Published in final edited form as:

Clin Pharmacol Ther. 2017 July ; 102(1): 106–114. doi:10.1002/cpt.586.

Patient perceptions of care as influenced by a large institutional pharmacogenomic implementation program

Ryan P. McKillip¹, Brittany A. Borden², Paige Galecki², Sandra A. Ham³, Linda Patrick-Miller⁴, Julianne P. Hall², Sheena Hussain², Keith Danahey^{2,5}, Mark Siegler^{2,4,6,7}, Matthew J. Sorrentino^{2,4}, Yasmin Sacro^{2,4}, Andrew M. Davis^{2,4}, David T. Rubin^{2,4}, Kristen Lipstreuer^{2,4}, Tamar S. Polonsky^{2,4}, Rita Nanda^{2,4}, William R. Harper^{2,4}, Jay L. Koyner^{2,4}, Deborah L. Burnet^{2,4}, Walter M. Stadler^{2,4}, Mark J. Ratain^{2,4,7}, David O. Meltzer^{3,4}, and Peter H. O'Donnell^{2,4,7}

¹The University of Chicago Pritzker School of Medicine, Chicago, Illinois, USA

²Center for Personalized Therapeutics, The University of Chicago, Chicago, Illinois, USA

³The Center for Health and the Social Sciences, The University of Chicago, Chicago, Illinois, USA

⁴Department of Medicine, The University of Chicago, Chicago, Illinois, USA

⁵Center for Research Informatics, The University of Chicago, Chicago, Illinois, USA

⁶MacLean Center for Clinical Medical Ethics, The University of Chicago, Chicago, Illinois, USA

⁷Committee on Clinical Pharmacology and Pharmacogenomics, The University of Chicago, Chicago, Illinois, USA

Abstract

Despite growing clinical use of genomic information, patient perceptions of genomic-based care are poorly understood. We prospectively studied patient-physician pairs who participated in an institutional pharmacogenomic implementation program. Trust/Privacy/Empathy/Medical Decision-Making (MDM)/Personalized Care (PC) dimensions were assessed through patient surveys after clinic visits at which physicians had access to preemptive pharmacogenomic results (Likert scale, 1-minimum/5-maximum; mean [SD]). From 2012–2015, 1,261 surveys were issued to 507 patients, with 792 (62.8%) returned. Privacy, Empathy, MDM and PC scores were significantly higher following visits when physicians considered pharmacogenomic results. Importantly, PC scores were significantly higher after physicians used pharmacogenomic

Correspondence: Peter H. O'Donnell, 5841 S. Maryland Ave, MC 2115, Chicago, IL 60637, phone: 773-702-4400, FAX: 773-702-3163, podonnel@medicine.bsd.uchicago.edu.

AUTHOR CONTRIBUTIONS

R.P.M. and P.H.O. wrote the manuscript; L.P.M., M.J.R., D.O.M., and P.H.O. designed the research; R.P.M., B.A.B., P.G., J.P.H., S.H., K.D., M.S., M.J.S., Y.S., A.D.M., D.T.R., K.L., T.S.P., R.N., W.R.H., J.L.K., D.L.B., W.M.S., and P.H.O. performed the research; R.P.M., B.A.B., P.G., S.A.H., J.P.H., S.H., K.D., and P.H.O. analyzed the data; K.D., D.O.M., and P.H.O. contributed new analytical tools.

CONFLICT OF INTEREST

Dr. O'Donnell, Dr. Ratain, and K. Danahey are named as co-inventors on a pending patent for the Genomic Prescribing System and are co-founders of PrescriptIQ, Inc. Dr. Ratain is a coinventor holding patents related to pharmacogenetic diagnostics and receives royalties related to *UGT1A1* genotyping. No royalties were received from the genotyping performed in this study.

SUPPLEMENTARY MATERIAL

Supplementary information is available at the *Clinical Pharmacology & Therapeutics* website.

information to guide medication changes (4.0[1.4] vs. 3.0[1.6], $P<0.001$) compared to prescribing visits without genomic guidance. Multivariable modeling controlling for clinical factors confirmed PC scores were more favorable following visits with genomic-influenced prescribing (OR=3.26 [1.31–8.14], $P<0.05$). Physicians appear to individualize care when utilizing pharmacogenomic results and this decision-making augmentation is perceived positively by patients.

Keywords

pharmacogenomics; implementation; patient-reported outcomes; attitudes/perceptions; precision medicine

INTRODUCTION

Pharmacogenomics is positioned to play a significant role in the advancement of personalized medicine due to its ability to inform medication choices based on a patient's individual genetic profile. The clinical application of pharmacogenomics has begun, and has the potential to change many aspects of medicine including the doctor-patient relationship and patient perceptions of care^{1,2}. Both the rate of adoption of pharmacogenomics for clinical use and the extent of any impact on the doctor-patient relationship will depend in part on patient attitudes toward the practice³.

