A National Study Among Diverse US Populations of Exposure to Prescription Medications with Evidence-Based Pharmacogenomic Information

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Tailoring pharmacogenomic (PGx) implementation to diverse populations is vital to promoting health equity. We assessed prescriptions for medications with potentially actionable PGx information to identify patient characteristics associated with differential PGx medication exposure. We analyzed the nationally-representative MEPS dataset of adults who reported receiving prescriptions between 2014 and 2021. PGx medications include those the FDA and CPIC designate as having drug-gene associations supported by scientific evidence. With the primary outcome being PGx prescriptions, we performed Poisson regression adjusted for all other relevant covariates. In our final population (*N* = 119,722, 72% White/20% Black/4% Asian/8% Hispanic), 61% were prescribed a PGx medication, 56% were female, and 97% held health insurance coverage. Adults with private health insurance (65%) or public Medicaid/Medicare coverage (32%) were more likely to have PGx prescriptions than the uninsured (3%). Individuals with cardiovascular conditions [adjusted IRR (aIRR) = 1.45, 95% CI 1.41, 1.48], high cholesterol [aIRR = 1.37, 95% CI 1.35, 1.40], high blood pressure [aIRR = 1.14, 95% CI 1.12, 1.16], and cancer [aIRR = 1.02, 95% CI 1.00, 1.04] were more likely to receive PGx prescriptions. Self-reported Blacks were less likely than Whites to receive PGx medications [aIRR = 0.92, 95% CI 0.90, 0.94], and among those with health conditions, the likelihood of PGx medication exposure for underrepresented groups (Blacks, Hispanics, and Asians) was lower than for Whites. Our study using a comprehensive list of PGx medications in a nationally representative dataset indicates that certain populations are differentially exposed to genomically informed medications. This may suggest that if implementing

Study Highlights

WHAT IS THE CURRENT KNOWLEDGE ON THE TOPIC?

☑ At present, there is a dearth of nationally representative evidence on: (i) exposure to medications with clinically actionable pharmacogenomic information within a diverse population and (ii) the impact pharmacogenomics may have on health disparities.

WHAT QUESTION DID THE STUDY ADDRESS?

☑ We set out to address three specific research questions: (i) at the national level, what characteristics are descriptive of exposure to prescription medications with evidence-based pharmacogenomic associations? (ii) since some commonly prescribed medications to treat chronic health conditions have pharmacogenomic associations, are specific health conditions (e.g., cancer) associated with increased likelihood of pharmacogenomic medication exposure? and (iii) is there differential exposure to PGx medications across populations (e.g., Black vs. White)?

WHAT DOES THE STUDY ADD TO OUR KNOWLEDGE?

☑ This study demonstrates differential exposure to prescription medications with evidence-based pharmacogenomic information. Our results show that individuals with chronic conditions, including a cardiovascular condition, high cholesterol, high blood pressure, and cancer were more likely to have PGx prescriptions. Overall, Black patients were less likely than White patients to receive prescriptions for PGx medications, and, particularly, among those with chronic conditions, the likelihood of exposure to PGx medications for underrepresented racial/ethnic groups (Blacks, Hispanics, and Asians) was comparatively lower than for Whites.

HOW MIGHT THIS CHANGE CLINICAL PHARMACOLOGY OR TRANSLATIONAL SCIENCE?

☑ Since most PGx information has historically been derived from populations of European descent, this study showing that US non-White populations less frequently receive prescriptions for medications with available PGx guidance highlights a potential additional obstacle to underrepresented groups deriving equal benefit from genomically-guided personalized medicine.

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a pharmacogenomics program based on reactive testing initiated by a prescription, a small underrepresentation of the Black population could be expected because of an underlying prescription disparity. Secondly, if implementing a pharmacogenomics program based on targeted preemptive testing, using clinical indication/comorbidity may be a reasonable way to enrich the population for prescriptions that would benefit from genotype tailoring.

Prescription medications play a large role in US healthcare and the management of health conditions. As chronic health conditions have been steadily increasing in the United States and globally, these medications are not only vital to day-to-day disease control but also may prevent or slow disease progression.[1] Almost half (48.6%) of Americans used at least one prescription drug in the past month, and about 1 of every 4 Americans used three or more prescription drugs in the past month.[2] Significant patient harm can result from preventable adverse drug events (ADEs).[3–5] Potentially inappropriate prescribing[6,7] and medication use are associated with worse health outcomes (e.g., hospitalizations and emergency department visits) and drug interactions.

