Precision Medicine Using Pharmacogenomic Panel-Testing

Current Status and Future Perspectives

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INTRODUCTION

Although drug treatment is often successful, adverse drug reactions (ADRs) and lack of efficacy present a significant burden for individual patients and society as a whole. ADRs are an important cause of emergency department visits and hospital admissions. A study in 2 large UK hospitals showed that 6.5% of hospital admissions were attributable to ADRs \cite{1}. In the United States, ADR-related morbidity and mortality have been estimated at $30 billion to $136 billion annually \cite{2}. In parallel, lack of efficacy also results in a significant burden. Its magnitude can be estimated by inspecting the number needed to treat of commonly used drugs \cite{3}, which are commonly more than 10. As a result, most patients will not benefit from drug treatment and, in contrast, may experience harm from unsuccessfully treated disease. It has been estimated that $100 billion a year is wasted on ineffective drug treatment \cite{4}.

Precision medicine aims to individualize or stratify application of pharmacotherapy, as opposed to the current population-based application, in an effort to optimize the benefit/risk ratio \cite{5,6}. By enabling identification of individuals who are at higher risk for ADRs or lack of efficacy, before drug initiation and potential harm, an individualized dose and drug selection may be applied to reduce this risk. An individual's germline genetic variation is a particularly promising

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predictive factor that can enable drug response prediction. This notion is supported by its pharmacologic plausibility and has been demonstrated in various studies [7–10]. Drug-gene interactions (DGIs) can be categorized into 3 groups (Fig. 1A–C): pharmacokinetic-dependent ADRs (see Fig. 1A), pharmacodynamic-dependent ADRs (see Fig. 1B), and idiosyncratic ADRs (see Fig. 1C).

Pharmacogenomics (PGx) uses an individual’s germline genetic profile to identify those who are at higher risk for ADRs or lack of efficacy (see Fig. 1D) [11–13]. This information can be used by health care professionals (HCPs) to guide dose and drug selection before drug initiation in an effort to optimize drug therapy [14]. Within germline PGx, the focus lies on inherited variation in genes, which play a role in drug absorption, distribution, metabolism, and elimination (ADME). To date, several randomized controlled trials (RCT) support the clinical utility of individual DGIs to either optimize dosing [15–18] or drug selection [19,20]. Following the completion of the Human Genome Project, the Royal Dutch Pharmacists Association anticipated a proximate future where patients would present themselves in the pharmacy with their genetic information. In anticipation, the Dutch Pharmacogenetics Working Group (DPWG) was established in 2005 with the objective to develop clear guidelines for HCPs on how to interpret and apply PGx test results [21,22]. In parallel, the Clinical Pharmacogenetics Implementation Consortium was initiated in 2008 and devises similar guidelines [23].

Significant debate persists regarding the optimal timing and methodology of testing for delivering PGx testing in clinical care [24]. Some support a pretherapeutic single gene–drug approach, in which a PGx test of a single relevant gene is ordered once a target drug is prescribed, while others advocate for a preemptive

![FIG. 1 Precision medicine using pharmacogenomic panel testing: current status and future perspectives. conc., concentration; PM, poor metabolizers; Rx, prescription.](image-url)
Despite the initiatives, a major hurdle preventing implementation is the absence of evidence presenting the collective clinical utility of a panel of PGx markers for preemptive PGx testing. Although several RCT support the clinical utility of individual gene-drug pairs, delivered in a single-gene reactive approach [15–20], evidence supporting clinical utility of the remaining DGIs for which recommendations are available when delivered in a preemptive panel approach is lacking. Significant debate persists regarding both the nature and the strength of evidence required for the clinical application of these remaining DGIs. Some argue an RCT is required for each individual DGI before clinical implementation is substantiated [35]. Others argue that a mandatory requirement for prospective evidence to support the clinical validity for each PGx interaction is incongruous and excessive [36–39]. Generating gold-standard evidence for each individual DGI for which PGx guidelines are available separately would require unrealistically large amounts of funds. On the other hand, extrapolating efficacy of all of these DGIs based on the conclusions of the previously mentioned RCTs, supporting clinical utility for a subset of individual DGIs, is also not substantiated.