Investigations of patient receptiveness to pharmacogenomic testing have revealed varying levels of interest. Previous research has shown that, while patients are generally receptive to pharmacogenomic testing, they often indicate privacy, cost, the risk of learning unwanted ancillary information, or the risk for insurance or employment discrimination as concerns or reasons for not consenting^{3–6}. As reported by Mikat-Stevens et al.⁷, primary care providers cite these same patient concerns as the primary ethical, legal, and social barriers to the integration of genetic testing into clinical practice^{8–13}. By interrogating only genes that are putatively important in drug prescribing, the ethical, legal, and social implications of pharmacogenomics are considered to be potentially less critical compared to other genetic tests¹. Therefore, many groups have proposed pharmacogenomics as a sensible starting point for introducing genetic testing to patients^{1,14,15}. However, there has been little investigation as to whether patient concerns are at all assuaged once pharmacogenomic information has been integrated into practice.

A prior survey-based study of 387 patients found that patients presented with a hypothetical pharmacogenomics-guided prescribing vignette reported lower medication adherence intention than those participants who were presented with a standard (non-pharmacogenomics-guided) prescribing vignette. Other aspects of the doctor-patient relationship, such as trust and perceived respect, were not significantly different between the two prescribing scenarios¹⁶. To date, no study has investigated these topics specifically in patients that have experienced care under a preemptive pharmacogenomics clinical model.

The objective of our study was to test whether incorporating pharmacogenomics into clinical decision making can improve patient perceptions of care. We utilized the infrastructure of a large preemptive pharmacogenomics implementation project at the University of Chicago,

the 1,200 Patients Project¹⁷. We hypothesized that the availability of patient-specific pharmacogenomic test results during care would improve patient perceptions of care, indicated by more favorable patient ratings of interactions with their provider.

RESULTS

Genotyped and non-genotyped patients represented those under the care of one or more of 17 participating providers across a diverse set of primary care and medicine subspecialty clinics (all 17 providers who were invited to participate agreed, and all providers recruited patients to this study). Of all case (genotyped) patients enrolled in the 1,200 Patients Project, 507 made at least one clinic visit during the study period and met survey eligibility requirements (see Supplementary Table 1 for criteria for survey administration). One thousand two hundred sixty-one surveys (1,261) were provided to the 507 case patients, and 792 (62.8%) were returned and eligible for analysis by 409 patients. Separately, of the 218 surveys provided to 159 control patients, 111 (50.9%) were returned and analyzable by 80 patients. The demographics of case and control patients that submitted analyzable surveys are shown in Table 1. Respondents were 52% female, averaged 63.7 years in age, and were predominantly white (62%). Education level, self-reported health, satisfaction with provider, and physician estimated time available were significantly different between the groups. Demographic characteristics were similar between case patients who returned at least one survey versus those who never returned a survey, with the exception that those who did not return at least one survey were younger (mean age 64.1 vs. 58.8, $P=0.002$) and had a higher predominance of African American patients (41.8% vs. 25.3%; Supplementary Table 2). Demographic characteristics were also similar between the control patients who did and did not return surveys, with the exception that the estimated provider minutes available were higher for patients who did not return surveys (26.4 vs. 23.2, $P=0.007$; Supplementary Table 2). The overall survey response rate of case patients was statistically higher than control patients (62.8% vs. 50.9%, $P<0.001$).

The median number of surveys submitted by case patients was 2 (range 1 – 12) and by control patients was 1 (range 1 – 4). Overall, patients scored physicians favorably. The lowest scoring dimension was Personalized Care, which also had the most variation among patients, with a mean score and standard deviation [SD] across all patient surveys of 3.0 [1.5]. Empathy and Medical Decision-Making (MDM) were the highest scoring dimensions and both dimensions showed the least variability among patients' ratings, with mean values of 4.8 for both and SDs of 0.6 and 0.4, respectively.

When analyzing the validity of the customized instrument for assessing five dimensions of the doctor-patient relationship, it was found that Empathy dimension scores positively correlated with self-reported health and satisfaction with physician ($P<0.01$). Trust dimension scores showed positive correlation with age and satisfaction with physician ($P<0.01$). These patterns are similar to those of established empathy and trust measurement tools^{18,19}.

Provider's Use of the Genomic Prescribing System (GPS)

Providers logged into the GPS during 621 of the 792 clinic visits for which a survey was returned by a case patient (78.4%). Comparing these GPS Log In visits to No Log In visits, Privacy (4.2 [1.3] vs. 3.9 [1.5], $P<0.01$), Empathy (4.9 [0.4] vs. 4.8 [0.4], $P<0.001$), MDM (4.9 [0.3] vs. 4.8 [0.3], $P<0.01$), and Personalized Care (3.4 [1.6] vs. 2.5 [1.4], $P<0.001$) dimensions scored significantly higher if the provider accessed the GPS (Figure 1). A one point difference on the Likert scale, e.g. moving from 4.0 to 5.0, is equivalent to moving the average patient response from “Agree” to “Strongly Agree”. Changes at a similar scale have previously been associated with significant changes to clinical outcomes^{20–25}. To better understand this improvement in scores across several dimensions, we measured whether these visits were associated with longer clinical encounters, noting that the mean estimated provider minutes available was approximately 5.6 minutes higher for GPS Log In visits than No Log In visits (29.2 [9.1] vs. 23.6 [7.1], $P<0.001$). This suggests that physicians were more likely to use the GPS when more time was available for the encounter.

