**Translational and
Clinical Pharmacology**

TCP

Original Article

Check for updates

Survey of physicians' views on the clinical implementation of pharmacogenomics-based personalized therapy

Woo-Young Kim (iD) [1,†], Ho-Sook Kim (iD) [1,2,3,*], Minkyung Oh (iD) [1,2], and
Jae-Gook Shin (iD) [1,2,3]

[1]Department of Pharmacology and PharmacoGenomics Research Center, Inje University College of
Medicine, Busan, Korea
[2]Center for Personalized Precision Medicine of Tuberculosis, Inje University College of Medicine, Busan,
Korea
[3]Department of Clinical Pharmacology, Inje University Busan Paik Hospital, Busan, Korea

OPEN ACCESS

*Correspondence to
Ho-Sook Kim
Department of Pharmacology and
PharmacoGenomics Research Center, Inje
University College of Medicine, 75 Bokji-ro,
Busanjin-gu, Busan 47392, Korea.
E-mail: hosuegi@gmail.com

†Current address: SPMED Co., Ltd. Busan,
Korea.

ORCID iDs
Woo-Young Kim (iD)
https://orcid.org/0000-0003-1234-4823
Ho-Sook Kim (iD)
https://orcid.org/0000-0001-6764-7261
Minkyung Oh (iD)
https://orcid.org/0000-0001-7584-5436
Jae-Gook Shin (iD)
https://orcid.org/0000-0002-5821-850X

ABSTRACT

Despite quantitative increases and qualitative advances in pharmacogenomics (PGx)
research, the clinical implementation of PGx-based personalized therapy has still been
limited. The objective of this study was to assess physicians' self-reported knowledge of PGx-
based personalized therapy, and to explore the most problematic and highest priority barriers
preventing physicians from applying PGx into clinical practice under the Korean healthcare
system. A 36-question survey was distributed to 53 physicians with various specialties in
Korea. In the physicians' self-perceived knowledge, twenty-eight physicians (53%) reported a
lack sufficient knowledge about PGx. The perceived largest barrier to clinical implementation
of PGx was the high cost of PGx testing, followed by a lack of PGx education for healthcare
providers or lack of clinical PGx experts. Physicians without clinical PGx experience or with
indirect experience reported that the largest barrier to clinical implementation of PGx was
the high cost of PGx testing, while physicians with clinical PGx experience pointed out that
a lack of patients' education was the major concern, followed by a lack of PGx education
for healthcare providers or lack of clinical PGx experts. The highest priority problem was
reported to be a lack of actionable guidelines for drug selection and dosing using PGx. In
conclusion, we should increase and expand extensive educational programs for healthcare
providers and patients, and to develop and establish a clinical decision support systems for
PGx-based personalized therapy in Korea.

Keywords: Pharmacogenomics; Physician; Survey

INTRODUCTION

Adverse drug reactions (ADRs) and treatment failures have long been considered as
major problems of pharmacotherapeutics. About 20–95% of these variabilities of drug
response have been accounted for by pharmacogenomics although various values has
been reported according to different drugs [1]. Pharmacogenomics (PGx) allows us to

Generated by xmlinkpress

understand the relationship between genetic variation and drug response, and to optimize specific medications, drug regimens, and drug dosages for an individual patient, leading to personalized pharmacotherapy in healthcare [2].

Over the past decade, with the completion of the reference human genome sequence, rapid advances in high throughput genomics technologies such as microarray and next generation sequencing (NGS) have significantly declined the cost of gene analysis, almost a 10,000-fold reduction compared with the cost of sequencing a human genome in 2004 [3], causing an exponential increase in PGx research [4]. Despite the quantitative increase and qualitative advances in the field of PGx research, its clinical implementation of PGx-based personalized therapy has remained limited [5].

