A review of consent practices and perspectives for pharmacogenetic testing

Aim: We aimed to understand consent practices for pharmacogenetic (PGx) testing. **Methods:** We conducted a literature review and analysis of consent forms from clinical laboratories offering PGx testing. **Results:** Our review of the literature shows a lack of consensus about the need for and type of informed consent for PGx testing. We identified 35 companies offering PGx testing and were able to confirm consent practices for 22 of those. We found a range of variability in the consent practices regarding the consent approach and information disclosed. **Conclusion:** Variability in the consent practices among laboratories offering PGx testing mirrors the ambiguous practices and recommendations reported in the literature. Establishing a minimal set of information to be disclosed to patients may help address the disparities in consent practice.

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The precision medicine movement is predicated on the use of personal information to improve clinical decision-making and health outcomes. One major part of this practice is pharmacogenetic (PGx) testing, which involves the analysis of genes associated with drug targets, metabolism and other relevant pathways to predict drug effectiveness and/or likelihood of an adverse response for a given drug. PGx testing is most likely to be ordered when a new medication with known drug–gene interaction is anticipated or needed, though some groups are assessing the utility of pre-emptive testing [1,2].

It is critical to consider the patient experience with testing as PGx testing is increasingly used to predict drug response, and as healthcare delivery embraces a more patient-centered care model aimed to improve outcomes and patient satisfaction [3]. In particular, it is unclear what type of consent process may be appropriate for PGx testing. The American Medical Association's Code

of Ethics states that physicians are obligated to present accurate medical facts and help patients make choices appropriate for each individual [4]. Only with accurate information enabling patient understanding can patients make an informed decision about their care. A test-specific consent is not typically required for individual tests as most clinical tests (e.g., complete blood count or liver enzyme analysis) pose very little risk and presumably no reasonable patient would decline testing. Instead, consent for clinical tests and other interventions may be obtained through a general consent for treatment to provide care deemed medically necessary. A test-specific consent may be needed for tests that present an increased physical risk to obtain the specimen (e.g., chorionic villus sampling or bone marrow biopsies) or potential psychological risk. For example, it is recommended that providers inform patients of the potential risk of discrimination or stigmatization for some infectious diseases like

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tuberculosis and HIV/AIDS, though testing typically requires verbal agreement rather than signed consent and counseling [5,6].

Genetic testing is one exception to the practice of not obtaining consent for clinical testing [7]. Compared with other clinical tests, genetic testing presents some different risks and limitations, which vary depending on the type of genetic test (e.g., diagnostic, susceptibility, HLA typing, viral typing) that may warrant disclosure of information about the test and potential risks to the patient [7,8]. Furthermore, an effective treatment is not available for many genetic conditions, and thus, confirmation of a diagnosis may not lead to any additional medical benefit. However, a genetic diagnosis may provide substantial personal benefit. Because of the nature of genetic testing, it is recommended that informed consent be an ongoing process of patient-centered, nondirective education and counseling that addresses not only clinical risks and benefits, but other implications as well in order to promote an informed choice [7]. Guidelines regarding informed consent and patient education have been developed for disease-based genetic tests [9], including whole genome and whole exome sequencing [10–12] and predictive testing for adult-onset disorders such as Alzheimer's disease [13] and cancer [14,15].

Although PGx testing is a genetic test, it differs from disease-based genetic testing as may have immediate clinical utility and does not typically have significant risks. However, despite the perceived lower risks, both patients and providers have recognized the value of pre-testing communication and patients expect to be engaged in decisions about PGx testing [16–19]. Furthermore, there are different types of PGx tests, which may warrant different consent processes – those which analyze variants in genes associated with drug metabolism or transport and those tests for genetic variants in drug targets, often referred to as companion diagnostics. Some of PGx tests are single-gene tests and others are gene panels [20]. In addition, PGx testing offered at the time of treatment may present lower risks/higher benefits than testing offered in advance of treatment when the patient is healthy as point-of-care testing may have greater clinical utility. Therefore, it is unclear if the different PGx tests and testing scenarios warrant a test-specific consent similar to disease-based genetic testing.