Of the 792 surveys returned by case patients, 263 (33.2%) related to clinic visits during which a medication change was made (stopping a drug, changing a dose, or starting a new prescription). Pharmacogenomic information provided by the GPS influenced a medication change at 70 of those 263 clinic visits (26.6%). Comparing dimension scores of Pharmacogenomic (PGx)-influenced Med Change visits to Traditional Med Change visits (medication changes made without the use of pharmacogenomics) identified the largest difference in dimension scoring in the entire study: Personalized Care (4.0 [1.4] vs. 3.0 [1.6], $P<0.001$) was a full point higher on average if the GPS was used to inform a medication change. Average Privacy, Empathy, and MDM dimension scores were also consistently higher after PGx-Influenced Med Change visits versus Traditional Med Change visits, however the differences were not statistically significant. Importantly, estimated provider minutes available was not significantly different between PGx-influenced Med Change visits and Traditional Med Change visits (26.9 [7.8] vs. 28.0 [10.2]).

Patients with Repeated Medication Change Visits

Eighteen case patients submitted at least one survey from both a PGx-influenced Med Change visit and a Traditional Med Change visit. Compared to clinic visits with a PGx-influenced Med Change, patients more strongly wished that their care was more individualized after Traditional Med Change visits (Figure 2). This coincided with significantly improved Personalized Care dimension scores after PGx-influenced Med Change visits compared to Traditional Med Changes among these patients (3.8 [1.5] vs. 2.8 [1.6], $P=0.023$). Trust, Privacy, Empathy, and MDM dimension scores were not significantly different between the two different types of encounters in these patients.

Case vs. Control

All five dimensions were rated higher by case patients than by control patients (Figure 3), coinciding with the underlying cohort composition differences that were observed. Trust (4.5 [0.7] vs. 4.0 [0.9], $P<0.01$), Privacy (4.0 [1.3] vs. 3.6 [1.3], $P<0.01$), and Personalized Care (3.1 [1.5] vs. 2.7 [1.5], $P<0.05$) scores from case patients were each at least 0.4 points higher on average versus control patients. Empathy (4.8 [0.6] vs. 4.6 [0.7], $P<0.01$) and MDM (4.9

[0.3] vs. 4.7 [0.7], $P<0.05$) dimension scores were also significantly higher in case patients, however the absolute differences compared to control patients were small (only 0.2 for each dimension).

Clinical Model

The percentages of encounters with an event of interest (score deemed high) ranged from Trust (62.5%) and Personalized Care (63.0%) to Privacy (74.8%), Empathy (86.6%), and MDM (89.1%). Many of the models showed null results when including all clinical covariates. However, even when including all clinical covariates, the multivariate model showed significantly higher Personalized Care scores associated with the use of pharmacogenomics (GPS Log In visits versus No Log Ins, Odds Ratio (OR)=1.83 [1.16 – 2.91, $P<0.05$]). Additionally, when comparing Personalized Care scores of GPS Log In visits to No Log In visits, year of encounter emerged as a significant covariate, with 2015 (later) encounters being associated with lower Personalized Care scores (OR=0.17 [0.09 – 0.35], $P<0.05$). Trust (OR=1.26 [0.83 – 1.92]), Privacy (OR=1.52 [0.97 – 2.38]), MDM (OR=0.92 [0.48 – 1.76]), and Empathy (OR=1.54 [0.86 – 2.75]) scores were not significantly different between GPS Log In and No Log In clinic visits.

Comparison of Personalized Care scores after PGx-influenced Med Changes to scores after Traditional Med Changes also identified important differences based on provider use of pharmacogenomics to inform prescribing. Even after controlling for other clinical factors, encounters with PGx-influenced Med Changes more often had high Personalized Care scores compared to Traditional Med Change visits (OR=3.26 [1.31 – 8.14], $P<0.05$) (Figure 4). As a means of determining whether this effect was likely due to the presence of pharmacogenomic information rather than simply being due to the fact that a medication change was occurring, we also compared Traditional Med Changes to visits when there was no medication change and found no significant differences in Personalized Care outcomes, (OR=1.22 [0.77 – 1.94]). Yet visits with PGx-influenced Med Changes were significantly more likely to have high Personalized Care scores compared to visits with no medication changes, (OR=3.98 [1.66 – 9.54], $P<0.05$). Lastly, similar to the prior finding, chronologically later encounters were also associated with lower Personalized Care scores, for both 2014 encounters (OR=0.52 [0.31 – 0.87], $P<0.05$) and 2015 encounters (OR=0.14 [0.07 – 0.28], $P<0.05$).

To account for the repeated measurements of patients with multiple surveys, as well as to understand whether these effects strengthened over time as patients' exposure to pharmacogenomic-based care grew, additional logistic regression models were run using only case and control patients' first surveys, as well as using the first surveys submitted by control patients and last surveys submitted by case patients. Comparing these models to our original results, there were two comparisons (Personalized Care scores after GPS Log In visits and after PGx-influenced Med Changes) that were no longer statistically significant, although the magnitude and directions of the effects were the same. The loss of statistical significance but not the loss of the relationship suggests that the ability to measure a statistical difference of the effect was simply not adequately powered with the first-last or first-first analyses (which excluded a number of surveys).

DISCUSSION

This prospective study demonstrates that making patient-specific pharmacogenomic information available to providers is strongly associated with improved patient perceptions of care. We found that providers deliver additional aspects of care individualization when accessing genomic results during prescribing, and that this augmentation in decision-making is perceptible to, and favorably viewed by, patients. Ours is the first study, to our knowledge, to prospectively explore the attitudes and perceptions of patients who are actively receiving care under a preemptive pharmacogenomics model.

