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Professional Perspectives About Pharmacogenetic Testing and Managing Ancillary Findings

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Aims: Pharmacogenetic (PGx) tests, intended to inform therapeutic decision making through prediction of patient likelihood to respond to or experience an adverse effect from a specific treatment, may also generate ancillary, or incidental, disease information unrelated to the purpose for which the test was ordered. To assess attitudes toward PGx testing, ancillary disease risk information, and related clinical issues, we conducted a series of focus groups among health professionals. *Results:* Twenty-one primary care and genetics professionals from Durham, NC, were recruited to participate in three focus groups (two of primary care professionals [PCPs] and one of geneticists). Overall, interest in PGx testing was positive, though enthusiasm was reserved among PCPs due to concerns about clinical utility, insurance coverage, delay of treatment, and ability to communicate and interpret ancillary disease risk information. Although many PCPs felt an obligation to disclose information about ancillary disease risk, geneticists did not believe that it was always necessary, noting the complexities of genetic risk results such as incomplete penetrance. *Conclusion:* This pilot study found that health professionals' interest in the use of PGx testing was limited by concerns about the lack of evidence of clinical utility and their ability to interpret and communicate ancillary disease risk information to patients. Additional educational resources, access to genetic specialists, and clear clinical guidelines about the use of PGx testing would greatly facilitate appropriate use of testing.

Introduction

Pharmacogenetic (PGx) testing involves the use of genetic tests to determine the optimal pharmaceutical therapy for a given individual. This testing approach is considered to be one of the most promising clinical applications in personalized medicine, with the potential to reduce adverse drug responses and improve treatment efficacy. Although PGx tests are generally believed to have fewer ethical and social implications than other predictive genetic tests (Roses, 2000), they have the potential to generate additional clinical information unrelated to the drug therapy question for which the test was ordered (Netzer and Biller-Andorno, 2004; Haga and Burke, 2008; Henrikson *et al.*, 2008). This additional, or ancillary, clinical information may relate to disease susceptibilities, prognosis, or other drug responses.

Few studies have explored health professional attitudes about PGx testing, and none have considered the issue of ancillary information or involved U.S.-based health professionals. Although recognizing the benefits of PGx testing, health professionals have reported concerns about patients' being/feeling pressured to be tested, potential discrimination, need for counseling, and informed consent (Rogausch *et al.*, 2006; Fargher *et al.*, 2007a; Hoop *et al.*, 2010). To gain a better understanding of the views of primary care professionals (PCPs) and genetics experts regarding PGx testing and specifically ancillary information, we conducted a series of focus groups. We selected these two groups of health professionals as they are involved in the development, introduction, and use of these tests. Further, no studies have included perspectives of geneticists. In particular, we aimed to explore each group's attitudes about the use of PGx testing, potential for ancillary information, role of genetics experts, and sharing of PGx information among healthcare professionals. These data will provide greater understanding of potential barriers to uptake of PGx testing and inform the development of practice guidelines, including management of ancillary information, to ensure the appropriate use and integration of PGx testing in the clinic.

Materials and Methods

Study population

To encourage open discussion among participants with similar backgrounds, we convened separate focus groups of PCPs and genetic professionals. Medical directors of Duke-affiliated primary care clinics were contacted to assess interest in conducting a focus group with physicians at their respective practices. Geneticists (board-certified genetic counselors, and laboratory and clinical geneticists) practicing at Duke

Institute for Genome Sciences & Policy, Duke University, Durham, North Carolina.

University Medical Center were invited to attend a separate focus group. A meal and $35 were provided as compensation for participation in the focus group. The study was approved by the Duke University Health System Institutional Review Board.

Focus group design

We developed a moderator guide to ensure uniformity regarding the material presented and questions asked between focus groups. Questions were intended to guide participants toward formulation of informed opinions regarding PGx testing and to elicit the thought processes behind those opinions. A hypothetical vignette was used to illustrate potential clinical and ethical issues that may arise with PGx testing, particularly regarding ancillary information.

Focus groups

Three focus groups of health professionals were convened between February and April 2009, two at primary care clinics affiliated with Duke University Medical Center and one on campus (geneticists). Consent was obtained from discussants upon arrival. Discussants were asked to complete a demographic questionnaire at the beginning of the session. Each focus group discussion was audio-recorded and transcribed.