In other countries including the United States (US) and Netherlands, surveys of doctors, pharmacists, and patients, etc. have examined the barriers to clinical implementation of PGx [5-8]. Most surveys revealed that biggest barriers were a lack of evidence for clinical effectiveness, a lack of actionable guidelines for the clinical implementation of PGx, and the high cost and reimbursement of the PGx test. Based on these results, many efforts are being made to overcome the problems with gradual success. For example, relevant government agencies such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA), etc., encourage the insertion of PGx information into drug labels, as a result, PGx information in drug label is increasing [9,10]. At present, 321 drugs have been approved by the US FDA and 134 drugs by EMA (accessed 15 January 2020) [9,10]. And actionable guidelines for PGx-based pharmacotherapy provided by PGx expert group such as Clinical Pharmacogenetics Implementation Consortium (CPIC) are increasing and providing the information on when to order PGx test and how to act in clinical practice [11]. Furthermore, the insurance coverage rate for PGx tests is also increasing although the insurance coverage and payments of the PGx tests varies by country and insurance provider [12].

Since 2017, the health insurance coverage for PGx testing has been gradually increasing in Korea, and now major genes for drug metabolism and pharmacokinetics (DMPK) including Cytochrome P450 (CYP) 2C9, CYP2C19, CYP2D6 and thiopurine methyltransferase etc. are covered by insurance [13,14]. However, clinical implementation of PGx-based personalized therapy is still very limited in Korea except for use in oncology area.

Despite this situation, the surveys on the barriers to clinical implementation of PGx-based personalized therapy have not been conducted in Korea. Because the healthcare system and insurance policy of Korea are different from those in the other countries such as United States and Europe, the most problematic and priority barriers to clinical uptake of PGx in Korea can be different from previous reports in other countries, and these surveys are virtually important. Among survey subjects including government, physicians, pharmacists and patients, survey of physicians seemed to be more urgent in Korea because PGx tests must be ordered by physicians and it must be preceded in Korea,

The objective of this study was to assess physicians' self-reported knowledge of PGx-based personalized therapy, and to explore the most problematic and highest priority barriers preventing physicians from applying PGx into clinic practice under the Korean healthcare system.

METHODS

This study was approved by the Institutional Review Board of Inje University Busan Paik Hospital (IRB approval number: 18-0217) before subjects were recruited.

The survey questionnaire was developed by adapting several tools reported in the literature [5-8] and translating the questions into the Korean language. When a draft of the questionnaire was ready, it was sent to several PGx experts and physicians in order to identify confusing questions or ambiguous terms. And then the questionnaire was revised based on their comments. The survey was comprised of four major parts, totaling 36 questions as follows; knowledge of terminology, clinical experience of PGx, barriers in clinical implementation of PGx-based personalized therapy, and demographic information. In order to decrease bias from sampling errors, more than ten physicians were carefully recruited into each of following group: physician with vs. without clinical experience of PGx; physician working in tertiary hospital vs. others; residents vs. specialists; surgeon vs. internal medicines.

The Korean hospital was classified as follows: clinics (up to 29 beds), small hospitals (30–100 beds), general hospitals (more than 100 beds), and tertiary hospitals, the requirements for whose qualifications are stated by Korean law [15]. General hospitals are hospitals equipped with more than 100 beds and several specialty departments as designated by law, and tertiary hospitals are large-sized university hospitals equipped with a full complement of services and departments, typically housing the most experienced and widest range of specialist doctors, which were selected by the government.

Physicians were classified as 'with experience,' 'with indirect experience' or 'without experience' of PGx testing. If the physicians had no experience conducting PGx research or clinically implementing PGx, but had observed or heard others' works, they were defined as indirectly experienced.

Firstly, physicians were asked to rate their understanding based on a five-point scale of 1 = expert (I fully understand everything related to the terminology including legal issues), 2 = very knowledgeable (I understand the terminology including its utilization in clinical practice although limited), 3 = knowledgeable (I understand only the meaning of the terminology), 4 = little knowledgeable (I have heard the terminology, but I do not understand it), 5 = not knowledgeable (I have never heard of the terminology).

In this study, the primary endpoint was the most severe and highest priority barriers preventing physicians from applying PGx to clinical therapeutics. In order to explore the most serious problem, physicians' perception of the severity of barriers were assessed using visual analog scale from 0 to 5: Physicians were requested to rank the barriers to clinical implementation of PGx from first priority to third.

