

# Prescription Drug Abuse & Addiction: Past, Present and Future: The Paradigm for an Epidemic

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*“Substance abuse affects a broader segment of West Virginia’s citizens and their state and local governments than any other single issue confronting us today”.<sup>1</sup>*

Governor Joe Manchin III

## Abstract

Prescription drug abuse has reached epidemic proportions in the United States and West Virginia is not immune. It is estimated that in 2009, the number of adolescents and adults with a substance abuse and/or dependence problem has reached 23.2 million in the US. There has been an alarming rate of increased sales of methadone, hydrocodone and oxycodone. This article addresses the scope of the problem of prescription drug abuse in West Virginia and the impact by and on the addicted individual. Addiction is a chronic relapsing neuropsychiatric illness manifested by compulsive drug seeking and use. It has created a substantive socioeconomic burden on our state. Prescription drug abuse and addiction increase medical expenses, drug related crime and unemployment. There are misconceptions regarding the etiology and treatment of addiction based on past clinical experience. The view of

addiction as volitional misconduct alone has been disproven scientifically. A more current understanding of neurobiological alterations caused by this disease, current treatment strategies and future directions will be presented. This article provides an understanding of prescription drug abuse and addiction’s contribution and impact on society’s health and social policy. Addressing the problem of prescription drug abuse requires an understanding of the disease of addiction, thus enhancing the effectiveness in diminishing the associated health and social costs. It is the article’s intent to illuminate the mutually symbiotic relationship of prescription drug abuse and the disease of addiction and subsequently provide recommendations toward the resolution of this most important issue.

## The Past...outmoded

Addiction has historically been considered a disease of “weak will or moral turpitude”. However, advances in brain imaging technology and the ability to accurately measure neurotransmitters over the past two decades has significantly improved our understanding of the neurobiology of addiction. Complex animal and human studies have led to evidence based science that recognizes “addiction as a disease”. This is a dramatic change from the long-standing misperception that the addicted patient is afflicted with the illness due to a lack of willpower. In 1997, National Institute on Drug Abuse (NIDA) published “Addiction is a Brain Disease and It Matters”, by Dr. Alan Leshner, the then current

director. This publication served a pivotal role in the introduction of the disease model of addiction based on emerging new research.<sup>2</sup> In 2007, Dr. Nora Volkow, as the current NIDA Director, presented “The Neurobiology of Free Will” at the American Psychiatric Association’s annual conference further enhancing the medical research community’s understanding of the drive of active addiction overriding individual personal needs. Consequently, the public is becoming better informed that the epidemic of addiction is the result of a disease. Public information of this disease is being disseminated by the media via educational programs and publications such as the 1998 PBS special *Moyers on Addiction: Close to Home*, the 2005 special issue of the journal *Nature*<sup>3</sup> on addiction, the 2007 HBO special, *Addiction: Why Can’t They Just Stop?* and Time Magazine’s 2007 cover story, “How We Get Addicted”.<sup>4</sup> Viewing addiction as a chronic medical illness makes the long-standing stigmatization no longer acceptable.

## The Present...an epidemic

The estimate of lifetime prevalence of a substance use disorder, in the general population, is approximately 10%.<sup>5,6</sup> According to the US Department of Health and Human Services in 2009, 23.2

## Objectives

*As a result of reading this article, the physician will better:*

1. *Be able to explain the socioeconomic impact of prescription drug abuse and addiction*
2. *Comprehend the neurobiology of addiction as result of prescription drug abuse*
3. *Be able to explain important components in effectively addressing prescription drug abuse and addiction in the future.*

million Americans age 12 or older experienced a substance use or abuse problem where treatment would have been indicated. Only 10% of these individuals received the indicated treatment at a specialty facility.<sup>7</sup> Estimates from the 2008 National Household Drug Use and Health Survey (NHDUHS) revealed the predominant reason for not receiving substance abuse treatment among persons age 12 or older who needed but did not receive treatment for the period 2005-2008 combined was "no health coverage and could not afford the cost (37.4%)". According to the Substance Abuse and Mental Health Services Administration (SAMHSA), the need for substance abuse treatment among Americans older than age 50 is likely to double by 2020.<sup>8</sup>

