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## Prescription medication changes following direct-to-consumer personal genomic testing: Findings from the Impact of Personal Genomics (PGen) Study

Deanna Alexis Carere, ScD, CGC<sup>1</sup>, Tyler VanderWeele, PhD<sup>2</sup>, Jason L. Vassy, MD, MPH, SM<sup>3,4,5</sup>, Cathelijne van der Wouden, PharmD<sup>6</sup>, J. Scott Roberts, PhD<sup>7</sup>, Peter Kraft, PhD<sup>2,\*</sup>, Robert C. Green, MD, MPH<sup>5,8,9,\*</sup>, and for the PGen Study Group<sup>#</sup>

<sup>1</sup>Department of Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, Canada <sup>2</sup>Department of Epidemiology, Harvard School of Public Health, Boston, MA, USA <sup>3</sup>Division of General Medicine and Primary Care, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA <sup>4</sup>VA Boston Healthcare System, Boston, MA, USA <sup>5</sup>Harvard Medical School, Boston, MA, USA <sup>6</sup>Department of Clinical Pharmacy and Toxicology, Leiden University Medical Center, Leiden, The Netherlands <sup>7</sup>Department of Health Behavior and Health Education, University of Michigan School of Public Health, Ann Arbor, MI, USA <sup>8</sup>Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, USA <sup>9</sup>Broad Institute, Cambridge, MA, USA

### Abstract

**Purpose**—To measure the frequency of prescription medication changes following direct-to-consumer personal genomic testing (DTC-PGT) and their association with the pharmacogenomic results received.

**Methods**—New DTC-PGT customers were enrolled in 2012 and completed surveys prior to return of results and 6 months post-results; DTC-PGT results were linked to survey data. ‘Atypical response’ pharmacogenomic results were defined as those indicating an increase or decrease in risk of an adverse drug event or likelihood of therapeutic benefit. At follow-up, participants reported prescription medication changes and health care provider consultation.

**Results**—Follow-up data were available from 961 participants, of which 54 (5.6%) reported changing a medication they were taking, or starting a new medication, due to their DTC-PGT results. Of these, 45 (83.3%) reported consulting with a health care provider regarding the change. Pharmacogenomic results were available for 961 participants, of which 875 (91.2%) received 1 *atypical response* result. For each such result received, the odds of reporting a prescription medication change increased 1.57 times (95% confidence interval = 1.17, 2.11).

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**Corresponding Author:** Robert C. Green, MD, MPH, Brigham and Women's Hospital and Harvard Medical School, EC Alumnae Building, Suite 301, 41 Avenue Louis Pasteur, Boston, MA 02115, (office) 617-264-5834, (fax) 617-264-3018, (cell) 617-966-3216, [rcgreen@genetics.med.harvard.edu](mailto:rcgreen@genetics.med.harvard.edu).

\*These authors contributed equally

#See acknowledgements for list of non-author members of the PGen Study Group

**Conclusion**—Receipt of pharmacogenomic results indicating atypical drug response is common with DTC-PGT, and associated with prescription medication changes; however, fewer than 1% of consumers report unsupervised changes at 6 months post-testing.

### Keywords

pharmacogenomics; pharmacogenetics; direct-to-consumer genetic testing; personal genomic testing; prescription medications; commercial genetic testing

## INTRODUCTION

Direct-to-consumer (DTC) personal genomic testing (PGT), whereby individuals purchase specific genetic analyses directly from private companies, has the potential to prompt inappropriate use of health care services.<sup>1</sup> In studies, however, this concern has not been borne out,<sup>2,3</sup> and one likely reason is that most health services are subject to gate-keeping,<sup>4</sup> and consumers can rarely access care without clinician involvement.

An exception to this *de facto* regulation mechanism lies in DTC pharmacogenomic testing. When the United States Food and Drug Administration (FDA) sent a Warning Letter to 23andMe, Inc. (23andMe) in November 2013, they speculated that the DTC-PGT company's customers might use their results to "self-manage their treatments through dose changes or even [abandonment of] therapies"<sup>5</sup> without contacting a physician or pharmacist. With the exception of a single cross-sectional survey that reported post-test medication changes in <5% of DTC-PGT consumers,<sup>6</sup> no empirical evidence exists to evaluate the validity of FDA's concerns; moreover, no study has evaluated the relationship between consumers' actual pharmacogenomic test results and post-PGT prescription medication changes.

