Adverse drug reactions (ADRs) are a striking failure and major unmet problem of modern medicine resulting in debilitating and lethal consequences for patients. ADRs are the 4\textsuperscript{th} – 6\textsuperscript{th} leading cause of death in Canada and the United States\textsuperscript{1-2}. Genetic factors play a key role in drug response and therefore contribute significantly to the risk of drug-induced harm. As such, the study of pharmacogenomics – that is the determination of the genetic predisposition regarding the response to medication – is a key component to understanding how to utilize medication in a safer and more effective manner, ensuring that the benefit of the medication is administered without the unintended consequences of ADRs. Indeed, the field of pharmacogenomics has been identified as one of the most promising areas for personalized medicine\textsuperscript{3}.

For example, through comprehensive genomic analyses, the Canadian Pharmacogenomics Network for Drug Safety (CPNDS)\textsuperscript{4} has identified the genomic factors responsible for a number of severe ADRs, including but not limited to codeine-induced infant and toddler death\textsuperscript{5-8}, cisplatin-induced ototoxicity\textsuperscript{9,10} and anthracycline-induced cardiotoxicity\textsuperscript{11-14}. To address these serious ADRs, pharmacogenomic clinical practice guidelines and tests have been developed that assess a given patients’ risk of suffering from these ADRs prior to the start of treatment such that better personalized therapy plans can be developed based on a drug’s risk/benefit profile for each patient\textsuperscript{15-17}.

Anthracyclines are the most frequently used chemotherapeutic in Canada and can cause congestive heart failure in up to 20\% of treated children\textsuperscript{18}. In the past, the risk of experiencing cardiotoxicity from anthracycline chemotherapy (the most commonly used class of drugs in children with cancer) could be described only generally as falling in the range of a few percent to an almost 100\% chance. The pharmacogenomic test, however, helps to better determine a patient’s specific risk before drug treatment is initiated. Based their genetic makeup, in two patients with the same diagnosis, one patient’s risk of serious drug-induced cardiotoxicity may be below 20\%, whereas the second patient’s risk of harm may be greater than 80\%.

Most importantly, this ability to quantify pharmacogenomic risk provides a vehicle for patients and their families to dictate the level of risk they are comfortable with in the paradigm of benefit-risk decision making in their cancer treatment. This is the very definition of patient-oriented care. For example, an estimated risk of serious drug-induced cardiotoxicity of <20\% may be completely acceptable given the significant mortality that accompanies a diagnosis of many types of cancer. However, a predicted risk of drug-induced harm of >80\% should require discussion of viable alternative and pre-emptive preventative therapy.

The development of pharmacogenomic tests is a key component to preventing severe ADRs such that for every serious ADR associated with medication use, for which genetic risk factors have been identified, a predictive test could be developed to allow for better risk/benefit profiling for each patient to inform treatment decision-making. With pharmacogenomics, we thus move closer to drug safety solutions instead of simply documenting drug-induced harm.

CPNDS is not the only group in the world focused on finding drug safety solutions offered through pharmacogenomics. The US FDA currently includes pharmacogenomic information in the label of more than 140 drugs – this number has steadily been rising and continues to do so as more pharmacogenomic discoveries are made linking the risk of ADRs to specific genetic markers. Drugs are used across all medical disciplines making it easy to justify why pharmacogenomics should be the highest of priorities in both patient care advancement and in the federal investment of research dollars.
Clinicians who want to integrate pharmacogenomic testing into their practices are faced with challenges. Access to tests means better profiling risks of therapy, before therapy begins. Delays in access to tests puts patients at risk of reactions for which predictive tests are available. We the undersigned believe that pharmacogenomics has the potential to drastically impact the use of medication making it safer, more effective and personalized to truly treat individual patient needs in the best possible way. It is an ethical responsibility for all of us – clinicians, hospital administrators and policy makers – to provide access to this service to all Canadian families battling disease and illnesses requiring medication.

References: