Online Appendix for Representation and Extrapolation: Evidence from Clinical Trials

by

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A Additional Discussion

A.1 Conditioning on Patient Characteristics

We document, using survey data from Research!America, that Black patients are less likely to hear about clinical trials, less likely to enroll in trials if recommended by their doctor, and cite (a lack of) trust as one of the reasons for their hesitancy in enrolling (Table I). Overall, this evidence suggests that there is racial disparity in access to and perceived benefits from trials.

A standard question is whether these gaps persist when conditioning on patient characteristics. Black patients statistically differ in characteristics like income, education, and insurance status, and these characteristics also influence participation and perception of clinical trials. Without controlling for such characteristics, the gaps presented could suffer from omitted variable bias.

However, recent work in economics and law highlights that conditioning on patient characteristics may also result in "included variable bias" (Ayres 2010). The key distinction is that an agent's practices, which seem neutral when conditioning on patient characteristics, can result in "substantial adverse impact on a protected group." Even if there is no "intentional discrimination," such practices are discriminatory unless they are essential for the task at hand (Ayres 2010). For example, recruiting from academic medical centers and not safety net hospitals might be taken as a neutral business practice (conditional on hospital access) but if minority and immigrant communities use the safety net system more often this could have a disparate impact.

On the supply side of clinical trials, the question of which characteristics to condition on is subtle. For example, education may not directly affect the ability of a patient to participate in a trial, suggesting that we should *not* control for education. On the other hand, education might affect the ability to provide informed consent and therefore be an appropriate control.[1] Similar arguments follow for prescription behavior – on the one hand, insurance and income often determine access to new medications.[2] On the other hand, the presence of systemic racial barriers in access to employment and insurance, including, importantly, a lack of universal health care and other safety net systems in the US, might suggest that income and insurance are mechanisms of discrimination.[3]

Empirically, we find that conditional or unconditional gaps are quite similar for clinical trial participation and new drug prescription rates. In Appendix Table C1, we show that the gaps in access to trials and beliefs on benefits from trials are unchanged when we control for income, education, and political affiliation. Regardless, the notion that conditional gaps are the "right" measure of disparity requires careful evaluation and should not be asserted without considering the specific context.

[1] Though the response to such a rationale might very well be that consent forms could be accessible to people with different literacy levels.

[2] Indeed, the two are linked in the U.S. through employer-sponsored health insurance.

[3] According to Alesina, Glaeser and Sacerdote (2001, p.189): "America's troubled race relations are clearly a major reason for the absence of an American welfare state."

A.2 Discussion of Recruitment Costs

Precise estimates on costs of patient enrollment are typically held as trade secrets and, thus, are difficult to pin down. In off-the-record conversations, industry stakeholders confirmed our intuition about why these costs are difficult to find: clinical research organizations (CROs) are widely believed to charge different amounts to recruit patients when working with different firm partners and, thus, are typically unwilling to reveal this information. To provide at least some information about the relative costs of recruitment, we below summarize a discussion with a marketing firm that partners with non-profit and governmental organizations as well as additional scholarly publications that report data on costs.

An executive at a marketing firm that specializes in health care recruitment cited a recent initiative, in which the sponsor had budgeted $25 per enrollee for marketing expenses. When efforts were made to target Black and Hispanic patients, estimated costs rose to $1600 per enrollee, as advertisements needed to be redesigned and new venues for recruiting patients identified. This anecdote is consistent with findings in Marquez et al. (2003), who detail challenges in recruiting minority patients to a study of age-related bone loss and fractures. They document a total expense of recruiting patients from minority groups that was 5-fold higher than the cost of recruiting White patients. Similarly, Rasouly et al. (2019) study alternative strategies to improve representation in genetic screening studies and find that the lowest cost methods yielded samples with "comparatively higher education levels and employment rates, and lower ethnic diversity." More generally, proposed best practices to increase enrollment of Black patients in clinical trials often involve additional resources: this includes adding "nurse navigators" to study teams who can visit community clinics and support enrollees, incorporating monetary incentives for physicians who can identify and recruit patients, and increasing in-kind incentives for participation (Fouad et al. 2016; Holmes et al. 2012; Arring et al. 2022; Dignan et al. 2011). Experts note that these cost differences stem, in large part, from a lack of historical efforts to build relationships and infrastructure.

A.3 Interaction Between Representation and Efficacy

The effect of representation on prescribing intention may differ based on the efficacy of the drug. Our model suggests that representation matters the least when a drug has very low or very high efficacy. Intuitively, if a drug is ineffective for all patients in a trial, then a physician will not prescribe it to Black patients, independent of their decision-making with regard to representation. Similarly, if a drug is a drastic improvement over existing treatments, then a physician will be willing to prescribe it to all patients, even those belonging to underrepresented groups. For more intermediate ranges of efficacy, we would expect representation to meaningfully impact a physician's prescribing intention.

In our experiment, we choose the domain of efficacy values to reflect typical values of FDA-approved oral antiglycemics. The efficacy range of these drugs – 0.5 to 2 percentage point reductions in A1c – is narrow. Although this choice allowed us to study our central question in a way that simulates real-world

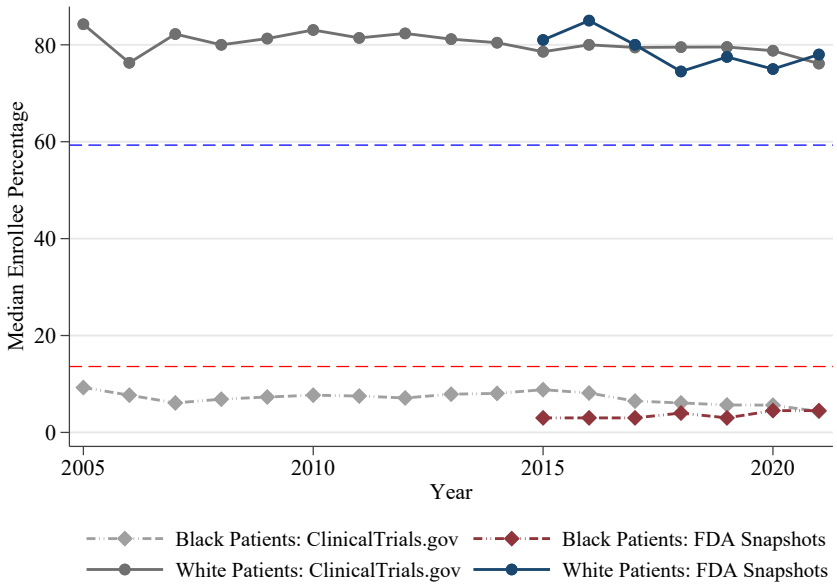
physician decisions, it did limit our ability to detect potential differences in the effect of representation on prescribing intention across different values of efficacy.

In Column (2) of Table C17, we observe that the coefficient on the interaction between efficacy and representation is not economically meaningful nor is it statistically significant. This confirms that the effect of representation on prescribing intention is essentially constant across the narrow range of efficacy we present in the experiment.

We also note that alternative models would predict that the effect of representation on prescribing intention is similar across all domains of efficacy. This would be the case, for example, in a model along the lines of "warm-glow giving" (Andreoni 1990), specifying that physicians (agents) directly derive utility from prescribing drugs tested in representative trials (donating to charity) independent of the reported efficacy (amount of donation). Investigating whether the effect of representation on prescribing intention varies for a larger domain of efficacy values is an avenue for future research.

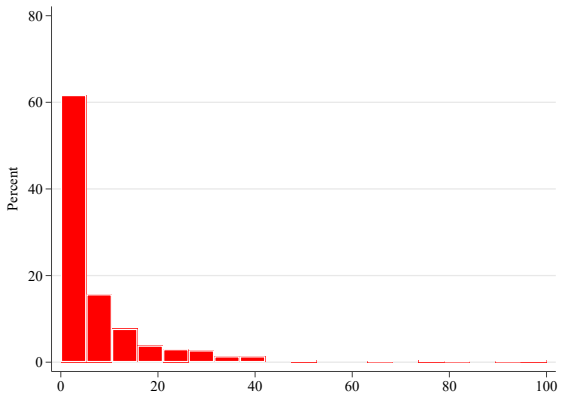
B Appendix Figures

Appendix Figure B1: Clinical Trials Participation in ClinicalTrials.gov and FDA Drug Trials Snapshots

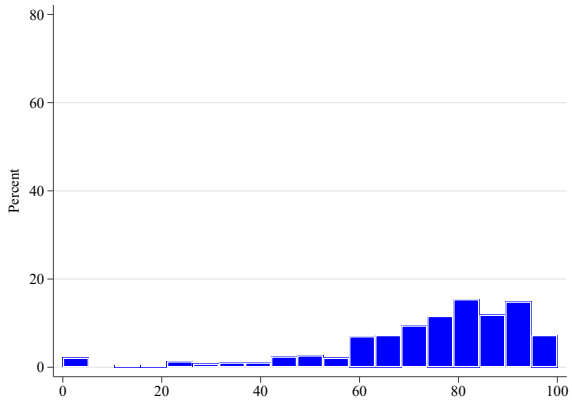


Notes: Figure plots the median enrollee shares by race in clinical trials, using data drawn from two databases: FDA Drug Trials Snapshots and ClinicalTrials.gov. FDA Drug Trials Snapshots includes race enrollment data on all pivotal trials for drugs approved between 2015 and 2021. Figure includes Clinicaltrials.gov data for completed trials that report Black and/or White enrollment rates, with a primary completion date between 2005 and 2021. Dashed lines plot the population shares by race in the U.S. population as reported in the 2020 U.S. Census (Black population share is 13.6 percent and non-Hispanic White population share is 59.3 percent; U.S. Census Bureau 2021). See Data Appendix H.1.1 and H.1.2 for details.

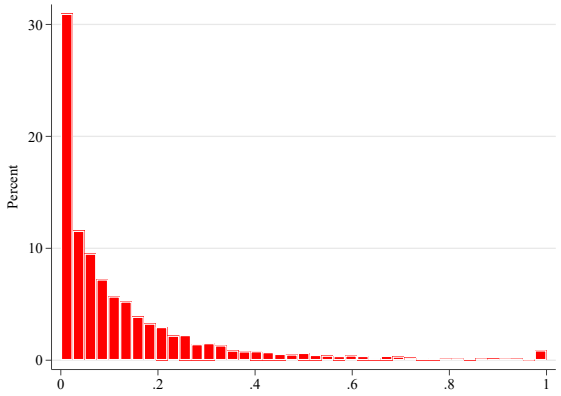
Appendix Figure B2: Trial Participation By Race



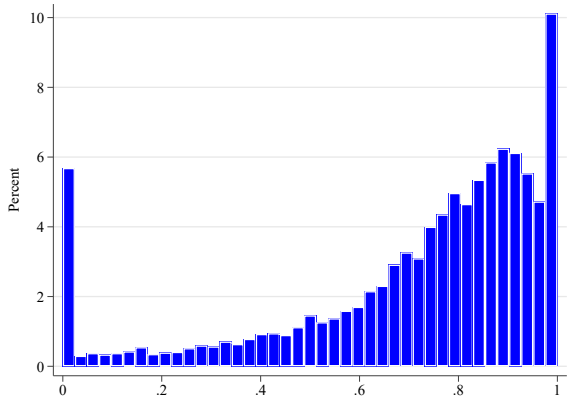
(a) FDA Drug Trials Snapshots, Black Patients



(b) FDA Drug Trials Snapshots, White Patients



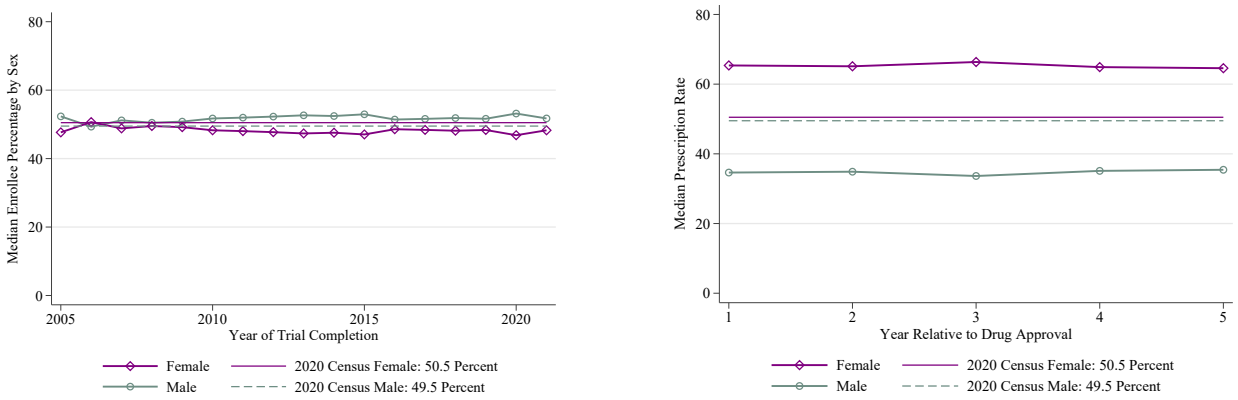
(c) ClinicalTrials.gov, Black Patients



(d) ClinicalTrials.gov, White Patients

Notes: Figure plots the racial composition of clinical trials separately for Black and White participants. Panels (a) and (b) use data drawn from the FDA Drug Trials Snapshots database. Panels (c) and (d) use data from ClinicalTrials.gov for completed trials that report Black and/or White enrollment rates. See Data Appendix H.1.1 and H.1.2 for details.

Appendix Figure B3: Development and Distribution of New Drugs by Sex

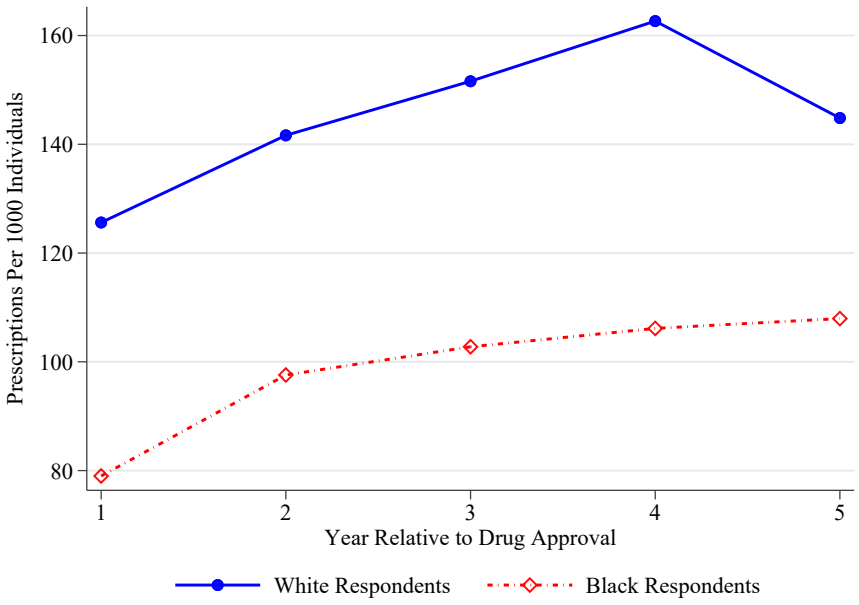


(a) Clinical Trials Participation

(b) Prescriptions of New Drugs

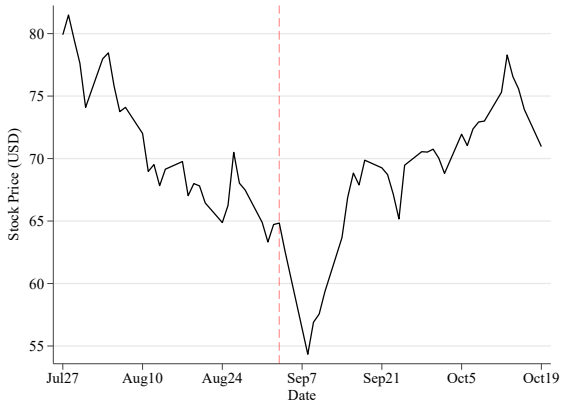
Notes: Figure replicates Figure I using data on sex instead of race. Panel (a) plots the median enrollee percentage by sex using data drawn from ClinicalTrials.gov for completed trials that report data on sex and have a primary completion date between 2005 and 2021. Panel (b) plots the median new drug prescription percentage by sex in each year relative to its approval using data from the Medical Expenditure Panel Survey. Straight lines in both panels plot population shares by sex in the U.S. as reported in the 2020 Census (Female population share is 50.5 percent, and Male population share is 49.5 percent; U.S. Census Bureau 2021). See Data Appendix H.1.1, H.2, and H.3.3 for details.

Appendix Figure B4: Prescribing Rates per Population

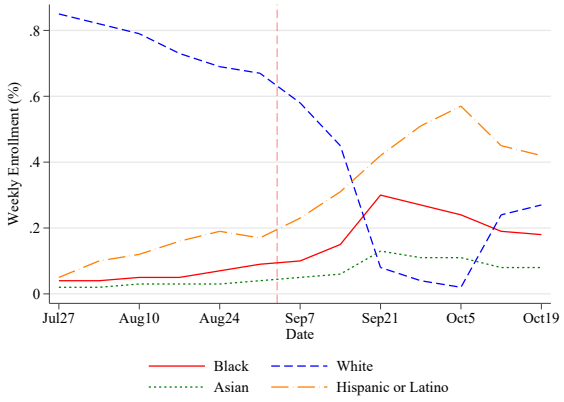


Notes: Figure plots the average number of new drug prescriptions in each year relative to marketing start date per 1000 individuals. The average number of prescriptions is plotted separately for Black and White individuals. Data are drawn from the Medical Expenditure Panel Survey. See Data Appendix H.2 for details.

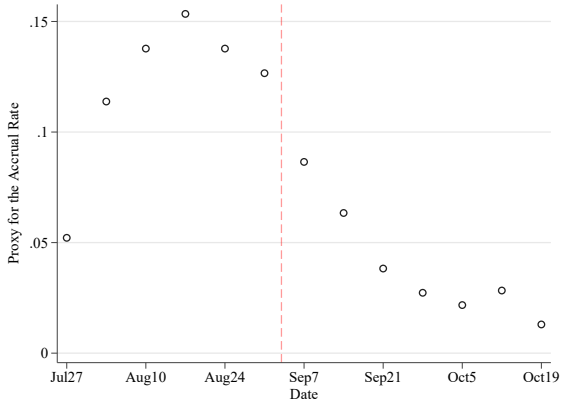
Appendix Figure B5: Moderna Stock Price and Trial Enrollment



(a) Moderna Stock Price



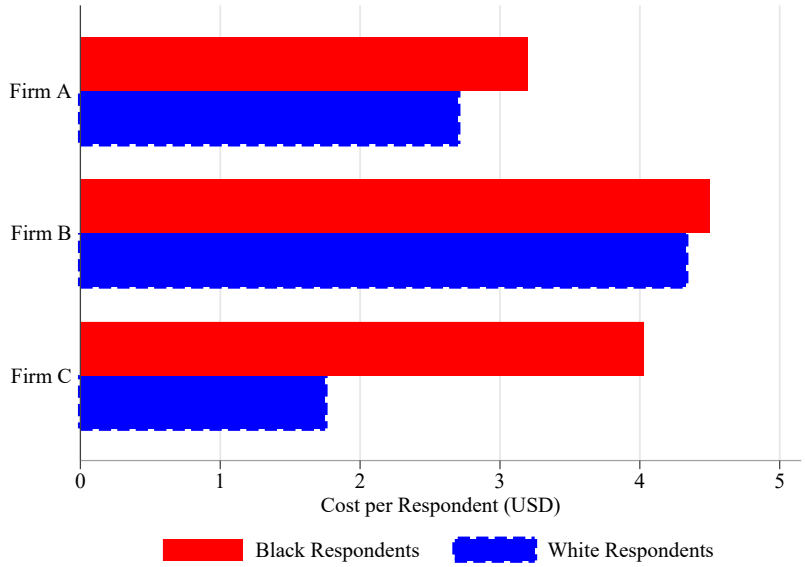
(b) Trial Enrollment by Race and Ethnicity



(c) Proxy for the Accrual Rate

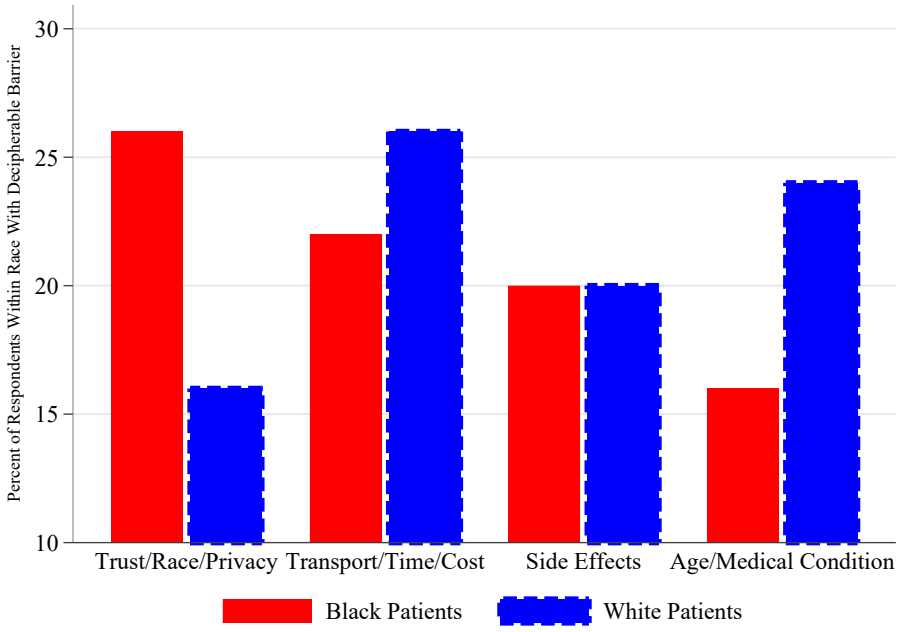
Notes: Panel (a) plots the Moderna Inc. stock price from July 27, 2020 through October 19, 2020. Data are from Yahoo!Finance Historical Stock Records. Panel (b) plots the share of new Moderna Covid-19 trial participants by race. Panel (c) plots a proxy for the accrual rate – the number of participants enrolled in the trial that week divided by the total trial enrollment, which was pre-specified by the company at 30,000 (National Institutes of Health 2020). Data for Panels (b) and (c) are from Moderna presentations and executive announcements. In all panels, the vertical line at September 3, 2020 marks the date of Moderna's public announcement of slowing down trial enrollment to ensure minority representation (Tirrell and Miller 2020). See Data Appendix H.3.6 and H.3.7 for details.

Appendix Figure B6: Recruitment Costs by Race across Firms



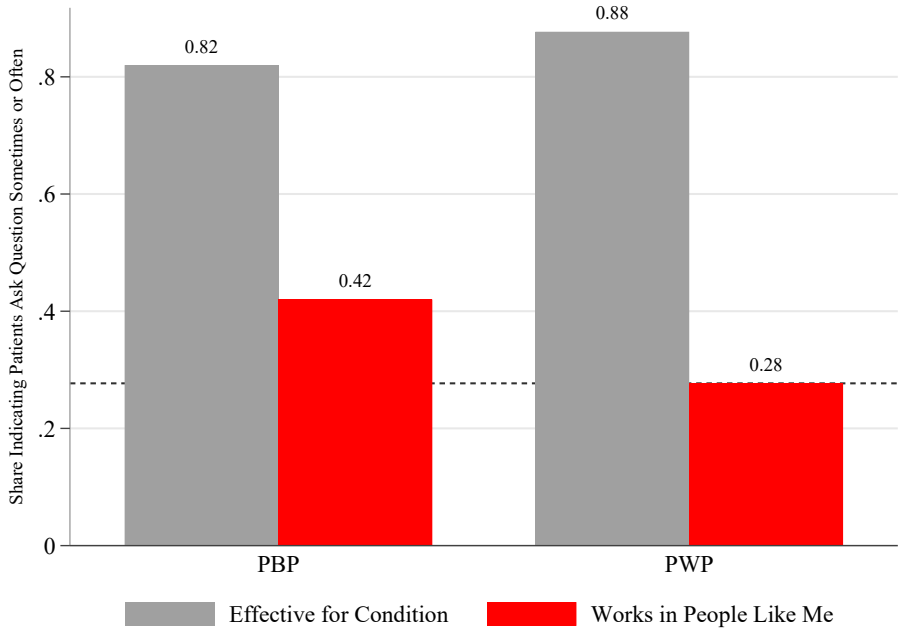
Notes: Figure plots the estimated per-respondent cost of recruiting survey participants on three online platforms. Quotes are provided by race for samples of 400 respondents (Firm A) and 600 respondents (Firms B and C). Data are from estimates solicited by the authors between January and June of 2022 from large marketing research firms, which have been used to recruit participants for online experiments in economics; firm names have been anonymized.

Appendix Figure B7: Leading Barriers to Clinical Trial Participation



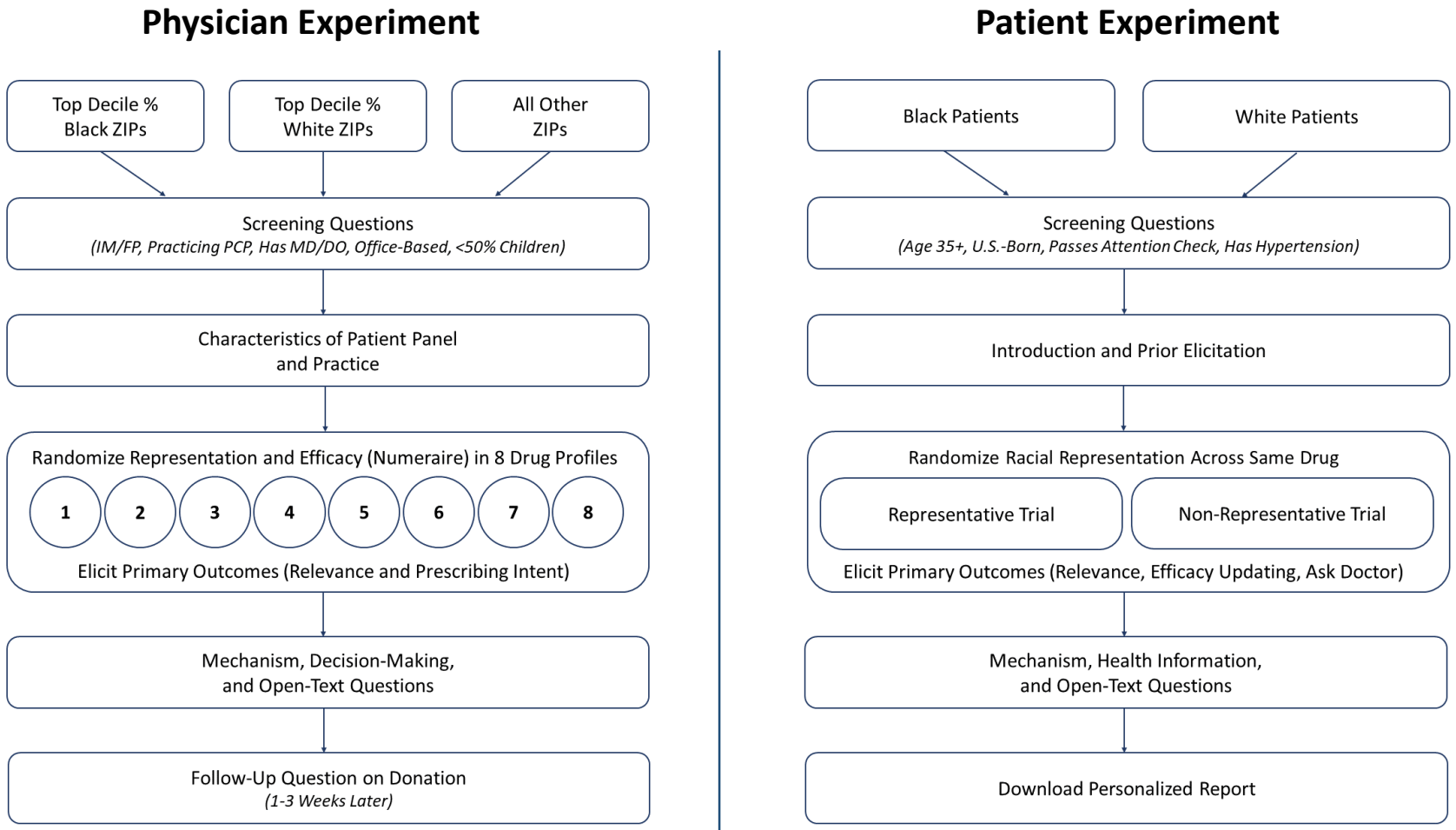
Notes: Figure presents the most commonly cited barriers to participating in clinical trials among patient respondents reporting they faced a decipherable barrier to participation, by respondent race. Open-text responses were independently coded by three coders (two research assistants and one graduate student) as corresponding to one of eight categories of barriers: (1) trust/race/privacy; (2) transport/time/cost; (3) side effects; (4) age/medical condition; (5) lack information; (6) not interested; (7) none/no barriers; and (8) indecipherable/unsure. In the event of disagreement between coders, the code selected by the majority was used; in the rare (N=4) event all coders disagreed, one of the codes was selected at random. In total, 36.0 percent of Black respondents and 36.8 percent of White respondents reported facing a decipherable barrier to trial participation; as visualized in the figure, the older age profile of White respondents corresponds to greater age-related barriers. Data are from the New Drug Patient Survey Experiment.

Appendix Figure B8: Patient Queries to Doctor When Prescribed New Medications



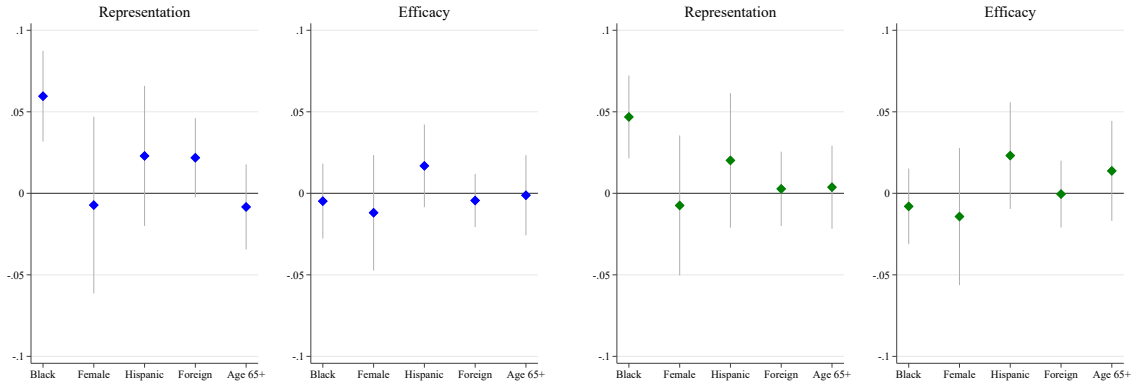
Notes: Figure plots the share of physicians who indicate that they have been asked the following questions by patients *frequently*: "Is the drug effective for my condition?" and "How do I know the drug will work in people like me?" *PBP* (Physicians treating Black patients) denotes physicians who report above the median percent Black patients in their patient panel. *PWP* (Physicians treating White patients) is defined similarly with respect to White patients. Data are from the Physician Survey Experiment.

Appendix Figure B9: Physician and Patient Experiment Flow



Notes: Overview of the Physician and New Drug Patient Survey Experiments.

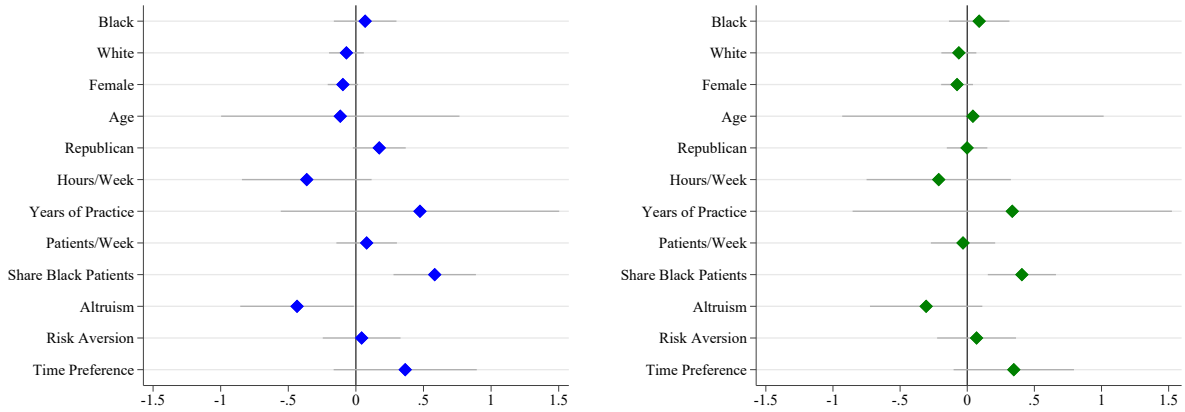
Appendix Figure B10: Association Between Physician Coefficients and Patient Characteristics



(a) Relevance (b) Prescribing Intention

Notes: Figure plots coefficient estimates from regressions of physician-specific coefficients for representative treatment or efficacy treatment on patient panel characteristics (expressed as the percentage of patients with a given demographic characteristic multiplied by 10). 95 percent confidence intervals using robust standard errors are drawn. Data are from the Physician Survey Experiment.

Appendix Figure B11: Association Between Physician-Specific Coefficients and Characteristics

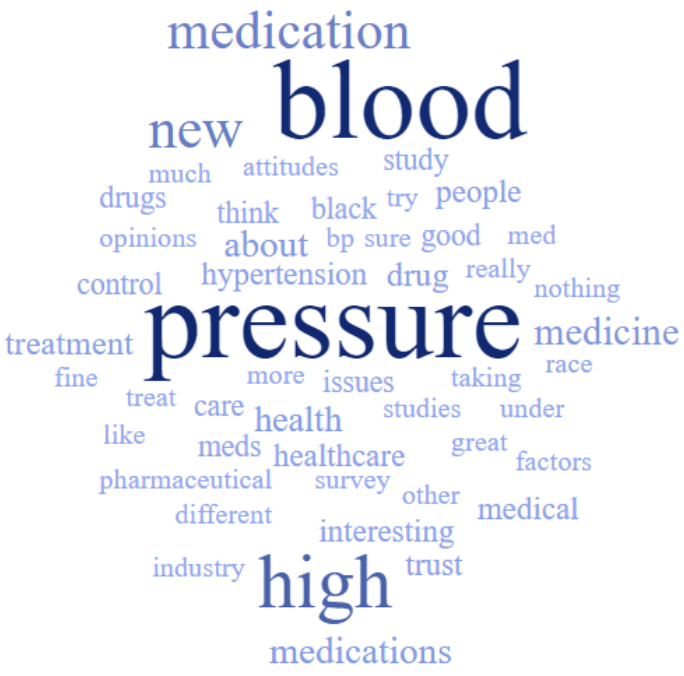


(a) Relevance

(b) Prescribing Intention

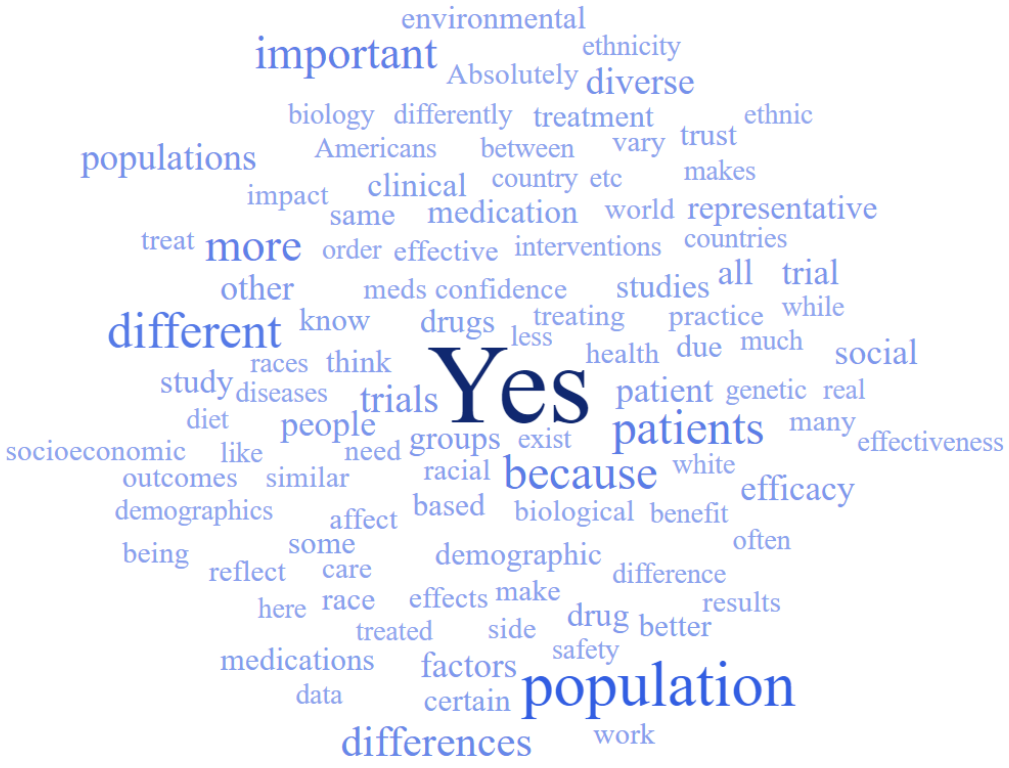
Notes: Figure plots coefficient estimates from regressions of physician-specific coefficients for representative treatment on physician characteristics. *Age, Hours/Week, Years of Practice, Patients/Week*, and *Share Black Patients* are divided by 100 for ease of visualization. *Altruism, Risk Aversion,* and *Time Preference* (measured on a 0-10 scale) are divided by 10 as well. 95 percent confidence intervals using robust standard errors are included. Data are from the Physician Survey Experiment.

Appendix Figure B12: Patient Respondents: Open-Text Responses



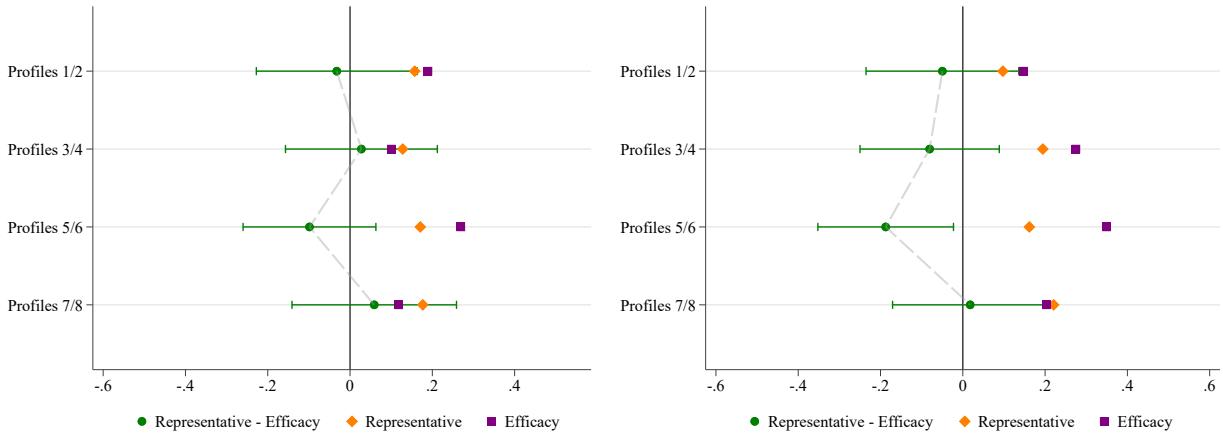
Notes: Word cloud of open-text responses of patient respondents' answers to the question at the end of the survey: "What do you think this study is about?" Data are drawn from the New Drug Patient Survey Experiment.

Appendix Figure B13: Physician Respondents: Open-Text Responses



Notes: Word Cloud of open-text responses of physicians' answers to the question: "Is it important for clinical trials to be representative of the U.S. population? Why or why not?" Data are from the Physician Survey Experiment.

Appendix Figure B14: Physician Experimental Results by Profile Order

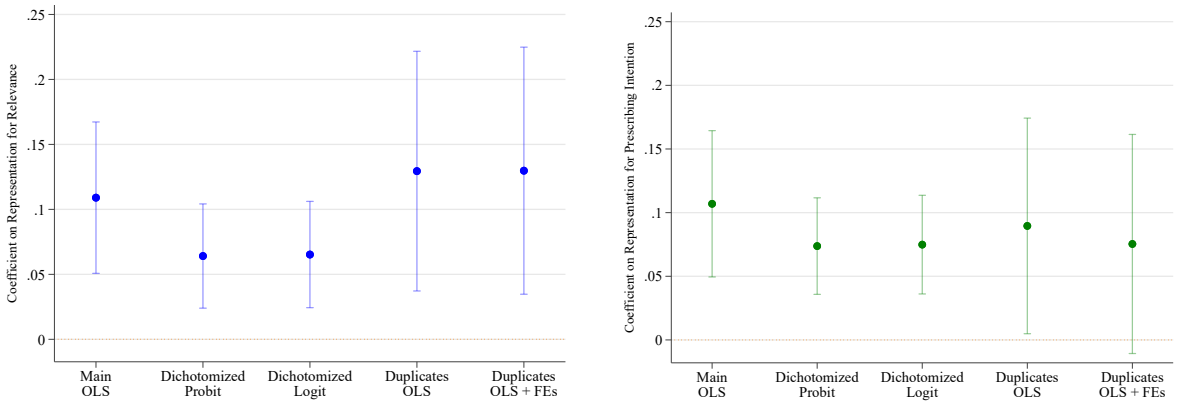


(a) Relevance

(b) Prescribing Intention

Notes: Figure plots the difference between coefficients on *Representative Treatment* and *Efficacy Treatment* as well as their point estimates for the outcomes of *Relevance* and *Prescribing Intention*, grouped by profile orders. *Representative* refers to the randomized percent Black in the trial unless otherwise indicated. *Efficacy* refers to the randomized percentage point drop in A1c. *Prescribing Intention*, *Representative* and *Efficacy* are standardized to a mean of 0 and a standard deviation of 1. Rx Mechanism fixed effects are included. For instance, the topmost orange data point in panel (b) shows the average effect across physicians of representation on prescribing intention across profiles 1 and 2, and the purple dot shows the same for the coefficient on efficacy. The green dot with error bars shows the difference between the two coefficients (*i.e.*, the label *Representation - Efficacy* refers to Representation minus Efficacy). Robust standard errors are clustered at the physician level. 95 percent confidence intervals for difference estimates are displayed. Data are drawn from the Physician Survey Experiment.

Appendix Figure B15: Physician Survey Experiment: Robustness Across Samples and Models

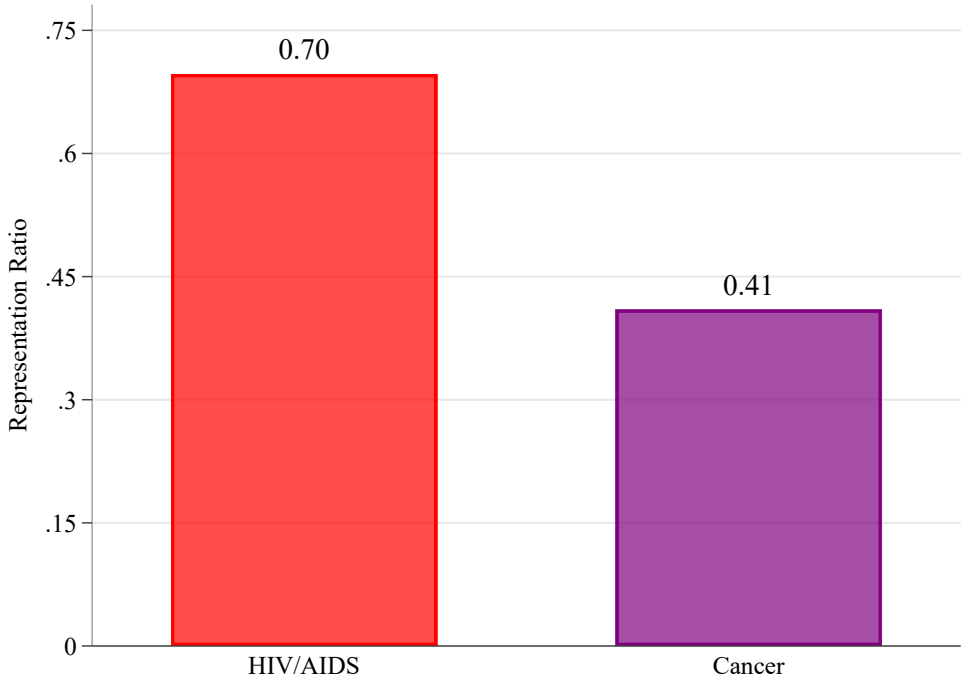


(a) Relevance

(b) Prescribing Intention

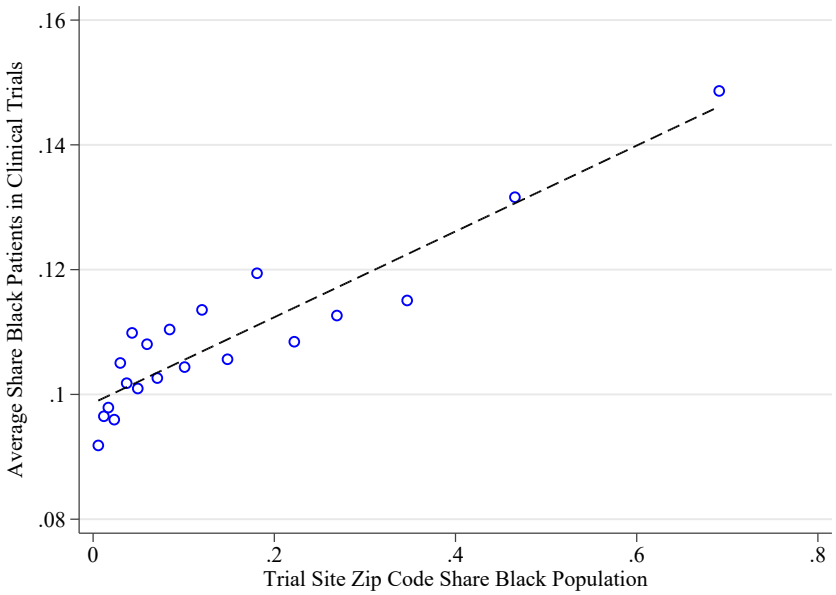
Notes: Figure plots coefficient estimates from a regression of *Prescribing Intention* on *Representation*. *Representation* is standardized for all specifications; *Relevance* and *Prescribing Intention* are standardized to a mean of 0 and standard deviation of 1 for OLS specifications and dichotomized at the median value for probit and logit specifications. The "Main OLS" specification corresponds to our pre-specified main equation. The "Dichotomized Probit" specification corresponds to a probit equation regressing dichotomized prescribing intention on *Representation* and *Efficacy* with profile order fixed effects and drug mechanism fixed effects, using robust standard errors clustered at the physician level. The "Dichotomized Logit" specification is identical to the probit specification but logistic regression is utilized instead. In both the probit and logit cases, the margin effects are plotted. The "Duplicates OLS" specification plots estimates from a regression of *Prescribing Intention* or *Relevance* on *Representation* with physician-by-efficacy fixed effects. Within our sample, we ensured that each physician saw two drug profiles with identical efficacy levels and different measures of representation; "Duplicates OLS" restricts consideration to this sample. The "Duplicates OLS + FEs" specification is identical to the "Duplicates OLS" but adds profile order fixed effects and drug mechanism fixed effects. 95 percent confidence intervals are shown; all coefficient estimates are statistically significant at the 95 percent level except "Duplicates OLS + FEs," which is significant at the 90 percent level. Data are from the Physician Survey Experiment.