We present data from the Impact of Personal Genomics (PGen) Study,<sup>7</sup> a longitudinal study of DTC-PGT customers of 23andMe and Pathway Genomics Corp. (Pathway) surveyed prior to, and 6 months following, return of results. Our analytic goals were three-fold: (1) to describe the frequency and types of pharmacogenomic results received by DTC-PGT consumers; (2) to describe the frequency and types of post-PGT prescription medication changes reported by DTC-PGT consumers; and (3) to test the hypothesis that receipt of pharmacogenomic results predicting an atypical drug response is associated with post-PGT prescription medication changes. In light of a previously documented association between receipt of DTC pharmacogenomic information, generally, and post-PGT health services usage,<sup>8</sup> we also evaluated in secondary analyses the association between receipt of atypical drug response results and three measures of health services usage.

## METHODS

### The Impact of Personal Genomics (PGen) Study

The PGen Study was initiated in 2011 by academic researchers at Harvard Medical School/Brigham and Women's Hospital (Boston, MA) and the University of Michigan School of Public Health (Ann Arbor, MI), and industry scientists at 23andMe<sup>9</sup> (Mountain View, CA) and Pathway<sup>10</sup> (San Diego, CA). The study was approved by the Partners Human Research

Committee and the University of Michigan School of Public Health Institutional Review Board.

New customers were recruited between March and July 2012. Emails with information about the study and an invitation to participate were sent by 23andMe to a consecutive series of 3,900 customers who ordered the company's service during this time period, and who had previously submitted a general consent to be contacted about research opportunities; of these, 1,249 (32.0%) provided online consent to the PGen Study. Separately, Pathway placed a banner advertisement for their services and the PGen Study on their webpage, and sent emails to approximately 30,000 members of PatientsLikeMe, a health-based social networking site.<sup>11</sup> In these communications, Pathway's PGT service was offered at a subsidized price of \$25, and after placing an order for PGT through one of these channels, customers were directed to a webpage inviting them to participate in the PGen Study. A total of 589 Pathway customers provided online consent.

Of the 1,838 individuals who consented, 1,648 (23andMe = 1,085; Pathway = 563) completed a baseline survey prior to receiving their PGT results. Eligibility criteria for follow-up, requiring receipt and access of health-related results within the study period, were met by 1,464 participants (23andMe = 947; Pathway = 517). Follow-up surveys were administered 2 weeks post-results (n = 1,046; response rate<sup>12</sup> = 71.4%) and 6-months post-results (1,042; 71.1%). Results were returned to customers by the companies and then transferred to academic researchers and linked to survey data. Complete details of the collaborative arrangement with the companies, participant recruitment, inclusion/exclusion criteria, and data collection (including a non-response bias analysis and full versions of the surveys) are published elsewhere.<sup>7,13</sup> Throughout the PGen Study, each company was represented by one research scientist, who was invited to comments on papers in progress. A pre-submission manuscript was sent to each representative for review and comment, but final discretion lay with the writing group, in particular the first author (DAC) and the PGen Study's co-Principal Investigators (JSR, RCG).

## Survey Instruments

At baseline, we measured age, race/ethnicity,<sup>14</sup> gender, income, education, self-reported health,<sup>15</sup> health insurance status, current prescription medication use (yes/no in 7 categories), and interest in obtaining pharmacogenomic information (three ordinal categories). Among participants who reported a physical exam in the last two years, we measured number of self-reported health care visits in the last year (shown to correlate strongly with medical records-based measures of health care visits<sup>16</sup>).

At 6-month follow-up, participants reported changes to their prescription medications "as a result of seeing [their company] results" (yes/no in 5 categories), whether or not they had consulted a health care provider before making the change, and what had prompted them to make the change(s) (free-text response). "Health care provider" was not further defined; therefore, reported consultations could capture interactions with non-physicians, alternative medicine practitioners, or other non-prescribing professionals (e.g., nurses). Participants were also asked: "Do you think you will use your [company] results to guide your future use of medication?" (yes/no/don't know).