The integration of genomic information into clinical practice depends on both patient attitudes regarding genetic testing as well as healthcare providers' understanding of the information^{26,27}. However, even when patients or providers might be positively inclined toward using genomic information to aid in decision-making, aspects of the doctor-patient relationship, such as trust, privacy, and perceived respect, may mediate or moderate the ultimate impact of precision medicine-guided care. Of the five dimensions of the doctor-patient relationship that were measured as part of this study, patient sentiment regarding Personalized Care stood out as being the most responsive to the use of pharmacogenomics. A primary appeal of pharmacogenomics to the public is the promise of tailored treatments that can enhance efficacy and reduce the likelihood of adverse effects^{4,6,28}. The improved Personalized Care dimension scores observed in this investigation indicate a positive response from patients to the ability of pharmacogenomics to deliver personalized medicine. Previous work has demonstrated that small changes to patient perceptions measured with similar survey tools can be associated with significant changes in clinical outcomes^{20–25}.

Trust and privacy findings were also intriguing. Trust scores, which measured a patient's belief that the provider had his or her best interest in mind when making clinical decisions, were not affected for the genotyped patients in this study by their providers' use of pharmacogenomics. Since trust scores were generally high to begin with among our genotyped patients, this may reflect the fact that patients already trusted their physician enough to be willing to consent to genotyping, and that the use of genomic information did not significantly amplify that level of trust. Notably, however, physician trust scores were significantly lower among the non-genotyped (control) patients in this study. This may reflect the fact that the treating physicians in this study were asked, in part, to enroll patients first for the genotyping group, and enrollment for the controls commenced later. This may have unintentionally led to patients with higher levels of trust in their physicians being selected by those physicians for genotyping, which itself may illustrate an important aspect of how the doctor-patient relationship impacts the actualization of precision medicine. Future randomized studies should examine this relationship in more detail.

In contrast, Privacy, which measured a patient's willingness to share personal genetic information, did correlate with the use of pharmacogenomics. Numerous prior studies have demonstrated that despite patients being generally receptive to the use of genetic information in their care, the public is often concerned with privacy of genetic information^{4,10,29,30}. The improved Privacy dimension scores in our investigation were observed in patients who consented for the 1,200 Patients Project and agreed to be genotyped—meaning these

patients knew this was a genomic study and therefore there was likely a higher general acceptance for use of genomic information. However, even among all patients who consented to be genotyped, patients were more amenable to openly discuss personal genetic information if physicians accessed the GPS. Understanding the direction of this effect will be important—is it that patients who are open to discussing/disclosing genetic information prompt their physicians to log-in and access genomic results? Or is it that patients who experience care under a genomically-guided model then develop increased comfort with sharing genetic information, once they see the potentially positive ways it can be used for their care by their provider? Qualitative studies by our group and others are ongoing to unravel these important questions. It is likely that both aspects—and both members of the doctor-patient relationship—will play integral roles in order to maximize the utility of precision medicine information.

We found that the mean estimated provider time available was approximately 5 minutes longer for GPS Log In visits than No Log In Visits. This may explain in part the broad improvement in scores after Log In visits in this study, but the finding most accurately suggests that physicians were perhaps more willing to use the GPS when more time was available for the encounter. Our findings do not necessarily demonstrate that providers actually spent more time in the room with a patient—only that more time was available—as time-in-room was not directly measured. Therefore, our data are consistent with the idea that either increased doctor-patient interaction time, and/or direct use of pharmacogenomics, or both, could have resulted in more favorable scores. To additionally consider this question, we also examined visits at which medication changes specifically occurred, and there was no difference in estimated provider minutes available for visits where pharmacogenomic results were used to influence the medication change (PGx-influenced Med Changes) versus visits at which pharmacogenomics were not used to influence medication changes (Traditional Med Change visits). Yet PGx-influenced Med Change visits had the highest improvement in patient-reported scores compared to Traditional Med Change visits for the entire study, strongly suggesting that it was not interaction time, but rather the availability and use of pharmacogenomic results that was perceived positively by patients.

This study had limitations. First, the providers and patients were part of a single, academic tertiary care institution, and thus may not be generalizable. Secondly, while our primary analysis involved only case patients who differed solely by whether their provider utilized or did not utilize pharmacogenomic results—and this analysis itself showed significant improvements in patient-reported measures across multiple domains for the ‘pharmacogenomics-utilized’ group—the secondary case-control comparisons, given the non-randomized design of this study, while also novel and notable, should importantly be measured and confirmed in future randomized studies. We are indeed currently planning a future randomized study which will incorporate these endpoints. Additional attempts to control for demographic differences between case and control patients in the secondary analyses were made by designing a multivariate clinical model, which incorporated numerous clinical factors potentially impacting the measured outcomes. For example, it was observed in our clinical model that later survey responses (2014, 2015) were also associated with lower Personalized Care scores. This may be a reflection of the enthusiasm for personalized medicine among patients who were the earliest enrollees, in contrast with the

