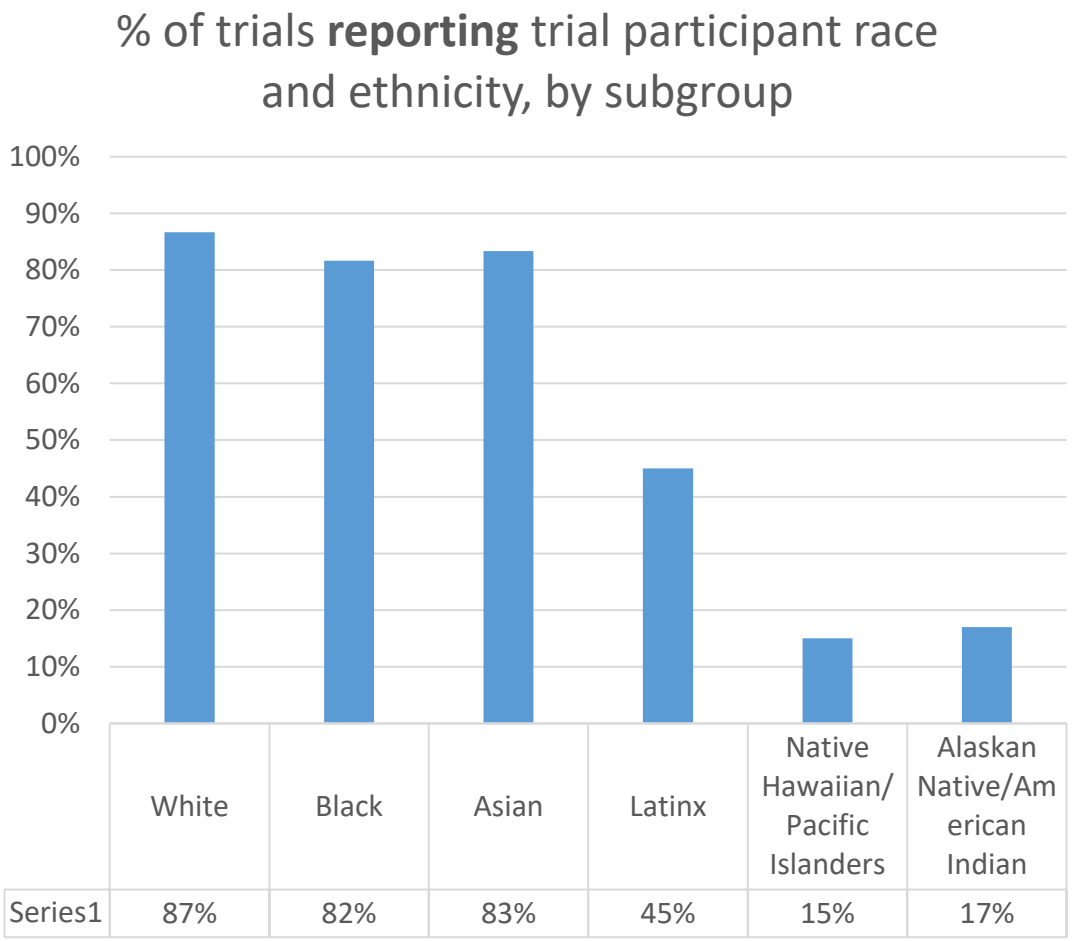

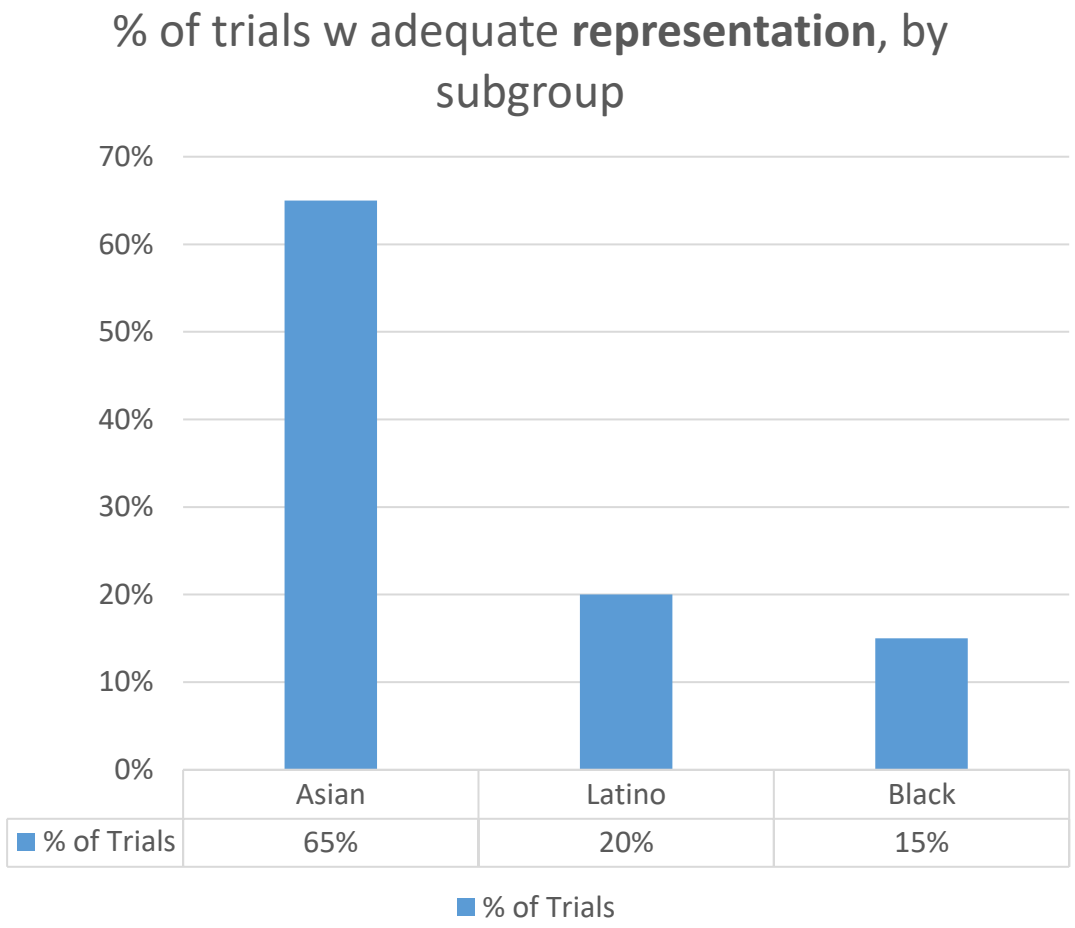

10% (6/62) of trials adequately represented black, white, asian and latino- identifying patients

