Abstract
Pharmacists, the most accessible of health care professionals, are well positioned to help prevent and treat substance use disorders and should prepare themselves to perform these functions. New research improves our knowledge about the pharmacological and behavioral risks of drug abuse, supports the clinical impression that drug dependence is associated with long-lasting neurochemical changes, and demonstrates effective pharmacological treatments for certain kinds of drug dependencies. The profession is evolving. Pharmacists are engaging in new practice behaviors such as helping patients manage their disease states. Collaborative practice agreements and new federal policies set the stage for pharmacists to assist in the clinical management of opioid and other drug dependencies. Pharmacists need to be well informed about issues related to addiction and prepared not only to screen, assess, and refer individual cases and to collaborate with physicians caring for chemically dependent patients, but also to be agents of change in their communities in the fight against drug abuse.

At the end of this article the pharmacist will be better able to:
1. Explain the disease concept of chemical dependence
2. Gather the information necessary to conduct a screen for chemical dependence
3. Inform patients about the treatment options for chemical dependence
4. Locate resources needed to answer questions about the effects of common drugs of abuse (alcohol, marijuana, narcotics, "ecstasy", and cocaine)
5. Develop a list of local resources for drug abuse treatment
6. Counsel parents who are concerned about drug use by their children
7. Counsel individuals who are concerned about drug use by a loved one.
8. Counsel individuals who are concerned about their own drug use

Introduction
Given the ongoing public attention paid to the problems of substance abuse and chemical dependence in American society, it is somewhat disappointing that few health care professionals are educated and trained in this area of clinical care [1]. Pharmacists are front-line health care
providers and arguably are the most accessible members of a health care team. They are expected to play a multitude of roles – custodian of the country's legitimate supply of Schedule II drugs, purveyor of clean needles in harm reduction public health endeavors, dispenser of addictions pharmacotherapy, provider of drug information, and drug educator – to name some of the more visible functions. Yet few pharmacists are adequately informed or prepared to assume these diverse functions as they relate to issues of substance abuse and chemical dependence [2].

While science has moved forward and clinical methods have improved, the drug abuse problem has grown more complex. No longer can we think in terms of a person being addicted to one drug or another. Rather it is frequently the case that an individual uses many different drugs often in combination. The issue is further complicated by the co-occurrence of substance abuse and mental illness. Even seasoned specialists find it difficult to disentangle the web of causation when the two conditions co-exist in one patient. It is clear that these are synergistic pathologies each exacerbating the symptoms of the other.

Stereotypes established decades ago continue to shape perceptions of "the drug problem" despite dramatic scientific advances in substance abuse research over the past 20 years. It is now well established and widely accepted that addiction is a brain disease [3] and that effective interventions properly deployed reduce the consequences of addiction for the individual and for society. Clinical techniques for screening and assessment have been shown to identify individuals who are likely to have the disease and to determine their treatment needs. Treatment techniques, including pharmacotherapy, have become more specialized and the rates of recovery among various segments of chemically dependent patients have improved. For instance, we know that 25% of alcoholic patients remain constantly abstinent during the year after treatment and an additional 10% significantly reduce alcohol consumption [4].

Surveys conducted in the United States on a regular basis [5] reveal a trend in which young people start experimenting with alcohol and illicit drugs earlier in life today than in years past. The list of "drugs of abuse" has expanded such that drugs easily available to the middle school student today were unknown or non-existent only ten years ago. Adolescence is an especially risky period of life for substance abuse involving powerful mind-altering drugs. Parents are justified in their fear and concern for the well being of their children.

Pharmacists may find themselves ill prepared to respond effectively when approached by patients, parents, and civic leaders who look to our profession for expertise in this area. Since substance abuse has been a somewhat arcane specialty area, health professionals for the most part have not been expected to possess a working knowledge of this issue. The coverage of the topic in health professions training programs has typically been superficial across the country [6]. However, recent legislation [7] passed by Congress is bringing the treatment of opiate addiction out of specialty clinics and into the offices of general practitioners. Pharmacists must understand substance abuse and chemical dependence at least as well as they understand other diseases.

What is addiction and how do people get it?
Addiction is a chronic, primary, progressive and fatal disease characterized by the compulsion to use drugs, with an associated loss of control over drug use, and continued use of drugs despite known problems [7]. More specific diagnostic criteria for a variety of individual substance related disorders are found in the DSM-IV [8] manual. Compulsion involves an inability to resist the desire to use a drug. Thus while most people let the thought of having a drink simply pass through their consciousness, for alcoholics the thought is an undeniable need that must be satisfied.

Loss of control is best understood as the inability to use in moderation consistently. For the average person, quitting after one, two, or three drinks is not a struggle. The alcohol-dependent drinker may plan to stop after just a few drinks, and occasionally may succeed, but it is with some effort. Repeated episodes of social drinking increase the risk that the alcohol dependent person will succumb to another incident of excessive drinking with subsequent adverse consequences. Thus, the stereotype of a constantly intoxicated daily user represents a small segment of drug dependent people.

Continued use despite problems can be misinterpreted as simply the repeated exercise of poor judgment. Unfortunately, by the time substance abusers have developed full-blown chemical dependence, they have constructed a wall of denial around themselves. Their perception of reality is twisted into the belief that drug use is the result of their misfortune. Rather, it is the frequent abuse of substances that leads to repeated negative consequences in their lives. Disrupted interpersonal relations, poor job performance, low self-esteem, and eventual ill health are the sequela of substance abuse and, taken together, may evolve into a perverted justification for self-medication.

While the question of the magnitude of the problem appears to be simple, answers vary according to how the estimate is made. One must distinguish between substance abuse and substance dependence, factor in...
differences among chemicals, consider regional variations, and recognize market specificity for particular illicit drugs. Using DSM-IV criteria, the bulk of epidemiological studies puts the figure for alcohol dependence at 13% to 18% of the American population [10]. The rates for other drugs except for tobacco are lower on a national basis, while the rate of abuse is higher overall than the rate of dependence for any particular substance.

