Representation and Extrapolation: Evidence from Clinical Trials

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20 February 2023

Motivation

- Innovation does not benefit everyone equally (Aghion et al., 2019; Jones and Kim, 2018; Kline et al., 2019).
- Research investments skew towards developing technologies appropriate for more profitable groups (Cutler, Meara and Richards-Shubik, 2012; Jaravel, 2019; Kremer and Glennerster, 2004; Michelman and Msall, 2021)
- Diffusion often occurs faster among the well-connected or well-educated (Agha and Molitor, 2018; Foster and Rosenzweig, 2010; Glied and Lleras-Muney, 2008; Hamilton et al., 2021; Papageorge, 2016; Skinner and Staiger, 2005, 2015)
- We explore another dimension of **innovation and inequality**. Does routine underrepresentation of certain groups from the R&D process contribute to disparities?

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- We explore another dimension of **innovation and inequality**. Does routine underrepresentation of certain groups from the R&D process contribute to disparities?
- Put differently, does *how* a technology is developed affect *who* adopts it?

Context: Clinical Trials and Racial Health Disparities

- Black patients are underrepresented in clinical trials that support new drug approvals in the U.S.
- Black patients are less likely to be on newly approved medications.

  Enrollment and Prescription Gap across Race | CDFs | Longer Time Series | Science Gap

  - Focus on racial gaps, though others exist, not to same degree and/or do not have same underlying life expectancy inequality.

    Across Gender | Life Expectancy Gap | By Condition

- Firms & regulators aware of these patterns – discuss two recent examples.

Diversity Challenges Slow Enrollment of Moderna's Late-Stage COVID-19 Vaccine Trial

October 12, 2020

Moderna has slowed enrollment of its phase 3 COVID-19 vaccine trial because it is experiencing challenges recruiting enough Black, Latino and Native American participants. The Cambridge, Mass.-based biotech company suggests this lack of diversity is preventing researchers from understanding how its COVID-19 vaccine candidate works in minority populations.

The late-stage 30,000-person study has been filled with mostly White volunteers, despite the fact that COVID-19 infects the Black community in the U.S. at almost three times the rate as the White community. Only around 7 percent of Moderna's vaccine trial consists of Black Americans as of Sept. 17,

Moderna Data

Moderna's stock falls 4% as CEO says enrollment in vaccine trial has been slowed to ensure diversity

Published: Sept. 4, 2020 at 2:50 p.m. ET

By Jaimy Lee

Referenced Symbols

MRNA +2.83% ▲ SPX +0.43% ▲

Shares of Moderna Inc. MRNA, +2.83% were down 4.6% in trading on Friday after the company's CEO told CNBC that it was slowing down enrollment in the Phase 3 clinical trial for its experimental COVID-19 vaccine to ensure diversity of the study's participants. The late-stage trial is expected to enroll about 30,000 participants and will be a crucial test to understanding whether the vaccine candidate can protect against infections with the virus. "We believe these efforts will improve the quality of the study and confidence in the vaccine by building evidence for benefit in the communities at highest risk of COVID-19," a company spokesperson said in an email. As of Aug. 24,

The New York Times

F.D.A. Panel Rejects Lilly's Cancer Drug Tested Only in China

The panel debated whether overseas trials could be applied to a more diverse U.S. population. The decision may affect other Chinese drug trials, and spotlights the high cost of immunotherapy.

The F.D.A.'s headquarters in Silver Spring, Md. The agency panel's decision stems from a longstanding debate: Should a drug tested only in another country be accepted without U.S. trials? Jim Lo Scalzo/EPA, via Shutterstock

By Gina Kolata

Feb. 10, 2022

Dr. Richard Pazdur, the powerful director of the F.D.A.'s oncology unit, explained on Thursday why he had backtracked from a far more welcoming attitude in 2019, when he said the agency might consider a checkpoint inhibitor tested solely in China.

"Over the past two or three years, this country has experienced tremendous social change," he said at the meeting. "We clearly heard from all patient groups that they want faces like theirs." That, he said, is also important to build confidence in the clinical trials and the drugs being tested.

Physician Perspective

"As a physician caring for patients in an urban safety net setting and wanting to provide the best evidence-based preventive care...I'd spend as much time on the science as I devoted to reinforcing with patients why they should still trust these guidelines and the process, despite the unrepresentative populations in the evidence base."

— Dr. Kirsten Bibbins-Domingo (Editor-in-chief, *JAMA*)

Back Information Dissemination

This Project

- We explore the consequences and causes of the persistent under-representation of Black patients from clinical trials on medical decision-making.
  1. Does representative data matter to physicians and patients?
  2. If so, why are such data not supplied endogenously by the market?

- To address the first question – conduct survey experiments with physicians and patients.
  - Cross-randomize drug efficacy ("the numeraire") with racial representation in trial for physician respondents.
  - Simpler but similar exercise for patient respondents.

- To address the second question – turn to a theoretical framework on similarity-based extrapolation.

Model Overview

- People learn more from samples that "look like them" *i.e.,* similarity-based extrapolation.
- Consistent with broad array of mental models and psychological processes as well as physician training in evidence-based medicine.
- All agents use the same mental model to interpret data, but increasing representation has a larger effect on Black patients due to their substantial and persistent under-representation in trials to date.
- Despite these benefits of representative data, our framework predicts that those who have benefited more from past medical breakthroughs are less costly to enroll in the present, leading to persistence in who is represented in the evidence base.

Preview of Empirical Findings

- Statistically (& medically) significant racial gaps in perceived benefits of new technology when trials are not representative.
  - Black patients view non-representative trials as less relevant for their care.
  - Physicians who treat Black patients are less likely to prescribe medications based on non-representative evidence.

- Gaps in perceived benefits are narrowed when patients and physicians are presented with more representative trial data.
  - Driven by gains to Black patients and their doctors without losses to White patients or their doctors over domain tested.

- Mechanism: Doctors and (to a greater extent) patients — lack confidence in extrapolating from samples that are not representative of them or their patients.

- Case studies: disease conditions with more representative trials tend to have higher diffusion of new drugs to Black patients.

Related literatures

- **Mental models** [*e.g.* Gilboa and Schmeidler (1995); Mullainathan, Schwartzstein and Shleifer (2008); Bordalo, Gennaioli and Shleifer (2020); Bordalo et al. (2022); Malmendier and Veldkamp (2022)]
- **Innovation and health inequality** [Cutler et al. 2012, Hamilton et al. 2021]
- **Incentives for health innovation** [Agha et al. 2022, Azoulay et al., 2020, Budish et al. 2015, Finkelstein 2004, Finkelstein 2007, Malani and Philipson 2011]
- **Physician Agency** [Ellis and McGuire 1986, Barnato 2017]
- **Medical care and discrimination** [Alsan and Wanamaker 2018, LaVeist et al. 2011, Obermeyer et al. 2019]
- **Technology adoption** [Conley and Udry 2010., Duflo et al. 2011, BenYishay and Mobarak 2019, Corral et al. 2020, Beaman et al. 2021, Suri and Udry 2022, Iversen and Ma 2022]
- **Trust and health inequality** [Alsan et al. 2019, Lowes and Montero 2021, Boulware et al. 2003, Hammond et al. 2010, Adam et al. 2017]
- **Survey experiments** [Alesina et al. 2022, Haaland et al. 2022, Kessler et al. 2019, Low 2021, Kesselheim et al. 2012, Kuziemko et al. 2015, Macchi 2021]
- **Legitimacy** [Persad 2017, Applbaum 2017 and 2019, Fricker 2007]

Outline

Institutional Context

The Drug Development Process

- **Regulation:** New drugs must demonstrate safety and efficacy to FDA before approval for sale.
  - Phase I, II, and III trial data. FDA Process
- **Private Sector:** Large share of trials sponsored by firms.
  - $\sim$30% of U.S.-regulated trials have a private sector primary sponsor, relative to $\sim$3% for U.S. government sponsors.
  - Median share Black is 3% in private sector trials, relative to 6% in government and non-profit academic. [ClinicalTrials.gov]
- **Revenue:** U.S. is $\sim$ 46% of global pharmaceutical revenues Market
- **Cost:** Clinical Trials are expensive – patient "accrual" rates cited as #1 reason for trial delays and (rarely) failures.
  - Benefits and cost of trial participation may vary across groups.

Licensed medicines

After a **clinical trial** has shown a new medicine is safe and effective, it must be granted a license before it can be made available for widespread use. The license confirms the health condition it can treat and the recommended dosage.

Licenses are granted by the **Medicines and Healthcare products Regulatory Agency (MHRA)** in the UK, by the European Commission, acting on advice from the **European Medicines Agency (EMA)** in Europe and by the **Food and Drug Administration (FDA)** in America. These bodies consider all the evidence to ensure that the medicine is safe and effective. The license they then grant means we can trust that the medicines we are offered will help rather than harm us.

Because different countries have different processes, some medicines can be available in some countries but not in others.

When a medication has a license from the MHRA that confirms it is safe and effective, it can be made available in the UK to buy privately at a price set by the pharmaceutical company that manufactures it.

Once the price of the medication is set, the National Institute for Health and Care Excellence (NICE) assesses the evidence for the effectiveness of the treatment and its cost. NICE recommends whether it should be funded by the National Health Service (NHS) and for which conditions and symptoms. The medicine should be available through the NHS within three months after NICE has made the funding decision.

Dissemination of New Drug Data

- Doctors learn about new drugs through journal articles, continuing medical education, pharmaceutical reps, social networks and embedded in clinical guidelines.
  - 72% of doctors asked by patients if "drug will work in people like me."
    Questions to Doctors
  - Evidence-based medicine training (required in U.S. accredited medical colleges) includes considering whether study sample is similar to own patients.
    EBM Patient Questions re: New Medicines
  - Qualitative evidence, presumption that most guidelines not based on representative data.
    Quotation
- Patients learn about new drugs mainly through doctors, but also social networks.
  - In the U.S., direct-to-consumer advertising (DTCA) also allowed.

Views on Science and Clinical Trials Among U.S. Respondents

Variable	(1) Black Respondents Mean/SD	(2) White Respondents Mean/SD	(3) Difference (1)-(2)
Confidence in Research Institutions	2.829	3.082	-0.253**
	(0.963)	(0.822)	
Heard of Clinical Trial	0.796	0.875	-0.079**
	(0.374)	(0.339)	
Would Enroll in Clinical Trial if Doctor Recommends	0.783	0.837	-0.054**
	(0.384)	(0.379)	
Trust Not Reason for Lack of Enrollment	0.432	0.536	-0.104***
	(0.463)	(0.514)	
Science is Beneficial	0.284	0.383	-0.099**
	(0.419)	(0.493)	
Would Get FDA-Approved Vaccine	2.907	3.069	-0.163
	(1.024)	(1.099)	
Kling-Liebman-Katz (KLK) Index	0.824	1.072	-0.248***
	(0.428)	(0.545)	

Racial Gaps in Perceived Benefits

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High Awareness of Clinical Trials... Yet Gaps Persist

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Racial Gaps in Barriers to Participation

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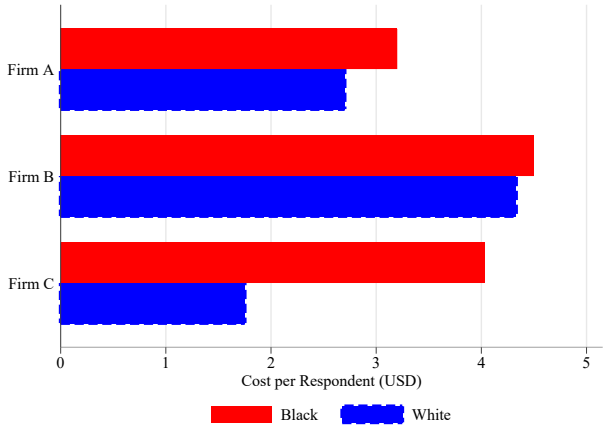
Recruitment Costs by Race across Firms



– Framework will endogenize cost differentials.

(Brief) Policy Timeline

Series of federal efforts to address representation in medical research though lack incentives or penalties. Persistent pattern. Longer Time Series

- **1993**: NIH Revitalization Act establishes guidelines for inclusion of women, minorities in medical research
- **1998**: FDA requires drug sponsors to report trial composition by race, sex when seeking approval
- **2000**: ClinicalTrials.gov platform established, with goal of increasing transparency of research
- **2015**: FDA Five-Year Plan lays out strategy for improving racial representation in trials, begins posting *pivotal* trial composition publicly
- **2022**: FDA issues draft guidance proposing that trial composition reflect eventual patient population

Organizing Framework

Purpose of Framework

1. Formalize how representation in the trial process affects perceived benefits of new drugs for patients and their doctors, yielding predictions we can then test experimentally.

2. Deepens understanding of why underrepresentation of Black patients is an equilibrium outcome, requiring us to move beyond experimental predictions and model the costs and benefits to firms conducting clinical trials.

3. Clarifies why patterns have been so persistent, identifying an intertemporal externality associated with a history of underrepresentation.

Pharmaceutical Firms Choose Recruitment Strategy τ

$$\Pi_\tau = s_\tau \times v_\tau - c_\tau$$

- s_τ: success probability of the trial
- v_τ: (mark-up per unit of demand$_\tau$)$\times$(demand$_\tau$)
- c_τ: cost of running trial

Assume that τ comes in three types, which imply different demographic compositions, and that there are only Black and White people:

1. $\tau = R$epresentative of overall US population
2. $\tau = W$hite people overrepresented
3. $\tau = B$lack people overrepresented

v_τ Depends on Demand and thus Perceived Benefits of Drug

- Assume doctors are agents for patients (rule out strategic behavior).
- Suppose treatment T to patient in dyad i satisfies $b_i \in \{0, \tilde{b}\}$, $\tilde{b} > 0$.
- Let θ be likelihood T works similarly well for patient as demonstrated in trial.
- Let x be patient characteristics.
  - Our case: uni-dimensional in $\{0, 1\}$, where $x_i = 1$ corresponds "Black".
  - $\bar{x}$ then equals the share Black in the trial.
- Trial data reports averages:

  $\bar{b}_T \equiv \tilde{b}_T \times \frac{k_T}{N_T}$ (average efficacy, where k_T is #successes, and N_T is sample size).
  $\bar{x}_T(x_i)$ (average share of group i).

- Perceived benefit of treatment for patient in dyad i given trial data h:

$$\hat{b}_i = \tilde{b} \times \mathbb{E}_i[\theta(x_i)|h].$$

Perceived Benefits and Similarity-Based Extrapolation

Key assumption: with probability $m > 0$ characteristic x_i matters for how well the treatment will work. Thus, for patients with characteristic x_i:
$\theta(x_i) \equiv \Pr(b_i = \tilde{b}|x_i)$.

- for patients: reflects learning from similarity.
- for doctors: reflects evidence-based medicine.

$$\hat{b}(x_i; h) = m\left(\tilde{b} \times \mathbb{E}[\theta(x_i)|h, x_i \text{ matters}]\right) + (1-m)\left(\tilde{b} \times \mathbb{E}[\theta(x_i)|h, x_i \text{ doesn't matter}]\right)$$

- To generate simple closed-form expressions for the above expectations, we assume priors over θ are in the Beta family.

  $\theta(x_i) \sim \text{Beta}(\alpha_i, \beta_i)$ Closed Form Expression

Implications for Beliefs

Proposition 1: If $m > 0$ is fixed and $\frac{k_T}{N_T}$ exceeds prior $\alpha_i/(\alpha_i + \beta_i)$ then:

1. Perceived benefit of treatment $\uparrow$ in efficacy: i.e., $\frac{\partial \hat{b}(x_i;h^T)}{\partial k_T} > 0$.
2. Perceived benefit of treatment for individual of group j $\uparrow$ in its representation: i.e., $\frac{\partial \hat{b}(x_i;h^T)}{\partial \bar{x}_T(x_i)} > 0$.
3. Diminishing returns to representation: i.e., $\frac{\partial^2 \hat{b}(x_i;h^T)}{\partial \bar{x}_T(x_i)^2} < 0$.

Details on Updating | Numerical Examples | Subgroups Reported Case | Subgroups Not Reported Case

Implications for Physician-Patient Behavior

Let $d(x_i; h^T) = \Pr\left(-\varepsilon_{iT} \leq \hat{b}(x_i; h^T) - n_T - p_T\right)$ be the likelihood a patient with characteristic x_i is treated when the treatment T is indicated, where:

- n_T: the non-price costs of prescribing or adhering to treatment T
- p_T: the price (*i.e.*, copay) for treatment T
- ε_{iT}: a stochastic shock that is i.i.d. across i according to $F_\varepsilon(\cdot)$

Corollary 3: Doctors are less likely to prescribe new drug (& patients less likely to demand and/or adhere) when their representation in trials is low.

- i.e., $\frac{\partial d(x_i;h^T)}{\partial \bar{x}_T(x_i)} > 0$
- Increasing representation has more of an effect for Black vs. White patients (given diminishing returns), i.e., $\frac{\partial^2 d(x_i;h^T)}{\partial \bar{x}_T(x_i)^2} < 0$

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We test predictions in Proposition 1 and Corollary 3 by making $\bar{x}_T(x_i)$ salient.

Behavior on Firm's v_τ

Summary of Theoretical Predictions and Empirical Results

- Other insights from model
  - Values of representative trials are higher (due mainly to diminishing returns).
  - But so are costs (due to history of underrep.)
  - Creates cycle of under-representation
  - Requires investment in inclusive infrastructure.