The paper-based survey was distributed to the 53 physicians and returned from November 2018 to January 2019 using physicians' societies and PGx research network in Korea. This survey was voluntary and participants were informed about anonymity and the potential use of the results for publication. Participants were invited directly via email or face to face.

Data were presented as count (percentage) for categorical variables and by mean ± standard deviation for continuous variables. Physicians' perceptions of problems associated with

clinical implementation of PGs were compared among groups with different experiences of PGx using the Kruskal-Wallis test for the most problematic problem and Fisher's exact test for the highest priority problem. The value of $p < 0.05$ was considered to be statistically significant. All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Characteristics of survey respondents

A total 53 physicians participated in the present study and all completed the survey without incomplete response. Their basic characteristics of participants are represented in **Table 1**. Of these, 37 (69.8%) were working at tertiary hospitals, and 13 (24.5%) were working at general hospital. There were no physician working at small-size hospitals or long-term hospitals among the respondents. The most common specialty of the respondents was psychiatry (26.4%), followed by thoracic surgery (24.5%), then internal medicine (20.8%). The specialists with more than 10 years' experiences were the largest group (43.4%).

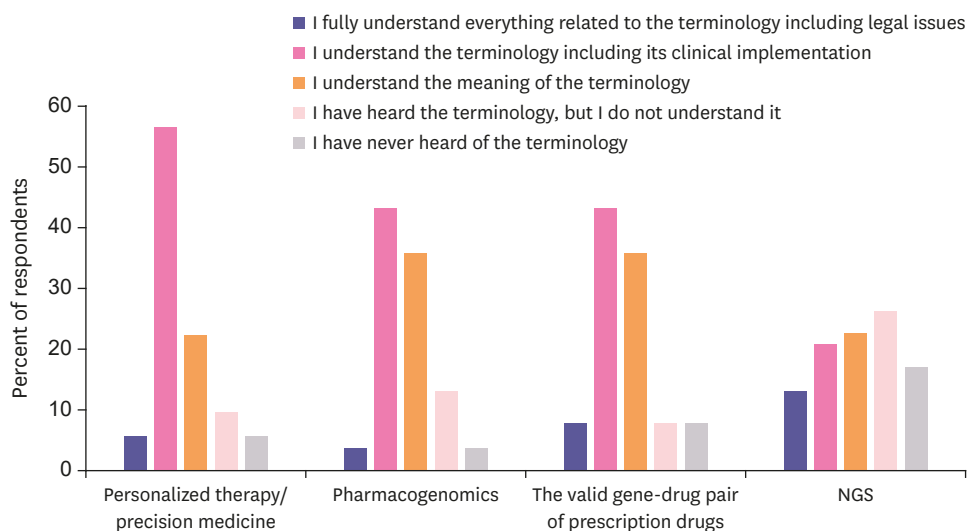### Self-reported level of knowledge

We explored physicians' perceptions and level of knowledge on the topics of 'Personalized therapy/Precision medicine,' 'PGx,' 'The drug-gene pairs known to be valid,' and 'NGS' (**Fig. 1**).

Table 1. Characteristics of physicians participating in this survey (n = 53)

Characteristics	Values
Gender	
Male	38 (72)
Female	15 (28)
Specialty	
Anesthesiology	1 (1.9)
Family medicine	3 (5.7)
General surgery	2 (3.8)
Internal medicine*	11 (20.8)
Neurology	1 (1.9)
Ophthalmology	2 (3.8)
Pathology	1 (1.9)
Pediatrics	5 (9.4)
Psychiatry	14 (26.4)
Thoracic surgery	13 (24.5)
Year of specialty	
Resident	13 (24.5)
Specialist (< 3 yr)	4 (7.6)
Specialist (3–5 yr)	3 (5.7)
Specialist (6–9 yr)	10 (18.9)
Specialist (≥ 10 yr)	23 (43.4)
Hospital classifications†	
Tertiary hospital	37 (69.8)
General hospital	13 (24.5)
Small hospital	0 (0.0)
Clinics	3 (5.7)