The "brain disease" view of addiction is supported by studies indicating that the brains of chemically dependent individuals are different from others in many important ways. The brain reward system is the center of attention of much of the new thinking about the disease of addiction. In the healthy brain this system reinforces human (and animal) behaviors that are life sustaining. Brain cells adapt to the introduction of chemicals and it is theorized that excessive bombardment of this system by drugs produces dysfunctional adaptations that become embedded in the neuronal circuitry [11]. Alan Leshner of the National Institute on Drug Abuse summarizes these differences as follows: "The addicted brain is distinctly different from the non-addicted brain, as manifested by changes in brain metabolic activity, receptor availability, gene expression, and responsiveness to environmental cues" [3]. Researchers conclude that constant drug use establishes new patterns of neuronal firing in the centers of the brain reward system so that the addicted brain is functionally and morphologically different from a non-addicted brain. For example, an addict responds to visual, olfactory, and auditory cues very differently than a non-addict. Thus, a line of white powder, the aroma of marijuana smoke, or a particular piece of music is associated with specific drug use behaviors for the addict, but for the non-addict these same cues carry no special meaning.

Risk factors for addiction have been identified. Genetic predisposition is generally regarded as a strong predictor for eventual disease. Thus, while the general population risk for alcoholism is about 13%, the risk hovers around 50% for sons of alcoholic fathers [12]. There is also a gender bias; males are more at risk than females [13]. Of course, the risk of addiction is stronger for some drugs than for others. One measure of the addiction potential of drugs is captured in the proportion of those who experiment with a drug who eventually become compulsive users at some point in their lives. Using this measure, the most addictive behavior is cigarette smoking that claims 40% to 60% of those who try cigarettes. Following cigarette smoking is cocaine abuse, wherein about 30% to 50% of experimenters become chemically dependent. Heroin addiction occurs in about 25% to 40% of experimenters. Alcohol addiction occurs in about 13% to 18% of those who experiment with it, while marijuana addiction occurs in about 6% to 9% of users [14,15].

While cocaine, heroin, and marijuana capture much media attention, studies confirm that tobacco and alcohol claim many more lives. Cigarette smoking accounts for 400,000 deaths annually and is considered the single most preventable cause of death in American. Alcohol-related deaths total about 100,000 and the remaining illegal drugs of abuse claim about 20,000 deaths per year for all drugs combined [16].

Why should pharmacists screen patients for substance use and addiction?

The goal of pharmacy education and training is to prepare clinicians for practice in a complex and demanding therapeutic environment. Pharmaceutical care is defined as: "the direct, responsible provision of medication-related care for the purpose of achieving definite outcomes that improve a patient's quality of life. The principal elements of pharmaceutical care are that care is directly provided to the patient, it is provided to produce definite outcomes, these outcomes are intended to improve the patient's quality of life and the provider (pharmacist) accepts personal responsibility for the outcomes."[17]

The American Pharmacists Association takes a similar position by stating: "The mission of Pharmacy is to serve society as the profession responsible for the appropriate use of medications, devices and services to achieve optimal therapeutic outcomes" [18]. To fulfill these goals, pharmacists must acquire a complete drug history for all patients under their care. It is considered routine practice to ask patients about prescription and over-the-counter medications, and in recent years, the importance of herbal product use has become apparent. However, it is doubtful that pharmacists routinely ask about nicotine or alcohol use and more unlikely that they question patients about illicit drug use. Yet these psychoactive chemicals exert powerful pharmacological effects, are known to be involved in a host of drug interactions, and have the capacity to provoke profound behavioral priorities. The failure to elicit information from patients about these drugs is an obvious omission in an otherwise comprehensive medication use history.

Cigarette use is associated with and exacerbates cardiovascular and pulmonary dysfunction. Nicotine is a vasopressor and cardiac stimulant, and smoke is an obvious pulmonary irritant. Thus, in the short run, any patient receiving prescription medication for any cardiovascular or pulmonary condition should be screened for tobacco use. Smokers need unambiguous information about the association between their tobacco use and their medical problem. However, asking about tobacco use should not be limited to patients with these medical conditions.
Guidelines developed by the Agency for Healthcare Research and Quality (AHRQ) stress the public health gains that can be achieved by questioning all patients about tobacco use and advising all smokers to quit [19]. Recent evidence suggests that pharmacists’ advice to quit smoking can produce significant increases in quit rates among smokers [20]. Therefore, even when a patient’s condition is unrelated to tobacco use, giving up smoking will improve the health of all smokers, and the health of their families will be improved by eliminating second hand smoke in the household.

There is a wealth of literature on nicotine pharmacology, tobacco use, and smoking cessation [21]. More detail on these facets of nicotine is readily accessible, and the evidence to justify pharmacists asking about tobacco use is strong. For the pharmacist who wants to build a practice around smoking cessation, certification programs are available.

Asking about alcohol use and screening for dependence can provide vital data for optimizing pharmacotherapy outcomes. Alcohol use should be avoided with many prescription medications [22]. While pharmacists are likely to provide ancillary labels warning patients about drug/alcohol interactions, can they assume the label is a sufficient deterrent to alcohol use? Although there are no data to answer this question directly, this author assumes that the warning is sufficient for those who use alcohol occasionally and who can abstain from drinking without difficulty. For the alcohol-dependent patient this warning may be impossible to heed. Special interventions will be needed to avoid potentially serious drug/alcohol interactions in an alcohol dependent patient.

The clinical ramifications of alcohol dependence run deeper than the acute problem of drug/alcohol interactions. A patient with alcohol (or any other chemical) dependence is operating under a set of life priorities that are different from those who are not chemically dependent. For the vast majority of patients dealing effectively with their illness, taking medications according to the doctor’s order should be a top priority. However, even in the general population, non-adherence to prescription drug administration schedules has been estimated to be on average 50% with a range of from 10% to 90% and is a likely cause of outpatient prescription drug failure [23]. One cause of prescription drug non-compliance is drug abuse. For instance, drug abuse is known to be associated with non-adherence to Highly Active Anti-Retroviral Therapy (HAART) [24]. The extent of non-adherence to other prescription medications that can be attributed to chemical dependence is unknown, but the issue cannot be addressed at all unless those at risk of alcohol or other drug dependence are identified.