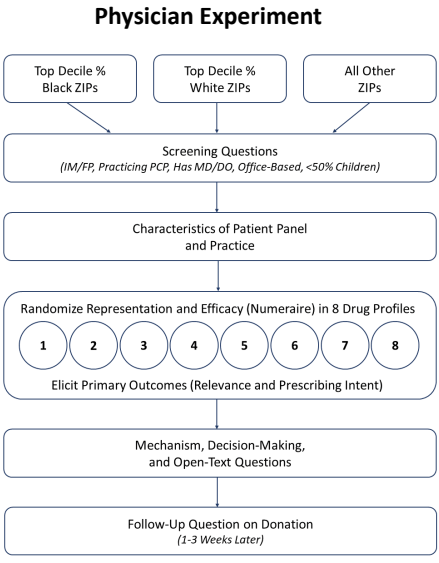
Cycle of Underrepresentation

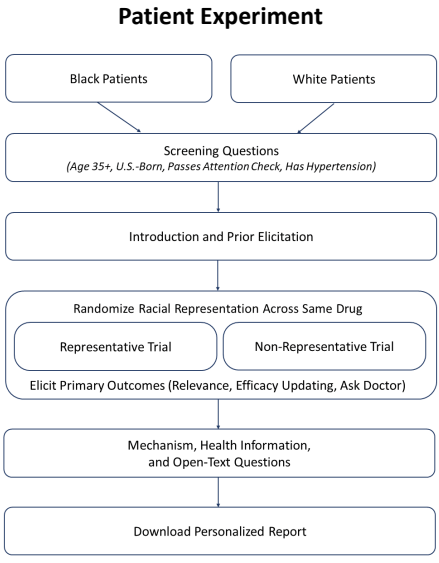
Theory	Predictions	Exhibits	Result Summary
Prop. 1.1; Cor. 3.1	Perceived benefits and demand for a new medication are increasing in trial-reported efficacy.	***Table III***	A 1 sd increase in efficacy increases physician prescribing intention by 0.28 sd.
Prop. 1.2; Cor. 3.2	Perceived benefits and demand for a new medication are increasing in representation of similar patients in clinical trials.	***Table III***	• For physicians, a 1 sd increase in representation increases prescribing intention by 0.11 sd. • For Black patients, being assigned to the representative treatment increases self-reported relevance for their own care ("relevance") and the likelihood that their posterior on efficacy is within a small neighborhood of the reported clinical-trial results ("loading on the signal") 0.78 sd and 19.9 pp, respectively.
Prop. 1.3; Cor. 3.3	Diminishing returns to representation.	***Figure II(d); Table III***	• For Physicians treating White Patients ("PWP"), we fail to reject the null hypothesis that a decrease in White representation (from existing high levels) does not change prescribing intention. • For White patients, we fail to reject the null hypothesis that a decrease in White representation (from existing high levels) does not change relevance or loading on the signal.
Cor. 4	• There are White-Black gaps in perceived benefits and demand for a new medication. • Increasing Black representation in clinical trials narrows these gaps.	***Figure III; Figure IV; Figure V***	• PWP have a mean prescribing intention of 6.46 while PBP who are exposed to non-representative trials have a mean prescribing intention of 4.90. The prescribing intention of PBP who are exposed to representative trials increases to 6.26 and is statistically indistinguishable from that of PWP. • Black patients who are shown the low representation trial are 26 pp less likely to load on the signal than White patients. Black patients shown the representative trials are only 5 pp less likely to load on the signal than White patients and this difference is statistically indistinguishable from 0.
Prop. 2; Cor. 2	Groups that were historically underrepresented have a lower propensity to participate in trials today than historically well-represented groups.	**Table I**	Black respondents are 9.9 pp less likely to perceive science as beneficial, 7.9 pp less likely to have heard of clinical trials and 5.4 pp less willing to participate in clinical trials when recommended by a doctor.
Prop. 3	In the absence of government regulation or other public-policy intervention, low representation of Black patients in clinical trials is a persistent equilibrium outcome.	**Figure I(a)**; SectionVI.1	• Black participation in pivotal trials remains low at a median of five percent over time. • In contrast to cancer trials, HIV/AIDS trials are associated with higher percent Black representation and greater prescribing of new therapies.

Notes: Formatting of the exhibits indicate the type of evidence: ***causal evidence***; **descriptive evidence**; suggestive evidence.

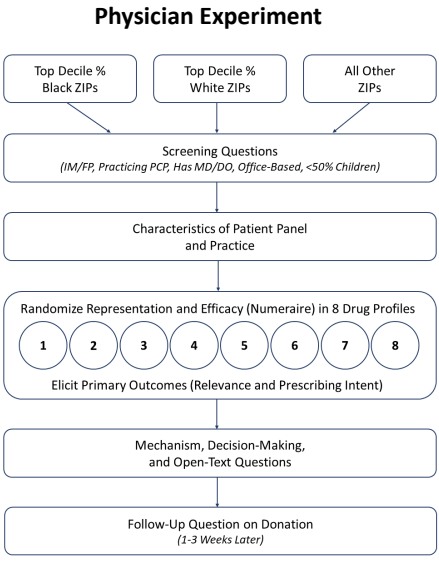
Physician and Patient Experiments

Overview


Physician Experiment
Top Decile % Black ZIPs
Top Decile % White ZIPs
All Other ZIPs
Screening Questions
(IM/FP, Practicing PCP, Has MD/DO, Office-Based, <50% Children)
Characteristics of Patient Panel and Practice
Randomize Representation and Efficacy (Numeraire) in 8 Drug Profiles
1
2
3
4
5
6
7
8
Elicit Primary Outcomes (Relevance and Prescribing Intent)
Mechanism, Decision-Making, and Open-Text Questions
Follow-Up Question on Donation
(1-3 Weeks Later)


Patient Experiment
Black Patients
White Patients
Screening Questions
(Age 35+, U.S.-Born, Passes Attention Check, Has Hypertension)
Introduction and Prior Elicitation
Randomize Racial Representation Across Same Drug
Representative Trial
Non-Representative Trial
Elicit Primary Outcomes (Relevance, Efficacy Updating, Ask Doctor)
Mechanism, Health Information, and Open-Text Questions
Download Personalized Report

Overview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Diverse Trial
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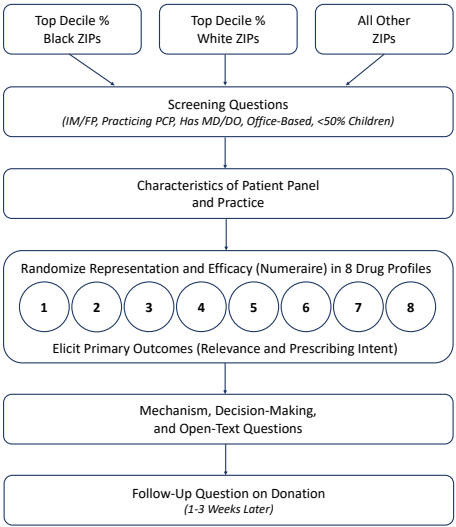
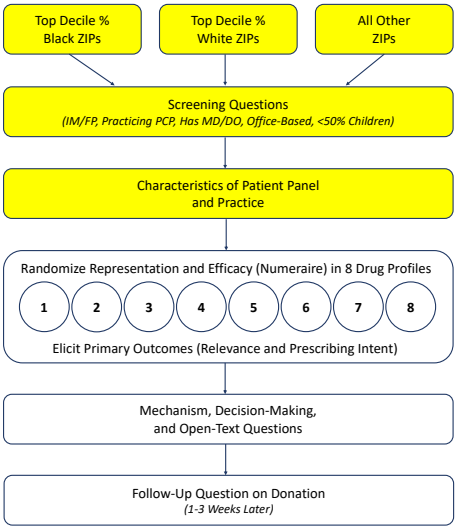
Physician Experiment: Overview



- Physicians are the gatekeepers (i.e., write prescriptions)
- Doctors are familiar with evaluating new medications
  - Doctors asked to rate several drugs
  - Randomized the racial composition of the trial and efficacy Drug Profile
  - Focus on diabetes: common primary care condition; several novel treatments have recently been developed
- Primary outcomes of interest:
  1. Drug's relevance for patient panel
  2. Prescribing intent

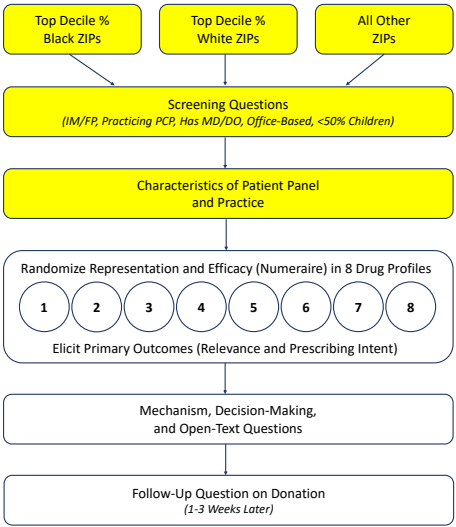
Physician Experiment: Sampling



Criteria for Inclusion

1. Actively practicing in primary care
2. Earned either a MD or DO
3. Work in an outpatient setting (i.e., hospitalists were not included)

Physician Experiment: Sampling



Criteria for Inclusion

1. Actively practicing in primary care
2. Earned either a MD or DO
3. Work in an outpatient setting (i.e., hospitalists were not included)

Recruitment

Compare to AMA

- Worked with a licensed vendor of the AMA Masterfile
- Over-sampled physicians from primarily Black and White ZIP codes

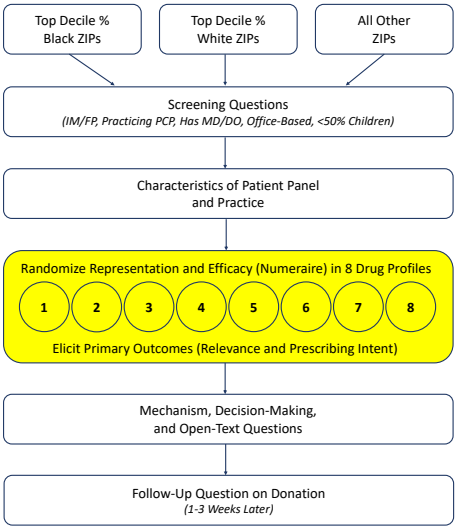
Segregation

- Sent out email invite outlining study on "views on clinical trials research"

Physician Email Invite

- Screen for inclusion criteria at survey start

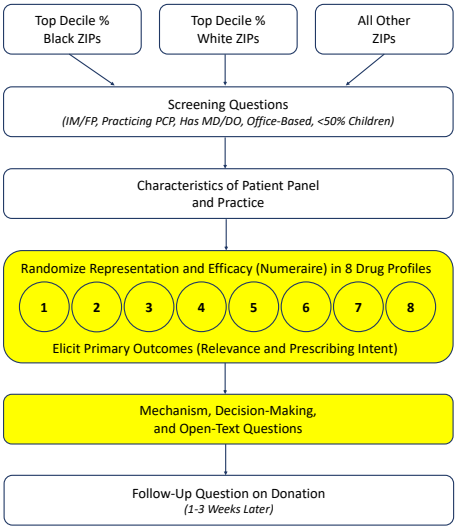
Physician Experiment: Study Flow



Respondents were asked to rate 8 hypothetical drug profiles (adapting from Kessler, Low, and Sullivan 2019; Low 2021; Kesselheim et al. 2012).

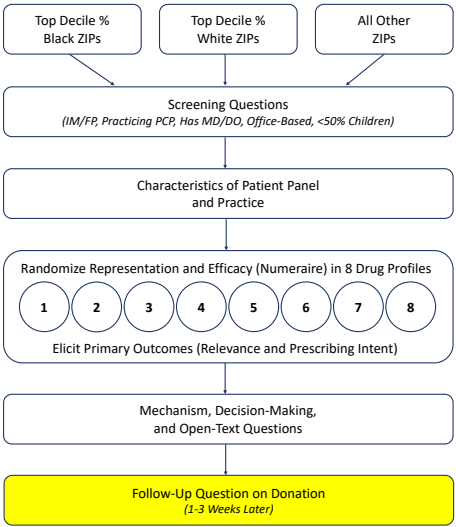
- Although vignettes were hypothetical, the drugs were based on recent therapies for diabetes. List of Drugs Example
- Randomly assigned an efficacy value ranging uniformly from 0.5% to 2% reduction in A1c.
- Randomly assigned percent trial subjects Black from 0% to 35%. Actual Distribution
  - Over-sampled low values (mimicking actual clinical trials).
  - Subjects of other races held constant at 10%. Percent White was 90% minus Black.

Physician Experiment: Study Flow



- Type of trial and sample size were constant across all profiles.
- After each profile, physician respondents were asked:
  1. To rate the relevance of the trial findings for patients in their care
  2. How likely they would be to prescribe the drug for patients in their care
- Following experiment, asked multiple-choice and open-ended questions to better understand mechanisms

Physician Experiment: Follow-up Donation

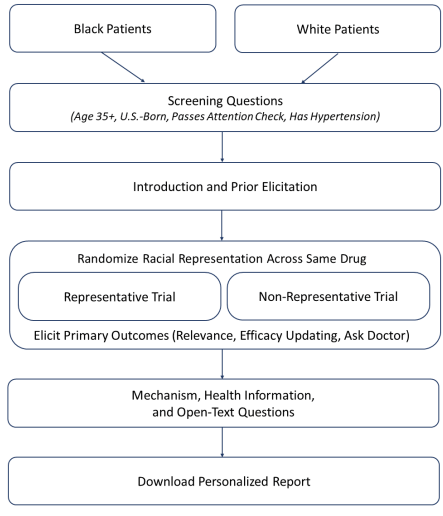


- 1-3 weeks after initial response (with two reminders) to limit experimenter demand
  Email
- 60% of physicians from the original sample responded
  $\Rightarrow$ No differences in physician characteristics compared to full sample Table
- Allocate $5 in donations between two campaigns to raise trial participation:
  1. Among historically under-represented minorities Donation Website
  2. Among the broader American public

Overview

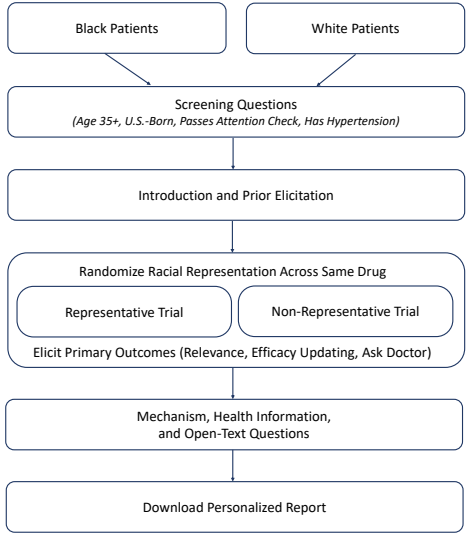
Physician Experiment

Patient Experiment



Patient Experiment: Overview

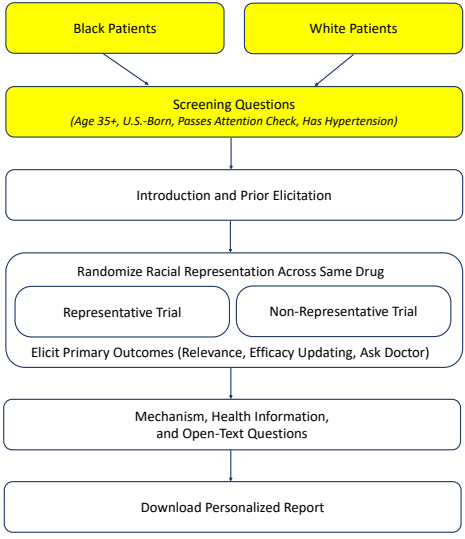
- Rationale:
  1. Patients' adherence behavior determines whether prescribed drugs will have salubrious effect
  2. Direct-to-consumer advertising in U.S.
  3. Doctors are agents for patients
- Randomized information on same drug
- Focus on hypertension: More adults with hypertension (45%) than diabetes (15%)
- Outcomes of interest:
  - Relevance for own health
  - Beliefs on the drug's efficacy
  - Willingness to "ask their doctor" about the new medication



Patient Experiment: Sampling and Recruitment

Criteria for Inclusion

- Self-reported non-Hispanic White or non-Hispanic Black race/ethnicity
- Being at or above age 35
- Endorsement of a diagnosis of high BP



Patient Experiment: Sampling and Recruitment

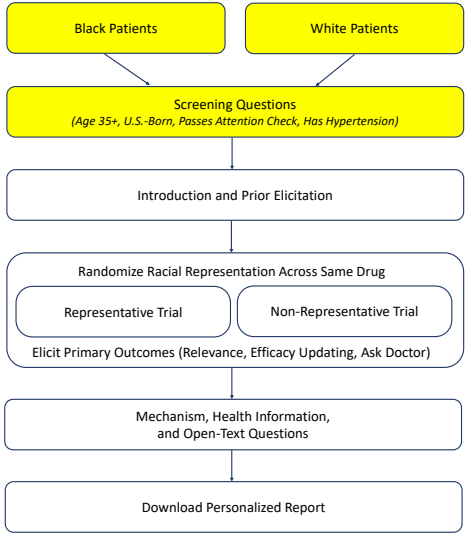
Criteria for Inclusion

- Self-reported non-Hispanic White or non-Hispanic Black race/ethnicity
- Being at or above age 35
- Endorsement of a diagnosis of high BP

Recruitment

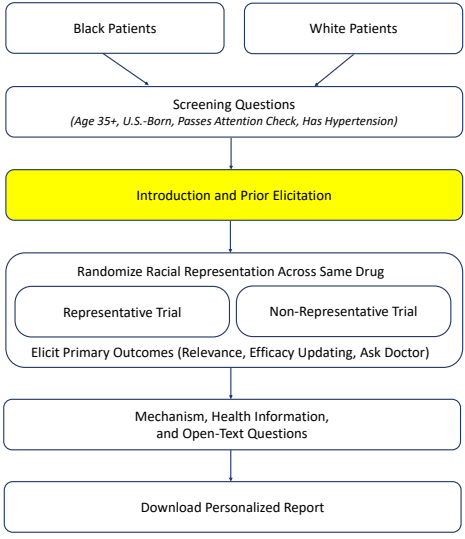
Compare to MEPS

- Recruited from the Lucid online survey platform
- Informed soliciting views on health care and interest in health research
- Entered latest systolic and diastolic BP as open text ⇒ Screen out non-sensible responses



