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Results of a national survey of Japanese pharmacists in relation to the application of pharmacogenomic testing for precision medicine

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Abstract

What is known and objective: Pharmacogenomics (PGx) testing can be effective for supporting precision medicine. The purpose of this study was to assess the knowledge, attitude and practice behaviors of pharmacists in relation to such testing through a survey. We also aimed to identify potential obstacles to implementation of PGx testing by pharmacists and the characteristics of hospital pharmacists involved.

Methods: We performed a web-based survey regarding PGx in Japan. The survey contained a questionnaire related to PGx, which consisted of 30 items and was made accessible via the official Japanese Society of Pharmaceutical Health Care and Sciences (JSPHCS) website. The characteristics of hospital pharmacists associated with involvement in PGx testing were evaluated using univariate and multivariate analyses.

Results and discussion: 1313 pharmacists responded to the survey. The results revealed that the majority of respondents recognized the role that germline PGx testing can play in determining individual drug responses, and that pharmacists have embraced the potential of PGx testing to improve patient care. However, only 26% of pharmacists were involved in PGx testing. We also found that most respondents (81.0%) believed that the lack of insurance coverage for PGx testing was a major barrier to its clinical implementation. Hospital pharmacists involved in PGx testing included certified pharmacists in JSPHCS and pharmacists who had studied PGx in university;

however, only 12.4% of pharmacists had received specific PGx-related education.

What is new and conclusions: The findings from this survey highlight the necessity to increase the number of PGx tests covered by insurance and the importance of effective education for its clinical implementation.

KEYWORDS

Precision medicine, Pharmacogenomics, Pharmacists, Questionnaire survey, Clinical implementation

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1 WHAT IS KNOWN AND OBJECTIVE

The cancer gene panel test was approved and covered in the national insurance system in June 2019 in Japan. Given the implementation of gene panel testing in clinical settings, precision medicine based on information pertaining to somatic mutations is expected to be widely available. Similarly, pharmacogenomics (PGx) testing for germline variants from a pharmacokinetic viewpoint, such as those encoding drug-metabolizing enzymes, could also be effective tools for supporting precision medicine. PGx, an important component of precision medicine, is expected to afford the most appropriate drug choice and/or dose adjustment for each individual. Genetic biomarkers that may avoid adverse drug reactions (ADRs) or predict the effects of drugs have been evaluated in clinical studies. To date, the Clinical Pharmacogenetics Implementation Consortium (CPIC®) has identified over 120 drugs impacted by approximately 30 genes with CPIC level A or B evidence that have sufficient evidence for prescribing recommended action. Recently, in some hospitals, genetic information related to drug selection and dose adjustment is used in clinical practice by prescribing physicians.[1-3] As PGx testing becomes more common, pharmacists and physicians will encounter enhanced PGx information in the near future. Germline PGx, an applicable branch of precision medicine, identifies patient's genotypes that alter the clinical outcome of the drug, hence preventing serious ADRs in individual patients.

There have been significant advances in PGx research over the past 20 years, but only a few

germline PGx tests have been covered by insurance and introduced into clinical practice compared to tests for somatic mutations. Although the introduction of germline PGx testing is considered to be in the clinical-implementation stage, this process has been delayed. There are several obstacles to the clinical implementation of PGx tests. Several reports indicate the presence of various hurdles regarding the widespread adoption of PGx testing in clinical settings, including its uncertain clinical utility, reimbursement, lack of PGx knowledge, insufficient education, and provider or patient interest.[4-8] Several reports suggested that pharmacists might be better at applying PGx tests as compared to physicians because of their education that includes analytical science.[9-11] Moreover, it is reported that pharmacists in the United States of America (USA) are actively participating in various types of PGx clinical services in an effort to address the challenges of clinical implementation of PGx testing.[5]

The clinical implementation of PGx testing is a major concern worldwide. Small-scale or physician-based surveys on PGx testing have been conducted until now.[12, 13] However, large-scale surveys of this topic focusing on pharmacists have not been performed, despite the fact that pharmacists are expected to be deeply involved PGx implementation process. In addition, very few studies have evaluated the characteristics of the health care professionals who are actually involved in PGx testing in clinical practice.[13, 14] A survey of this nature targeting pharmacists and aimed at the realization of precision medicine which by focusing on germline PGx testing has not

been carried out in Japan. Although the testing of somatic mutations related to drug selection has a great impact in the field of oncology, germline PGx testing regarding dose adjustment for each individual is also an important implications for pharmacotherapy. Therefore, here, we performed a large-scale questionnaire survey of pharmacists regarding the actual situation of PGx tests in medical practice. The purpose of this study was to survey a broad baseline data for PGx, including an assessment of the knowledge, attitude, practice behaviors, obstacles, and preferred information sources of Japanese pharmacists. Second, we aimed to identify the characteristics of hospital pharmacists involved the ordering of PGx tests.