Finally, participants reported three post-PGT outcomes previously shown by Bloss *et al.*<sup>8</sup> to be associated with receipt of DTC pharmacogenomic information: sharing of PGT results with a health care provider (yes/no); follow-up tests, medical exams, or procedures ordered on the basis of their PGT results (yes/no); and number of health care visits since PGT (6 month interval). The first of these outcomes was measured with a survey item which asked participants with whom they had shared their results (9 available responses, including 3 health care provider categories: “Primary Care Provider,” “Genetics specialist (e.g., genetic counselor, clinical geneticist),” and “Other medical professional.”) If participants selected “Other medical professional,” they were asked to identify the type of medical professional from a list. “Primary Care Provider” was not further defined in the survey, and was therefore open to participant interpretation (i.e., may have included non-physician medical practitioners and alternative medicine providers). The second of these outcomes was measured with a single survey item that read: “As a result of seeing your genetic information from [company], have you had any tests, medical exams, or procedures?” The inclusive wording of this item was designed to capture services received in response to any PGT result (e.g., disease risk estimates, genetic carrier status), not only pharmacogenomic information. Note that in Bloss *et al.*, investigators evaluated the impact on health services usage of receiving *any* DTC pharmacogenomic information (without consideration of the content of that information) within a sample of consumers that were randomized to either receive or not receive pharmacogenomic results; here, we instead evaluated the impact of receiving *atypical* pharmacogenomic results within a sample of consumers who all received pharmacogenomic reports.

### Personal Genomic Testing Results

Participants received pharmacogenomic information within their comprehensive PGT reports. 23andMe customers received up to 8 pharmacogenomic results, presented as a relative risk for each adverse outcome (or relative benefit for treatment efficacy traits) compared to someone in the general population of the same ethnicity. Pathway customers received up to 9 pharmacogenomic results, presented as either “normal,” “beneficial effect,” or “adverse effect.”

### Statistical Analyses

Data were obtained from PGen Study participants who submitted both baseline and 6-month surveys, and who had complete data for age, gender, race/ethnicity, education, self-reported health, interest in pharmacogenomic PGT results, baseline prescription medication use, and changes to prescription medications post-PGT. Analyses were restricted to those participants whose pharmacogenomic results were available to researchers. Pharmacogenomic results were classified as either *atypical response* (increased relative risk of an adverse drug event; increased or decreased likelihood of therapeutic benefit) or *typical response* (average risk of an adverse event; typical therapeutic response). We summarized baseline participant characteristics, and frequency of *atypical response* results and post-PGT prescription medication changes, with descriptive statistics.

We performed logistic regression of ‘reporting any change to a prescription medication’ (and in separate models, each type of change) on the number of *atypical response*

pharmacogenomic results received. We used similar models to test the association of *atypical response* results with: (1) sharing PGT results with a health care provider; and (2) undergoing additional tests, exams, or procedures post-PGT. Finally, we performed linear regression of ‘change in number of health care visits from pre-PGT to post-PGT’ on number of *atypical response* pharmacogenomic results received. The number of visits in the past year reported at baseline was divided by 2 for this analysis.

Analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC), and models were fitted using PROC GLM (linear regression) and PROC LOGISTIC (logistic regression). Models of post-PGT outcomes were adjusted for age, gender, race/ethnicity, education, health insurance status, PGT company, self-reported health, and baseline interest in pharmacogenomic results. The model for change in mean health care visits was additionally adjusted for number of health care visits reported at baseline (divided by 2). Because household income is associated with both health services utilization<sup>17</sup> and prescription medication adherence,<sup>18</sup> we evaluated the impact of adjusting for income in those participants for whom these data were available. Statistical significance was set at  $p < 0.05$ .

### Qualitative Analyses

Free text responses to the question about medication changes were reviewed by DAC for two themes: use of pharmacogenomic results to guide medication changes; and use of other PGT results to guide medication changes.

## RESULTS

### Participants and Pharmacogenomic Results

Thirty-nine participants were excluded due to missing data on self-reported health ( $n = 2$ ) or post-PGT prescription medication changes ( $n = 37$ ). A further 42 participants (all from 23andMe) were excluded because their pharmacogenomic results were not available to researchers. These participants had 1+ genetic relatives with a linked 23andMe account – i.e., relatives who had ordered 23andMe testing prior to or following the PGen Study, and indicated a familial relationship during registration. Given the possibility of revealing personal information about individuals who did not consent to the PGen Study, the genetic results of participants with linked relatives were withheld by 23andMe. Baseline socio-demographic characteristics of the final sample ( $n = 961$ ) are shown in Table 1. Of these 961 participants, 876 (91.2%) received at least one result indicating atypical drug response (mean =  $1.81 \pm 1.04$ , range = 0 – 5) (Table 2).