Pharmacogenomics (PGx) offers the promise of helping providers deliver personalized medication treatments based on how an individual's genes influence drug response. By optimizing medication therapy (e.g., medication selection and/or dose adjustment), pharmacogenomics may help avoid adverse events or improve drug efficacy. Large prospective randomized studies have now suggested measurable benefits associated with PGx-informed prescribing.[8] Medications with well-defined pharmacogenomic associations now have actionable prescribing recommendations[9], and such medications are actually overrepresented among highly prescribed medications in the United States.[10] In fact, about 30 of the most commonly prescribed drugs with potential for pharmacogenetic clinical action account for over 15% of all prescriptions.[11] Furthermore, approximately 90–95% of individuals have an actionable genotype for at least one gene associated with drug response.[12]

However, the utility of PGx in directing healthcare delivery to diverse patient groups where individuals descend from a wide variety of ancestral backgrounds is uncertain. The majority of pharmacogenomic discovery studies have been conducted in populations of primarily European descent, and evidence has shown that not all PGx implementation strategies are clinically generalizable across patient populations.[13,14] This potential bias of traditionally using mostly European-descent population data in pharmacogenomic discovery research has resulted in implementation challenges, including the fact that important non-European ancestrally-restricted or ancestrally-enriched variants from underrepresented groups are either not yet identified or not included in clinical implementation testing panels, thereby limiting the clinical applicability of some first-generation clinical "PGx tests" for diverse populations.[13,15–20] Use of preemptive pharmacogenomics is not currently considered a standard of care for guiding most prescriptions and for most prescribing settings. Concerns also exist that the inequitable diffusion of pharmacogenomic technologies has preferentially benefited certain populations at the expense of others.[21] Due to wide variation and inconsistency in the use of pharmacogenomics within clinical care and the lack of diversity in pharmacogenomic clinical trials across the country, nationally representative evaluations have remained challenging.

In this study, we sought to identify the incidence of prescriptions for medications with evidence-based pharmacogenomic associations in a diverse, nationwide patient population. We also set out to address three specific research questions: (i) at the national level, what characteristics are descriptive of exposure to prescription medications with evidence-based pharmacogenomic associations? (ii) since some commonly prescribed medications to treat chronic health conditions have pharmacogenomic associations, are specific health conditions (e.g., cancer) associated with increased likelihood of pharmacogenomic medication exposure?; and (iii) is there differential exposure to PGx medications across populations (e.g., Black vs. White)? We acknowledge that potential differences in the prescribing rates of PGx medications within self-reported racial/ethnic groups may not consistently represent disparities, but rather, depending on the context and specific medication could represent appropriate prescribing. Nevertheless, we intended this analysis as a starting point for examining potential disparities in the application of prescription optimization that might be offered by pharmacogenomic information.

METHODS

Data and study population

We evaluated consolidated data from the nationally-representative Medical Expenditure Panel Survey (MEPS)[22] between 2014 and 2021. MEPS is a publicly available dataset that includes information on US healthcare use (including office-based and hospital services, prescription drugs, and other healthcare services) and costs. Unique to the MEPS data is that patients in sampled households are asked to sign authorization forms permitting the data collection contractor to contact their healthcare providers and pharmacies to request both medical records and billing data.[23] Therefore, MEPS data provide clinical validation of patient-reported healthcare utilization and expenditures. This study period from 2014 to 2021 reflects the years MEPS has been administered following the completion of a major shift in national genetic testing reimbursement policy by the end of 2013.[24] For each year, we identified US adults (age 18 years or older) who reported having at least one prescription medication. Then, we compiled a complete dataset of all prescription medications reported by each survey respondent during the study period. Our final dataset consisted of pooled cross-sectional survey results collected annually over the study period (2014–2021). This dataset was not longitudinal, and it did not follow individual survey respondents over time.

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Prescription medications with pharmacogenomic associations

Prescription medications were separated into two groups: (i) medications with known, evidence-based pharmacogenomic associations (PGx medications) and (ii) medications without pharmacogenomic associations. "PGx medications" were defined as those listed by the US Food and Drug Administration (FDA) Table of Pharmacogenetic Associations[25] or those identified by the Clinical Pharmacogenetics Implementation Consortium (CPIC) with an evidence level A/B as having well-supported gene-drug associations.[26] The FDA includes pharmacogenetic associations with data: (i) supporting therapeutic management recommendations, (ii) indicating a potential impact on safety/response, and (iii) demonstrating impact on the way a drug is metabolized.[25] Since providers take into account different sources and strengths of evidence and determine prescribing decisions based on their judgment about which treatments are appropriate for individual patients, we were inclusive of all of the FDA's cited pharmacogenomic associations with potential impact. We combined medications with pharmacogenomic associations from either of these sources into one composite list of potentially "actionable" PGx medications. We consolidated our final list of PGx medications in June 2022 (**Table S1**).

