This review aims to provide useful references and publications in the field of ethics and pharmacogenomics. Publications that merely address scientific and technical aspects of this science (such as fundamental or clinical studies) will not appear here, unless: (1) they mention or comment on ethical issues; (2) they propose an accessible description or definition of pharmacogenomics and comment on its potential or future developments; (3) they explicitly address the scope or limitations of the results generated by pharmacogenomics studies in general; (4) they constitute general guidelines or statements.

Global pharmacogenomics: Impact of population diversity on the distribution of polymorphisms in the CYP2C cluster among Brazilians

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Suarez-Kurtz G, Genro JP, de Moraes MO, Ojopi EB, Pena SD, Perini JA, Ribeiro-Dos-Santos A, Romano-Silva MA, Santana I, Struchiner CJ

**Authors’ abstract:** The impact of biogeographical ancestry, self-reported ‘race/color’ and geographical origin on the frequency distribution of 10 CYP2C functional polymorphisms (CYP2C8*2, *3, *4, CYP2C9*2, *3, *5, *11, CYP2C19*2, *3 and *17) and their haplotypes was assessed in a representative cohort of the Brazilian population (n=1034). TaqMan assays were used for allele discrimination at each CYP2C locus investigated. Individual proportions of European, African and Amerindian biogeographical ancestry were estimated using a panel of insertion-deletion polymorphisms. Multinomial log-linear models were applied to infer the statistical association between the CYP2C alleles and haplotypes (response variables), and biogeographical ancestry, self-reported Color and geographical origin (explanatory variables). The results showed that CYP2C19*3, CYP2C9*5 and CYP2C9*11 were rare alleles (<1%), the frequency of other variants ranged from 3.4% (CYP2C8*4) to
17.3% (CYP2C19*17). Two distinct haplotype blocks were identified: block 1 consists of three single nucleotide polymorphisms (SNPs) (CYP2C19*17, CYP2C19*2 and CYP2C9*2) and block 2 of six SNPs (CYP2C9*11, CYP2C9*3, CYP2C9*5, CYP2C8*2, CYP2C8*4 and CYP2C8*3). Diploptype analysis generated 41 haplotypes, of which eight had frequencies greater than 1% and together accounted for 96.4% of the overall genetic diversity. The distribution of CYP2C8 and CYP2C9 (but not CYP2C19) alleles, and of CYP2C haplotypes was significantly associated with self-reported Color and with the individual proportions of European and African genetic ancestry, irrespective of Color self-identification. The individual odds of having alleles CYP2C8*2, CYP2C8*3, CYP2C9*2 and CYP2C9*3, and haplotypes including these alleles, varied continuously as the proportion of European ancestry increased. Collectively, these data strongly suggest that the intrinsic heterogeneity of the Brazilian population must be acknowledged in the design and interpretation of pharmacogenomic studies of the CYP2C cluster in order to avoid spurious conclusions based on improper matching of study cohorts. This conclusion extends to other polymorphic pharmacogenes among Brazilians, and most likely to other admixed populations of the Americas.

Pharmacoeconomic evaluation of warfarin pharmacogenomics.
You JH.

Author’s abstract: Introduction: The merit of applying pharmacogenomics in the induction phase of warfarin therapy for personalized dosing is controversial and highly dependent on its cost-effectiveness. Areas covered: Published studies on pharmacoeconomics of warfarin pharmacogenomic application are reviewed. A literature search was done using Medline and Embase covering the period 2000 - 2010. Decision tree and Markov modeling were the most frequently used methods in the reviewed reports. Studies incorporating clinical efficacy data of genotype-guided dosing algorithm had shown that warfarin pharmacogenomics would improve quality-adjusted life-years (QALYs) gained. Nevertheless, it was unlikely to be cost-effective for general patients. Influential factors to improve the cost-effectiveness included low genotyping cost, high effectiveness in improving anticoagulation control/event rate, and applying warfarin pharmacogenomics to patients with high bleeding risk or at practice sites with suboptimal management of anticoagulation control. Expert opinion: Warfarin pharmacogenomics would improve QALYs and could possibly be cost-effective in selected patient groups or practice sites.

Valuing pharmacogenetic testing services: A comparison of patients' and health care professionals' preferences

Authors' abstract: OBJECTIVE: The study compared the preferences of patients and healthcare professionals for the key attributes of a pharmacogenetic testing service to identify a
patient’s risk of developing a side effect (neutropenia) from the immunosuppressant, azathioprine.

METHODS: A discrete choice experiment was posted to a sample of patients (n=309) and health-care professionals (HCPs) (n=410), as part of the TARGET study. Five attributes, with four levels each, described the service as follows: level of information given; predictive ability of the test; how the sample is collected; turnaround time for a result; who explains the test result. Data from each sample were first analyzed separately and responses were compared by 1) identifying the impact of the scale parameter, and 2) estimating marginal rates of substitution.

RESULTS: The final analysis included 159 patients and 138 HCPs (50% & 34% response rates). Estimated attribute coefficients from the patient and HCP sample differed in size, after taking into account the impact of the scale parameter. Patients and HCPs had similar preferences for predictive accuracy of the test and were willing to wait 2 days for a 1% improvement in test accuracy. Patients preferred to obtain more information and were willing to wait 19 days compared to 8 days for HCPs for providing higher levels of information.