Asking about the use of illegal drugs and screening for dependence on these chemicals is a daunting task. One must first establish a professional belief that these questions are driven by therapeutic concerns and dispel hesitation created by feeling that one is intruding into a forbidden area of another’s life. The concerns regarding drug interactions and life priorities discussed in relation to alcohol use are equally of concern in the case of illicit drug use and dependence. However, the stigma associated with illicit drug use is greater than that associated with alcohol or nicotine use. Therefore, the pharmacist must proceed with sensitivity, respect, and confidentiality. Patients should understand that the questions are routine and that honest answers are critical to the safe and effective use of their prescription medication.

Any drug history should be conducted in as confidential an atmosphere as possible in the practice environment. These are basic professional concerns heightened to the level of potential legal liability with the introduction of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Given the likelihood that patients will be hesitant to answer questions about drug use in an open area, facilities for private discussion should be provided when it is evident that the therapeutic conversation includes sensitive areas of a person's history. Assurance of confidentiality can allay patient fears related to disclosure of personal information.

**How can pharmacists screen patients for substance abuse and addiction?**

Asking about non-therapeutic drug use and screening for chemical dependence are two separate activities with different therapeutic goals. A thorough accounting of a person's non-therapeutic drug use can mitigate drug interactions if the patient can comply with a pharmacist’s warnings concerning mixing alcohol or other substances with prescription medication. Some patients conform to this advice because they are not compulsive drug users and can exert control over their drug use when convinced of the necessity to abstain.

The AHRQ recommends that all patients be asked about tobacco use at every visit. In effect, tobacco use should be treated as a vital sign and smoking status should be ascertained at the first visit as "non-smoker", "former smoker" or "current smoker." These choices should be incorporated as check off options on the drug history form in the pharmacy computer. Since adult non-smokers are unlikely to initiate smoking in later life this group need not be asked repeatedly. Former smokers are always at risk of relapse and thus should be questioned periodically about their status and given positive feedback for sustaining abstinence. All current smokers should be advised with each visit to quit smoking for the benefit of their
health and guided to effective therapies if they acknowledge a desire to quit.

Asking about alcohol use requires a bit more finesse. An opening question such as "How do you use alcohol?" is non-threatening and unlikely to be regarded as being intrusive. Preceding this question with a statement regarding the duty of pharmacists to warn patients about untoward drug reactions and the confidentiality of the information will emphasize the protected nature of the conversation and its therapeutic intent. "It's important for your safety that you tell me the truth about this" is language emphasizing the practical reason for your questions. Asking about illegal drugs is a more sensitive issue and one may initially be hesitant to venture into this area of questioning. After ascertaining tobacco use and alcohol use, a natural follow-up question is "Do you take any other kinds of drugs?".

Clearly, patients should be cautioned to refrain from all tobacco, alcohol, and illegal drug use while taking prescription medication when the combination would be harmful. It is also clear that some patients will not be able to conform to this behavioral change. "If you find that you are unable to refrain from drug use during the period of prescription therapy, I strongly recommend that you seek assistance" is a statement that could spark a turning point in the life of individuals who otherwise may feel in total control of their drug use. A brochure on this subject can effectively convey the message while insuring confidentiality.

The issue of screening for addiction as a practical activity for the dispensing pharmacist may stimulate much debate. In the busy environment of the community pharmacy, there is little time to fulfill the required aspects of dispensing, much less to take on additional tasks. However, the same has been said about most other health practice settings. Screening strategies have been developed for use in today's hectic and fast paced health care delivery environment. CAGE is an example of the extent to which questions can reliably screen for alcoholism. The questions are:

1. Have you ever felt the need to Cut down on your drinking?
2. Have you ever been Annoyed by criticism of your drinking?
3. Have you ever felt Guilty about your drinking?
4. Have you ever needed an Eye opener (a morning drink) to steady your nerves, get rid of a hangover, or get the day started?

Since CAGE is a screening tool it cannot render a diagnosis and is not a substitute for a thorough assessment. However, a single "yes" response is considered a positive screen and should trigger a referral to a substance abuse specialist for a full assessment [25]. Some critics have felt that questions should screen for both alcohol and other drugs and for abuse as well as dependence. Two questions have emerged that address these issues: 1) "Have you ever felt you wanted or needed to cut down on your drinking or drug use in the last year?", and 2) "In the last year have you ever drunk or used drugs more than you meant to?" A "yes" to either question is a positive screen [26]. Williams and Vinson have further distilled the screening for problem drinking to one question. "When was the last time you had more than 5 drinks (4 for women) in one day?" Problem drinking, defined as either past-month hazardous drinking or past-year DSM-IV alcohol use disorder [9], is considered present in anyone who answers the question with a date that falls within the last 3 months [27].

What do patients need to know about addiction treatment?

Patients need to know how their medications work and what the role of medication is in the treatment of chemical dependence. The increasing emphasis being placed on training physicians to screen, assess, and treat chemical dependence, coupled with new policies and advances in addiction pharmacotherapy predicts that a larger proportion of substance abusers and chemically dependent patients will receive treatment. Many of them will bring prescriptions related to their outpatient management into community pharmacies across the country. From nicotine transdermal patches used in the treatment of tobacco addiction, to disulfiram and naltrexone for alcoholism, to buprenorphine for the treatment of opioid dependence, outpatient pharmacotherapy for addiction is becoming more commonplace. Patients need counseling related to these therapies as much as for other disease states.

The passage of the Drug Addiction Treatment Act by the U.S. Congress in 2000, coupled with the approval by the Food and Drug Administration in October 2003 of buprenorphine sublingual tablets for the treatment of opioid dependence (Subutex ® and Suboxone ®), may make this a routine prescription intervention. Pharmacists should become familiar with the fundamental biological facts related to opioid dependence and the pharmacotherapeutic approaches for medical withdrawal and maintenance [28].

Table 1 lists the agents currently approved by the Food and Drug Administration for the outpatient treatment of tobacco, alcohol, and opioid addiction. Details on the pharmacology and use of these medications are available.
from usual compendia on prescription products. No prescription medications are currently approved for the outpatient treatment of chemical dependence to other drugs such as marijuana or cocaine.

Patients should understand that medication alone is insufficient for the long-term successful treatment of chemical dependence. For addiction pharmacotherapy, the medication is an adjunct in an overall treatment program. The goals of addiction pharmacotherapy are to achieve and/or sustain abstinence from the patient’s drug of choice. Patients should be informed that their active involvement. Family participation can significantly support a successful addiction recovery.