Chronic health conditions

The chronic health conditions included in our analysis were defined by the Agency for Healthcare Research and Quality (AHRQ) who administers and publishes the MEPS data. AHRQ prioritizes this select group of chronic health conditions[27] that include top drivers of morbidity and mortality in the United States: cancer, diabetes, high cholesterol, high blood pressure (or hypertension), cardiovascular conditions (e.g., coronary heart disease), and respiratory conditions (e.g., emphysema). We also generated a numerical count variable representing the number of these chronic health conditions reported at the person level.

Descriptive and statistical analyses

Descriptive analyses were performed to characterize the total study population of MEPS respondents (pooled from 2014 to 2021), persons with pharmacogenomic medication exposure, and individuals without pharmacogenomic exposure. To produce nationally representative estimates, annual population weights were incorporated to derive the percentages indicated for each group.

Poisson regression models were constructed to examine the likelihood of pharmacogenomic medication exposure using the number of PGx medication prescriptions as the primary outcome. Other variables used for analysis included the following: race/ethnicity, age, sex, region, income, educational attainment, health insurance, number of chronic conditions, and number of unique drugs prescribed in a year. For all statistical analyses, the modeling coefficients were expressed as incidence rate ratios unadjusted and adjusted for all other relevant covariates (e.g., age), and 95% confidence intervals were calculated. All analyses were conducted using Stata 15.1.

Ethics statement

This study was reviewed by The University of Chicago Institutional Review Board and was determined to be exempt as it relied on publicly available data.

RESULTS

Demographics

Our final dataset (2014–2021) included 119,722 unweighted MEPS survey respondents that had at least one prescription medication, the majority of which had experienced exposure to medications with pharmacogenomic (PGx) associations (61%). The study population with at least one PGx prescription was majority White (72%), had a median age of 60 years (range: 18–85), majority female (56%), and over half (53%) had an educational attainment of a high-school degree or less (**Table 1**). The overwhelming majority (97%) of respondents with PGx medication exposure had health insurance coverage. This health insurance was either public (32%) or private (65%) health insurance coverage. In unadjusted analyses, we found that adults with any type of health insurance coverage [IRR = 1.70, 95% CI 1.57, 1.83] but especially those with coverage through public health insurance programs (e.g., Medicaid and Medicare) [IRR = 2.36, 95% CI 2.19, 2.55] were more likely to have prescriptions for PGx medications. Following adjustment for patient demographics (e.g., race/ethnicity) of the uninsured, publicly insured, and privately insured populations, these observed differences by insurance status were no longer statistically significant.

Polypharmacy increases PGx information relevance

Additionally, the population exposed to PGx medications had multiple comorbidities with a median of two health conditions (range: 0–14) and polypharmacy with a median number of 5 prescription medications (range: 0–14). Not surprisingly, we found a direct relationship between the increased likelihood of exposure to PGx medications and the number of health conditions and unique prescriptions (**Table 2**). Compared to those with no health conditions, individuals with more than one health condition were at minimum 42% more likely to be exposed to PGx medications [0 vs. 2–3 health conditions, aIRR = 1.42, 95% CI 1.37, 1.47]. Even after adjustment, the likelihood of exposure to PGx medications more than doubled for individuals with multiple medication prescriptions compared to those with only one prescription medication (**Table 2**). Compared to the population under 65 years of age, older adults (65 years and older) were more likely to be exposed to PGx medications (**Table 2**). Though the majority of the study population was female, adjusted analyses showed women were less likely to have prescriptions for PGx medications [aIRR = 0.89, 95% CI 0.88, 0.91].

Specific chronic conditions are more likely to confer PGx medication likelihood

Among patients with chronic conditions, the majority reported prescriptions for pharmacogenomic medications: 83% with diabetes, 72% with high cholesterol, 69% with cancer, 68% with high blood pressure, 64% with a cardiovascular condition, and 52% with a respiratory condition (**Table 3**). Specific health conditions increased the likelihood of PGx medication exposure (**Table 4**). Individuals with a cardiovascular condition [aIRR = 1.45, 95% CI 1.41, 1.48], high cholesterol [aIRR = 1.37, 95% CI 1.35, 1.40], high blood pressure [aIRR = 1.14, 95% CI 1.12, 1.16], and cancer [aIRR = 1.02, 95% CI 1.00, 1.04] were more likely to have PGx prescriptions.