The National Institute on Drug Abuse (NIDA) estimated the cost of drug abuse in the United States to be 246 billion dollars in 1992.<sup>3</sup> Current estimates of the financial burden to society due to substance abuse exceeds half a trillion dollars annually.<sup>9</sup> The West Virginia partnership to promote community well-being estimates "In 2006, the total cost to West Virginia for substance abuse was 1.86 billion with 470 million related to direct costs to the consequences of substance abuse".<sup>1</sup> The intangible personal costs to society are immeasurable. Prescription drug use and abuse have significantly increased in the United States and West Virginia. In the 10 years (1997 - 2007) the per capita retail purchases of methadone, hydrocodone and oxycodone in the United States increased 13-fold, 4 fold and 9-fold, respectively. Nationally, 4.8% of individuals 18-25 use pain relievers for non-medical reasons and 5.2 million age 12 years and older have used prescription medications non-medically in the past year during 2002-2005.<sup>10</sup> Prescription drug abuse and addiction are epidemic in the United States with West Virginia leading the way.

From 1999 to 2004, deaths as result of unintentional drug poisoning increased 68% nationwide. West Virginia experienced the Nation's largest increase in unintentional drug poisoning mortality rates (550%). In 2006, those overdose deaths in West Virginia were associated with non-medical use and diversion of pharmaceuticals, primarily opioid analgesics. Diversion was highest among the 18-24 year age group with the decedents lacking prescription documentation for one or more contributing pharmaceuticals 91% of the time. Although opioid analgesics were the most prevalent drug class, 79.3% of decedents had multiple substances contributing to their fatal overdose. Opioid analgesics were involved in 93% of deaths with only 44.4% ever having been prescribed these drugs. Psychotherapeutic drugs were involved in 49% of deaths with Benzodiazepines being most commonly involved (78.5%). Alcohol was a significant contributing factor in the vast majority of fatal prescription drug overdoses. Prescription opioid analgesics played a dominant role in deaths with a secondary contribution from psychotherapeutics. Virtually all of the individuals experiencing prescription drug related deaths showed signs of drug abuse. Risk factors included being male, lower education, living in impoverished counties of the state and having a positive family history. Many users are naïve to the potentiative and synergistic effects contributing to the lethality of combining these drugs. This lack of understanding and/or concomitant usage of alcohol provides some accounting for the escalation of unintentional pharmaceutical overdose fatalities. This, potentially, partly explains why methadone was found to be responsible for more single-drug deaths and was involved more than any other drug.<sup>10</sup>

In a society which has gotten very comfortable with "a pill for

everything" philosophy there is another issue in addition to unintentional drug overdoses to be considered. Prescription drug abuse is affecting our children and therefore our future. The drug of choice for adolescents age 12-18 is no longer marijuana, but prescription drugs. These are easily obtained from medicine cabinets within the home, from friends and family with the majority reporting that the friend or relative received the drug from a single clinician.<sup>11</sup> The problem of adolescent substance abuse and addiction with associated co-morbidities is widespread. Adolescent addiction is a developmental disorder with peak onset between ages 15 and 21. The onset of addiction prior to age 15 statistically increases disease severity and duration.<sup>12,13</sup> Many adolescents are potentially self medicating co-existing psychiatric disorders such as depression, a well known major comorbid factor in the development of marijuana dependence.<sup>12</sup> Other contributing factors include; genetic predisposition, childhood trauma, disruptive or addictive child rearing environments, poor school performance and substance abusing friends. It is well known traumatized adolescents have greater difficulty learning addiction recovery skills.<sup>14</sup> A deeper understanding is needed in the relationship of addiction as a disease and prescription drug abuse in adolescents and adults.