These non-pharmacological interventions represent the "Achilles heel" in addiction treatment. They are part of the recovery process often overlooked or ignored by both patients and health care providers. The well-informed clinician recognizes that this focus is as vital to the success of addiction treatment as is, for example, blood glucose monitoring and diet control to the treatment of diabetes. Thus, when counseling a patient who is undergoing prescription therapy for chemical dependence, these non-pharmacological interventions should be encouraged.

| Drug of Abuse | Prescription Medication | Usual SIG | Notes | Support Systems |
|---------------|-------------------------|-----------|-------|-----------------|
| Tobacco       | a) Nicotine Substitution NT51<br>Polarclex gum<br>Nasal spray<br>Inhaler<br>Lozenge<br>b) Bupropion SR | a) various dosing protocols.<br>b) 150 mg once daily × 3 days then; 150 mg B.I.D. | a) Stop tobacco use before initiating treatment<br>b) Contraindicated in patients with a history of bulimia, anorexia nervosa, seizure, or currently taking an MAOI or another product containing bupropion. | Nicotine Anonymous [http://www.nicotine-anonymous.org](http://www.nicotine-anonymous.org)<br>American Lung Association [http://www.lungusa.org](http://www.lungusa.org)<br>American Cancer Society [http://www.cancer.org](http://www.cancer.org)<br>American Heart Association [http://www.americanheart.org](http://www.americanheart.org) |
| Alcohol       | a) Disulfiram<br>b) Naltrexone<br>c) Benzodiazepines | a) 500 mg once daily × 1 – 2 weeks, then 235 mg P.O. once daily<br>b) 50 mg P.O. once daily<br>c) dose varies on the basis of the specific agent, level of alcohol tolerance, history of past withdrawal, and presenting symptoms of withdrawal. | a) Stop before and avoid all alcohol use while taking this prescription.<br>b) Contraindicated in patients with severe myocardial disease or coronary occlusion. Punishment when people drink.<br>c) Reduces the "high" from alcohol<br>d) For detoxification only. | Alcoholics Anonymous (A.A.) [http://www.alcoholics-anonymous.org](http://www.alcoholics-anonymous.org)<br>Alanon [http://www.al-anon.org](http://www.al-anon.org)<br>Rational Recovery [http://rational.org](http://rational.org) |
| Opioids       | a) Naltrexone<br>b) Methadone<br>c) LAAM<br>d) Buprenorphine The use of other opioids for the treatment of opioid dependence is a violation of federal law. | a) 50 mg P.O. once daily<br>b) 20 – 120 mg P.O., once daily<br>c) 80 – 100 mg P.O., every other day.<br>d) 4 to 16 mg/day sublingually for maintenance. | a) Will precipitate withdrawal if taken within 7 to 10 days of last opioid use.<br>b & c) Use for maintenance and detoxification tightly regulated by FDA<br>d) Sublingual tablet approved by FDA for medical withdrawal and maintenance. C-III drug. | Narcotics Anonymous (N.A.) [http://www.na.org](http://www.na.org)<br>Naranon [http://www.naranon.com](http://www.naranon.com)<br>Buprenorphine subscribers: [http://buprenorphine.samhsa.gov](http://buprenorphine.samhsa.gov)<br>Local resources for substance abuse and addiction treatment and group and family therapy. |

1 Nicotine Transdermal System 2 L-alpha-acetyl-methadol
ported the substance abuse of the husband or wife. When the opportunity arises, the pharmacist should recommend spousal participation in a support program designed for their needs. These are Al-Anon and Nar-Anon for the spouses of alcohol and opioid dependent patients, respectively. The goal of this referral is to help the spouse recognize enabling behaviors and to stop them. Just as the affected individual is consciously unaware of the insidious development of chemical dependence, the spouse often fails to realize that his or her behavior is deeply enmeshed in the behavior of the dependent partner.

Enabling is recognized as a characteristic of co-dependency under the family disease view of substance use disorders [29]. The therapeutic approach to the co-dependent person is to help him or her detach from the intricacies of the dependent person’s disease and treatment. While this may seem paradoxical to the notion of a family disease model of addiction, only by detaching can the spouse work to reduce their own emotional distress and improve their own coping. As the spouse becomes healthier, the addicted partner is forced to confront his or her issues directly without the co-dependent person running interference, taking partial responsibility, and softening the impact of the disease.

Parents of drug using teens are another group who may ask the pharmacist’s advice on matters of substance abuse and addiction. On-line resources can address many questions of pharmacological fact; however some websites proselytize the drug culture and provide biased and non-factual material. In contrast, the National Institute on Drug Abuse (NIDA) maintains a website that offers valid factual information on commonly abused drugs. In addition, the site http://www.nida.nih.gov provides access to publications in a variety of formats from newsletters to condensed “fact sheets” that can be downloaded, printed, and offered to pharmacy patrons.

Parents have a legitimate fear that drug abuse can disrupt their child’s healthy development. Unfortunately, the distinction between normal adolescent inquisitiveness and pathology, while important, is not easily made. Youthful experimentation in many areas of life is common and to be expected. Alcohol and other drugs, especially marijuana, are easily accessible to youth but, with the exception of tobacco, use becomes habitual and hazardous in only a small percentage. Alcohol, tobacco, and marijuana in that order appear year after year in surveys of school-aged populations as the drugs most often experimented with and used frequently.

The literature on adolescent drug abuse and prevention suggests several concepts germane to our understanding of these issues. Two of these are risk factors and protective factors. As the terms imply, risk factors are aspects of life that are associated with a greater likelihood of drug abuse, while protective factors work to reduce the potential for drug abuse. The research is not clear-cut on these associations; some factors may work differently in different stages of life and in different groups of individuals. In addition, the impact of a risk factor can be mediated by other intervening considerations and some risk factors are co-related [30]. Generally, the notion of risk and protective factors is informative in discussions with parents, since risk factors can be reduced and protective factors enhanced as a means of intervention [31].