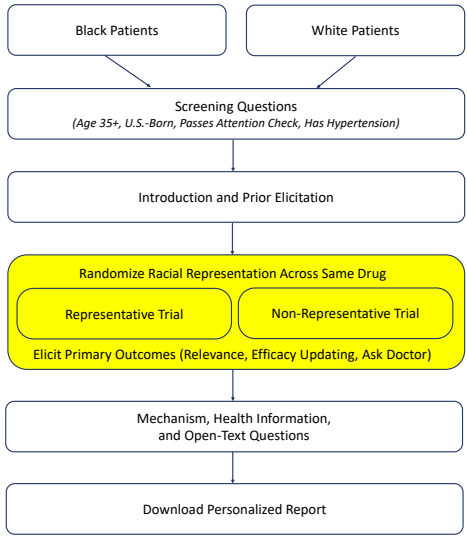
Patient Experiment: Study Flow

- First educated patient respondents on clinical trials:
  - New medications to treat BP are studied and aim to improve BP control, reduce complexity, or decrease side effects
  - No guarantee that new medication will be improvement ⇒ Must be tested
- Introduced novel antihypertensive medication (95% hadn't heard about it)
- Asked about anticipated effect (i.e., prior) on respondents systolic blood pressure (in mmHg)



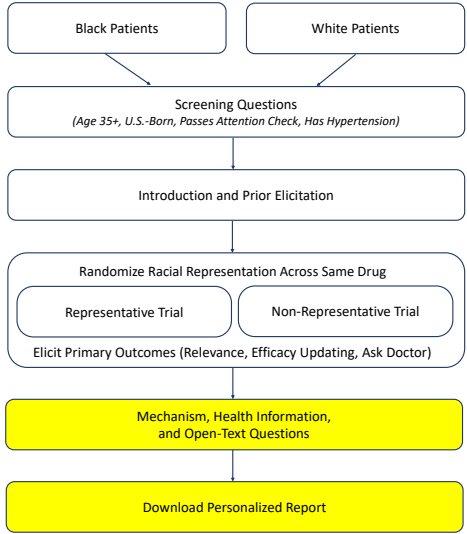
Patient Experiment: Study Flow

- Provided with findings from actual clinical trial for the drug Example
- Black share of <1% vs. 15% – all other characteristics were held constant Actual Distribution
- After viewing the trial profile, patients were asked:
  1. To express their posterior belief about the drug's efficacy
  2. How relevant the findings of the trial were for their hypertension
  3. Whether they would be interested in ''asking their doctor" about the medication



Patient Experiment: Study Flow

- Following experimental portion:
  - Asked multiple-choice and open-ended questions to better understand mechanisms
  - Elicited additional health information (such as insurance status and previous medications taken)
  - Respondents able to download personalized report



Social Desirability and Experimenter Demand

Social Desirability and Experimenter Demand

Physician Survey Balance Table

- Adapted incentivized resume rating approach (Kessler et al. 2019, Low 2021, Kesselheim et al., 2021)
- Noted that responses would be incorporated into a report to NIH and NASEM – 72% elected to receive a copy Subsample Results
- No strong order effects, suggesting not learning over the course of experiment Results by Profile Order
- Verified that survey responses correlate with donation behavior Results

Social Desirability and Experimenter Demand

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- No strong order effects, suggesting not learning over the course of experiment Results by Profile Order
- Verified that survey responses correlate with donation behavior Results

Patient Survey Balance Table

- Stated at the outset that respondents should answer truthfully; hypertensive patients - intrinsically interested in new therapies Experimental Intro
- Randomized *across*, not *within* – difficult to infer research aim when rating one trial only Word Cloud
- Pattern of results by race not consistent with social desirability (see below)
- 42% take-up of personalized report to be shared with provider Subsample Results

Estimation

Physician Survey Experiment

$$Y_{jk} = \alpha_0 + \alpha_1 \text{Representation}_{jk} + \alpha_2 \text{Efficacy}_{jk} + \rho_k + \mu_j + \sigma_{jk} + \epsilon_{jk}, \qquad (1)$$

where j denotes a drug and k denotes a unique physician respondent. Y_{jk} denotes our primary outcomes of interest.

Estimation

Physician Survey Experiment

$$Y_{jk} = \alpha_0 + \alpha_1 \text{Representation}_{jk} + \alpha_2 \text{Efficacy}_{jk} + \rho_k + \mu_j + \sigma_{jk} + \epsilon_{jk}, \quad (1)$$

where j denotes a drug and k denotes a unique physician respondent. Y_{jk} denotes our primary outcomes of interest.

Patient Survey Experiment

$$Y_{i(r)} = \beta_0 + \beta_1 1_{i(r)}^{representativeness} + X'_{i(r)}\Omega + \epsilon_{i(r)}, \quad (2)$$

where $1^{representativeness}$ is an indicator capturing the difference between receiving the information that the percent Black of trial participants was 15% as opposed to less than 1%.

Main Findings

Main Results: Physician Survey

	No Controls	
	Relevance	Prescribe
	(1)	(2)
Representation	0.163***	0.179***
	(0.039)	(0.036)
Efficacy	0.165***	0.229***
	(0.038)	(0.039)
Representation × Patient Percent Black		
Efficacy × Patient Percent Black		
p-value: Representation=Efficacy		
p-value: Representation=$\frac{1}{2}$(Efficacy)		
Doctor FEs	No	No
Profile Order FEs	No	No
Rx Mechanism FEs	No	No
Observations	1,096	1,096

Main Results: Physician Survey

	No Controls		*Main Specification*	
	Relevance	Prescribe	Relevance	Prescribe
	(1)	(2)	(3)	(4)
Representation	0.163***	0.179***	0.109***	0.107***
	(0.039)	(0.036)	(0.029)	(0.029)
Efficacy	0.165***	0.229***	0.189***	0.281***
	(0.038)	(0.039)	(0.029)	(0.032)
Representation × Patient Percent Black				
Efficacy × Patient Percent Black				
p-value: Representation=Efficacy			0.057	<0.001
p-value: Representation=$\frac{1}{2}$(Efficacy)			0.655	0.314
Doctor FEs	No	No	Yes	Yes
Profile Order FEs	No	No	Yes	Yes
Rx Mechanism FEs	No	No	Yes	Yes
Observations	1,096	1,096	1,096	1,096

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Profile Order FEs	No	No	Yes	Yes
Rx Mechanism FEs	No	No	Yes	Yes
Observations	1,096	1,096	1,096	1,096

Main Results: Physician Survey

	No Controls		*Main Specification*		*Share Black Interactions*	
	Relevance	Prescribe	Relevance	Prescribe	Relevance	Prescribe
	(1)	(2)	(3)	(4)	(5)	(6)
Representation	0.163***	0.179***	0.109***	0.107***	0.007	-0.005
	(0.039)	(0.036)	(0.029)	(0.029)	(0.038)	(0.039)
Efficacy	0.165***	0.229***	0.189***	0.281***	0.179***	0.285***
	(0.038)	(0.039)	(0.029)	(0.032)	(0.036)	(0.043)
Representation × Patient Percent Black					0.004***	0.004***
					(0.001)	(0.001)
Efficacy × Patient Percent Black					0.000	-0.000
					(0.001)	(0.001)
p-value: Representation=Efficacy			0.057	<0.001		
p-value: Representation=$\frac{1}{2}$(Efficacy)			0.655	0.314		
Doctor FEs	No	No	Yes	Yes	Yes	Yes
Profile Order FEs	No	No	Yes	Yes	Yes	Yes
Rx Mechanism FEs	No	No	Yes	Yes	Yes	Yes
Observations	1,096	1,096	1,096	1,096	1,096	1,096

Main Results: Physician Survey

	No Controls		*Main Specification*		*Share Black Interactions*	
	Relevance	Prescribe	Relevance	Prescribe	Relevance	Prescribe
	(1)	(2)	(3)	(4)	(5)	(6)
Representation	0.163***	0.179***	0.109***	0.107***	0.007	-0.005
	(0.039)	(0.036)	(0.029)	(0.029)	(0.038)	(0.039)
Efficacy	0.165***	0.229***	0.189***	0.281***	0.179***	0.285***
	(0.038)	(0.039)	(0.029)	(0.032)	(0.036)	(0.043)
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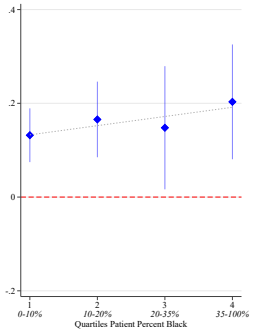
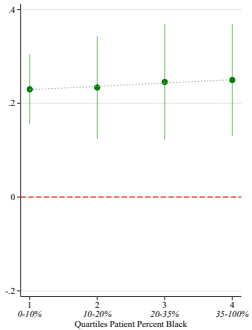
Observations	1,096	1,096	1,096	1,096	1,096	1,096

Heterogeneity Among Physicians by Racial Composition of Patient Panel

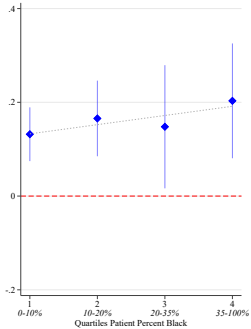


Efficacy on Relevance

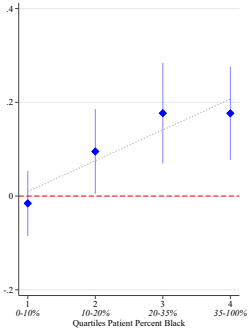


Efficacy on Prescribing

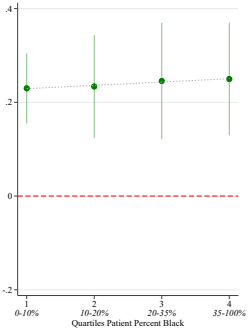
Heterogeneity Among Physicians by Racial Composition of Patient Panel



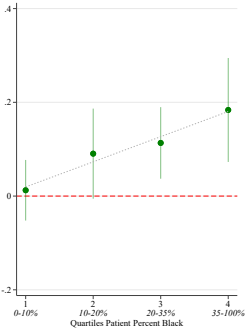
Efficacy on Relevance



Representation on Relevance



Efficacy on Prescribing



Representation on Prescribing

Omnibus | Association with MD Characteristics

Association Between Physician-Specific Coefficients and Trial Donations

	(1)	(2)
Coefficient on Representation	1.279***	1.229***
	(0.449)	(0.436)
Coefficient on Efficacy		0.199
		(0.621)
Constant	3.534	3.485
Observations	82	82

Notes: Table reports OLS estimates regressing dollars donated to a campaign promoting clinical trial participation among under-represented minorities (out of a possible $5) on individual physician coefficients using all standardized variables. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5 and 1 percent level, respectively.

Internal Validity | Results With Follow-up Sample | Characteristics Comparison

Main Results: Patient Survey

	Relevance	
	Black Patients (1)	White Patients (2)
Representative Treatment	0.781***	0.172
	(0.167)	(0.159)
p-value: Black=White		.008
Control Mean	-0.26	-0.23
Observations	139	136

Main Results: Patient Survey

	Relevance		*Ask Doctor*	
	Black Patients (1)	White Patients (2)	Black Patients (3)	White Patients (4)
Representative Treatment	0.781***	0.172	0.021	0.006
	(0.167)	(0.159)	(0.077)	(0.079)
p-value: Black=White		.008		.893
Control Mean	-0.26	-0.23	0.70	0.70
Observations	139	136	139	136

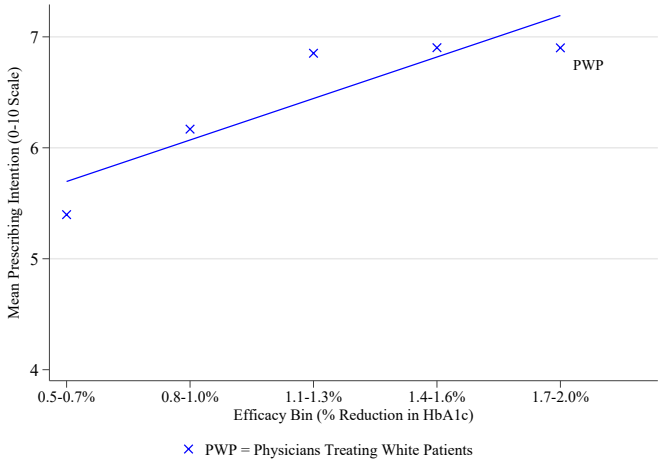
Main Results: Patient Survey

	Relevance		*Ask Doctor*		*Loading on Signal*	
	Black Patients (1)	White Patients (2)	Black Patients (3)	White Patients (4)	Black Patients (5)	White Patients (6)
Representative Treatment	0.781***	0.172	0.021	0.006	0.199**	-0.057
	(0.167)	(0.159)	(0.077)	(0.079)	(0.083)	(0.086)
p-value: Black=White		.008		.893		.030
Control Mean	-0.26	-0.23	0.70	0.70	0.33	0.59
Observations	139	136	139	136	139	136

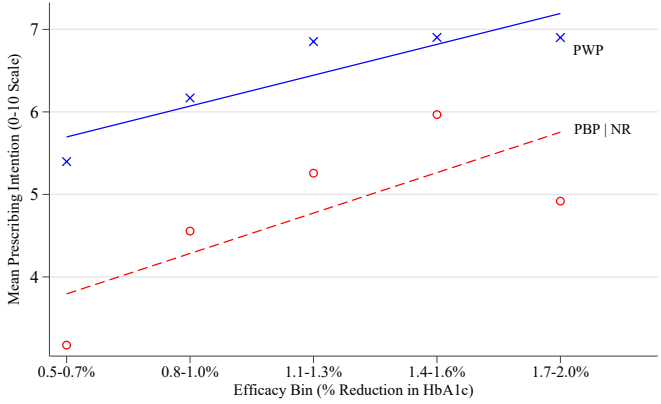
Heterogeneity

Representation and Inequality

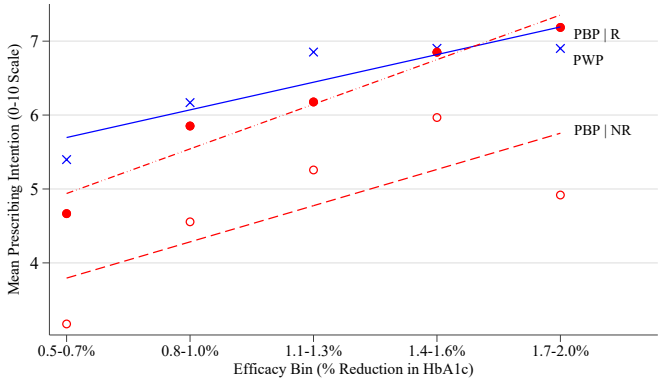
Physician Prescribing Intent by Patient Composition and Trial Representation



Physician Prescribing Intent by Patient Composition and Trial Representation

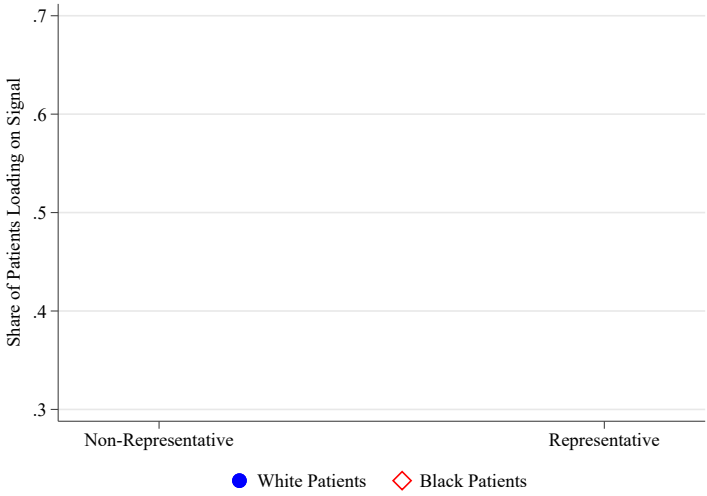


Physician Prescribing Intent by Patient Composition and Trial Representation

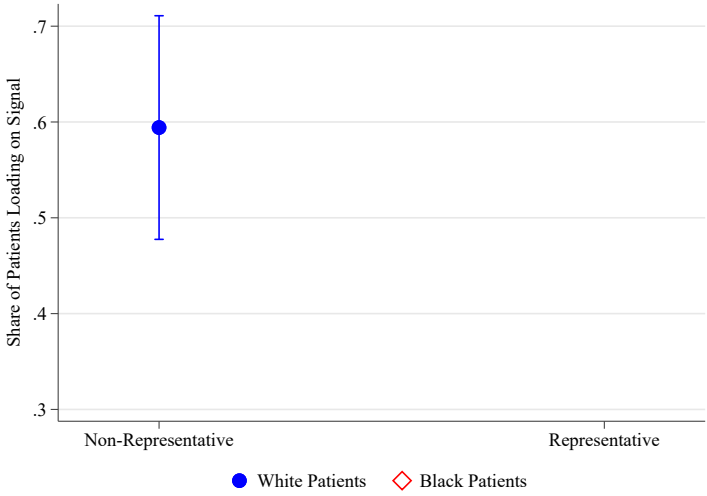


Quartiles

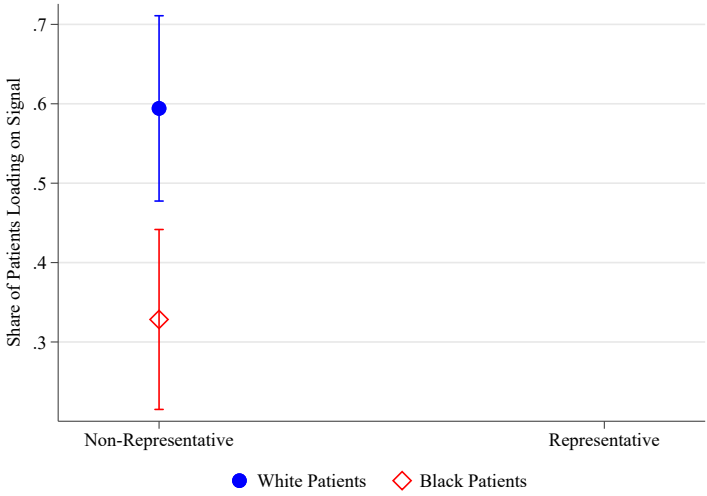
Patient Updating on Efficacy



Patient Updating on Efficacy



Patient Updating on Efficacy



Patient Updating on Efficacy

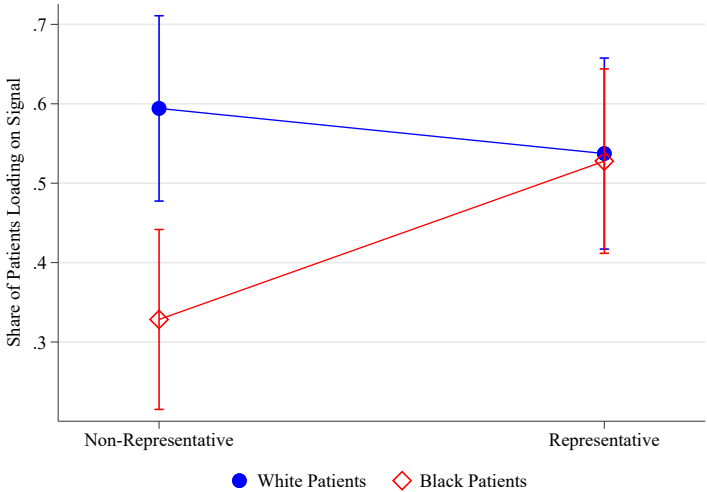


Table Priors Posteriors

Robustness

1. Double-robust LASSO-chosen controls [Chernozhukov et al. 2018] Patients
2. Subsample of physicians that requested report
3. Subsample of patients that downloaded clinical information Patients
4. Reweighting by MEPS data Patients
5. Non-linear models
6. Subsample of Physician observations which hold efficacy constant