Given the novelty of PGx tests and differences with disease-based genetic tests, we sought to better understand current consent practices for PGx testing as required by the testing laboratories. Here, we report our findings from a literature review on the current practices and recommendations about consent for PGx testing and an analysis of consent forms from PGx testing laboratories, excluding laboratories exclusively

providing companion diagnostic testing since these tests are required for treatment. We recognize that healthcare providers and institutions may have their own consent policies in addition to the laboratory consent policies to promote patient engagement and for different testing scenarios (e.g., pre-emptive testing), which we do not address in this paper. With the limited information about consent practices for PGx testing, our findings describe current practices, which may be useful for laboratories or practitioners considering methods of informed consent for PGx testing.

Methods

Literature review

We conducted a literature review for papers commenting or reporting on the practice of consent for PGx testing in clinical settings in October–November 2015. We systematically searched several databases (PubMed, EMBASE and ISI Web of Knowledge). Search terms used included ‘pharmacogenetic’, ‘pharmacogenomic’ and ‘consent’. In addition, we utilized the ‘related citations’ function in PubMed to identify similarly indexed publications as well as reviewed the references of selected publications to further identify relevant publications for our analysis. Non-English publications were excluded. Both authors reviewed the list of titles from the search queries and excluded papers that did not address PGx testing or that addressed only PGx for companion diagnostics. Publications were identified as either review/commentaries or research reports, and then divided into PGx testing for research or clinical purposes given the different requirements of the consent process in research and clinical settings.

Analysis of informed consent & test requisition forms for clinical PGx testing

We reviewed test requisition and consent forms from laboratories offering clinical PGx testing in USA. The review was conducted in October 2015–March 2016. We reviewed the test requisition forms as well as traditional consent forms since some laboratories include a statement of consent within a patient information section on the requisition form. We chose to limit our analysis to only laboratories located in USA due to potential differences in consent practices and regulatory requirements in other countries. Clinical PGx testing laboratories were identified first through the Genetic Testing Registry [21]. We identified additional clinical PGx laboratories based on our knowledge and experience in the field of PGx, and through a web-based search using search terms ‘pharmacogenetic’ or ‘pharmacogenomic’ and ‘testing’ or ‘test’ and ‘laboratory’.

We reviewed the website of each testing laboratory for availability of a consent form or test requisition

form. For those without the consent form accessible online, we requested a copy through a customer service associate. Test requisition and/or informed consent forms were downloaded and analyzed. Specifically, we reviewed the consent forms for eight types of information that are legally required of consent forms for genetic testing in some states [22,23]: a general description of the test, purpose of the test, consideration of genetic counseling, potential results and/or meaning of a positive result, description of the disease/condition being tested, individuals to whom results will be disclosed, storage and/or destruction of sample following testing and medical risks and benefits. We noted if the consent forms addressed either physical, medical, psychological or informational risks of testing, information that is generally considered pertinent when making an informed decision about testing [24,25]. In addition, we recorded the type of consent (none, physician assent, patient consent, both), whether a separate patient consent form was available or a statement of consent or patient information was included on the test requisition form, the reading level (Flesch–Kincaid), page length and word count, the type of test (single-gene or panel testing) and type of laboratory (commercial, academic). We report summary statistics of our findings.

Results

Literature review

The initial literature search identified 318 publications. Following curation based on titles and abstracts, the number of relevant papers was reduced to 40 papers. Publications were excluded if they were not specific to PGx or consent (i.e., they addressed all types of genetic testing, or all types of ethical, legal and social implications not specific to consent), or if they discussed consent and/or return of PGx test results as part of exome sequencing or biobanking (presumably the consent process for those practices is more complicated than PGx testing as a clinical test). These papers were further divided to consent for PGx in the research setting (16 papers) or clinical setting (16 papers) or both (seven papers). The bulk of the identified publications ($n = 23$) were commentaries or perspectives with little or no data about actual consent practices for PGx testing. Many of the commentaries provided recommendations for information or components of consent that should be addressed when providing testing in the research or clinical setting.