### The Chronic Medical Illness Model of Addiction

Addiction is a chronic medical illness; therefore, the comparisons of diagnosis, treatment and outcomes are similar to that of other chronic illnesses such as, type II diabetes mellitus, asthma and hypertension. There are accepted diagnostic criteria available in the DSM IV that provides a reliable, valid and refined differentiation of use, abuse and dependence disorders.<sup>15</sup> The

utilization of short screens similar to the CAGE<sup>16</sup> questionnaire, the AUDIT,<sup>17</sup> and the MAST<sup>18</sup> applied during a medical evaluation followed with the application of standardized diagnostic criterion has been proven reliable.<sup>19,20</sup> These well-known multiple question screening tools vary in degrees of usability in the primary care setting and in their ability to identify more severe unhealthy drinking (i.e., dependence). A single-question screen: "How many times in the past year have you had X or more drinks in a day?" (where X was 4 drinks for women and 5 drinks for men); was 82% sensitive and 79% specific for unhealthy alcohol consumption. A positive result is >1 occasion for both males and females. This screen is a useful tool in the busy primary care setting,<sup>21</sup> similar to using a finger-stick glucose measurement in diabetes screening.

It has been shown that screening followed with brief interventions by physicians can affect the motivational change among patients and positively impact the long-term health outcomes. Studies specific to substance abuse and addiction have shown abstinence increased and HIV seroconversion decreased in opiate dependent individuals when provided motivational counseling from a health educator.<sup>22</sup> The presence of cocaine in the urine of pregnant mothers getting some treatment for addiction and counseling in the context of their prenatal visits has been shown to be significantly decreased at delivery compared to addicted pregnant mothers who received routine prenatal care only.<sup>23</sup>

The treatment of addiction requires both long-term management and acute interventions. Similarly, asthma and diabetes are managed chronically with the utilization of maintenance measures and acutely with more immediate treatment. This principle should also be applied in the management of the addicted

patient where relapse occurs at a rate of 40-60% in the first year following treatment.<sup>24,25</sup> Treatment effectiveness is dependent upon compliance with the treatment recommendations. According to McLellan, et al, there is a significant degree of non-compliance with medication and behavioral treatment recommendations which contributes to relapse rates of 30-50% and 50-70% of adult patients with diabetes and asthma respectively.<sup>19</sup> Non-compliance leading to relapse is known to occur in both addictive and non-addictive illnesses and should be managed rather than viewed as treatment failure.

### **Nature and Nurture**

Evidence shows a significant genetic contribution to the risk of addiction comparable to other chronic illnesses. A multitude of twin studies have shown significantly higher rates of dependence among twins than non-twin siblings. There is a higher rate of dependence among monozygotic than dizygotic twins.<sup>26,27</sup> Twin studies of hypertension, diabetes and asthma show a significant component of heritability.<sup>28,29,30</sup> As with other chronic illnesses a genetic predisposition and the environmental trigger must often co-exist before disease occurs. For example, exposure to asbestos in a patient with a genetic predisposition to lung cancer is more likely to result in the development of carcinoma of the lung than the exposed patient without this genetic predisposition.<sup>31</sup>

The voluntary initiation of drug use does not distinguish drug dependence from other medical illnesses. Many other diseases are affected by voluntary choice especially when taking into account genetic, environmental and cultural factors. Excessive salt intake, for example, can contribute to the development of hypertension when combined with the genetic

predisposition for salt sensitivity, cultural stress and exogenous obesity. The initiation of alcohol use can be extremely pleasurable to some individuals (or not). The pleasant sensation induced by a casual drink at the end of the day is familiar and safe for many people. However, this recreational usage progresses to tolerance and dependence for some individuals. Studies have shown sons of alcohol dependent fathers have a higher degree of tolerance to alcohol and are less likely to experience hangovers than sons of non-alcoholic dependent fathers.<sup>32</sup> Conversely, the "flushing" response to alcohol in the inherited presence of aldehyde dehydrogenase genotype (associated with alcohol metabolism) leads to an unpleasant initial reaction to voluntary alcohol use resulting in very few alcoholics being found with this genotype.<sup>33</sup>