Results for Physicians

Mechanisms

Extrapolation from Clinical Trial Data

	Panel A: Black Patients and PBP			
White to Black Patients	*Confidence*			
	Not at All	Some	Moderate	High
	(1)	(2)	(3)	(4)
Black Patients	39.6%	28.1%	25.2%	7.2%
PBP	3.5%	28.1%	61.4%	7.0%

	Panel B: White Patients and PWP			
Offshored to U.S. Patients	*Confidence*			
	Not at All	Some	Moderate	High
	(1)	(2)	(3)	(4)
White Patients	21.3%	36.8%	32.4%	9.6%
PWP	1.5%	21.5%	61.5%	15.4%

Question Wording | Large Table | Table with Rationale

Physician Quotes: Open Text Responses

Is representation important? Why or why not?

- *"Yes. To help find out if there are any differences and to help med support decisions that I make. I think patients would appreciate knowing that they were considered."*
- *"Yes. It should be obvious that a trial tells you what happens in the population studied. Extrapolating to others is an uncertain endeavor."*
- *"Yes, to instill more confidence in prescribing to all groups."*
- *"Yes absolutely! We all have the same biology but it makes the patient trust a medication more if they know someone who looks like them was in the trial."*
- *"Absolutely. There is a lot of inherent mistrust of the pharmaceutical industry from marginalized and disenfranchised communities (which are also usually communities of color and/or immigrants). The more medications are studied across a broad array of Americans, the more I can get my patients (and myself) to trust those meds."*

Word Cloud

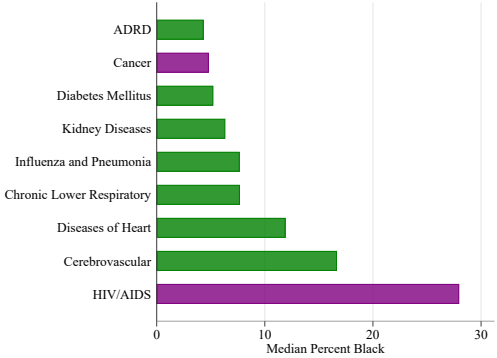
Patient Quotes: Open Text Responses

Please explain to your response to the last question [relevance].

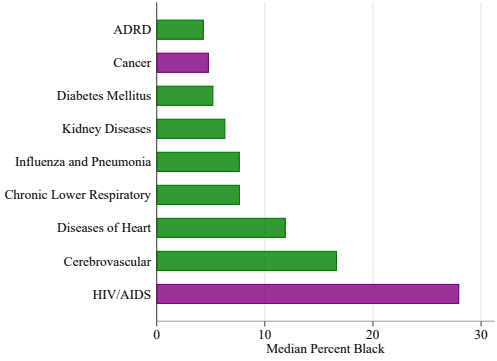
- Black patients in control group
  - "If the study only consisted of 1% of blacks, the study do not represent the black population of blacks with hypertension."
  - "I am not even sure this applies to people of color since your percentage of survey or study participants was so low."
- Black patients in treatment group
  - "BECAUSE 15% OF THOSE IN THE STUDY WERE AFRICAN AMERICAN AS I AM"
  - "A good number of my ethnicity were in this study."
  - "I'm interested in one pill daily versus three"

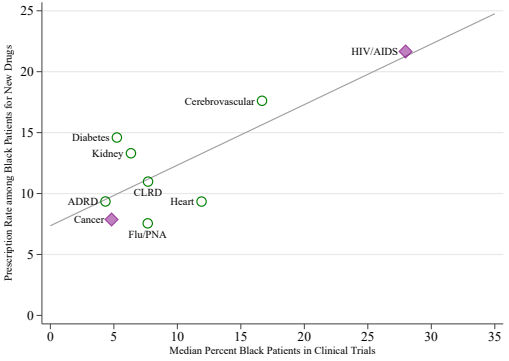
Case Studies: Inclusive Infrastructure

Trial Representation by Condition and Association with New Drug Prescribing



Trial Representation by Condition and Association with New Drug Prescribing





Clinical Trial Sites at Safety Net Hospitals

	DSH Index	UCMP Care
	(1)	(3)
HIV/AIDS (Cancer Comparison)	0.110***	0.019***
	(0.008)	(0.007)
Constant	0.475	0.176
Observations	197,240	182,929

Clinical Trial Sites at Safety Net Hospitals

	DSH Index		UCMP Care	
	(1)	(2)	(3)	(4)
HIV/AIDS (Cancer Comparison)	0.110***		0.019***	
	(0.008)		(0.007)	
HIV/AIDS (ADRD Comparison)		0.161***		0.054***
		(0.012)		(0.010)
Constant	0.475	0.423	0.176	0.141
Observations	197,240	6,804	182,929	5,997

Conclusion

Conclusion

- Representation in clinical trials matters for both Black patients and the physicians who treat them.
  - Patients update more on efficacy and doctors are more willing to prescribe drugs of **same** efficacy if trial sample is more representative.
  - Magnitude is substantial relative to efficacy.
  - Physicians appear to be acting as good agents for patients.

Conclusion

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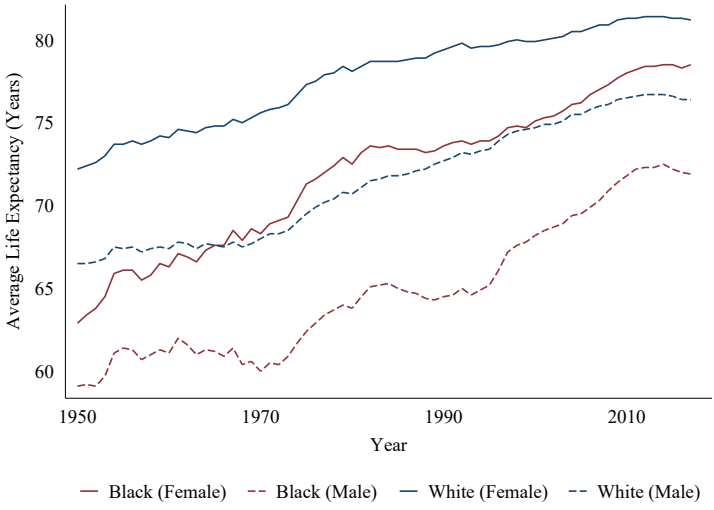
  - Patients update more on efficacy and doctors are more willing to prescribe drugs of **same** efficacy if trial sample is more representative.
  - Magnitude is substantial relative to efficacy.
  - Physicians appear to be acting as good agents for patients.
- Suggests policies that break the cycle of underrepresentation by encouraging inclusive infrastructure in clinical trials could have large social returns.

Conclusion

- Representation in clinical trials matters for both Black patients and the physicians who treat them.
  - Patients update more on efficacy and doctors are more willing to prescribe drugs of **same** efficacy if trial sample is more representative.
  - Magnitude is substantial relative to efficacy.
  - Physicians appear to be acting as good agents for patients.
- Suggests policies that break the cycle of underrepresentation by encouraging inclusive infrastructure in clinical trials could have large social returns.
- Thank you!

Appendix: Life Expectancy By Race and Sex



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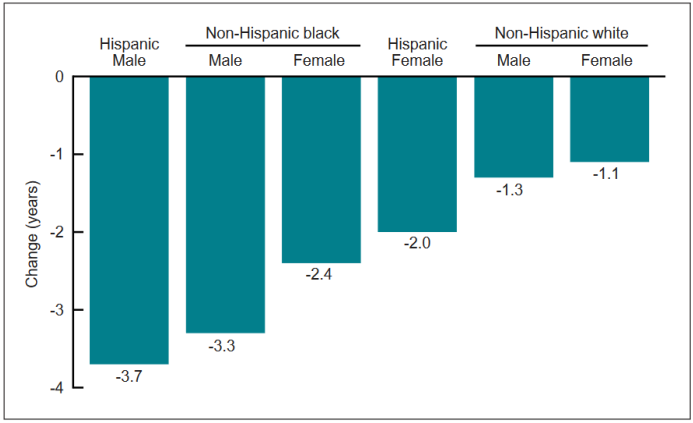
Widening Gradients with COVID-19

Appendix: Widening Gradients with COVID-19

Figure 4. Change in life expectancy at birth, by Hispanic origin and race and sex: United States, 2019–2020



NOTES: Life expectancies for 2019 by Hispanic origin and race are not final estimates; see Technical Notes. Estimates are based on provisional data for 2020. Provisional data are subject to change as additional data are received.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality data.

Back to Motivation Life Expectancy Gap

Inequality in Death Rates within Heart Disease and Diabetes

Age-adjusted heart disease death rates per 100,000 (2018)			
	Non-Hispanic Black	**Non-Hispanic White**	**Non-Hispanic Black / Non-Hispanic White Ratio**
Men	270.6	213.1	1.3
Women	168.6	130.7	1.3
Total	212.0	168.1	1.3

Source: CDC 2021. National Vital Statistics Report, Vol. 69, No. 13. Table 10.
https://www.cdc.gov/nchs/data/nvsr/nvsr69/nvsr69-13-508.pdf [PDF | 2.05MB]

Age-adjusted diabetes death rates per 100,000 (2018)			
	Non-Hispanic Black	**Non-Hispanic White**	**Non-Hispanic Black / Non-Hispanic White Ratio**
Male	47.6	24.3	2.0
Female	33.1	14.3	2.3
Total	39.3	18.9	2.1

Source: CDC 2021. National Vital Statistics Report, Vol. 69, No. 13. Table 10.
https://www.cdc.gov/nchs/data/nvsr/nvsr69/nvsr69-13-508.pdf [PDF | 2.05MB]

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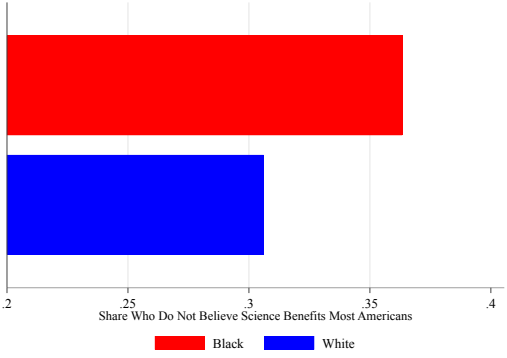
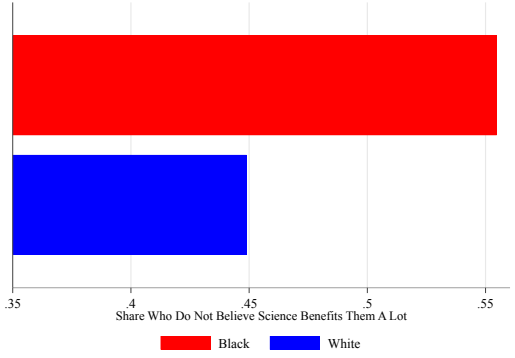
Appendix: Views on Scientific Innovation





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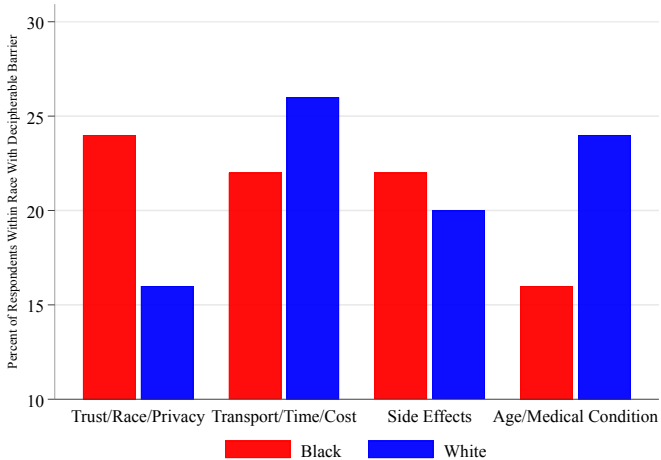
Source: Research!America America Speaks Survey, 2021.

Appendix: Leading Barriers to Clinical Trial Participation

Patient Open Text Responses



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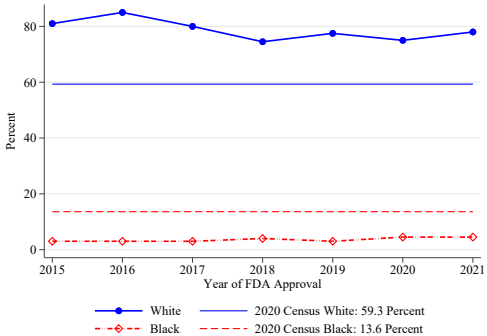
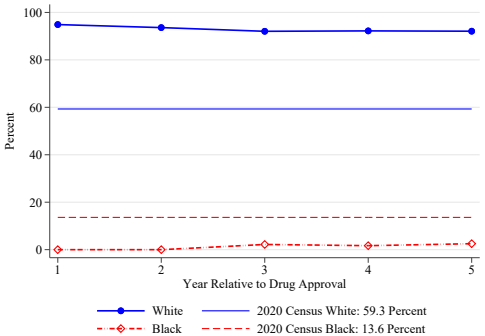
Innovation and Inequality

Clinical Trials (inputs)



Prescriptions (outputs)



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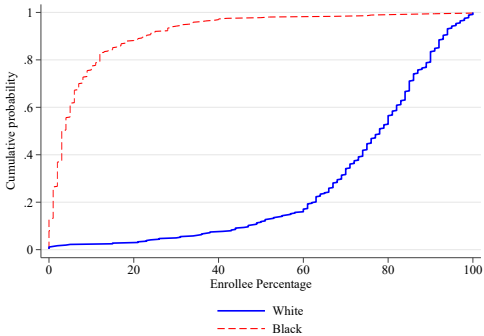
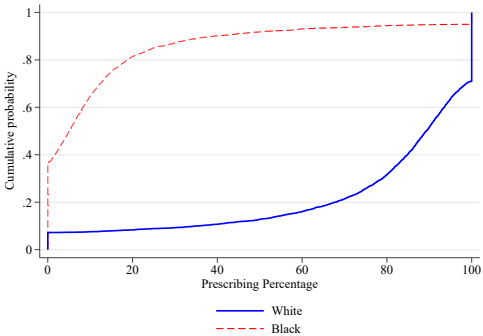
Innovation and Inequality

Clinical Trials (cdf)



Prescriptions (cdf)



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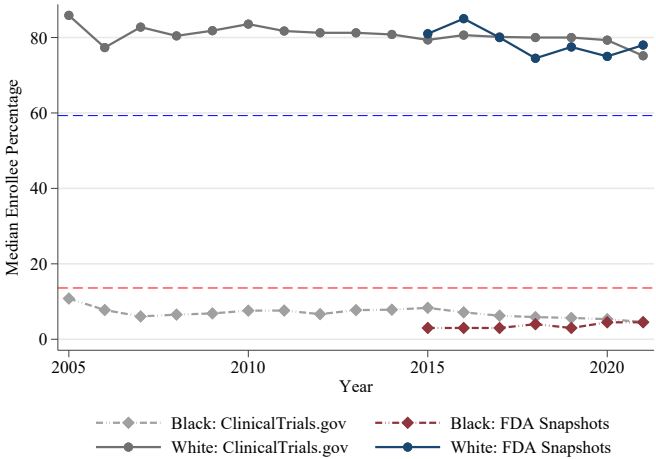
Innovation and Inequality: Longer Time Series