patients who were later to enroll. Despite these differences, the salient observations from this study and the primary outcomes remained statistically and clinically significant for the pre-specified analysis of the case-only (genotyped) group, which avoided the potential biases of the non-randomized case-control comparisons. The survey response rate of case patients was 62.8%, which compares quite favorably with similar large scale studies examining patient-reported outcomes^{31–33}. Furthermore, while we cannot know the perspectives of non-responders definitively, the clinical and demographic characteristics of survey responders versus non-responders were nearly identical. Nevertheless, we cannot exclude the possibility that the 37.2% of case patients who did not return surveys may include patients who were overall more dissatisfied with their care. We do however note the consistency across our study's multiple analyzed dimensions showing scores either being superior or non-inferior when pharmacogenomics were incorporated. Lastly, although we observed associations that suggest that pharmacogenomics has a significant positive effect on patient perceptions of personalized care and other dimensions of the doctor-patient relationship, further work will be needed to confirm a causal relationship and to better understand the drivers (i.e., provider versus patient attitudes, or both) of those interdependencies.

A patient's willingness to consent to genetic testing can be complicated by multiple concerns of both the patient and the provider. Our results demonstrate that thoughtful integration of pharmacogenomic information at the point-of-care provides an opportunity to address patient concerns about trust, privacy, and MDM while enhancing a patient's sense that the doctor is providing individualized care. As the use of pharmacogenomics continues to expand, understanding more completely the effects on patient attitudes will become increasingly important for the design of appropriate implementation guidelines.

MATERIALS AND METHODS

1,200 Patients Project

The 1,200 Patients Project was created to more fully realize the possibilities of personalized medicine by offering broad, preemptive pharmacogenomic testing^{34,35}. The project's physicians were recruited by the study's principal investigator (P.H.O.), through a process of stakeholder interviews and informed consent. All 17 providers who were approached for participation agreed, representing a diverse set of specialties across medicine (eight general internists, three oncologists, two cardiologists, one hepatologist, one nephrologist, one gastroenterologist, and one pulmonologist). Patients were then recruited to the 1,200 Patients Project if they were receiving care from one of the participating physicians. Case patients were genotyped for selected markers that are associated with actionable pharmacogenomic information. The pharmacogenomic information specific to each case patient was shared with the patient's physician through an online web portal, which we refer to as the GPS^{34,35}. The GPS translated pharmacogenomic test results into clinical decision-support at the point-of-care. The medications included in GPS with actionable pharmacogenomic information have been previously reported³⁴. Control patients were enrolled concurrently with case patients but were not genotyped as part of the project. Additional details regarding the recruitment of case and control patients and sample size are included in the Supplemental Methods.

Clinic Assessments

Patients enrolled in the 1,200 Patients Project were given anonymous surveys to complete after clinic visits depending on certain criteria as outlined in Supplementary Table 1. Research staff independent of the providers gave surveys to case and control patients (after they saw their provider) to complete before leaving clinic. If patients were unable to complete the surveys in the clinic, they were mailed or emailed to patients within one week of the patient's visit. Surveys were solicited between October 2012 and May 2015. For each clinic visit, the research team monitored whether the physician logged in to the GPS, and captured (based on post-visit physician documentation, click log reviews of GPS use, and independent review of the electronic medical record) whether the pharmacogenomic information in the GPS influenced a medication change decision. At each clinic visit, it was the physician's decision whether to inform the patient if the GPS was accessed and if pharmacogenomic information was used. Details about how it was formally determined whether pharmacogenomic information altered a medication decision are included in the Supplemental Methods.

Survey Instruments

The surveys contained a customized instrument for assessing five dimensions of the doctor-patient relationship, including Trust, Privacy, Empathy, MDM, and Personalized Care. These dimensions were selected based on constructs suggested by a comprehensive literature review, discussion topics at several national pharmacogenomics meetings, feedback from relevant stakeholders, as well as relevance to personalized medicine and inclusion within existing doctor-patient relationship measurement tools³⁶. Previous work using similar measurement tools has shown that small differences in Likert-type scores can be associated with significant changes in clinical outcomes and patient adherence^{20–25}. Each dimension consisted of 1 to 4 questions, and responses were based on a 5 point Likert scale (Agree Strongly=5, Agree Somewhat=4, Not Sure=3, Disagree Somewhat=2, Disagree Strongly=1). Each dimension score was a mean of the sum of the questions in the dimension scale. In addition, the surveys asked patients to rate their current health and their overall satisfaction with their provider (see Supplementary Figure 1 for a copy of the full patient survey). Development and pre-testing of the survey was performed with members of the University of Chicago Survey Lab and Center for Health and the Social Sciences, and with additional external reviewers with experience in survey methodology. Revisions were made accordingly to produce the final version of the survey that was used in this study. Additional details on the development and pre-testing of the survey instruments are described in the Supplemental Methods.

Individual surveys were included in the analysis if at least half of the questions were completed. Individual questions that were left blank or answered inappropriately (e.g. multiple responses when only one was requested) were excluded from analysis of that item. Because enrollment into the genotyped versus non-genotyped cohort was non-randomized, the demographics of case and control patients were compared. Results of Trust and Empathy scores were compared with validated trust and empathy measurement tools based on their association with certain demographic characteristics^{18,19}. A similar exercise was not

performed for Privacy, MDM, and Personalized Care, as there were no existing and validated measurement tools known to the investigators.