Appendix Figure B16: Representation Relative to Disease Burden



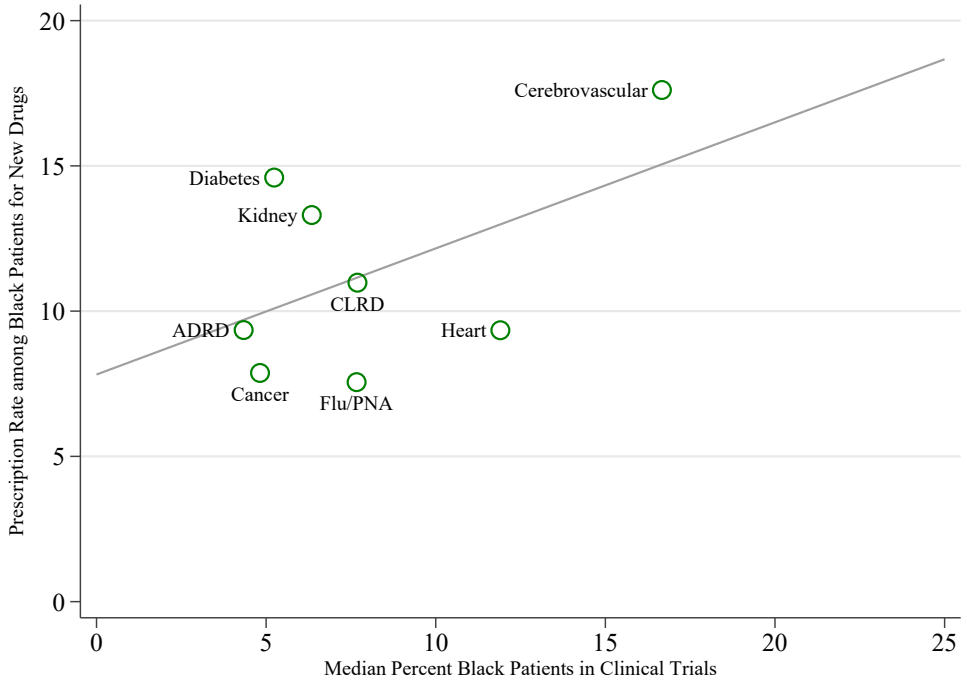
Notes: Figure plots the representation ratios of cancer and HIV/AIDS in Black patients relative to disease burden. *Representation Ratio* is defined as the median percent Black in trials in a disease category divided by the Black disease burden (share of Black deaths among all deaths from the condition in the United States). Enrollment data are from ClinicalTrials.gov for completed trials that report Black patient enrollment rates. Disease burdens are from Centers for Disease Control and Prevention (2021) and Heron (2021). See Data Appendix H.1.1 for details.

Appendix Figure B17: Racial Composition of Clinical Trials and Trial Site Zip Codes



Notes: Figure plots the binned average percent Black in clinical trials and the average percent Black of trial site zip codes. Enrollment data are drawn from ClinicalTrials.gov for completed trials that report Black patient enrollment rates and have trial sites in the United States. Data on trial site zip code demographics are drawn from the 2019 American Community Survey (ACS). See Data Appendix H.1.1 and H.3.3 for details.

Appendix Figure B18: Prescription Rates and Trial Representation (Excluding HIV-AIDS)



Notes: Figure plots the correlation between the prescription rate of new medications to Black Americans and the median percent Black in pivotal trials. We construct the prescription rate as the percentage of newly marketed drugs (on the market for five or fewer years) received by Black Americans in the ten leading causes of death (excluding unintentional injuries and suicide) in the United States Heron (2021). The y-axis value of Cancer includes supportive outpatient therapies. CLRD, Diabetes, Heart, Kidney, and Flu/PNA indicate Chronic Lower Respiratory Diseases, Diabetes Mellitus, Diseases of Heart, Kidney Diseases, and Influenza and Pneumonia, respectively. Prescription data are from the Medical Expenditure Panel Survey, and trial composition data are from ClinicalTrials.gov. See Data Appendix H.1.1 and H.2 for details on data construction.

C Appendix Tables

Appendix Table C1: Views on Science and Clinical Trials among U.S. Respondents – with SES Controls

	Confidence in Research Institutions		*Heard of Clinical Trial*		*Would Enroll if Doctor Recommends*		*Trust Not Reason for Lack of Enrollment*		*Science is Beneficial*		*Would Get FDA-Approv. Vaccine*	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)
Black	-0.253**	-0.273**	-0.079***	-0.076***	-0.054**	-0.046*	-0.104***	-0.090***	-0.099**	-0.106**	-0.163	-0.054
	(0.115)	(0.123)	(0.020)	(0.022)	(0.022)	(0.023)	(0.029)	(0.032)	(0.045)	(0.046)	(0.119)	(0.128)
Constant	3.082	3.329	0.875	0.909	0.837	0.871	0.536	0.528	0.383	0.595	3.069	3.436
Covariates	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Observations	940	927	2843	2757	2658	2584	2031	1948	971	955	922	907

Notes: Table reports OLS estimates from a regression of survey responses among Black and White individuals across a number of questions regarding science. Covariates include an indicator for whether the individual's income is above the median, an indicator for whether the individual has a college degree, and an indicator for whether the individual supports the GOP. Data are from a nationally representative survey conducted by Research!America in the years 2013, 2017, and 2021. See Data Appendix H.3.5 for details. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C2: Physician Survey Experiment Balance Table

	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)
F-Statistic	0.76	1.21	1.70	1.32
Number of Observations	137	137	137	137

Notes: Table displays results from separate regressions of the mean and range of *Representation* and *Efficacy* values randomly assigned to physicians on a host of physician and physicians' patient panel characteristics. For *Physician Years Practice*, respondents selected an interval from a multiple choice list; *Grp* refers to the group (selected interval) chosen by the respondent, instead of the numerical value indicated. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C3: Comparison between Physician Survey Respondents and AMA Masterfile Physicians by Strata

	Top Decile Share Black ZIPs		*Bottom Decile Share Black ZIPs*		*All Other ZIPs*		*Differences*		
	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)
Phys: 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)
Phys: 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)
Phys: 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)
Phys: 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

Notes: Table reports means and differences between physicians that participated in the survey experiment and all those coded as internal medicine or family practice in the U.S. who practice in similar zip codes. Data are drawn from the Physician Survey Experiment, U.S. News and World Report, the 2014 version of the AMA Masterfile Directory, and the 2019 American Community Survey. See Data Appendix H.3.1, H.3.2, and H.3.3 for details. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C4: Characteristics of Physicians Responding to Follow-Up Question

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)
MD Hours/Week (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)
Observations	137	82	219

Notes: Table compares the baseline physician and patient panel characteristics of all physician respondents to those responding to the follow-up question. For *Physician Years Practice (Mdpt)*, *Physician Patients/Week (Mdpt)*, and *Patient Percent Foreign (Mdpt)*, respondents were asked to select an interval from a list of options; we assigned each physician the *midpoint* of the interval selected when calculating summary statistics. Robust standard errors are used when comparing characteristics between the two groups. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C5: Comparison Patient Respondents for Survey on New Drug to MEPS Respondents

	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. Survey weights are utilized. "Under FPL" refers to the household income of the respondent being under the 2021 federal poverty line, around $30k for a four-person household (ASPE 2022). See Data Appendix H.2 for details. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C6: Patient Experimental Results on New Drug – Robustness

Panel A: Patients Demanding Personalized Report

	Relevance		*Ask Doctor*		*Loading on Signal*	
	Black Patients	White Patients	Black Patients	White Patients	Black Patients	White Patients
	(1)	(2)	(3)	(4)	(5)	(6)
Representative Treatment	0.615**	0.380	0.104	0.000	0.071	-0.019
	(0.258)	(0.253)	(0.113)	(0.126)	(0.106)	(0.059)
Observations	63	52	63	52	63	52

Panel B: Using MEPS Person Weights

	Relevance		*Ask Doctor*		*Loading on Signal*	
	Black Patients	White Patients	Black Patients	White Patients	Black Patients	White Patients
	(1)	(2)	(3)	(4)	(5)	(6)
Representative Treatment	0.781***	0.166	0.042	0.008	0.132*	-0.076
	(0.173)	(0.161)	(0.077)	(0.081)	(0.068)	(0.056)
Observations	139	136	139	136	139	136

Panel C: LASSO-Selected Controls

	Relevance		*Ask Doctor*		*Loading on Signal*	
	Black Patients	White Patients	Black Patients	White Patients	Black Patients	White Patients
	(1)	(2)	(3)	(4)	(5)	(6)
Representative Treatment	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: Relevance is standardized to a mean of 0 and standard deviation of 1. Panel (a) reports estimates from Equation 3 restricting to patients demanding the personalized report. Panel (b) reports estimates weighting each observation based on the mean person weight in the 2019 Medical Expenditure Panel Survey by combinations of the following sociodemographic characteristics: race (Black or White), age (35–44, 45–64, or 65+), region (South vs. non-South), college degree, income (0-30k, 30-110k, 110k+), health insurance status (insured or uninsured), and usual place of care (has usual place or does not have usual place). Nine patient survey respondents have combinations of characteristics not represented in the MEPS, and are assigned person weight equal to the mean person weight in the MEPS. Results are robust to dropping these individuals (available upon request). Panel (c) reports estimates from double-selection LASSO linear regression. Potential controls included age, sex, education, and health variables among others. Robust standard errors clustered in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C7: Patient Survey on Clinical Trial Participation: Balance Table

Variable	(1) All Respondents	(2) Representative Arm	(3) Non-Representative Arm	(4) Difference
Black	0.423	0.424	0.421	0.003
	(0.495)	(0.496)	(0.496)	(0.060)
Male	0.467	0.439	0.496	-0.057
	(0.500)	(0.498)	(0.502)	(0.061)
Age Group	3.188	3.144	3.233	-0.089
	(1.037)	(1.060)	(1.014)	(0.126)
BA or Higher	0.386	0.360	0.414	-0.054
	(0.488)	(0.482)	(0.494)	(0.059)
Insured	0.967	0.964	0.970	-0.006
	(0.179)	(0.187)	(0.171)	(0.022)
Takes BP Medication	0.912	0.906	0.917	-0.011
	(0.284)	(0.292)	(0.276)	(0.035)
Past Nonadherence	0.107	0.101	0.113	-0.012
	(0.309)	(0.302)	(0.318)	(0.038)
Heard of Tribenzor	0.044	0.043	0.045	-0.002
	(0.206)	(0.204)	(0.208)	(0.025)
Observations	272	139	133	272

Notes: Table compares the baseline demographic, economic, and health characteristics of respondents receiving information on a representative trial to those receiving information on a non-representative trial.

Appendix Table C8: Patient Survey on New Drug: Balance Table

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)
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

Notes: Table compares the baseline demographic, economic, and health characteristics of respondents receiving information on a representative trial to those receiving information on a non-representative trial.

Appendix Table C9: Patient Survey Experiments Attrition by Arm

	Attrition Post-Randomization			
	Survey on New Drug		Survey on Clinical Trial	
	(1)	(2)	(3)	(4)
Representative Treatment	0.011		-0.004	
	(0.030)		(0.035)	
Black		0.036		0.040
		(0.030)		(0.036)
Sample Mean	0.074	0.074	0.099	0.099
Observations	297	297	302	302

Notes: Table reports OLS estimates regressing an indicator for *Attrition Post-randomization* on indicators for *Representative Treatment* (*i.e.*, assignment to the 15 percent Black trial) and Black race for two separate surveys. The primary survey refers to the original experiment which was designed to measure patient assessment of a new drug after receipt of clinical trial evidence. The secondary survey refers to a later experiment designed to assess willingness of patients to participate in future clinical trials. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C10: Physician Survey Experiment Attrition and Randomized Attributes

	Mean of Values Over Trials		*Range of Values Over Trials*	
	Representation	Efficacy	Representation	Efficacy
	(1)	(2)	(3)	(4)
Attrition	-0.477	-0.016	0.911	0.014
	(0.851)	(0.059)	(1.550)	(0.090)
Sample Mean	12.025	1.277	25.782	1.159
Observations	145	145	145	145

Notes: Table displays results from separate regressions of the mean and range of *Representation* and *Efficacy* values randomly assigned to physicians on an indicator for respondent attrition post-randomization. Of those randomized, 5.5 percent of respondents attrited from the survey. Robust standard errors are shown. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C11: Representation and Willingness to Participate in Future Clinical Trials

Panel A: Black Patients

		Mechanisms					
	Willingness to Participate	Researchers are not Trustworthy	Does not Apply to Me	Risk Side Effects	Does not Provide New Information	Does not Protect my Information	Financial Burden
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Representative Treatment	0.385**	-0.413**	-0.215	-0.327*	-0.060	0.204	-0.061
	(0.177)	(0.189)	(0.178)	(0.194)	(0.200)	(0.199)	(0.199)
Control Mean	-0.15	0.34	0.00	0.10	0.07	-0.02	0.09
Observations	115	115	115	115	115	115	115

Panel B: White Patients

		Mechanisms					
	Willingness to Participate	Researchers are not Trustworthy	Does not Apply to Me	Risk Side Effects	Does not Provide New Information	Does not Protect my Information	Financial Burden
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Representative Treatment	-0.114	-0.054	0.021	-0.006	-0.302**	0.036	0.013
	(0.164)	(0.156)	(0.164)	(0.154)	(0.150)	(0.150)	(0.152)
p-value: Black Patients=White Patients	0.038	0.141	0.328	0.193	0.329	0.499	0.765
Control Mean	0.02	-0.06	0.07	0.06	0.12	-0.08	-0.05
Observations	157	157	157	157	157	157	157

Notes: Column (1) reports OLS estimates for the outcome of *Willingness to Participate* on a sample of Black patients (Panel (a)) and White patients (Panel (b)). *Willingness to Participate* reflects whether a patient respondent would participate in a new study testing a different blood pressure medication after being randomly assigned to the representative treatment. Respondents were next asked the extent to which they agreed or disagreed with a series of statements including "Study researchers are not trustworthy" (*Researchers are not Trustworthy*), "Study findings will not apply to me" (*Does not Apply to Me*), "Study participation will risk side effects" (*Risk Side Effects*), "Study will provide no new information" (*Does not Provide New Information*), "Study will not protect my personal health information" (*Does not Protect my Information*), and "Study will be a financial burden" (*Financial Burden*). All variables are standardized to have a mean of 0 and a standard deviation of 1. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C12: Patient Change in Beliefs and Trial Representation

	Posterior Belief				*Update Exp. Dir.*		*Conf. in Beliefs*	
	Black Patients	White Patients	Black Patients	White Patients	Black Patients	White Patients	Black Patients	White Patients
	(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)				
Control Mean	12.552	13.072	12.552	13.072	0.731	0.913	1.403	1.420
Observations	139	136	139	136	139	136	139	136

Notes: Table reports OLS estimates for different measures of patient beliefs. In Columns (3)–(4), the *Prior on Efficacy* variable refers to confidence in posteriors on efficacy. *Posterior Belief* is the patient's expected efficacy of the drug (ranging from 0-25 mmHg reduction in blood pressure) post-treatment. *Update Exp. Direction* is a binary variable indicating whether the patient updated their beliefs in the expected direction post-treatment (*i.e.* updated down if efficacy beliefs were higher than results of the trial, updated up if beliefs were lower than results of the trial). *Confidence in Beliefs* is measured 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.

Appendix Table C13: Heterogeneity Among Patients by Expectation of 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

Notes: Table reports the OLS estimates for the outcome of *Relevance*, *Ask Doctor*, and *Load on Signal* on the interaction with trust and the main effect for Black and White patients. *Expectation of Trustworthiness (Exp. Trust.)* represents the patients' response to the question, "Generally speaking, you would say that: 'Most people can be trusted' or 'Most people cannot be trusted."' *p-value: Expt. Trust. 1=0* reports the *p*-value of the test between the coefficients of an indicator for treatment group (1 or 0) interacted with the expectation of trustworthiness. *Relevance* is standardized to a mean of 0 and standard deviation of 1. *Load on Signal* and *Ask Doctor* are binary. Columns (1), (3), and (5) report the estimates for Black patients, and Columns (2), (4), and (6) report the estimates for White patients. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C14: Extrapolation from Clinical Trial Data among Physicians and Patients

	Confidence				*Rationale*	
	Not at All	Some	Moderate	High	Perceived Biol. Factors	Perceived Social & Envir. Factors
	(1)	(2)	(3)	(4)	(5)	(6)
Panel A: Extrapolation from White to Black Patients						
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						
	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%

Notes: Table reports clinical trial data extrapolation confidence and rationale among patients and physicians. Panel (a) reports confidence in extrapolation across race and Panel (b) reports confidence in extrapolation across geography. Columns (1)–(4) report the percentage of respondents at each confidence level. If a respondent did not select "High" confidence in extrapolation, they were asked to provide a rationale. Column (5) reports the percentage of respondents who cite perceived biol. factors as the rationale for not having "High" confidence in extrapolation. Column (6) reports the percentage of respondents who cite perceived social and envir. factors as the rationale for not having "High" confidence in extrapolation. *PBP* (Physicians treating Black Patients) denotes physicians who report above the median percent Black patients in their patient panel. *PWP* (Physicians treating White Patients) is defined similarly with respect to White patients. Data are drawn from the New Drug Patient Survey Experiment and the Physician Survey Experiment.