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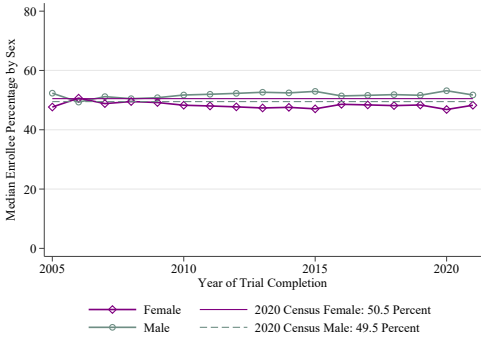
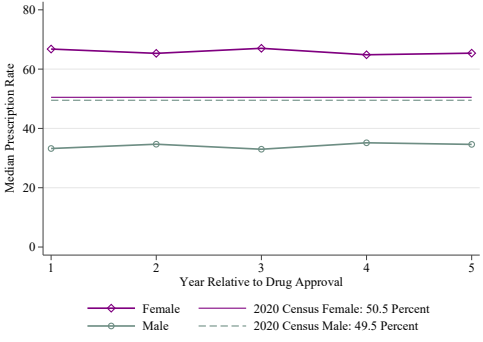
Policy History

Trial Participation and Prescriptions of New Drugs by Gender

Clinical Trials



Prescriptions



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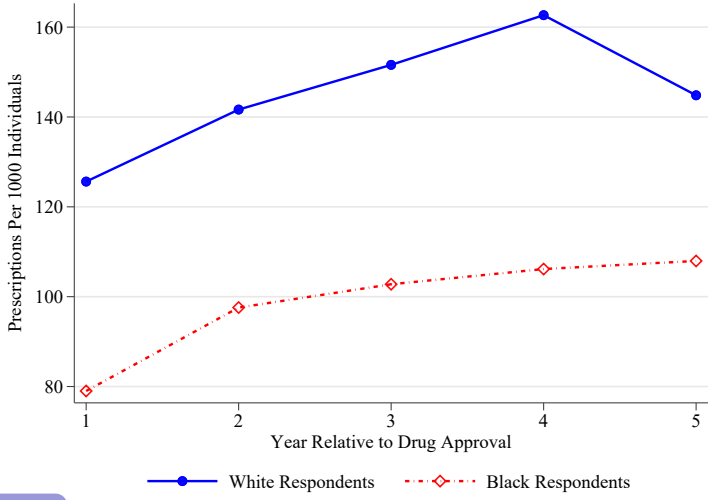
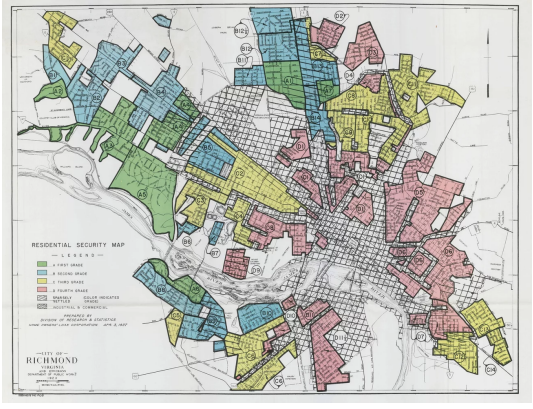
Innovation/Inequality: Outputs (Prescriptions)



Race, Racism and Medical Research

Racism in Medicine

- Long history of discriminatory, low-quality care [*e.g.* drapteomania]
- Highly salient events have intensified mistrust [*e.g.* Tuskegee Syphilis Study]
- Systemic inequities affects health outcomes [*e.g.* redlining]



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Why Might Racial Representation Matter?

1. (Perceptions of) heterogeneous treatment effects [physicians *or* patients believe race is correlated with treatment efficacy for many different reasons.]
2. Inclusion as signal – allows one to learn more about results of process [similarity-based extrapolation *or* legitimacy]
   - #2 could be driven by #1.

Subtle aspect – we empirically document that:

- #2 matters even in the absence of confirming #1
- *i.e.,* Representation matters even without information regarding heterogeneous treatment effects by race.

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Appendix: Evidence-Based Medicine

EBM/EBP Steps

1. ASK - Convert the need for information into a focused clinical question. Use the PICO framework.

2. ACQUIRE - Track down the best evidence with which to answer that question.

3. APPRAISE - Critically appraise the evidence for its validity, impact, and applicability.

4. APPLY - Integrate the evidence with your clinical expertise and your patient's characteristics and values.

5. ASSESS - Assess the results of your intervention.

Two Cardinal Rules of EBM

1. *Not all evidence is created equal* - A hierarchy of evidence guides clinical decision-making.

2. *Evidence alone is never enough* - Competent physicians balance risks and benefits of management strategies in the context of patient values and preferences.

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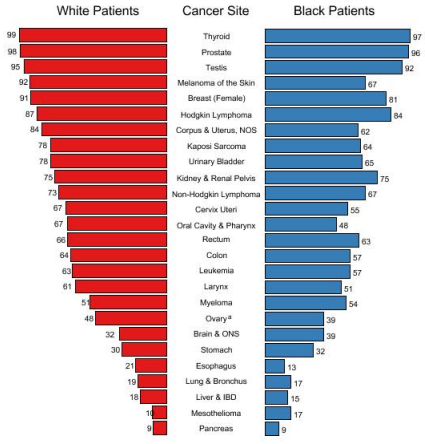
Appendix: Racial Disparities in Life Expectancy from Cancer

Figure 1.11



Source: SEER 18 areas (San Francisco, Connecticut, Detroit, Hawaii, Iowa, New Mexico, Seattle, Utah, Atlanta, San Jose-Monterey, Los Angeles, Alaska Native Registry, Rural Georgia, California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey and Georgia excluding ATL/RG).

[a] Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.

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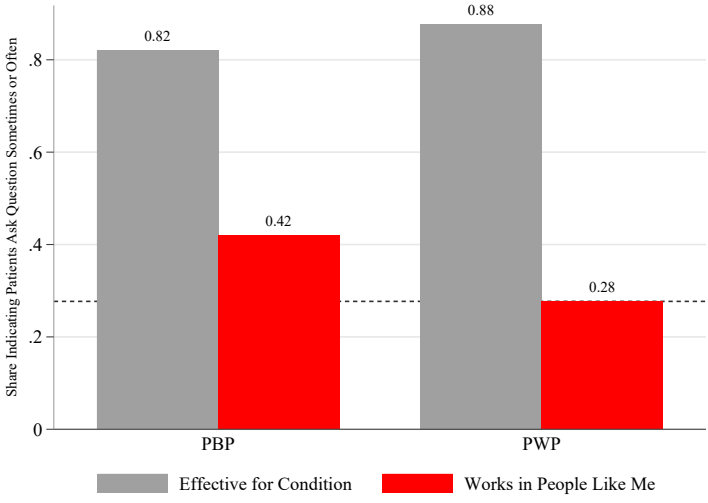
Patient Questions to Physicians when Starting New Rx



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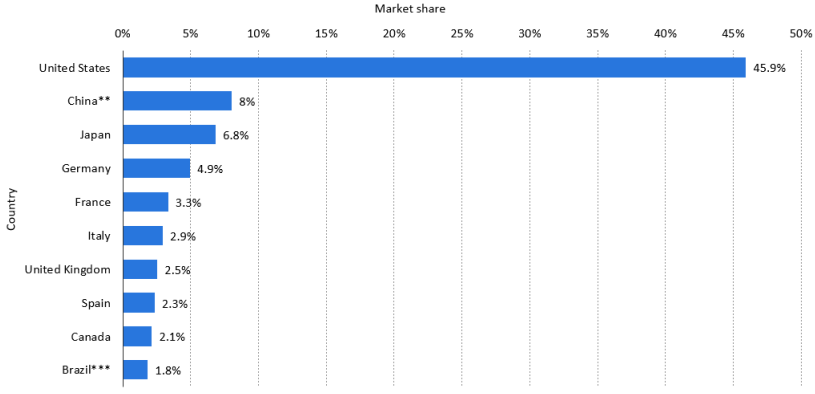
Appendix: U.S. Share of Pharmaceutical Sales (2020)



Note(s): United States

Further information regarding this statistic can be found on page 8.

Source(s): IQVIA; ID 245473

HARVARD LIBRARY

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Appendix: FDA Process Drug Approval

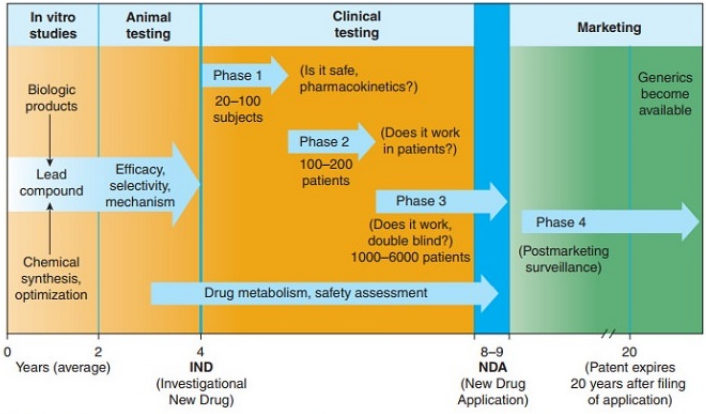

FIGURE 5–1 The development and testing process required to bring a drug to market in the USA. Some of the requirements may be different for drugs used in life-threatening diseases (see text).

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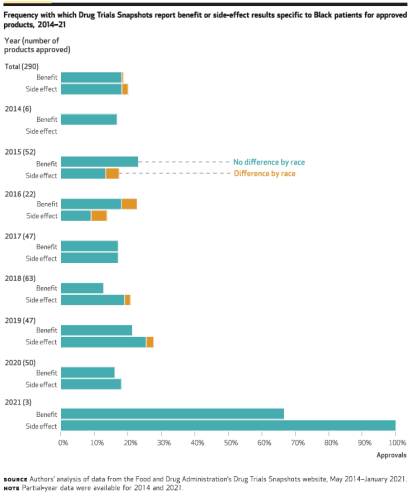
Appendix: Reporting of Black Specific Results



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Source: Green et al. (2020): "Despite The FDA's Five-Year Plan, Black Patients Remain Inadequately Represented In Clinical Trials For Drugs", Health Affairs

Appendix: Example Drug Profile

Drug Name: Afinaglutide

Mechanism of Action: Increases levels of incretin, which enhance glucose-dependent insulin secretion
Study Type: Double blind active-comparator control trial
Drug Efficacy: Lowers Hemoglobin A1C in patients with poorly controlled diabetes by 1.5%
Sample Size: 1500 subjects
Sample Demographics: 7% Black, 83% white, 10% other

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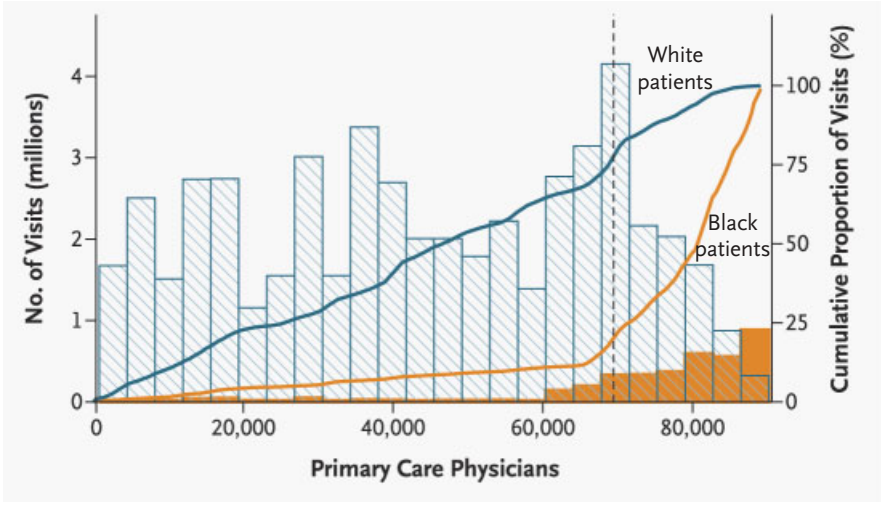
Appendix: Segregation in Health Care System



Bach et al. (2004) "Primary Care Physicians Who Treat Blacks and Whites", NEJM

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Appendix: List of Hypothetical Drugs Shown to Physicians

Drug Name	Mechanism of Action
Atenaburide	Stimulates insulin secretion from pancreatic beta cells
Istapiride	Stimulates insulin secretion from pancreatic beta cells
Benzapizide	Stimulates insulin secretion from pancreatic beta cells
Islogliptin	Inhibits the enzyme DPP-4 from deactivating incretins that stimulate insulin release
Methylgliptin	Inhibits the enzyme DPP-4 from deactivating incretins that stimulate insulin release
Dolagliptin	Inhibits the enzyme DPP-4 from deactivating incretins that stimulate insulin release
Metaglitazone	Increases insulin sensitivity of fat, muscle, and liver tissue
Seraglitazone	Increases insulin sensitivity of fat, muscle, and liver tissue
Loraglitazone	Increases insulin sensitivity of fat, muscle, and liver tissue
Iscagliflozin	Blocks the protein SGLT2 from absorbing glucose in the kidney, so that it is excreted in urine
Paragliflozin	Blocks the protein SGLT2 from absorbing glucose in the kidney, so that it is excreted in urine
Sotagliflozin	Blocks the protein SGLT2 from absorbing glucose in the kidney, so that it is excreted in urine
Betaglutide	Increases levels of incretin, which enhance glucose-dependent insulin secretion
Afinaglutide	Increases levels of incretin, which enhance glucose-dependent insulin secretion
Fenaglutide	Increases levels of incretin, which enhance glucose-dependent insulin secretion

Notes: Table shows the names and mechanisms of action of the 15 hypothetical drugs shown in the physician survey. Profiles for all drugs ranged in efficacy from 0.5% to 2% and in percent Black of trial subjects from 0% to 35%.

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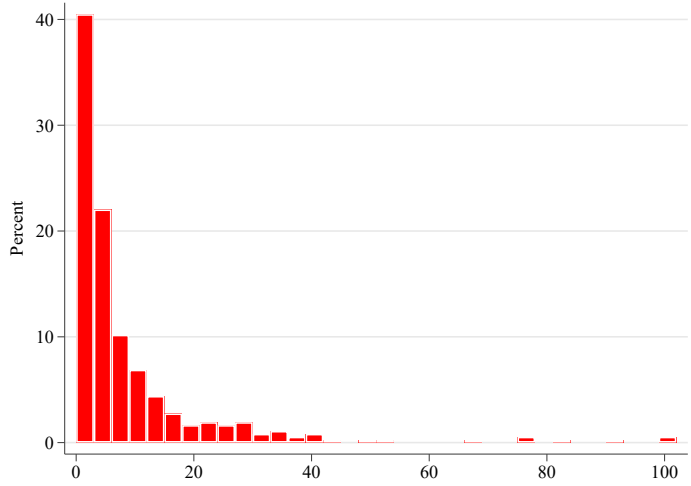
Appendix: Distribution of Trials by Share Black



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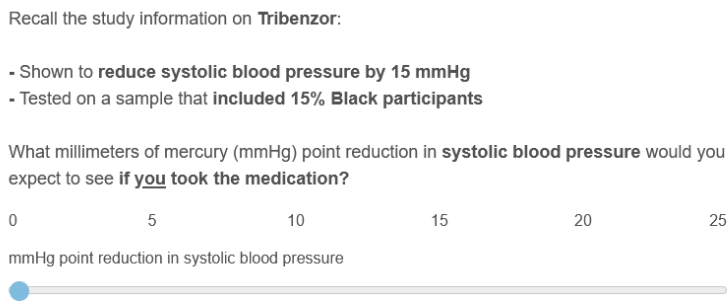
Appendix: Example Trial Profile



Participants needed to move the slider in order to advance the screen.

Doctor Invitation – Baseline Survey

HARVARD Kennedy School
MALCOLM WIENER CENTER
for Social Policy

Dear Dr. PHYSICIAN_NAME,

You have been randomly selected to participate in a study to investigate how physicians use information from clinical trials to treat their patients.

Researchers at Harvard University are conducting this study. The study is funded by an independent research center at Harvard, and is not connected with any pharmaceutical company. This study has been approved by the Institutional Review Board.

Your views are highly valuable and we greatly appreciate your willingness to participate. **As a token of our appreciation, we will give you a $100 honorarium if you pass a few screening questions and complete the survey.**

Your anonymized views will be used to draft a report to the National Institutes of Health and National Academy of Medicine regarding the types of research that clinicians find most useful for their practice.

We will also send you a copy of this report, if you would like. Simply click "yes" at the end of the survey to receive it.

This survey includes questions about your background and clinical practice, then asks you to rate 8 hypothetical drugs. All data associated with this survey are located on a secure server at Harvard. The survey takes about 15 minutes to complete.

Please click on the link below to access the survey. The link to the survey will expire in 4 days. Thank you for your help.

https://harvard.az1.qualtrics.com/jfe/form/SV_898DCxd11ZoL2Rg?Q_DL=HD52bVT9EdDESfV_898DCxd11ZoL2Rg_MLRP_djhzTq2daQrFX9A&Q_CHL=email

Sincerely,

Marcella Alsan, M.D., M.P.H., Ph.D.
Professor of Public Policy
Harvard University

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Doctor Invitation – Follow-Up

HARVARD Kennedy School
MALCOLM WIENER CENTER
for Social Policy

Dear Dr. PHYSICIAN_NAME,

On behalf of our research team, I would like to personally thank you for taking the time to complete our survey on clinical practice.

Based on your responses, I am writing with one follow-up question. **Our research team is planning on donating to a non-profit, the Center for Information and Study on Clinical Research Participation (CISCRP), to support recruitment efforts for clinical trials.** We would like your input on how our donation should be allocated.