CONCLUSIONS: Patients demanded accurate and timely information from health-care professionals about why it was necessary to have a pharmacogenetic test and what the test results mean. In contrast, health-care professionals appear to focus more exclusively or entirely upon the predictive accuracy and waiting time for a test result.

Why, When, and How Should Pharmacogenetics Be Applied in Clinical Studies?: Current and Future Approaches to Study Designs
Stingl Formerly Kirchheiner JC, Brockmöller J.

Authors' abstract: The growing interest in incorporating pharmacogenetics (PGx) into drug development and clinical practice raises several questions: which study designs best reveal relevant pharmacogenetic biomarkers, best clarify specific hypotheses in PGx, and result in the largest gain of clinical evidence in this field? In this review, we present and compare a variety of PGx-related study designs. The type and quality of evidence gained by each category of study design is evaluated, and an appropriate timeline for the integration of pharmacogenetic studies into drug development is proposed. A summary of the pros and cons of the different study designs might help investigators decide how best to incorporate PGx into drug research. Using different scenarios to explain how genetic polymorphisms influence drug action, we illustrate how this knowledge can be translated into individualized drug choices, individualized dosage determination based on pharmacogenetic diagnostics, and other types of monitoring in order to make drug therapies safer and more effective.
Development and implementation of a pharmacist-managed clinical pharmacogenetics service


Authors’ abstract: Purpose: The development and implementation of a pharmacist-managed clinical pharmacogenetics service are described. Summary: A pharmacist-managed clinical pharmacogenetics service was designed and implemented at an academic specialty hospital to provide clinical pharmacogenetic testing for gene products important to the pharmacodynamics of medications used in the hospital’s patients. A series of accredited educational seminars were conducted for our pharmacists to establish competencies in providing pharmacogenetic consults for the genes to be tested by the clinical pharmacogenetics service. The service was modeled after and integrated with an already-established clinical pharmacokinetics service. A steering committee was formed to evaluate the use of available tests, new evidence for implementation of additional tests, and other service quality metrics. All clinical pharmacogenetic test results are first reported to one of the pharmacists, who reviews the result and provides a written consultation. The consultation includes an interpretation of the result and recommendations for any indicated changes to therapy. In 2009, 136 clinical pharmacogenetic tests were performed. The service has been met with positive clinician feedback. The successful implementation of this service highlights the leadership role that pharmacists can take in moving pharmacogenetics from research to patient care. Conclusion: The development of and experience with a pharmacist-managed clinical pharmacogenetics service are described. The program’s success has depended on collaboration between the clinical laboratory and pharmacists, and pharmacists’ pharmacogenetic recommendations have been well accepted by prescribers.

Pharmacogenetic tests in cancer chemotherapy: what physicians should know for clinical application


Authors’ abstract: Significant efforts to develop pharmacogenomic predictors have been made to guide more effective and safer chemotherapy. Although a considerable amount of data has been generated from numerous experimental or clinical studies, there is a large gap between pharmacogenomic knowledge and clinical application. This review will focus on eight pharmacogenetic tests including TYMS, DPYD, UGT1A1, CYP2D6, EGFR, KRAS, FCGR3A, and BRCA1/2 to predict toxicity or response to commonly used chemotherapeutic agents. We will discuss the current level of evidence, if the current pharmacogenetic tests are appropriate for clinical application, and how to integrate the pharmacogenomic information into routine clinical practice.
Personalized Medicine  
Part 3: Challenges Facing Health Care Plans in Implementing Coverage Policies for Pharmacogenomic and Genetic Testing  

Authors’ abstract: This is the third article in a three-part series on the future of personalized medicine. Part 3 focuses on trends in health plan insurance policies and coverage for genetic tests.

Upsetting categories? The consequences of pharmacogenomics for making knowledge-based reimbursement decisions in Sweden  
Sjögren E.  

Author’s abstract: This paper contributes to an understanding of pharmacogenomics-in-the-making by foregrounding a regulatory setting in which these technologies must be situated: decision-making about pharmaceutical reimbursement. Health care assessment organizations have been introduced in many countries to systematically address the issue of health care coverage. Using the example of Sweden, the process of deciding reimbursement status is shown to hinge on the creation of stable and clinically feasible categories of patients, diseases and drug responses. Through a series of analogous examples concerning conventional pharmaceuticals, it is argued that current mechanisms for categorizing reimbursable drugs could be upset when pharmacogenomic advances provide a means of making patients more specific objects of regulatory intervention. By extension, this has implications for the form of solidarity that is produced.

Perceptions and benefits of receiving pharmacogenetic research results to codeine-prescribed breastfeeding mothers: A pilot study  
Madadi P, Joly Y, Avard D, Chitayat D, Koren G.  

Authors’ abstract: Sixty-two codeine-prescribed breastfeeding mothers from a pharmacogenetic study were interviewed regarding the communication of individual CYP2D6 genotype results and overall research findings. All participants wanted to receive the results of their individual genetic tests; however, individuals placed different values on the usefulness of this information toward future medical decisions. Receiving one’s pharmacogenetic test results was not associated with a negative psychosocial impact. Thirty-three percent of the participants wished to withhold these results from their physicians. Participants' expectations seem to dictate the extent of transparency of pharmacogenetic research results.  
Note: the same issue of Clinical Pharmacology & Therapeutics (88(6)) gathers several articles on pharmacogenetics.