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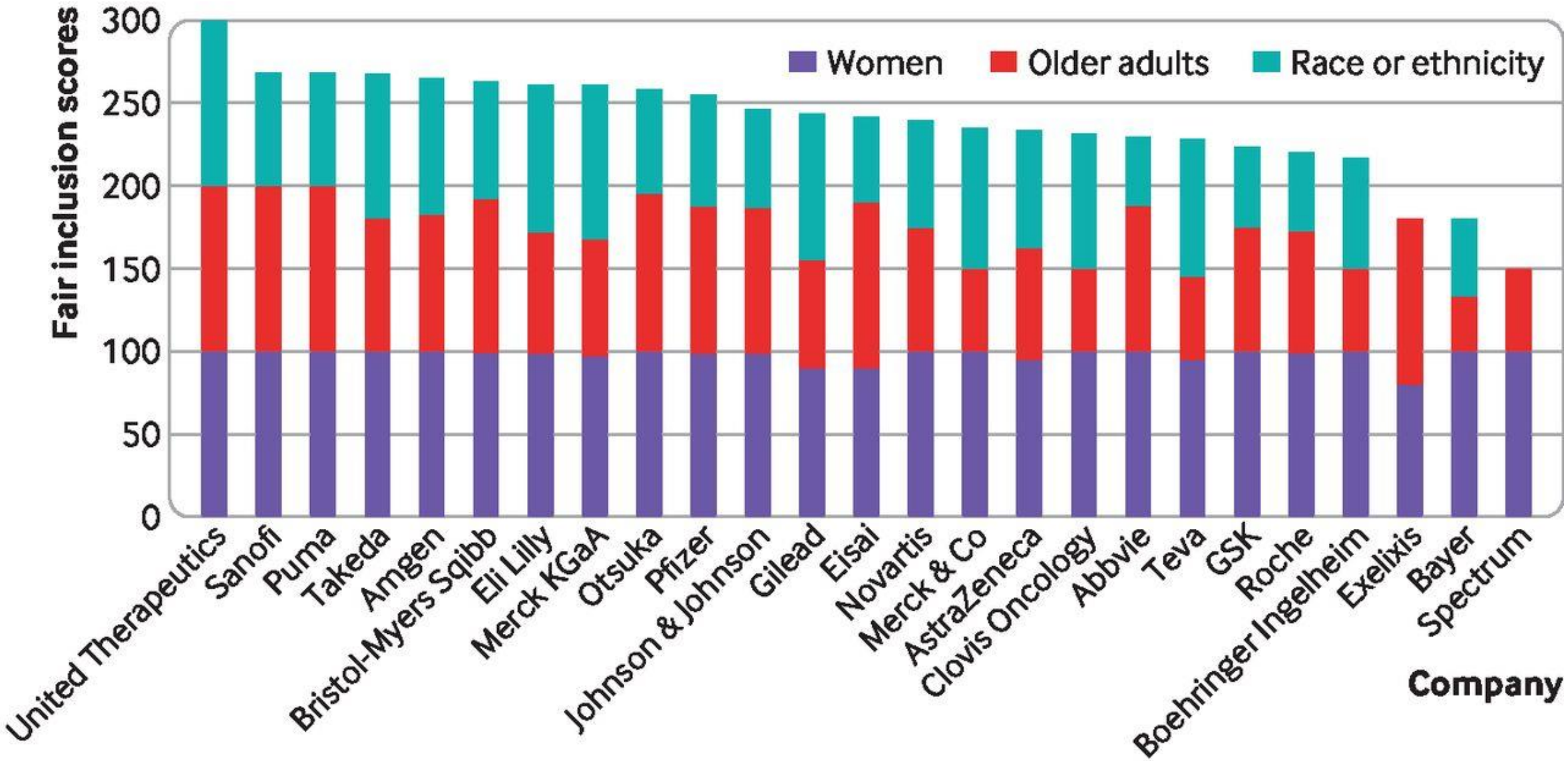
Figure. Company rankings on fair inclusion of women, older adults, and racially and ethnically minoritized patients in research, for novel oncology therapeutics approved by the US FDA, 2012-17.



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	Transparency scores				Representation scores				Fair inclusion scores			
Company	**Overall transparency**	Sex	Older Adults	Race/ Ethnicity	**Overall representation**	Women	Older Adults	Race/ Ethnicity	**Overall fair inclusion**	Women	Older Adults	Race/ Ethnicity
United Therapeutics	**100**	100	100	100	**100**	100	100	100	**100**	100	100	100
Puma	**89**	100	100	67	**85**	100	N/A	70	**89**	100	100	68
Sanofi	**89**	100	100	67	**90**	100	100	70	**89**	100	100	68
Takeda	**94**	100	83	100	**89**	100	90	76	**89**	100	80	88
Amgen	**94**	100	100	83	**82**	100	65	82	**88**	100	83	83
BMS	**86**	100	100	58	**88**	99	85	79	**88**	99	93	71
Eli Lilly	**92**	100	75	100	**89**	98	93	78	**87**	99	73	89
Merck KGaA	**100**	100	100	100	**85**	90	80	N/A	**87**	98	70	93
Otsuka	**89**	100	100	67	**83**	100	90	60	**86**	100	95	63
Pfizer	**88**	100	90	73	**81**	98	83	62	**85**	99	88	68
J&J	**89**	100	100	67	**77**	98	75	58	**82**	99	88	60
Gilead	**92**	100	75	100	**72**	80	60	77	**81**	90	65	88
Eisai	**78**	100	100	33	**83**	80	100	70	**81**	90	100	52
Novartis	**88**	100	92	72	**70**	100	48	63	**80**	100	74	65
Merck & Co	**83**	100	50	100	**87**	100	N/A	73	**79**	100	50	87
AstraZeneca	**81**	100	59	83	**75**	90	75	59	**78**	95	67	72
Clovis Oncology	**72**	100	50	67	**98**	100	N/A	95	**77**	100	50	81
Abbvie	**69**	100	75	33	**100**	100	100	100	**76**	100	88	42
Teva	**72**	100	50	67	**95**	90	N/A	100	**76**	95	50	83
GSK	**87**	100	83	78	**65**	100	75	20	**75**	100	75	49
Roche	**76**	100	82	45	**74**	98	67	57	**73**	99	74	47
Boehringer Ingelheim	**61**	100	50	33	**100**	100	N/A	100	**72**	100	50	67
Exelixis	**67**	100	100	0	**80**	60	100	N/A	**60**	80	100	0
Bayer	**63**	100	33	56	**85**	100	100	56	**60**	100	33	46
Spectrum	**50**	100	50	0	**100**	100	N/A	N/A	**50**	100	50	0
Median	***87***	***100***	***83***	***67***	***85***	***100***	***85***	***72***	***81***	***100***	***75***	***68***
Q3	***90***	*100*	*100*	*92*	***93***	*100*	*100*	*85*	***87***	*100*	*94*	*85*

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Original Investigation | Health Policy

Reporting of Study Participant Demographic Characteristics and Demographic Representation in Premarketing and Postmarketing Studies of Novel Cancer Therapeutics

Tanvee Varma, BA; Joshua D. Wallach, PhD, MS; Jennifer E. Miller, PhD; Dominic Schnabel, MPH; Joshua J. Skydel, BS; Audrey D. Zhang, MD; Michaela A. Dinan, PhD; Joseph S. Ross, MD, MHS; Cary P. Gross, MD

Abstract

IMPORTANCE Adequate representation of demographic subgroups in premarketing and postmarketing clinical studies is necessary for understanding the safety and efficacy associated with novel cancer therapeutics.

OBJECTIVE To characterize and compare the reporting of demographic data and the representation of individuals by sex, age, and race in premarketing and postmarketing studies used by the Food and Drug Administration (FDA) to evaluate novel cancer therapeutics.

DESIGN, SETTING, AND PARTICIPANTS In this cross-sectional study, premarketing and postmarketing studies for novel cancer therapeutics approved by the FDA from 2012 through 2016 were identified. Study demographic information was abstracted from publicly available sources, and US cancer population demographic data was abstracted from US Cancer Statistics. Analyses were conducted from February 25 through September 21, 2020.

MAIN OUTCOMES AND MEASURES The percentages of trials reporting sex, age, and race/ethnicity were calculated, and participation to prevalence ratios (PPRs) were calculated by dividing the percentage of study participants in each demographic group by the percentage of the US cancer population in each group. PPRs were constructed for premarketing and postmarketing studies and by cancer type. Underrepresentation was defined as PPR less than 0.8.