Data are presented as number (%).
*Internal medicine (n = 11) includes cardiology (n = 1), nephrology (n = 1), gastroenterology (n = 3), pulmonology (n = 4), allergy and clinical immunology (n = 1), rheumatology (n = 1); †The Korean hospital was classified as follows: clinics (up to 29 beds), small hospitals (30–100 beds), general hospitals (more than 100 beds), and tertiary hospitals. General hospitals are hospitals equipped with more than 100 beds and several specialty departments as designated by law, and tertiary hospitals are large-sized university hospitals equipped with a full complement of services and departments, typically housing the most experienced and widest range of specialist doctors, which were selected by the government.

Figure 1. Self-reported knowledge of physicians in response to our survey. Physicians were asked to rate their understanding on a five-point scale, from no knowledge (I have never heard of the terminology) to expert knowledge (I fully understand everything related to the terminology including legal issues), on the topics of personalized therapy/precision medicine; pharmacogenomics; known valid drug-gene pairs; NGS. NGS, next generation sequencing.

The results showed the majority of the physicians considered themselves as very knowledgeable (30%) or knowledgeable (12%) about the personalized therapy/precision medicine. Surprisingly, 9 physicians (17%) considered themselves to have little knowledgeable or not knowledgeable about PGx and 19 participants (36%) understood only the meaning of PGx.

Although there was no statistically significant relationship between baseline characteristics including level of specialty and self-perceived knowledge, residents reported a better understanding of all terminologies than specialist with more than 10 years experiences (P = 0.073) due to their more recent education from medical college. Not surprisingly, physician with PGx experience understood the terminologies better than those without PGx experience (P = 0.001) (data not shown).

Of the total 53 respondents, 35 physicians (66.0%) indicated that they had experience with PGx tests in clinical practice. Among them, 19 physicians had direct PGx experience. Of those 19, 13 physicians reported that PGx testing helped their patient's care and influenced the decision of drug selection or dosing. But no one said it had no effect.

All physicians were asked if PGx could allow personalized therapy (i.e. reduce ADRs and therapeutic, failure and maximize drug efficacy) (**Fig. 2**). Almost respondents (75%) believed that PGx could allow personalized therapy; and the remaining respondents (25%) were neutral, no respondents believed that it could not.

Physicians' perception of the barriers to incorporating PGx into clinical practice

According to the physicians' perceived severity of each barriers (visual scale from 0 to 5), the largest barrier to clinical implementation of PGx was the high cost of PGx testing (severity: 3.7 ± 1.0), followed by a lack of PGx education for healthcare providers or a lack of clinical PGx experts (3.6 ± 1.1) as shown in **Table 2**. Interestingly, the physicians without clinical
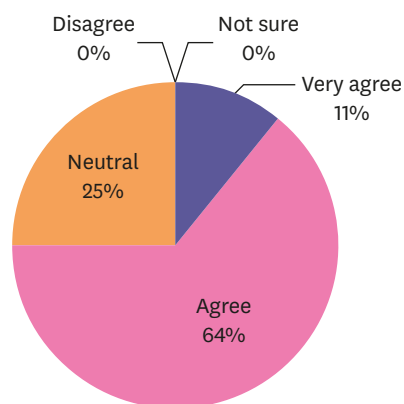
Figure 2. Physicians views on the benefits of PGx testing; PGx testing could reduce adverse drug reactions and therapeutic, failure and maximize drug efficacy (n = 53).
PGx, pharmacogenomics.

