Body System: Population-Based Care		
Session Topic: Pharmacogenomics		
Educational Format		**Faculty Expertise Required**
REQUIRED	Interactive Lecture	Expertise in the field of study. Experience teaching in the field of study is desired. Preferred experience with audience response systems (ARS). Utilizing polling questions and engaging the learners in Q&A during the final 15 minutes of the session are required.
OPTIONAL	Problem-Based Learning (PBL)	Expertise teaching highly interactive, small group learning environments. Case-based, with experience developing and teaching case scenarios for simulation labs preferred. Other workshop-oriented designs may be accommodated. A typical PBL room is set for 50-100 participants, with 7-8 each per round table. Please describe your interest and plan for teaching a PBL on your proposal form.

Professional Practice Gap	**Learning Objective(s) that will close the gap and meet the need**	**Outcome Being Measured**
• Family physicians have statistically significant and meaningful gaps with regard to diagnosing genetic syndromes, and underestimate the significance of inherited and acquired genetic variation on drug response (i.e., drug susceptibility or drug resistance). • Physicians are often unsure about pharmacogenomics testing in clinical practice, including the interpretation of test results, knowing when testing is appropriate and understanding testing costs and insurance coverage of testing. • Physicians are often unprepared to address legal and ethical issues associated with pharmacogenetic testing. • Physicians are often uncertain about prescribing recommendations associated	1. Evaluate the availability, efficacy, and utility of pharmacogenomics testing. 2. Consider pharmacogenomics testing in terms of predictive value, cost, and payer reimbursement. 3. Develop plans to incorporate appropriate pharmacogenomics testing, as indicated by FDA drug labels. 4. Counsel patients regarding legal or ethical issues associated with pharmacogenetic testing. 5. Evaluate barriers to routine use of pharmacogenetics in a clinical setting.	Learners will submit written commitment to change statements on the session evaluation, indicating how they plan to implement presented practice recommendations.

with pharmacogenomics testing results. • Medical Residents are often inadequately trained in genomic medicine.		

ACGME Core Competencies Addressed (select all that apply)			
X	Medical Knowledge		Patient Care
X	Interpersonal and Communication Skills		Practice-Based Learning and Improvement
	Professionalism		Systems-Based Practice

Faculty Instructional Goals

Faculty play a vital role in assisting the AAFP to achieve its mission by providing high-quality, innovative education for physicians, residents and medical students that will encompass the art, science, evidence and socio-economics of family medicine and to support the pursuit of lifelong learning. By achieving the instructional goals provided, faculty will facilitate the application of new knowledge and skills gained by learners to practice, so that they may optimize care provided to their patients.

- Provide up to 3 evidence-based recommended practice changes that can be immediately implemented, at the conclusion of the session; including SORT taxonomy & reference citations
- Facilitate learner engagement during the session
- Address related practice barriers to foster optimal patient management
- Provide recommended journal resources and tools, during the session, from the American Family Physician (AFP), Family Practice Management (FPM), and Familydoctor.org patient resources; those listed in the References section below are a good place to start
  - Visit http://www.aafp.org/journals for additional resources
  - Visit http://familydoctor.org for patient education and resources
- Provide evidence for evaluating the availability, efficacy, and utility of pharmacogenomics testing.
- Provide recommendations for considering pharmacogenomics testing in terms of predictive value, cost, and payer reimbursement.
- Provide recommendations and strategies for developing plans to incorporate appropriate pharmacogenomics testing, as indicated by FDA drug labels.
- Provide strategies and resources for counseling patients regarding legal or ethical issues associated with pharmacogenetic testing.
- Provide strategies for overcoming barriers to routine use of pharmacogenetics in a clinical setting.

