**Pharmacogenomics in the UK National Health Service: opportunities and challenges**

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**Abstract**

Despite increasing interest in pharmacogenomics, and the potential benefits to improve patient care, implementation into clinical practice has not been widespread. Recently, there has been a drive to implement genomic medicine into the UK National Health Service (NHS), largely spurred on by the success of the 100,000 Genomes Project. The UK Pharmacogenetics and Stratified Medicine Network, NHS England and Genomics England invited experts from academia, the healthcare sector, industry and patient representatives to come together to discuss the opportunities and challenges of implementing pharmacogenomics into the NHS. This report highlights the discussions of the workshop to provide an overview of the issues that need to be considered to enable pharmacogenomic medicine to become mainstream within the NHS.

**Introduction**

Implementation of pharmacogenomics (the study and clinical application of the genomic determinants of drug response) is being undertaken in many centers in the USA, but this is not nationwide and often focused on highly specialized academic centers, driven by champions. To date, there has been no implementation on a whole country basis. The UK National Health Service (NHS) is a single integrated healthcare system, which provides free care to all patients at the point of need. Recently, there has been a government backed drive to implement genomic medicine into the NHS, largely spurred on by the success of the 100,000 Genomes Project. This represents an unprecedented opportunity to implement pharmacogenomics for over 60 million people to provide a more efficient service with improved healthcare outcomes.

The UK spends approximately £16.8 billion per year on prescription drugs and this will soon rise to £20 billion, but currently they are not effective in 50–75% of patients being treated [[1](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B1)]. Less than optimal efficacy of drugs, and patients suffering adverse drug reactions (ADRs), place a huge burden at an individual patient level, and also on the resources of the NHS in terms of consumable costs and clinical contact time. ADRs alone account for 6.5% of hospital admissions [[2](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B2)], and 14.7% of extended hospital stays [[3](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B3)], equating to 8000 hospital beds being occupied at any one time, at a cost of £1.6 billion per year. Incorporating pharmacogenomics into the prescribing process has the potential to deliver safer, more effective treatments, at optimal cost, to support the NHS develop the ‘medicines value program’ [[4](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B4)].

In order to understand the opportunities and challenges of implementing pharmacogenomics into the NHS, the UK Pharmacogenetics and Stratified Medicine Network, NHS England and Genomics England developed a collaborative workshop which brought together key stakeholders [[5](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B5)]. The findings of this workshop ([Table 1](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#T1)) will also help inform other worldwide organizations how best to incorporate pharmacogenomics into their healthcare systems.

**Using genomics for drug choice & drug dose**

The number of gene–drug pair associations which warrant a change in the drug or its dose in individuals carrying particular genetic variants is increasing all the time. This is evidenced by the number of drug–gene associations listed by the US FDA [[6](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B6)], and the increasing number of Clinical Pharmacogenetics Implementation Consortium guidelines and the Dutch Pharmacogenomic Working Group guidelines [[7](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B7)]. A number of genotyping approaches exist for these gene–drug pair associations. To date, most centers provide single gene tests, rather than panel or exome or whole-genome sequencing (WGS), for pharmacogenomic testing. Furthermore, the availability of pharmacogenomic testing depends on the particular gene–drug pair being tested; for example, *HLA-B\*57:01* genotyping is available in many countries prior to the prescription of abacavir. Wider implementation of pharmacogenomic testing however has been slow and limited.

WGS is becoming more widely available and is developing at pace both in terms of the chemistry and bioinformatic analysis. However, coverage of sequencing remains limited in some areas of the genome, particularly for short-read sequencing, and so the use of pharmacogenomics information from WGS to determine the drug of choice, and the most effective dose, is not without its challenges [[8](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B8)]. Clearly, for those patients where sequencing has been part of their diagnosis (for example, for a rare disease), the availability of a whole-genome sequence could pre-emptively guide drug choice for known variants without any additional cost or delay to their treatment. As WGS becomes ever more affordable, and pharmacogenomics knowledge increases, the number of drug–gene interactions identified will steadily increase. It may eventually become cost–effective to sequence the genomes of the whole population at a certain age, or at the onset of disease, to guide prescribing of their treatment. Excitingly, as sequencing becomes more mainstream, there is the potential for a dramatic paradigm shift in clinical care to include genomic medicine. In the 100,000 Genomes Project in the UK, WGS has been undertaken in individuals with rare diseases and various cancers, with results being returned to clinicians [[9](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B9)]. This also provides an excellent platform to pre-emptively provide pharmacogenomic data to clinicians at the point of prescribing. This is currently being rolled out through a pilot on dihydropyrimidine dehydrogenase variants in patients receiving 5-fluorouracil [[10](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B10)]. It is focusing on four variants initially, but as our knowledge of the functionality of other variants increases (through either functional testing *in vitro* or real-world evidence), then it will be possible to add these additional variants to prescribing information.