Table 2. Physicians' perceived severity of each barriers preventing them from applying PGx to clinical therapeutics using visual analog scale from 0 to 5

Contents	Total (n = 53)	Clinical experience with PGx testing		
		Without experience (n = 19)	Indirect experience (n = 16)	With experience (n = 18)
Difficulties in accessing PGx testing in the workplace	3.2 ± 1.5	2.9 ± 1.7	3.4 ± 1.2	3.4 ± 1.6
High cost of PGx testing	3.7 ± 1.0	3.9 ± 1.1	3.8 ± 0.8	3.4 ± 1.1
Long turnaround time for PGx testing	3.2 ± 1.2	3.6 ± 1.3	3.2 ± 1.0	2.9 ± 1.2
Difficulty in interpreting genotyping results	2.9 ± 1.3	3.5 ± 1.0	2.6 ± 1.2	2.6 ± 1.5
Lack of evidence of the clinical utility of PGx	2.6 ± 1.2	2.8 ± 1.2	2.8 ± 1.0	2.1 ± 1.3
Lack of actionable guidelines for drug selection and dosing	3.2 ± 1.1	3.2 ± 1.2	3.5 ± 0.7	3.0 ± 1.3
No automated decision support system for prescription	3.1 ± 1.3	3.1 ± 1.6	2.9 ± 1.2	3.3 ± 1.1
Lack of PGx education for healthcare providers or lack of clinical PGx experts	3.6 ± 1.1	3.7 ± 1.3	3.5 ± 0.9	3.8 ± 1.1
Lack of patient's education	3.3 ± 1.3	3.2 ± 1.5	2.7 ± 1.2	3.9 ± 0.7

PGx, pharmacogenomics.

PGx experience or with indirect experience perceived that the largest barrier was the high cost of PGx testing, while physicians with clinical PGx experience perceived that the largest barrier was a lack of patients' education about PGx, followed by a lack of PGx education for healthcare providers or lack of clinical PGx experts.

As shown in **Table 3**, respondents were directed to rank the problem in order from first priority to third. Interestingly, all ranking from first to third were a lack of actionable guidelines for drug selection and dosing.

Table 3. Physicians' perception of the most priority problems related to the clinical implementation of PGx based personalized therapy (n = 53)

Contents	Ranking		
	1st	2nd	3rd
Difficulties in accessing PGx testing in the workplace	9 (17.0)	4 (7.6)	4 (7.6)
High cost of PGx testing	10 (18.9)	7 (13.2)	6 (11.3)
Long turnaround time for PGx testing	2 (3.8)	7 (13.2)	5 (9.4)
Difficulty in interpreting genotyping results	1 (1.9)	4 (7.6)	1 (1.9)
Lack of evidence of the clinical utility of PGx	5 (9.4)	7 (13.2)	8 (15.1)
Lack of actionable guidelines for drug selection and dosing	12 (22.6)	10 (18.9)	11 (20.8)
No automated decision support system for prescription	1 (1.9)	6 (11.3)	7 (13.2)
Lack of PGx education for healthcare providers or lack of clinical PGx experts	7 (13.2)	8 (15.1)	6 (11.3)
Lack of patient's education	6 (11.3)	0 (0)	5 (9.4)

PGx, pharmacogenomics.

DISCUSSION

This is the first survey to assess physicians' self-reported knowledge of PGx-based personalized therapy, and to explore what physicians' perceived to be the most problematic and highest priority barriers to the clinical implementation of PGx under the Korea health system. We demonstrated that the most problematic barrier was perceived to be the high cost of PGx testing, which was consistent with previous study [5].

While the health insurance under Korea HIRA has covered most known valid PGx genes including DMPK since early 2017 [13], 70% of this survey respondents reported little or no knowledge about insurance coverage for PGx tests (data not shown). This indicates that the insurance system for offsetting the cost of PGx testing is not well known to physicians. It is supporting that there is an urgent priority to educate physicians about which PGx tests are covered by HIRA insurance system as well as PGx itself.