2 METHODS

2.1 Survey method and content

We performed an anonymous web-based survey regarding PGx among Japanese pharmacists who were members of the Japanese Society of Pharmaceutical Health Care and Sciences (JSPHCS). Many of the members of this society are hospital pharmacists. The survey outline was notified by a flyer and mailing list to the pharmacist members of JSPHCS. The survey was voluntary and the participants were informed that personally identifiable information was not going to be released and that personal information was protected. The online survey contained an explanatory cover letter. The questionnaire were consisted of 30 items and further categorized

into four sections: (1) demographics, (2) attitude and practice behaviors, (3) information sources and knowledge, and (4) general way of thinking, perception, and barriers regarding the clinical implementation of PGx testing. The survey was designed using Google Forms© and was made accessible via the official JSPHCS website.

2.2 Statistical analysis

For each question, response frequencies were aggregated to analyze the responses in this survey. Demographics, knowledge, attitudinal, and practice factors that affected PGx testing were evaluated using chi-squared tests as univariate analysis. Potential factors with *P* values < 0.05 by univariate analysis were included in multivariate analysis. The factors associated with the adoption of PGx testing were identified using a stepwise, multivariate logistic regression analysis. The results of multivariate analysis were reported as odds ratios (ORs) with 95% confidence intervals (CIs) and *P* values. All statistical tests were two-sided, and *P* values < 0.05 were considered statistically significant. All statistical analyses were performed using the EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).[15]

3 RESULTS

3.1 Questionnaire response rate and respondent characteristics (SECTION 1, Table 1)

Of the 12,552 members of JSPHCS who were approached, 1,313 pharmacists cooperated and completed the questionnaires. The percentage of respondents was 10.5%. No missing data were found throughout the full set of questions, because we created this survey using Google Forms© and set it for all questions to be answered. In this survey, the percentage of holders of professional certifications in JSPHCS was 38.2%, which was approximately 10% higher than the whole of the JSPHCS members. The characteristics of the cohort used in this survey are listed in **Table 1**.

3.2 Attitude and practice behaviors regarding PGx testing (SECTION 2, Table 2)

The content of all survey questions and the corresponding answers are presented in **Tables 2–4**.

Almost all respondent pharmacists (93.6%) reported that they believe PGx tests are useful for personalized medicine, and 72.6% of respondents believe that their current work requires PGx knowledge (**Table 2**). More than half (56.7%) of the pharmacists answered that they know the term “precision medicine.” However, only 12.5% of respondents answered that they understand PGx well (Likert scale score, 3 and 4), and pharmacists who had received PGx education in their

university curriculum represented only 12.4% of the cohort. Moreover, regarding their involvement in PGx testing in the past year, those respondents who answered that they had never been involved in PGx testing were 74.3%, and 25.7% had been actually involved (≥1/month) (**Table 2**). **Fig. 1** shows the purpose of the involvement of pharmacists in PGx testing if there was more than one involvement per month. In 24.6% of cases, the purpose of their involvement in PGx testing was to confirm the appropriate dose of the selected drug and to select the optimal drug (these were the most frequent answers).

When asked about how much genetic information might be involved in individual differences in pharmacotherapy, most respondents answered 10%–30% (39.6%), followed by 30%–50% (29.0%) and 50%–80% (14.3%) (**Table 2**).

3.3 Information sources and knowledge (SECTION 3, Table 3)

When asked where they obtained information and how they learned about PGx, the respondents reported that the source of information on the adaptation of PGx testing, which reflect on prescriptions, were academic journals most frequently (42.4%), followed by medical package inserts (39.5%). Regarding the source of learning about PGx, academic conferences (seminars/lecture meeting) were reported to be the most common source (46.9%). However, 34.0% of the respondents reported that they had not learned about PGx. A proportion of the

pharmacists (30.8%) reported that they can identify five or more drugs that would be useful for PGx testing (**Table 3**).

We set up five questions that address PGx knowledge in this survey questionnaire. The percentage of correct answers to knowledge questions 1 to 5 was 57.9%, 12.5%, 20.3%, 51.6%, and 72.7%, respectively (**Table 3**). Respondents who answered more than four questions correctly (≥80%) were regarded as having good knowledge. One-hundred and twenty-two pharmacists (13.8%) answered more than four questions correctly (Knowledge tests in Table 3).

3.4 Perception of, general way of thinking about, and obstacles to the clinical implementation of PGx testing (SECTION 4, Table 4)

The majority of respondents agreed that pharmacists need to have knowledge about PGx (93.1% for Likert scale score 3 plus 4, agree totally or partly; 6.9% for Likert scale score 1 plus 2, disagree totally or partly) (**Table 4 and online appendix A1**).Similarly, many respondents (75.2%) agreed totally or partly that healthcare professionals should consult pharmacists on the appropriate use of PGx testing, but only 18.2% (Likert scale score 3 plus 4) of respondents agreed totally or partly that they could provide information to other healthcare professionals regarding the appropriate use of PGx testing (**Table 4 and online appendix A1**). The results of PGx tests

could be adequately applied to patient drug selection, dose adjustments, or monitoring by 32.2% (Likert scale score 3 plus 4) of the respondents (**Table 4 and online appendix A1**).