CISCRP currently has two initiatives:

- Campaign A, which aims to boost trial participation among the general American public, and
- Campaign B, which focuses on boosting clinical trial participation among Americans from under-represented minority communities.

For every physician who replies, we will donate $5 to CISCRP. Of the $5 we donate on your behalf, how much would you like to go to Campaign A and how much would you like to go to Campaign B? Please indicate your choice below.

I would like the research team's $5 donation to be split in the following manner:

$0 to Campaign A $5 to Campaign B	**$1 to Campaign A $4 to Campaign B**	**$2 to Campaign A $3 to Campaign B**	**$3 to Campaign A $2 to Campaign B**	**$4 to Campaign A $1 to Campaign B**	**$5 to Campaign A $0 to Campaign B**

Thank you so much again for your participation. Please note that responding to the follow-up question is voluntary. If you would like a payment of $5 for your time, please click here. Feel free to contact me at rxmd_study@hks.harvard.edu if you have any questions or feedback on our study.

With warmest regards,

Marcella Alsan, M.D., M.P.H., Ph.D.
Professor of Public Policy
Harvard University

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Appendix: Encouraged Truthful Responses – Patient

You will now answer a series of questions regarding treatments for your high blood pressure.

Please answer carefully and honestly. To make sure that this exercise is helpful for your own medical care, we will provide a personalized summary of your responses in the following sections that you can share with your health care provider. If you wish, you may download this information at the end of the survey.

To move to the next page, click the button below.

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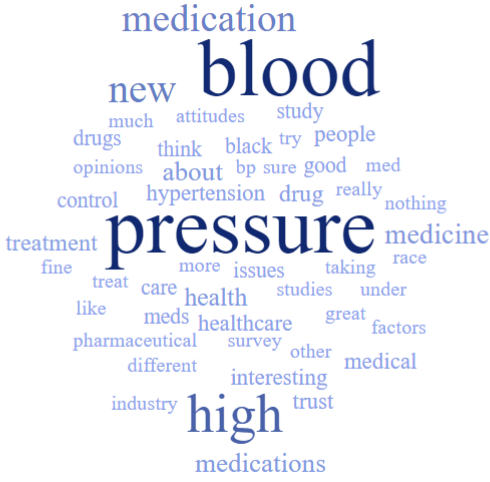
Appendix: "What do you think this study is about?"



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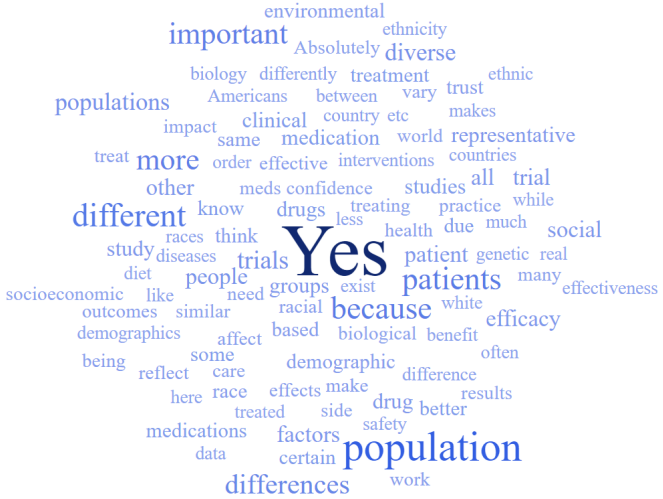
Appendix: "Is it important for clinical trials to be representative of the U.S. population? Why or why not?"



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Sample Characteristics - Representativeness of Physicians

	Top Decile Share Black ZIPs		*Bottom Decile Share Black ZIPs*		*All Other ZIPs*		*Differences*		
Variable	AMA Physicians	Survey Respondents	AMA Physicians	Survey Respondents	AMA Physicians	Survey Respondents	Top Decile Black ZIPs	Bottom Decile Black ZIPs	All Other ZIPs
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
MD: Male	0.548	0.559	0.618	0.543	0.569	0.558	-0.011	0.075	0.010
	(0.498)	(0.501)	(0.486)	(0.505)	(0.495)	(0.502)	(0.065)	(0.084)	(0.076)
MD: Age	44.587	49.254	48.388	48.543	46.470	50.349	-4.667***	-0.155	-3.879**
	(10.948)	(10.405)	(10.464)	(10.239)	(10.488)	(10.433)	(1.346)	(1.709)	(1.573)
MD: Yrs Since Deg	16.827	16.275	19.622	15.310	18.386	17.711	0.552	4.312**	0.676
	(10.953)	(10.398)	(10.424)	(9.332)	(10.597)	(9.016)	(1.444)	(1.706)	(1.444)
MD: Med School Rank	99.205	67.745	84.494	79.448	90.693	85.763	31.460***	5.045	4.930
	(37.596)	(46.052)	(41.779)	(45.826)	(40.724)	(43.509)	(6.392)	(8.374)	(6.965)
ZIP: South	0.462	0.441	0.124	0.057	0.323	0.186	0.021	0.067*	0.137**
	(0.499)	(0.501)	(0.329)	(0.236)	(0.468)	(0.394)	(0.065)	(0.039)	(0.059)
ZIP: Poverty Rate	26.635	25.688	11.678	9.063	13.699	13.023	0.947	2.615***	0.676
	(11.123)	(10.178)	(9.384)	(4.970)	(9.398)	(12.884)	(1.317)	(0.834)	(1.942)
ZIP: Black	0.537	0.550	0.002	0.002	0.090	0.089	-0.014	0.000	0.001
	(0.207)	(0.211)	(0.002)	(0.002)	(0.094)	(0.093)	(0.027)	(0.000)	(0.014)
ZIP: Hispanic	0.203	0.185	0.109	0.045	0.168	0.119	0.018	0.064***	0.049**
	(0.214)	(0.194)	(0.209)	(0.047)	(0.193)	(0.129)	(0.025)	(0.008)	(0.019)
ZIP: Asian	0.041	0.047	0.016	0.018	0.077	0.081	-0.006	-0.002	-0.004
	(0.059)	(0.066)	(0.031)	(0.027)	(0.100)	(0.066)	(0.009)	(0.005)	(0.010)
ZIP: Age 18 and Under	0.231	0.230	0.210	0.218	0.202	0.193	0.001	-0.008	0.009
	(0.053)	(0.044)	(0.059)	(0.047)	(0.060)	(0.059)	(0.006)	(0.008)	(0.009)
ZIP: Age 65 and Over	0.127	0.130	0.208	0.207	0.158	0.161	-0.003	0.002	-0.003
	(0.038)	(0.033)	(0.084)	(0.048)	(0.063)	(0.063)	(0.004)	(0.008)	(0.009)
ZIP: Insured	0.885	0.888	0.933	0.952	0.926	0.945	-0.003	-0.019***	-0.020***
	(0.065)	(0.065)	(0.051)	(0.035)	(0.050)	(0.042)	(0.008)	(0.006)	(0.006)
Observations	16,651	59	9,376	35	143,623	43	16,710	9,411	143,666

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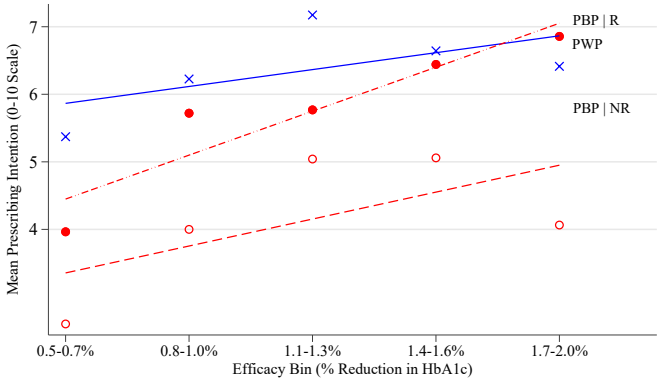
Appendix: Physician Prescribing Intent by Patient Composition and Trial Representation (Top Quartile Specification)



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Donation Details

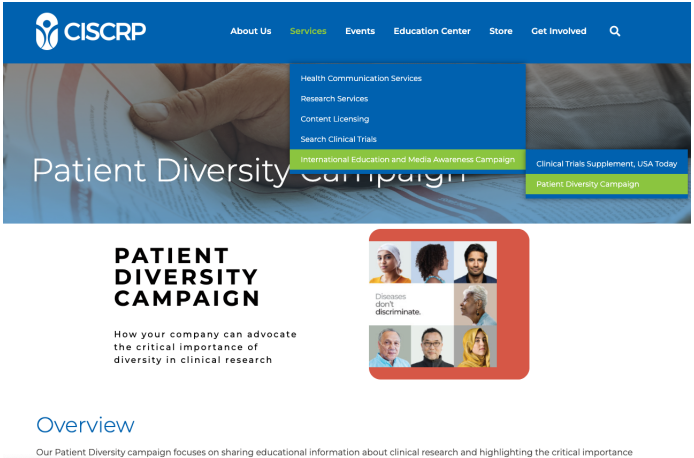

Figure: CISCRP Donation Website

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Sample Characteristics - Representativeness of Patients

	Non-Hispanic Black			Non-Hispanic White		
	MEPS	Survey	Difference	MEPS	Survey	Difference
	(1)	(2)	(3)	(4)	(5)	(6)
Male	0.424	0.360	0.064	0.518	0.426	0.092**
	(0.494)	(0.482)	(0.044)	(0.500)	(0.496)	(0.043)
Age 45-64	0.498	0.482	0.016	0.411	0.382	0.029
	(0.500)	(0.501)	(0.046)	(0.492)	(0.488)	(0.043)
Age 65+	0.386	0.295	0.091**	0.508	0.478	0.030
	(0.487)	(0.458)	(0.042)	(0.500)	(0.501)	(0.044)
BA or Higher	0.194	0.331	-0.136***	0.311	0.243	0.068*
	(0.396)	(0.472)	(0.042)	(0.463)	(0.430)	(0.038)
Under FPL	0.385	0.374	0.011	0.216	0.279	-0.063
	(0.487)	(0.486)	(0.044)	(0.412)	(0.450)	(0.039)
Insured	0.917	0.942	-0.026	0.965	0.919	0.046*
	(0.277)	(0.234)	(0.022)	(0.184)	(0.274)	(0.024)
Observations	1,153	139	1,292	4,146	136	4,282

Notes: Table compares the patient survey respondents, all of whom reported having hypertension, to individuals with hypertension in the 2019 Medical Expenditure Panel Survey (MEPS). Survey weights are utilized. *, **, *** refer to statistical significance at the 10, 5 and 1 percent level, respectively.

Patient Experiment Details | MEPS-Weighted Results

Appendix: Physician-Specific Coefficients and Patient Characteristics

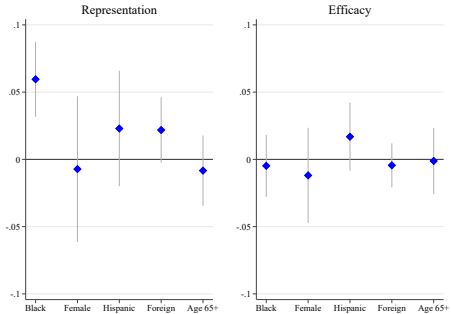

Figure: Relevance

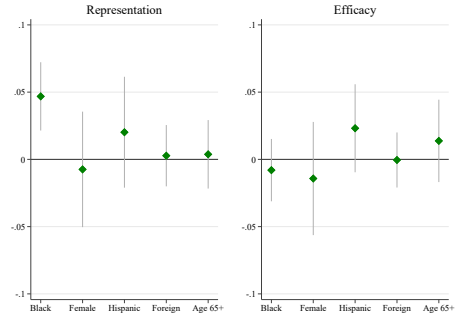

Figure: Prescribing Intention

Appendix: Physician-Specific Coefficients and Patient Characteristics

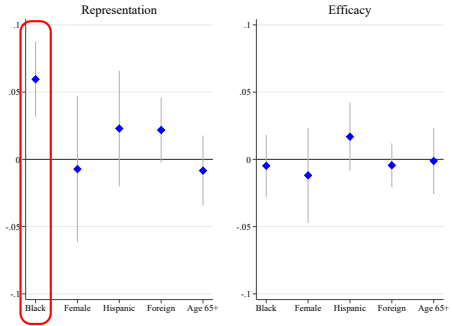

Figure: Relevance

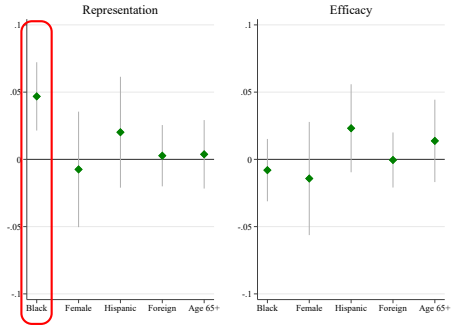

Figure: Prescribing Intention

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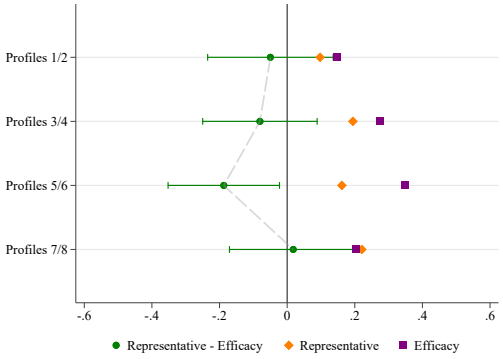
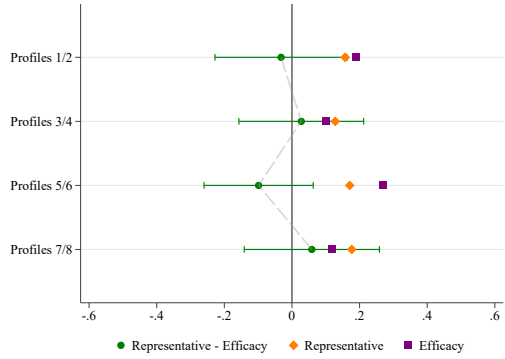
Physician Survey Results by Profile Order





Internal Validity | Physician Robustness

Appendix: Representative Trials and Beliefs About Drug Efficacy

	Posterior Belief				Update Exp. Dir.		Conf. in Beliefs	
	Black	White	Black	White	Black	White	Black	White
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Representation	2.003**	-0.147	1.776**	0.032	0.144**	-0.077	0.170	0.133
	(0.809)	(0.654)	(0.786)	(0.629)	(0.067)	(0.057)	(0.127)	(0.116)
Prior on Efficacy			0.105*	0.109***				
			(0.059)	(0.041)				
Observations	139	136	139	136	139	136	139	136
Outcome Control Mean	12.552	13.072	12.552	13.072	0.731	0.913	1.403	1.420

Notes: Table reports OLS estimates. In columns 7-8, the "Prior on Efficacy" variable refers to confidence in priors on efficacy. Confidence in beliefs is measured using the question "How confident are you in your above response regarding how much your blood pressure would fall by if you took Tribenzor?" on a 1-4 Likert scale, with 4 indicating "high confidence." Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5 and 1 percent level, respectively.

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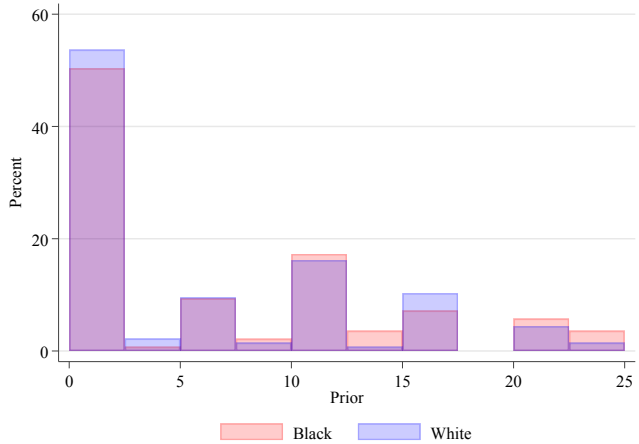
Appendix: Representative Trials and Beliefs About Drug Efficacy



Notes: Kolmogorov-Smirnov test fails to reject the null that the prior are identical across race (p-value=0.960)

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Appendix: Representative Trials and Beliefs About Drug Efficacy

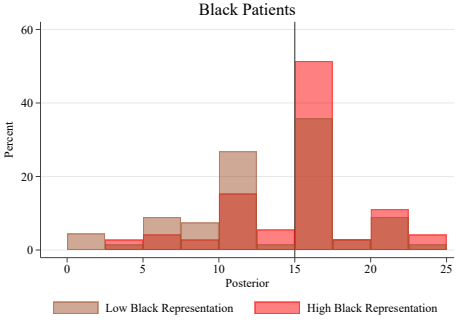

Figure: Black Patients

Notes: Kolmogorov-Smirnov test rejects the null that the posteriors are identical (p-value = 0.026)

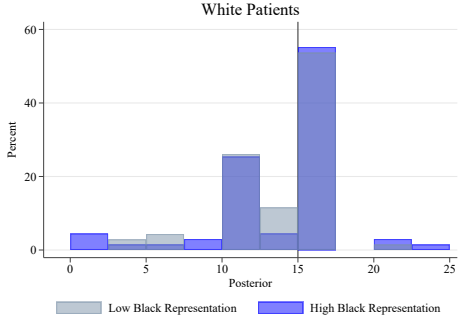

Figure: White Patients

Notes: Kolmogorov-Smirnov test fails to reject the null that the posteriors are identical (p-value=0.789)

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Appendix: Physician-Specific Coefficients and Physician Characteristics