Regardless of the inconvenience, there is still a demand for evidence substantiating patient benefit and cost-effectiveness, to enable stakeholders to practice evidence-based medicine. The Ubiquitous Pharmacogenomics Consortium (U-PGx), a European Consortium funded by the Horizon 2020 program, aims to generate such evidence [34]. The U-PGx consortium set out to quantify the collective clinical utility of a panel of PGx markers (50 variants in 13 pharmacogenes) within a single trial (the PREPARE study, ClinicalTrials.gov: NCT03093818) as a proof-of-concept across multiple potentially clinically relevant DGIs [34,40]. It is a block RCT aiming to enroll 8100 patients across 7 European countries. Additional outcomes include cost-effectiveness, process indicators for implementation, and provider adoption of PGx.

In the meantime, several smaller randomized and observational studies indicate the cost-effectiveness of PGx panel–based testing in psychiatry and polypharmacy patients [41–44]. Observed cost savings ranged from $218 [42] to $2778 [45] per patient. Others have modeled the cost-effectiveness of one-time genetic testing to minimize a lifetime of ADRs and concluded an incremental cost-effectiveness ratio (ICER) of $43,165 per additional life-year and $53,680 per additional quality-adjusted life-year, therefore considered cost-effective [46]. However, cost-effectiveness may vary across ethnic populations, as a result of differences in allele frequencies, differences in prescription

**THE LACK OF EVIDENCE OF (COST-) EFFECTIVENESS SUPPORTING A PHARMACOGENOMICS-PANEL APPROACH**

Several of the reported hurdles obstructing the implementation of PGx-panel testing are currently being addressed by various initiatives, in both the United States and the European Union. Overviews of these initiatives have previously been published [24,34]. Despite these initiatives, a major hurdle preventing
patterns, and differences in health care costs and ICER cost-effectiveness thresholds. The study designed by the U-PGx consortium (the PREPARE Study) will enable the quantification of the cost-effectiveness over a 12-week time horizon.

Clinical trials and prospective cohorts typically measure short-term benefits of PGx testing, whereas the time horizon for the benefits and risks of PGx testing is over a lifetime and therefore unable to be captured within regular trials. As such, the life-long cost-effectiveness of one-time preemptive panel-based testing to prevent ADRs is yet undetermined. Other methodologies, such as Markov models, can be deployed to simulate effectiveness over longer time horizons. The results of such models will be of interest to reimbursement policymakers, who require evidence that panel-based testing will yield downstream improved health outcomes at acceptable costs. Therefore, once the effectiveness of PGx-panel testing has been established, future research should model the cost-effectiveness of preemptive PGx testing to prevent a lifetime of ADRs. Optimally, such an analysis could be run on a longitudinal cohort of patients for which both prescription data and PGx results are available. Furthermore, such a data set could be used to explore the optimal timing and subgroup application of testing to optimize cost-effectiveness.

FINDING THE OPTIMAL TARGET POPULATION AND TIMING FOR DELIVERING PHARMACOGENOMICS

The optimal target population and time at which panel-based testing should be performed remain to be determined. In the most progressive application of PGx panel-testing could be performed when no drug initiation is indicated, in anticipation of future drug prescriptions. However, if no drug is initiated in the near future, PGx testing would be a waste of resources. Alternatively, in a more efficient scenario, panel testing could be performed once a patient plans to initiate a drug for which PGx testing may be useful and reuse these results when future DGIs are encountered. Such a model was deployed in a pilot study [47], whereby pharmacists requested a PGx-panel test when patients planned to initiate one of 10 drugs for which PGx guidelines are available. Here, 97% of patients (re)used PGx-panel results for at least one, and 33% for up to 4 newly initiated prescriptions with possible DGIs within a 2.5-year follow-up. In this case, 24% were actionable DGIs, requiring pharmacotherapy adjustment. This high rate of reuse indicates that such a model may be promising for delivering PGx panel-based testing. As an alternative model, another initiative at Vanderbilt University Medical Center has used a prediction model to select patients who may benefit from PGx testing in the near future algorithmically and using prescription data [48,49].

In addition to undetermined timing and methodology, the most optimal target group for testing is also yet undetermined. Current studies have identified potential patient subgroups for which preemptive PGx-panel testing may be most useful. Some initiatives have selected patients with particular indications in psychiatry [43,44,50,51]. Others have selected patients with particular characteristics, such as polypharmacy and elderly patients [41,42].