All respondents were asked about the benefits and issues of PGx testing, preferred learning format, and barriers to the clinical implementation of PGx (multiple answers, top three selected). The majority of respondents chose “Improving the efficacy of pharmacotherapy” (95.3%), "Reducing adverse effects” (91.7%), and “Reduction of medication costs” (46.9%) as the benefits that patients would obtain from PGx testing (**Table 4**). Regarding questions addressing the knowledge and attitudes needed to optimize pharmacotherapy based on the results of PGx testing, many respondents selected “Knowledge on basic concepts of PGx” (72.4%), “Knowledge on pharmacokinetics” (60.5%), and “Knowledge on genetics” (54.3%) (**Table 4**). As for the required system, “Insurance approval for PGx testing” (75.2%), "Inclusion in clinical practice guidelines” (67.0%), and “Evidence that PGx improves clinical outcomes” (58.9%) were selected by many respondents (**Table 4**). Regarding the dissemination of PGx-related education, many respondents asked JSPHCS to “Hold basic educational lectures” (67.3%) and “Provide the latest information through symposia” (63.1%). Educational books on PGx (65.3%) and e-learning courses (60.9%) were chosen by over 50% of respondents as the preferred PGx learning format in the future (**Table 4**). When asked about barriers to the clinical implementation of the PGx test, most respondents selected “Not covered by insurance” (81.0%), followed by “Requiring expenses for analysis”

(61.2%) (**Table 4**).

3.5 Multivariate analyses of predictors of PGx testing in hospitals

Hospital pharmacists are most likely directly involved in PGx testing. Therefore, the characteristics of pharmacists', who were involved in PGx testing in their hospitals, were examined using the answers obtained from hospital pharmacists.

Several demographic, knowledge, attitudinal, and practical characteristics were shown to be associated with the involvement in PGx testing by univariate analysis (**online appendix A2**).

A multivariate analysis adjusted for 8 characteristics revealed that professional certifications in JSPHCS ($P = 0.0016$), thinking that the current work requires PGx knowledge ($P < 0.0001$), knowing the term "Precision medicine" ($P < 0.0001$), inclusion of PGx learning in the university educational curriculum ($P = 0.0106$), and being able to identify five or more drugs that would be useful for PGx testing ($P < 0.0001$) were retained as significant characteristics of the hospital pharmacists involved in PGx testing (**Table 5**).

DISCUSSION

In this questionnaire survey focused on pharmacists across Japan, we found that most Japanese pharmacists accept the basic principle that PGx has clinical relevance. Although respondents were

receptive to the incorporation of PGx testing into clinical practice, their knowledge was generally insufficient and their applicability for PGx testing was relatively low. In addition, based on the results of SECTION 4 of the survey, a large gap was identified between the pharmacists' perception of PGx and their clinical practice (online appendix A2). Only 12.4% of the pharmacists in the current survey reported having received education in PGx in their university curriculum, and only one quarter of all respondents had ordered a PGx test in a clinical setting.

The application of the findings of PGx research in daily clinical practice requires assessing the current situation and overcoming many obstacles. The multivariate analysis revealed the characteristics of hospital pharmacists who adopted PGx testing. The characteristic with the highest odds ratio was “Thinking that the current work requires PGx knowledge,” and the ability to identify five or more drugs for which PGx testing was required, and the inclusion of lectures regarding PGx education in the university curriculum were shown to actually affect PGx testing. These results were consistent with previous reports that showed that pharmacists and physicians who felt well informed about PGx testing and had received pharmacogenetics education were more likely to adopt PGx testing.[13, 16, 17] Although the percentage of correct answers on the knowledge tests was not identified as a significant independent characteristic in the multivariate analysis, pharmacists with a higher percentage of correct answers were more likely to be involved in PGx tests. This analysis also found that the acquisition of board certification and/or specialty

pharmacists had an impact on the involvement in PGx testing. The successful clinical implementation of PGx requires continuing education.[13, 16] The findings of this survey strongly suggest that enhancing PGx education and increasing the availability of training for pharmacists will be crucial for accelerating the implementation of PGx testing; i.e., having an interest in PGx, increasing PGx knowledge, and placing pharmacists in environments where PGx knowledge is required may promote the implementation of PGx testing in clinical practice.

The majority of respondents believed that a lack of insurance coverage was the major barrier to the clinical implementation of PGx testing. Despite the growth of the field of PGx research and the discovery of an increasing number of genetic variations, germline PGx testing is rarely performed clinically, and very few are covered by insurance. At present, the only two germline PGx tests that are covered by insurance in Japan are the *UGT1A1* polymorphisms in irinotecan and the *NUDT15* polymorphisms in thiopurines. In fact, the *UGT1A1* genetic test, which started receiving insurance coverage in 2008, was found to be the most widely performed PGx test (81.8%) in our previous survey of 121 medical institutions in Japan.[18] Therefore, we believe that it is important to increase the number of PGx tests that are covered by insurance. For inclusion in insurance coverage, high-quality clinical trials to verify the clinical utility of PGx tests need to be conducted, and it is expected that the number of PGx tests with reimbursement will increase if their usefulness is demonstrated. Somatic gene panel testing is being explored in cancer genomic

medicine,[19, 20] and several tests are being reimbursed by insurance. Thus, the introduction of panel testing for germline PGx may also be a useful tool in this setting. A large randomized controlled trial is currently underway in Europe to verify the utility of a panel test for germline genetic profiling to guide optimal drug and dose selection.[21]