An issue that needs to be considered when implementing on a country-wide scale is whether the capacity for testing is available. This has clearly been an issue recently with COVID-19 testing globally, and in order to avoid genomics labs being overwhelmed, initially, it may be worthwhile concentrating on the pharmacogenetics opportunities for the most important drugs, selected by volume of prescription, cost and health burden, and those drugs associated with ADRs or poor efficacy. For example, the IMPACT trial, approved by Health Canada, is analyzing how eight genes may affect a patient’s metabolism and their response to 33 antidepressant and antipsychotic medications [[11](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B11)]. There is already strong evidence that genetic variants are associated with the development of ADRs [[12](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B12)]. This has been most striking for HLA alleles, where variants in the *HLA* region on the short arm of chromosome 6 have been linked to off target ADRs for up to 30 different drugs [[13](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B13)]. A clinical study recently estimated that around 80% of healthy volunteers have at least one *HLA* risk allele [[14](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B14)]. Any multigene panel test developed to identify variations in the *HLA* region must be flexible enough to incorporate additional variants as they become linked to drug response phenotypes. Furthermore, although HLA tests have largely been used for predicting susceptibility to serious ADRs, they may also have alternative uses as described previously [[15](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B15)]. For example, drug labels frequently ask for laboratory monitoring for serious ADRs for everybody who is prescribed the particular drug. In the future, it may be possible to use HLA testing to stratify monitoring when the drug is required clinically, so that those at risk can be monitored frequently, while those who do not carry the risk allele could be monitored less frequently or not at all. Evidence in this area is needed and would help to demonstrate how pharmacogenomic stratified monitoring has the potential to reduce the number of clinical appointments.

Evaluating the effectiveness of incorporating genomic medicine into the UK prescribing process will be challenging. Abacavir is often quoted as an exemplar of the clinical effectiveness of genomic testing [[16](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B16),[17](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B17)]. However, the strength of association seen with abacavir and *HLA-B\*57:01* is much greater than that seen with other drug–gene associations, and this can therefore be considered an outlier. Implementing testing for other gene–drug pairs where the evidence may not be so strong, will need an assessment of the likely clinical utility and its cost–effectiveness. Novel study designs will be required to evaluate prescribing decisions based on pharmacogenomics data, as traditional randomized controlled trials will mostly be neither feasible nor appropriate. Recruiting patients into pharmacogenomics ‘quality improvement programs’ on the day of admission to hospital, or via another randomization approach, will help determine if prescribing based on genomic medicine delivers any improvements in patient outcome. In relation to cost–effectiveness, this may vary depending on the population frequency of the implicated allele. Even with abacavir and *HLA-B\*57:01*, although cost–effectiveness has been shown in many countries, there are some countries where it was felt not to be cost–effective to implement this genetic test [[18](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B18)]. Given the changing demographics and increasing burden of polypharmacy, a pooled analysis of all ADRs associated with genetic variants associated with multiple drugs being taken by patients may provide more robust evidence of a health economic benefit.

**Developing pharmacogenomics testing**

A genomic diagnostic test must be cost–effective, easy to analyze the results and have suitable support systems in place for clinicians to access and interpret the data, to be of benefit to patients. As our knowledge of drug–gene interactions increases, it will become more likely that in the short term pre-emptive array-based technologies will be the most practical in terms of cost, turnaround time, convenience and capacity to genotype multiple prespecified variants, rather than individual gene variants. It is also possible, however, that as sequencing technologies are becoming more widely accessible and cheaper, array-based technologies may be replaced by sequencing approaches. Indeed, in cancer, sequencing panels are becoming more widely used in an attempt to identify the many different variants that can affect the function of a cancer predisposing gene [[19](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B19)].