Differential likelihood of PGx-associated prescriptions by race/ethnicity

We also observed differential exposure to PGx medications across underrepresented racial/ethnic groups. Notably, Blacks were less likely than Whites to receive prescriptions for PGx medications

Table 1 Patient characteristics, MEPS 2014-2021 (weighted)

		At least one prescription event		
	Total survey respondents	At least one prescription	At least one PGx prescription	No PGx prescriptions
(unweighted) *N*=	**189,685**	**119,722**	**75,186**	**44,536**
Variable	%	%	%	%
Race/ethnicity				
White (Non-Hispanic)	63	69	72	66
Black (Non-Hispanic)	12	11	10	11
Hispanic	16	12	11	14
Asian (Non-Hispanic)	6	5	4	6
Age				
Median (Range)	48 (18, 85)	55 (18, 85)	60 (18, 85)	44 (18, 85)
Under 65	79	71	61	86
65–74	12	17	22	9
75–84	6	9	13	4
85+	3	4	5	2
Female	52	57	56	60
Highest degree earned				
No degree	11	10	10	10
HS degree	42	42	43	39
College degree	19	19	17	22
Graduate degree	11	12	12	13
Income status				
Poor (<100% FPL)	11	11	12	9
Near poor (100% to <125% FPL)	4	4	4	3
Low income (125% to <200% FPL)	12	12	13	11
Middle Income (200% to <400% FPL)	28	28	27	28
High Income (≥400% FPL)	44	46	44	49
Region				
Northeast	17	17	17	17
Midwest	21	22	23	21
South	37	38	38	37
West	23	22	21	23
Full year insurance				
Uninsured	8	4	3	6
Public	23	27	32	18
Private	69	69	65	76
Number of chronic health conditions				
Median (Range)	1 (0, 14)	2 (0, 14)	2 (0, 14)	1 (0, 11)
None	40	25	14	42
1	22	22	18	30
2–3	24	32	38	23
4–5	10	14	21	4
6+	4	6	9	1
Number of unique prescriptions				
Median (Range)	1 (0, 47)	4 (1, 47)	5 (1, 47)	2 (1, 19)
None	35	—	—	—

(Continued)

Table 1 (Continued)

	Total survey respondents	At least one prescription event		
		At least one prescription	At least one PGx prescription	No PGx prescriptions
1	14	22	7	44
2–3	19	29	23	38
4–5	12	18	23	12
6–7	8	12	17	4
8–9	5	7	11	1
10+	8	12	19	1

All percentage values reflect nationally representative population-based weights. Totals may not sum to 100 due to rounding and unknown/missing values not being shown. Number of Health Conditions—AHRQ defined chronic health conditions in MEPS. Number of unique prescription medications of any type. For race/ethnicity, Other (non-Hispanic) not displayed as comprised less than 4% of the study population.

overall [aIRR = 0.92, 95% CI 0.90, 0.94] (**Table 2**). Additionally, among those with a chronic health condition, the likelihood of exposure to PGx medications for underrepresented racial/ethnic groups (Blacks, Hispanics, and Asians) was comparatively lower than for Whites (**Figure 1**). Significant differences in predicted PGx medication exposure between Blacks and Whites were observed for multiple chronic health conditions. Compared to White patients with the same chronic conditions, Black patients experienced a decrease in the likelihood of having prescriptions for PGx medications of about 38% when they reported having a diagnosis of diabetes, 30% with a diagnosis of high blood pressure, and 22% with a diagnosis of a cardiovascular condition (**Figure 1**).

