According to recent data briefs from the Center for Disease Control and Prevention (CDC), in 2007, pain-reliever overdose killed more people in the USA than cocaine and heroin combined [1]. Since 1999, deaths among women from prescription painkiller overdose have increased nearly 400 % [2]. Over 40% of these deaths are attributed to one class of pain-relievers, the opioids [1,2]. In 2011, opioid overdose killed more Americans than traffic fatalities. Data published on the National Institute of Drug Abuse (NIDA) website [3] show a steady increase in the number of opioid prescriptions over the past two decades. Other data compiled and analyzed independently [4] support the CDC and NIDA observations, and further point to some disturbing trends. Although the number of opioid prescriptions has gone up, the number of Americans filling opioid prescriptions declined and the days of medication per prescriptions rose by 8.4%. Most of the long-term opioid users are elderly; yet, young adults (22-44 yrs.) filled more prescriptions, for longer time per prescription. About 20% of these individuals use opioids for non-medical reasons. Opioid abusers and misusers include elderly, as well as college students [4]. Opioid abuse is affecting urban and rural populations [5]. American Veterans are victims of this epidemic [6] as are high school students [3]. In 2010, one out of every 12 high school seniors in USA reported abusing/misusing opioids [3]. Finally, opioid use has been shown to act as a gateway to heroin addiction [4]. Thus, opioid addiction due to their misuse or abuse is now considered a public health crisis in the USA [7] as well as other nations [8-10]. However, this problem is not limited only to opioid addiction due to abuse and misuse. New evidence also indicates iatrogenic opioid dependence and/or addiction [11], although at least one report argues to the contrary [12]. During 1999-2009, there was a parallel increase in opioid sales, treatment facilities admissions, and opioid overdose deaths in the US [1,2]. More Americans are affected by chronic pain than cancer, diabetes and all vascular disorders combined [13]. The chronic pain diagnoses, number of opioid prescriptions and admission numbers for prescription opioid abuse treatment also show a parallel growth in numbers [4] leading some experts to argue that chronic pain and prescription opioid abuse are co-existing disorders [14,15].

It is clear from the foregoing analysis that opioid abuse/addiction is a rapidly growing public health issue affecting different populations globally. A number of important preventive steps such as prescription drug monitoring and compliance guidelines [16], policy and legal interventions [17], and addiction/dependence management through medication [8] have been in place, with mixed results [18-20]. Clearly, opioid-associated death is a complex problem and solving it may require a combination of multiple approaches. One tactic, which remains rather underutilized, is pharmacogenomics (PGx). During the past few years, considerable evidence has accumulated to substantiate the view that PGx has the potential to positively affect this issue in three different ways:

Application

Significant progress has already been made in understanding how genetic variations influence metabolism of codeine, the opiate agonist, which is also a constituent of many top-selling medications [21-25]. Specifically, CYP2D6 gene variants that result in drastically different pharmacokinetics of codeine metabolism and hence patient health outcomes have been reported [21-24]. One article also reports using codeine PGx to resolve a suspected opioid overdose case [25]. Wider application of codeine PGx has also been shown to reduce accidental overdosing, unintentional health complications and associated costs [26,27]. It is time for the regulatory agencies to make CYP2D6 genotype testing mandatory before prescribing codeine-containing medications.

Education

Lack of awareness and/or training of health care professionals, specifically primary care physicians [28-30], nurse practitioners [31] and pharmacists [32] is reported to be a major factor hindering the broader application of the approach referred above. Using available continuing education programs and developing targeted programs specifically addressing when, where and how the PGx information should be sought and used would further expand the scope of application and improve healthcare outcomes as well as reduce costs.

Research

Addiction is a complex, multi-genic trait [33-35]. Most of the current applicable studies and results on PGx of pain relievers are focused on single candidate gene examples [36-39]. However, with advances in genome wide association studies [40], reduction of technology costs in whole genome sequencing/analyses, and larger numbers of trained health care professionals working in this area, new research will lead to a better understanding and characterization of genomic determinants underlying addiction behavior. This in turn will offer novel ways to manage, even cure addiction behavior. Targeted funding support from governmental and non-governmental sources will play a crucial role in furthering knowledge, identifying new target gene candidates and discovering new treatment modalities.

In summary, addiction to pain relievers is a major public health issue across the world. Significant research in opiate PGx has already provided tools and technologies that positively influence health care outcomes and reduce treatment costs via improved dosing decisions. Regulatory agencies are urged to make CYP2D6 genotype testing mandatory before prescribing codeine-containing medications. Broader application of these tools and technologies is possible through continuing education and training of practicing health care professionals. Use of advanced tools and technologies of PGx
research will further improve identification and application of genetic determinants underlying addiction to various pain relievers. Targeted funding support from governmental and non-governmental sources for research projects in this area will further strengthen our abilities to take pain out of pain reliever medication.

References