Needs Assessment

In 2007-2010, almost one-half of all Americans reported taking one or more prescription drugs in the past 30 days.[1] Drugs are a frequently used therapy for reducing morbidity and mortality and improving the quality of life of Americans, and reflects 9.7% of all national health expenditures; totally $263 billion in 2011.[1] Medications were provided or prescribed at 73% of outpatient department visits in 2011; most commonly, analgesics (41.1 million); antidiabetic agents (15.6 million); antihyperlipidemic agents (14.5 million); antidepressant (14.3 million); immunostimulants (12.9 million); anxiolytics, sedatives, and hypnotics (12.3 million);

bronchodilators (10.9 million); anticonvulsants (10.4 million); dermatological agents (10.2 million); antiplatelet agents (10.1 million); and beta-adrenergic blocking agents (10.1 million).[2] More specifically, in 2010, medications were provided or prescribed at 85% of office visits to general/family practices.[3] On average, active members of the AAFP write an average of 125 prescriptions per week; in fact, family physicians overall prescribed, administered, or suggested 26% of all medication in 2009.[4]

Drug safety and efficacy is of particular importance since adverse drug reactions are responsible for nearly 7% of all hospital admissions.[5] Deaths from drug overdose have been rising steadily over the last two decades in the U.S., with nearly 9 out of 1 poisoning deaths caused by drugs.[6] Medication errors are common among patients who are being treated for multiple chronic conditions.[7,8] Medication errors are also common among pediatric patients, who are at higher risk of experiencing medication errors than adults because of the need for a dose calculation based on a patient's age, weight (mg/kg), body surface area (mg/m^2), and clinical condition.[9,10] Unintentional poisoning killed 838 U.S. children in 2010; and in 2011, U.S. poison centers received more than 1.4 million calls involving poison exposures for children 19 and younger, with nearly 80 percent of these calls involving children under 6, and roughly half of them involved exposures to medications.[11] Data from a recent American Academy of Family Physicians (AAFP) CME Needs Assessment survey indicates that family physicians do have a knowledge gap related to optimally managing and preventing poisoning from drug overdose.[12] Pharmacogenomics has the potential to allow clinicians to create customized medical treatment, based on an individual's genetic profile.[13] As such, there also exists great potential to reduce adverse drug reactions.[14,15]

As medicine continues to advance, the evolving science of genomics and increasing body of genetic knowledge will impact the health of the public. Advances in technologies related to pharmacogenomics will impact therapeutic selections for individualized patient care and family physicians will continue to need cost effective methods to counsel patients, as well as knowledge to apply this information in overall care. Genetics for physicians is no longer simply interviewing patients to obtain relevant risk factors including "red flags" and "family history." There are social implications for individuals and families and ethical considerations, with potential impact to other family members.[16,17] For example, patients often reject genetic or genomic testing because they are afraid of genetic discrimination from insurance companies by denying coverage or from employers in employment decision; however, in 2008, the US Senate passed Genetic Information Nondiscrimination Act (GINA) to protect an individual's genetic information from insurance and employer discrimination.[17] Technologic advances have made it easier to test for specific genetic mutations and entire genomes can be mapped. Less clear is what to do with a "variant of uncertain significance," meaning something has been recognized as "not normal;" however, the interpretation is unclear. Family physicians should be prepared to address these issues with their patients, especially in light of recent stories in the media about at-home genetic test kits and expectations arising from the Human Genome Project over the past decade, physicians are increasingly required to have a greater understanding of genetic testing and counseling. Physicians must be prepared to counsel patients who bring in results from at-home genetic tests, as they pose a real risk for confusion and misinterpretation by consumers.[18-20]

While pharmacogenomics testing has potential to improve the safety and effectiveness of many drug therapies, studies suggest that physicians lack knowledge on the topic pharmacogenomics generally; and specifically, availability of tests, interpretation of test results, and making sound clinical judgements about the impact of these tests on the selection of appropriate drug therapies.[21,22] Pharmacogenomics is a rapidly growing field, making it increasingly challenging for physicians to remain up to date on new pharmacogenomic testing that impacts the prescription and clinical monitoring of drug therapy.[23,24] In fact, data from a recent American Academy of Family Physicians (AAFP) CME Needs Assessment survey indicate that family physicians have statistically significant and meaningful gaps with regard to diagnosing genetic syndromes, and underestimate the significance of inherited and acquired genetic variation on drug response.[12]

The AAFP Medical Genetics Curriculum Guideline for Medical Schools and Residency recommends that a medical resident should be able to demonstrate the ability to apply knowledge of the range of genetic approaches to treatment of disease (including pharmacogenomics and gene therapy).[25] As such, many residency programs have started to include more genomic medicine training in their programs; however, some studies suggest that as many as 40% of fourth-year residents have not received any instruction in genomic medicine, and the majority of residents have a self-reported "poor" or "fair" consultative ability to discuss pharmacogenetics test results with patients.[26] Several studies have also identified barriers to routine use of pharmacogenomics in clinical settings, include the following:

- Logistics of performing timely genotyping in a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory
- Electronic health records (EHRs) do not support formats needed to record genetic results
- Lack of prospective genotype-directed randomized clinical trials validating the advantage of using pharmacogenetic based dosing over standard of care treatment algorithms
- Inexperience and lack of knowledge of many clinicians in interpreting and acting on pharmacogenetic information
- Paucity of clear recommendations for pharmacogenetic testing by professional associations
- Lack of a robust infrastructure to provide decision support for genomic medicine
- Cost and reimbursement issues
- Ethical and medico-legal concerns.

Primary care physicians are often comfortable ordering a pharmacogenetic test or interpreting test results, often citing a general lack of education in this area.[5,21,27] These barriers need to be addressed for pharmacogenetics to become a routine part of health care.[23,28-30]

Physicians may improve their care of patients by engaging in continuing medical education that provides practical integration of current evidence-based guidelines and recommendations into their standards of care, including, but not limited to the following:[27]

- Codeine should be avoided in CYP2D6 ultrarapid metabolizers because of the potential for toxicity.
- Codeine, and possibly tramadol, should be avoided in CYP2D6 poor metabolizers because of possible lack of effectiveness.

- In poor CYP2C19 metabolizers who are undergoing percutaneous coronary intervention for acute coronary syndromes, ticagrelor (Brilinta) or prasugrel (Effient) should be considered as an alternative to clopidogrel (Plavix) for antiplatelet therapy.

These recommendations are provided only as assistance for physicians making clinical decisions regarding the care of their patients. As such, they cannot substitute for the individual judgment brought to each clinical situation by the patient's family physician. As with all clinical reference resources, they reflect the best understanding of the science of medicine at the time of publication, but they should be used with the clear understanding that continued research may result in new knowledge and recommendations. These recommendations are only one element in the complex process of improving the health of America. To be effective, the recommendations must be implemented. As such, physicians require continuing medical education to assist them with making decisions about specific clinical considerations.

Additionally, the American Board of Family Medicine (ABFM) created a new Clinical Self-Assessment (CSA) Genetics Module that is slated to be released in 2015. Competencies to be addressed include genomic concepts and terminology, interpretation of genomic testing, family history, application of genomics, public health and policy implications, recognition and management of genetic disorders, and ethical, legal, and social implications. Assisting AAFP members to sustain American Board of Family Medicine (ABFM) Maintenance of Certification is one of the important strategies associated with educational objectives that support the AAFP mission and vision.[31]

Resources: Evidence-Based Practice Recommendations/Guidelines/Performance Measures

- Pharmacogenetics: Using Genetic Information to Guide Drug Therapy[27]
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines[32-39]
- Genetic factors in drug metabolism[40]
- (AAFP) Medical Genetics. Curriculum Guidelines[25]
- At-home genetic tests[18]
- U.S. Food and Drug Administration. Genomics[41]
- U.S. Food and Drug Administration. Table of Pharmacogenomic Biomarkers in Drug Labeling[42]
- Thinking on paper: documenting decision making[43]
- Engaging Patients in Collaborative Care Plans[44]
- FamilyDoctor.org. Genetic Testing: What You Should Know (patient education)[45]

References

1. National Center for Health Statistics. Health - United States 2013 - With Special Feature on Prescription Drugs. In: U.S. Department of Health & Human Services, ed. Washington DC 20402: U.S. Government Printing Office; 2013:511.

2. Centers for Disease Control and Prevention. National Hospital Ambulatory Medical Care Survey: Factsheet. 2011. http://www.cdc.gov/nchs/data/ahcd/NHAMCS_2011_opd_factsheet.pdf.

3. Centers for Disease Control and Prevention. National Ambulatory Medical Care Survey: Factsheet General/Family Practice. 2010. http://www.cdc.gov/nchs/data/ahcd/NAMCS_2010_factsheet_general_family_practice.pdf. Accessed Feb 2015.

4. American Academy of Family Physicians (AAFP). Member Profile Report. Leawood KS: AAFP; 2015.

5. Haga SB, Burke W, Ginsburg GS, Mills R, Agans R. Primary care physicians' knowledge of and experience with pharmacogenetic testing. *Clinical genetics.* Oct 2012;82(4):388-394.

6. Centers for Disease Control and Prevention. Prescription Drug Overdose. 2014; http://www.cdc.gov/homeandrecreationalsafety/overdose/. Accessed July, 2014.

7. Brown M, Sinsky CA. Medication adherence: we didn't ask and they didn't tell. *Family practice management.* Mar-Apr 2013;20(2):25-30.

8. Koper D, Kamenski G, Flamm M, Bohmdorfer B, Sonnichsen A. Frequency of medication errors in primary care patients with polypharmacy. *Family practice.* Jun 2013;30(3):313-319.

9. Aseeri MA. The impact of a pediatric antibiotic standard dosing table on dosing errors. *The journal of pediatric pharmacology and therapeutics : JPPT : the official journal of PPAG.* Jul 2013;18(3):220-226.

10. National Safety Council. Poisoning. 2014; http://www.nsc.org/safety_home/HomeandRecreationalSafety/Poisoning/Pages/Poisoning.aspx. Accessed July, 2014.

11. Centers for Disease Control and Prevention. A National Action Plan for Child Injury Prevention: Reducing Poisoning Injuries in Children. 2013; http://www.cdc.gov/safechild/nap/overviews/poison.html. Accessed July, 2014.

12. AAFP. 2012 CME Needs Assessment: Clinical Topics. American Academy of Family Physicians; 2012.

13. Burke W, Brown Trinidad S, Press NA. Essential elements of personalized medicine. *Urologic oncology.* Feb 2014;32(2):193-197.

14. Lee JW, Aminkeng F, Bhavsar AP, et al. The emerging era of pharmacogenomics: current successes, future potential, and challenges. *Clinical genetics.* Jul 2014;86(1):21-28.

15. Phillips KA, Veenstra DL, Oren E, Lee JK, Sadee W. Potential role of pharmacogenomics in reducing adverse drug reactions: a systematic review. *JAMA : the journal of the American Medical Association.* Nov 14 2001;286(18):2270-2279.

16. Rieder MJ, Carleton B. Pharmacogenomics and adverse drug reactions in children. *Frontiers in genetics.* 2014;5:78.

17. Li A, Meyre D. Jumping on the Train of Personalized Medicine: A Primer for Non-Geneticist Clinicians: Part 3. Clinical Applications in the Personalized Medicine Area. *Current psychiatry reviews.* May 2014;10(2):118-132.

18. Frosst P, Wattendorf DJ. At-home genetic tests. *American family physician.* Feb 1 2006;73(3):540-541.

19. Annes JP, Giovanni MA, Murray MF. Risks of presymptomatic direct-to-consumer genetic testing. *The New England journal of medicine.* Sep 16 2010;363(12):1100-1101.

20. Sturm AC, Manickam K. Direct-to-consumer personal genomic testing: a case study and practical recommendations for "genomic counseling". *Journal of genetic counseling.* Jun 2012;21(3):402-412.

21. Johansen Taber KA, Dickinson BD. Pharmacogenomic knowledge gaps and educational resource needs among physicians in selected specialties. *Pharmacogenomics and personalized medicine.* 2014;7:145-162.

22. Stanek EJ, Sanders CL, Taber KA, et al. Adoption of pharmacogenomic testing by US physicians: results of a nationwide survey. *Clinical pharmacology and therapeutics.* Mar 2012;91(3):450-458.

23. Bielinski SJ, Olson JE, Pathak J, et al. Preemptive genotyping for personalized medicine: design of the right drug, right dose, right time-using genomic data to individualize treatment protocol. *Mayo Clinic proceedings. Mayo Clinic.* Jan 2014;89(1):25-33.

24. Stanek EJ, Sanders CL, Frueh FW. Physician Awareness and Utilization of Food and Drug Administration (FDA)-Approved Labeling for Pharmacogenomic Testing Information. *Journal of personalized medicine.* 2013;3(2):111-123.

25. American Academy of Family Physicians (AAFP). Medical Genetics. *Curriculum Guidelines* 1999; Reprint No. 258:http://www.aafp.org/dam/AAFP/documents/medical_education_residency/program_directors/Reprint258_Genetics.pdf. Accessed Feb, 2015.

26. Haspel RL, Rinder HM, Frank KM, et al. The current state of resident training in genomic pathology: a comprehensive analysis using the resident in-service examination. *American journal of clinical pathology.* Oct 2014;142(4):445-451.

27. Chang KL, Weitzel K, Schmidt S. Pharmacogenetics: Using Genetic Information to Guide Drug Therapy. *American family physician.* Oct 1 2015;92(7):588-594.

28. Welch BM, Kawamoto K. The need for clinical decision support integrated with the electronic health record for the clinical application of whole genome sequencing information. *Journal of personalized medicine.* Dec 18 2013;3(4):306-325.

29. Overby CL, Erwin AL, Abul-Husn NS, et al. Physician Attitudes toward Adopting Genome-Guided Prescribing through Clinical Decision Support. *Journal of personalized medicine.* 2014;4(1):35-49.

30. Shuldiner AR, Palmer K, Pakyz RE, et al. Implementation of pharmacogenetics: the University of Maryland Personalized Anti-platelet Pharmacogenetics Program. *American journal of medical genetics. Part C, Seminars in medical genetics.* Mar 2014;166C(1):76-84.

31. American Academy of Family Physicians (AAFP). Vision & Strategic Plan. 2015; http://www.aafp.org/about/the-aafp/vision.html. Accessed Feb, 2015.

32. Clancy JP, Johnson SG, Yee SW, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for ivacaftor therapy in the context of CFTR genotype. *Clinical pharmacology and therapeutics.* Jun 2014;95(6):592-597.

33. Crews KR, Gaedigk A, Dunnenberger HM, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for codeine therapy in the context of cytochrome P450 2D6 (CYP2D6) genotype. *Clinical pharmacology and therapeutics.* Feb 2012;91(2):321-326.

34. Crews KR, Gaedigk A, Dunnenberger HM, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for cytochrome P450 2D6 genotype and codeine therapy: 2014 update. *Clinical pharmacology and therapeutics.* Apr 2014;95(4):376-382.

35. Johnson JA, Gong L, Whirl-Carrillo M, et al. Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 genotypes and warfarin dosing. *Clinical pharmacology and therapeutics.* Oct 2011;90(4):625-629.

36. Leckband SG, Kelsoe JR, Dunnenberger HM, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for HLA-B genotype and carbamazepine dosing. *Clinical pharmacology and therapeutics.* Sep 2013;94(3):324-328.

37. Martin MA, Hoffman JM, Freimuth RR, et al. Clinical Pharmacogenetics Implementation Consortium Guidelines for HLA-B Genotype and Abacavir Dosing: 2014 update. *Clinical pharmacology and therapeutics.* May 2014;95(5):499-500.

38. Muir AJ, Gong L, Johnson SG, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for IFNL3 (IL28B) genotype and PEG interferon-alpha-based regimens. *Clinical pharmacology and therapeutics.* Feb 2014;95(2):141-146.

39. Relling MV, McDonagh EM, Chang T, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for rasburicase therapy in the context of G6PD deficiency genotype. *Clinical pharmacology and therapeutics.* Aug 2014;96(2):169-174.

40. Belle DJ, Singh H. Genetic factors in drug metabolism. *American family physician.* Jun 1 2008;77(11):1553-1560.

41. U.S. Food and Drug Administration. Genomics. *Drugs* 2013; http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/. Accessed Feb, 2015.

42. U.S. Food and Drug Administration. Table of Pharmacogenomic Biomarkers in Drug Labeling. 2014; http://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm. Accessed Feb, 2015.

43. Edsall RL, Moore KJ. Thinking on paper: documenting decision making. *Family practice management.* Jul-Aug 2010;17(4):10-15.

44. Mauksch L, Safford B. Engaging Patients in Collaborative Care Plans. *Family practice management.* 2013;20(3):35-39.

45. FamilyDoctor.org. Genetic Testing: What You Should Know. 1999; http://familydoctor.org/familydoctor/en/prevention-wellness/staying-healthy/healthy-living/genetic-testing-what-you-should-know.html. Accessed August, 2013.