Statistical Analysis

Trust, Privacy, Empathy, MDM, and Personalized Care dimension scores were calculated for each individual survey using the survey responses. For the primary analysis, we sought to identify whether responses varied depending on the provider's use of the GPS and the extent of such usage. Among the surveys returned by case patients, mean dimension scores were calculated for surveys associated with clinic visits in which the physician logged in to the GPS ("GPS Log In") and visits when the GPS was not utilized ("No Log In"). To learn whether dimension scores varied based on whether providers used GPS pharmacogenomic information to inform treatment decision-making, surveys associated with case patient clinic visits when a medication change was made (stopping, changing, or starting a new prescription) were identified. Mean dimension scores were calculated for surveys associated with clinic visits when the medication change was made using information in the GPS ("PGx-influenced Med Change") and from visits when the GPS did not influence the medication change ("Traditional Med Change"). Dimension scores of each group were compared using the Mann-Whitney two-sample rank-sum test in three separate analyses (case vs. control, GPS Log In vs. No Log In, and PGx-influenced Med Change vs. Traditional Med Change). Results are reported as mean [SD]. Additionally, case patients were identified who had submitted a survey for at least one clinic visit with a PGx-influenced Med Change and at least one clinic visit with a Traditional Med Change. This allowed for a comparison of dimension scores within a group of patients—who were all genotyped—for whom the only detectable variable between compared visits was the provider's use of GPS to inform a medication change. Dimension scores of PGx-influenced Med Change clinic visits were compared to Traditional Med Change visits using the Wilcoxon signed-rank test. A secondary analysis was performed in which dimension scores were compared between case and control patients. In instances when a respondent submitted multiple surveys because of having more than one clinic visit, responses were weighted so that each patient's total encounters counted as one patient.

A clinical model using logistic regression and mixed modeling was developed to evaluate factors associated with the selected dimensions and adjust for patient demographics and clustering effects of patients' physicians. Clinical and demographic characteristics included age, gender, race, education, number of medical problems, number of medications, self-reported health, extent of provider experience with the GPS, year of study, and overall satisfaction with provider. Dimension scores were dichotomized and logistic regression calculated the ORs associated with an event of interest (high score). For Trust, Empathy, and MDM, summed scales that averaged "agree somewhat" or less were the reference group, and sums that included any "agree strongly" were the event of interest. Personalized Care was dichotomized as "agree somewhat" or "agree strongly" versus non-agreement (reference group). Privacy was dichotomized similarly, including "not sure" in the event group. The same groups used in the Mann-Whitney rank-sum analyses were compared using the logistic regression. Given that multiple surveys were submitted by some patients, we performed additional modeling to further minimize clustering effects and understand whether a

measurable change occurred over time. These exploratory analyses were performed using only the first surveys submitted by case and control patients, as well as using the last visit for cases and the first visit for controls. All results are presented as OR with [95% confidence interval].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors wish to thank Susanne B. Haga, Ph.D. and Kenneth A. Rasinski, Ph.D. for their assistance and feedback during development of the survey instrument. This work was funded by The University of Chicago Pritzker School of Medicine Summer Research Program; National Institutes of Health (NIH) grants #5T35DK062719-28, K23 GM100288-01A1, and 5 U01 HL105198-09; The William F. O'Connor Foundation; The University of Chicago Bucksbaum Institute for Clinical Excellence; and a Central Society for Clinical and Translational Research Early Career Development Award.

References

1. Johnson JA. Pharmacogenetics in clinical practice: how far have we come and where are we going? *Pharmacogenomics*. 2013; 14:835–843. [PubMed: 23651030]
2. Hapgood R. The potential and limitations of personalized medicine in the doctor-patient relationship. *Pharmacogenomics*. 2003; 4:685–687. [PubMed: 14596632]
3. Lachance K, et al. Opinions, hopes and concerns regarding pharmacogenomics: a comparison of healthy individuals, heart failure patients and heart transplant recipients. *Pharmacogenomics J*. 2015; 15:13–19. [PubMed: 24980785]
4. Haga SB, O'Daniel JM, Tindall GM, Lipkus IR, Agans R. Survey of U.S. Public Attitudes Towards Pharmacogenetic Testing. *Pharmacogenomics J*. 2012; 12:197–204. [PubMed: 21321582]
5. Haddy CA, Ward HM, Angley MT, McKinnon RA. Consumers' views of pharmacogenetics--A qualitative study. *Res Social Adm Pharm*. 2010; 6:221–231. [PubMed: 20813335]
6. Haga SB, Tindall G, O'Daniel JM. Public Perspectives About Pharmacogenetic Testing and Managing Ancillary Findings. *Genet Test Mol Biomarkers*. 2012; 16:193–197. [PubMed: 22047505]
7. Mikat-Stevens NA, Larson IA, Tarini BA. Primary-care providers' perceived barriers to integration of genetics services: a systematic review of the literature. *Genetics in Medicine*. 2015; 17:169–176. [PubMed: 25210938]
8. Freedman AN, et al. US physicians' attitudes toward genetic testing for cancer susceptibility. *Am J Med Genet A*. 2003; 120A:63–71. [PubMed: 12794694]
9. Acheson LS, Stange KC, Zyzanski S. Clinical genetics issues encountered by family physicians. *Genet Med*. 2005; 7:501–508. [PubMed: 16170242]
10. Rogausch A, Prause D, Schallenberg A, Brockmüller J, Himmel W. Patients' and physicians' perspectives on pharmacogenetic testing. *Pharmacogenomics*. 2006; 7:49–59. [PubMed: 16354124]
11. Friedman LC, Cooper HP, Webb JA, Weinberg AD, Plon SE. Primary care physicians' attitudes and practices regarding cancer genetics: a comparison of 2001 with 1996 survey results. *J Cancer Educ*. 2003; 18:91–94. [PubMed: 12888383]
12. Walter FM, et al. Experiences and expectations of the new genetics in relation to familial risk of breast cancer: a comparison of the views of GPs and practice nurses. *Fam Pract*. 2001; 18:491–494. [PubMed: 11604369]
13. Robins R, Metcalfe S. Integrating genetics as practices of primary care. *Soc Sci Med*. 2004; 59:223–233. [PubMed: 15110415]