There have been no report to compare the physicians' perceived barriers to clinical implementation of PGx between the physicians with and without clinical PGx experience. In this study, we found that the two groups (the physicians with and without PGx experience) perceived the barriers to clinical implementation of PGx was different: Physicians with PGx experience perceived the largest barrier to be a lack of patient education, followed by lack of healthcare providers' PGx education, or a lack of clinical PGx experts; but the physicians without clinical PGx experience or with indirect experience perceived that the largest barrier to be the high cost of PGx testing. Cancer patients who are at high risk for serious ADR and treatment failure leading to death have been willing to try new therapy and pleased to personalized therapy. In reality, they have been likely to more benefit from PGx-based personalized therapy [16]. These seems to cause significant differences in patients' attitude towards PGx between anti-cancer drugs and other drugs. Physicians with clinical PGx experience in this study indicated that it was difficult and time consuming to educate and persuade patients to incorporate PGx into clinical practice except oncology. They also reported that it was very difficult to keep up with rapidly changing PGx issues related to legal matters, insurance coverages and clinical utilization, etc. And thus, they indicated that clinical PGx experts and continuous education for health care providers are necessary. Responses of physicians without clinical PGx experience seemed to be caused by little knowledge about PGx including decreased cost and insurance coverage of PGx tests. It is also supporting that it is very important and necessary to educate and re-educate physicians about PGx-based personalized therapy.

These days, several educational program can be used through offline meetings such as PGx symposium and workshop, online resource such as PharmGKB, education from direct-to provider and point-of-care education (education embedded in clinical decision support system [CDSS] alerts, inbox messaging and result reports) if possible. Rohrer Vitek et al. [17] evaluated the PGx education methodologies and reported the general consensus that regardless of the type and number of educational strategies, initial training was inadequate and they required ongoing education.

Knowledge about pharmacology as well as PGx itself is needed to apply PGx to clinics. And thus it is expected that clinical pharmacologists play an important role in educating physicians and patients about clinical pharmacogenomics. In addition, as clinical pharmacogenomics experts, clinical pharmacologist can provide clinical PGx consultations

to support patient care. It may result in more efficient and effective PGx implementation along with more effective CDSS alerts.

Our results indicated that the most urgent problem as perceived by physicians, was a lack of actionable guidelines for drug selection and dosing. After PGx testing, physicians don't know how to act with many drugs in clinical practice. And thus the development of standardized actionable guidelines for PGx-based personalized therapy should be a high priority. These days, PGx expert groups such as CPIC, are actively publishing PGx guidelines although the number of guidelines is still limited [11]. As clinical pharmacogenomic experts, clinical pharmacologists should actively participate in the PGx expert working group and make an effort to develop PGx guidelines.

In the physicians' self-reported knowledge, more than half of respondents (53%) reported that they lack knowledge about PGx. This result is consistent with Selkirk et al.'s finding [6]. Of note, our survey found that residents self-reported a better understanding of the terminologies related to PGx compared to specialists with more than 10 years' experience, without statistical significance due to small sample size. This finding can be attributed to recent inclusion of PGx into undergraduate medical curriculum. But Selkirk et al. [6] reported that there was no difference in perceived knowledge based on graduation date. They assessed ages as a continuous variables while in this current study we focused on recently educated group of residents and handled the years of experience as a categorical variables. It may account for the discrepancy between two surveys. Other studies have reported that knowledge is based on experience [18,19]. Unsurprisingly, our survey also found that physicians with PGx experience self-reported a better understating of PGx issues compared to those without PGx experience.

A large systematic review reported that the most common obstacle preventing genomic medicine from entering into clinical practice was a lack of sufficient knowledge [20]. Genomic medicine is a relatively broader concept compared to PGx, which is the field of study that looks into genes (our DNA) and their interaction with our health. Similar to PGx, the main problems of clinical application seem to be evolving from a lack of evidence, to a lack of clinical guidelines, to a lack of health insurance coverage. In addition, as the number of studies on the implementation of PGx has increased recently, different solutions for overcoming the obstacles have been emphasized dependent on their healthcare system including PGx [21]. In this survey, the need for education and training of clinical PGx experts was increasing. Based on the current survey, we should strengthen our efforts to increase the extensive PGx educational programs for healthcare providers and patients, and to develop and establish CDSS for PGx-based personalized therapy in Korea.

