

## **Sigma's 30th International Nursing Research Congress**

### **Clinical Pharmacogenetics From a Nursing Perspective: Personalizing Drug Therapy**

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Precision medicine is the approach to patient care that is focused on finding the most appropriate medication based on the interplay between genetic, environmental, and lifestyle factors to improve patient outcomes. An important part of selecting the appropriate medicine and appropriate dose for the right patient at the appropriate time is testing for genetic variations that influence drug metabolism or transport. If a healthcare provider knows a person's pharmacogenetic test results, these results could be used to identify patients that may experience treatment inefficacy and to minimize adverse drug events. Nurses are familiar with how patients respond differently to identical treatments and can enhance patient outcomes by adopting a precision medicine approach to patient care. The long-term goal is to make pharmacogenetic testing part of routine care. However, a major obstacle to effective implementation of pharmacogenetic testing is the lack of adequate knowledge of healthcare providers on interpretation of these test results.

Pharmacogenetic testing is relatively easy and minimally invasive for patients, involving either a simple blood draw or saliva collection. The test is to identify variations in genes coding for proteins that are responsible for drug disposition, especially drug-metabolizing enzymes. The most common type of genetic variation that exist in these genes is a change at one nucleotide in the DNA sequence of the gene called a single nucleotide variation (SNV). These variations can alter the function of the respective enzyme and subsequently alter a person's ability to metabolize or transport certain drugs. Often a person's pharmacogenetic test results are reported as a phenotype based on their genotype. The predicted phenotypes, also called the individual's "metabolizer status", are classified as poor, intermediate/reduced, extensive, rapid, or ultra-rapid depending on which genetic variants (alternative alleles) are present. As part of the reporting, an asterisk-based nomenclature is used, where \*1 is often the reference allele and assigned based on an individual lacking the alternative allele. To assist with interpretation of pharmacogenetic test results, the Clinical Pharmacogenetics Implementation Consortium (CPIC®) and the Dutch Pharmacogenetics Working Group (DPWG) provide guidelines, with dosing recommendations for clinically actionable pharmacogenetic test results. Currently differences in recommendations exist between the guidelines, but efforts are underway to harmonize the CPIC® and DPWG guidelines.

Nurses have a critical role to play in implementation of pharmacogenetic testing. For nurses to adopt a precision health approach and implement pharmacogenetic testing, they need to be aware of the CPIC® and DPWG guidelines and how to use the guideline recommendations. Nurses can improve the trust relationship with patients by explaining why a dosing adjustment or medication change was made based on pharmacogenetic test results. When discussing or administering medications, nurses can be alert to and verify with the prescriber if atypical drug doses are observed and regularly monitor and report adverse effects. Nurses can document patient education efforts as well as document patient response to medications.

In addition, advanced practice nurses (APNs) need to be able to assess which individuals would benefit from pharmacogenetic testing instead of testing all individuals or individuals based on receiving a prescription for a particular medication. Being able to identify those patients who would benefit the most from testing due to concerns about inefficacy or toxicity is particularly important in resource-constrained environments. Nurses are perfectly positioned in primary and specialty care settings to apply test results within the clinical context.

Every patient presents a unique challenge to the pharmacogenetic interpretation of his or her case. This makes it difficult to automate interpretation of test results and requires a knowledgeable provider to assess each patient's genotype and medications. Pharmacogenetic test interpretation should not be confined to the medication of interest. It is also necessary to assess drug-gene interactions of existing medications to explain symptoms, inform selection of alternative treatment options, and improve efficacy of the patient's medication profile. With sufficient knowledge and experience, all nurses will become more confident in applying pharmacogenetic results within the clinical context.

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**Title:**

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**References:**

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### **Abstract Summary:**

Precision medicine is the approach to patient care that is focused on finding the most appropriate medication based on the interplay between genetic, environmental, and lifestyle factors to improve patient outcomes. With sufficient knowledge and experience, all nurses will become more confident in applying pharmacogenetic results within the clinical context.

### **Content Outline:**

#### 1. Introduction

A. The promise of pharmacogenomics (genetic variants in one or few genes as opposed to the entire genome) testing sits at the heart of precision medicine.

B. A major obstacle to effective implementation of pharmacogenomics testing is the lack of adequate knowledge of healthcare providers on interpretation of these test results.

#### 2. Body

A. Nurses understand that patients respond differently to identical treatments.

1. Family history has long served as a source of genetic information.

2. Both drug-gene and drug-drug interactions (DDIs) may contribute to this variability.

B. For a growing list of medications, a patient's pharmacogenotype helps determine drug response and adverse drug effects.