14. Aronson SJ, Rehm HL. Building the foundation for genomics in precision medicine. *Nature*. 2015; 526:336–342. [PubMed: 26469044]
15. Relling MV, Evans WE. Pharmacogenomics in the clinic. *Nature*. 2015; 526:343–350. [PubMed: 26469045]
16. Butrick M, et al. Patient reactions to personalized medicine vignettes: An experimental design. *Genet Med*. 2011; 13:421–428. [PubMed: 21270639]
17. O'Donnell PH, et al. Adoption of a clinical pharmacogenomics implementation program during outpatient care-initial results of the University of Chicago '1,200 Patients Project': AMERICAN JOURNAL OF MEDICAL GENETICS PART C (SEMINARS IN MEDICAL GENETICS). *American Journal of Medical Genetics Part C: Seminars in Medical Genetics*. 2014; 166:68–75.
18. Weng HC, et al. The effect of surgeon empathy and emotional intelligence on patient satisfaction. *Advances In Health Sciences Education: Theory And Practice*. 2011; 16:591–600. [PubMed: 21287265]
19. Thom DH, Ribisl KM, Stewart AL, Luke DA, et al. Further validation and reliability testing of the Trust in Physician Scale. *Medical care*. 1999; 37:510–517. [PubMed: 10335753]
20. Rakel D, et al. Perception of Empathy in the Therapeutic Encounter: Effects on the Common Cold. *Patient Educ Couns*. 2011; 85:390–397. [PubMed: 21300514]
21. Hojat M, et al. Physicians' empathy and clinical outcomes for diabetic patients. *Acad Med*. 2011; 86:359–364. [PubMed: 21248604]
22. Attar HS, Chandramani S. Impact of physician empathy on migraine disability and migraineur compliance. *Ann Indian Acad Neurol*. 2012; 15:S89–94. [PubMed: 23024571]
23. Tanco K, Rhondali W, Park M, Liu D, Bruera E. Predictors of Trust in the Medical Profession among Cancer Patients Receiving Palliative Care: A Preliminary Study. *J Palliat Med*. 2016; 19:991–994. [PubMed: 27148816]
24. Lee YY, Lin JL. The effects of trust in physician on self-efficacy, adherence and diabetes outcomes. *Soc Sci Med*. 2009; 68:1060–1068. [PubMed: 19162386]
25. Ratanawongsa N, et al. Communication and medication refill adherence: the Diabetes Study of Northern California. *JAMA Intern Med*. 2013; 173:210–218. [PubMed: 23277199]
26. Peterson JF, et al. Attitudes of clinicians following large-scale pharmacogenomics implementation. *The Pharmacogenomics Journal*. 2015; doi: 10.1038/tpj.2015.57
27. Unertl KM, Field JR, Price L, Peterson JF. Clinician perspectives on using pharmacogenomics in clinical practice. *Personalized Medicine*. 2015; 12:339–347. [PubMed: 26635887]
28. Issa AM, Tufail W, Hutchinson J, Tenorio J, Baliga MP. Assessing patient readiness for the clinical adoption of personalized medicine. *Public Health Genomics*. 2009; 12:163–169. [PubMed: 19204419]
29. Rothstein MA, Hornung CA. *Pharmacogenomics*. John Wiley & Sons, Inc; 2003. Public Attitudes about Pharmacogenomics; 1–27. (Director, rk A. R. H. F. B. C. of L. and M.)at <<http://onlinelibrary.wiley.com/doi/10.1002/047142613X.ch1/summary>>
30. Dorfman EH, et al. Pharmacogenomics in diverse practice settings: implementation beyond major metropolitan areas. *Pharmacogenomics*. 2015; 16:227–237. [PubMed: 25712186]
31. Cohen G, Forbes J, Garraway M. Can Different Patient Satisfaction Survey Methods Yield Consistent Results? Comparison Of Three Surveys. *BMJ: British Medical Journal*. 1996; 313:841–844. [PubMed: 8870568]
32. Jha AK, Orav EJ, Zheng J, Epstein AM. Patients' Perception of Hospital Care in the United States. *New England Journal of Medicine*. 2008; 359:1921–1931. [PubMed: 18971493]
33. Hull SC, et al. Patients' attitudes about the use of placebo treatments: telephone survey. *BMJ*. 2013; 347:f3757. [PubMed: 23819963]
34. Hussain S, et al. Disease-Drug Database for Pharmacogenomic-Based Prescribing. *Clin Pharmacol Ther*. 2016; doi: 10.1002/cpt.364
35. O'Donnell PH, et al. The 1200 Patients Project: Creating a New Medical Model System for Clinical Implementation of Pharmacogenomics. *Clinical Pharmacology & Therapeutics*. 2012; 92:446–449. [PubMed: 22929923]

36. Eveleigh RM, et al. An overview of 19 instruments assessing the doctor-patient relationship: different models or concepts are used. *Journal of Clinical Epidemiology*. 2012; 65:10–15. [PubMed: 22118265]

STUDY HIGHLIGHTS

What is the current knowledge on the topic?