Appendix Table C15: Physician Experimental Results – Robustness

	Relevance Non-Standard	Prescribing 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. Column (1) reports estimates from Equation 2 with the outcome *Relevance*; in contrast to the primary specification, the outcome is not standardized. Column (2) shows results using *Prescribing Intention*; in contrast to the primary specification, the outcome is not standardized. *Efficacy* is the change in A1C associated with the drug, which has a range of 0.5 to 2.0 percentage points. *Representation* is the share of Black patients in the trial, which ranges from 0 to 35 percent. See main text for a discussion of these ranges. Column (3) reports estimates from Equation 2. Columns (4)–(6) report estimates for the outcome of *Prescribing Intention*, standardized to a mean of 0 and standard deviation of 1. Column (4) shows results restricting the sample to those demanding the NIH/NASEM report. Column (5) displays results restricting the sample to those responding to the follow-up question. Column (6) reports estimates from double-selection LASSO linear regression with potential controls including age, sex, education, and health variables among others. Robust standard errors clustered at the physician level are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C16: Characteristics of Patients Demanding Report

	All Patients	Demanded Report	Difference Between Groups
	(1)	(2)	(3)
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

Notes: Table compares the baseline characteristics of all patient respondents to those demanding the personalized report. Robust standard errors are used when comparing characteristics between the two groups. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C17: Physician Experimental Results – Additional Results

	Main Specification (1)	Interacted Specification (2)	Continuous Patient Black (3)	Above Median Black (4)	High Black vs. White Strata (5)	High Black vs. Other Two Strata (6)
Representation	0.107***	0.107***	-0.005	0.051	-0.022	0.062
	(0.029)	(0.029)	(0.039)	(0.035)	(0.050)	(0.039)
Efficacy	0.281***	0.281***	0.285***	0.280***	0.259***	0.302***
	(0.032)	(0.032)	(0.043)	(0.040)	(0.076)	(0.048)
Representation × Efficacy		-0.004				
		(0.023)				
Representation × Patient Percent Black			0.004***			
			(0.001)			
Efficacy × Patient Percent Black			0.000			
			(0.001)			
Representation × Above Median Black				0.134**		
				(0.058)		
Efficacy × Above Median Black				0.006		
				(0.065)		
Representation × Top Decile Black ZIP					0.194***	0.107*
					(0.065)	(0.057)
Efficacy × Top Decile Black ZIP					-0.013	-0.051
					(0.085)	(0.061)
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
Observations	1,096	1,096	1,096	1,096	752	1,096

Notes: Table reports OLS estimates for the outcome of *Prescribing Intentention*, standardized to a mean of 0 and standard deviation of 1. Column (1) reports estimates from Equation 2. Column (2) includes the two-way interaction between *Representation* and *Efficacy* (see Subsection A.3 for further explanation). Column (3) includes interactions between *Representation* and *Patient Percent Black* (reported patient panel percent Black), *Efficacy* and *Patient Percent Black*, and the main effect of patient panel percent Black (the latter is not reported here). Column (4) includes interactions between *Representation* and *Above Median Black* (an indicator for above the median patient panel percent Black), *Efficacy* and this indicator, and the main effect of above the median patient percent Black (the latter is not reported). Column (5) includes interactions between *Representation* and *Top Decile Black ZIP* (an indicator for belonging to a zip code in the top decile of population percent Black), *Efficacy* and this indicator, and the main effect (not reported here) among the sample of physicians either from the top decile or bottom decile of population percent Black. Column (6) reports results from the same specification as Column (5) but estimated among physicians from all three sampling strata (top decile population percent Black, bottom decile population percent Black, and all other deciles). Robust standard errors clustered at the physician level are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C18: Overall Sentiment and Screen Time
New Drug Patient Survey Experiment

	Overall Sentiment		*Duration (Min.)*	
	Black Patients	White Patients	Black Patients	White Patients
	(1)	(2)	(3)	(4)
Representative Treatment	0.039	0.180	-2.672	1.750
	(0.114)	(0.112)	(2.758)	(1.783)
p-value: Black=White		0.376		0.176
Constant	0.045	0.014	17.595	12.522
Observations	139	136	139	136

Notes: Columns (1) and (2) report OLS estimates for *Overall Sentiment*, a scale from -1 to 1 measuring overall sentiment as implied by open-text responses. Respondents were asked to explain why or why not a given drug was relevant for their own medical care immediately following exposure to the treatment. Continuous sentiment scores (from -1 to 1 with 1 being the most positive) are predicted using the Valence Aware Dictionary and Sentiment Reasoner (VADER). If the score of an open-text response is greater than or equal to 0.1, a measure of overall sentiment is coded as 1; if the score is less than or equal to -0.1, a measure is coded as -1; otherwise a measure is coded as 0. Columns (3) and (4) report OLS estimates where the outcome *Duration* is the total time a respondent spent completing the survey in minutes. *Black Patients* denotes the group where the patients self-report their race as Black, and *White Patients* denotes the group where the patients self-report their race as White. *Representative Treatment* is an indicator for whether the respondent was assigned to see data from a representative trial (treatment group). To test the null hypotheses that the coefficients for Black and White patients are equal, the *p*-values for both regressions are reported, respectively. Robust standard errors are reported in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C19: Trial Sites and Safety Net Hospitals

	(1)	(2)	(3)
HIV/AIDS (Cancer Comparison)	0.110***		
	(0.008)		
HIV/AIDS (ADRD Comparison)		0.161***	
		(0.012)	
Cancer (ADRD Comparison)			0.050***
			(0.010)
Constant	0.475	0.423	0.425
Observations	197,240	6,804	195,863

Notes: Table reports OLS estimates from a regression of an indicator for whether a trial site is located at a safety net hospital (SNH). Each observation represents a specific site associated with a unique clinical trial and the data are limited to Cancer, HIV/AIDS, and ADRD trials. Following Popescu et al. (2019), we define an SNH as a hospital in the top quartile within the state it is located in either receiving a disproportionate share of funding from Medicaid or high uncompensated care. In this table, we use the Disproportionate Share Hospital (DSH) Index to define an SNH. See the Data Appendix for more detailed definitions of this variable. *HIV/AIDS (Cancer Comparison)* is an indicator variable equal to one if a trial site studies HIV/AIDS and zero if a trial site studies cancer. *HIV/AIDS (ADRD Comparison)* is an indicator variable equal to one if a trial site studies HIV/AIDS and zero if a trial site studies ADRD. *Cancer (ADRD Comparison)* is an indicator variable equal to one if a trial site studies cancer and zero if a trial site studies ADRD. Trial site information is drawn from ClinicalTrials.gov. See Data Appendix H.1.1 and H.3.8 for details. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C20: Neighborhood Demographics of HIV/AIDS, Cancer, and ADRD Study Sites

Variable	(1) HIV/AIDS	(2) Cancer	(3) ADRD	(4) HIV vs. Cancer	(5) HIV vs. ADRD	(6) Cancer vs. ADRD
Share Male	0.495	0.490	0.488	0.006***	0.008***	0.002***
	(0.042)	(0.042)	(0.036)	(0.001)	(0.001)	(0.001)
Share Under 18	0.160	0.183	0.182	-0.023***	-0.022***	0.001
	(0.077)	(0.070)	(0.066)	(0.001)	(0.001)	(0.001)
Share 65+	0.135	0.151	0.166	-0.016***	-0.031***	-0.015***
	(0.068)	(0.078)	(0.100)	(0.001)	(0.002)	(0.001)
Share Non-Hispanic White	0.482	0.587	0.576	-0.105***	-0.093***	0.013***
	(0.237)	(0.231)	(0.233)	(0.004)	(0.005)	(0.003)
Share Non-Hispanic Black	0.195	0.144	0.131	0.051***	0.065***	0.013***
	(0.214)	(0.172)	(0.158)	(0.003)	(0.004)	(0.002)
Share Hispanic	0.191	0.156	0.181	0.035***	0.009**	-0.026***
	(0.194)	(0.170)	(0.198)	(0.003)	(0.004)	(0.002)
Share Non-Hispanic Asian	0.096	0.078	0.078	0.018***	0.017***	-0.001
	(0.098)	(0.086)	(0.085)	(0.001)	(0.002)	(0.001)
Share Non-Hispanic AIAN	0.003	0.004	0.003	-0.001***	-0.000*	0.001***
	(0.006)	(0.012)	(0.007)	(0.000)	(0.000)	(0.000)
Share Non-Hispanic NHPI	0.001	0.001	0.001	-0.000	0.000	0.000
	(0.007)	(0.007)	(0.005)	(0.000)	(0.000)	(0.000)
Share with Health Insurance	0.916	0.920	0.917	-0.004***	-0.000	0.004***
	(0.061)	(0.057)	(0.059)	(0.001)	(0.001)	(0.001)
Share with Private Insurance	0.679	0.709	0.708	-0.030***	-0.028***	0.002
	(0.178)	(0.153)	(0.144)	(0.002)	(0.003)	(0.002)
Share with Public Insurance	0.321	0.316	0.320	0.005**	0.001	-0.003*
	(0.145)	(0.126)	(0.127)	(0.002)	(0.003)	(0.002)
Share in Poverty	0.154	0.137	0.135	0.017***	0.019***	0.002**
	(0.050)	(0.048)	(0.042)	(0.001)	(0.001)	(0.001)
Share SNAP Recipients	0.050	0.044	0.044	0.006***	0.006***	-0.000
	(0.024)	(0.022)	(0.021)	(0.000)	(0.000)	(0.000)
Observations	4,811	48,324	5,973			
F Test *p*-value				<.001***	<.001***	<.001***

Notes: Table displays the average demographic characteristics of hospital service areas in which study sites for HIV/AIDS, cancer, and Alzheimer's disease and related dementias (ADRD) are located. HIV/AIDS, Cancer, and ADRD sites represent sites from Clinical Trials.gov. Each site is included once for a given condition. F Test *p*-value is from a regression of the *HIV vs. Cancer*, *HIV vs. ADRD*, and *Cancer vs. ADRD* indicator on all characteristics. See Data Appendix for details. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

Appendix Table C21: Neighborhood Demographics of HIV/AIDS, Cancer, and ADRD Study Sites with Substantial Federal Investment

Variable	(1) HIV/AIDS	(2) Cancer	(3) ADRD	(4) HIV vs. Cancer	(5) HIV vs. ADRD	(6) Cancer vs. ADRD
Share Male	0.495	0.485	0.492	0.010*	0.003	-0.007
	(0.052)	(0.038)	(0.032)	(0.006)	(0.008)	(0.006)
Share Under 18	0.148	0.130	0.159	0.019*	-0.011	-0.029**
	(0.083)	(0.076)	(0.076)	(0.010)	(0.013)	(0.013)
Share 65+	0.122	0.111	0.148	0.011	-0.026**	-0.037***
	(0.058)	(0.064)	(0.103)	(0.008)	(0.012)	(0.013)
Share Non-Hispanic White	0.458	0.509	0.481	-0.051*	-0.023	0.028
	(0.234)	(0.207)	(0.238)	(0.028)	(0.039)	(0.037)
Share Non-Hispanic Black	0.219	0.171	0.184	0.048*	0.036	-0.013
	(0.227)	(0.196)	(0.185)	(0.027)	(0.036)	(0.033)
Share Hispanic	0.184	0.150	0.212	0.033	-0.029	-0.062*
	(0.195)	(0.165)	(0.231)	(0.023)	(0.034)	(0.032)
Share Non-Hispanic Asian	0.104	0.128	0.086	-0.023*	0.018	0.041***
	(0.092)	(0.091)	(0.075)	(0.012)	(0.015)	(0.015)
Share Non-Hispanic AIAN	0.003	0.003	0.004	-0.001	-0.002*	-0.001
	(0.005)	(0.006)	(0.008)	(0.001)	(0.001)	(0.001)
Share Non-Hispanic NHPI	0.001	0.002	0.001	-0.002	-0.000	0.002
	(0.001)	(0.013)	(0.002)	(0.001)	(0.000)	(0.002)
Share with Health Insurance	0.923	0.933	0.919	-0.010	0.004	0.014
	(0.063)	(0.055)	(0.060)	(0.008)	(0.010)	(0.010)
Share with Private Insurance	0.682	0.742	0.666	-0.060**	0.016	0.076**
	(0.193)	(0.175)	(0.176)	(0.024)	(0.031)	(0.030)
Share with Public Insurance	0.317	0.266	0.348	0.052**	-0.030	-0.082***
	(0.161)	(0.155)	(0.147)	(0.020)	(0.026)	(0.026)
Share in Poverty	0.163	0.149	0.147	0.014**	0.016**	0.002
	(0.049)	(0.046)	(0.047)	(0.006)	(0.008)	(0.008)
Share SNAP Recipients	0.055	0.046	0.048	0.009***	0.007*	-0.002
	(0.024)	(0.024)	(0.024)	(0.003)	(0.004)	(0.004)
Observations	135	114	54			
F Test *p*-value				<.001***	<.001***	.140

Notes: Table displays the average demographic characteristics of hospital service areas in which study sites for HIV/AIDS, cancer, and Alzheimer's disease and related dementias (ADRD) are located. HIV/AIDS sites represent sites from the HIV Prevention Trials Network (HPTN), HIV Vaccine Trials Network (HVTN), and AIDS Clinical Trials Group (ACTG). Cancer sites represent National Cancer Institute (NCI)-designated cancer centers, National Comprehensive Cancer Network (NCCN) member institutions, and Association of American Cancer Institutes (AACI) cancer centers. ADRD sites represent National Institute on Aging (NIA)-funded Alzheimer's disease research centers. As some sites belong to multiple networks, each site is included once for a given condition. F Test *p*-value is from a regression of the *HIV vs. Cancer*, *HIV vs. ADRD*, and *Cancer vs. ADRD* indicator on all characteristics. See Data Appendix H.3.3 and H.3.4 for details. Robust standard errors are in parentheses. *, **, *** refer to statistical significance at the 10, 5, and 1 percent level, respectively.

D Qualitative Findings – Selected Quotes

Table D1: Physician Quotes on Extrapolating from the Physician Survey Experiment

Extrapolation Across Race		
Subthemes	Selected Quotes	Physician
Social and Envir. Factors	"I would feel confident that a White-only sample could demonstrate safety, but I would be less confident about its real-world effectiveness for Black patients, given that Black patients have different lived experiences that result in differential experiences of health care and health outcomes."	PBP
	"Race is a social construct, not a biological construct. We risk mistreating Black patients by assuming differences are biological rather than social."	PWP
	"Race is a construct based on skin color not necessarily reflective of biology. Differences in efficacy are multifactorial including a variety of patients gives me confidence the drug will help my patients."	PBP
Biol. Factors	"Genetic variations exist in certain demographic groups. For instance, a high proportion of those of East Asian descent are fast metabolizers of Plavix."	PBP
	"It is unclear if genetic/racial differences would affect the mechanism of action for a particular drug."	PWP
	"Other classes of medications have shown variation in effectiveness among different ethnic groups."	PWP
	"Drugs may work differently for black and white patients due to genetic differences. The presence or absence of certain genes may affect the efficacy of a drug, and affect the incidence of side effects."	PWP
Combination of Factors	"I don't think we understand the connections and interactions between some biological predispositions and some socioeconomic factors, but studies in the past have shown some drugs to work differently in Black and white patients."	PWP
	"There may be subtle differences in genetic, biology and social/environmental situations."	PWP
Not Confident in Data	"I am more suspicious of findings in research and researchers who exclude certain groups. Including Latino patients."	PBP
	"Drugs may work differently in Black and white patients, so it is preferable to have a diverse population in the study. However, it is often necessary to make a decision based on incomplete data."	PWP
	"It can not be automatically assumed that drugs will work equally without sufficient data."	PWP
	"The external validity of the study is limited if the study demographics don't represent the patient being treated."	PBP
Norms/Preferences	"Studies should be done with a broader racial demographic prior to FDA approval."	PBP
	"I would prefer if a trial included the population that I treat."	PBP
	"Drug trials should account for different races as a confounding variable."	PBP

Extrapolation Across Geography		
Subthemes	Selected Quotes	Physician
Social and Envir. Factors	"Would be confident in safety, but not confident in effectiveness given different lived experiences (social, environmental, cultural) between US and other countries."	PBP
	"It depends on what the sampling is again. Different lifestyles, diets, and activity levels can play a part in changing results based on the study demographics. For instance, Rybelsus reported weight loss in a study for DM2 conducted in Japan where the average weight of the patient receiving the therapy is decently less than my average patient with the same condition. They have greater weight loss with my patient population than the predicted amount based on the study."	PWP
Biol. Factors	"Depending on racial or ethnic background of the population in the sample not being much in US or outside US."	PBP
	"It depends on the race, not the country."	PBP
Combination of Factors	"I would need to know racial and demographic/social factors that may influence the drug's effectiveness, etc."	PWP
	"It cannot be assumed that drugs will work equally in different populations without appropriate data."	PWP
	"As above, I feel there are subtle differences in genetic, biological, as well as social and environmental situations."	PWP
Not Confident in Data	"I do not know enough about studies outside the US to be confident in them."	PWP
	"I worked on protocols in Thailand and the level of falsifying data by technicians doing the assays was shocking."	PBP
	"Other countries may have less stringent measures of safety and efficacy compared to the United States."	PWP
	"Limited information is given to know how the study was conducted and on what population."	PBP
	"I need to know more about the country and study methods."	PBP
	"I would have to evaluate if high standards were upheld."	PBP
Dependent on Study Location	"It would depend upon the country. I would expect Western European and Canadian trials to be similar to my particular patient population."	PWP
	"It depends where the study was done, and what the population was."	PBP

Notes: Table displays quotes that demonstrate several themes from physician's open-text survey responses in the Physician Survey Experiment. Any physician who did not select that they were "Highly" confident in extrapolating clinical trial data from Black patients to White patients or from patients outside the U.S. to U.S. patients were given a set of potential reasons (see Table IV and Appendix Table C14), and then asked to explain why they had chosen a given response. *PBP* (Physicians treating Black Patients) denotes physicians who report above the median percent Black patients in their patient panel. *PWP* (Physicians treating White Patients) is defined similarly with respect to White patients.