- http://www.nida.nih.gov/Infofax/lessons.html

When parents ask a pharmacist about drug effects, there may be an underlying and undisclosed concern about drug use by their child. Thus, the question; “Is marijuana addictive?” may be heard as; “Is my child addicted to marijuana?” This particular question about the nature of marijuana is perhaps one of the most confusing. Since discontinuation of marijuana even after prolonged heavy use is not associated with a physical withdrawal syndrome, few people acknowledge its addictive potential. However, when addiction is defined by compulsive use, loss of control, and continued use despite problems, the reality of addiction to marijuana is evident. As discussed earlier, the road to addiction traverses some predictable territory.

While some amount of experimentation is normative for adolescents, parents should be concerned when they find evidence of the following signs of progression:

a. Using drugs alone
b. Stockpiling drugs
c. Changing friends
d. Willingness to take increasing risks to use drugs
e. Using drugs at inappropriate times
f. Becoming defensive when asked about drugs or drug use practices
g. Carrying drugs

CRAFFT is a screening questionnaire designed specifically for adolescents [32]. It asks these questions:

Have you ever ridden in a Car driven by someone (including yourself) who was high or had been using alcohol or drugs?
Do you ever use alcohol or drugs to relax, feel better about yourself?

Do you ever use alcohol or drugs while you are by yourself (Alone)?

Do you ever forget things you did while using alcohol or drugs?

Do your family or friends ever tell you that you should cut down on your drinking or drug use?

Have you ever gotten into trouble while you were using alcohol or drugs?

A score of 2 or more "yes" responses is a positive screen. Parental action is warranted when such signals are seen. Parents should act swiftly to change those things that can be changed in both the risk and protective dimensions. Of course, a preferred strategy would be for parents to be consistently and supportively engaged in the lives of their children so that positive bonds are created during childhood and carried into the adolescent years of their children's lives.

**Drug effects**

Psychoactive drugs can be classified into three broad categories, 1) depressants, 2) stimulants, and 3) psychedelics. Some details of the effects of popular drugs in these categories can be found in Table 2 (see Additional File 1) and in more detail at the NIDA website identified earlier. While the details of street drug pharmacology are fascinating and sometimes critical, the overarching basic actions characteristic of each category are sufficient to address many inquiries. Furthermore, drug users themselves cannot be certain that the drug they bought is the drug they set out to purchase. The illicit drug market provides no quality assurance, no guarantee of purity, or even the capacity of the buyer to ascertain the qualitative (much less the quantitative) properties of the material purchased. These uncertainties reduce critical care of overdose victims to symptomatic and supportive responses and antidotal therapy on trial and error basis [33].

Depressant drugs like alcohol, heroin, barbiturates, benzodiazepines, anesthetics, solvents, and gamma-hydroxybutyrate (GHB) cause sedation. The initial effect may be liberating and disinhibiting, but as the blood level rises, the user becomes more impaired and exhibits signs of muscle incoordination, difficult speech, unsteady gait, and a general unawareness of the surroundings. In a toxic overdose the person may succumb to the potentially fatal effects of respiratory depression and cardiovascular collapse. These agents produce addiction with concurrent physical dependence. Abrupt discontinuation after pro-

Stimulant drugs like cocaine, amphetamine (and other phenethylamines), and caffeine produce excitation during the action phase of the biphasic effect. The initial effect at a low blood level enhances clarity of thought and increases performance speed without increasing errors. As the blood level rises, these enticing effects are followed by confusion, disorganization of thinking, and performance errors. The physical effects of overdose include paranoid psychosis along with potentially fatal cardiovascular accidents and seizure. Since there is no physical dependence, there is no pharmacological intervention for detoxification; however, profound rebound depression is a predictable aftermath of heavy stimulant abuse.

Psychedelics like lysergic acid diethylamide (LSD), marijuana, and methylene-dioxy-methamphetamine (MDMA, "ecstasy") distort normal perceptions through mechanisms that are not entirely clear. The psychoactive effects of cannabis are thought to be mediated through specific cannabinoid receptors in the brain located in regions responsible for cognition, memory, and movement. These receptors respond to the endogenous ligand anandamide and are present in only low levels in the brain stem, which may explain the lack of lethality of cannabinoids [34].

LSD and MDMA are not active at the cannabinoid receptor, and no cross tolerance between cannabis and these agents is seen. LSD and MDMA share structural features with serotonin, and it appears to be the affinity of these agents for 5-HT₂ receptors that correlate with psychedelic potency. These receptors are highly concentrated in the cerebral cortex, and the effects of these agents on perceptual and cognitive functions are likely to be mediated predominantly through this brain region [35]. Evidence also exists that ties 5-HT₂ receptors to the function of the locus coeruleus (LC). The LC receives an abundance of somatic, visceral, and other sensory inputs that converge from all regions of the body. The LC has been likened to a novelty detector [36]. The response of LC neurons to sensory stimulate is enhanced by LSD.

While neuroanatomy and the geography of the brain are understood in great detail, a psychodynamic model as it relates to psychedelic drug action may be helpful in this context. Freud developed concepts of id, ego, and super-
ego to explain the internal conflict of the human psyche. The unconscious id represents our primal impulses, the partially conscious superego represents the internalization of societal rules, high moral values, and desire to act honorably, and the conscious ego mediates the conflict between them. Ego also functions to organize our sense perceptions into a reality shared with others in our world, particularly the senses of time, person, and place. Ego has also been called the guardian of the unconscious mind. To use a computer metaphor, the brain is the hardware and the mind is the software.

The senses are distorted and the perception of reality changes when ego function is disturbed by psychedelic drugs. This may be fascinating at low intensity, but as the effect increases the fascination may give way to fear. An individual who then attempts to resist the drug effect may move into a state of emotional conflict thought to be the basis of a "bad trip" [37]. Although some psychedelic agents, in particular MDMA, can induce dose related toxicity (see Table 2, Additional File 1) many of the acute adverse effects of psychedelic drugs are related to behaviors resulting in accidental injury or fatality.

Recently emerging "drugs of abuse" include gamma-hydroxy-butyrate (GHB) and methylene-dioxy-methamphetamine (MDMA, "ecstasy"). These agents have received substantial attention in the media. Although the number of users of these agents is small compared to the more commonly abused alcohol and marijuana, parents may have concerns and pharmacists should have sufficient knowledge to discuss them at community events.