We identified few reports of consent practices for clinical PGx testing. Current clinical practices in Europe indicate that informed consent is not always requested by physicians conducting PGx testing [26]. For example, Hedgecoe [27,28] reports that clinicians felt

that *HER2* testing does not require specialized consent and that physicians rarely tell their patients that the test is being conducted or that it is a genetic test. In the research setting, variability also exists with informed consent for PGx testing. ‘Significant deficiencies’ were reported in a review of research consent forms for PGx studies [29] and participants desired resources supplemental to the consent form like a brochure or video [30].

The lack of a standard practice of consent for PGx testing was addressed in a number of publications identified in the literature review. For example, while some providers perceive PGx testing differently from routine clinical testing, it is not considered quite in the same category as disease-based genetic testing that warrants patient consent and potentially counseling [19]. In addition, provider attitudes about consent may vary based on their experience with PGx testing. A survey of psychiatrists revealed that 91% of those who had not yet ordered PGx testing indicated that they would obtain verbal consent and 55% would obtain written consent [16–19]. Of those who had ordered PGx tests, the actual practice of obtaining verbal consent aligned with that reported of the non-experienced group (98%), but was significantly lower for written consents (17%) [16–19]. Furthermore, some physicians may not distinguish between PGx tests and other clinical tests ordered as part of a standard clinical workup, potentially accounting for the lack of reported informed consent for PGx tests [26–28]. Provider decisions to obtain consent for well-established tests such as *HER2/NEU* (a genetic marker used to identify patients who may benefit from a targeted cancer therapy) have been reported to be impacted by the clinical stage at diagnosis, the providers’ attitude toward testing and the potential for false hopes based on test result [27].

Mirroring the variability reported in clinical and research practices in the literature, there is also great variability in perspectives shared in the literature. Not all providers believe informed consent is unnecessary for PGx testing. Some providers feel that consent is warranted when testing may reveal secondary information, as in the case of Alzheimer’s specialists considering *APOE* gene testing [28]. Other surveys of providers (Psychiatrists and General Practitioners) report that many providers believed that informed consent was absolutely necessary [19,31,32].

Several scholars have indicated that limited or no patient communication/consent is needed given the immediate clinical application and the perceived lower risks of PGx testing compared with disease-based genetic testing [28,33–35]. Buchanan *et al.* [36] suggested that “In low-risk situations, to avoid genetic exceptionalism, PGx tests should be treated like other routine laboratory tests, in which minimal explanation and patient

assent suffice.” In contrast, some scholars note that the risks and limitations of PGx testing may be very similar to the challenges and risks presented by disease-based genetic testing, and if so, warrant consent [37–40]. As was also acknowledged in the provider surveys, some commentaries noted the potential risk of secondary findings with PGx tests that would warrant informed consent [34,37–39,41]. Thus, some recommend that the consent process for PGx testing entail disclosure of the risks of testing (e.g., discrimination and stigmatization) and potential familial implications [38,39].

If consent should be obtained for clinical PGx testing, no clear consensus emerged from the literature review about the content of the informed consent or whether a verbal or written consent would be appropriate. As a result, decisions about the consent process may require test-specific considerations. However, both researchers and clinicians recognize the need for guidance and standardization regarding consent for PGx testing [42,43].

Some groups have considered the key elements to be included in a consent form for PGx studies [44,45]. For example, as part of the consent process, clinicians and researchers may consider including the purpose of testing, an overview of the potential results and how they will be returned to the patient, risks and benefits of testing, potential for secondary findings and storage of sample and results, though the suggested amount of detail shared for each topic is variable [36,38,39,44]. Robertson [38] suggests that a patient signatory be obtained for obtaining and testing DNA, but indicates that the consent process surrounding the acquisition of the signature not be overly burdensome, and may be satisfied by a simple oral explanation of testing and the need for a DNA sample. The Nuffield Council on Bioethics reported that written consent may be appropriate for PGx tests that reveal incidental findings [34].

Patient cohorts or the general public also vary in their opinions about consent, with some believing that

Table 1. Features of pharmacogenetic testing laboratories and summary of analysis of consent forms and test requisitions (n = 35).