Addressing potential confounders

Confounders such as access to care and severity of disease may introduce challenges to interpreting rates of PGx medication prescribing across racial/ethnic populations. Therefore, our analysis next incorporated measures to address these potential confounders. First, we analyzed for all study patients the total number of recorded chronic conditions, as a measure of overall health fitness/severity (these were conditions recorded at medical visits, meaning these were chronic conditions known to a treating provider). There was no difference in the number of chronic conditions between self-reported Whites and Blacks (**Table S2**). Second, prior research has suggested that rates of overall prescription drug use reflect underlying patterns of healthcare access and disease treatment.[28] To this end, we evaluated the number of overall prescription medications for all patients in our study by race/ethnicity and found that Whites and Blacks were prescribed identical median numbers of unique medication prescriptions, with almost identical patterns of polypharmacy (**Table S2**). Similar trends were observed between Whites and Hispanics (**Table S2**). This suggests that the patients in our study were receiving similar frequencies of prescriptions to treat an identical number of chronic conditions, lessening the possibility that significant differences in chronic disease undertreatment existed by race/ethnicity. Finally, while cost considerations for prescriptions could not be directly compared using the available data, our final study population was one with high rates of health insurance coverage (97% of individuals had health insurance), and almost all PGx medications in the analysis set are available in generic forms (**Table S1**), facts that likely mitigate significant influences of prescription drug cost as explaining the race/ethnicity findings in the dataset. We appropriately caution that extensions of these findings to uninsured populations should not be made.

DISCUSSION

The current study assessed the prescribing patterns for pharmacogenomic medications within a diverse US adult population derived from the nationally representative Medical Expenditure Panel Survey dataset. To our knowledge, this analysis is the first nationally representative study evaluating PGx medication exposure following expansions in reimbursement and health insurance coverage policy for genetic testing. Our results show that individuals with chronic conditions, including a cardiovascular condition, high cholesterol, high blood pressure, and cancer were more likely to have PGx prescriptions. However, Black patients were less likely than White patients to receive prescriptions for PGx medications overall, and, particularly, among those with chronic conditions, the likelihood of exposure to PGx medications for underrepresented racial/ethnic groups (Blacks, Hispanics, and Asians) was comparatively lower than for Whites. While we acknowledge that fewer PGx medication prescriptions to some underrepresented groups may not actually reflect a disparity (i.e., depending on the context and specific medications, these differences may represent appropriate prescribing), we view these findings as representing a potential missed opportunity for the prescription optimization that pharmacogenomic information offers. When combined with the fact that most PGx information has historically been derived from European-descent populations, these findings that US non-White populations less frequently receive prescriptions for medications with available PGx guidance underscores a possible additional obstacle to underrepresented groups being able to derive equal benefit from genomically-guided personalized medicine.

We found that individuals with chronic conditions were more likely to have PGx prescription medications. Finding a direct

Table 2 Characteristics that predict exposure to PGx medications, 2014–2021

	Unadjusted			Adjusted		
Independent variables	**IRR**	***P*-value**	**95% CI**	**aIRR**	***P*-value**	**95% CI**
Race/ethnicity						
White (Non-Hispanic)	—	—	—	—	—	—
Black (Non-Hispanic)	0.91	<0.001	(0.88, 0.95)	0.92	<0.001	(0.90, 0.94)
Hispanic	0.78	<0.001	(0.75, 0.81)	0.99	0.353	(0.97, 1.01)
Asian (Non-Hispanic)	0.70	<0.001	(0.66, 0.75)	1.00	0.812	(0.96, 1.03)
Age						
Under 65	—	—	—	—	—	—
65–74	1.98	<0.001	(1.93, 2.04)	1.10	<0.001	(1.08, 1.12)
75–84	2.31	<0.001	(2.24, 2.37)	1.12	<0.001	(1.10, 1.15)
85+	2.30	<0.001	(2.20, 2.40)	1.11	<0.001	(1.07, 1.14)
Sex						
Male	—	—	—	—	—	—
Female	0.92	<0.001	(0.90, 0.94)	0.89	<0.001	(0.88, 0.91)
Highest degree earned						
No degree	—	—	—	—	—	—
HS diploma	0.93	<0.001	(0.90, 0.97)	1.00	0.996	(0.98, 1.02)
College degree	0.71	<0.001	(0.68, 0.74)	0.95	0.001	(0.93, 0.98)
Graduate degree	0.77	<0.001	(0.73, 0.81)	0.95	<0.001	(0.92, 0.97)
Income status						
Poor (<100% FPL)	—	—	—	—	—	—
Near poor (100% to <125% FPL)	1.05	0.021	(1.01, 1.10)	0.98	0.226	(0.96, 1.01)
Low income (125% to <200% FPL)	0.97	0.116	(0.94, 1.01)	0.99	0.458	(0.97, 1.01)
Middle income (200% to <400% FPL)	0.82	<0.001	(0.79, 0.85)	0.98	0.060	(0.96, 1.00)
High income (≥400% FPL)	0.73	<0.001	(0.71, 0.76)	0.97	0.006	(0.95, 0.99)
Region						
Northeast	—	—	—	—	—	—
Midwest	1.06	0.010	(1.01, 1.11)	1.01	0.399	(0.99, 1.04)
South	1.04	0.056	(1.00, 1.09)	0.99	0.309	(0.96, 1.01)
West	0.90	<0.001	(0.86, 0.94)	0.96	0.003	(0.94, 0.99)
Full-year insurance						
Uninsured	—	—	—	—	—	—
Public only	2.36	<0.001	(2.19, 2.55)	1.04	0.136	(0.99, 1.09)
Any private	1.44	<0.001	(1.34, 1.56)	0.99	0.811	(0.95, 1.04)
Number of health conditions						
None	—	—	—	—	—	—
1	1.61	<0.001	(1.54, 1.68)	1.19	<0.001	(1.15, 1.24)
2 to 3	3.04	<0.001	(2.94, 3.15)	1.42	<0.001	(1.38, 1.47)
4 to 5	5.18	<0.001	(5.00, 5.37)	1.61	<0.001	(1.55, 1.66)
6+	7.02	<0.001	(6.75, 7.29)	1.75	<0.001	(1.69, 1.82)
Number of unique prescriptions						
1	—	—	—	—	—	—
2 to 3	2.96	<0.001	(2.84, 3.07)	2.71	<0.001	(2.61, 2.82)
4 to 5	5.90	<0.001	(5.67, 6.14)	4.89	<0.001	(4.69, 5.10)
6 to 7	8.84	<0.001	(8.50, 9.21)	6.80	<0.001	(6.52, 7.10)
8 to 9	11.52	<0.001	(11.06, 12.00)	8.39	<0.001	(8.03, 8.76)

