



Scientific Facts on Psychoactive Drugs

Tobacco, Alcohol, and Illicit Substances

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Level 2 - Details on Psychoactive Drugs

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This Digest is a faithful summary of the leading scientific consensus report produced in 2004 by the World Health Organization (WHO):
"Neuroscience of psychoactive substance use and dependence"

The full Digest is available at: <http://www.greenfacts.org/en/psychoactive-drugs/>

i This PDF Document is the Level 2 of a GreenFacts Digest. GreenFacts Digests are published in several languages as questions and answers, in a copyrighted user-friendly Three-Level Structure of increasing detail:

- Each question is answered in Level 1 with a short summary.
- These answers are developed in more detail in Level 2.
- Level 3 consists of the Source document, the internationally recognised scientific consensus report which is faithfully summarised in Level 2 and further in Level 1.

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1. What are psychoactive drugs and how much are they used?

Psychoactive drugs are substances that can change the consciousness, mood, and thoughts of those who take them. They include legal drugs, such as tobacco and alcohol; as well as illicit drugs, such as cannabis, amphetamines, ecstasy, cocaine, and heroin.

Overall, the use of tobacco, alcohol, and other controlled drugs is growing rapidly and this is contributing significantly to the global burden of disease.

1.1 How many people smoke tobacco?

The percentage of smokers is growing rapidly in developing countries, particularly China, and among women. Currently, 50% of men and 9% of women in developing countries smoke, as compared with 35% of men and 22% of women in developed countries.

When comparing different regions of the world, the average consumption of cigarettes is highest in Asia and the Far East, with the Americas and Eastern Europe following closely.

Table 1. Prevalence of smoking among adults and youths in selected countries [see Annex 3, p. 14]



Annual cigarette consumption per person. Source: WHO Tobacco Atlas [see <http://www.who.int/tobacco/en/atlas8.pdf>]



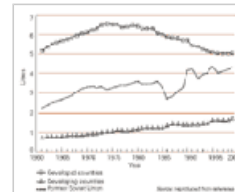
See also GreenFacts' Tobacco Study [see <http://www.greenfacts.org/en/tobacco/index.htm>]

1.2 What are the trends in alcohol consumption?

Like tobacco, alcohol is widely available and marketed aggressively in most parts of the world.

Alcohol consumption is increasing in **developing countries** – especially in Asia – and in countries of the **former Soviet Union**.

In the past twenty years, the consumption of alcohol has decreased in **developed countries**. Nonetheless, the average alcohol consumption remains highest in the developed world compared to the developing world and the former Soviet Union.



Adult (15+) Per Capita Alcohol Consumption by Development Status [see Annex 2, p. 13]

1.3 How many people use illicit drugs?

Worldwide, it is estimated that about 200 million people use some type of illicit drug, such as cocaine, heroin, cannabis, or amphetamines. Illicit drugs are more widely used among males than females and among young people than older people.

Cannabis is the most commonly used illicit drug. Among people aged 15 and above, 3.9% have used cannabis at least once between 2000 and 2001.

After cannabis, the most frequently used illicit drugs are **amphetamines**, **opioids**, and **cocaine**. Eight percent of youths



See also GreenFacts' Alcohol Study [see <http://www.greenfacts.org/en/alcohol/index.htm>]



Cannabis is the most commonly used illicit drug.

in Western Europe and more than 20% of those in the USA reported having used at least one type of illicit drug other than cannabis in their lifetimes.

The number of people who inject drugs is also increasing and this has implications for the spread of HIV. Worldwide, 5% of adults living with HIV/AIDS were infected through injecting psychoactive drugs. However, this proportion is even higher in some regions: 50-90% in Eastern Europe, Central Asia, East Asia, and the Pacific regions, and 25-50% in North America and Western Europe. Therefore, treatment and prevention of drug injection can help to prevent the spread of HIV.

2. How do psychoactive drugs affect health?

2.1 What is the health burden attributable to psychoactive drugs?

Psychoactive drugs impose a substantial health burden on society. Damage to human life is often described in terms of loss of "disability-adjusted life years" (DALYs). This measure takes into account the number of years lost due to premature deaths as well as the years spent living with disability.

Worldwide, psychoactive drugs are responsible for 8.9% of all DALYs lost. The main impact is not due to illicit drugs (0.8% of DALYs) but to alcohol (4%) and tobacco (4.1%).

The health burden attributable to tobacco and alcohol is particularly high for men in developed countries, mainly Europe and North America. Indeed, tobacco and alcohol combined are considered responsible for over a third of all male deaths in developed countries (26.3% are attributed to tobacco and 8% to alcohol). Moreover, the impact of tobacco is expected to increase in other parts of the world.