Table D2: Inclusive Infrastructure: Site Selection and Community Engagement Quotes from *NASEM (2022)* Report

Subthemes	Selected Quotes	Role
Intentional Site Selection	"And so if you want to be inclusive, you need to then think about how many from that population you want to enroll and begin to work towards that goal. That's number one. I think that goes into the framework of intentionality, right? We need to be intentional."	Study Investigator
	"You have to want to do it because expediency will kick in that you need to close the study in one year and you want to get those patients enrolled. But I do think if you start to plan from the beginning to have an inclusive group, that's important."	
	"I think in some sense the clinics did that for us, like if this is a clinic that largely serves the homeless population downtown and we partner with that clinic, we don't need to do a lot of extra stuff to reach those patients. Making sure those clinics were priorities for us and we did adjust a lot of our approach in working with the clinic."	Study Investigator
Physical and Linguistic Access	"They're coming into the clinic like three days a week to get . . . lab samples and that is a lot of driving, that's a lot of time to . . . have to take off work, or have to take away from family. And not all patients are privileged enough to be able to take time off and come to the center every day."	Study Coordinator
	"And so travel to centers.. it's a big barrier... so assisting in transportation centers is important if that's required. Remote monitoring is important because I think why bring people back just to check that they're ok when it can be done remotely."	Study Investigator
	"There were two language translations that were required in order to do our study... if you don't have those materials prepared and you don't anticipate the need to have those materials a priori, it sort of becomes a self-fulfilling prophecy in that you're not going to accrue well or at all in those populations."	Study Investigator
Community Members Inform Protocol	"Get the input of those who are actually working within the communities. . . I think you will come up with a lot of different ways how . . . to diversify their cohort."	Study Coordinator
	"We have community advisory boards that are built very early in the process and each site has a different community advisory board because the issues that come up with each geographic location are very different and the communities to serve are very different. . . We try to get a good representation of age and gender and different types of work and the experience in the community."	Study Investigator
	"You would go to the community . . . and say 'I have an idea for research. I'd like your opinion on what the community might feel about this. Am I trying to get too many people? What would I need to establish a relationship? How can I help you to help me hire out of the community so that they can have people that are easily accessible to ask questions?"	Study Coordinator

Subthemes	Selected Quotes	Role
Building Trust with Community	"This one community that I'm thinking about has been a little historically suspicious because of bad experiences they've endured of medical research and perhaps academic medical research and so sending out a single notice is not going to be sufficient in order to have meaningful recruitment of these groups. It's really going to start with building relationships of trust and then later availing those groups of opportunities."	Study Investigator
	"I would give a talk and try to sit with people. And we had food afterwards usually, so we could all just sit and talk casually. But they're telling me, over and over again, there's just a lot of distrust in the medical community and I get it, I understand why."	Study Investigator
Relationships with Community Partners	"And so we do try to give back. We don't just recruit, we always try to give back to the community. I think that's really important if you want to have a relationship with the community, you don't just take. Whatever that community is, we try to teach you, we go to health fairs, we try to give something back."	Study Investigator
	"Our academic partners have been working with these community organizations and actually have community health workers who worked with them on other projects. It's easy to take them from one project to another until they have this track record. And it works really nicely for them because they have built in trust already."	Study Investigator
	"It's a two-way street. I don't just go to them when I have a study. And I can't expect them to be open and ready to help me with every study and I'm not truly there for them. It's not only me, but it's like having this kind of relationship that is enduring and takes time to build. And it's not a trivial commitment. It's a real long-term commitment. And so we built these relationships with our community partners for now more than a decade and have been and those relationships come with both give and take of information."	Study Investigator
Reciprocal Relationships with Participants	"You really can't separate participating in a trial from how a person feels the system treats them. What surprised me is that it cuts across socioeconomic classes. Even my fellow African American physicians express some concerns you would not expect them to express. It's percolating in the back of their minds."	Study Investigator
	"Yeah, incentives, we paid them. And then establishing that personal connection with them because they were letting us into their homes with these video recorders and things. I would talk to them on the phone each week. And sometimes these conversations would last 15 minutes, sometimes they would last two hours. Where we would just chat about 'How's it going?' I really tried to get to know them on a personal level."	Study Investigator

Subthemes	Selected Quotes	Role
	"That's why we don't force, everything's voluntary. . . They can withdraw at any time. We make sure that they instill that in anything that we do, no forcing answering questions. Their well-being is first, the study goes second. And then it just always comes first with us because we just put them first. So they put the study first."	Study Investigator

Notes: Table displays quotes from researchers and physicians on inclusive infrastructure policies. Quotes are drawn from NASEM (2022) and STAT News (2020).

E Survey Appendix

E.1 Physician Survey Panel

For the Physician Survey Experiment, we recruited 137 physicians from the United States using a physician contact information database from Redi-Data Inc. We contacted 12,192 primary care physicians to participate in the study, and 1.8 percent of those contacted started the study.[4] Respondents were channeled through demographic questions to ensure that the individual met the pre-specified criteria for our final sample (see Section IV.1.1 for details). The survey was run in March 2022. Respondents were paid only if they fully completed the survey. The compensation for survey completion was $100. The median time for survey completion was 18 minutes.

E.2 Patient Survey Panel

For the Patient Survey Experiment, we recruited 275 individuals from the United States using a survey company, Lucid. The survey was run in March 2022. Lucid partners with suppliers that provide panels of respondents to which they email survey links.[5] Respondents who clicked on the link were first channeled through demographic questions and questions about High Blood Pressure/Hypertension to ensure that the individual met the pre-specified criteria for our final sample. Respondents were paid only if they fully completed the survey. Respondents were blocked from completing the survey multiple times or reattempting the survey if they were screened out. The pay per survey completed was around $3. The median time for the completion of the survey was 11 minutes.

[4]Due to DUA restrictions and IRB guidance regarding protecting subject privacy, we are not able to release the contact information of the physicians we contacted. See replication materials for de-identified datasets.

[5]See more information on Lucid panels at https://luc.id/quality/. Luc.id, in e-mail correpsondence, further explained they use API suppliers on a Marketplace platform. They source from hundreds of different suppliers with varying sizes and demographics.

E.3 Survey Materials

Appendix Exhibit E1: Invitation Email Sent to Physicians

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_djbzTq2daQrFX9A&Q_CHL=email

Sincerely,

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

You may email nikhil_shankar@hks.harvard.edu if you would like more time to complete the survey or if you would like a reminder in 2 days to complete the survey.

Click here to opt out of future emails.

Appendix Exhibit E2: Example Drug Profile

HARVARD UNIVERSITY

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

Appendix Exhibit E3: List of Hypothetical Drugs Shown to Participating 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. Hypothetical drug names were created by importing the most commonly prescribed diabetes drugs by medication class in the Medical Expenditure Panel Survey (MEPS) to ascertain common drug name suffixes for each class and then replacing the prefixes in these drug names with common generic drug name prefixes as published by the National Library of Medicine. Following this process, a total of 15 hypothetical drug names were used in the survey (3 per medication class). Profiles for all drugs ranged in efficacy from 0.5 percent to 2 percent and in percent Black of trial subjects from 0 percent to 35 percent.

Appendix Exhibit E4: Physician Survey

Link to Survey: https://harvard.az1.qualtrics.com/jfe/form/SV_eEugbM54Kx87Fk2

- Screeners include:
  1. MD/DO degree
  2. Family practice or internal medicine
  3. <50 percent pediatrics
  4. Currently practice primary care

Appendix Exhibit E5: Physician Survey Outcomes: Question Wording

Outcome Name	Question Text	Response Options
	Primary Outcomes	
Relevance	• How relevant are the findings from this trial for patients with poorly controlled diabetes in your care?	[On a scale of 0 (Not relevant at all) to 10 (Very relevant)]
Prescribe	• Thinking about your patient panel in particular, how likely would you be to prescribe [DRUG NAME] for patients with poorly controlled diabetes in your care?	[On a scale of 0 (Very unlikely to prescribe) to 10 (Very likely to prescribe)]

Appendix Exhibit E6: Follow-Up Email Sent to Physicians

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

Click here to opt out of future emails.

Notes: The order of the campaigns was randomized at the individual level, with the diverse campaign denoted as Campaign A for half the respondents and denoted as Campaign B for the other half of the respondents.

Appendix Exhibit E7: Patient Survey

Link to Survey: https://harvard.az1.qualtrics.com/jfe/form/SV_eyyp71a6ifHhJf8

- Screeners include:
  1. Race (Non-Hispanic Black/White)
  2. Age (35+)
  3. Hypertension (may have some additional diagnoses but may not select all)
  4. Reasonable value for blood pressure
  5. Never taken survey before
  6. Correctly answer attention question

Appendix Exhibit E8: Patient Survey Outcomes: Question Wording

Outcome Name	Question Text	Response Options
	Primary Outcome	
Relevance	• How relevant are the findings from this study for treating your high blood pressure?	[On a scale of 0 (Not relevant at all) to 10 (Very relevant)]
	Secondary Outcomes	
Belief Updating	• What millimeters of mercury (mmHg) point reduction in systolic blood pressure would you expect to see if you took the medication?	[On a scale of 0 to 25]
Ask Doctor	• Would you be interested in asking your doctor (or other primary care provider) about Tribenzor?	[Yes or No]

F Model Appendix

F.1 Model Details

We assume people update their beliefs from trial data on treatment T according to the following equations, which then enter into $\hat{b}(x_i;h^T)$ analogously to how the prior parameters do in Equation 1:

$$\alpha(x_i;h^T) = \alpha(x_i;h^{T-1}) + \bar{x}_T(x_i) \times k_T \tag{4}$$
$$\beta(x_i;h^T) = \beta(x_i;h^{T-1}) + \bar{x}_T(x_i) \times N_T - \bar{x}_T(x_i) \times k_T \tag{5}$$
$$\alpha(h^T) = \alpha(h^{T-1}) + k_T \tag{6}$$
$$\beta(h^T) = \beta(h^{T-1}) + N_T - k_T. \tag{7}$$

F.2 The Value and Cost of Recruiting Strategies to the Firm

Pharmaceutical firms choose a trial-*r*ecruitment strategy r in compact space R to maximize profit

$$\Pi_r = s_r \times v_r - c_r,$$

where $s_r \in [0,1]$ is the success probability of the trial, $v_r \geq 0$ is the value of a successful trial to the firm, and $c_r \geq 0$ is the cost to the firm of running the trial. Both the value and cost to the firm of recruitment strategy r depend on patients' and doctors' assessments of the benefits of treatment, which in turn influence trial-participation and treatment decisions.

For simplicity, suppose each firm only develops a single treatment and there are a continuum with measure one of patient-doctor dyads.[6]

Given recruiting strategy r, the value to the firm of the treatment if brought to market is given by

$$v_r = \mathbb{E}\left[\sum_{i=0,1} \sigma(x_i) \times (p - mc) \times d(x_i;h^T) | r\right],$$

where $\sigma(x_i)$ equals the share of people who both have characteristics x_i as well as a condition for which the treatment is indicated, p is the price the firm charges for treatment, mc is the marginal cost of treatment, $d(x_i;h^T)$ is the demand for treatment at price p among patients with characteristics x_i for whom the treatment is indicated, and $\mathbb{E}[\cdot|r]$ equals the firm's expectation under recruiting strategy r.

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

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

where $f \geq 0$ 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.) and $h(\cdot)$ 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.

Note, there are two channels by which *historical underrepresentation* increases the cost for a firm to enroll a more representative trial participation sample. First, patients with underrepresented characteristics x_i become less likely to participate in the trial when targeted, so firms have to reach out to more patients to achieve a given level

[6]This simplifies the analysis by allowing us to abstract from dynamic considerations, where a firm might be concerned that its trial-recruitment decisions today could influence their own recruitment costs in the future. What's important for the analysis is merely that a firm does not internalize *all* the benefits from increasing trial representation – *e.g.*, how this will lower future recruitment costs for *other* firms.

of representation. Second, the patient pool becomes less representative under the status-quo recruitment strategy over time in the absence of any intervention.

F.3 Further Results

Corollary F.2. *Given Proposition 1 and physician-patient dyad's decision making process, the demand for a new medication $d(x_i;h^T)$ is influenced by the reported efficacy and representation of a clinical trial T in the following ways:*

1. $\frac{\partial d(x_i;h^T)}{\partial k_T} > 0$*: demand for a new medication is increasing in the efficacy observed in the clinical trial.*
2. $\frac{\partial d(x_i;h^T)}{\partial \bar{x}_T(x_i)} > 0$*: demand for a new medication is increasing in the representation of patients with similar characteristics.*
3. *Assuming that $F_\varepsilon()$ is convex, $\frac{\partial^2 d(x_i;h^T)}{\partial \bar{x}_T(x_i)^2} < 0$. That is, the degree to which increasing representation in a clinical trial increases demand is decreasing in the existing representation of a patient's group.*

Corollary F.3. *Let $G_b(h^T) = \hat{b}(x_i = 0;h^T) - \hat{b}(x_i = 1;h^T)$ and $G_d(h^T) = d(x_i = 0;h^T) - d(x_i = 1;h^T)$ be the difference between White and Black patients in perceived benefits and demands for a new medication after observing trial T, respectively. Assuming that clinical trial T has a higher share of White patients relative to Black patients $\bar{x}(x_i = 0) > \bar{x}(x_i = 1)$ and that the perceived benefits, based solely on the history of trials h^{T-1}, for Black patients is less than or equal to that for White patients, then*

1. $G_b(h^T) > 0$ *and* $G_d(h^T) > 0$*: There exists a gap in perceived benefits and demand for novel drugs between White patients and Black patients. White patients have higher perceived benefits and demand relative to Black patients.(Existence of Gaps)*
2. *Increasing Black representation to $\bar{x}'(x_i = 1) > \bar{x}(x_i = 1)$, closes the gap in perceived benefits $G_b(h^T) \geq G_b(h^{T'})$ and demand for novel drugs $G_d(h^T) \geq G_d(h^{T'})$. (Representation Closes Gaps)*

Proposition F.3. *Suppose firms have access to a status-quo technology for recruiting patients to clinical trials, which firms use to* invite *Black and White patients to participate in the trial in proportions $\bar{x}_T^a$ and $(1-\bar{x}_T^a)$, respectively. The actual trial representation of these groups under the status quo, $\bar{x}_T^{sq}$ and $(1-\bar{x}_T^{sq})$, generally differs from the invited proportions – and this may vary by group (i.e., there may be differences in accrual rates across groups.) Specifically, 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 F.4. *Proposition F.3 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 $d(x_i = 1;h^{T-1}) < d(x_i = 0;h^{T-1})$.*

F.4 Numerical Examples

Example 1. For a numerical example, suppose people are certain characteristic x_i matters, so $m = 1$. Suppose further that $\alpha(x_i;h^{T-1}) = \beta(x_i;h^{T-1}) = 100$ for all x_i, $\tilde{b} = 100$, $k_T = 750$, and $N_T = 1000$. Then the following table shows the perceived benefit of the treatment for White ($x_i = 0$) and Black ($x_i = 1$) patients as a function of Black trial representation ($\bar{x}$).