Environmental and other influences such as comorbid mental illness, low-self-esteem, poor social skills, poor coping mechanisms, exposure to physical or sexual abuse, poor parental influences, poor school performance, peers who abuse substances, male gender, and poverty<sup>7,19</sup> can lead individuals to seek pleasure by reactivating the dopaminergic system (see Neurobiology). In patients without the genetic predisposition for addiction, it is less likely that this disease will be established even in the presence of at risk behaviors. The overall addiction vulnerability is related to genetic influences, environmental conditions, other complex personality traits, stress responses and comorbid issues including self-medication of undiagnosed psychiatric illness, codependency, family of origin issues, poor coping skills, etc.

### **The Neurobiology**

Chronic exposure to an addictive drug can "hi-jack" the neural circuits of the susceptible brain

causing enhanced “plasticity” in the neural circuits related to reward, motivation, and learned behavior. This circuit is contained in the ventral tegmental area connecting the limbic cortex through the mid-brain to the nucleus accumbens. Although by different mechanisms, alcohol, opiates, cocaine and nicotine activate the dopaminergic system, resulting in the euphoria associated with drug use. Administration of an addictive substance increases synaptic dopamine levels in the brain creating euphoria and enhanced sense of well-being.<sup>34,35,36</sup> This occurs predominantly by the neurons of the ventral tegmental area (VTA) releasing dopamine into the nucleus accumbens and the prefrontal cortex.<sup>4,35,36,37</sup> Volitional behaviors become habits and then compulsions through pavlovian

learning. The brain adapts replacing appropriate reward for survival activities like quenching thirst, satisfying hunger, sleeping and sex with the drive for activation of the dopaminergic system. Repeated activation eventually leads to chronic changes in the neuroregulatory mechanism.<sup>34,35,36</sup> This neuro-adaptive transformation occurs at a higher rate if the initial’s substance exposure occurred during adolescence when there is a greater degree of synaptic plasticity.<sup>37</sup> Other neuroendocrine substances and structures involved include, but not limited to, serotonin, norepinephrine, N-methyl-D-aspartate receptors, opioid peptide receptors,  $\gamma$ -Aminobutyric acid (GABA) systems, dynorphin, acetylcholine, corticotrophin releasing factor, adrenocorticotrophic hormone, and corticosterone.<sup>34,36,37</sup>

## Pharmacotherapy

Increased understanding of the pathophysiology of addiction has led to medications useful in the treatment of addiction.<sup>38</sup> Nicotine, bupropion and varenicline are good examples of pharmacologic agents utilized in the treatment of cigarette smoking. Opioid dependence has been successfully treated with the partial agonist buprenorphine,<sup>39</sup> and methadone is known to reduce opiate use, the spread of infectious diseases and crime.<sup>38</sup> The opioid antagonist naltrexone competitively blocks the actions of heroin resulting in neither dysphoria or euphoria in abstinent patients.<sup>40,41</sup> The GABA agonist acamprosate has been shown to decrease craving and relapse to alcohol use.<sup>42</sup> Disulfiram is well-known to be useful in the prevention of relapse in individuals

dependence

vulnerability

fixation

addiction

obsession

helplessness

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with alcohol dependence.<sup>43</sup> These agents are infrequently prescribed, despite being indicated and proven effective. With the knowledge now available, this is comparable to withholding an antihypertensive agent from a hypertensive patient. Medications coupled with adjunctive lifestyle modifications can be of therapeutic benefit.