Table 3. Percentage of total global mortality and DALYs attributable to tobacco, alcohol and illicit substances [see Annex 4, p. 14]

2.2 What main harmful effects are caused by psychoactive drug use?

Mostly, people use psychoactive drugs because they expect some benefit, either getting pleasure or avoiding pain. However, using these drugs can cause harm in the short and longer term.

The main harmful effects of drug use are as follows:

	Short-term	Long-term
Health effects	Deaths and injuries caused by driving after drinking alcohol or after other drug use, other accidents, suicide, assaults (at least for alcohol) overdose (for drugs such as opioids and alcohol).	For alcohol this includes liver cirrhosis. For cigarette smoking this includes lung cancer, emphysema and other chronic illnesses. For heroin taken by injection and through the sharing of needles, this includes the possibility of contracting HIV or hepatitis B and C.
Social problems	For example a sudden break in a relationship or an arrest.	For example neglecting work and family duties.

3. How does drug addiction affect the functioning of the brain?

3.1 What is drug addiction?

Drug addiction, also referred to as drug dependence, is a disorder of the brain brought on by the use of psychoactive drugs. These drugs affect some of the normal processes in the brain related to perception, emotion, and motivation, thus affecting behaviour and thoughts.



Psychoactive drugs affect the brain
Source: WHO

People are diagnosed as drug dependent if they have shown or experienced three or more of the following, at some time during the previous year:

1. A strong desire or sense of compulsion to take the drug.
2. Difficulty in controlling when they start or stop taking the drug and how much they take.
3. Withdrawal, which refers to unpleasant physical and psychological symptoms when the use of the drug is reduced or discontinued.
4. Evidence of tolerance, such as needing increased doses of the drug to achieve the effects originally produced by lower doses.
5. Progressive neglect of other pleasures or interests because of drug use, increased amount of time spent getting or using the drug or recovering from its use.
6. Persistence in using the drug despite clear evidence that it is causing harm

The above criteria for dependence include health and social consequences. Two of them, withdrawal and tolerance, are easily measured biologically. Others are becoming measurable using improved brain imaging techniques such as magnetic resonance imaging (MRI).

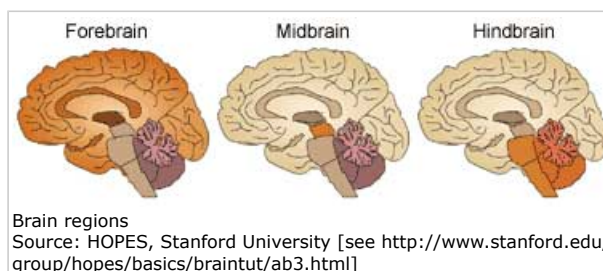
3.2 What brain mechanisms are affected?

Psychoactive drugs alter communication between brain cells. Individual brain cells (neurons) communicate with one another through a series of biological messengers called neurotransmitters. These neurotransmitters are released from the neuron sending the message and bind to receptors on the neuron receiving the message.

Some psychoactive substances are able to mimic the effects of neurotransmitters. Others interfere with normal brain function by blocking it, or by altering the way neurotransmitters are stored, released, and removed.

The human brain is organized into a number of different regions with highly specialized functions

- The **hindbrain** is vital to staying alive because it controls breathing and wakefulness.
- The **midbrain** is involved in learning and reinforcing behaviours — such as eating and drinking — that lead to pleasure and to life preservation. This area thus plays an important role in drug dependence.



- The **forebrain** is very complex and its outer layer (the cerebral cortex) controls the ability for abstract thought and planning.

When drug-dependent people are exposed to stimuli that provoke cravings, specific regions of their forebrain become activated.

Moreover, some other parts of the brain have been shown to work abnormally after drug use or dependence.

3.3 How do different psychoactive drugs act in the brain?

Different psychoactive drugs have different ways of acting in the brain to produce their effects. They bind to different receptor types, and can increase or decrease the activity of neurons through a range of mechanisms. Consequently, they have different effects on behaviour, different rates of development of tolerance, different withdrawal symptoms, and different short-term and long-term effects.

The most common psychoactive drugs can roughly be divided into four groups:

- **Depressants**, such as alcohol, sedatives/hypnotics and volatile solvents, that diminish the activity of the central nervous system. *Overview of effects [see Annex 1, p. 12]*
- **Stimulants**, such as nicotine, cocaine, amphetamines and ecstasy, that increase the activity of the central nervous system. *Overview of effects [see Annex 1, p. 12]*
- **Opioids**, such as morphine and heroin, that relieve pain, dull the senses, and induce sleep. *Overview of effects [see Annex 1, p. 12]*
- **Hallucinogens** such as PCP and LSD, that can distort perceptions to induce delusions or hallucinations. *Overview of effects [see Annex 1, p. 12]*

Cannabis, though classified in the present study as a hallucinogen, also displays characteristics of depressants and stimulants.