RESULTS From 2012 through 2016, the FDA approved 45 cancer therapeutics. The study sample included 77 premarketing studies and 56 postmarketing studies. Postmarketing studies, compared with premarketing studies, were less likely to report patient sex (42 studies reporting [75.0%] vs 77 studies reporting [100%]; $P < .001$) and race (27 studies reporting [48.2%] vs 62 studies reporting [80.5%]; $P < .001$). Women were adequately represented in premarketing studies (mean [SD] PPR, 0.91; 95% CI, 0.90-0.91) and postmarketing studies (mean PPR, 1.00; 95% CI, 1.00-1.01). Although older adults and Black patients were underrepresented in premarketing studies (older adults: mean PPR, 0.73; 95% CI, 0.72-0.74; Black patients: mean PPR, 0.32; 95% CI, 0.31-0.32), these groups continued to be underrepresented in postmarketing studies (older adults: mean PPR, 0.75; 95% CI, 0.75-0.76; Black patients: mean PPR, 0.21; 95% CI, 0.21-0.21).

CONCLUSIONS AND RELEVANCE This study found that older adults and Black patients were underrepresented in postmarketing studies of novel cancer therapeutics to a similar degree that they were underrepresented in premarketing studies. These findings suggest that postmarketing studies are not associated with improvements to gaps in demographic representation present at the time of FDA approval.

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Key Points

Question Are the demographic characteristics of patients enrolled in premarketing and postmarketing studies used by the US Food and Drug Administration (FDA) to evaluate the safety and efficacy of novel cancer therapeutics clearly reported and representative of the US cancer population?

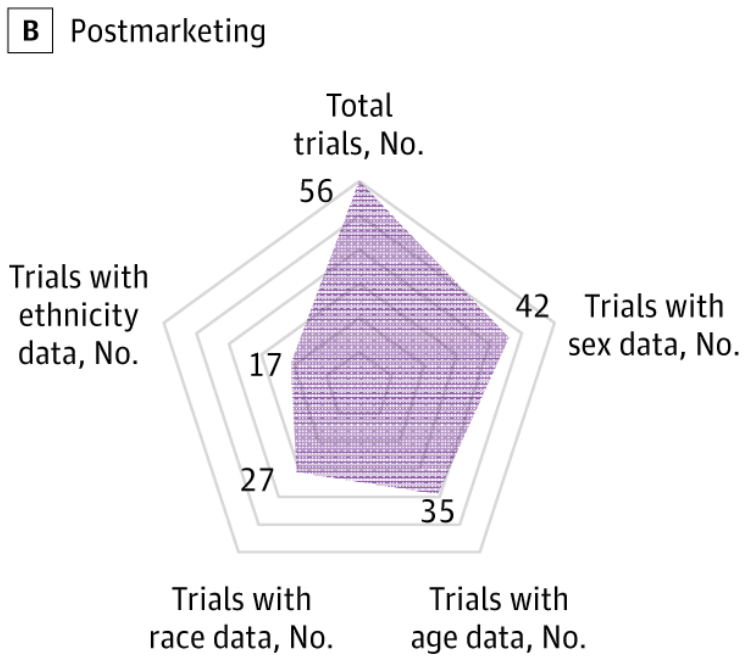
Findings In this cross-sectional study of 77 premarketing studies and 56 postmarketing studies for FDA-approved cancer therapeutics, there was inconsistent reporting of demographic data and underrepresentation of older adults and Black patients in premarketing and postmarketing studies of cancer therapeutics.

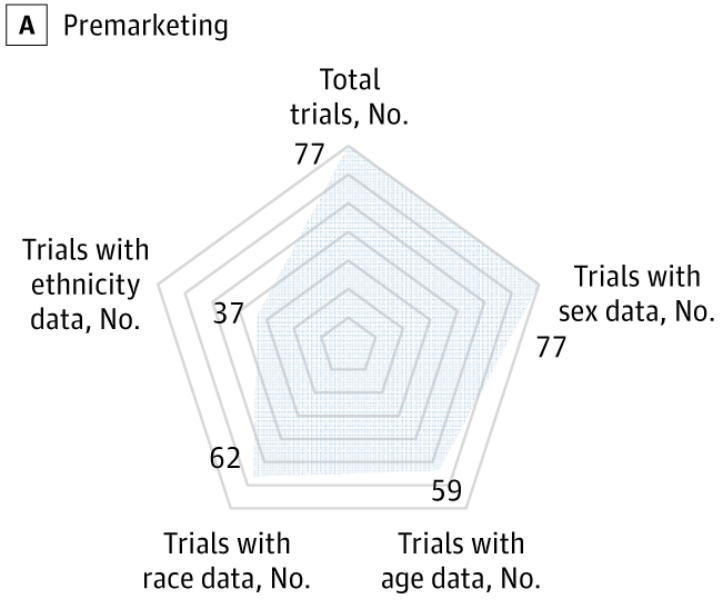
Meaning Premarketing and postmarketing studies used by the FDA to evaluate novel cancer therapeutics may not adequately represent the US cancer population.

+ Invited Commentary
+ Supplemental content

Author affiliations and article information are listed at the end of this article.

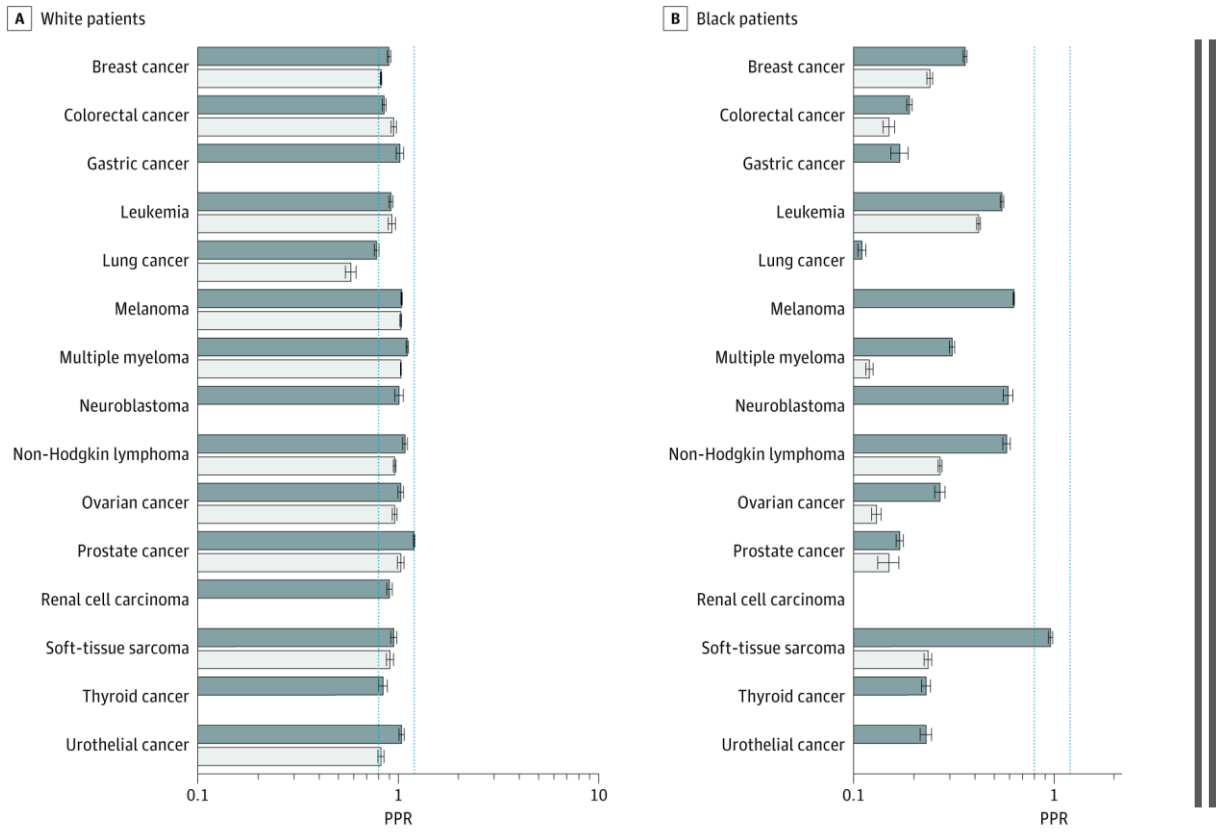
Varma, T., Wallach, J, Miller, JE., et al, Reporting of Study Participant Demographic Characteristics and Demographic Representation in Pre + Post-marketing Studies of Novel Cancer Therapeutics, JAMA Netw Open. 2021;4(4):e217063