(Continued)

Table 2 (Continued)

Independent variables	Unadjusted IRR	Unadjusted *P*-value	Unadjusted 95% CI	Adjusted aIRR	Adjusted *P*-value	Adjusted 95% CI
10+	16.71	<0.001	(16.07, 17.37)	11.50	<0.001	(11.02, 11.99)

Adjusted and unadjusted odd ratios come from Poisson regression model used to predict PGx medication exposure. We adjust over the following covariates: race, age, sex, geography, income, education, insurance, number of chronic medical conditions, and the number of unique medications prescribed in a year.

Table 3 Exposure to PGx medications among adults with chronic conditions, MEPS 2014–2021 (weighted)

		Chronic condition					
	Total survey respondents	Cancer[a]	Cardiovascular condition[b]	Respiratory condition[c]	Diabetes	High blood pressure	High cholesterol
(unweighted) *N*=	**189,685**	**19,652**	**91,328**	**24,934**	**15,595**	**65,389**	**58,427**
	%	%	%	%	%	%	%
At least one prescription event	65	89	85	81	97	89	88
At least one PGx prescription	40	69	64	52	83	68	72
No PGx prescriptions	60	31	36	48	16	32	28

[a]At least one reported of any type of cancer. [b]At least one cardiovascular condition including coronary heart disease, angina, heart attack, stroke, hypertension, high cholesterol, and other heart disease. [c]At least one respiratory condition included emphysema and asthma. Percentages reflect rounding.

Table 4 Chronic health conditions that predict exposure to PGx medications, 2014–2021

Chronic health condition	Unadjusted IRR	Unadjusted *P*-value	Unadjusted 95% CI	Adjusted aIRR	Adjusted *P*-value	Adjusted 95% CI
None	—	—	—	—	—	—
Cancer[a]	1.61	<0.001	(1.56, 1.65)	1.02	0.013	(1.00, 1.04)
Cardiovascular condition[b]	3.05	<0.001	(2.98, 3.13)	1.45	<0.001	(1.41, 1.48)
Respiratory condition[c]	1.22	<0.001	(1.19, 1.27)	0.89	<0.001	(0.87, 0.90)
Diabetes	2.11	<0.001	(2.05, 2.16)	1.00	0.618	(0.99, 1.02)
High blood pressure	2.29	<0.001	(2.24, 2.34)	1.14	<0.001	(1.12, 1.16)
High cholesterol	2.50	<0.001	(2.45, 2.56)	1.37	<0.001	(1.35, 1.40)

[a]At least one reported of any type of cancer. [b]At least one cardiovascular condition including coronary heart disease, angina, heart attack, stroke, hypertension, high cholesterol, and other heart disease. [c]At least one respiratory condition included emphysema and asthma. Results of Poisson regression models of PGx medication exposure. Adjusted analyses include: race/ethnicity, age, sex, region, income level, educational attainment, insurance coverage, and number of unique prescription medications.