GHB is best understood as a depressant agent similar in effect to ethanol and benzodiazepines. Street names include liquid X, salty water, scoop, and soap. It is most frequently sold and ingested as a liquid. The pharmacology of GHB was the topic of a recent thorough review of the scientific literature [38]. GHB is a short chain fatty acid naturally occurring in mammalian tissue and functioning as a neurotransmitter or neuromodulator at GHB receptors in the brain. The effects of GHB are evident within 15 to 30 minutes after ingestion of a little as 10 mg/kg with peak levels being reached in 25–45 minutes. Sedative effects are seen with doses in the 20–30 mg/kg range and 60 mg/kg and higher doses can produce coma.

In comparison to alcohol, there are important similarities and differences. On one hand, GHB exhibits cross-tolerance with ethanol and produces synergistic effects when ingested concurrently. This synergism has earned GHB the reputation as a "date rape" drug along with the benzodiazepine rohypnol. GHB mixes easily with alcoholic drinks and can quickly and surreptitiously be added to an unsuspecting victim’s glass or bottle. GHB also alleviates alcohol withdrawal distress.

On the other hand, animal data suggest differences between GHB and ethanol. Rats trained to discriminate between GHB and saline do not substitute ethanol. In other words, these animals recognize a difference between ethanol and GHB. On a cellular level, there appears to be no overlap between the two agents. Ethanol has been shown to have significant activity at GABA<sub>A</sub> and NMDA receptors while GHB shows only weak effects on NMDA receptors and is devoid of GABA<sub>A</sub> effects. Pre-clinical studies support a conclusion that physical dependence is more difficult to induce with GHB than with ethanol, and GHB withdrawal distress appears to be less severe than that of alcohol.

In contrast to ethanol, GHB induces sleep without disrupting the sleep cycle. This ability to induce a physiological sleep may be exploited therapeutically in the treatment of narcolepsy. It is suggested that patients with this disorder suffer with extreme daytime sleepiness and related symptoms because they experience profound sleep disturbances throughout the night. GHB reduces daytime symptoms of narcolepsy by eliminating the sleep disturbances and restoring a more natural sleep pattern. By comparison, alcohol induced sleep is unnatural in that suppression of REM and slow wave sleep leaves the individual unrested and unstable the next day.

It is the ability of GHB to induce slow wave sleep that appears to explain its attraction for body builders. Growth hormone is released from the anterior pituitary during this stage of sleep. Despite its use for this purpose a recent literature review produced no empirical evidence that GHB-induced hormone release yielded any increase in muscle mass.

The Food and Drug Administration banned the sale of GHB in 1990. Although the chemical is being developed for medicinal use by legitimate pharmaceutical companies, the current supply of GHB for recreational use is from illegal sources. Liquid samples of GHB obtained in an illicit market show large variations in concentration. At best, users are guessing the ingested dose even when the volume is carefully measured. The rapid absorption and inaccurate dosing have led to cases of acute poisoning, especially when GHB is taken in combination with alcohol or another sedative agent.

Seizures of illicit MDMA by the Drug Enforcement Administration have risen sharply in the past two years, consistent with reports of increasing "ecstasy" use among teens. The use of this drug, which has many street names in addition to the more common "ecstasy", has been
closely tied to dance parties called "raves." These are often promoted as alcohol free events, giving parents a false sense of security that there is no affiliated drug use. Rave participants are likely to be teens, and the events are commonly held in open-air locations or in large indoor venues such as warehouses. A rave may go on late into the night and may not break up until sunrise.

The scientific literature is at odds with some popular conceptions of MDMA safety. One trendy website can be found at http://www.dancesafe.org. An examination of this homepage reveals links to other sites that provide information biased toward favorable perspectives on MDMA toxicity. The sense that one gets from information available at this site disagrees considerably with information from government sources http://www.nida.nih.gov and from reports in scientific journals.

A recent review of the medical literature summarizes the scientific data on MDMA effects [39]. MDMA is an amphetamine structure as its name implies, but the added moiety substantially alters the pharmacological response. The effect is more akin to psychedelic than to stimulant agents. Thus, the more striking response is that of a psychedelic with stimulant overtones. Effects on the neurotransmitter serotonin are at the center of concern over MDMA, both in terms of psychoactive response and toxicity. Animal studies reveal that the most likely mechanism of action is enhancement of serotonin neurotransmission through blockade of reuptake after its release. However, this does not constitute an entire explanation since the recent selective serotonin reuptake inhibitor (SSRI) antidepressants do not induce the same effects nor display similar toxicity as MDMA and there is no evidence of their abuse. Like other psychedelic agents, MDMA acts selectively at 5-HT2 (5-hydroxytryptamine type 2) receptors [40]. This differential serotonergic action, coupled with the stimulant qualities of the drug, make MDMA particularly suited to the rave scene and its participants.

The main appeal of MDMA appears to be its ability to produce a sensation of attachment and connection to others. The drug produces a sense of emotional and physical well-being, a desire to communicate with others, and a strong feeling of belonging to the group [41]. Individuals under the influence of the drug want physical contact. For young people struggling with the angst of self-identity and group membership, these effects fulfill a deep need common among adolescents.

The use of MDMA comes with risks. A particularly troublesome pattern of toxicity results from an overload of serotonergic activity which may be aggravated by the rave conditions, i.e., crowded environment, high ambient temperature, loud sound, and possible dehydration. Hyperthermia is a central feature of this toxicity. Body temperatures as high as 43°C (109°F) have been reported [39]. Fatalities from MDMA are related to this extreme body temperature that can produce hyperthermic seizures, rhabdomyolysis (muscle breakdown), disseminated intravenous coagulation, and renal failure. Other vexing, but less critical, undesirable effects include bruxism (tooth grinding), trismus (jaw tightening), nausea, blurred vision, and tremor. Lollipops and baby pacifiers are the paraphernalia used by rave participants to reduce the dental complications of the drug effects.