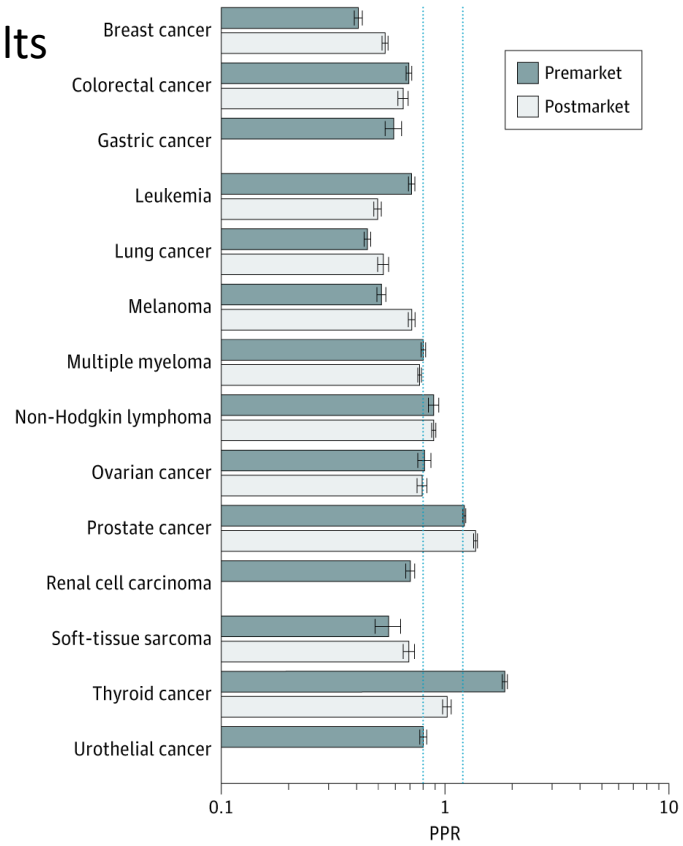


- Demographic Data Availability

Black identifying patients and older adults were under-represented in pre and post-marketing trials



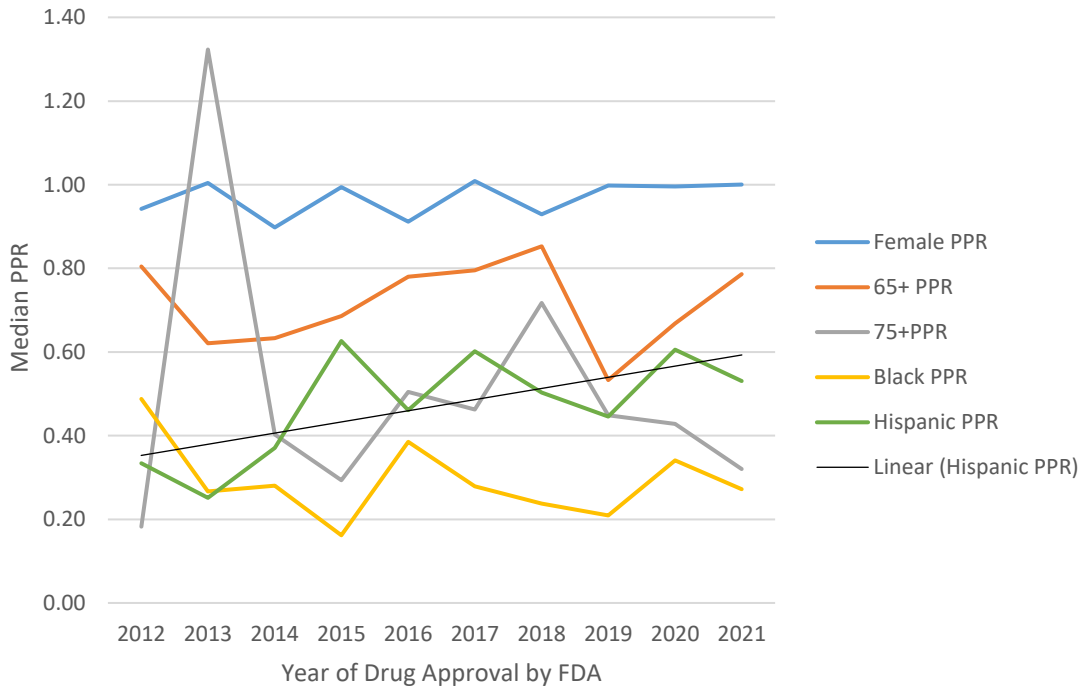
Older adults



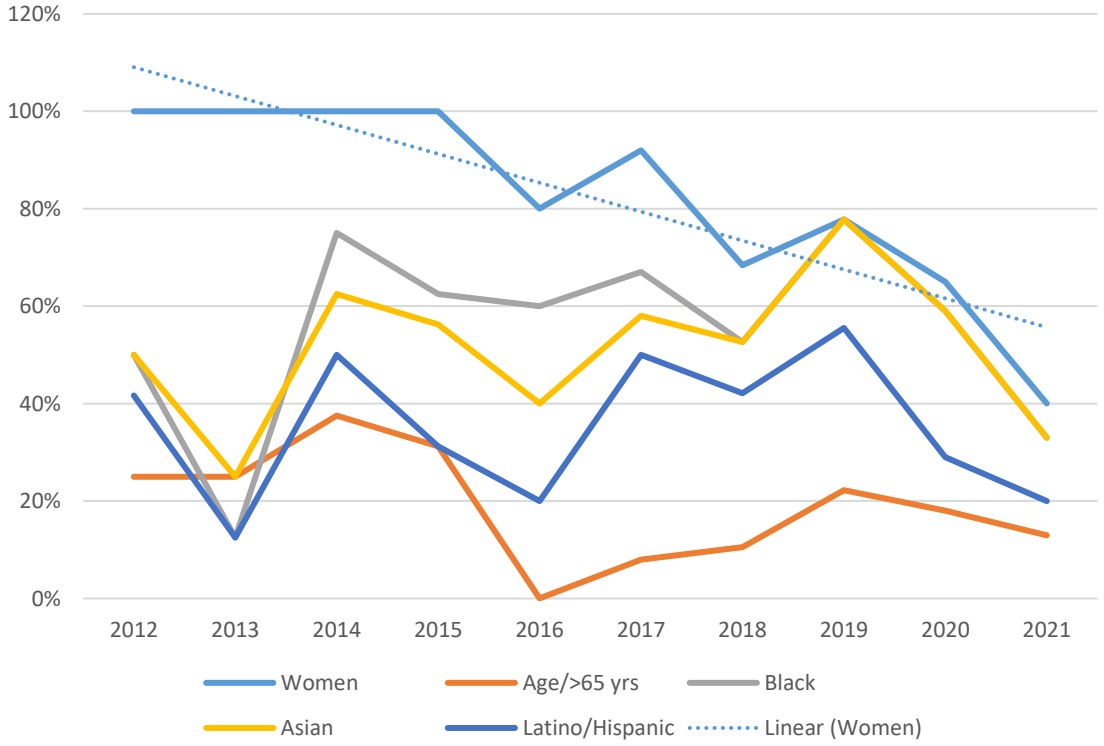
Varma, T., Wallach, J, Miller, JE., et al, Reporting of Study Participant Demographic Characteristics and Demographic Representation in Pre + Post-marketing Studies of Novel Cancer Therapeutics, JAMA Netw Open. 2021;4(4):e217063