relationship between the increased likelihood of exposure to PGx medications and the number of health conditions was expected, especially given the increased role of medication management for patients with chronic illness.[1] Yet we additionally found there was differential PGx exposure across specific chronic condition groups. While descriptive analysis of chronic condition rate ratios reflects instances (e.g., high cholesterol) that are indications for the measurements and other instances (e.g., high blood pressure) that are correlated with indications for medications on the PGx list, overall we observed that PGx medication therapy across chronic conditions was not uniform. While the findings are descriptive in nature and thus have a limitation of not being true predictive models, nevertheless, given the observed variation in the frequency of PGx medication exposure, patients with certain chronic conditions may derive greater benefit from targeted pharmacogenomic-guided prescribing. Future research is needed to determine the underlying factors contributing to this inconsistent diffusion of PGx medications. Other papers describe PGx prevalence in various populations, such as those diagnosed with a single chronic condition like cancer[29] or those reflecting diversity in genetic ancestry.[30] Our analysis builds upon this prior research in further emphasizing the importance of performing pharmacogenomic studies in populations reflective of our global diversity.

The dearth of evidence on the impact pharmacogenomics may have on health disparities[31] provides additional value to our study which illuminates differential PGx medication exposure across demographic populations. Health disparities are costly for patients left behind who may experience ADEs or suboptimal treatment, incur high medical costs, and experience premature death.[32] There are also societal costs due to health inequities for the overall health system via excess medical care expenditures as well as from economic losses due to premature deaths each year.[33–38] Whether the observed prescribing patterns reflect appropriate clinical care or provide evidence of health disparities in genomic medicine will

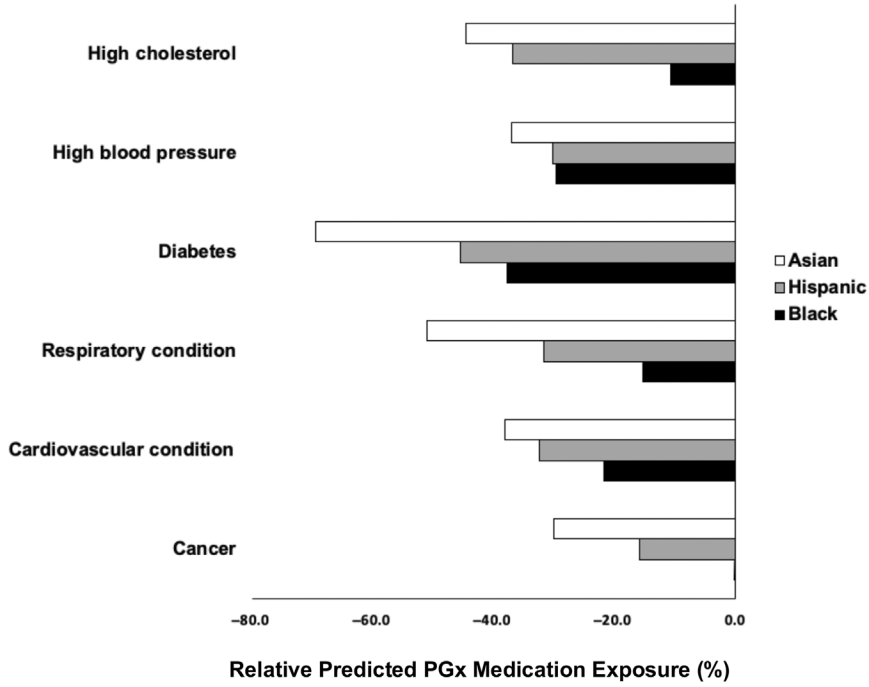

Figure 1 Relative predicted PGx medication exposure for underrepresented racial/ethnic populations with chronic health conditions compared to Whites, 2014–2021. White study participants represent the reference group for comparison. Percentages represent the absolute difference in the relative risk between underrepresented study groups and the White reference group. Negative % values indicate the magnitude of the decrease in the likelihood of prescriptions for PGx medications compared to Whites.

have meaningful implications for the clinical utility of pharmacogenomics in a diverse patient population.