### Post-PGT Prescription Medication Changes

Fifty-four participants (5.6% of 961) reported changing a prescription medication they were already taking, or starting a new medication, by 6-month follow-up (Table 3). Of these, 46 (85.2%) reported consulting a health care provider before doing so. Among those who reported baseline use of a prescription medication within the measured categories ( $n = 537$ ), 39 (7.3%) reported a change to a prescription medication they were already taking, and 34 of them (87.2%) reported consulting a health care provider.

We observed a significant association between *atypical response* pharmacogenomic results and reported prescription medication changes (Table 4): for each *atypical response* result received, participants had a 1.57 times greater odds (95% CI = 1.17 – 2.11) of reporting a change to a prescription medication within 6 months of undergoing PGT. This relationship held for all specific types of medication changes with the exception of raising the dose of a medication (Table 5). Due to the small number of events per change category, and concerns about model instability, here we adjusted for only those variables that were significantly associated with changing a prescription medication in the main model, plus PGT company.

Looking ahead, 166 participants (17.3% of 961) did not think they would use their results to guide their future use of medication, while 471 (49.0%) thought they would, and 324 (33.7%) did not know. Within these three groups (no/yes/not sure), the frequency of having received at least one atypical drug response result was 85.5%, 94.5%, and 89.2%, respectively, while the frequency of having already reported making a change to a prescription medication at 6-month follow-up was 0.6%, 10.8%, and 0.6%, respectively.

### Post-PGT Health Services Usage

Forty-nine participants did not discuss their results with anyone. Overall, 336 (35.0% of 961) reported sharing with a health care provider, including 260 (27.1%) with a primary care provider, 31 (3.2%) with a genetics specialist, and 157 (16.3%) with a different medical professional. Other medical professionals with whom participants reported sharing their results included a/an: physician assistant, nurse, or medical assistant (n = 32), obstetrician/gynecologist (17), oncologist (10), surgeon (10), anesthesiologist (4), pediatrician/child's physician (4), nutritionist (3), reproductive endocrinologist (2), and other specialist (115, encompassing a variety of free-form responses).

Follow-up tests, examinations, and procedures based on PGT results were reported by 105 (10.9% of 961) participants. Among the 752 participants for whom data were available at both time points, the median number of health care visits in the 6 months both prior to and following PGT was 2.0 (Wilcoxon signed rank test: S-statistic = 567; p = 0.90). There was no significant association between the number of positive pharmacogenomic results received and any of these post-PGT outcomes after multivariable adjustment (Table 4).

### Qualitative Data and Case Studies

Thirty-eight of the participants who reported changing a prescription medication provided free-text responses regarding their motivations (Table S1). Of these, 15 made reference to a pharmacogenomic result motivating their medication change. For example, a 59-year-old with an increased risk of methotrexate toxicity reported:

[My] [d]octor had planned on putting me on methotrexate for inflammation at my next office visit, but once he [saw] the genome study he decided to put me on a different drug instead, which has worked well without the side effects.

Four responses attributed the change to some other personal genomic testing result. For example, a 46-year-old whose PGT results indicated an elevated risk of coronary heart disease reported:



The heart disease possibility lead [*sic*] to the comprehensive blood panel test, which showed I'm off the charts when it comes to cholesterol. This resulted in prescriptions for Crestor [rosuvastatin] and Niaspan [niacin].

Twenty responses did not reference a specific PGT result. As further examples of the types of medication changes reported, two cases are presented below:

*Case 1:* Ms. X is a Caucasian woman in her 50s who reported baseline use of medication for heart disease, anxiety/depression, diabetes, high cholesterol, and menopause symptoms. She also reported a family history of heart disease and high cholesterol. Ms. X received two atypical pharmacogenomic results: an increased likelihood of statin therapeutic benefit, and an increased risk of statin-induced myopathy. She explains: "Since I am sensitive to statins but have high cholesterol/triglycerides, I decided to cut my TriCor [fenofibrate] dosage to every other day." She did not consult with her physician before making this change.

*Case 2:* Ms. Y is a Caucasian woman in her 30s who reported baseline use of oral contraceptives. Ms. Y received three atypical pharmacogenomic results: increased metabolism of warfarin; reduced efficacy of treatment for Hepatitis C; and increased risk of venous thromboembolism with estrogen supplementation. She explains that she "[s]topped taking birth control for a trial period and [is] now starting back on a lower dose due to increased risk for venous thromboembolism." She reports consulting with her physician regarding this change.