In addition to the acute toxic and undesirable effects of MDMA, users are at risk of after-effects and long-term neurotoxicity. The hangover effects of MDMA use include lethargy, anorexia, decreased motivation, and, in some cases, anhedonia (loss of feeling of pleasure). More troubling than these short-term effects is the growing body of literature that points to long-term dysfunction that may be caused by damage to serotonin neurons in the central nervous system. Evidence from laboratory studies in animals, brain imaging in humans, and clinical observations of heavy "ecstasy" users by and large are consistent with serotonergic neuro-degeneration. Animal studies in various species show MDMA induced degeneration of serotonergic axons with repeated administration, a decrease in concentrations of both serotonin and its metabolite, 5-hydroxy-indole-acetic-acid (5-HIAA), and a disturbing reorganization pattern of serotonin neurons in which projections to distant sites are pruned back with a concomitant overgrowth (sprouting) to proximal sites. Positron emission tomography (PET) studies in humans reveal dysfunction in 5-HT transport systems in heavy "ecstasy" users vs. controls weeks to years after use. The severity of dysfunction correlates with the extent of use [42]. Fear of brain atrophy among "ecstasy" users has arisen from studies using proton magnetic resonance spectroscopy [43,44]. Clinical evidence suggests that changes in mood and behavior among heavy "ecstasy" users are consistent with serotonergic dysfunction. Although the measure of "heavy" use encompasses a wide range (30 to 1000 incidents of use), the heavy users seem to be those engaged in weekly exposure and multiple doses at each incident. Disruptions in memory, executive function (planning and making choices among alternatives) and learning are common findings in studies of this group. Sleep disturbances have been noted along with mood depression, anxiety, and increased impulsiveness.

The usual single dose of MDMA in a recreational setting is 75 to 150 mg. The effects begin within 20 to 40 minutes, with the initial experience being stimulation. Emotional changes and subjective effects follow and last three to four hours. As the effects of the first dose wane, users often take

http://www.harmreductionjournal.com/content/1/1/3
a "booster" dose to keep the experience going. MDMA is eliminated from the body through liver metabolism and urinary excretion of metabolites. Current urine testing for drugs of abuse does not identify MDMA specifically, which is a shortcoming for clinicians treating abusers of this drug. It is possible to adjust the testing protocol to detect MDMA on an amphetamine screen by lowering the cut-off level. This will produce a false positive for amphetamine but will result in the sample being sent for a second assay where MDMA can be identified as the substance present.

There is no legitimate source of MDMA in the United States. Thus, users must rely on an illicit distribution network. Most of the MDMA sold in the U.S. comes from European production sites. The buyer is at an extreme disadvantage in that he or she cannot be certain of the contents of any particular product sold under the many "brand" names of "ecstasy" tablets. Chemical analysis of purported MDMA samples makes the point. The dance-safe.org website provides a link to lab results of MDMA tablet testing. A posting of 100 samples (from July to November 2001) revealed that 53% of the samples were unadulterated MDMA (no quantitative data available), 13% of the samples were MDMA plus other psychoactive ingredients, with ketamine and caffeine being the most prevalent, and the remaining 34% of the samples contained no MDMA, but were made up of a variety of chemicals including dextromethorphan, acetaminophen, caffeine, ketamine, ephedrine, and methamphetamine, either alone or in combination.

**Building and using a local list of resources**

The local Yellow Pages lists substance abuse and addiction services under the following headings: 1) Alcoholism & Drug Abuse Information & Treatment Centers, 2) Drug Abuse & Addiction Information & Treatment Centers, and 3) Information & Referral Services Drug Abuse & Addiction. An on-line search of http://www.bigyellow.com will yield a listing under these categories by state.

| Risk Factors                                      | Protective Factors                                      |
|--------------------------------------------------|--------------------------------------------------------|
| Chaotic home environment                         | Strong and positive bonds with family                  |
| Parental substance abuse or mental illness       | Parental monitoring                                    |
| Ineffective parenting                            | Clear rules of conduct that are consistently enforced within the family |
| Affiliations with deviant peers                  | Involvement of parents in the lives of their children |
| Adolescent's perception of approval of drug-using behaviors in family, work, school, peers and community environments | Adoption of conventional norms about drug use |
| Lack of nurturing                                 | Bonds with other pro-social institutions such as school, and church |
| Failure in school performance                    | Success in school performance                          |

* Table adapted from NIDA infofax "Lessons from Prevention Research"

Table 3: Risk and Protective Factors Related to Adolescent Drug Abuse*

Treatment resources can be divided into several categories in line with the continuum of care concept applied to addiction therapy. The continuum of care concept is to initiate treatment with the least intrusive intervention that will succeed for the patient. Accordingly, treatment options range from outpatient counseling and education programs to intensive inpatient experiences. The most urgent and severe treatment needs occur when a chemically dependent person initiates abstinence and begins to experience withdrawal distress. This is most likely to occur among those addicted to depressant drugs such as alcohol, opioids, anti-anxiety agents, and soporifics. These agents produce a state of physical dependence and abrupt discontinuation is physically painful, and in the case of alcohol and sedative drugs, potentially fatal.

Building a readily available list of local resources is helpful in that people are most likely to accept a referral in their time of need. A person who expresses a desire for help today may have been unwilling to accept a referral yesterday and by tomorrow the urgency may have passed. Research indicates that individuals go through stages in their approach to making life changes. These stages of change can be determined by questioning and the intervention geared to the person's readiness for change [45]. The five stages are conceptualized as 1) pre-contemplation, 2) contemplation, 3) preparation, 4) action, and 5) maintenance. A clinical strategy called "motivational interviewing" has been built around this change theory [46].

Table 4 presents basic elements of the readiness or stage of change theory, intervention approaches, and some suggested language for talking with patients in each stage. Levinson et al. offer a very practical guide for employing this model in patient oriented clinical practice [47].

Patients rarely succeed on their first attempt at change. One need only consider something in his or her own life that needs to change to realize that old patterns die hard.
Thus, pharmacists should anticipate that advice given once needs to be reinforced with reminders over time. In addition, the stage of change theory warns of relapse, and predicts that people cycle through the stages several times. The individual should re-engage the behavior modification with a renewed commitment to change, a greater level of understanding about themselves and their problem, and an increased intensity of resolve to improve his or her life. The pharmacist can help the patient recognize that in order to “relapse” one has to have succeeded in initiating the change in the first place. The pharmacist can periodically instill optimism by pointing out that the individual is farther along the path of permanent change than they were initially.