Patient receptiveness is one of several barriers to the integration of pharmacogenomics in clinical practice. There have been no formal, prospective examinations of patients' attitudes/perspectives regarding genomic-based care within an implementation setting wherein physicians had preemptive pharmacogenomic results available.

What question did this study address?

We hypothesized that physicians' consideration of patient pharmacogenomic information during prescribing would improve patient perceptions of care.

What this study adds to our knowledge

This prospective study demonstrates that making patient-specific pharmacogenomic information available to providers is strongly associated with improved perceptions of care from the patient's perspective. Providers deliver additional aspects of care individualization when accessing genomic results, and this augmentation in decision-making is perceptible to patients.

How this might change clinical pharmacology or translational science

Integration of point-of-care pharmacogenomic information provides an opportunity to address patient concerns about trust, privacy, and medical decision-making. Understanding effects of pharmacogenomics on patient attitudes is integral for the design of future gene-based medicine implementations.

Figure 1. Doctor-patient relationship dimension scores among case patients. GPS Log In visits were associated with significantly higher Privacy, Empathy, MDM, and Personalized Care dimension scores. * $P < 0.01$. P values were calculated using Mann-Whitney. Error bars represent the standard error of the mean.

Figure 2.

Personalized Care responses from patients (N=18) who submitted surveys after clinic visits when there was a Traditional Med Change and after clinic visits when there was a PGx-Influenced Med Change. The Personalized Care doctor-patient relationship dimension score in these patients was more likely to be favorable after a visit with a PGx-Influenced Med change, (3.8 [1.5] vs. 2.8 [1.6], $P=0.023$). Statistical comparisons were made using the Wilcoxon signed-rank test.

Figure 3. Doctor-patient relationship dimension scores among case and control patients based on patient survey responses. * $P < 0.01$. ** $P < 0.05$. P values were calculated using Mann-Whitney. Error bars represent the standard error of the mean.

Figure 4.

Odds ratio and 95% confidence interval plots of identified covariates ($P < 0.05$) as predictors of high Personalized Care ratings among case patients. After controlling for other covariates, patients were significantly more likely to score Personalized Care favorably after PGx-influenced Med Changes compared to clinic visits with Traditional Med Changes.

Table 1

Characteristics of case and control survey respondents

	Case Patients	Control Patients	Total	P-value
Total	409 (100)	80 (100)	489 (100)	
Gender				0.31
Female	210 (51.2)	46 (57.5)	256 (52.3)	
Age at visit 1				0.52
Mean (SD)	64.1 (14.7)	61.9 (17.1)	63.7 (15.2)	
Race/ethnicity				0.24
White	261 (63.8)	44 (55)	305 (62.4)	
Black	106 (25.9)	28 (35)	134 (27.4)	
Other	42 (10.3)	8 (10)	50 (10.2)	
Educational attainment				0.03
<High school	10 (2.5)	4 (5.0)	14 (2.9)	
High school/GED	52 (12.8)	18 (22.5)	70 (14.5)	
Some college	81 (20)	15 (18.8)	96 (19.9)	
College graduate	110 (27.1)	22 (27.5)	132 (27.3)	
Graduate school	153 (37.7)	18 (22.5)	171 (35.4)	
Health status				0.0008
Poor	6 (1.5)	6 (7.6)	12 (2.5)	
Fair	36 (8.9)	12 (15.2)	48 (9.9)	
Good	114 (28.2)	26 (32.9)	140 (28.9)	
Very good	161 (39.8)	28 (35.4)	189 (39.1)	
Excellent	88 (21.7)	7 (8.9)	95 (19.6)	
Satisfaction with provider				0.006
Very dissatisfied	1 (0.3)	0 (0)	1 (0.2)	
Somewhat dissatisfied	3 (0.7)	0 (0)	3 (0.6)	
Somewhat satisfied	7 (1.7)	7 (8.9)	14 (2.9)	
Very satisfied	392 (97.3)	72 (91.1)	464 (96.3)	
Number of surveys				0.0005
1	216 (52.7)	55 (68.8)	271 (55.4)	
2	94 (23)	21 (26.3)	115 (23.5)	
>2	99 (24.2)	4 (5)	103 (21.1)	
Number of medications, mean (SD)	5.1 (2.9)	5.0 (2.4)	5.1 (2.8)	0.86
Days between visits, mean (SD)	104.4 (53.9)	103.9 (61)	104.3 (54.9)	0.97
Estimated provider minutes available, mean (SD) ^a	26.9 (7.7)	23.2 (5.5)	26.3 (7.5)	<0.0001

Values are represented as no. (%).

SD, Standard Deviation.

^a Calculated as total provider minutes in clinic divided by number of patients seen that day.