	$\bar{x} = .05$	$\bar{x} = .1$	$\bar{x} = .2$
$\hat{b}(x_i = 0;h^T)$	70.65	70.45	70
$\hat{b}(x_i = 1;h^T)$	55	58.33	62.5

There are two noteworthy features of this numerical exercise. First, as seen in the second row of the table, representation significantly matters for the perceived treatment efficacy of groups with low representation. Second,

comparing the two rows, trial representation of 80 percent versus 95 percent makes essentially no difference to the perceived benefits of treatment to highly-represented White patients, but trial representation of 20 percent versus 5 percent makes a big difference to the perceived benefits of treatment to poorly-represented Black patients.[7]

Returning to Example 1, modify it slightly to suppose that instead of describing treatment T it describes the most similar past treatment to treatment T. Then the table shows how historical representation influences priors for a novel treatment. Indeed, Black-patients' prior expectations for the novel treatment are $\tilde{b}_T \times .625$ if their representation in the previous trial was 20 percent and are only $\tilde{b}_T \times .55$ if their representation in the previous trial was 5 percent. This shows how, even when all groups begin with the same priors for $T-1=0$, beliefs diverge when some groups are systematically more represented in trials than others. This shows how a failure to represent groups in a trial today creates an externality where it's more difficult to represent those groups in a trial tomorrow.

To illustrate, return to the earlier numerical example with $\bar{x}_Z = \bar{x}_Z^a = .1$. Suppose that the non-monetary cost of participating in the trial equals $n = 55$ and that $F_\varepsilon(\cdot)$ is logistic. In this case, if the firm sticks with the status-quo recruitment technology in period T (*e.g.*, because f is sufficiently large), then $\bar{x}_T = \bar{x}_T^{sq} = .06$. This shows that one period of underrepresentation leads Black trial participation to drop by almost half.

F.5 Proofs

Proof of Proposition 1. Note that

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

where, by Equations (4)-(7),

$$\frac{\alpha(x_i;h^T)}{\alpha(x_i;h^T)+\beta(x_i;h^T)} = \frac{\alpha(x_i;h^{T-1})+\bar{x}_T(x_i)\times k_T}{\alpha(x_i;h^{T-1})+\beta(x_i;h^{T-1})+\bar{x}_T(x_i)\times N_T} \tag{8}$$

$$\frac{\alpha(h^T)}{\alpha(h^T)+\beta(h^T)} = \frac{\alpha(h^{T-1})+k_T}{\alpha(h^{T-1})+\beta(h^{T-1})+N_T}. \tag{9}$$

The three parts of the proposition follow from the fact that the partial derivatives of Equations (8)-(9) with respect to k_T and $\bar{x}_T(x_i)$ are positive, and the second derivatives of these two equations with respect to $\bar{x}_T(x_i)$ are negative. □

Proof of Corollary 1. Immediate from Proposition 1 and from demand increasing in perceived benefits.

□

Proof of Proposition 2. When the fixed costs f are sufficiently large, then $\bar{x}_T = \bar{x}_T^{sq}$, which is increasing in $\bar{x}_Z$ by Corollary 1 and Proposition F.3. □

Proof of Corollary F.2. The demand for a novel drug is $1 - F_\varepsilon\left(-\left(\hat{b}(x_i;h^T) - n_T - p_T\right)\right)$. The first two parts of this corollary follow from applying the chain rule and the fact that the demand is increasing in perceived benefits (any c.d.f. is an increasing function) and perceived benefits are increasing in k_T and $\bar{x}_T(x_i)$ (Proposition 1).

[7] Instead of boosting the perceived benefits of treatment to Black patients by doubling representation, fixing the size of the sample, the firm could do so by doubling the size of the sample, fixing Black representation. However, it seems unlikely that the latter would be less expensive to the firm or society, motivating our focus on the former.

To show the third part, note that

$$\frac{\partial^2 d(x_i;h^T)}{\partial \bar{x}_T(x_i)^2} = F_\varepsilon^{'}\left(-\left(\hat{b}(x_i;h^T)-n_T-p_T\right)\right)\frac{\partial^2 \hat{b}(x_i;h^T)}{\partial \bar{x}_T(x_i)^2} - \left(\frac{\partial \hat{b}(x_i;h^T)}{\partial \bar{x}_T(x_i)}\right)^2 F_\varepsilon^{''}\left(-\left(\hat{b}(x_i;h^T)-n_T-p_T\right)\right).$$

By assumption, $F_\varepsilon^{''}(.) \geq 0$; by properties of c.d.fs $F_\varepsilon^{'}(.) > 0$; and by proposition 1 $\frac{\partial \hat{b}(x_i;h^T)}{\partial \bar{x}_T(x_i)} > 0$ and $\frac{\partial^2 \hat{b}(x_i;h^T)}{\partial \bar{x}_T(x_i)^2} < 0$. Plugging these comparative statics into the above equation, it is immediate that $\frac{\partial^2 d(x_i;h^T)}{\partial \bar{x}_T(x_i)^2} < 0$. □

Proof of Corollary F.3. The first part of this corollary follows immediately from Proposition 1 and Corollary F.2.

For the second part, note that $\bar{x}(x_i=0)+\bar{x}(x_i=1)=1$. Therefore, an increase in $\bar{x}(x_i=1)$ implies a decrease in $\bar{x}(x_i=0)$. By Proposition 1 and Corollary F.2, this implies that demand and perceived benefits increases for Black patients and decreases for White patients when $\bar{x}(x_i=1)$ increases. The gaps $G_b(h^T)$ and $G_d(h^T)$ then decrease by definition. □

Proof of Proposition F.3. Immediate application of Bayes' rule. □

Proof of Corollary F.4. Immediate. □

G Institutional Details

G.1 Policy Efforts to Improve Representation in U.S. Government Sponsored Clinical Trials Research

Federal policies aimed at improving representation in clinical research date back at least five decades, and mostly include regulations targeted at federally-funded researchers. Following the passage of the Civil Rights Act of 1964, the National Institutes of Health (NIH) General Clinical Research Centers added notices to grant applications warning that racial discrimination was illegal. Eventually, all domestic grant applicants to the Department of Health and Human Services (HHS) were required to file an assurance of compliance with Title 6 of the Civil Rights Act of 1964, which prohibits discrimination based on race, color, religion, national origin, or sex in services and establishments that require federal funding.

While Title 6 barred discrimination by sex, federal agencies struggled for decades to balance representation of women in clinical trials with attempts to protect pregnant women and fetuses from potentially harmful exposures to unproven drugs.[8] Healthy males were considered the "norm" in study populations, and many researchers believed that including female participants would confound trial results due to factors such as fluctuations in hormone levels (see Epstein 2007 for an excellent history). In response to concerns about these potential harms, the FDA distributed new guidelines in 1977, "General considerations for the clinical evaluations of drugs," that banned women of childbearing potential from Phase I and early Phase II trials with limited exceptions. As documented in Michelman and Msall (2021), this policy change reduced investment into drugs aimed toward female patients. This policy was rescinded in 1993.

In 1985, the U.S. Public Health Service Task Force on Women's Health Issues released a report indicating that low representation of women in clinical trials had resulted in suboptimal health care for women. The task force recommended increasing participation of women in clinical trials, including women of child-bearing potential, and also advised that more research be supported on diseases with a high prevalence among women.

The NIH responded to the taskforce's report by adopting the Inclusion of Women and Minorities in Clinical Research policy in 1986. Although broadly intended to provide information on differences in drug safety and efficacy by sex and race/ethnicity, its implementation was slow and incomplete. Guidelines were developed in

[8] In the early 1960s, maternal exposure to the sedative thalidomide during pregnancy led to widespread fetal death and birth defects across Europe and Canada. Congress responded by passing the Kefauver- Harris Amendments in 1962, which strengthened the FDA's authority to oversee drug development and testing.

1989, but the resulting requirements for researchers were inconsistently applied. In 1990, the NIH founded the Office for Research on Women's Health (ORWH) and Office of Minority Programs (OMP) in 1990.

The FDA responded to the U.S. Public Health Service's report in 1987 with new guidelines encouraging new drug sponsors to use animals of both sexes in pre-clinical drug safety studies. The following year, the FDA released guidance in which it recommended analyzing data from clinical pharmacology studies by sex, race, and age. These recommendations, however, were not binding.

The 1993 NIH Revitalization Act included additional reforms. Designed to ensure that clinical research could determine differential effects of interventions by sex and race/ethnicity, the Revitalization Act included the following stipulations: Phase III clinical trials should have sufficient numbers of participants to allow for subgroup analyses, populations should not to be excluded from trials due to cost, and the NIH must maintain outreach efforts to include women and minority populations in trials. In 1994, the FDA Office of Women's Health was established to coordinate policies regarding the inclusion of women in clinical trials.

In 1997, Congress enacted regulation requiring the FDA and NIH to review and develop guidance on the inclusion of women and minorities in clinical trials. To comply, the FDA issued the demographic rule in 1998, which revised New Drug Applications (NDAs) to require safety and efficacy data presented by gender, age, and racial subgroups and dosage modifications identified for specific subgroups. In contrast to the non-binding 1980s guidance, the rule gave the FDA the authority to refuse any NDA that did not appropriately analyze safety and efficacy data and applied to all sponsors, regardless of federal funding. Additionally, the demographic rule required sponsored to present data on participation in Investigational New Drug (IND) applications by sex, age, and race. Congress passed a law in 2000 that permitted the FDA to place clinical holds on IND studies if men or women were excluded from clinical trials studying a serious or life-threatening illness on the grounds of threats to reproductive potential.

Under Section 907 of the FDA Safety and Innovation Act of 2012, the FDA issued guidance in 2014 outlining rules regarding sex-specific patient enrollment, data analysis, and reporting of study information. In 2015 the FDA launched the FDA Drug Trials Snapshots database, which provides information about the populations participating in clinical trials associated with new drug applications. FDA Snapshots data must report whether differences in benefits or side effects were detected by sex, race, ethnicity, or age.

G.1.1 Efforts to Expand Reach of Clinical Trial Recruitment

Cancer research centers have recently implemented a variety of initiatives aimed at boosting recruitment from underrepresented communities; see, for example, https://ncorp.cancer.gov/about/ and https://www.cancer.gov/about-nci/organization/crchd for details. The NIH has recently expanded research networks for ADRD to address low represesentation of Black and Hispanic populations in trials; see https://www.nia.nih.gov/news/nih-expands-alzheimers-and-related-dementias-centers-research-network for details on trial sites in North Carolina and Texas. The CDC's National Healthy Brain Initiative Road Map Series has, in parallel, focused on building partnerships with state and local public health agencies to support ADRD efforts in communities https://www.cdc.gov/aging/healthybrain/roadmap.htm.

G.1.2 Participant Compensation

In light of the facts documented in Table VI and Appendix Figure B17, extending participation incentives to offset the personal cost of participating in trials is especially important. Transportation subsidies, stipends to offset lost wages and childcare costs, and guaranteed coverage of any supplemental medical care not included in the trial can ensure that geographically distant trials remain accessible to patients (NASEM 2022).[9]

[9]Most of the literature on improving representation and incentives revolves around ensuring that time and monetary costs are not an undue burden that disproportionately deters certain low socioeconomic groups from participating. Although there is some concern that incentives may still carry the possibility of undue influence, a recent NASEM report clarifies that undue influence occurs when individuals take actions that are not reasonable (NASEM 2022, p.∼100-101). Participation in a trial should always be reasonable for the targeted individual, or else the trial should not pass ethical review. Additionally, incentives should not be used with the goal of "changing the minds" of otherwise hesitant participants.

G.2 Background on ClinicalTrials.gov

ClinicalTrials.gov, a registry of clinical trials maintained by the U.S. National Library of Medicine, was established in 2000. Under the Food and Drug Administration Modernization Act of 1997 (FDAMA), the FDA and NIH were directed to develop an online registry of clinical trials that contained details on all drug efficacy studies associated with approved Investigational New Drug (IND) applications (Food and Drug Administration 2022 Sections 312 & 812). A precursor to ClinicalTrials.gov, the AIDS Clinical Trials Information Services (ACTIS), provided a template.[10]

At its inception, the registry included only a small minority of clinical trials performed domestically and worldwide, with the database largely comprised of NIH-sponsored trials. The completeness of the registry, however, grew over time with the introduction of additional federal and non-governmental reforms. In 2005, the International Committee of Medical Journal Editors (ICMJE) began to require trial registration as a condition of publication, motivating many academics to become careful about registering their trials (ICMJE 2022). Two years later, the FDA Amendments Act (FDAAA) mandated registration and results reporting on ClinicalTrials.gov for all trials studying FDA-regulated drugs. The law authorizes penalties of up to $10,000 per day and the current or future withholding of federal grant funds for violating these provisions (Food and Drug Administration 2020). Following the FDAAA, registration of trials substantially increased.

The FDA's efforts to increase clinical trial diversity and trial transparency grew interrelated over the most recent decade. In 2010, the Affordable Care Act (ACA) required the collection and reporting of demographic data of clinical trial participants; however, a subsequent review by the FDA demonstrated many inconsistencies in industry's adherence to these requirements, particularly with respect to race reporting. In response to these deficiencies, a new FDA rule came into effect in 2017 requiring the submission of "baseline or demographic characteristics measured in the clinical trial, including age, sex/gender, race, [and] ethnicity" for FDA-regulated drugs, if such demographics were collected under the protocol. The enactment of this rule resulted in a large rise in the share of trials reporting race/ethnicity data.

[10]Consistent with the discussion in our final section, ACTIS was founded under pressure from HIV/AIDS activists, who demanded greater transparency in research.

Appendix Exhibit G1: Timeline of Federal Initiatives to Increase Representativeness of Clinical Trials

Year	Action
1965	NIH General Clinical Research Centers add notices to grant applications warning that racial discrimination is illegal.
1986	NIH adopts the Inclusion of Women and Minorities in Clinical Research policy, which is aimed at ensuring that clinical trials are designed to provide information about sex and race/ethnicity differences, but the policy is slow to be implemented and inconsistently applied.
1988	New FDA guideline recommends analyzing data from clinical pharmacology studies for safety and efficacy by sex, race, and age.
1993	NIH Revitalization Act directs the NIH to establish guidelines for the inclusion of women and minorities in clinical research.
	FDA withdraws policy banning women of childbearing potential from participating Phase I and early Phase II trials, except in the case of life-threatening conditions and with certain other exceptions; the policy had been in place since 1977.
1993	FDA Office of Women's Health is established to guide the agency around policies on the inclusion of women in clinical trials.
1998	FDA Demographic rule revises new drug application (NDA) content to require safety and efficacy data by gender, age, and racial subgroups.
2000	ClinicalTrials.gov, an online registry of clinical trials co-developed by FDA and NIH, is established. The registry initially includes information largely only on NIH-sponsored trials.
2005	International Committee of Medical Journal Editors (ICMJE) requires trial registration as a condition of publication, raising the number of academics registering on ClinicalTrials.gov.
2007	FDA Amendments Act introduces reporting requirements for FDA-approved products and penalties for failure to comply (including withholding of federal grant funding and fines of up to $10,000 per day).
2010	Affordable Care Act (ACA) requires the collection and reporting of demographic data for clinical trial participants.
2015	FDA's Five Year Plan aims to make pivotal trials (efficacy studies used as basis for new drug approval) more representative of U.S. population and starts publishing of data on composition (the FDA Drug Snapshots).
2017	FDA Reauthorization Act (FDARA) made a reference encouraging the "enrollment of more diverse patient populations."
	FDA rule requiring the submission of age, sex/race, and ethnicity data for trial subjects (if collected) on ClinicalTrials.gov goes into effect.
	Requirement for Drug Snapshots to provide information about the trial populations and differences in efficacy/side effects by sex, race, ethnicity, and age.
2020	FDA releases non-binding, industry-focused guidance on enhancing the diversity of clinical trial populations and that calls for broadening eligibility criteria and improving trial recruitment.