Under reporting + under representation remain a challenge for most demographic subgroups *(forthcoming study)*

Median participation to prevalence scores for women, older adults, Black and Latino-identifying participants in pivotal trials supporting FDA approval of novel oncology therapeutics, 2012-2021



% of pivotal trials w/ transparent reporting, by participant demographic group + FDA approval year, for novel oncology therapeutics, 2012-2021



Low scoring organizations improve practices in response to ratings

The NEW ENGLAND JOURNAL of MEDICINE

SOUNDING BOARD

Accountability Measures — Using Measurement to Promote Quality Improvement

Mark R. Chassin, M.D., M.P.P., M.P.H., Jerod M. Loeb, Ph.D., Stephen P. Schmaltz, Ph.D., and Robert M. Wachter, M.D.

Measuring the quality of health care and using those measurements to promote improvements in the delivery of care, to influence payment for services, and to increase transparency are now commonplace. These activities, which now involve virtually all U.S. hospitals, are migrating to ambulatory and other care settings and are increasingly evident in health care systems worldwide. Many constituencies are pressing for continued expansion of programs that rely on quality measurement and reporting.

In this article, we review the origins of contemporary standardized quality measurement, with a focus on hospitals, where such programs have reached their most highly developed state. We discuss some lessons learned from recent experience and propose a conceptual framework to guide future developments in this fast-moving field. Although many of the points we make are relevant to all kinds of quality measurement, including outcome measures, we focus our comments on process measures, both because these account for most of the measures in current use and because outcome measures have additional scientific challenges surrounding the need for case-mix adjustment. We write not as representatives of the Joint Commission articulating a specific new position of that group, but rather as individuals who have worked in the fields of quality measurement and improvement in a variety of roles and settings over many years.

A BRIEF HISTORY OF HOSPITAL QUALITY MEASUREMENT AND REPORTING IN THE UNITED STATES

Although the ubiquity of quality measurement and reporting makes it difficult to remember a health care landscape without them, these trends are remarkably recent. In 1998, the Joint Commission launched its ORYX initiative, the first national program for the measurement of hospital quality, which initially required the reporting only of nonstandardized data on performance measures.[1] In 2002, accredited hospitals were required to collect and report data on performance for at least two of four core measure sets (acute myocardial infarction, heart failure, pneumonia, and pregnancy)[2]; these data were made publicly available by the Joint Commission in 2004.

When the program started, no consensus existed regarding the kinds of measures on which data should be gathered by hospitals, no data on quality of care were collected systematically by hospitals, and little information on nationally standardized measures of hospital quality was available to the public. Few hospitals used national data on quality measures to improve clinical care processes; in fact, hospitals strongly resisted collecting data on quality measures and reporting them publicly.

The changes over the past decade have been breathtaking. The National Quality Forum has endorsed more than 600 quality measures.[3] In 2004, the Centers for Medicare and Medicaid Services (CMS) began financially penalizing hospitals that did not report to the CMS the same performance data they collected for the Joint Commission, and in 2005, the CMS began its own public reporting.[4,5] Today, hospitals provide data to the Joint Commission from a selection of 57 inpatient measures; currently, 31 of these are publicly reported, and there are plans to add the remaining, newly implemented measures over time.[6,7] The CMS also includes additional data on patient satisfaction and outcomes (death and readmissions) for common medical conditions such as pneumonia and heart failure.

Strategic Management Journal
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Received 12 November 2008; Final revision received 19 December 2009

HOW FIRMS RESPOND TO BEING RATED

AARON K. CHATTERJI[1] and MICHAEL W. TOFFEL[2]*
[1] *Fuqua School of Business, Duke University, Durham, North Carolina, U.S.A.*
[2] *Harvard Business School, Boston, Massachusetts, U.S.A.*

While many rating systems seek to help buyers overcome information asymmetries when making purchasing decisions, we investigate how these ratings also influence the companies being rated. We hypothesize that ratings are particularly likely to spur responses from firms that receive poor ratings, and especially those that face lower-cost opportunities to improve or that anticipate greater benefits from doing do. We test our hypotheses in the context of corporate environmental ratings that guide investors to select 'socially responsible,' and avoid 'socially irresponsible,' companies. We examine how several hundred firms responded to corporate environmental ratings issued by a prominent independent social rating agency, and take advantage of an exogenous shock that occurred when the agency expanded the scope of its ratings. Our study is among the first to theorize about the impact of ratings on subsequent performance, and we introduce important contingencies that influence firm response. These theoretical advances inform stakeholder theory, institutional theory, and economic theory. Copyright © 2010 John Wiley & Sons, Ltd.

INTRODUCTION

Information asymmetry has long been understood to complicate market transactions (Akerlof, 1970). Incomplete information prevents buyers from knowing when to believe suppliers' claims about product attributes that are not directly observable prior to purchase. Independent agencies that rate and rank products and companies can help consumers overcome information asymmetries. Such agencies operate in a wide variety of contexts, rating consumer products (Consumer Reports), services (Michelin's guidebooks), and corporate debt (Moody's).[1] These rating schemes are institutions designed to achieve a common objective: to provide credible information to help company stakeholders such as potential buyers, employees, and investors overcome an information disadvantage. Better informed stakeholders can make better decisions about which products to purchase, in which stocks or bonds to invest, and with which companies to seek employment.

Prior scholarship has found evidence that independent company ratings can affect the behavior of consumers and investors. However, scholars have

Keywords: information disclosure; environmental performance; corporate social responsibility; industry self-regulation; ratings
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[1] Companies are subjected to an increasing number of ratings and rankings, from 'Best Places to Work' (*Fortune*, 2008; HRC, 2008) to assessments of environmental and social responsibility (Chatterji and Levine, 2006). In fact, a recent survey counted more than 183 public lists across 38 countries of companies rated or ranked on the basis of their reputation for corporate citizenship, employee relations, leadership, innovation, and other characteristics (Fombrun, 2007).

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J Environ Health. 2005 Mar;67(7):32-6, 56; quiz 59-60.

Impact of restaurant hygiene grade cards on foodborne-disease hospitalizations in Los Angeles County.

Simon PA[1], Leslie P, Run G, Jin GZ, Reporter R, Aguirre A, Fielding JE.
Author information

Abstract
Although health departments routinely inspect restaurants to assess compliance with established hygienic standards, few data are available on the effectiveness of these efforts in preventing foodborne disease. The study reported here assessed the impact on foodborne-disease hospitalizations in Los Angeles County of a restaurant hygiene grading system that utilized publicly posted grade cards. The grading systm was introduced in January 1998. Hospital discharge data on foodborne-disease hospitalizations were analyzed for Los Angeles County and, as a control, for the rest of California during the period 1993-2000. Ordinary least-squares regression analysis was done to measure the effect of the grading progam on these hospitalizations. After baseline temporal and geographic trends were adjusted for, the restaurant hygiene grading program was associated with a 13.1 percent decrease ($p < .01$) in the number of foodborne-disease hospitalizations in Los Angeles County in the year following implementation the program (1998). This decrease was sustained over the next two years (1999-2000). The results suggest that restaurant hygiene grading with public posting of results is an effective intervention for reducing the burden of foodborne disease.