An important issue to consider for pharmacogenetic testing is the turnaround time. This obviously depends on the context for prescribing a particular drug. For example, should it be a routine laboratory test with the results reported within a defined period (ideally within one week) or is there a need for point-of-care (POC) testing in acute settings to provide immediate results? With reactive pharmacogenetic testing, efficient test turnaround times will be critical to meet the demands of the proposed model as: clinicians do not have the resources and time to amend existing workflows to recall patients to alter a prescription as additional pharmacogenomics information becomes available; and many ADRs occur soon after starting a new drug, and so any delay in test turnaround time could attenuate the positive health impact of utilizing pharmacogenomics data in the prescribing process. Incorporating a facility for clinicians to state a time frame for the patient commencing a drug treatment would help laboratories prioritize their order of sample analysis, and harness existing workflows to deliver results before treatment begins. For example, widespread pharmacogenomic testing incorporated in routine pre-operative assessment clinics could provide genetic information for postoperative analgesic prescribing for drugs such as codeine. POC testing also needs to be available for some drugs where there is a need not to delay treatment, for example, in determining the dose of warfarin [[20](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B20)], or before the use of clopidogrel in percutaneous coronary intervention [[21](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B21)]. In both these instances, the utility of POC testing has been demonstrated, and allows treatment to be commenced immediately to maximize the benefits of the drugs.

Pharmacogenomics is currently available at specialist research active hospitals in a growing number of countries. In order to provide the evidence for more wide-scale use, the European Ubiquitous Pharmacogenomics Consortium (U-PGx) is researching the major challenges/obstacles for the implementation of pharmacogenomics testing in patient care, taking into account the diversity of healthcare systems and citizens across Europe. Specifically, U-PGx is investigating if the emerging approach of pre-emptive genotyping an entire panel of important pharmacogenomics markers is cost effective and results in a better clinical outcome for patients. The opportunities and challenges in providing a panel test in U-PGx have been highlighted in recent papers [[22](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B22),[23](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B23)]. The outcome of this initiative, along with other large-scale US projects [[24](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B24)], will be integral to the ongoing development of the evidence underpinning the value of pharmacogenomics. Furthermore, the rollout of such projects will create the opportunity to build the evidence base for both clinical utility and cost–effectiveness of pharmacogenomics-based prescribing in real-world settings using readily accessible data sources. Such evidence is important as it will increase the ‘buy in’ of healthcare professionals to implement the routine use of pharmacogenomics in the NHS and other international healthcare systems.

**Opportunities & challenges for introducing pharmacogenomics into the NHS**

**National genomic testing service**

The UK has already made significant investment in genomic medicine by setting up the 100,000 Genomes Project to aid the diagnosis and potentially the treatment of patients suffering from either previously undiagnosed rare diseases or certain cancers [[9](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B9)]. Big data collected from this project, and from other initiatives such as the UK Biobank, will offer a way forward to identify variants of clinical relevance. The Genomic Medicine Service [[25](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B25)], an infrastructure of nationwide genomic laboratories that links the Genomic Medicine centers established for the 100,000 Genomes Project with other services, such as support from clinical geneticists, has already been set up in England. Patient genomic data held at a single trusted research environment will facilitate research via the Genomics England Clinical Interpretation Partnerships [[9](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B9)]. With respect to pharmacogenomics, although the initial intention is to have ‘test-broad-report-narrow’ approach (see below), the availability of WGS data linked to clinical phenotypes will allow the identification of identifying gene–drug interactions and help to establish which interactions need to be included into the National Genomic Test Registry which has been set up for the Genomic Medicine Service.

More broadly, reconfiguration of national genomic laboratories, and the creation of sustainability and transformation partnerships and integrated care services [[26](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B26)] that integrate local primary and secondary care services closer together in England, are bringing about pronounced changes in the NHS. For example, if a general practitioner (GP) requests a pharmacogenomic test that prevents hospitalization, the patient and the sustainability and transformation partnership both benefit, rather than it being perceived the GP has had to subsidize the hospital service by carrying out the test. These changes represent clear opportunities to introduce a comprehensive national pharmacogenomics service.