Conversely, concerns remain about the cost effectiveness of these tests. In addition to assessing the clinical utility of the PGx tests, demonstrating their cost effectiveness is likely to be one of the major challenges in this field of clinical research. In a review of articles that conducted economic evaluation studies of drugs with PGx information in the Food and Drug Administration's Table of Pharmacogenomic Biomarkers in Drug Labeling, of 44 economic evaluation studies on 10 drugs that were evaluable, 13 studies (30%) reported that PGx-guided strategy was more cost effective (PGx was more effective at acceptable additional cost) than alternative strategies, and 12 studies (27%) reported that it was dominant (PGx was more effective at lower cost).[22] The gathering of evidence of both the clinical utility and the cost effectiveness of PGx testing may drive decisions on reimbursement. Therefore, we believe that it is of paramount importance to obtain convincing clinical evidence, including that pertaining to cost effectiveness, by conducting randomized controlled trials and/or large observational studies to validate the clinical utility of PGx testing.

This study had limitations. Although the survey covered a large number of pharmacists, it is

unclear whether the results are representative of Japanese pharmacists as a whole; i.e., the response rate was low and we cannot deny the possibility that only highly conscious pharmacists participated in this survey. In addition, similar limitations in generalizability stem from the fact that this survey was conducted only among Japanese pharmacists and its results are not representative of the global pharmacist community.

ADRs are a major concern for patients receiving pharmacotherapy, even in the present day, and it was reported previously that ADRs represent the fourth and sixth leading cause of death in the USA.[23] A review article of recent observational studies in Europe reported that 3.5% of patients were hospitalized because of ADRs, and 10.1% of patients were found to have developed ADRs during their hospital stays.[24] Many factors affect the occurrence of ADRs, including age, organ function, comorbidities, and concomitant medications. In addition to the factors mentioned above, genetic polymorphisms also most likely play an important role in this context. As the clinical implementation of PGx testing progresses and PGx information becomes more readily available in clinical settings, these results can be used in advance to optimize drug selection and perform dose adjustment. Moreover, this is also expected to significantly reduce the incidence of ADRs and improve the quality of pharmacotherapy. We believe that pharmacists are an ideal professional group to evaluate the challenges of pharmacotherapy and implement evidence-based solutions from precision medicine research.

WHAT IS NEW AND CONCLUSION

The survey found that pharmacists in Japan have embraced the potential of PGx testing to improve patient care. The majority of pharmacists recognized the role of germline PGx testing in determining individual drug responses. However, there were a limited number of pharmacists who were actually involved in PGx testing. Therefore, it is important to bridge this gap between pharmacists' perceptions and practices by enhancing educational programs for the clinical implementation of PGx testing.

Figure legends

Fig. 1

What was the purpose of your involvement in the cases in which PGx testing was performed? (≥1 case/month)

(1) Only confirmation of the PGx tests results performed

(2) To confirm the validity of the dose selection for the drug in question

(3) To assess the dosage of the drug to be administered in advance

(4) To select the optimal drug used for treatment

(5) To assess the risk of side effects in patients in advance

(6) To confirm the cause of the side effects that occurred in the patient

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CONFLICT OF INTEREST

All the authors have no conflict of interest to declare with respect to this manuscript.

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Ethics approval

The study was approved by the Institutional Review Board of each institution. This study was conducted in accordance with Ethical Guidelines for Medical and Health Research Involving Human Subjects issued by the Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare, Japan.