2019 GPS Transparency. Data-sharing analysis

- **33%** of companies scored 100% on data sharing
- **50%** improved their procedures

		Pre 30 day amendment window						Post 30 days
Company	No. of NDA trials	Policy provides access to analysis-ready dataset & CSR	Policy explains how data may be requested	Company publicly reports # & outcome of requests	Policy specifies data will be shared by deadline	% of covered trials registered	Data-sharing score	Data-sharing score
Valeant	17	0%	0%	0%	0%	71%	**14%**	**14%**
Gilead	10	0%	0%	0%	0%	100%	**20%**	↑ **80%**
Merck	35	100%	100%	0%	0%	83%	**57%**	↑ **80%**
AstraZeneca	10	100%	100%	0%	0%	90%	**58%**	↑ **78%**
Allergan	45	100%	100%	0%	0%	96%	**59%**	**59%**
BMS	13	100%	100%	0%	0%	100%	**60%**	↑ **80%**
Amgen	35	100%	100%	100%	0%	31%	**66%**	**66%**
Pfizer	0	100%	100%	100%	0%	NA	**75%**	**75%**
Novartis	6	100%	100%	100%	0%	100%	**80%**	↑ **100%**
Janssen/J&J	5	100%	100%	100%	100%	100%	**100%**	**100%**
Novo Nordisk	46	100%	100%	100%	100%	100%	**100%**	**100%**
Roche	1	100%	100%	100%	100%	100%	**100%**	**100%**
Median	**12**	**100%**	**100%**	**50%**	**0%**	**100%**	**63%**	↑ **80%**
% of companies meeting data-sharing measure							**(3/12)25%**	**(4/12) 33%**


Celgene
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Our Approach
Message from the Chairman and CEO
Materiality
Corporate Responsibility at Celgene
Celgene and the Sustainable Development Goals
External Recognition
Patients First
Pre-Approval Access
Patient Support
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Business with Integrity
Funding
Home Page > Celgene Corporate Responsibility > Our Approach to Corporate Responsibility > Message from the Chairman and CEO
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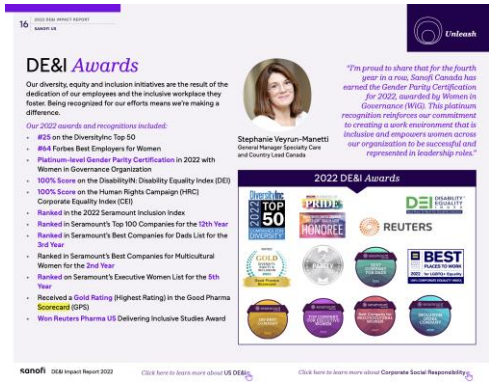
MESSAGE FROM THE CHAIRMAN AND CEO
Celgene Corporation exists to discover, develop and deliver innovative medicines that can improve and extend patients' lives worldwide. It is our purpose and our mission.
In the 14 years I have been a part of Celgene, I've had the privilege of seeing our organization produce transformational medicines that are helping hundreds of thousands of patients. During that time, Celgene has grown from an early-stage start-up to a global company with more than 8,500 employees, eight marketed products and a research engine with nearly 160 ongoing clinical trials and 30 novel agents in development across 40 indications.
As we strive to achieve our mission, we continue to focus on meeting the expectations of all stakeholders. This year's corporate responsibility report highlights how Celgene and its employees are working to make a difference in the lives of patients, communities and economies around the world.
We are at a very important time in our company's journey to help patients and create increased value for our stockholders. Over the next two years, we expect to advance five late-stage products toward regulatory approval -- fedratinib, luspatercept, ozanimod, liso-cel and bb2121. These therapies represent the promise of our industry-leading investments in research, and the beginning of our next wave of innovation that is delivering multiple new product candidates expected to enter mid-stage clinical development during this same period.
MARK J. ALLES
CHAIRMAN AND CHIEF EXECUTIVE OFFICER
Our work to discover and develop these therapies is meaningless if patients cannot access them. As a result, patient access is a vital part of our mission and central to our efforts. For patients being treated with Celgene medicines in the U.S., we have and will continue to offer co-pay assistance for eligible commercially insured patients and free product for qualified patients who are uninsured or underinsured, are unable to afford their medication, and meet other criteria.
To help address patients' medical needs in low- and middle-income countries, Celgene is a member of Access Accelerated, a partnership of 24 biopharmaceutical companies developing innovative and sustainable solutions to improve access to treatment and care for non-communicable diseases, including cancer. In the first year of this program, 62 company programs operating in 88 countries are contributing to the mission of Access Accelerated.
To that end, we are working with the Academic Model Providing Access to Healthcare (AMPATH) program in partnership with the Government of Kenya to deliver healthcare services and strengthen health system capacity around important health-related initiatives. This program includes multiple myeloma care, pharmacovigilance, patient education and pharmacy residency programs.
We also recently introduced Celgene Cancer Care Links™, a grant program designed to support cancer healthcare capacity through partnerships in resource-constrained countries. This adds to our continued efforts to support health-related philanthropic programs, science education, and local community activities for Celgene sites and affiliates around the world.
I am extremely proud of the work we do on behalf of patients with serious unmet medical needs and by Celgene's dedicated and diverse workforce. Our employees embody a remarkable culture at Celgene that was recently recognized by Forbes as one of the World's Best Employers, ranking 9th out of the 2,000 largest companies worldwide. In 2018, we took steps to further enhance this standing as we expanded the benefits provided to our employees -- such as flexible work arrangements and increased paid parental leave for our U.S. employees. We recognize and appreciate how vital our employees are to the patients we seek to serve and are continually seeking to further strengthen our culture and engagement.
To help ensure a sustainable future and a healthy environment, we have become a member of the Environmental Protection Agency's Green Power Partnership, which recognizes companies committed to using renewable energy sources. Today, 73 percent of our electricity for U.S. office facilities is derived from renewable energy sources. We continue to advance toward our 2020 environmental goals to reduce emissions, increase purchasing of renewable energy, decrease water withdrawal and decrease solid waste generation. We achieved LEED® certification this year for the recently remodeled Conference Center and office building on our main campus. This follows the successful certification last year of our main campus expansion.
As part of our focus on business with integrity, we joined the Pharmaceutical Supply Chain Initiative in 2018. This group of major healthcare companies is working to establish and promote responsible practices that will improve social, health, safety and environmental sustainability outcomes for biopharmaceutical company supply chains. Additionally, Celgene ranked in the top five for Clinical Trial Transparency by the Bioethics International Good Pharma Scorecard.
Through our efforts across these critical areas, we continue to meet our responsibilities to stakeholders, remaining focused on our mission to improve patients' lives, while applying the highest standards of ethics, integrity and purpose.
We remain steadfastly committed to our mission, as we work to discover, develop and deliver to patients new and even more effective ways to improve and extend the lives of patients around the world.
MARK J. ALLES
Chairman and Chief Executive Officer


gsk
Good pharma scorecard
"2 of 10 reviewed companies disclosed all trials and complied with legal disclosure requirements for their 2012 approved drugs."
-New York University School of Medicine