## Relapse

Healthcare professionals perceive relapse rates of diabetics, hypertensives and asthmatics as acceptable and even expected in many cases. Yet, the relapse to drug or alcohol use following discharge is often considered “treatment failure”. It is essential to realize that a relapse in a patient suffering from addiction is no different than an exacerbation of other chronic medical illnesses. The immediate and profound desire for the re-administration of an addictive drug is common. The re-initiation of use following a period of abstinence, despite potential negative consequences, is counterintuitive. The awareness of potentially negative consequences is not necessarily protective or preventative. This is due to possibly permanent pathophysiologic changes in the reward circuitry which occur with chronic administration of addictive substances. Physical signs of withdrawal are short lived. Motivational and cognitive impairments may resolve over a period of months, but the tolerance to drugs may never return to normal. Neurobiological changes in the brain, impulse dysregulation and alterations of decision making all impact executive function. People, places or things previously associated with drug/alcohol use can induce conditioned physiologic reactions resulting in profound “craving” for the drug/alcohol. Cravings in the absence of good recovery skills and unresolved co-morbid issues can result in relapse. These

physiologic responses have been well documented using positron emission tomography (PET) examinations of the limbic and control brain regions further confirming that addiction is a disease with definable, reproducible, anatomical and biochemical brain alterations.<sup>44</sup>

## Discussion

Although there are other important aspects to the supply and demand continuum related to prescription drug abuse and addiction not addressed in this article, it was the authors’ intent to focus on the interrelationship of prescription drug abuse related to addiction. The disease of addiction is a major driving force to the prescription drug abuse problem we are facing in West Virginia today. It is obvious that addiction is a disease and shares many common features with other chronic illnesses resulting in as many health problems as there are social problems. The evidence showing neurobiological and neuroplastic alterations in the brain’s “circuitry” provide confirmation that prescription drug abuse related to addiction is an incurable, chronic medical illness. The stigma of the drug addict as “weak or bad people” unwilling to live a more socially acceptable moral life is being replaced with a better understanding of the addicted individual as a “sick person”, who may or may not be, trying to get well. The public is no longer naïve because many of us have a loved and respected friend or family member who suffers from the disease of addiction. There is no better antidote to the stigmatization than the personal experience of knowing one or more individuals in successful long-term recovery.

Even if addiction is the result of voluntary behavior initially, the brain chemistry in the addicted individual is different from the non-addicted brain and must be treated as if he or she is in a different brain

state (much like the schizophrenic, diabetic in ketoacidosis, cirrhotic with hepatic encephalopathy and Alzheimer’s patient). We need to continue narrowing the gap between the scientific knowledge and the public perception about prescription drug abuse and addiction in order to enhance our ability to address this problem.

Federal studies show that the best drug treatment programs pay for themselves over time, especially when utilizing strong motivation to facilitate the treatment process. A combination of sanctions or rewards from personal, professional and/or legal relationships can increase the utilization of treatment and retention rates, as well as, the success of interventions.<sup>14,45</sup> A good example is law enforcement’s “drug court diversion” to treatment initiatives.<sup>11,45</sup> Evidence shows treatment response benefits of reduced drug use improved personal health and reduced social pathology, but not a cure for addiction. A comprehensive study conducted in 2000 of the cost benefit of drug treatment services estimated that for every \$1 spent on treatment, \$7 are saved in the form of reduced medical expenses, costs of crime and the increased employment earnings.<sup>46,47</sup> Every man, woman, and child in America pays nearly \$1,000 annually to cover the costs of unnecessary health care, extra law enforcement, motor vehicle crashes, crime, and lost productivity due to substance abuse.<sup>48</sup> The management of addictive disease and co-occurring disorders in a continuing care model of treatment must include consideration of; a chronic disease requiring long-term follow up, integration of healthcare, the possibility of dual diagnosis, the level of detoxification, relapse prevention, pharmacotherapy, psychosocial recovery, educational needs and other factors based on the American Society of Addiction Medicine Placement Criteria.<sup>49</sup> If effective education and prevention programs

were implemented nationwide, substance abuse initiation would decline for 1.5 million youth and be delayed on average for 2 years, which reduces subsequent problems later in life. In 2003, it is estimated that 10.2% fewer youth would have used marijuana, 30.2% fewer would have used cocaine and 8% fewer would have smoked regularly. With an average cost of effective school based programs in 2002 at \$220 per pupil (only 20% of American youth were exposed to effective prevention programs in 2005), these programs could have saved an estimated \$18 per \$1 invested if implemented nationwide.<sup>50</sup> The education and treatment of addiction needs to continue the shift from acute treatment alone (detoxification, stabilization and discharge) to the model applied to other chronic illnesses.