Even after adjusting for the overall number of unique medication prescriptions, we found that Blacks were less likely than Whites to receive prescriptions for PGx medications. Moreover, chronic health conditions disproportionately impact populations of underrepresented racial/ethnic groups.[39] In this analysis of the chronically ill population, among patients with the same chronic health condition, Blacks were consistently less likely than Whites to have prescriptions with pharmacogenomic associations. In fact, we observed a reduced likelihood of PGx medication exposure when comparing racial/ethnic populations underrepresented in pharmacogenomic studies (Blacks, Hispanics, and Asians) with Whites for multiple chronic health conditions. Prior research has indicated that medically underserved populations with geographic barriers to healthcare access may particularly benefit from pharmacogenomically-guided medication therapy.[40] While we did not observe variation in PGx medication exposure due to geography, additional studies of how geographic and area-level social risk factors[41] may influence genomic medicine are critical to ensuring the equitable implementation of pharmacogenomics across clinical care settings.

This study's results indicating the significance of patient population characteristics across insurance types to PGx medication exposure aligns with earlier work demonstrating that non-elderly adults enrolled in Medicaid, a public health insurance program serving those with lower incomes, had the highest incidence of PGx drug use.[42] Public insurance programs serving vulnerable populations (e.g., lower income and older adults) have been at the forefront of establishing reimbursement mechanisms for pharmacogenomic testing.[24,43,44] This may have meaningful implications for the beneficiaries of these programs with complex health needs in terms of facilitating access to pharmacogenomic-guided prescribing. Future research should investigate the role of safety-net public health insurance programs in promoting the uptake of PGx-guided prescribing in genomic medicine.

No study is without limitations. Though the MEPS data allowed for the evaluation of patient-reported and validated medication prescriptions, we were unable to confirm actual medication adherence once prescriptions were filled. Drug dosage information is not contained within the MEPS dataset, meaning that for a few medications where dose may affect whether PGx recommendations exist (e.g., when amitriptyline is used for sleep vs depression treatment), this nuance was not considered. Additionally, the MEPS data do not indicate whether a given prescription is new, or incident, as opposed to a "renewal" of an already-chronic medication; this could have implications for the potential utility/applicability of some medication-level PGx information. Finally, receipt of pharmacogenomic testing is not included in the MEPS survey, so we are unable to associate PGx medication exposure with confirmed pharmacogenomic testing. Separately, the lower likelihood of PGx medication exposure for certain patient populations must be placed into context by considering potential confounders like access to care, severity of disease (e.g., comorbidities), and out-of-pocket costs. As drivers of both general healthcare disparities as well as PGx-specific

disparities, these confounding factors or those possibly unmeasured might rather indicate potential undertreatment of chronic disease. Our analysis of potential confounding across racial/ethnic populations did not find evidence that access to prescription medications or comorbidities biased our results on PGx medication exposure. While uninsured individuals likely face increased difficulty affording prescription drugs,[45] our study population had high rates of health insurance coverage with 97% of individuals having health insurance to assist in mitigating the costs of prescription drugs. However, this does limit the generalizability of our findings for uninsured populations. Finally, we adopted liberal inclusion criteria for FDA and CPIC-published PGx associations to provide an assessment at the national level of differential exposure rates that future sub-group analyses of drug-gene pairs can further delineate. Our more liberal PGx inclusion criteria may not mean that a prescribing difference is warranted for each PGx prescription difference, but we utilized this broader definition as a starting point to highlight the potential for disparities in suboptimal prescribing based on the totality of pharmacokinetic, toxicity, and/or clinical outcomes differences for patients. Evidence of differential exposure to genomically-informed medications is a critical first step in distinguishing the underlying potential drivers of disparities, determining patient populations most likely to benefit from PGx testing, and ultimately closing the gap of knowledge on the impact pharmacogenomics may have on health disparities.[31]

This study reveals that medications with pharmacogenomic associations and currently available clinical guidelines are being prescribed at different rates. The rapid rate of technological advancement in genomics and the development of genomic databases including greater ancestral diversity, will likely uncover new genetic variants to inform medication therapy. Alongside these innovations, it will be important to monitor prescribing patterns for medications with pharmacogenomic associations as well as to initiate studies on the clinical utility of pharmacogenomics across diverse patient populations.

SUPPORTING INFORMATION

Supplementary information accompanies this paper on the *Clinical Pharmacology & Therapeutics* website (www.cpt-journal.com).

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CONFLICT OF INTEREST

The authors declared no competing interests for this work. As an Associate Editor for *Clinical Pharmacology & Therapeutics*, Peter O'Donnell was not involved in the review or decision process for this paper.

AUTHOR CONTRIBUTIONS

L.S., J.J., R.D.G., M.E.D., O.I.O., and P.H.O. wrote the manuscript; L.S. and P.H.O. designed the research; L.S. and J.J. performed the research. L.S. and J.J. analyzed the data.

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