Alternatively, consumers who have an interest in their PGx profile may also obtain their PGx test results outside the realm of health care and without the intervention of an HCP. In 2018, direct-to-consumer (DTC) PGx testing for specific DGIs was approved by the Food and Drug Administration (FDA). However, in contrast to DTC tests provided before 2013, the FDA has approved only a limited scope of 33 variants in 8 genes, and providers have mandated the need to retest. Concerns of DTC PGx testing have been reported to relate to patient actions (eg, to stop taking a prescribed medication or adjusting the regimen based on genotype without consultation with a health provider) [52]. However, a longitudinal study of DTC consumers showed that only 5.6% of consumers reported changing a medication they were taking or starting a new medication because of their PGx results. Of these, 45 (83.3%) reported consulting with an HCP regarding the change [53]. Nonetheless, the involvement of HCPs will optimize the use of PGx results when delivered in a DTC setting. In the same longitudinal study, the authors found that 63% of consumers planned to share their results with a primary care provider. However, at 6-month follow-up, only 27% reported having done so, and 8% reported sharing with another HCP. Among participants who discussed results with their PCP, 35% were very satisfied with the encounter, and 18% were not at all satisfied. These results indicate that PGx testing in a DTC model may be a safe model for obtaining PGx testing.

THE LACK OF TOOLS SUPPORTING IMPLEMENTATION OF PHARMACOGENOMICS-PANEL TESTING

Development of a Pharmacogenomics Panel to Facilitate Implementation

Another important challenge hampering adoption of preemptive panel testing is the lack of standardization
regarding variants included in such panels. Standardization would enable clinicians to understand PGx test results without extensive scrutiny of the alleles included in the panel. Despite the identification of standardization as a potential accelerator for PGx adoption, exchange, and continuity [54], there are currently no standards defining which variants should be tested [55,56]. Although some initiatives have developed standardized panels of relevant variants within individual genes [57], and other initiatives across multiple genes [58], a panel covering widely accepted genetic variants reflecting an entire set of guidelines is not yet available. Thus, in order to facilitate the clinical implementation of PGx testing, the U-PGx consortium set out to develop a pan-European panel based on actionable DPWG guidelines, called the “PGx-Passport” [59]. Here, germline variant alleles were systematically selected using predefined criteria regarding allele population frequencies, effect on protein functionality, and association with drug response. A “PGx-Passport” of 58 germline variant alleles, located within 14 genes (CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP3A5, DPDY, F5, HLA-A, HLA-B, NUDT15, SLCO1B1, TPMT, UGT1A1 and VKORC1), was composed. This "PGx-Passport" can be used in combination with the DPWG guidelines to optimize drug prescribing for 49 commonly prescribed drugs. An advantage of the approach is that the number of clinically interpretable results within their "PGx-Passport" is maximized, while costs remain reasonable.

Importantly, the presented panel will not be able to fully identify those at risk for unwanted drug response. The overall ability of a panel to predict drug response is dependent on, first, the predictive utility of genetic variation to predict drug response and, second, the ability to adjust pharmacotherapy to reduce the risk of unwanted effects among high-risk individuals. In the following sections, the current limitations of both domains are further elaborated.

**Current predictive utility of genetic variation to predict drug response**

Even though multiple genetic variants have been discovered, the authors currently restrict testing to a subset of these variants. However, restricting testing to individual variants disregards untested or undiscovered variants that may also influence the functionality of the gene product. Therefore, the functionality of the gene product cannot be fully predicted (see Fig. 1E). Reasons for restriction of testing are twofold. First, technical limitations regarding the sequencing of complex loci prevent complete determination of both the gene of interest and other areas in the genome, which may have an effect on the gene product. Determining genetic variation is specifically difficult in highly polymorphic genes, such as the HLA genes, or genes located near pseudogenes, such as CYP2D6. Although sequencing of these loci is technically possible, it are costly and time-consuming. Second, even if one were to determine all genetic variation, the downstream effect on protein functionality may be unknown and therefore impossible to interpret clinically [60].