**Implementing a genomic service into the NHS**

A pragmatic approach that automatically offers genetic testing to patients newly prescribed a drug(s) where there is already a pharmacogenomics clinical guideline available will encourage implementation. The number of headline drug–gene pairs targeted during this early stage of implementation will be dependent on the initial funding allocation given to the rollout of pharmacogenomics across the NHS, the frequency of prescribing and the clinical need for the chosen therapeutics. NHS England have convened an expert group to review the evidence for known drug–gene associations and to recommend which variants to incorporate into the Standardized NHS England Test Directory. Based on the strength of evidence underpinning their drug–gene associations and the severity of their associated genotype-influenced clinical response (efficacy and/or ADR), the key drugs to consider for the initial test directory should include clopidogrel, warfarin, azathioprine and 5-fluoropyrimidines. The magnitude of benefit to patients and the NHS will increase as the implementation of genomic medicine occurs across the various therapeutic areas.

As the cost of genotyping additional variants diminishes, adopting a ‘test-broad-report-narrow’ approach, whereby common and rare variants in multiple pharmacogenes are simultaneously genotyped but only those variants with the strongest evidence base are reported into the patient’s electronic health record, would maximize value. Details of the remaining variants would be stored and released into medical records as evidence for their clinical relevance accrues. This approach would future proof the test and save on costs of retesting patients as new variants emerge. Decisions on the actual technology utilized for the tests left to the discretion of the provider genomic laboratories would encourage innovation as technologies advance, and accommodate local preferences and expertise.

More extensive information on a gene-by-gene basis is required before it is safe to recommend if genomic testing should follow either a sequencing or panel approach. In some cases, where multiple functionally relevant rare variants occur in a single gene, sequencing may be required rather than a targeted genotyping approach. For example, while array-based genotyping of more than the 50 known pathogenic *RYR1* variants [[27](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B27)] (associated with malignant hyperthermia, a life-threatening reaction to specific anaesthetic drugs) is feasible and sits in a single workflow, sequencing will capture additional rare variants outside the array panel. However, these additional rare variants have uncertain significance and so would not be included in the patient’s medical records and so would not alter clinical decisions. As an expert group have defined the Standardized National Test Directory (and it is updated annually), any compensation claims brought against the NHS by patients (or others) for not identifying rare variants beyond the directory would be without merit. To mitigate against patient confusion, the information sheet within the informed consent process could clearly state that the panel test cannot identify every genomic risk or ADR.

**Data management & Information technology**

Genomic sequencing produces large amounts of complex data, much of which may not be relevant to decisions on patient treatment but has enormous research value. Clinicians require support from specialist bioinformaticians to develop algorithms that identify the clinically actionable genetic variants within sequencing data to incorporate pharmacogenomics routinely into clinical practice. To help clinicians incorporate pharmacogenomics into rational prescribing decisions, computerized decision support systems (CDSS) that analyze patient’s genomic data and flag up any relevant variant–drug interactions are required. These CDSS must produce targeted and strictly evidence-based reports to avoid confusion and ensure only those findings that have sufficient evidence to be clinically actionable for prescribing are reported. An important aspect will be to link the development of multiple research discovery CDSS and implementation platforms together to help fully utilize all the datasets collected and keep them up to date with advances in real time.

CDSS are in their infancy but will become available in time. Therefore, in the short term, key clinically actionable pharmacogenetics findings associated with severe ADRs, could be incorporated in a way similar to the recording of drug allergies on the front page of a person’s electronic GP and hospital records. However, in the longer term, it is critical to link these complex, rapidly evolving, systems to patient’s electronic medical record data to utilize pharmacogenomics for prescribing in real time. The ultimate vision is for support algorithms to interrogate all key clinical parameters influencing drug response (such as BMI, sex, renal and liver function, diagnostic and genomic data embedded in the patient’s clinical record) to recommend to the GP, or prescriber, the most appropriate treatment for the individual.

However it must be noted, while the majority of primary practices use an electronic prescribing system, only approximately a third of existing NHS hospitals in England use electronic patient health records. Thus, current healthcare records are fragmented and information does not flow consistently between NHS sectors and community pharmacies. For example, information on treatment during a hospitalization episode can easily become buried and not transferred back into primary care records. Therefore, a national rollout will be required to extend information technology (IT) capabilities and provide a single source of patient information, visible to all sectors of NHS care providers including community healthcare and pharmacy services.