REFERENCES

1. Wang L, McLeod HL, Weinshilboum RM. Genomics and drug response. N Engl J Med 2011;364:1144-1153.
   PUBMED | CROSSREF

2. Flynn AA. Pharmacogenetics: practices and opportunities for study design and data analysis. Drug Discov Today 2011;16:862-866.
   PUBMED | CROSSREF

3. Burt T, Dhillon S. Pharmacogenomics in early-phase clinical development. Pharmacogenomics 2013;14:1085-1097.
   PUBMED | CROSSREF

4. Pirmohamed M. Pharmacogenetics: past, present and future. Drug Discov Today 2011;16:852-861.
    PUBMED | **CROSSREF**

5. UnitedHealth Center for Health Reform & Modernization. Working paper: personalized medicine: trends and prospects for the new science of genetic testing and molecular diagnostics. https://www.unitedhealthgroup.com/newsroom/2012/0312whitepaper7personalizedmedicine.html/. Accessed January 15, 2020.

6. Selkirk CG, Weissman SM, Anderson A, Hulick PJ. Physicians' preparedness for integration of genomic and pharmacogenetic testing into practice within a major healthcare system. Genet Test Mol Biomarkers 2013;17:219-225.
    PUBMED | **CROSSREF**

7. Unertl KM, Jaffa H, Field JR, Price L, Peterson JF. Clinician perspectives on using pharmacogenomics in clinical practice. Per Med 2015;12:339-347.
    PUBMED | **CROSSREF**

8. Haga SB, Burke W, Ginsburg GS, Mills R, Agans R. Primary care physicians' knowledge of and experience with pharmacogenetic testing. Clin Genet 2012;82:388-394.
    PUBMED | **CROSSREF**

9. U.S. Food and Drug Administration. Table of pharmacogenomic biomarkers in drug labeling. https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling/. Accessed January 15, 2020.

10. European Medicines Agency. https://www.ema.europa.eu/. Accessed January 15, 2020.

11. PharmGKB. https://www.pharmgkb.org/. Accessed January 15, 2020.

12. Park SK, Thigpen J, Lee IJ. Coverage of pharmacogenetic tests by private health insurance companies. J Am Pharm Assoc (2003) Forthcoming 2019.
    PUBMED | **CROSSREF**

13. HIRA. Criteria for health insurance coverage. https://www.hira.or.kr/rd/insuadtcrtr/InsuAdtCrtrList.do?pgmid=HIRAA030069000000&WT.ac=보험인정기준바로가기/. Accessed January 15, 2020.

14. Kim S, Yun YM, Chae HJ, Cho HJ, Ji M, Kim IS, et al. Clinical pharmacogenetic testing and application: laboratory medicine clinical practice guidelines. Ann Lab Med 2017;37:180-193.
    PUBMED | **CROSSREF**

15. Kim AM, Cho S, Kim HJ, Jung H, Jo MW, Lee JY, et al. Primary care patients' preference for hospitals over clinics in Korea. Int J Environ Res Public Health 2018;15:15.
    PUBMED | **CROSSREF**

16. Marsh S, McLeod HL. Cancer pharmacogenetics. Br J Cancer 2004;90:8-11.
    PUBMED | **CROSSREF**

17. Rohrer Vitek CR, Abul-Husn NS, Connolly JJ, Hartzler AL, Kitchner T, Peterson JF, et al. Healthcare provider education to support integration of pharmacogenomics in practice: the eMERGE Network experience. Pharmacogenomics 2017;18:1013-1025.
    PUBMED | **CROSSREF**

18. Hofman KJ, Tambor ES, Chase GA, Geller G, Faden RR, Holtzman NA. Physicians' knowledge of genetics and genetic tests. Acad Med 1993;68:625-632.
    PUBMED | **CROSSREF**

19. Wilkins-Haug L, Hill LD, Power ML, Holzman GB, Schulkin J. Gynecologists' training, knowledge, and experiences in genetics: a survey. Obstet Gynecol 2000;95:421-424.
    PUBMED | **CROSSREF**

20. Scheuner MT, Sieverding P, Shekelle PG. Delivery of genomic medicine for common chronic adult diseases: a systematic review. JAMA 2008;299:1320-1334.
    PUBMED | **CROSSREF**

21. Krebs K, Milani L. Translating pharmacogenomics into clinical decisions: do not let the perfect be the enemy of the good. Hum Genomics 2019;13:39.
    PUBMED | **CROSSREF**