Unleash
DE&I Awards
Our diversity, equity and inclusion initiatives are the result of the dedication of our employees and the inclusive workplace they foster. Being recognized for our efforts means we're making a difference.
Our 2022 awards and recognitions included:
#25 on the DiversityInc Top 50
#64 Forbes Best Employers for Women
Platinum-level Gender Parity Certification in 2022 with Women in Governance Organization
100% Score on the DisabilityIN: Disability Equality Index (DEI)
100% Score on the Human Rights Campaign (HRC) Corporate Equality Index (CEI)
Ranked in the 2022 Seramount Inclusion Index
Ranked in Seramount's Top 100 Companies for the 12th Year
Ranked in Seramount's Best Companies for Dads List for the 3rd Year
Ranked in Seramount's Best Companies for Multicultural Women for the 2nd Year
Ranked on Seramount's Executive Women List for the 5th Year
Received a Gold Rating (Highest Rating) in the Good Pharma Scorecard (GPS)
Won Reuters Pharma US Delivering Inclusive Studies Award
Stephanie Veyrun-Manetti
General Manager Specialty Care and Country Lead Canada
"I'm proud to share that for the fourth year in a row, Sanofi Canada has earned the Gender Parity Certification for 2022, awarded by Women in Governance (WiG). This platinum recognition reinforces our commitment to creating a work environment that is inclusive and empowers women across our organization to be successful and represented in leadership roles."
2022 DE&I Awards
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We're proud Sanofi's commitment to #clinicaltrials transparency has earned the top score of 100% on the @BioethicsIntl 2017 Good Pharma Scorecard: prn.to/2BAWOSz
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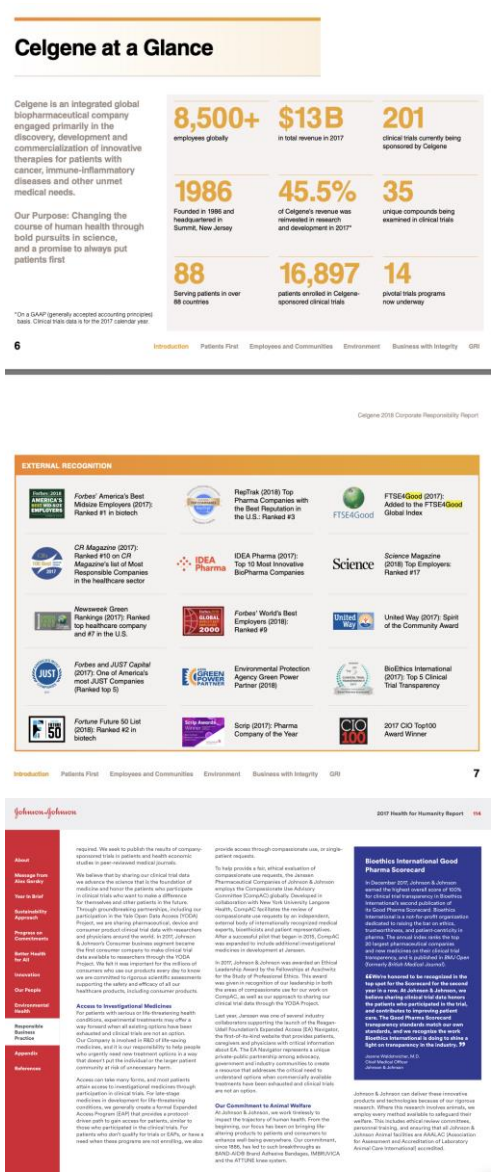
CLINICAL TRIAL TRANSPARENCY
2017
Bioethics International
Good Pharma Scorecard
8:45 AM - 5 Dec 2017


Celgene at a Glance
Celgene is an integrated global biopharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for patients with cancer, immune-inflammatory diseases and other unmet medical needs.
Our Purpose: Changing the course of human health through bold pursuits in science, and a promise to always put patients first
8,500+ employees globally
$13B in total revenue in 2017
201 clinical trials currently being sponsored by Celgene
1986 Founded in 1986 and headquartered in Summit, New Jersey
45.5% of Celgene's revenue was reinvested in research and development in 2017*
35 unique compounds being examined in clinical trials
88 Serving patients in over 88 countries
16,897 patients enrolled in Celgene-sponsored clinical trials
14 pivotal trials programs now underway
*On a GAAP (generally accepted accounting principles) basis. Clinical trials data is for the 2017 calendar year.
6
Introduction Patients First Employees and Communities Environment Business with Integrity GRI
Celgene 2018 Corporate Responsibility Report
EXTERNAL RECOGNITION
Forbes' America's Best Midsize Employers (2017): Ranked #1 in biotech
RepTrak (2018) Top Pharma Companies with the Best Reputation in the U.S.: Ranked #3
FTSE4Good (2017): Added to the FTSE4Good Global Index
CR Magazine (2017): Ranked #10 on CR Magazine's list of Most Responsible Companies in the healthcare sector
IDEA Pharma (2017): Top 10 Most Innovative BioPharma Companies
Science Magazine (2018) Top Employers: Ranked #17
Newsweek Green Rankings (2017): Ranked top healthcare company and #7 in the U.S.
Forbes' World's Best Employers (2018): Ranked #9
United Way (2017): Spirit of the Community Award
Forbes and JUST Capital (2017): One of America's most JUST Companies (Ranked top 5)
Environmental Protection Agency Green Power Partner (2018)
BioEthics International (2017): Top 5 Clinical Trial Transparency
Fortune Future 50 List (2018): Ranked #2 in biotech
Scrip (2017): Pharma Company of the Year
2017 CIO Top100 Award Winner
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Better Health for All
Innovation
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Appendix
References
Bioethics International Good Pharma Scorecard
In December 2017, Johnson & Johnson earned the highest overall score of 100% for clinical trial transparency in Bioethics International's second publication of its Good Pharma Scorecard. Bioethics International is a not-for-profit organization dedicated to raising the bar on ethics, trustworthiness, and patient-centricity in pharma. The annual index ranks the top 20 largest pharmaceutical companies and new medicines on their clinical trial transparency, and is published in BMJ Open (formerly British Medical Journal).
"We're honored to be recognized in the top spot for the Scorecard for the second year in a row. At Johnson & Johnson, we believe sharing clinical trial data honors the patients who participated in the trial, and contributes to improving patient care. The Good Pharma Scorecard transparency standards match our own standards, and we recognize the work Bioethics International is doing to shine a light on transparency in the industry. 99
Access to Investigational Medicines
Our Commitment to Animal Welfare


Corporate Responsibility
2017/2018 OVERVIEW
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RATED
SILVER
DIVERSITY, EQUITY & INCLUSION
2023
Good Pharma Scorecard
Awarded for diversity and transparency in oncology trials
Eisai

Limitations

- Public cancer incidence data have gaps
  - patient demographic data are mainly available for broad cancer types, while many therapeutics target specific cancer types.
  - missing some race and ethnicity
  - there are accuracy questions

- Cannot disaggregate trial enrollment by country, using public data sources.

Clinical Trial Diversity—Will We Know It When We See It?

Tanvee Varma, BA; Cary P. Gross, MD; Jennifer E. Miller, PhD

There is widespread consensus on the need to improve clinical trial diversity, with policy efforts spanning decades. In 2022, the US House of Representatives passed legislation, Food and Drug Amendments of 2022, requiring sponsors to develop and submit diversity action plans for certain types of trials, defining enrollment goals by age group, sex, race and ethnicity, geographic location, and socioeconomic status along with rationales for such goals.[1] This legislation would codify the draft guidance introduced by the US Food & Drug Administration (FDA) in 2022 recommending that the industry submit race and ethnicity plans for its trials to the FDA.[1]

While the policy efforts are helpful, vital gaps limit their effectiveness. First, these efforts do not clearly define adequate trial diversity. Second, they lack guidance on suitable enrollment goals, making it difficult to assess whether success has been achieved. Third, epidemiological data for various health conditions are needed to set enrollment goals. This editorial aims to address these gaps.