	N	Percentage
Type of laboratory		
Reference laboratories (offers multiple tests)	20	57%
Laboratories offering PGx testing only [†]	15	43%
Commercial lab	30	86%
Academic lab	5	14TT%
Type of PGx test offered		
Offers single-gene PGx tests only	8	23%
Offers panel PGx tests	17	49%
Offers both single-gene and panel	10	29%
Laboratories with accessible informed consent	22	63%
Type of consent		
Patient-signed PGx-specific consent form	3	14%
Patient-signed general genetic testing consent form	8	36%
Patient-signed consent statement within requisition form	4	18%
Provider assent only required	1	5%
No consent/assent collected by lab	6	27%
Readability	Average	Range
Word count (overall)	568.2	68–1040
Word count (patient consent embedded in test requisition)	231.5	68–430
Word count (patient consent as a separate form)	680.4	363–1040
Flesch–Kincaid Reading Ease score (overall) [‡]	39.8	24–76.1
Flesch–Kincaid Reading Grade (overall) [§]	12.5	5.6–16.9

[†]Includes laboratories offering PGx and toxicology testing, but no other gene-based tests.

[‡]Calculated based on average number of syllables per word and words per sentence (0–100 scale; 0 = very difficult and 100 = very easy).

[§]Text ranked on a US grade-school level based on the average number of syllables per word and words per sentence.

PGx: Pharmacogenetic.

PGx testing requires consent particularly if it reveals secondary information [46], whereas others stated a preference for a brief verbal notification about testing from their provider instead of a formal signed consent form [47]. Some evidence suggests that patients may have difficulty understanding concepts of PGx [48,49]. Providers that advocate for informed consent for PGx testing have also recognized the challenges of achieving truly meaningful informed consent. In pediatric populations, informed consent is not possible and it may be difficult to achieve assent of an appropriately aged child [50]. Findings from the literature review suggest a more patient-friendly consent process is needed, potentially supplemented by additional educational materials [37–38,50–51]. However, scholars believe that it is unlikely that genetic counseling is necessary [37–39], except in unique circumstances of high risk.

Analysis of consent forms for PGx testing

To better understand the current consent process for PGx testing, we reviewed test requisition and consent forms from laboratories offering clinical PGx testing. Of the 35 laboratories identified in our study, 30 (86%) are commercial laboratories (Table 1); 15 of those are reference laboratories that offer a range of clinical genetic and nongenetic tests. Fifteen laboratories are specialty laboratories that offer PGx testing only. Overall, eight laboratories offer single-gene PGx testing only, 17 offer a panel of PGx genes and ten offer both single-gene tests and panels, with some offering the option of customized panels.

A total of 14 laboratories provided access to the test requisition or consent form on their website; those who do not were contacted via their online request form or a toll-free telephone number. We received no response from nine laboratories and two laboratories declined to provide the consent form to a non-provider (one stated on its website that consent was only required for residents of the state of New York, but did not provide us with a copy of the consent). One laboratory is a new company that is not yet providing testing. In total, we were able to confirm the consent process for 22 laboratories.

Of the 22 laboratories with available consent or test requisition forms, six laboratories (laboratories 1, 16, 19, 22, 24 and 25) indicated that they do not require a patient-signed consent form for testing (four commercial laboratories/two academic laboratories), though some suggest that the provider obtain consent and one laboratory requires consent when participating in research conducted by the lab. One of the laboratories (laboratory 22) includes patient-friendly PGx-specific information about the test appended to the requisition form and suggests that the provider encourage the

patient to read it, but requires neither a provider nor patient signature acknowledging provision or review of the statement, respectively. Four laboratories (laboratories 3, 10, 18 and 31; all commercial) include a brief (average word count 232) consent statement within the test requisition form and patient signature is required in that section. Overall, seven of the eight laboratories that do not require consent or include a consent box on the test requisition form are commercial laboratories; four offer PGx testing only.

The remaining 11 laboratories use an informed consent form similar to what is typically used for disease-related genetic testing. Specifically, eight laboratories (laboratories 6, 8, 13, 17, 20, 26, 27 and 32) use a generic genetic testing consent form that requires a patient signature (mean word count 644; five commercial/three academic laboratories, seven reference laboratories/one PGx-only). The consent forms are a separate document from the test requisition form and include language applicable for any type of genetic test, including PGx testing, provided by the laboratory. Three laboratories (laboratories 4, 12 and 15) have a separate consent form requiring a patient signature that is specific to PGx testing (average word count 729). Eight of the 12 laboratories requiring a separate consent are laboratories at academic medical centers; ten are reference laboratories offering multiple types of genetic tests.