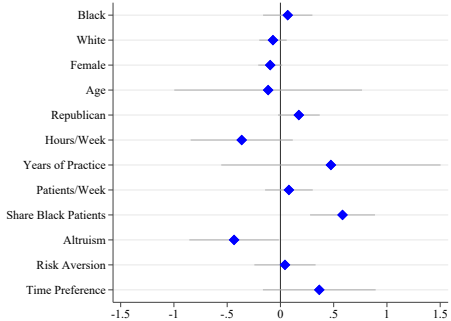

Figure: Relevance

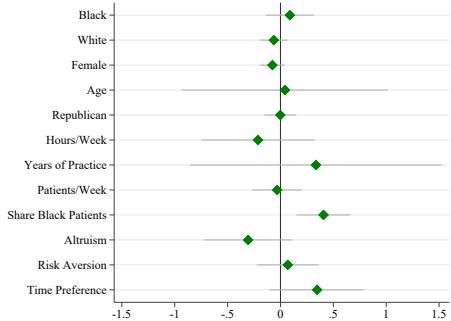

Figure: Prescribing Intention

Appendix: Physician-Specific Coefficients and Physician Characteristics

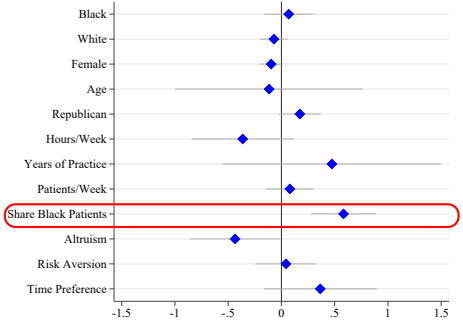

Figure: Relevance

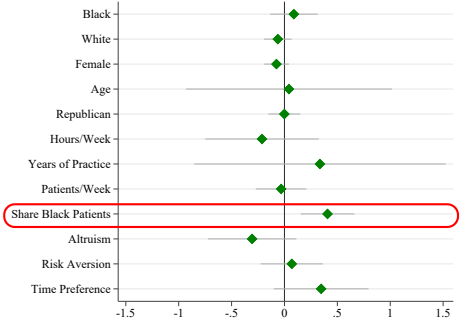

Figure: Prescribing Intention

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Appendix: Characteristics of Physicians Responding to Follow-Up

Variable	(1) All Physicians	(2) Responded to Follow-Up	(3) Difference Between Groups
Physician is Black	0.088	0.085	0.002
	(0.284)	(0.281)	(0.039)
Physician is White	0.606	0.683	-0.077
	(0.490)	(0.468)	(0.067)
Physician is Male	0.555	0.585	-0.031
	(0.499)	(0.496)	(0.069)
Physician Age	49.416	50.341	-0.925
	(10.319)	(9.918)	(1.420)
Physician is Republican	0.190	0.159	0.031
	(0.394)	(0.367)	(0.054)
Physician Hours/Week	32.978	32.768	0.210
	(13.740)	(13.159)	(1.889)
Physician Years Practice (Mdpt)	16.460	17.293	-0.833
	(8.398)	(8.487)	(1.177)
MD Patients/Week (Mdpt)	64.164	65.098	-0.933
	(30.941)	(30.872)	(4.316)
Patient Percent Black	25.388	26.024	-0.637
	(23.131)	(23.792)	(3.264)
Patient Percent Female	53.664	53.659	0.006
	(11.858)	(11.708)	(1.648)
Patient Percent Children	7.803	7.902	-0.100
	(8.058)	(7.780)	(1.111)
Patient Percent 65+	41.584	41.061	0.523
	(18.727)	(16.604)	(2.508)
Patient Percent Foreign (Mdpt)	27.591	26.037	1.555
	(25.308)	(25.236)	(3.530)
Top Decile Black ZIP	0.431	0.415	0.016
	(0.497)	(0.496)	(0.069)
Bottom Decile Black ZIP	0.255	0.280	-0.025
	(0.438)	(0.452)	(0.062)
Altruism (0-10)	7.394	7.280	0.114
	(1.447)	(1.468)	(0.203)
Risk Preference (0-10)	5.730	5.683	0.047
	(2.088)	(1.956)	(0.285)
Time Preference (0-10)	7.854	7.927	-0.073
	(1.353)	(1.395)	(0.191)
Observations	137	82	219

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Appendix: Characteristics of Physicians Demanding Report

Variable	(1) All Physicians	(2) Demanded Report	(3) Difference Between Groups
MD is Black	0.088	0.122	-0.035
	(0.284)	(0.329)	(0.040)
MD is White	0.606	0.602	0.004
	(0.490)	(0.492)	(0.065)
MD is Female	0.445	0.429	0.017
	(0.499)	(0.497)	(0.066)
MD Age	49.416	50.255	-0.839
	(10.319)	(10.221)	(1.360)
MD is Republican	0.190	0.194	-0.004
	(0.394)	(0.397)	(0.052)
MD Hours/Week	32.978	34.224	-1.246
	(13.740)	(14.292)	(1.849)
MD Years Practice (Mdpt)	16.460	16.607	-0.147
	(8.398)	(8.410)	(1.112)
MD Patients/Week (Mdpt)	64.164	64.148	0.016
	(30.941)	(29.919)	(4.038)
Patient Percent Black	25.388	25.705	-0.318
	(23.131)	(23.927)	(3.104)
Patient Percent Female	53.664	53.265	0.399
	(11.858)	(12.109)	(1.583)
Patient Percent Children	7.803	7.469	0.334
	(8.058)	(8.099)	(1.068)
Patient Percent 65+	41.584	42.133	-0.549
	(18.727)	(17.824)	(2.429)
Patient Percent Foreign (Mdpt)	27.591	28.316	-0.725
	(25.308)	(25.995)	(3.386)
Top Decile Black ZIP	0.431	0.429	0.002
	(0.497)	(0.497)	(0.066)
Bottom Decile Black ZIP	0.255	0.255	0.000
	(0.438)	(0.438)	(0.058)
Altruism (0-10)	7.394	7.480	-0.085
	(1.447)	(1.318)	(0.185)
Risk Preference (0-10)	5.730	5.786	-0.056
	(2.088)	(2.047)	(0.274)
Time Preference (0-10)	7.854	8.020	-0.166
	(1.353)	(1.193)	(0.171)
Number of Observations	137	98	

Back Physician Robustness

Appendix: Characteristics of Patients Demanding Report

Variable	(1) All Patients	(2) Demanded Report	(3) Difference Between Groups
Black	0.505	0.548	-0.042
	(0.501)	(0.500)	(0.056)
Male	0.393	0.426	-0.033
	(0.489)	(0.497)	(0.055)
Age Group	5.876	5.870	0.007
	(1.117)	(1.166)	(0.126)
BA or Higher	0.287	0.287	0.000
	(0.453)	(0.454)	(0.050)
Insured	0.931	0.948	-0.017
	(0.254)	(0.223)	(0.027)
Takes BP Medication	0.889	0.886	0.003
	(0.315)	(0.319)	(0.035)
Past Nonadherence	0.171	0.165	0.006
	(0.377)	(0.373)	(0.042)
General Trust	0.527	0.557	-0.029
	(0.500)	(0.499)	(0.056)
Pharma Trust	1.636	1.730	-0.094
	(0.801)	(0.798)	(0.089)
Doctor Trust	2.324	2.322	0.002
	(0.689)	(0.695)	(0.077)
Public Health Trust	1.945	2.104	-0.159*
	(0.863)	(0.799)	(0.094)
Altruism	6.793	7.357	-0.564**
	(2.188)	(1.812)	(0.231)
Risk Preference	5.422	5.861	-0.439
	(2.516)	(2.509)	(0.279)
Time Preference	6.993	7.348	-0.355
	(1.985)	(2.086)	(0.224)
Heard of Tribenzor	0.047	0.043	0.004
	(0.213)	(0.205)	(0.023)
Prior on Efficacy	5.782	5.696	0.086
	(7.131)	(7.514)	(0.805)
Observations	275	115	390

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Appendix: Results for Doctors Responding to Follow-up

	Main Specification		*Div-Eff Interaction*		*Black Interactions*	
	Relevance	Prescribe	Relevance	Prescribe	Relevance	Prescribe
	(1)	(2)	(3)	(4)	(5)	(6)
Representation	0.104***	0.071**	0.103**	0.070**	-0.002	0.002
	(0.039)	(0.034)	(0.040)	(0.035)	(0.050)	(0.046)
Efficacy	0.213***	0.315***	0.213***	0.315***	0.173***	0.275***
	(0.036)	(0.044)	(0.036)	(0.044)	(0.038)	(0.055)
Representation x Efficacy			0.019	0.016		
			(0.034)	(0.030)		
Representation x Patient Percent Black					0.004***	0.003**
					(0.002)	(0.001)
Efficacy x Patient Percent Black					0.001	0.001
					(0.002)	(0.002)
Number of Observations	656	656	656	656	656	656
Doctor FEs	Yes	Yes	Yes	Yes	Yes	Yes
Profile Order FEs	Yes	Yes	Yes	Yes	Yes	Yes
Rx Mechanism FEs	Yes	Yes	Yes	Yes	Yes	Yes

Notes: Table reports OLS estimates from Equation 1. Relevance, prescribing intent, reprsentation, and efficacy are standardized to a mean of 0 and standard deviation of 1. Robust standard errors clustered at the physician level are in parentheses. *, **, *** refer to statistical significance at the 10, 5 and 1 percent level, respectively.

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Appendix: Patient Survey Results Weighted Using MEPS

	Relevance		*Ask Doctor*		*Loading on Signal*	
	Black Respondents	White Respondents	Black Respondents	White Respondents	Black Respondents	White Respondents
	(1)	(2)	(3)	(4)	(5)	(6)
Representatation	0.781***	0.155	0.042	0.010	0.184**	-0.051
	(0.173)	(0.161)	(0.077)	(0.081)	(0.085)	(0.086)
Observations	139	136	139	136	139	136

Notes: Table reports OLS estimates. Relevance is standardized to a mean of 0 and standard deviation of 1. "Loading on Signal" is an indicator equal to one if the respondent's posterior was within 1 mmHg of the signal (i.e., between 14 and 16) and zero otherwise. Robust standard errors clustered in parentheses. *, **, *** refer to statistical significance at the 10, 5 and 1 percent level, respectively.

Robustness Checks Representativeness Table

Appendix: Patient Survey Results with LASSO-Chosen Controls

	Relevance		*Ask Doctor*		*Loading on Signal*	
	Black Respondents	White Respondents	Black Respondents	White Respondents	Black Respondents	White Respondents
	(1)	(2)	(3)	(4)	(5)	(6)
Representation	0.781***	0.172	0.021	0.006	0.144**	-0.077
	(0.164)	(0.158)	(0.077)	(0.079)	(0.066)	(0.056)
Observations	139	136	139	136	139	136

Notes: Table reports estimates from double-selection LASSO linear regression. Potential controls included age, sex, education and health variables among others. Relevance is standardized to a mean of 0 and standard deviation of 1. "Loading on Signal" is an indicator equal to one if the respondent's posterior was within 1 mmHg of the signal (i.e., between 14 and 16) and zero otherwise. Robust standard errors clustered in parentheses. *, **, *** refer to statistical significance at the 10, 5 and 1 percent level, respectively.

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Extrapolation from Clinical Trial Data among Physicians and Patients

Panel A: Extrapolation from White to Black Patients						
White to Black Patients	*Confidence*				*Rationale*	
	Not at All	Some	Moderate	High	Perceived Biol. Factors	Perceived Social & Envir. Factors
	(1)	(2)	(3)	(4)	(5)	(6)
Black Patients	39.6%	28.1%	25.2%	7.2%	31.0%	45.7%
White Patients	19.1%	37.5%	31.6%	11.8%	33.3%	29.2%
PBP	3.5%	28.1%	61.4%	7.0%	32.1%	45.3%
PWP	4.6%	35.4%	50.8%	9.2%	35.6%	37.3%

Panel B: Extrapolation from Offshored to U.S. Patients						
Offshored to U.S. Patients	*Confidence*				*Rationale*	
	Not at All	Some	Moderate	High	Perceived Biol. Factors	Perceived Social & Envir. Factors
	(1)	(2)	(3)	(4)	(5)	(6)
Black Patients	33.8%	34.5%	22.3%	9.4%	21.4%	54.8%
White Patients	21.3%	36.8%	32.4%	9.6%	19.5%	43.9%
PBP	3.5%	19.3%	66.7%	10.5%	9.8%	60.8%
PWP	1.5%	21.5%	61.5%	15.4%	10.9%	70.9%

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Patient Enrollment: Supply and Demand

Demand and **Supply** side factors affect trial composition

- **Demand:** Trial sponsors may
  - Recruit through physician networks or large medical centers [Hughson et al. 2016]
  - Recruit in foreign countries [Petryna 2009]
  - Recruit without actively engaging minority communities [Haley et al. 2017]
- **Supply:** Potential patients may
  - Mistrust medicine/medical research [Alsan-Wanamaker 2018; Research!America 2021]
  - Lack knowledge of clinical trials [Research!America]
  - Have limited access to racially concordant providers [Alsan et al. 2019]
  - Have limited access to primary care [Landon et al. 2021]

Back to Research!America

Moderna Stock Price and Trial Enrollment

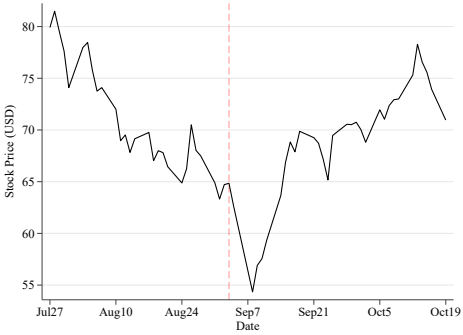

Figure: Stock Price

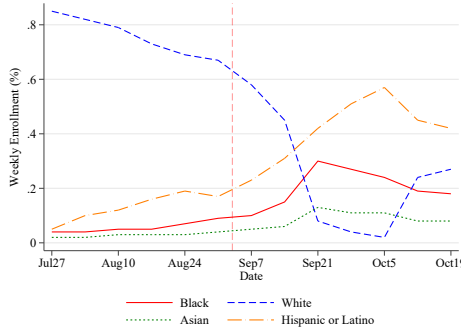

Figure: Enrollment Patients

Model Appendix: Closed Form Expressions

If $\theta(x_i)$ is distributed according to Beta distributions prior to the trial data for treatment T, with parameters $(\alpha(x_i; h^{T-1}), \beta(x_i; h^{T-1}))$ conditional on x_i mattering and parameters $(\alpha(h^{T-1}), \beta(h^{T-1}))$ conditional on x_i not mattering, then:

$$\hat{b}(x_i; h^{T-1}) = m \times \underbrace{\left(\tilde{b} \times \frac{\alpha(x_i; h^{T-1})}{\alpha(x_i; h^{T-1}) + \beta(x_i; h^{T-1})}\right)}_{\text{prior estimate of } \hat{b} \text{ conditional on } x_i \text{ mattering}}$$

$$+ (1 - m) \times \underbrace{\left(\tilde{b} \times \frac{\alpha(h^{T-1})}{\alpha(h^{T-1}) + \beta(h^{T-1})}\right)}_{\text{prior estimate of } \hat{b} \text{ conditional on } x_i \text{ not mattering}}.$$

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Model Appendix: Closed Form Expressions

- Expression multiplying m:

$$= \tilde{b} \times \frac{\alpha_{\text{Black}} + (k_{\text{White}} + k_{\text{Black}}) \times \bar{x}}{N \times \bar{x} + \alpha_{\text{Black}} + \beta_{\text{Black}}}.$$

- Expression multiplying $(1 - m)$:

$$= \tilde{b} \times \frac{\alpha_i + k}{N + \alpha_i + \beta_i}.$$

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Model Appendix: Priors and Historical Under-representation

- Whether or not x_i matters, the person believes

$$\theta(x_i) \sim \text{Beta}(\alpha_i, \beta_i)$$

- So, prior to seeing trial data, the person perceives

$$\begin{aligned}\hat{b}_i &= \tilde{b} \times \mathbb{E}_i[\theta(x_i)|\text{historical data}] \\ &= \tilde{b} \times \frac{\alpha_i}{\alpha_i + \beta_i}\end{aligned}$$

- Historical trial data enters by influencing (α_i, β_i)
  - Suppose (α_i, β_i) only depends on group membership, so we'll write (α_i, β_i) for $i \in \{\text{White, Black}\}$
- The assumption here is that a historical lack of representation in historical clinical trials reduces $\alpha_i/(\alpha_i + \beta_i)$
  - One micro-foundation: patients' posteriors from the most similar past treatment become their priors for the new treatment

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Model Appendix: Updating with Current Trial Data

- Suppose $m_i = 1$: everybody is certain x_i matters
  - This case is too stark, but is simple to analyze and instructive

- If sub-group analyses were reported, then a person would end up believing:

$$\begin{aligned}\hat{b}_i &= \tilde{b} \times \mathbb{E}_i[\theta(x_i)|\text{trial data}, \text{historical data}] \\ &= \tilde{b} \times \frac{\alpha_i + k(x_i)}{N(x_i) + \alpha_i + \beta_i},\end{aligned}$$

where

- $k(x_i)$ equals the number of successes among trial participants with characteristics x_i
  - Let $k_{\text{White}} = k(x_i = \text{White})$, $k_{\text{Black}} = k(x_i = \text{Black})$
- $N(x_i)$ equals the number of trial participants with characteristics x_i
  - Let $N_{\text{White}} = N(x_i = \text{White})$, $N_{\text{Black}} = N(x_i = \text{Black})$

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Model Appendix: Case When Subgroup Analyses Are Reported

- If sub-group analyses were reported, then White patients would end up believing:

$$\hat{b}_{\text{White}} = \tilde{b} \times \frac{\alpha_{\text{White}} + k_{\text{White}}}{N \times (1 - \bar{x}) + \alpha_{\text{White}} + \beta_{\text{White}}}$$

  and Black patients would end up believing

$$\hat{b}_{\text{Black}} = \tilde{b} \times \frac{\alpha_{\text{Black}} + k_{\text{Black}}}{N \times \bar{x} + \alpha_{\text{Black}} + \beta_{\text{Black}}}$$