It is perhaps important to state that the COVID-19 pandemic has hastened the development of IT capabilities and digital communications. Nevertheless, since there are several providers for primary care IT facilities, and there will be several systems in hospitals, it should be possible for healthcare providers with CDSS to embed the pharmacogenomics data into their local system to provide point of prescribing recommendations on their local prescribing platform to increase usability. However, they must include a mechanism to download updates on the interpretation of pharmacogenomics variants, and incorporate any new clinical guidelines in a timely fashion. It is especially important to include any new evidence of drug–gene interactions into the records of those patients on long-term medications. Some centers in the US [[28](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B28),[29](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B29)], including St. Judes Children’s Research Hospital [[30](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B30),[31](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B31)], have been early adopters of pharmacogenomics so learning from their experiences of developing CDSS systems, from both the academic healthcare institutions, and the associated software companies, will help the UK to develop a suitable system. Working with data companies, especially large organizations such as Google or Microsoft, would support the NHS handle such complex big datasets. Where electronic medical records are not available in certain hospitals, it will still be important to make sure that pharmacogenomic testing becomes embedded in testing and reporting pathways which are used for other diagnostic tests to ensure that health inequalities are not inadvertently introduced, or exacerbated, by the introduction of pharmacogenomic testing.

Ethical issues including data ownership, secure storage, anonymization and access by health professionals need resolving. The debate continues on whether data should be stored on NHS patient electronic health records, or held by the individual. Smart phones are becoming almost ubiquitous so patient held health record apps would provide the patient with some control of their data and ‘live prescriptions’ could be offered to provide a more efficient service. An alternative option would be to provide patients with a plastic card linked to their centralized data records. Large data computing companies will try to implement commercial systems if no decisions on data are forthcoming.

**Challenges of implementing pharmacogenomics into the NHS**

The NHS (like most healthcare systems globally) is overstretched and the situation has been made worse by the COVID-19 pandemic. Patients’ needs are becoming more complex and clinicians have to deal with multiple conditions during relatively short consultations. It is not clear where staff will find the time to gain training on pharmacogenomics, or the incentive to change their working practice to incorporate genomic medicine. Staff at all levels within the NHS must be encouraged to focus more on the effective use of medicines and take responsibility to ensure patients receive optimized treatment regimens, as currently there are no national referral pathways for prescription review in complex patients. Prescribers require simple, clear and clinically relevant information to support the implementation of pharmacogenomics. For example, “this patient is a poor metabolizer of drug x and so requires an increased dose of x mg/day”, or “this is a pediatric/elderly patient with impaired liver and kidney function and so requires a lower dose”. Combining the expertise of the genomics testing service with clinical pharmacologists, pharmacists and the prescribing clinician into a multidisciplinary service team will help to improve patient treatment plans. Once the National Pharmacogenomics Testing Strategy has been determined, incorporating information about adjusting treatment into the British National Formulary framework would support prescribing decisions as most clinicians subscribe to the British National Formulary.

‘First-generation’ drug–gene tests already available are particularly important to improve the prescribing for patients with complex polypharmacy needs and could be the prototype for implementing pharmacogenomics in the NHS. These ‘first-generation’ pharmacogenomic tests, such as *CYP2C19* for clopidogrel, and *CYP2C9/VKORC1* for warfarin, may become less relevant as new drugs (e.g., ticagrelor or apixaban, respectively) are introduced. Nevertheless, they remain important as some patients will require older drugs as the newer drugs may be contraindicated for various reasons; they provide valuable learning and experience in implementing genomic-guided prescribing which can be extrapolated to the newer compounds, as and when genomic determinants for drug response are identified for the new drugs; and lessons learnt in a country such as the UK may still be valuable for resource-poor settings where the use of older drugs may be preferred for cost reasons.

**Financial support**

Where pharmacogenomics is available in routine clinical practice, funding is either by the patient, insurer or by the national healthcare service of the clinician requesting the test. The full costs of implementing pharmacogenomics testing are difficult to assess and perceived as potentially expensive, even though testing may ultimately produce cost savings. NHS England ring fenced funding would offer the best value for money and be most equitable for patients. Any eligibility restrictions for patients should be minimized upon service launch but it would be prudent to assess each drug, or group of drugs, and each condition, for the risk of exceptionally large demand occurring to ensure robust service delivery. Experience in the Netherlands suggests that, while a gradual growth in demand for pharmacogenomics testing activity year-on-year might occur (van Schaik, personal communication), there would be no immediate overwhelming demand for tests. Reviewing the eligibility criteria on an annual basis will help prevent large volumes of requests swamping the service and maintain a cost–effective service.