Notes: Table lists major policy initiatives by the FDA, NIH, and HHS to increase diversity and improve representativeness of clinical trials. Information is, largely, drawn from resources on diversity, equity, and inclusion compiled by the National Institutes of Health, the National Library of Medicine (via ClinicalTrials.gov), and the FDA.

H Data Appendix

H.1 Clinical Trials Data

We draw on two publicly available sources of clinical trials data: ClinicalTrials.gov and the FDA's Drug Trials Snapshots database.

H.1.1 ClinicalTrials.gov

We collected clinical trials records from the Aggregate Analysis of ClinicalTrials.gov (AACT) data, a publicly available relational database that contains information on all studies registered on ClinicalTrials.gov (Tasneem et al. 2012).[11] In our analyses, we used the `baseline-counts`, `baseline-measurements`, `countries`, `facilities`, `funding`, and `studies` files. It is useful to note that – to the best of our knowledge – many data files in ClinicalTrials.gov have not been extensively used by researchers and that the purpose is not primarily for research so it requires substantial cleaning which may be imperfect. We narrowed our sample to trials that were reported as "completed" to ensure that demographic composition and enrollment statistics were finalized.

For instance, many entries in ClinicalTrials.gov are missing data on demographic composition and trial outcomes. In some cases, this is due to changes in reporting requirements over time: between 2008 and 2017, only trials that were conducted under an ever-approved IND – that is, trials that supported either a successful U.S. drug application or U.S.-based marketing for an approved product – were required to report results to ClinicalTrials.gov. After 2017, all trials conducted under an IND registered with the FDA were subject to reporting requirements (FDA 2022). In other cases, missing data reflects widespread noncompliance with reporting requirements. For these reasons, we also use FDA Snapshort reports (described below).

Often times we use the "close to raw" ClinicalTrials.gov information in the figures. When needed for the analysis, we classify clinical trials by disease category using Medical Subject Headings (MeSH) associated with each trial. We downloaded the 2021 version of the MeSH tree number database from the National Library of Medicine (NLM). We then grouped MeSH heading to create disease categories by searching keywords in the data (see Appendix Exhibit H1), and merged this information with the `browse-conditions` file. We selected disease categories of interest based on the top ten causes of death in the U.S. in 2019 -– diseases of the heart, cancer, chronic lower respiratory diseases, cerebrovascular diseases, Alzheimer's disease, diabetes mellitus, kidney diseases, and influenza and pneumonia (Heron 2021). We also chose to include HIV/AIDS, as it presents an example of well-represented clinical trials (see Section VI.2 for details).[12] We used these data to create Figure VI, and Appendix Figures B1, B2, B3, B16, and B18.[13]

Additionally, we use data from ClinicalTrials.gov for our analysis of trial sites (in, for example, Table VI). We used the `facilities` file and restricted the sample to sites located in the United States. We then restricted our sample to sites for trials studying HIV/AIDS, ADRD, or cancer.[14] We used these data to produce Table VI; Appendix Figure B17; and Appendix Tables C19, C20, and C21. To compute the share of trials with primary sponsors from government and industry, as reported in Section II, we used the `funding` file to identify sponsors, the countries file to restrict to trials in the United States, and the studies file to restrict to completed trials.

[11] We downloaded a version of this database on 15 October, 2021. Dataset versions are released frequently and changes in compliance rules for ClinicalTrials.gov mean that historical records *may* change between versions.

[12] We excluded accidents and intentional self-harm from the sample because there are no prescription medicines indicated for these causes of death, specifically. We selected 2019 as the reference year to exclude Covid-19 deaths.

[13] For Appendix Figures B1 and B3, we further restricted our sample to 2005-2021 since very few trials completed prior to 2005 reported the demographic composition of enrollees.

[14] Note that we do not restrict our sample to completed trials for these tables and figures, because we are interested in site selection of all U.S.-based trials.

Appendix Exhibit H1: Search Terms for Disease Categories

Category	Search Terms
Diseases of Heart	"heart"
Diabetes Mellitus	"diabetes mellitus"
Kidney Diseases	"nephritis", "nephro"
Cerebrovascular	"cerebrovascular", "intracranial","stroke"
Chronic Lower Respiratory	"asthma", "bronchiectasis", "bronchitis", "emphysema", "pulmonary disease, chronic"
Influenza and Pneumonia	"influenza","pneumonia"
Cancer	"cancer", "carcinoma", "leukemia", "lymphoma", "melanoma", "myeloma" "neoplasms","neoplastic", "tumor", "sarcoma"
HIV/AIDS	"aids", "hiv"
ADRD	"alzheimer", "dementia"

Notes: Table lists search terms used to group MeSH headings into disease categories in Table VI; Figure VI; Appendix Figures B16 and B18; and Appendix Tables C19, C21, and C20. If a MeSH heading includes any of the search terms, it will be included in the corresponding category.

H.1.2 FDA Drug Trial Snapshot Reports

In contrast to ClinicalTrials.gov, the FDA Drug Trials Snapshots reports provide complete information on the demographic composition of pivotal trials associated with new drug applications approved by the FDA. Per the agency, their goal is to provide data on clinical trial evidence to patients and is "part of an overall FDA effort to make demographic data [associated with trials] more available and more transparent."[15] A standard entry corresponds to a drug and includes the following information:

- Drug name and sponsor
- Drug approval date
- Approved indications and method of use
- Any differences in clinical trial evidence by sex, race, or age
- Side effects
- Demographic composition of trials by age, sex, race, ethnicity, location
- Trial design

Beginning in 2015, the FDA's Center for Drug Evaluation and Research (CDER) has published reports containing these data for all new drug approvals. We collected PDFs of Drug Trials Snapshots summary reports for each available year (2015–2021) and digitized tables containing demographic data on trials. Data were extracted using OCR tools.

Although FDA Snapshots data include information on the number of trials associated with each drug approval, it aggregates data to the drug-level rather than the trial-level.[16] That is, FDA Snapshots data indicate the *total* share of Black and White patients enrolled across all trials, but not trial-specific enrollment figures. A key advantage of using the FDA Drug Trials Snapshots database is that information on the demographic composition of trials is nearly complete. We used these data to produce Figure I; and Appendix Figures B1 and B2.

[15] See https://www.fda.gov/media/97210/download for additional details.

[16] For example, "*The FDA approved ADLYXIN primarily based on evidence from nine clinical trials of 4,508 patients with type 2 DM. The trials were conducted in the United States, Canada, Europe, Australia, South America, Africa, and Asia. The FDA also considered data from one separate trial of 6,068 patients with type 2 DM who recently suffered heart attack. The trials were conducted in the United States, Canada, Europe, Africa, and Asia.*" See https://www.fda.gov/drugs/drug-approvals-and-databases/drug-trials-snapshots-adlyxin

H.2 Prescribing Data

To construct prescribing rates for new drugs (in, for example, Figure I) we combined FDA data with the Medical Expenditure Panel Survey (MEPS). We use the product file from the FDA, which includes information on the National Drug Code (NDC) – unique 11-digit identifiers for drugs assigned by the agency reported at the manufacturer-product-package level – marketing start date and marketing category of pharmaceutical products.[17] We restrict to New Drug Applications (NDA) and abbreviated new drug applications (ANDA) pharmaceutical products with unique NDCs. The MEPS data are from two sources, IPUMS (for patient-level demographic information) and the Agency for Healthcare Research and Quality (AHRQ) which hosts the MEPS prescribed medicines files (these data are not yet available on IPUMS). The prescribed medicines data files cover the years 1996 to 2019, we exclude the last three years as they are missing Clinical Classification Software (CCS) codes which are necessary to produce new drug prescriptions by condition. The MEPS prescribed medicines files include the unique MEPS respondent identifier, medication name, NDC, CCS code and year prescription was started. Data from MEPS prescribed medicine files are merged both to the patient demographic information (using the unique patient identifier) as well as to the FDA product file (using NDC).

We then compute the age of drugs prescribed to respondents in MEPS (*i.e.*, the number of years between when the manufacturer first marketed the drug in the U.S. and when the patient started taking the drug).[18] For the purpose of certain exhibits (one in the main text and several in the appendix) we define a new drug as a drug first taken by the respondent within 5 years of its marketing date.

We use the CCS codes to group the MEPS observations by diagnosis, allowing us to calculate the prescription rates across disease categories (in, for example, Figure VI). CCS codes collapse diagnosis and procedure codes from the International Classification of Diseases, 9th Revision, Clinical Modification (IDC-9-CM), which contains over 14,000 diagnosis codes and 3,500 procedure codes, into 260 disease categories.[19] We selected disease categories based on the top ten causes of death in the U.S. in 2019 as per Section H.1.1.

The CCS code does not always map to using a prescription drug directly for a given condition. For example, a patient may be diagnosed with diabetes mellitus, but be prescribed an antidepressant. In the MEPS data, the observation will report the NDC for the antidepressant, but the CCS code for diabetes mellitus. Hence, the antidepressant will appear in the diabetes mellitus disease category. We recognize this limitation of the data, though the drugs that appear with the highest frequency appropriately map to the disease category. Furthermore, drugs not associated with the disease are generally associated with comorbidities and have associated trials (*i.e.,* diabetes-associated neuropathy, cancer-associated prophylaxis or pain management). Specific clinical trials relied on by oncologists, for instance, would be limited to cancer patients testing these drugs for management.[20] This process yielded a patient-drug-prescription year-level data set, which contains 357,312 observations corresponding to 3,509 products, 44 prescription-start-years, and 64,015 distinct MEPS respondents. We used these data to produce Figures I and VI; and Appendix Figures B3, B4, and B18.

H.3 Additional Data Sources

H.3.1 Physician Socio-Demographic Information

The American Medical Association (AMA) masterfile, distributed by Medical Marketing Service Inc., provided additional information at the physician-level such as location of birth, medical school code and year of graduation, location of practice, and specialty. We used these data to calculate average physician characteristics at the zip code-level.

We recruited physicians by securing their contact information from Redi-Data Inc. We requested physicians who are 1) aged 30-70; 2) hold a DO or MD degree; and 3) actively practice primary care in an office setting.[21]

[17] The NDC are in different formats in MEPS and FDA product data sets, and thus required cleaning. We followed an approach similar to Roth (2018) to create a crosswalk.

[18] We remove observations for which the relative year was negative (*i.e.*, the patient reported that they started taking the drug before the marketing start year).

[19] See more details on CCS codes at https://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp.

[20] We also note that the prescribing data are lagged relative to the clinical trial data in Figure VI though this is consistent with the model presented in Section III – specifically the importance of history and the prior formation process.

[21] See replication file for more detail on Redi-Data access.

Data in this section are used to produce Appendix Table C3 and C4.

H.3.2 U.S. Medical Schools

We obtained data on U.S. medical school codes from the Texas Medical Board website and created a data set using Adobe Acrobat converter. Additionally, we used rankings from U.S. News and World Report 2022 medical school research rankings, and manually created a data set.[22] We used these data to produce Appendix Table C3.

H.3.3 U.S. Census and ACS Data

The 2019 American Community Survey (ACS) provides zip code-level population and socioeconomic demographic 5-year estimates. We used these data to produce Appendix Figure B17, Appendix Tables C3, C20, and C21. We obtained U.S. Black population share and White population share from the 2020 U.S. Census website and incorporate these shares into Figure I and Appendix Figure B1.

H.3.4 Clinical Trial Network Site Locations for Cancer, HIV/AIDS, and ADRD

We built a data set of clinical trial network site locations using information gathered from multiple network websites for cancer, HIV/AIDS, and ADRD. For cancer trial network sites, we used information from the National Cancer Institutes (NCI), National Comprehensive Cancer Network (NCCN), and Association of American Cancer Institutes (AACI). For HIV/AIDS we used information from data from the HIV Prevention Trial Network (HPTN), AIDS Clinical Trial Group (ACTG), and HIV Vaccine Trials Network (HVTN). For ADRD, we collated information from the NIA Alzheimer's Disease Research Center (ADRC). All website information is contained in the Appendix References. Trial network site data are used to produce Appendix Table C21.

H.3.5 Research!America Survey Data

The nonprofit Research!America fields national surveys that are used to gauge public opinion on attitudes toward medical, health, and scientific research. We use data from three survey waves: 2013, 2017, and 2021, recoding responses to facilitate data construction in Table I and C1. The variable Science is Beneficial is equal to 1 if a respondent believes that science benefits all or most people in the U.S. and themselves. See Appendix Table H2.

[22] Medical schools given a ranking ranging between two numbers in U.S. News were assigned the midpoint of those two numbers in the data set, and those that were unranked were assigned a ranking of 124 as the U.S. News rankings stop at 124.

Appendix Exhibit H2: Research!America Codebook

	Variable	Question	Raw Responses	Recoded Responses	Years	Black Respondents (Obs.)	White Respondents (Obs.)
(1)	Confidence in Research Institutions	"How confident are you in research institutions?"	1: A great deal 2: Some 3: Not much 4: None at all 5: Not sure	1: None at all 2: Not much 3: Some 4: A great deal Missing: Not sure	2021	215	815
(2)	Heard of Clinical Trial	"Have you ever heard of a clinical trial?"	1: Yes 2: No 3: Not sure	0: No 1: Yes Missing: Not sure	2013 2017 2021	659	2184
(3)	Would Enroll if Doctor Recommends	"If your doctor found a clinical trial for you and recommended you join, how likely would you be to participate in a clinical trial?"	1: Very likely 2: Somewhat likely 3: Not likely 4: Would not participate 5: Not sure	1: Would not participate 2: Not likely 3: Somewhat likely 4: Very likely Missing: Not sure	2013 2017 2021	637	2021
(4)	Trust Not Reason for Lack of Enrollment	"Which of the following do you think is a reason that individuals don't participate in clinical trials?"	0: Not select lack of trust 1: Selected lack of trust	0: Selected lack of trust 1: Not select lack of trust	2013 2017	581	1450
(5)	Would Get FDA-Approved Vaccine	"What is the likelihood of getting COVID vaccine if it was FDA-approved?"	1: Very likely 2: Somewhat likely 3: Not very likely 5: Not sure	4: Very likely 3: Somewhat likely 2: Not likely Missing: Not sure	2021	121	801
(6)	Science is Beneficial	"In general, do you think the work that scientists do benefits all, most, or very few people in this country?" – "In general, to what extent do you think the work that scientists do benefits you?"	1: All 2: Most 3: Some 4: Very few 5: Not sure – 1: To a great extent 2: Somewhat 3: A little 5: Not sure	0: No 1: Yes	2021	134	837

Notes: Table lists variables constructed using Research!America data, the corresponding question, the response options, the years the question was asked, and the number of observations for Black and White respondents.

H.3.6 Moderna Enrollment Information

Information on Moderna's Phase III trial enrollment target (30,000 participants) were publicly announced by Chief Executive Officer Stéphane Bancel (National Institutes of Health 2020). Data on the weekly racial composition of new enrollees are from a presentation by Chief Development Officer Melanie Ivarrson to the National Academies of Sciences Engineering and Medicine on March 29, 2021. Data on the weekly accrual rate are from a figure published on the Moderna Therapeutics Inc. website. We eyeballed the data from the figures and used them to produce the panels of Appendix Figure B5.

H.3.7 Stock Prices

Data on the Moderna Therapeutics Inc.(MRNA) stock price are from the Yahoo!Finance database. We obtained the closing price and volume for the dates July 27, 2020–October 19, 2020. These data are used to produce Appendix Figure B5.

H.3.8 Safety Net Hospitals

There is not an official safety net hospital designation. Therefore, we use the two definitions provided in Popescu et al. (2019). The first definition is whether the hospital is in the state's top quartile of share of uncompensated care, where uncompensated care is charity care plus non-Medicare and non-reimbursable Medicare bad debt. The second definition applies if the hospital is in the top quartile with respect to the Allowable Disproportionate Share (DSH) percent. Data on uncompensated care are from the American Hospital Association Annual Survey and the DSH Index is published in Annual Hospital Provider Cost Report produced by CMS. These designations were merged with trial site information from Clinical Trials and are used to produce Table VI and Appendix Table C19.

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