1. Many healthcare clinics are able to determine the pharmacogenotypes of clinic patients.

2. In the U.S., people can now order their own pharmacogenotyping in direct-to-consumer tests.

3. The long-term goal is to make pharmacogenotyping part of routine care.

C. Pharmacogenotyping is a relatively easy test for patients.

1. The test involves a simple blood draw or saliva collection.

2. The test results identify variations in human genes regulating drug disposition, especially drug-metabolizing enzymes.

3. Variations can alter a person's ability to metabolize certain drugs.

a. People have different therapeutic responses to drugs.

b. Adverse drug events can be minimized.

D. The most common type of genetic variation is a single nucleotide polymorphism (SNP).

1. Figure: Cytosine (C) changes to thymine (T) which changes the base pairs from cytosine and guanine (CG) to thymine and adenine (TA).

2. SNPs alter a person's ability to metabolize certain drugs.

E. To assist with interpretation of pharmacogenetic test results, the Clinical Pharmacogenetics Implementation Consortium (CPIC®) (<https://cpicpgx.org/>) and the Dutch Pharmacogenetics Working Group (DPWG) provide guidelines, with dosing recommendations for clinically actionable pharmacogenetic test results.

1. The predicted phenotypes also called the individual's "metabolizer status" are classified as poor, intermediate/reduced, extensive, rapid, or ultra-rapid and can be deduced from the presence of genetic variants (alternative alleles).

2. The guidelines use an asterisk-based nomenclature, where \*1 is often the reference allele and assigned based on an individual lacking the alternative allele.

3. Efforts are currently underway to harmonize CPIC and DPWG guidelines.

F. Many prescribed medications are substrates, inhibitors, and inducers of CYP enzymes.

1. Substrates bind (interact) to CYP enzymes and are converted into active or inactive forms (metabolites).

2. Sometimes, the administered medication is an inactive prodrug, which requires conversion to active form by the CYP system to convey its therapeutic effect.

3. Inhibitors are medicines/compounds that decrease the function of the CYP enzyme, while inducers increase the function.

4. A list of common CYP substrates, inhibitors, and inducers are listed at <http://medicine.iupui.edu/clinpharm/ddis/main-table/>.

5. Certain medicines can be categorized as having more than one effect (e.g. fluoxetine is a substrate and inhibitor).

G. As pharmacogenomics knowledge accumulates, healthcare institutions have implemented genotype-guided therapy in clinical practice.

1. In seven European countries-The Ubiquitous Pharmacogenomics (U-PGx) Consortium.

2. In the U.S.-The IGNITE Network.

3. Sample of a de-identified patient report.

H. Nurses can adopt a precision health approach.

1. Patient education- Explain why a dosing adjustment or drug change was made based on pharmacogenetic test results.

2. Medications

a. Be alert to and verify atypical drug doses.

b. Regularly monitor and report adverse effects.

3. Documentation

a. Clarify and verify drug doses

b. Document patient education efforts

c. Document response to medications.

I. Advanced Practice Nurses (APNs) can adopt a precision medicine approach.

1. APNs can do all of the aforementioned (H).

2. APNs need to be able to assess which individuals would benefit from pharmacogenetic testing instead of testing all individuals or individuals based on receiving a prescription for a particular medication.

a. Being able to identify those patients who would benefit the most from testing due to concerns about inefficacy or toxicity is particularly important in resource-constrained environments.

b. APNs are perfectly positioned in primary and specialty care settings to apply test results within the clinical context.

3. Conclusion

A. Every patient presents a unique challenge to the pharmacogenetic interpretation of his or her case.

1. This makes it difficult to automate interpretation of test results and requires a knowledgeable provider to assess each patient's genotype and medications.

2. Pharmacogenetic test interpretation should not be confined to the medication of interest.

3. It is also necessary to assess drug-gene interactions of existing medications to explain symptoms, inform selection of alternative treatment options, and improve efficacy of the patient's medication profile.

B. With sufficient knowledge and experience, all nurses will become more confident in applying pharmacogenetic results within the clinical context.

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**Author Summary:** Dr. Fulton is an assistant professor at the Indiana University School of Informatics and Computing and a former clinical assistant professor at the IU School of Nursing. A nurse practitioner with more than 20 years' experience, Dr. Fulton just completed an NIH-funded clinical pharmacology fellowship at the Indiana University School of Medicine, specializing in personalized medicine.