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Figure 1

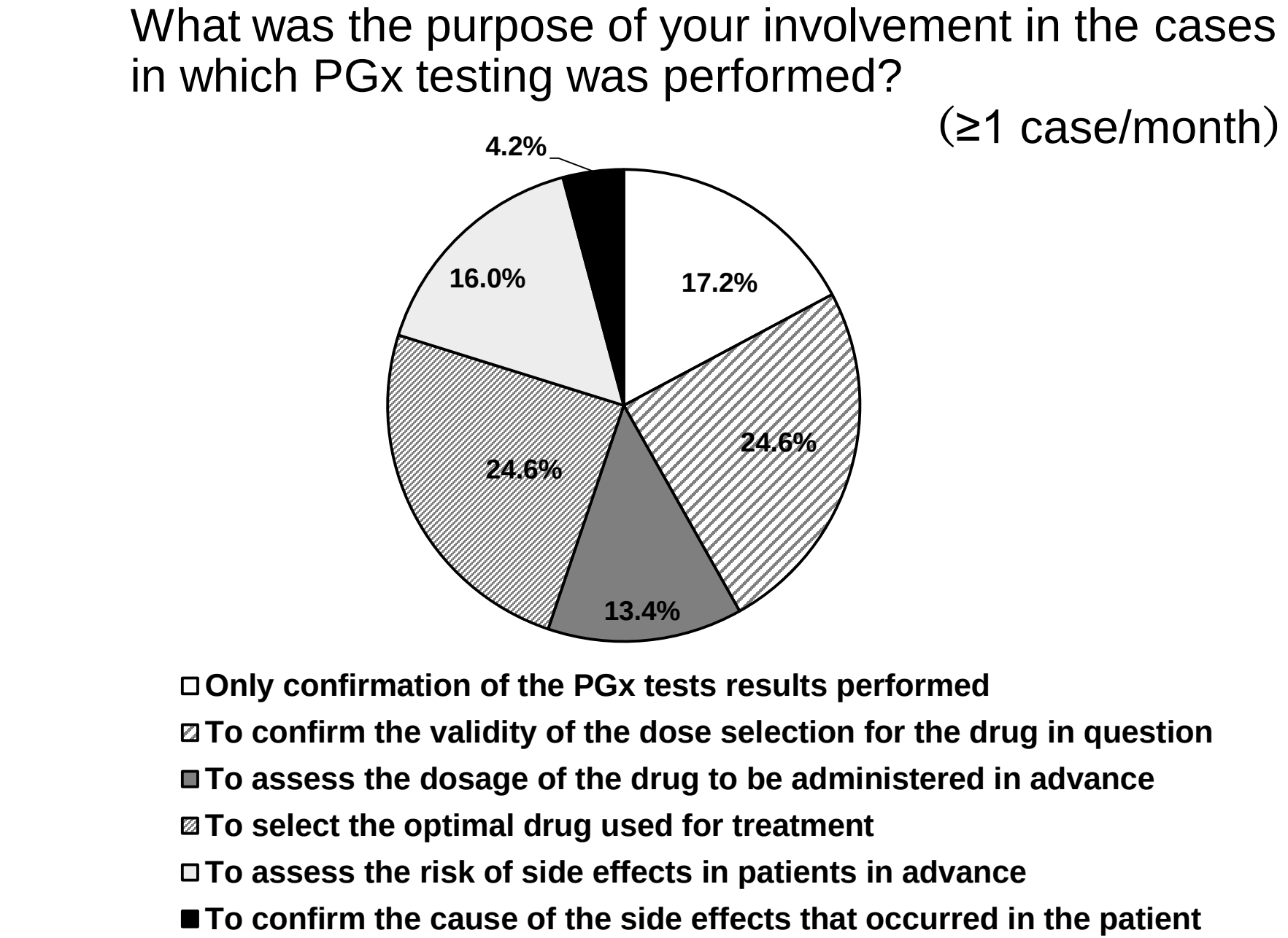

What was the purpose of your involvement in the cases in which PGx testing was performed?
(≥1 case/month)
4.2%
16.0%
17.2%
24.6%
24.6%
13.4%
Only confirmation of the PGx tests results performed
To confirm the validity of the dose selection for the drug in question
To assess the dosage of the drug to be administered in advance
To select the optimal drug used for treatment
To assess the risk of side effects in patients in advance
To confirm the cause of the side effects that occurred in the patient

Table 1 Baseline demographic information of the respondent pharmacists (SECTION1: demographics)

Characteristic	n (%)
Total survey respondents	1313
Institution	
Hospital	1067(81.3%)
Clinic	3(0.2%)
Community pharmacy	85(6.5%)
University	131(10.0%)
Administrative organ	5(0.4%)
Company	12(0.9%)
Other	10(0.8%)
Practice setting (Prefectures)	
Tokyo and prefectures including ordinance-designated cities	824(62.8%)
Other	489(37.2%)
Professional certifications in JSPHCS*	
Certified Pharmacist	380(28.9%)
Supervisory pharmacist	200(15.2%)
Board-certified Oncology Pharmacist	162(12.3%)
Board-certified Senior Oncology Pharmacist	90(6.9%)
Board-certified Pharmacotherapy Specialist	16(1.2%)
Board-certified Senior Pharmacotherapy Specialist	9(0.7%)
None	812(61.8%)
Years since pharmacist license acquisition	
Less than 1 year	16(1.2%)
1 to less than 5 years	136(10.4%)
5 to less than 10 years	182(13.9%)
10 to less than 20 years	550(41.9%)
20 to less than 30 years	262(20.0%)
More than 30 years	167(12.7%)

* Includes duplicate answers

Table 2 Survey questions and responses (SECTION 2: attitude and practice behaviors)

Survey questions	
Do you think PGx tests are useful for personalized medicine?	
○Yes	1229 (93.6%)
○No	84 (6.4%)
Do you think you need PGx knowledge for your current work?	
○Yes	953 (72.6%)
○No	360 (27.4%)
Do you know the term "precision medicine"?	
○Yes	744 (56.7%)
○No	569 (43.3%)
I understand PGx well.	
(Disagree ○1 ○2 ○3 ○4 Agree)	
1	815(62.1%)
2	334 (25.4%)
3	121 (9.2%)
4	43 (3.3%)
Did your university education curriculum include PGx lectures?	
○Yes	163 (12.4%)
○No	958 (73.0%)
○Unknown	192 (14.6%)
How many times (monthly average) have you been involved in cases where PGx tests were performed in the last one year?	
○Zero	976 (74.3%)
○1 case/month	149 (11.3%)
○2-5 cases/month	129 (9.8%)
○6-10 cases/month	34 (2.6%)
○11-20 cases/month	14 (1.1%)
○≥ 21 cases/month	11 (0.8%)