Healthcare providers have an important role in education regarding; addiction treatment and prescription drug abuse, the risk of drug interactions, overdose and the proper prescribing and administration of addictive medications. The American Society of Addiction Medicine and others are actively addressing these and

many other important aspects in the research and treatment of addiction as a disease. Addiction medicine is now a mainstream medical society recognized by the American Medical Association and has established an American Board of Addiction Medicine.<sup>11</sup> Irrespective of the underlying science of addiction, the massive health and social problems that drug addiction brings is not just epidemic in West Virginia, but across the nation, maybe even should be more appropriately referred to as pandemic. The interest and safety of the public are best served when regulatory agencies and experts develop a process allowing for early intervention, evaluation, treatment and follow-up of the addicted patient.<sup>51</sup>

### Conclusion

The current and future impact of prescription drug abuse and addiction on society is being evaluated. A new paradigm, which would include health care reform legislation encompassing parity of insurance coverage for mental health and substance use disorders, is imminent. Funding of evidence based addiction research, treatment and education of the

healthcare community and the public is greatly needed. Addiction screening, brief interventions, diagnosis, medication management and referrals when indicated should be a mandatory component of all medical school, residency, and non-physician healthcare providers training program curricula. This should also be part of continuing educational programs to ensure the skill set and resources are available in the institution of these services. They would then be more routinely incorporated into clinical practice with associated future benefit to patients and society. It is important that practitioners adapt to the advances made in the care and monitoring strategies as they are in the treatment of other chronic illnesses.

As stated by the Governor of West Virginia, we need to “Implement a long-term approach that will sustain a meaningful and effective system addressing the entire substance abuse continuum: Prevention, Early Intervention, Treatment, and Recovery”.<sup>1</sup> The formation of the Governor’s Prescription Drug Abuse Advisory Board exemplifies such an effort. It is the authors’ belief that this combined effort and education

## Drug or Alcohol Problem? Mental Illness?

If you have a drug or alcohol problem, or are suffering from a mental illness you can get help by contacting the West Virginia Medical Professionals Health Program. Information about a practitioner’s participation in the program is confidential. Practitioners entering the program as self-referrals without a complaint filed against them are not reported to their licensing board.

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of our children (prior to exposure), the healthcare profession as a whole during and subsequent to training and the public is the key to resolving the issue of prescription drug abuse and addiction. Clinicians have a critical role, not only in preventing the diversion of prescription drugs, but also in the treatment of addiction acutely and the long-term as with any other chronic medical illness affecting our society. Collaboration of legislators, legal authorities, the clinicians and healthcare community, including organized medicine, and the public will provide the ability to stop living in the problem and begin to live in the solution. As representatives of the healthcare profession and the public, we ask... what are we going to do about it?

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*The complete Bibliography can be accessed at [www.wvmp.org](http://www.wvmp.org).*

## CME POST-TEST

1. What is the estimated number of individuals over the age of 12 years who have a substance abuse and/or addiction problem in the United States?
  - a. 1 million
  - b. 5 million
  - c. 10 million
  - d. 23.2 million
  - d. 50 million
2. What is currently considered to be the "drug of choice" in adolescences in the United States?
  - a. Marijuana
  - b. Cocaine
  - c. Gamma-hydroxybutyrate (GHB)
  - d. Inhalants
  - e. Prescription drugs
3. Which one of the following neurotransmitter is most involved in euphoria, reward, motivation, abuse, and addiction?
  - a. Dopamine
  - b. Norepinephrine
  - c. Serotonin
  - d.  $\gamma$ -Aminobutyric acid (GABA)