## DISCUSSION

Among DTC-PGT customers enrolled in the PGen Study, 91.2% received at least one pharmacogenomic result indicating atypical drug metabolism, a proportion consistent with prior estimates. For example, a 2014 study<sup>19</sup> found that, among 9,589 hospital patients offered preemptive genotyping for 5 drug-gene interactions, 8,760 (91.4%) received at least one positive result. Further roll-out of pharmacogenomic testing in the general population, whether commercial or clinic-based, could have a far-reaching impact given the likelihood of identifying atypical variants in most individuals.

Fewer than 6% of participants changed a prescription medication in response to their PGT results 6 months post-testing, and <1% reported doing so without consulting a health care provider. A 2012 cross-sectional, post-testing survey of PGT customers from three companies<sup>6</sup> found similar self-reported rates of medication changes: among 1,048 customers, 4.4% reporting changed a prescription medication, and 0.4% reported doing so without consulting a physician. While the infrequency of medication changes made without provider consultation is encouraging, it should be reiterated that the definition of "health care provider" was not specified; therefore, some participants may have reported interactions with non-prescribing professionals (e.g., nurses, alternative medicine practitioners).

Here, the number of atypical pharmacogenomic results received was associated with the probability of changing a prescription medication post-PGT; on the other hand, participants' explanations of what prompted these changes made clear that *other* PGT results (e.g., genetic risk estimate for coronary heart disease) and post-PGT follow-up care (e.g., serum

cholesterol testing) also played a role. Future evaluations of the impact of DTC-PGT on prescription medication should consider the broader testing experience, including non-pharmacogenomic results and any clinical follow-up that may lead to changes to a consumer's prescription medication regimen.

The potential utility of pharmacogenomic results is limited by the pharmacological treatment needs of a particular individual at a particular time. This may explain, in part, why so few participants – relative to the 91.2% receiving a positive pharmacogenomic result, and the 49.0% who predict using their results to guide future medication decisions – reported changing a prescription medication in our study. Moreover, despite inclusion of pharmacogenomic information on an increasing number of product inserts, use of genetic testing to guide medication selection and dosing remains limited.<sup>20</sup> Why participants did or did not believe that they would use their pharmacogenomic results to guide future use of medication is unclear, although participants who thought they would use their results in the future had more frequently received an atypical drug response result and more frequently reported already having made a medication change by 6-month follow-up. Multiple explanations for these trends are plausible: e.g., consumers may believe that atypical response results are inherently more “actionable” than typical response results; consumers who have already made some change prompted by their results may as a result be more optimistic about their future potential; or certain consumers may simply be more likely to engage with and utilize their PGT results in managing their own health care, both immediately following testing and in the future, due to personal characteristics or their original motivations for seeking PGT.

In a recent study of DTC pharmacogenomic testing, Bloss *et al.* reported that, compared to participants who had not yet received their pharmacogenomic results, those that had received them reported more physician visits, higher rates of sharing their results with a physician, and more physician-ordered follow-up services.<sup>8</sup> Although Bloss *et al.* do not attempt to explain why receipt of pharmacogenomic information prompts greater health services usage in their study, they do suggest that pharmacogenomic information may be more likely than other PGT-derived information (e.g., disease risk estimates) to be added to the medical record (because of its perceived actionability), and – therefore – more likely to be used in medical decision making. If these explanations are correct, then we might reasonably expect atypical drug response (“red flag”) results to more acutely motivate medical interactions and interventions than typical drug response results. Our study, however, which finds no association between receipt of atypical pharmacogenomic results and these same health care outcomes, add a layer of complexity to this picture: although receipt of pharmacogenomic information, generally, may lead to increased healthcare utilization, the content of those results appears, in fact, to play a limited role in this effect. Population characteristics could also explain the lack of observed effect: for example, the mean of nearly 7 reported health care visits in the past year within our sample is higher than expected in the United States population,<sup>21</sup> and the distribution of this variable suggests our estimates are disproportionately influenced by a small number of high-frequency health care users. Our study further provides anecdotal evidence of both potential harms and potential benefits to consumers of DTC pharmacogenomic testing. In Case 1, a consumer reduces, without physician consultation, her dose of a cholesterol-lowering fibrate in response to a result



indicating increased risk of myopathy from statins. The consumer has therefore misinterpreted her PGT results and applied them too broadly: there is currently no evidence from the Pharmacogenomics Knowledgebase (PharmGKB)<sup>22</sup> of an effect of the statin-related SNPs for which this consumer was tested on drugs in the fibrate class. Given this consumer's reported personal and family history of heart disease, diabetes, and cholesterol, the risk of adverse health outcomes associated with failure to adhere to her cholesterol-lowering medication regimen likely far exceed the probability of statin-induced myopathy (if she were taking a statin).<sup>23</sup>