However, progress in the interpretation of functional consequences of such uncharacterized variations may support future interpretation in silico [61], in vitro, or in vivo [62]. Importantly, a study has shown that 92.9% of genetic variation in ADME genes is rare, and an estimated 30% to 40% of functional variability in pharmacogenes can be attributed to these variants [63]. In addition to the downstream functionality, the penetrance (ie, the potential of a variant to accurately predict the genetic component of drug response) is also unknown. The penetrance is a function of both the variant’s effect on protein functionality and the extent to which the protein functionality is associated with clinical outcome. Significant debate persists regarding both the nature and the strength of evidence required for the clinical application of variant alleles of unknown functionality. Because the strength of these functions differs across genes and DGIs, the authors do not foresee a one-size-fits-all consensus regarding and evidence threshold across all DGIs, but rather a different evidence threshold per individual DGI based on the genetics and pharmacology of the interaction. For example, in the case of the TPMT-thiopurine interaction, the effect of TPMT variation on protein functionality has been firmly established because it exhibits behavior similar to monogenetic codominant traits [64]. Therefore, identified variants in TPMT (*3A/*3B/*3C) are considered to have sufficient evidence to be applied in the clinic. The clinical interpretation has been clinically validated in a study specifically investigating clinical effects in patients carrying these variants [18]. On the other hand, clinically relevant variant alleles in CYP2D6 are based on the pharmacology of the interaction. For example, the flecainide-CYP2D6 interaction is based on the associations between decreasing CYP2D6 activity leading to increasing flecainide plasma levels, which in turn leads to increased risk for flecainide intoxication. Therefore, all identified variants in CYP2D6, shown to have a significant effect on CYP2D6 enzyme activity, are considered clinically applicable. As such, both the functional effects and the penetrance of many rare variants are yet
unknown. As an additional complication, these may also differ across substrates and drug responses. Even more fundamentally, variants may impact each other’s functionality, and therefore, individual variants may have different functionalities depending on the absence or presence of other variants.

Another significant limitation, which is applicable to PGx testing and interpretation as it is performed today, is that predicted phenotypes are interpreted as categories rather than continuous scores, and it is assumed the sum of both alleles equals total metabolic capacity (see Fig. 1F). For example, for CYP2D6, patients are categorized into normal metabolizers, intermediate metabolizers, poor metabolizers, or ultrarapid metabolizers. However, the actual CYP2D6 phenotype is likely normally distributed [65,66]. Imposing categorization, as opposed to the interpretation of the actual diplotype, therefore sacrifices information in order to simplify clinical interpretation. In the process, the functionality of each allele is interpreted individually, and it is assumed that the sum of these activity scores equals the total activity of the diplotype. Furthermore, these categorizations are currently substrate independent, even though the effects on metabolic capacity are known to differ between substrates [67].

**Current ability to adjust pharmacotherapy to optimize outcomes**

In addition to the ability of genetic variation to predict drug response, the second component determining the utility of PGx-guided pharmacotherapy is the ability to adjust pharmacotherapy to the specific genetic variants. Currently, there are 2 options to reduce the risk of ADRs and lack of efficacy: (1) selecting another drug and (2) adjusting the dose (see Fig. 1H).

A successful example of choosing an alternative therapy to avoid an ADR is preemptive testing for HLA-B*57:01 to guide drug selection for abacavir or another antiretroviral. Here, 0% of the prospectively screened group versus 2.7% of the control group experienced immunologically confirmed hypersensitivity [19]. In this example, the PGx intervention and subsequent adjustment completely eliminated the risk of hypersensitivity.

An example of adjusting the dose to reduce the risk of ADRs is preemptive testing for TPMT to guide dose selection of thiopurines to reduce the risk of severe hematologic ADRs [18]. In contrast to the previously described abacavir/HLA-B*57:01 example, this intervention has a smaller effect size. Here, severe hematologic ADRs still occurred in 2.6% of TPMT variant carriers who received an adjusted dose, compared with 22.9% of TPMT variant carriers treated with a normal dose. Although dose adjustment prevented ~89% of severe hematologic ADRs, the remaining ~11% could not be prevented by this intervention. Indeed, this could partially be a result of the sensitivity of TPMT testing not reaching 100%, but could also be due to the fact that dose reduction was not sufficient for avoiding this ADR. Furthermore, the incidence of severe hematological ADRs among noncarriers of TPMT variants was 7.3%, indicating that other (genetic) factors, such as NUDT15, may play a role in the risk of severe hematological ADRs.