To what extent do you think genetic information might be involved in individual differences in pharmacotherapy?	
◯0%–10%	141 (10.7%)
◯10%–30%	520 (39.6%)
◯30%–50%	381 (29.0%)
◯50%–80%	188 (14.3%)
◯ ≥ 80%	83 (6.3%)

Table 3 Survey questions and responses: SECTION 3 (Information sources and knowledge)

Survey questions	
Where do you obtain information on PGx testing and adapting the results to the prescription of drug treatment? (Please choose all of the appropriate answers)	
□The pharmaceutical package insert	518 (39.5%)
□Academic journals	557 (42.4%)
□Pamphlet provided by companies (materials, etc.)	397 (30.2%)
□Genetic testing laboratory	52 (4.0%)
□Japanese Society of Pharmaceutical Health Care and Sciences (JSPHCS)	188 (14.3%)
□Other academic associations	204 (15.5%)
□Websites in foreign countries	69 (5.3%)
□Educational videos on YouTube	6 (0.5%)
□Other internet sites	164 (12.5%)
□Pharmacists	185 (14.1%)
□Doctors	144 (11.0%)
□None	345 (26.3%)
How did you learn PGx? (Please choose all of the appropriate answers)	
□University (classes/textbooks)	170 (12.9%)
□Self-learning using educational books	293 (22.3%)
□Academic conferences (seminars/lecture meetings)	616 (46.9%)
□Academic journals	307 (23.4%)
□Internet	252 (19.2%)
□Other materials	93 (7.1%)
□Not learned	447(34.0%)
Can you identify five or more drugs that would be useful for PGx testing?	
○Yes	405 (30.8%)
○No	908 (69.2%)
Knowledge tests	

Q1 Which of the following cytochrome P450 (CYP) molecular species has the highest frequency of poor metabolizer (PM) in Japanese populations? (Please choose one, the most appropriate answer)	
○CYP1A2	24 (1.8%)
○CYP2C9	206 (15.7%)
●CYP2C19	760 (57.9%)
○CYP2D6	190 (14.5%)
○CYP3A4	133 (10.1%)
Q2 Which PGx tests do you think are covered by insurance in Japan? (Please choose all of the appropriate answers)	
□ABCB1	91 (6.9%)
□ABCG2	49 (3.7%)
□CYP2C9	272 (20.7%)
□CYP2C19	404 (30.8%)
□CYP2D6	270 (20.6%)
□CYP3A5	100 (7.6%)
□DPD	83 (6.3%)
□NAT2	211 (16.1%)
■UGT1A1	1109 (84.5%)
■NUDT15	350 (26.7%)
Q3 Which of the following drugs may be useful for clinical applications of PGx testing? (Please choose six, the most appropriate answers)	
□amlodipine	114 (8.7%)
□ipragliflozin	330 (25.1%)
■irinotecan	1271 (96.8%)
■carbamazepine	950 (72.4%)
■clopidogrel	984 (74.9%)
■tacrolimus	1133 (86.3%)
□prasugrel	454 (34.6%)
■azathioprine	1002 (76.3%)
□rabeprazole	539 (41.1%)
■warfarin	1101 (83.9%)

Q4 Which of the following drugs may have a reduced therapeutic effect if the drug metabolism enzymatic activity is reduced by genetic polymorphism? (Please choose one, the most appropriate answer)	
○digoxin	134 (10.2%)
○omeprazole	249 (19.0%)
●clopidogrel	678 (51.6%)
○vancomycin	22 (1.7%)
○voriconazole	230 (17.5%)
Q5 Which of the following genes has been reported to cause the hereditary breast and ovarian cancer syndrome for which olaparib, a PARP inhibitor, is indicated? (Please choose one, the most appropriate answer)	
○ABCG2	52 (4.0%)
●BRCA	954 (72.7%)
○EGFR	31 (2.4%)
○HER2	208 (15.8%)
○KRAS	68 (5.2%)

Notes: ● and ■ are correct answers for each question.

Table 4 Survey questions and responses (SECTION 4: general way of thinking, perception, and obstacles to the clinical implementation of PGx testing)

Survey questions	
Pharmacists need to have knowledge about PGx.	
(Disagree ○1 ○2 ○3 ○4 Agree)	
1	27 (2.1%)
2	64 (4.9%)
3	391 (29.8%)
4	831 (63.3%)
Healthcare professionals should consult pharmacists on the appropriate use of PGx testing.	
(Disagree ○1 ○2 ○3 ○4 Agree)	
1	71 (5.4%)
2	255 (19.4%)
3	580 (44.2%)
4	407 (31.0%)
I can accurately apply the results of a PGx test to patient's drug selection, dose adjustment, or monitoring.	
(Disagree ○1 ○2 ○3 ○4 Agree)	
1	538 (41.0%)
2	352 (26.8%)
3	297 (22.6%)
4	126 (9.6%)
I can provide information to other healthcare professionals regarding the appropriate use of PGx testing.	
(Disagree ○1 ○2 ○3 ○4 Agree)	
1	729 (55.5%)
2	345 (26.3%)
3	163 (12.4%)
4	76 (5.8%)