Despite their differences, psychoactive drugs do share similarities in the way they affect regions of the brain involved in motivation, which is relevant to the development of drug dependence.

4. How does drug addiction develop?

4.1 How do drug users become drug dependant?

The development of drug addiction can be seen as a learning process. A person takes a drug and experiences the psychoactive effect, which is highly rewarding or reinforcing, and which activates circuits in the brain that will make it more likely that this behaviour will be repeated.

However, the rewarding effects of drugs alone cannot account for why some psychoactive drugs can lead to all of the behaviours associated with addiction.

Similarly, physical dependence on drugs, as evidenced by withdrawal symptoms when drug use is discontinued, may contribute to drug use and addiction, but cannot alone explain



The development of drug addiction can be seen as a learning process
Source: WHO

why drug addiction develops and is maintained, especially after long periods of abstinence. A complex interplay of psychological, neurobiological and social factors appears to be responsible.

The development of drug addiction can be explained by the effects of the drug on specific areas of the brain that increase an individual’s motivation to use the drug.

The brain has evolved to guide and direct behaviour toward stimuli that are critical to survival such as those associated with food, water, mating, and avoiding danger. These stimuli are recognized by the brain as important because they activate specific “circuits” in the midbrain.

Psychoactive drugs artificially activate these same circuits very strongly and “trick” the brain into responding as if the drugs and their associated stimuli (environments, people, objects) were biologically needed.

With repeated exposure, the brain “learns” the relationship between the drug and drug-related stimuli, causing a stronger and stronger desire or craving for the drug. For example, the mere sight of a cigarette or the smell of tobacco can cause such a strong desire to smoke in tobacco-dependent people that it overwhelms them and makes them relapse to tobacco use, even after long periods of abstinence.

4.2 How can genetic factors influence drug use and addiction?

Many environmental and individual factors (including genetic disposition) converge to increase or decrease the odds that a particular individual will use a psychoactive drug, and to what extent.

Risk and protective factors for drug use

	Risk factors	Protective factors
Environmental factors	<ul style="list-style-type: none"> • availability of drugs, • poverty, • social change, • peer culture, • occupation, • cultural norms, • attitudes, • policies on drugs, tobacco & alcohol. 	<ul style="list-style-type: none"> • economic situation, • situational control, • social support, • social integration, • positive life events.
Individual factors	<ul style="list-style-type: none"> • genetic disposition, • victim of child abuse, • personality disorders, • family disruption & dependence problems, • poor performance at school, • social deprivation, • depression & suicidal behaviour, 	<ul style="list-style-type: none"> • good coping skills, • self-efficacy, • risk perception, • optimism, • health-related behaviour, • ability to resist social pressure, • general health behaviour.

In addition to social and cultural factors, genetic differences largely contribute to person-to-person differences in psychoactive drug use and dependence. Studies of patterns of genetic inheritance in families, in identical and fraternal twins, and in adopted individuals, provide information on the extent to which inherited factors play a role in drug dependence. Tobacco use, opioid dependence, as well as alcohol use and dependence, have been shown to be significantly heritable. Gene research seeks to identify the genes that are involved.

Dependence on these drugs is caused by the interaction of several genes with environmental factors. Hence, exposure to drugs could have a much greater effect on somebody who carries a genetic vulnerability to drug dependence than on someone who does not. This partly explains why many of those who experiment with drugs at some point in their lives do not become dependent.

The inherited differences involved in drug use and dependence vary for each drug:

- for **tobacco**, differences in the genes involved in the metabolism of nicotine,
- for **alcohol**, differences in the genes involved in the metabolism of alcohol and inherited differences in certain brain cell receptors (for serotonin, dopamine and GABA), and
- for **opioids**, inherited differences in the brain cell receptors for opioids and in the enzymes that metabolize opioids.

Genetic differences may influence many aspects of a person's drug use. For instance, they may influence how pleasurable a drug is, to what extent it harms health (overdose or long-term effects), how strong the withdrawal symptoms and cravings are, and how the person develops tolerance.

5. Why do drug addiction and mental illness often coexist?

Drug addiction is more frequent in individuals who have a mental illness compared to individuals without any mental disorder. Likewise, people who are drug dependent are more likely to suffer from mental disorders than non-dependent people. This indicates either a shared neurobiological basis for both afflictions, or an interaction of effects at some level.