**Education of patients**

The public are already aware of the growing number of direct-to-consumer genomic testing services, but do not fully appreciate these tests require validation to be clinically relevant. Careful management of public expectations of receiving their prescribed medication based on pharmacogenomics is essential so genomic medicine retains support and does not appear elitist. Patients must understand more research is still required to identify clinically relevant drug–gene interactions to encourage them to donate their samples/data. Genomics becoming part of the National Curriculum in schools would help the next generation understand the benefits of pharmacogenomics.

Existing genetic counseling services are not needed for pharmacogenomics testing implementation, and in any case do not have the nationwide capacity to provide patients with an understanding of genomic testing, or to take formal consent from those patients eligible for a ‘national pharmacogenomics program’. In the majority of cases, the prescriber, or member of their multidisciplinary team, will be responsible for taking patient consent for testing. Clinical pharmacologists and pharmacists could also provide patients with information on complex molecular and genetic diagnostics tests through an onward referral pathway. As with other routine tests, verbal consent alone may be sufficient, particularly when testing is restricted to a panel of pharmacogenes and is for clinical care. However, clearly, written informed consent should be obtained if the genetic data obtained from patients, particularly in the case of WGS, will be used for future research.

As well as the ‘push’ from Health Education England (or other national education bodies), a ‘pull’ from the public would aid the understanding of pharmacogenomics. Media support from scriptwriters for popular TV shows including a story involving pharmacogenomics and exploring the relevant issues in dramas would significantly increase awareness. A documentary by leading televisions channels would help to educate the public and gain support for the adoption of genomic medicine.

**Education & training of practitioners**

The cancer field is successfully leading the way with the use of pharmacogenomics without any major concerns about education. This likely reflects a focus on both improving efficacy through the introduction of targeted therapies and the reduction of the serious ADRs that can result from chemotherapy. However, most NHS clinicians currently lack awareness of how genomic medicine has the potential to improve the treatments they prescribe and so additional education and training is required for some sectors. Undergraduates and junior doctors receive insufficient pharmacogenomics teaching, even as part of their genomics lectures, during their academic studies, which potentially creates a major barrier to pharmacogenomics becoming routine practice [[32](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B32),[33](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B33)]. It is essential that there is an assessment of the knowledge base at all levels from undergraduate to postgraduate, and pharmacogenomics becomes part of the medical curriculum, as well as continuing throughout professional development.

Education for clinicians should cover the science underpinning pharmacogenomics, clinical evidence to date and exemplars of actionable drug–gene associations. Detailed knowledge of the type of variant and biostatistical methods for identifying the variant are not required. However, clinician concerns such as the time burden associated with obtaining consent for a pharmacogenomics test, interpreting the result and conveying the information to the patient should be addressed. For medical students, the national Prescribing Safety Assessment examination [[34](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B34)], and potentially a future national medical licensing examination, afford the opportunity to set national standards on pharmacogenomics medical education. Health Education England have developed the ‘genomics education program’ with online training packages and MSc qualifications to meet a range of educational needs [[35](https://www.futuremedicine.com/doi/10.2217/pgs-2020-0091#B35)]. The wide range of educational resources available including face-to-face links with local champions, grand rounds, eLearning modules, short podcasts, videos and infographics and so on, all support dissemination of knowledge. Medical academies and the Royal Colleges have an important role to play in the continued training of healthcare professionals. Linking online additional bite size educational material to CDSS pharmacogenomics patient reports would help clinicians keep pace with pharmacogenomics and specifically with developments regarding clinically actionable drug–gene associations.

Explaining pharmacogenomics test results to patients may present new challenges and currently many clinicians will not have the time, knowledge or confidence to discuss such results with their patients. An accompanying national strategy to improve genomic literacy among healthcare professionals, especially if this is focused on pharmacogenetic indications that are directly relevant to their own clinical practice, will underpin confidence in using the tests and relieve concerns regarding discussing results with patients. Slow implementation and dealing with single variants initially will give clinicians time to develop their knowledge and counseling skills. The implementation of pharmacogenomics into any healthcare system does not need to be dependent on a single sector, for example, medical professionals, but should be developed around multidisciplinary teams including pharmacists and nurses. This would enable the process of when to order the tests, how to interpret results and when to take a prescribing decision to become seamlessly integrated into current clinical pathways as a normal part of the care of a patient, in the same way as biochemical testing is currently carried out.