Case 2, meanwhile, highlights the potential for DTC-PGT to democratize access to genetic information<sup>24</sup> and motivate patient engagement: here, a consumer and her provider together decide to lower her dose of oral contraceptives, in response to an increased risk of deep vein thrombosis with estrogen supplementation. On the other hand, genetic screening for thrombosis risk prior to prescription of estrogen-containing oral contraceptives is not currently recommended in the absence of a family history due to the low absolute risk of thrombosis, even among those with a genetic predisposition.<sup>25</sup> Existing guidelines do, however address incorporation of genetic risk information when already known: in the absence of a family history, women using estrogen-containing oral contraceptives should avoid additional risk factors, such as obesity and smoking; in the presence of a family history, women should avoid estrogen-containing oral contraceptives altogether.<sup>26</sup> Given that that family history of thrombosis is often unknown or unreliable,<sup>27</sup> and that equally effective low-estrogen and non-estrogen-containing contraceptive options exist, one could argue that regardless of the clinical utility of population screening for thrombosis risk, PGT has, for this consumer, provided a tangible benefit in the form of a patient-physician dialogue and informed decision-making about the use of estrogen.

Strengths of the PGen Study include the longitudinal collection of data, recruitment of new customers from two leading PGT companies, and incorporation of individual-level genetic information with extensive survey data. Limitations include the potential for selection bias due to the collection of voluntary survey data, and the exclusion of participants from certain analyses due to missing data. In addition, our sample may not be typical of the DTC-PGT consumer population circa 2012 because of the recruitment strategies employed, in particular for Pathway customers. Users of a health-based social networking site were directly targeted and offered subsidized testing, and therefore we may expect some enrichment of our sample for individuals who would not typically have pursued testing independently, owing to a lack of awareness or sensitivity to price.

Our post-PGT measures are limited to 6 months of follow-up, encompass the effects of all PGT-obtained genetic risk information (not only pharmacogenomic information), and rely entirely on self-report; these outcome measures could be improved by the incorporation of medical records data. However, since we were particularly interested in determining the frequency of prescription medication changes made *without* clinician involvement, self-reported data collection was essential. Further, owing to the way in which prescription medication changes and physician consultation were measured, we were unable to identify those participants who may have *considered* making a prescription medication change, but consulted with a health care provider and ultimately decided against making the change.

Therefore, the role of the health care provider in post-PGT decision-making surrounding prescription medications is likely not fully captured in our study.

Finally, our findings may be generalizable to consumers obtaining pharmacogenomic information via DTC-PGT (although it should be noted that as of 2016, neither 23andMe nor Pathway currently offer pharmacogenomic testing via the DTC model), but are likely not applicable to recipients of clinician-mediated pharmacogenomic testing. PGen Study participants tended to be high-earning, frequent prescription medication users, with high levels of health insurance coverage; thus, how pharmacogenomic information is used by consumers to self-manage their care may differ in groups without these qualities, particularly among those with low income or poor insurance coverage of prescription medications.

In conclusion, receipt of positive pharmacogenomic results via direct-to-consumer personal genomic testing is associated with post-testing prescription medication changes, but the proportion of consumers who report making such a change in the 6 months following testing is small. Further investigation of how physician consultation in the post-PGT period motivates, or discourages, such changes is warranted.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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‡Non-author members of the PGen Study at the time of publication are as follows: Joel B Krier, Margaret H Helm, Sarah S Kalia, Kurt D Christensen, Lisa S Lehmann, Harvard Medical School and Brigham and Women's Hospital; Mack T Ruffin IV, Lan Q Le, Jenny Ostergren, University of Michigan School of Public Health; Wendy R Uhlmann, Mick P Couper, University of Michigan; Joanna L Mountain, Amy K Kiefer, 23andMe; Adrian Vilalta, Pathway Genomics; Scott D Crawford, Survey Sciences Group; L Adrienne Cupples, Clara A Chen, Catharine Wang, Boston University; Stacy W Gray, Dana-Farber Cancer Institute; Barbara A Koenig, University of California San Francisco; Kimberly Kaphingst, University of Utah; Sarah Gollust, University of Minnesota.