The average Flesch–Kincaid reading grade for all consent forms analyzed as well as the information page (laboratory 22) is 12th grade (range: 5.6–16.9). Two of the informed consent documents reviewed (laboratories 15 and 22) were written below a high school reading level. Overall, the average Flesch–Kincaid reading ease score is 39.8 (range: 24.0–76.1), which falls within the category of difficult reading level (the higher the score, the easier to read). The average Flesch–Kincaid reading ease score for the four consent statements within the requisition form is 34.8 (range: 25.3–48.5) compared with an average score of 35.5 (range: 24.0–44.6) for the eight generic genetic consent forms and 53.7 (range: 35.0–76.1) for the three PGx-specific consent forms and the one information form that includes PGx-specific information.

We conducted a content analysis of each consent document available from the 15 laboratories that require patient signatures (laboratories 3, 4, 6, 8, 10, 12, 13, 15, 17, 18, 20, 26, 27, 31 and 32) as well as the information sheet provided by one laboratory (laboratory 22) though it does not require a patient signature (Table 2). Overall, eight of the 16 documents reviewed include all 8 components of informed consent required by some state laws; one addresses seven elements, four address six elements, two address five and two address

Table 2. Content analysis of consent forms/test requisitions for the eight elements of informed consent and illustrative quotes.

Component of consent	Laboratories including this element on consent form, n (%)	Sample text
General description	16 (100)	"The DNA test(s) detect small differences (variants) in DNA which can affect the way drugs work and are metabolized in your body and/or detect potential side effects"
Purpose of test	14 (91)	"Pharmacogenomics testing determines how genetic makeup affects my response to medication"
Genetic counseling recommendation	10 (73)	"Genetic counseling is recommended prior to, as well as following genetic testing"
Potential results/meaning of results	11 (73)	"DNA results may: indicate whether or not you have this condition or are at risk for developing this condition. Indicate whether or not you are a carrier for this condition, predict that another family member has or is at risk for developing this condition, predict that another family member is a carrier of this condition"
Description of disease being tested	16 (100)	"Genotyping of CYP2C9, CYP2C19 and VKORC1 for metabolism status to determine proper initial dosage of warfarin to avoid bleeding events and overdose"
Disclosure of results	15 (91)	"Because of the complexity of genetic testing and the important implications of the test results, results will be reported only through a physician, genetic counselor or other identified healthcare provider"
Storage/destruction of sample	16 (100)	"The sample will be destroyed at the end of the testing process or not more than 60 days after the sample was taken..."
Medical risks and benefits	11 (73)	"Side effects of having blood drawn are uncommon, but may include dizziness, fainting, soreness, pain, bleeding, bruising and, rarely, infection. Other risks that may be experienced as a result of this testing include: related emotional issues, impact on life – changing decisions, potential genetic discrimination (e.g., in employment and insurance areas) and loss of confidentiality"

four (average 6.8 out of 8). The components of consent most often excluded were a statement about genetic counseling (6/16), the risks of testing (5/16) and the potential results or meaning of a positive result (5/16). Eight laboratories also included a statement about potential results, or the meaning of a positive result, with one (laboratory 12), listing the possible PGx results (poor metabolizer, intermediate metabolizer, normal metabolizer, rapid metabolizer) and an interpretation of each result. All consents included a test name/gene name or description of the gene (or disease or condition, i.e., drug response) being tested, sometimes simply as a check-box or space to write-in a test name (for generic consent forms) and all included a statement regarding the storage or destruction of a sample. Almost all (15/16) consent documents included a statement regarding protection of privacy including details

about with whom test results would be disclosed, with many referencing the Health Insurance Portability and Accountability Act and/or the Genetic Information Non-discrimination Act. A subset analysis of the four test requisition forms that required patient signature within the form (not on a separate consent) addressed an average of 5 of 7 informational points (compared with an average of 6.5 for others).