**Conclusion**

The implementation of pharmacogenomics into any healthcare system is complex. The UK NHS is an integrated healthcare system, and implementation of pharmacogenomics for the whole population (>60 million) will not only be complex, but highly challenging. It would however represent the first example of the implementation of pharmacogenomics for a whole country-wide healthcare system, and as such the challenges are far outweighed by the potential opportunities to improve the care of patients.

**Future perspective**

The ability to provide a patient with the right drug at the right dose and at the right time to maximize efficacy and minimize toxicity is an ambitious but laudable goal. Personalization of drug therapy already occurs to some extent based on patient factors such as age and interacting medications, and concomitant diseases, such as renal impairment. The development of genomic testing to improve drug therapy is thus an evolution of the practice of medicine. Genomic testing should not be used in isolation but should be combined with clinical and environmental factors for the patient, leading to the development of multimodal algorithms. Implementation of such dosing algorithms will need the development of sophisticated decision support systems, which are dynamic, and readily modifiable to continually optimize patient outcomes using the paradigm of a learning health system. As we develop ever more sophisticated biomarkers (for example, those from other -omics technologies) and utilize artificial intelligence, such computerized decision support systems will become a critical part of any healthcare system so that well-trodden clinical pathways can be modified (but not disrupted) without too much effort, and therefore reduce the resistance from clinicians to change their clinical practice.

**Author contributions**

This report is based on a workshop that invited experts to come together in discussion groups to determine the opportunities to introduce pharmacogenetics into the UK NHS to improve healthcare; identify the challenges and offer solution on how best to overcome such challenges. RM Turner, WG Newman and E Bramon acted as chair/rapporteur for discussion groups, directing discussions and compiling reports of discussions, and edited the draft report. RM Turner also presented findings at the event. CJ McNamee organized/managed event, complied initial draft of report, incorporated rapporteur notes, comments and drafted final edit. WL Wong and S Misbah acted as rapporteurs of discussion groups contributing their notes of the discussions to the report, WL Wong offered comments on report. S Hill and M Caulfield were involved in the conception of the event, offered advice on content/format of the event and viewed final report. M Caulfield also presented findings at the event. They will be taking the findings of the event forward. M Pirmohamed offered advice on content/format of workshop, chaired and oversaw the event, presented findings, edited the initial draft and provided approval of the final version of the report to be published, acting as author for correspondence and will be taking findings of the event forward.

**Disclaimer**

The content of this article represents the collective views of the attendees rather than those of any individual organization represented at the workshop.

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**Table 1. Opportunities and challenges for implementing pharmacogenomics for a whole healthcare system.**

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| --- | --- | --- |
| **Specific issues** | **Challenges** | **Mitigation** |
| Type of genetic testing | Choice can vary from single gene, panels to whole exome/genome, each of which has its own advantages and disadvantages | Phased approach which can progress from single gene/variants, to panel based to whole-genome sequencing as technologies improve and costs decrease |
| Gene–drug pair associations to be included | No standardized list and variable numbers in different parts of the world | Include associations with the best evidence, and may have to use a phased strategy starting with a smaller number and increasing slowly. |
| Capacity for testing | On a country wide scale there may be concerns that the system may be overwhelmed | Limit the gene–drug pair associations included and have strict eligibility criteria for testing |
| Turnaround time for testing | If turnaround time is poor, the test will not be clinically useful and uptake may be low | Determine optimal turnaround time based on the drug, disease indication and clinician input |
| Clinical effectiveness of pharmacogenetic testing | Evidence for the effectiveness of individual gene–drug pair associations may vary, and evidence for panel or sequencing approaches may be absent | Model the clinical effectiveness of panel-based testing using literature data. Implement real-world assessment of effectiveness using electronic health record data |
| Cost–effectiveness of pharmacogenetic testing | Cost–effectiveness available for individual drugs but may be absent for panel approaches | Model the cost–effectiveness of panel-based testing using literature data. Implement real-world assessment of effectiveness using electronic health record data |
| Interpretation of pharmacogenomic test results | Knowledge about pharmacogenomics in healthcare professionals is poor | Inclusion of pharmacogenomic education in curricula and in clinical professional development courses for all professions |
| Lack of public awareness of pharmacogenomics | Poor awareness may lead to unrealistic expectations and/or poor uptake | Increase public education including clear information leaflets and materials. Online trusted resources also important |
| Decision support systems to help in interpretation and prescribing | Intelligent decision support systems are lacking | Start off with basic decision support and build up capabilities over time |