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**Table 1**

Baseline characteristics of PGen Study Participants (n = 961)

	No.	%
Male	385	40.1
Race		
Caucasian	824	85.7
African-American	23	2.4
Asian	32	3.3
>1 Race/Other	82	8.5
Hispanic/Latino ethnicity	48	5.0
Highest Level of Education		
< College degree	196	20.4
College degree	295	30.7
Some graduate school	342	35.6
Doctoral-level degree	128	13.3
Annual Household Income		
< \$40,000	166	17.3
\$40,000 – \$69,999	176	18.3
\$70,000 – \$99,999	199	20.7
\$100,000 – \$199,999	288	30.0
\$200,000	121	12.6
Missing	11	1.1
Health Insurance		
Yes	916	95.3
No	43	4.5
Unsure	2	0.2
Personal Genomic Testing Company: Pathway	384	40.0
Any Prescription Medication Use	537	55.9
Blood thinners	69	7.2
Heart disease	209	21.8
Anxiety/depression	259	27.0
Diabetes	39	4.1
High cholesterol	176	18.3
Menopause symptoms <sup>a</sup>	55	9.5
Oral contraceptives <sup>a</sup>	104	18.1
Self-Reported Health		
Excellent	142	14.8
Very Good	385	40.1
Good	288	30.0
Fair	107	11.1
Poor	39	4.1
Interest in Pharmacogenomic Results		

	No.	%
Not at all interested	74	7.7
Somewhat interested	362	37.7
Very interested	525	54.6

  

	mean $\pm$ standard deviation (range)
Age, years	46.6 $\pm$ 15.6 (19–94)
Health Care Visits in the Last Year <sup>b</sup>	6.8 $\pm$ 8.6 (0–75)

<sup>a</sup>Evaluated among women only (n = 576)

<sup>b</sup>n = 752; includes only participants who reported having a physical exam within the past 2 years

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**Table 2** Pharmacogenomic results in the PGen Study, stratified by personal genomic testing company (n = 961)

Drug/Response Tested	23andMe (n = 577)						Pathway (n = 384)					
	SNPs Tested			Results, n (%)			SNPs Tested			Results, n (%)		
	N/A <sup>a</sup>	TYP	ATYP	N/A <sup>a</sup>	TYP	ATYP	N/A <sup>a</sup>	TYP	ATYP	N/A <sup>a</sup>	TYP	ATYP
Abacavir ↑Risk: hypersensitivity reaction	rs2395029	1 (0.2)	541 (93.7)	35 (6.1)	rs3828917	0 (0.0)	356 (92.7)	28 (7.3)				
Clonidine ↓Efficacy	rs4244285, rs4986893, rs28399504, rs12248560, rs41291556	55 (9.5)	422 (73.2)	100 (17.3)	rs4244285, rs4986893	0 (0.0)	279 (72.7)	105 (27.3)				
Warfarin ↑Dose Sensitivity	rs12777823, rs1799853, rs1057910, rs9923231	3 (0.5)	137 (23.7)	437 (75.8)	rs1799853, rs1057910, rs9923231	1 (0.3)	210 (54.7)	173 (45.0)				
Estrogen Supplementation ↑Risk: venous thromboembolism	rs6025, rs1799963, rs505922	263 (45.6)	291 (50.4)	23 (4.0)	rs6025, rs1799963	120 (31.2)	246 (64.1)	18 (4.7)				
Pegylated interferon-α regimens ↓Efficacy	rs8099917	0 (0.0)	366 (63.4)	211 (36.6)	---	---	---	---				
Fluorouracil ↑Risk: toxicity	rs3918290	0 (0.0)	570 (98.8)	7 (1.2)	---	---	---	---				
Succinylcholine ↑Risk: postanesthesia apnea	rs1799807, rs28933389, rs28933390	0 (0.0)	550 (95.3)	27 (4.7)	---	---	---	---				
Thiopurines and purine analogs ↑Risk: toxicity	rs1800462, rs1800460, rs1142345	0 (0.0)	526 (91.2)	51 (8.8)	---	---	---	---				
Aminoglycoside antibiotics ↑Risk: ototoxicity	---	---	---	---	rs267606617	0 (0.0)	383 (39.9)	1 (0.1)				
Carbamazepine ↑Risk: hypersensitivity reaction	---	---	---	---	rs3909184, rs2844682	0 (0.0)	380 (99.0)	4 (1.0)				
Methotrexate ↑Risk: toxicity	---	---	---	---	rs1801133	0 (0.0)	167 (43.5)	217 (56.5)				
Statins ↑Efficacy	---	---	---	---	rs20455	0 (0.0)	149 (38.8)	235 (61.2)				
Statins ↑Risk: myopathy	---	---	---	---	rs4149056	233 (60.7)	143 (37.2)	8 (2.1)				

Abbreviations: N/A, not applicable; TYP, typical drug metabolism/response result; ATYP, atypical drug metabolism/response result; SNP, single nucleotide polymorphism

<sup>a</sup>Some individuals were not eligible to receive certain results due to gender or ethnicity.