**Enable Recording of Pharmacogenomics-Panel Results for Future Use**

To enable preemptive PGx testing, it is imperative that the PGx test results are recorded in the electronic medical records (EMRs) for future use (see Fig. 1G). Within a pilot study, the authors found that both pharmacists and general practitioners (GPs) are able to record PGx results in their EMRs as contraindications (96% and 33% of pharmacists and GPs, respectively), enabling the deployment of relevant guidelines by the CDSS when a DGI is encountered at both prescribing and dispensing [47]. In contrast, a recent study showed that genotyping results were sparsely communicated and recorded correctly; only 3.1% and 5.9% of reported genotyping results were recorded by GPs and pharmacists, respectively, within a similar follow-up time of 2.36 years [68].

**FUTURE PERSPECTIVES**

**Generating Evidence for Effectiveness of Precision Medicine Approaches**

In an era where digitalization is driving data accumulation and a concomitant increase in stratification of patient groups and a more precise diagnosis, we are moving toward the utilization of real-world data to support precision medicine (see Fig. 1I). Several investigators have pointed out that precision medicine, and genomic medicine, in particular, would benefit from a convergence of implementation science and a learning health system to measure outcomes and generate evidence across a large population [69,70]. However, this requires standardization of outcomes in EMRs to enable aggregation of phenotype data across large populations for both discovery and outcomes assessment within a genomic medicine implementation [71]. Many nationwide, large-scale initiatives are generating prospective longitudinal evidence supporting
precision medicine approaches [72–74]. For example, a landmark project specifically generating evidence for PGx is the All of Us project [75]. Alternatively, pragmatic clinical trials offer researchers a means to study precision medicine interventions in real-world settings [76,77]. In contrast to traditional clinical trials that are performed in ideal conditions, these pragmatic trials are conducted in the context of usual care [77]. Pragmatic clinical trials easily transition into existing health care infrastructures and therefore make them particularly appealing to comparative effectiveness research and the evidence-based mission of learning health care systems [78,79]. An example of such a pragmatic trial for generating evidence for preemptive PGx testing is the I-PICC study [80].

In parallel, evolving digital health technologies are driving data accumulation. Data collected by sensors (in smartphones, wearables, and ingestibles), mobile apps, and social media can be processed by machine learning to support medical decision making [81]. Raw sensor data can also be processed into digital biomarkers and endpoints [82]. This development may be particularly useful for endpoint definition in disease areas where biological endpoints are lacking, such as in psychiatry and neurology, to enable quantification of disease progression and drug response. For example, novel digital endpoints are being developed to stratify mental health conditions and predict remission using passively collected smartphone data [83]. Another example is the development of a digital biomarker for Parkinson disease using motor active tests and passive monitoring through a smartphone [84]. For precision medicine, in particular, we may also be more able to stratify patient groups into responders and nonresponders with improved endpoint development in these disease areas. Increased stratification of patient groups on the basis of genetic, (digital) biomarker, phenotypic, of psychosocial characteristics will drive more precise diagnoses and pharmacotherapy optimization [85,86]. This trend will drive demand for innovations for more efficient study designs because of increasing numbers of indications, whereas resources to fund these trials remain constant [87].

**Determining Optimal Timing and Target Group for Pharmacogenomics-Panel Testing**

Consensus regarding who should be tested, and when it is most cost-effective to perform preemptive panel-testing, remains undetermined [28]. Moreover, the most cost-effective technique to determine the PGx profile is also undetermined. As novel DGI s are discovered, it may be more efficient to sequence whole genomes, to avoid testing of additional variants through genotyping over time. Clinically relevant PGx variants can successfully be extracted from sequencing data using bioinformatics pipelines [88,89]. As the cost of sequencing techniques decrease, genotype-based testing will become obsolete. In this case, it may be more cost-effective to perform population-wide sequencing at birth, to ensure the maximization of instances in which a PGx result is available when a DGI is encountered. However, whole-exome sequencing and whole-genome sequencing are increasingly applied for other medical indications and objectives [90,91]. As this development expands, determining the cost-effectiveness of implementing PGx testing may become redundant, because the information on PGx variants becomes secondary findings, free of additional costs.