- Fixing trial efficacy on sub-group $i \in \{\text{White}, \text{Black}\}$, k_i/N_i, and assuming this efficacy exceeds prior beliefs, $\alpha_i/(\alpha_i + \beta_i)$:

$$\frac{\partial \hat{b}_{\text{Black}}}{\partial \bar{x}} > 0, \ \frac{\partial^2 \hat{b}_{\text{Black}}}{\partial \bar{x}^2} < 0, \ \frac{\partial \hat{b}_{\text{White}}}{\partial (1 - \bar{x})} > 0, \ \frac{\partial^2 \hat{b}_{\text{White}}}{\partial (1 - \bar{x})^2} < 0$$

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Model Appendix: Case When Subgroups Are Not Reported

Assume that when sub-group analyses aren't reported, doctors and patients fill-in with constant treatment effects *in the trial*:

- White patients end up believing:

$$\hat{b}_{\text{White}} = \tilde{b} \times \frac{\alpha_{\text{White}} + (k_{\text{White}} + k_{\text{Black}}) \times (1 - \bar{x})}{N \times (1 - \bar{x}) + \alpha_{\text{White}} + \beta_{\text{White}}}$$

  and Black patients end up believing

$$\hat{b}_{\text{Black}} = \tilde{b} \times \frac{\alpha_{\text{Black}} + (k_{\text{White}} + k_{\text{Black}}) \times \bar{x}}{N \times \bar{x} + \alpha_{\text{Black}} + \beta_{\text{Black}}}$$

- Fixing aggregate trial efficacy, $(k_{\text{White}} + k_{\text{Black}})/N$, and assuming this efficacy exceeds prior beliefs, $\alpha_i/(\alpha_i + \beta_i)$:

$$\frac{\partial \hat{b}_{\text{Black}}}{\partial \bar{x}} > 0, \ \frac{\partial^2 \hat{b}_{\text{Black}}}{\partial \bar{x}^2} < 0, \ \frac{\partial \hat{b}_{\text{White}}}{\partial (1 - \bar{x})} > 0, \ \frac{\partial^2 \hat{b}_{\text{White}}}{\partial (1 - \bar{x})^2} < 0$$

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Model Appendix: Numerical Examples of Mapping

- If $(\alpha_i, \beta_i) = (100, 100)$ for $i =$ White, Black, $\tilde{b} = 100$, $k_{\text{White}} + k_{\text{Black}} = 750$, $N = 1000$, $\bar{x} = .05$:
  - $\hat{b}_{\text{White}} = 70.65$
  - $\hat{b}_{\text{Black}} = 55$
- If $(\alpha_i, \beta_i) = (100, 100)$ for $i =$ White, Black, $\tilde{b} = 100$, $k_{\text{White}} + k_{\text{Black}} = 750$, $N = 1000$, $\bar{x} = .1$:
  - $\hat{b}_{\text{White}} = 70.45$
  - $\hat{b}_{\text{Black}} = 58.33$
- If $(\alpha_i, \beta_i) = (100, 100)$ for $i =$ White, Black, $\tilde{b} = 100$, $k_{\text{White}} + k_{\text{Black}} = 750$, $N = 1000$, $\bar{x} = .2$:
  - $\hat{b}_{\text{White}} = 70$
  - $\hat{b}_{\text{Black}} = 62.5$

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Model Appendix: Numerical Take-aways

- Numerical analyses reveal that representation of 80% vs. 95% makes essentially no difference for $\hat{b}_{\text{White}}$, but 20% vs. 5% makes a big difference for $\hat{b}_{\text{Black}}$
- Instead of boosting $\hat{b}_{\text{Black}}$ by increasing representation $\bar{x}$, could do so by increasing the trial size N
  - However, it would be necessary to double the trial size to have the same impact on $\hat{b}_{\text{Black}}$ as doubling representation
  - And it seems unlikely that this would be cheaper for the firm (or society) than working to double representation

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Model Appendix: Cost of Recruitment c_τ

The demand for participating in a trial is defined similar to the demand for new drugs $d(x_i; h^T)$, in that it depends on perceived drug benefit.

Suppose firms have a status-quo technology for recruiting patients to trials:

- $\bar{x}_T^a$: invited proportion of Black patients in the trial
- $\bar{x}_T^{sq}$: actual proportion of Black patients in the trial

Under **status quo** recruitment technology, trial representation of Black patients is lower since the demand for trial participation of Black patients falls below that of White patients.

- *i.e.*, $\bar{x}_T^{sq} < \bar{x}_T^a$ when $d(x_i = 1; h^{T-1}) < d(x_i = 0; h^{T-1})$.

Formalization Back

Model Appendix: Demand for Trial Participation and Cost of Recruitment

We assume that firms pay the following cost to increase representation from $\bar{x}_T^{sq}$ to $\bar{x}^r$:

$$
\begin{aligned}
c_r &= f \times 1(\bar{x}^r \neq \bar{x}_T^{sq}) + h\left(\frac{\bar{x}^r - \bar{x}_T^{sq}}{d(x_i = 1; h^T)} \times N - \frac{(1 - \bar{x}_T^{sq}) - (1 - \bar{x}^r)}{d(x_i = 0; h^{T-1})} \times N\right) \\
&= f + h\left((\bar{x}^r - \bar{x}_T^{sq}) \times N \times \frac{d(x_i = 0; h^{T-1}) - d(x_i = 1; h^{T-1})}{d(x_i = 0; h^{T-1}) \times d(x_i = 1; h^{T-1})}\right),
\end{aligned}
$$

- $f \geq 0$ is a fixed cost to deviating from the status-quo recruitment strategy (*e.g.*, due to costs of moving the trial location, setting up a new recruitment infrastructure, etc.)
- $h(\cdot)$ is an increasing function that takes as its argument the number of additional patients who need to be targeted to increase Black representation from $\bar{x}_T^{sq}$ to $\bar{x}^r$, holding the overall trial sample fixed at N

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Model Appendix: Actual Trial Representation under the Status Quo

Proposition 2: Let $d(x_i; h^{T-1}) = \Pr\left(-\varepsilon_{iT}^{trial} \leq \hat{b}(x_i; h^{T-1}) - n_T^{trial}\right)$ be the likelihood a patient with characteristic x_i participates in a trial when invited. Then, the share of Black trial participants under the status quo recruitment technology is given by:

$$\bar{x}_T^{sq} = \frac{d(x_i = 1; h^{T-1}) \times \bar{x}_T^a}{d(x_i = 1; h^{T-1}) \times \bar{x}_T^a + d(x_i = 0; h^{T-1}) \times (1 - \bar{x}_T^a)}.$$

Corollary: Proposition implies that Black trial representation will be lower than its invited representation under the status quo technology when the demand for trial participation of Black patients falls below that of White patients. Formally, $\bar{x}_T^{sq} < \bar{x}_T^a$ when $d(x_i = 1; h^{T-1}) < d(x_i = 0; h^{T-1})$.

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Model Appendix: Cycle of Underrepresentation Formalization

Proposition 3: Suppose the most similar treatment Z to T outperformed patients' prior expectations. When the fixed costs f to deviating from the status-quo recruitment technology to inclusive infrastructure are sufficiently large, then underrepresentation of Black patients in the historical trial leads to further underrepresentation of Black patients in the current trial:

$$\frac{\partial \bar{x}_T}{\partial \bar{x}_Z} > 0.$$

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Robustness: Results for Physicians

	Relevance Non-Standard	Presribe Non-Standard	Main Specification	Report Demand Sample	Follow-up Sample	LASSO Controls
	(1)	(2)	(3)	(4)	(5)	(6)
Representation	0.024***	0.025***	0.107***	0.121***	0.071**	0.168***
	(0.006)	(0.007)	(0.029)	(0.032)	(0.034)	(0.033)
Efficacy	0.957***	1.519***	0.281***	0.278***	0.315***	0.224***
	(0.147)	(0.175)	(0.032)	(0.038)	(0.044)	(0.038)
Doctor FEs	Yes	Yes	Yes	Yes	Yes	No
Profile Order FEs	Yes	Yes	Yes	Yes	Yes	Yes
Rx Mechanism FEs	Yes	Yes	Yes	Yes	Yes	Yes
Observations	1,096	1,096	1,096	784	656	1,096

Notes: Table reports OLS estimates from Equation 1. Columns (3)-(6) report OLS results on the outcome prescribing intention. Robust standard errors clustered at the physician level are in parentheses. *, **, *** refer to statistical significance at the 10, 5 and 1 percent level, respectively.

Back to Robustness Checks | Results by Profile Order | Threats to Internal Validity | Report Demanded Characteristics Comparison | Follow-up Sample Characteristics Comparison

Robustness: Patient Survey Results Among Those Demanding Report

	Relevance		*Ask Doctor*		*Loading on Signal*	
	Black Respondents	White Respondents	Black Respondents	White Respondents	Black Respondents	White Respondents
	(1)	(2)	(3)	(4)	(5)	(6)
Representative Treatment	0.615**	0.380	0.104	0.000	0.336***	0.006
	(0.258)	(0.253)	(0.113)	(0.126)	(0.119)	(0.143)
Observations	63	52	63	52	63	52

Robustness Checks | Threats to Internal Validity | Characteristics Comparison

Open-Text and Manipulation Check Questions

"Suppose a new drug is shown to be safe and effective in a study with only White patients. How confident are you that it would be safe and effective among Black patients with the same condition?"

"Suppose a new drug is shown to be safe and effective in a study that includes only patients recruited outside of the United States, how confident are you that it would be safe and effective among patients within the United States who have the same condition?"

- Anyone who expressed less than high confidence were queried on main reason for not holding high confidence.

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Balance in Physician Survey – Characteristics of Trials

	Mean of Values over Trials		*Range of Values Over Trials*	
	Representation	Efficacy	Representation	Efficacy
	(1)	(2)	(3)	(4)
Physician Age	0.017	0.007	-0.094	-0.002
	(0.015)	(0.014)	(0.094)	(0.003)
Physician is Male	0.123	-0.344*	0.912	-0.009
	(0.185)	(0.191)	(1.082)	(0.037)
Physician is White	-0.108	0.017	0.300	-0.051
	(0.201)	(0.206)	(1.111)	(0.041)
Physician Hours/Week	-0.009	0.005	-0.039	-0.003**
	(0.007)	(0.005)	(0.037)	(0.001)
Physician Years Practice (Grp)	-0.090	-0.060	-0.320	0.011
	(0.108)	(0.103)	(0.650)	(0.023)
Physician Holds MD	0.164	-0.088	-0.627	0.013
	(0.271)	(0.261)	(1.445)	(0.059)
Patient Percent Black	0.007	0.005	0.052	-0.001
	(0.006)	(0.006)	(0.038)	(0.002)
Patient Percent White	0.009	-0.001	0.060*	-0.000
	(0.006)	(0.006)	(0.034)	(0.002)
Patient Percent Hispanic	0.008	0.002	0.062	-0.001
	(0.007)	(0.007)	(0.041)	(0.002)
Altruism (0-10)	0.014	0.001	0.482	-0.021
	(0.069)	(0.081)	(0.402)	(0.015)
Risk Preference (0-10)	0.037	0.071*	-0.357	0.003
	(0.047)	(0.042)	(0.283)	(0.009)
Time Preference (0-10)	0.071	-0.021	0.452	0.012
	(0.080)	(0.069)	(0.443)	(0.015)
Constant	-1.960*	-0.356	22.475***	1.423***
	(1.043)	(0.883)	(5.430)	(0.238)
Observations	137	137	137	137

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Balance in Patient Survey

Variable	(1) All Respondents	(2) Representative Arm	(3) Non-Representative Arm	(4) Difference
Black	0.505	0.518	0.493	0.025
	(0.501)	(0.501)	(0.502)	(0.061)
Male	0.393	0.388	0.397	-0.009
	(0.489)	(0.489)	(0.491)	(0.059)
Age Group	5.876	5.914	5.838	0.075
	(1.117)	(1.126)	(1.110)	(0.135)
BA or Higher	0.287	0.281	0.294	-0.014
	(0.453)	(0.451)	(0.457)	(0.055)
Insured	0.931	0.942	0.919	0.023
	(0.254)	(0.234)	(0.274)	(0.031)
Takes BP Medication	0.889	0.891	0.887	0.003
	(0.315)	(0.313)	(0.318)	(0.038)
Past Nonadherence	0.171	0.194	0.147	0.047
	(0.377)	(0.397)	(0.355)	(0.045)
General Trust	0.527	0.540	0.515	0.025
	(0.500)	(0.500)	(0.502)	(0.060)
Pharma Trust	1.636	1.669	1.603	0.066
	(0.801)	(0.880)	(0.713)	(0.097)
Doctor Trust	2.324	2.309	2.338	-0.029
	(0.689)	(0.700)	(0.680)	(0.083)
Public Health Trust	1.945	1.971	1.919	0.052
	(0.863)	(0.908)	(0.817)	(0.104)
Altruism	6.793	6.748	6.838	-0.090
	(2.188)	(2.123)	(2.258)	(0.264)
Risk Preference	5.422	5.273	5.574	-0.300
	(2.516)	(2.612)	(2.415)	(0.304)
Time Preference	6.993	6.914	7.074	-0.160
	(1.985)	(2.094)	(1.872)	(0.240)
Heard of Tribenzor	0.047	0.058	0.037	0.021
	(0.213)	(0.234)	(0.189)	(0.026)
Prior on Efficacy	5.782	5.928	5.632	0.296
	(7.131)	(7.489)	(6.770)	(0.861)
Observations	275	139	136	275

Back

Heterogeneity Among Patients by Expectation of Others' Trustworthiness

	Relevance		*Ask Doctor*		*Load on Signal*	
	Black Patients	White Patients	Black Patients	White Patients	Black Patients	White Patients
	(1)	(2)	(3)	(4)	(5)	(6)
Treatment x (Expt. Trust.=1)	1.049***	0.190	0.291***	-0.000	0.190	-0.171
	(0.236)	(0.209)	(0.104)	(0.099)	(0.123)	(0.109)
Treatment x (Expt. Trust.=0)	0.562**	0.141	-0.211*	0.011	0.211*	0.115
	(0.235)	(0.249)	(0.108)	(0.132)	(0.113)	(0.136)
Expt. Trust.	-0.276	0.060	-0.142	0.089	-0.032	0.159
	(0.269)	(0.245)	(0.115)	(0.116)	(0.117)	(0.122)
p-value: Expt. Trust. $1 = 0$	0.146	0.880	0.001	0.947	0.901	0.104
Observations	139	136	139	136	139	136

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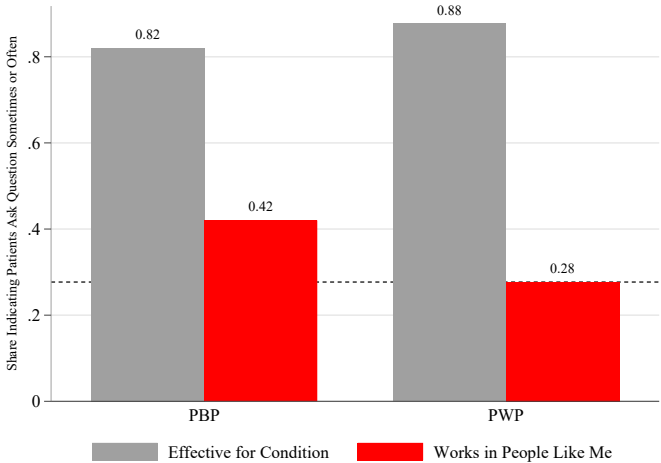
Patient Questions about New Medicines



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Extrapolation from Clinical Trial with Rationale

Panel A: Black Patients and Their Physicians (PBP)						
White to Black Patients	*Confidence*				*Rationale*	
	Not at All	Some	Moderate	High	Perceived Biol. Factors	Perceived Social & Envir. Factors
	(1)	(2)	(3)	(4)	(5)	(6)
Black Patients	39.6%	28.1%	25.2%	7.2%	31.0%	45.7%
PBP	3.5%	28.1%	61.4%	7.0%	32.1%	45.3%

Panel B: White Patients and Their Physicians (PWP)						
Offshored to U.S. Patients	*Confidence*				*Rationale*	
	Not at All	Some	Moderate	High	Perceived Biol. Factors	Perceived Social & Envir. Factors
	(1)	(2)	(3)	(4)	(5)	(6)
White Patients	21.3%	36.8%	32.4%	9.6%	19.5%	43.9%
PWP	1.5%	21.5%	61.5%	15.4%	10.9%	70.9%

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Implications of Physician-Patient Beliefs and Behavior on Firm's v_τ

- Demand for White over-represented trials exceeds Demand for Black over-represented trials ($v_W > v_B$) [# of White patients > # of Black patients]
- Demand for Representative trials exceeds Demand for White over-represented trials ($v_R > v_W$) [# of patients > # of White patients]

$\implies v_R > v_W > v_B$.

However, after accounting for effects of **historical underrepresentation** on recruitment **cost** using the status-quo recruitment technology:

$\implies \Pi_W > \Pi_R > \Pi_B$.

Back Details on Cost (of Recruitment) Function

Framework Implies a Cycle of Underrepresentation

1. Trials in the past have not been representative of Black patients.
2. The lack of representation decreases perceived benefits of treatments for Black patients and physicians who treat them.
3. (1) and (2) raise costs of recruiting diverse samples.
4. Trials today are not representative of Black patients.
5. And the cycle continues ...

Could break cycle and equalize cost of recruitment between groups; but firms can free ride on other firms ⇒ individual firms underinvest in *inclusive infastructure*

Back Formalization