Reported changes to prescription medications 6 months after personal genomic testing, stratified by health care provider consultation status (n = 961)

**Table 3**

	Consulted HCP		Did not consult HCP		Total	
	n	%	n	%	n	%
Any reported change to a prescription medication	45	4.7	9 <sup>a</sup>	0.9	54	5.6
Started taking a medication	13	1.4	0	0.0	13	1.4
Stopped taking a new medication	23	2.4	5	0.5	28	2.9
Raised the dose of a current medication	5	0.5	0	0.0	5	0.5
Lowered the dose of a current medication	11	1.1	2	0.2	13	1.4
Switched from one medication to another	14	1.5	1	0.1	15	1.6

Abbreviations: HCP, health care provider

<sup>a</sup> 1 participant who reported making a change to a prescription medication without consulting a HCP did not indicate that any of these specific changes were made.

**Table 4**

Regression of post-PGT health care outcomes on number of atypical response pharmacogenomics results received

	Univariable	Multivariable <sup>a</sup>	Multivariable with Income
Events/Sample Size, n		OR <sup>b</sup> (95% CI) p-value	
Made a change to a prescription medication			
54/961	1.65 (1.28, 2.12)	1.53 (1.14, 2.04)	1.57 (1.16, 2.11) <sup>d</sup>
	< 0.001	0.004	0.003
Shared personal genomic testing results with a health care provider			
336/912	1.24 (1.09, 1.41)	1.12 (0.97, 1.30)	1.14 (0.99, 1.32) <sup>e</sup>
	0.001	0.11	0.07
Had tests, exams, or procedures as a result of genomic information			
105/961	1.14 (0.94, 1.39)	1.08 (0.88, 1.33)	1.07 (0.87, 1.33) <sup>d</sup>
	0.17	0.47	0.51
Sample Size		$\beta$ <sup>b</sup> (95% CI) p-value	
Change in mean number of health care visits per year <sup>c</sup>			
752	0.05 (-0.29, 0.40)	0.03 (-0.32, 0.38)	0.07 (-0.29, 0.42) <sup>f</sup>
	0.76	0.88	0.71

Abbreviations: CI, confidence interval; OR, odds ratio; PGT, personal genomic testing

<sup>a</sup>Multivariable models adjusted for baseline age, gender, race, ethnicity, education, health insurance status, self-reported health, interest in pharmacogenomic information, and PGT company.

<sup>b</sup>Odds-ratio/mean change per positive pharmacogenomic test result received

<sup>c</sup>Additionally adjusted for frequency of health care visits at baseline

<sup>d</sup>n = 950 due to missing data on income for 11 participants

<sup>e</sup>n = 902 due to missing data on income for 10 participants

<sup>f</sup>n = 744 due to missing data on income for 8 participants

**Table 5**

Logistic regression of specific medication changes reported post-PGT on number of atypical response pharmacogenomic results received (n = 961)

	Events, n	Univariable	Multivariable <sup>a</sup>
		OR (95% CI) p-value	OR (95% CI) p-value
Started taking a medication	13	2.11 (1.29, 3.44) 0.003	2.01 (1.18, 3.42) 0.01
Stopped taking a new medication	28	1.62 (1.15, 2.29) 0.005	1.48 (1.02, 2.16) 0.04
Raised the dose of a current medication	5	0.53 (0.20, 1.39) 0.19	0.46 (0.16, 1.32) 0.15
Lowered the dose of a current medication	13	2.11 (1.29, 3.44) 0.003	1.94 (1.14, 3.30) 0.02
Switched from one medication to another	15	2.31 (1.46, 3.66) < 0.001	2.10 (1.24, 3.54) 0.006

Abbreviations: CI, confidence interval; OR, odds ratio; PGT, personal genomic testing

<sup>a</sup>Multivariable models adjusted for age, gender, hispanic ethnicity, self-reported health, and PGT company.