**Improving Predictive Utility of Genetic Variation to Predict Drug Response**

Recent advances have been made to improve the ability to determine an individual’s genetic variation. Technical limitations regarding the sequencing of complex loci may be overcome by advances in long-read sequencing technologies and synthetic long-read assembly [92]. As a result, an increasing number of variants with unknown functionality will need to be interpreted. Because of the vast increasing number of rare variants, it is impossible to determine functionality in traditional expression systems. To overcome this challenge, advances have been made in the development of in silico methods to predict functionality. However, these methods are based on genes that are evolutionarily highly conserved. Because many ADME genes are only poorly conserved, steps have been taken to calibrate in silico models on data sets. For example, recently investigators developed a novel computational functionality prediction model optimized for pharmacogenetic assessments, which substantially outperformed standard algorithms [62].

Nonetheless, these models still do not enable prediction of the functionality of synonymous mutations, intronic variants, or variants in noncoding regions of the genome. Recent initiatives have provided an alternative method for the interpretation of variants with unknown functionality using machine learning [65,93], one using an existing data set for model training and the other using a mock data set. In the first, the investigators trained a neural network model on the long-read sequencing profiles of CYP2D6 of 561 patients and used the metabolic ratio between tamoxifen and endoxifen as an outcome measure. The model explains 79% of the interindividual variability in CYP2D6.
activity compared with 55% with the conventional categorization approach. In addition, this model is capable of assigning accurate enzyme activity to alleles containing previously uncharacterized combinations of variants. The suggested model has provided a method to determine predicted phenotype on a continuous scale. Indeed, enzyme activity may be expected to be normally distributed within a population and therefore better described by such a scale. A future is envisioned where phenotypes can be predicted more precisely by using all of an individual’s genetic variation, as opposed to limiting the view only to those variants included in a tested panel.

Following a further understanding of the effects of individual variants to inform phenotype prediction on a continuous scale, one can imagine that this phenotype prediction will ultimately become substrate specific on top of gene specific. More fundamentally, in PGx, the view is currently limited to a single DGI, whereas multiple genes may be involved in the metabolism of drugs and their metabolites. If one were to expand their view to multiple genes involved to predict drug response, the predictive utility will further improve. To incorporate genetic variations of multiple genes, polygenic risk scores may prove useful [94].

Although genetics is considered the causal anchor of biological processes [95], the biological mechanism underlying drug response may be downstream of a genetic variant. In these cases, genetics will have no predictive utility for drug response (see Fig. 1J, top left). Therefore, incorporating processes downstream of the genome, such as the epigenome [96], transcriptome, microbiome [97], and metabolome [98], may further optimize the ability to predict drug response to enable more accurate stratification of patient populations. Combining these profiles in a systems medicine approach may have a synergistic effect.

Improving Ability to Adjust Pharmacotherapy to Optimize Outcomes
In the future, pharmacotherapy adjustment may be further improved by imminent technologies, such as 3-dimensional (3D) printing to enable personalized dosing and delivery [99]. Currently, the DPWG calculates specific dose adjustments based on pharmacokinetic studies and rounds the recommended dose to the nearest corresponding marketed dose for clinical feasibility. The utilization of 3D-printing technologies may enable rapid compounding of tablets with a specific dose based on an individual’s genetic profile. In any case, adjustment of the pharmacotherapy will always be limited by the safety profile of available drugs. Opportunely, over the last decades, newly developed drugs have been shifting from unspecific small molecules to more targeted drugs in the form of humanized monoclonal antibodies [100], cell therapies [101], and gene therapies [102] with fewer off-target ADRs.

Recording Pharmacogenomics-Panel Results for Future Use
Future initiatives should focus on the development of automated sharing of PGx results across EMRs. In the Netherlands, such an initiative has been launched but requires patient consent before it can be used. The National Exchange Point (“Landelijk Schakel Punt” [LSP]) is a nationwide secured EMR infrastructure to which nearly all HCPs can access [103]. Only when a patient has provided written consent for the LSP can a professional summary of the local pharmacy or GP EMR, including PGx results, be downloaded by another treating HCP in the same region, unless the patient chose to shield this information. Alternatively, providing the PGx results directly to patients may resolve the issue in terms of communicating and recording PGx results; for example, using the MSC safety-code card as used in the PREPARE study [104,105].

SUMMARY
In conclusion, developments in evidence generation and in genetic sequencing and interpretation will revolutionize current stratified medicine to enable true precision medicine, whereby multiple -omics profiles of an individual are combined to predict drug response and optimize pharmacotherapy accordingly.

DISCLOSURE
The authors have nothing to disclose.

REFERENCES