What are the benefits that patients would obtain from PGx testing? (Please choose up to three of the most appropriate answers)	
□Improving the efficacy of pharmacotherapy	1251 (95.3%)
□Reducing adverse effects	1204 (91.7%)
□Improving patient understanding of the disease or treatment	229 (17.4%)
□Improving patient adherence to pharmacotherapy	202 (15.4%)
□Reduction of medication costs	616 (46.9%)
□No benefit to the patients	18 (1.4%)
What knowledge and attitude do you need to optimize pharmacotherapy based on the results of PGx testing? (Please choose up to three of the most appropriate answers)	
□Knowledge on genetics	713 (54.3%)
□Knowledge on pharmacology	467 (35.6%)
□Knowledge on pharmacokinetics	794 (60.5%)
□Knowledge on basic concepts of PGx	951 (72.4%)
□Knowledge on legal regulations (including ethics)	438 (33.4%)
□Practical ability to apply knowledge	401 (30.5%)
What do you think is needed as the required system to optimize pharmacotherapy based on results of PGx tests? (Please choose up to three of the most appropriate answers)	
□Support of the facility at which you work	564 (43.0%)
□Expert advice and assistance	287 (21.9%)
□Insurance approval for PGx testing	988 (75.2%)
□Inclusion in clinical practice guidelines	880 (67.0%)
□Evidence that PGx improves clinical outcomes	774 (58.9%)
□Service in which research institutions, such as universities, conduct PGx analysis	156 (11.9%)
What do you hope for the JSPHCS regarding the dissemination of PGx? (Please choose up to three of the most appropriate answers)	
□Email distribution of the latest information on PGx	476 (36.3%)
□Publishing educational books	679 (51.7%)
□Providing the latest information through symposia	829 (63.1%)
□Holding basic educational lectures	884 (67.3%)

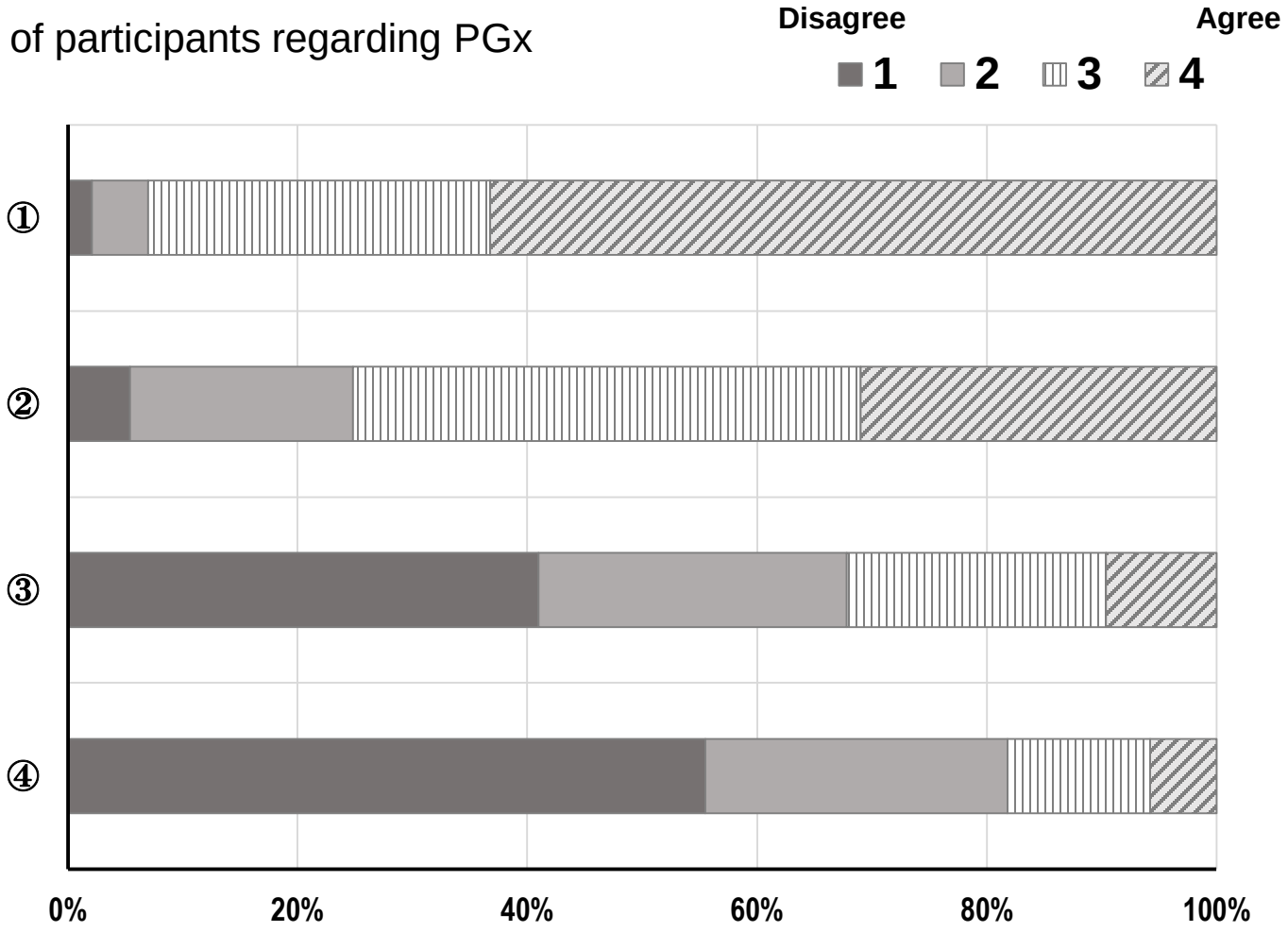
□Providing the mentioned example of documents for application to ethics committee	184 (14.0%)
□Coordination of multi-institutional studies on PGx	244 (18.6%)
□Setting up a consultation desk for PGx research	235 (17.9%)
What is the preferred format to learn more about PGx in the future? (Please choose all of the appropriate answers)	
□Educational books on PGx	858 (65.3%)
□Scientific articles	484 (36.9%)
□Accredited learning courses	597 (45.5%)
□Apps on mobile devices, such as smartphones	423 (32.2%)
□e-learning courses	800 (60.9%)
□Involvement in clinical research related to PGx	399 (30.4%)
□Other	54 (4.1%)
What obstacles do you think hamper the clinical implementation of PGx testing? (Please choose all of the appropriate answers)	
□Not covered by insurance	1064 (81.0%)
□Insufficient and uncertain evidence for PGx testing	579 (44.1%)
□Difficulty in obtaining patient understanding	294 (22.4%)
□Difficulty in obtaining the approval of physicians	284 (21.6%)
□Difficulty in obtaining the approval of medical stuff	136 (10.4%)
□Lack of understanding regarding the analytical method of genetic polymorphisms	479 (36.5%)
□Lack of understanding of the interpretation of the results of genetic polymorphism analyses	582 (44.3%)
□Lack of workforce	587 (44.7%)
□Requiring expenses for analysis	803 (61.2%)
□Troublesome application to ethics committee	525 (40.0%)
□Other	40 (3.0%)
□None (no barrier)	13 (1.0%)