Defining Adequate Representation

One gap in the current policy efforts is a lack of clarity on how sponsors should conceptualize adequate representation of demographic subgroups in diversity plans. There are 2 leading approaches in the literature for conceptualizing adequate trial representation, a country-population and a condition-based approach.

The country-population approach suggests that trial participants belonging to a specific segment of the population, or demographic, should be enrolled in proportion to the country's estimates of proportions of the population who lie within that demographic.[2] For the US, this would mean enrolling 50.5% female participants, 13.6% Black participants, and the like, for all trials, regardless of a trial's indication.[3] This disease-neutral approach contrasts with the condition-based approach, which suggests that participant demographic characteristics should mirror those of the patient population with the study's targeted condition.[4] A close reading of policy efforts suggests a preference for a condition-based approach with deference to research sponsor (such as pharmaceutical companies or the National Institutes of Health) and investigator judgment. Guidance from the FDA[1] suggests using the country-population approach when disease incidence across a range of racial and ethnic populations is unknown.

A problem with this policy flexibility is that different approaches can yield markedly different enrollment goals. As shown in the **Figure**, using the US country-population approach for a melanoma trial enrolling 500 patients yielded an enrollment goal of 14% for Black patients vs 0.5% using the condition-based approach.[5] The country-population approach yields an enrollment goal 28 times larger than the condition-based approach. Similarly, for a multiple myeloma trial enrolling 500 patients, the condition-based approach yielded an enrollment goal of 9% for patients identifying as Latinx, vs 19% using the US country-population approach, amounting to a 200% difference.[5]

Setting Enrollment Goals

A second gap is the lack of guidance on how to set and justify enrollment goals. The literature[6] generally uses enrollment goals for a specific demographic group proportionally, matching 80% to 120% of the proportion that demographic group comprises within a defined population (in our case, a country or a patient population). Proportionally representing less than 80% is considered underrepresentation. For example, if Latinx patients represent approximately 20% of the US population, using a country-population approach, we would aim to enroll 16% to 24% of trial participants who identify as Latinx.

Setting enrollment thresholds is not as straightforward as it may seem. First, neither FDA guidance nor legislation addresses the inclusion of global trial participants in enrollment goals and diversity plans. Clarification is necessary, as two-thirds of pivotal trial participants are from non-US sites and trial data may not extrapolate across geographic regions.[7]

Second, this approach often fails to yield samples large enough for subanalyses. Setting an enrollment goal for Black patients in our melanoma trial example using the condition-based approach yielded an enrollment goal of 0.5%, or 3 of 500 people enrolled (Figure). A subanalysis is impossible with only 3 patients, raising questions about the rationale for mandating diversity plans. This challenge arises for studies involving racial and ethnic groups constituting a small proportion of the US population (eg, American Indian or Alaska Native patients) or rare diseases.

Data Gaps

A third policy gap is the lack of accessible demographic data on the disease incidence or prevalence needed to design and evaluate enrollment goals using the condition-based approach, as recommended in some policies.[1] Although there are several condition-specific registries with patient demographic data, they need improvement. US Cancer Statistics, a Centers for Disease Control and Prevention database[5] of newly diagnosed cancer cases and deaths, has rigorous demographic data; however, it is missing some race and ethnicity data, and there are questions about its accuracy.

Further, patient demographic data are mainly available for broad cancer types, while most therapeutics target specific cancer types. For example, non-Hodgkin lymphoma is included, but mantle cell lymphoma, a type of non-Hodgkin lymphoma, is not. Mantle cell lymphoma more often affects men, compared with non-Hodgkin lymphoma (75% vs 55%).[8] Similarly, demographic data for patients with lung cancer are available in the US Cancer Statistics but not for patients with lung cancer who have *EGFR* variations. The prevalence of *EGFR* variation potentially differs by ancestry. It is imperative to develop and disseminate more complete incidence data for more conditions and across demographic subgroups.

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Thank you! Questions?

Jennifer E. Miller, PhD

- Associate Professor, Yale School of Medicine
- Founding President, Bioethics International
- Director, Good Pharma Scorecard
- Jennifer.e.miller@yale.edu
- @millerbioethics

Discussion Questions

1. How can stakeholders such as research institutions, funders (e.g., NIH), and research journals, work together to implement cohesive representation metrics and policies?
2. Based on early efforts, are there any emerging challenges to implementing FDA diversity plans?
3. What are the potential pitfalls of instituting universal representation policies?
4. What metrics are needed to evaluate the success of representation policies?
5. How can we best incorporate intersectionality into our approach to measurement and metrics development?
6. What steps are needed to synergize these measurement dimensions across stakeholder groups?
7. Can real-world data based approaches help? If so, how?
8. How can the FDA best work with regulatory agencies in other countries to unify and harmonize how representation is measured?

Break

1:25-1:35PM ET

Session 2: Building Capacity for Representative Trials in Community Settings

Moderator: Andrea Thoumi, Duke-Margolis
Nadine Barrett, Duke CTSI Center for Equity in Research
Perla Nunes, Julius L. Chambers Biomedical Biotechnology Research Institute
Yasmeen Long, FasterCures
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Discussion Points

1. Making overt efforts to acknowledge and intervene on systemic and structural contributors to poor trial representation are essential components of improving representative trial enrollment.
2. Diversifying the healthcare and clinical trial workforce are integral to capacity building and fostering trust and accountability within the clinical trial enterprise.
3. Community-engaged strategies are most successful when they are approached as genuine relationships with ongoing communication, opportunities for feedback, meaningful efforts to engage with community members outside of trial activities, and sustainable investment in community priorities.

Discussion Questions

1. What strategies can be used to replicate and scale successful community engagement initiatives across various clinical sites?
2. What are examples of initiatives that have helped to build or restore trust among potential trial participants that have experienced historic and contemporary structural racism or discrimination within health systems?
3. What state, federal, or institutional policies are current barriers to fair compensation for trial participants?
4. What resources and funding structures can be mobilized to support access and information barriers faced by potential trial participants?
5. What funding resources can be used to enable resource strained clinical sites/systems to conduct clinical trials?

Fireside Chat

Mark McClellan, Duke-Margolis
Kirsten Bibbins-Domingo, JAMA/USCF

Session 3: Defining the Role of Various Stakeholders in Improving Trial Representation

Moderator: Mark McClellan, Duke-Margolis
Sara Calvert, Clinical Trials Transformation Initiative
Carla Rodriguez-Watson, Reagan Udall Foundation for the FDA
Salina Waddy, National Center for Advancing Translational Sciences
Megan McKenzie, Genentech
Silas Buchanan, Institute for eHealth Equity

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

Discussion Questions

1. What are the primary factors industry sponsors should consider when implementing representation goals?
2. What steps should researchers, industry, and broader stakeholder groups take to acknowledge historic and current practices that discourage marginalized populations from trial participation?
3. What approach(es) should industry sponsors and academic researchers that do not currently have established relationships with patient groups and communities use to start the relationship-building process?
4. If fair payment for participation in clinical trials becomes more common, what changes need to be made to funding paradigms for clinical trials?
5. What role can journals play as a final opportunity for transparency on trial representativeness?
6. What should stakeholders be doing now to implement point-of-care and decentralized trials to advance more equitable access to clinical research?

Closing Remarks

Thank You!

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