Data analysis

Transcripts were first analyzed for accuracy and completeness before data analysis. To facilitate analysis, the authors used NVivo 8.0 software (QSR International) to partition the transcripts according to sections of discussion dictated by the moderator guide. Before coding, themes were independently identified by each author; consensus was reached on the themes through discussion among the authors. The themes were used to designate similar responses and opinions voiced by participants regarding questions posed by the moderator. The transcripts were then independently coded according to the designated selected themes by two members of the research team (S.B.H. and G.T.) using a qualitative content analysis approach. Disparities in coding were resolved through discussion and re-analysis of relevant sections of the transcript. This analytical approach allowed for comparative interpretation of concerns, issues, and opinions between groups.

Results

Characteristics of focus group discussants

A total of 21 health professionals, mostly women and white, participated in three focus groups. The PCP focus groups (quotes from these groups are denoted "PCP-FG") included a physician assistant, nurse practitioners, family medicine physicians, and internists. The geneticists' focus group (quotes from this group are denoted "Genetics-FG") included M.D. and Ph.D geneticists and genetic counselors (Table 1).

Table 1. Characteristics of Focus Group Discussants

	Health professionals (n = 21) (%)
Female	15 (71)
Race	
African–American	1 (5)
White	17 (81)
American Indian/Alaskan Native	0 (0)
Asian	3 (14)
Age (years)	
18–29	n/a
30–39	n/a
40–49	n/a
50–59	n/a
60–69	n/a
70+	n/a
No response	n/a
Year of graduation	
1970–79	2 (9)
1980–89	6 (29)
1990–99	8 (38)
2000 or later	5 (24)
Board certification	
Physician assistant	1 (5)
Nurse practitioner	2 (9)
Family medicine (M.D.)	4 (19)
Internal medicine (M.D.)	5 (24)
Medical genetics (M.D./Ph.D.)	3 (14)
Genetic counselor	6 (29)

General interest in PGx testing

Overall, discussants were interested in PGx testing and recognized the immediate benefit to improve drug therapy outcomes.

However, enthusiasm for PGx testing appeared to be lower among PCPs than among geneticists. Many PCPs felt that the technology was ahead of the clinical evidence and that current prescribing practices were preferred. For example, when discussing use of the warfarin PGx test to determine proper dosage, many PCPs still felt that clinical-based trial and error was the best way to determine the correct dosage, though some were more open to testing. They were divided on delaying treatment while waiting for test results to be returned. For severe adverse effects and drugs with narrow therapeutic windows, PCPs indicated that they would be more inclined to consider ordering PGx testing. Some PCPs raised concerns about insurance coverage.

- "[M]ost of the time when you're with like warfarin, or something like that, you're going to—you're making a decision that day that you want to start [immediately]…and you're not going to want to wait around." [Male-PCP-FG#1]
- "With warfarin, probably because of just the difficulty of use, getting the dose adjusted properly and people being high or being low and we can't explain that, I think that makes sense. I don't see the delay in that as a big barrier." [Male-PCP-FG#3]

Obligation to disclose ancillary information

We presented a hypothetical scenario about a patient who has PGx testing to predict her risk of a serious adverse effect associated with a specific asthma medication being considered. The PGx test could also reveal her risk of colon cancer.

Although many PCPs felt that ancillary risk information would scare patients, they felt that it was their duty to disclose this information, particularly if the condition was treatable. However, geneticists felt that it was not always necessary to disclose the presence of PGx ancillary risk information to patients and that the decision depended on the type and severity of the disease as well as its penetrance.

- "In a situation where it's the Alzheimer's, then I think you have to have a discussion with the patient ahead of time, before doing the testing, because there is a risk to having that knowledge." [Male-PCP-FG#3]

Many PCPs acknowledged that they themselves would be unlikely to understand the significance of the ancillary risk information, given their limited knowledge and experience with genetic testing. Therefore, referral to a specialist may be most appropriate. In addition, PCPs believed that it would be challenging to communicate genetic disease risk information, particularly for patients with low literacy and given the time constraints of a typical appointment.

- "I think the part that is daunting for me is having these conversations are so time-intensive, and trying to do it in a way that is understandable to the patient, and it's like, oh, I've got to do this discussion now." [Male-PCP-FG#3]
- "We are going to do this test, but we also might find out information that we didn't really want to know, and are you okay with that? It's like, how to explain that to somebody who might have a high school education or something like that." [Male-PCP-FG#3]

Although geneticists felt that it was their duty to help educate their physician peers to ensure that they accurately interpret the test result, they did not feel that their personal input or referral was needed for each case.