**Collegial response**

When a pharmacist develops chemical dependence, the whole profession suffers. As members of a professional community, our individual image is affected by the behavior of other pharmacists. In some respects our reputation rests on someone else’s shoulders. Professionals have a self-regulating duty. Individual pharmacists and the licensing boards that regulate the profession have ethical, moral, and legal responsibilities to protect the public safety and to ensure the viability of the profession.

Over the past 25 years, alcohol and other drug abuse in the workplace were found to be the single largest contribution to the problem of employee impairment and lost productivity. In its nascent form, the employee assistance program (EAP) was a job-based alcoholism program. It has since grown in scope and scale to handle a host of employee problems. The success of the EAP is attributed to the fact that it offers constructive techniques for dealing with employees’ problems in ways that are oriented toward conflict reduction in the workplace [48]. The EAP has emerged as a friend to both employer and employee, winning the support of both management and labor.

As early as 1982, the American Pharmaceutical Association adopted policies that “...pharmacists should not practice while subject to physical or mental impairment due to the influence of drugs – including alcohol – or other causes that might adversely affect their abilities to function properly in their professional capacities” and favoring a rehabilitative approach to the problem of impaired

| Modality                                      | Duration and characteristics of care                                                                 | Clientele                                                                 |
|----------------------------------------------|-------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| Detoxification                               | Alcohol – 3 to 5 days inpatient. Usually with benzodiazepine tapering. Opioids – 10 to 180 days outpatient using methadone or buprenorphine. | Those displaying or at risk for severe alcohol or opioid withdrawal distress. |
| Intensive Outpatient Therapy (IOP)           | 3 to 5 weeks. Patients live off-site and attend therapy for 4 to 6 hours per day.                    | Those recently discharged from detoxification protocols or who require aggressive initiation of therapy. |
| Individual, Group, and Family Outpatient Therapy | 6 to 24 months. Clients attend hourly sessions once a week to discover and deal with issues related to their disease. The least intrusive modality for patients with chemical dependence. | Those discharged from IOP and need continued recovery support (most patients) and those deemed able to establish sobriety with minimal intervention. |
| Education and Information Programs           | 4 to 6 weeks. Classes run in cycles providing information about substance abuse and its varied consequences | Substance abusers not diagnosed chemically dependent who may respond to information and reason. |
| Therapeutic Community                         | 12 to 36 months. Clients reside at the facility entering with no status and earning privileges as their recovery matures | Individuals are often court referred or otherwise coerced into treatment by parents or authorities. |
| Inpatient Treatment Center                   | Typically 1 to 4 weeks (although some individuals may stay longer). Live-in facility where patients are steeped in recovery activities and philosophy. Alcohol or opioid detoxification may be done on premises. | Chemically dependent patients with or without physical dependence. Clients may have been unsuccessful in outpatient treatment or are first time admissions deemed to be unlikely to succeed in outpatient care. |
| Half-Way facility                            | 1 year or longer. Recovery centered housing where housemates gain mutual support from each other’s sobriety. Many are based on 12-step recovery traditions. | Clients in recovery who have been unable to sustain sobriety in standard community housing or who are homeless. |
| Opioid Maintenance in certified treatment programs | Greater than 180 days of daily oral dosing with methadone or buprenorphine, or every-other-day dosing with LAAM or buprenorphine. | Patients who are > 18 years of age, have at least a 1 year history of addiction, and are physically dependent on an opioid. |
| Opioid maintenance in office based practices | Buprenorphine prescribed by authorized primary care physicians and dispensed by local pharmacies. | Patients who are deemed by the physician to be in need of pharmacotherapy for opioid dependence. |
pharmacists [49]. These policies reflect the recognition that the problems of substance abuse and addiction are at least as prevalent in the health professions (including pharmacy) as they are in the general population [50,51]. When a pharmacist observes a colleague practicing while impaired, she or he has an ethical duty to act. In some states, this means a report must be made to the Board of Pharmacy. In other states, the report is made to a collegial assistance program, most-typically called the Pharmacist Recovery Network (PRN), or to an “umbrella” assistance program serving a number of, or all, health professions. Such programs have been built around the EAP model. A rehabilitative approach is superior to a punitive approach in the discovery and treatment of impaired pharmacists [52]. Failure to act ignores the problem, endangers the public health, and prolongs the period of dysfunction for the affected pharmacist. These programs may use recovery contracts that usually employ urine testing for drugs of abuse as a means of supporting recovery. Recovery rates exceeding 80% are anecdotally reported for such programs.

### Additional pharmacy roles

In addition to offering the categories of treatment practices described in this text, pharmacists can speak in schools, churches, and other community organizations in need of substance abuse education. Pharmacists also possess the academic credentials to teach courses at community colleges and universities on the topic of substance abuse pharmacology. Additionally, they can conduct staff training on this topic at addiction treatment centers in their locale in the process of strengthening their therapeutic associations with those entities. As his or her knowledge of substance abuse increases and becomes more refined, the pharmacist can transpose this expertise into a consult service to these same centers where staff members struggle to understand the complexities of addiction pharmacotherapy.

### Summary

Pharmacists are accessible, knowledgeable, and respected health professionals. The frontier of practice has been rapidly expanding into areas of clinical pharmacotherapy, information services, disease state management, and other unique niches in the health services delivery environment. However, the community pharmacist continues to be the most visible pharmacy practitioner with whom the public interacts on a daily basis. Taken in whole measure, community pharmacists represent a largely untapped public health resource.

The country is rapidly moving forward with policies and programs that will expand access to drug abuse treatment services. Treatment of these problems is moving into environments of primary care and pharmacists will become directly involved in this process. The time has come for the pharmacy profession to seize the opportunities that are emerging as these changes come about.

### Competing interests

None declared.

### Additional material

**Additional File 1**

There is one additional file. The filename is Tommasello_Table 2. It is in Excel format, and is Table 2 for this paper. Click here for file
51. Blazer LK, Mansfield PK: A Comparison of Substance Use Rates Among Female Nurses, Clerical Workers and Blue Collar Workers. Journal of Advanced Nursing 1995, 21(2):305-313.

52. Tommasello AC: The Effects of State Policies on Addiction Intervention in the Health Professions: The Case of Pharmacy. Dissertation, University of Maryland 2000.