Table 5 Multivariate analysis of predictors of pharmacogenomic testing adoption

	OR	95% CI	*P* value
Professional certifications in JSPHCS	1.623	1.202–2.247	0.0016
Thinking that current work requires PGx knowledge	6.098	3.584–10.299	<0.0001
Knowing the term “Precision medicine”	2.370	1.706–3.300	<0.0001
PGx was included in the university educational curriculum	1.776	1.143–2.747	0.0106
Be able to identify five or more drugs that would be useful for PGx testing	2.415	1.767—3.300	<0.0001

Online appendix A1

Self-perception of participants regarding PGx



① Pharmacists need to have knowledge about PGx.
② Healthcare professionals should consult pharmacists on the appropriate use of PGx testing.
③ I can accurately apply the results of a PGx test to patient's drug selection, dose adjustment, or monitoring.
④ I can provide information to other healthcare professionals regarding the appropriate use of PGx testing.

Online appendix A2: Factors used for the adoption of pharmacogenomic testing: univariate analysis

	Pharmacogenomics testing adoption		
Survey response (N = 1067)	**No (n = 752) Non-adopters**	**Yes (n = 315) Adopters**	***P* value**
Practice setting			0.537
Tokyo and prefectures including ordinance-designated cities (n = 647)	451(69.7)	196(30.3)	
Other	301(71.7)	119(28.3)	
Professional certifications in JSPHCS			<0.0001
No	507(77.2)	150(22.8)	
Yes	245(59.8)	165(40.2)	
Years since pharmacist license acquisition			0.642
≥10 years	532(70.0)	228(30.0)	
<10 years	220(71.7)	87(28.3)	
Do you think PGx tests are useful for personalized medicine?			<0.0001
No	71(94.7)	4(5.3)	
Yes	681(68.6)	311(31.4)	
Do you think you need PGx knowledge for your current work?			<0.0001
No	256(93.8)	17(6.2)	
Yes	496(62.5)	298(37.5)	
Do you know the term “precision medicine”?			<0.0001
No	405(84.7)	73(15.3)	

Yes	347(58.9)	242(41.1)	
Did your university education curriculum include PGx lectures?			<0.0001
No or Unknown	689(72.3)	264(27.7)	
Yes	63(52.3)	51(44.7)	
I know well about PGx (Disagree ○1 ○2 ○3 ○4 Agree)			<0.0001
No (Likert scale, 1 and 2)	51(46.8)	58(53.2)	
Yes (Likert scale, 3 and 4)	701(73.2)	257(26.8)	
Can you identify five or more drugs that would be useful for PGx testing?			<0.0001
No	602(79.7)	153(20.3)	
Yes	150(48.1)	162(51.9)	
Percentage of correct answers to knowledge questions (≥80%): Knowledge tests Q1–Q5			0.0413
No	656()	259(28.3)	
Yes	96(63.2)	56(36.8)	