As genetic tests typically tend to raise more 'informational' risks than physical risks, we considered both types in our analysis. Overall, we found that 11 of the 16 laboratory consents included a description of one or more risks of testing. Ten of the 12 laboratories that used a separate consent document included information about one or more types of risk compared with one of the four laboratories that included a brief statement and patient signature box on the test requisition form.

Overall, we found that five laboratories disclosed risks of discrimination, two disclosed psychological risks, eight disclosed potential for discovery of nonpaternity or other familial implications and four disclosed physical risks of a blood draw or tissue acquisition necessary for testing. Although several papers identified in the literature review highlight the potential for incidental findings as a feature of PGx tests that warranted consent, we reviewed the consent forms to determine how often this was disclosed. We found that three laboratories disclosed the potential for incidental findings (specifically, risks for identifying genetic changes associated with other unrelated diseases).

Other notable disclosures on the consents included test limitations, use of results in research, availability of additional patient resources and details of the method used to collect the sample and/or conduct testing. Some PGx-specific consents include statements about clinical implications of testing, including some warnings for patients regarding the need to consult with a medical professional before altering drug regimens or that other factors in addition to genes can impact drug response.

Discussion

Findings from our literature review indicate that PGx testing appears to fall into a gray zone between limited or absent disclosure/consent similar to most clinical tests and an extensive informed consent standard for disease-based genetic testing. Aligning with our literature review findings, we found a range of variability in current consent practices among laboratories offering PGx testing. Of 35 laboratories that we identified that offer PGx testing, we were able to confirm the consent process of 22 laboratories. About half of these laboratories ($n = 12$, 55%) required a patient signature on a separate informed consent similar to that required of most genetic tests. Another four laboratories (18%) required patient signature in a box on the test requisition form. Our findings align with consent practices of other molecular genetic tests, whereby only about half of surveyed laboratories require informed consent prior to testing [52,53].

Depending on the type of consent required, the amount and detail of information disclosed varied greatly. Not surprisingly, less information was included in a consent box within the test requisition form compared with separate consent forms. The wide variability in consent length and content is not unprecedented with novel genetic and genomic applications. A recent comparison of written consent forms for genetic testing also showed variability in the type of information disclosed, with several laboratories using the same consent form for single and panel-based testing [54,55]. Despite concerns about incidental findings and its prominence

with the use of genomic tests (whole genome or exome testing [54–56]; chromosomal microarrays [57]), this potential was only disclosed by three laboratories. Perhaps due to the use of more targeted testing platforms (i.e., genotyping for common variants), the issue of incidental findings is of less concern for PGx testing.

Researchers and clinicians alike recognize the need for guidance and standardization regarding consent for PGx testing [42,43]; however, defining a uniform guideline may be challenging due to the variety of PGx tests available, purpose of testing (and when testing is performed) and perceived harms. The laboratory may be limited in its ability to develop consent forms for each potential use. For complex PGx tests, such as panel-based tests, laboratories could organize patient handouts and consent forms using a ‘tiered and binned’ approach that focuses on key themes rather than gene-specific information [58]. Development of multiple ‘tiers’ of information to which providers may tailor discussions based on patient needs resulted in increased patient knowledge and patient-reported informed decision [59]. Similar approaches have also been proposed for personal genome testing [60].

Yet providers may implement different consent practices as they deem appropriate and feasible. Some providers may perceive PGx tests similar to other clinical tests, necessary to inform drug selection, and therefore, believe that no discussion or consent is needed [27]. For PGx tests ordered preemptively, such as part of a health screen, they may warrant a different consent process than testing ordered at the point of care (when a medication is needed). For instance, patients electing to have preemptive testing may develop anxiety about test results in advance of necessary treatment that would be impacted by these results. Further, a preemptive test may have no clinical utility for a particular patient if he or she is never prescribed a drug impacted by the test results. Thus, the consent process for preemptive testing may entail more information about the future utility of the results while minimizing potential concerns about the patient’s overall health. For testing provided at the point of care, the immediate utility of results may reduce any psychological impact and the consent process would be focused on the use of PGx testing to inform treatment selection and dosing.