- "What you want is to educate the primary care frontline person about how to manage that information for their own patients, because that's what their questions are always to us. 'Okay, so you found this, now what do I do for my patient?' " [Female-Genetics-FG#2]

In addition to believing that automatic referrals to geneticists were unnecessary, geneticists also felt that PCPs should devote time in a follow-up appointment to discuss the results of a PGx test. However, PCPs felt that this was an unrealistic option, and many cited that either they or their patients simply did not have the time or resources to return for a second appointment.

Storage of PGx test results

Discussants also recognized the value of convenient access to PGx test results, believing that due to its importance, PGx test results should be stored somewhere easily accessible to other healthcare providers as needed. Pharmacists, in particular, may benefit from having access to a patient's PGx test results.

- "That may even make sense to put it on our medication portion of our EMR, under the allergy section.…So anybody going to add a medication would see that up there in bold up the top." [Male-PCP-FG#3]

Discussion

PGx tests hold great promise to improve outcomes through tailored drug treatment based on patients' genetic risk of adverse effects and/or likelihood of drug response. Their potential to generate additional clinical information unrelated to the drug therapy, however, poses some challenges regarding the disclosure and management of PGx test results as well as the potential uptake of testing by physicians and patients. Our study is the first to investigate health professionals' attitudes and interest toward PGx testing in general as well as ancillary information related to PGx testing in the United States.

Similar to other reports of professional attitudes toward PGx testing in general (Rogausch *et al*., 2006; Fargher *et al*., 2007a), interest among our participants was positive, though less so with PCPs, potentially due to geneticists' greater familiarity with the field and/or favorable biases. PCPs' concerns included their ability to adequately interpret and communicate test results, a finding not previously reported, as well as the lack of demonstrated clinical utility of the test, and practical considerations such as timing of test and insurance coverage. These findings contrast with European and U.K. health professional concerns about patient harms, pressure, and access (Rogausch *et al*., 2006; Fargher *et al*., 2007a; Hoop *et al*., 2010). However, similar concerns about uncertain clinical utility have been noted with respect to disease-based testing (Escher and Sappino, 2000; Mountcastle-Shah and Holtzman, 2000; Freedman *et al*., 2003; Levy *et al*., 2007; Park *et al*., 2007). Despite these concerns, other studies have found a high likelihood of use of new genetic tests such as PGx testing among PCPs (Park *et al*., 2007; Shields *et al*., 2008) and early adopters (Fargher *et al*., 2007b; Hoop *et al*., 2010).

In addition, opinions about responsibility for recognizing and managing ancillary information varied. PCPs were concerned about their ability to interpret and communicate disease risk information, particularly given their limited knowledge of genetics, a finding confirmed in several studies (Hofman *et al*., 1993; Hunter *et al*., 1998; Menasha *et al*., 2000; Emery and Hayflick, 2001; Wideroff *et al*., 2005). In contrast to PCPs general belief that patients should be informed of ancillary disease risk information, geneticists' noted some of the complexities of interpreting genetic risk (e.g., incomplete penetrance) and thus commented that disclosing some types of ancillary risk information may not be appropriate. While geneticists recognized that they could serve as an educational resource to physicians, they did believe involvement in all cases was necessary. Although time did not allow us to discuss the impact of ancillary information on uptake, other studies have suggested that this is not a major factor influencing health professional adoption (Shields *et al*., 2008).

This study has some limitations. Given the small sample size and recruitment from one region, the opinions of our focus group discussants may not be representative of the community of PCPs or geneticists. Thus, findings from this preliminary study will also need to be confirmed through larger studies in other geographic locales and medical specialties. As responses to hypothetical scenarios are often positively biased (Persky *et al*., 2007), further studies are also needed to test the impact of real clinical situations. To assess attitudes of a larger and more representative population, we are surveying a national sample of these groups and the data

gathered from this study have informed development of the three respective surveys on these issues.

With robust clinical evidence, uptake of PGx testing can occur rapidly (Lai-Goldman and Faruki, 2008). However, increasing physician awareness about new PGx tests and genetic risk associations in general are needed to increase physicians' confidence and ability to appropriately integrate PGx testing into clinical practice and communicate test results and possibly ancillary risk information. Geneticists can play a key role in the development of such education efforts, and our small cohort of geneticists agreed that this was an appropriate role for their profession. Strengthening partnerships with local genetic specialists as well as with testing laboratories may not only help facilitate uptake of new PGx tests (Faruki *et al*., 2007) but also provide guidance regarding the management of potential ancillary information.

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