At this early stage of clinical use of PGx testing in general, patient education is a critical part of the PGx testing process that can be achieved through the informed consent process. Informed consent cannot only promote informed decision making, but can prepare patients for outcomes of testing and increase the likelihood of patients’ comprehension of the test result. With improved comprehension, patients can understand the significance of the results to their current medications

as well as future medications and reduce duplicate testing. The consent process requires active discussion with the patient to address any questions or concerns and ensure truly informed consent. The patient–provider discussion should be tailored to address patient concerns instead of a recitation of statements on the consent form. This movement away from the common elements disclosed in a consent form and toward focusing on patient concerns or misunderstanding has been reported for more complex genomic testing [61].

If it is determined that a verbal consent alone is satisfactory for PGx testing, the advantages and disadvantages of verbal consent must be considered. For example, a discussion about testing may not be viewed by patients with the same gravitas as a signed consent form, or patients may fail to recognize it as part of the consent process [62]. Also, the information disclosed in patient–provider discussion may vary substantially due to providers' knowledge [63–66], so provider education is essential and discussion tips may help standardize discussions. We identified only one guideline on the use of the HER-2 testing that included talking points for discussing test results, but it did not address pre-testing communication and consent [67]. Based on our experience, we have recommended key information to discuss with patients offered PGx testing [68]. Though written consent may not be necessary, patients may become overloaded with information provided during discussions about medication and testing [69] and thus, patient educational materials are needed to supplement provider discussions and enable patients to review additional information at a later time; a need for educational materials was also recognized in our literature review [37–38,50–51]. However, the materials must be written at a level suitable for the general public. In addition, clinical decision support could be developed to prompt providers to discuss key features of PGx testing with patients. Clinical decision support has already been developed to alert providers about patients for whom PGx testing is clinically indicated (e.g., based on prescription ordered), or recommendation for adjustments to dosing or drug selection based on test results [47,70]. Considering the increased utilization of electronic medical records and patient portals, it may be possible to easily provide supplementary patient educational materials about testing or to print and distribute to the patient without online access to enhance patient understanding and optimize the limited time in an office visit.

Study limitations

Some limitations of this study should be noted. Analysis of consent forms was limited to only those accessible online or kindly provided by the laboratory. Providers

may have other means of communicating information to patients about PGx testing that this study does not review. The use of readability formulae to analyze consent forms are useful as a quantitative method to compare the consent forms, but they may be unreliable as they do not consider many other factors that affect reading ease [71]. In addition, this analysis represents a snapshot of laboratory consent requirements. With the evolution of PGx testing and anticipated greater patient and provider familiarity, consent practices will likely coevolve.

Conclusion

The variability in laboratory consent practices may reflect the ambiguous status and shifting perception about PGx testing. Laboratories may choose to have minimal or no consent requirements due to perceived lower risks of PGx tests compared with disease-based genetic tests, similar to consent practices for other clinical tests or biomarkers used for drug selection and dosing. Yet, the accepted practices of consent for traditional genetic tests still appear to influence some consent practices for PGx tests. Determination of a core set of information to disclose to patients about PGx testing may help standardize the process and ensure that the appropriate amount and type of information is disclosed to the patient; however, it will be important to consider the diversity of PGx tests, timing of testing and delivery settings during the process. Development of patient educational resources and provider discussion points can greatly facilitate patient understanding and patient–provider communication, respectively, to ensure informed medical decision making.

Future perspective

In the next 5–10 years, we anticipate the use of PGx testing will become more routine. With increased provider and patient familiarity with these tests, written consents are likely to be considered unnecessary and consent practices will mirror that of other types of accepted clinical tests. Furthermore, with advances in whole genome and whole exome sequencing, PGx information can be revealed through these tests, negating the need for individual PGx tests and consent for each test. In the interim, both patient and provider education remain important elements for the safe and appropriate use of PGx testing.

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Executive summary

- Little empirical research has explored patient communication and consent processes for clinical pharmacogenetic testing.
- A literature review revealed that there is variability in opinions regarding consent for pharmacogenetic testing with some scholars suggesting that the consent should be similar to traditional genetic testing whereas others believe limited consent is adequate.
- We find that consent practices currently used by testing laboratories are also variable, mirroring the ambiguous practices and recommendations reported in the literature.

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