This may be explained by different hypotheses:

1. Drug dependence and mental illness may be based on the same processes in the nervous system.
2. Drug use may help to ease some of the symptoms of the mental illness or the side effects of medication.
3. Drug use may precipitate mental illnesses or lead to biological changes that are involved in mental illnesses.

There is some evidence for all of these hypotheses. For instance, many psychoactive drugs can produce psychiatric-like syndromes. For example, amphetamines and cocaine can induce psychotic-like symptoms. Hallucinogenic substances can affect perception, thinking, and feeling, and produce hallucinations, which are an aspect of some psychoses. Furthermore, psychoactive drug use regularly changes a person's mood, producing either happy feelings or depressive symptoms, especially during withdrawal.

Research on the link between drug dependence and mental illness has only been carried out in a few countries and the results may not be applicable to other cultures.

For example, a US study has shown that people with mental disorders are 4.5 times more likely to be drug-dependent and 2.3 times more likely to be alcohol-dependent at some stage in their lives compared to people without any mental illness.

People who are dependent on drugs such as alcohol, tobacco, and cocaine have been shown to be more likely to suffer from mental disorders such as depression compared with non-dependent people. For instance, a US study has shown that 38 to 44% of people who

are alcohol-dependent have suffered from major depression, compared with 7% in non-dependent individuals.

6. How can addiction to psychoactive drugs be prevented and treated?

Drug addiction is treated with medications and with behavioural therapies, a kind of psychotherapy. A combination of the two appears to be the most effective approach. Many treatments have been very successful but some remain controversial for ethical reasons. New and better treatments are being developed.

It remains unclear whether a treatment should be considered successful only if a person gives up the drug completely, or if reducing the amount or the frequency of drug-taking can also be considered a success.

6.1 What are the different approaches to treating drug addiction with medications?

A variety of medications and behavioural treatments have been shown to be effective in treating drug addiction.

In terms of treatments with **medications**, two options are:

1. **Medications or procedures that interfere with the action of drugs in the body.** For example, some medicines block the pleasurable effects of drugs while others cause unpleasant reactions when combined with the drug and therefore make the drug repugnant to the user. The main problem with these medicines is that drug dependent patients often do not take the medication regularly, thereby making the treatment ineffective. It also remains ethically controversial whether a patient who does not consent to a treatment can be forced to follow it or whether treatments with other, potentially irreversible, effects should be used.
2. **Substitution or maintenance treatment.** Drug users are given a substance that acts like the drug in some ways without inducing some of its more harmful effects. This option has been widely used to treat dependence to opioids with methadone and other substances substituted for heroin. It aims to help drug users avoid previous illegal and harmful drug-taking habits and the associated risks of death, crime, and disease. Even though substitution therapies are effective in reducing harm to society (e.g., criminal activity) or to the individual (e.g. HIV infection), they contribute to the continuation of the dependence which raises ethical issues.



Methadone is a medication used as a substitute for heroin
Source:
Methadonetreatment.net

Table 5. Pharmacological treatments for substance dependence [see Annex 5, p. 15]

6.2 What are the different behavioural therapies for treating drug addiction?

Behavioural therapies try to replace the motivation to use drugs with the motivation to engage in other behaviours. They aim to help people 'unlearn' their drug-taking behaviour, learn new ways to respond to cravings, and develop new skills in order to remain drug-free. Such therapies include the provision of psychotherapy, psychosocial support, and counselling to encourage behavioural and emotional change. These therapies rely on the same principles of learning and motivation that are used to describe the development of dependence.

There are four types of behavioural therapies:

- **Cognitive behavioural therapies** focus on identifying what triggers drug-taking and on learning new ways to respond to cravings.
- **Relapse prevention therapies** are techniques aimed at developing greater self-control in order to avoid relapse, for instance by identifying emotional and environmental triggers of craving and drug use.
- **Contingency management techniques** use rewards and punishments to help people stop using a drug.
- **Motivational enhancement therapy** works by motivating the patients by asking their opinion on specific drug-related behaviours and by exploring the goals they want to achieve.

6.3 What ethical issues are raised by research on drug addiction?

The rapid pace of change in the field of neuroscience research brings with it a host of new ethical issues in both research and treatment, which will need to be addressed.

An influential set of moral principles guide the ethics of biomedical research. The principles of:

- **Autonomy:** People must voluntarily consent to treatment or research participation and any information they give to a researcher must remain private.
- **Non-maleficence:** The risks of participating in the research must be as small as possible.
- **Beneficence:** The benefits to society and to participants must be greater than the risks.
- **Justice:** The risks and benefits of research must be distributed fairly.

However, research on drug dependence is changing quickly and this raises new ethical issues, both regarding research on animals and on humans. For example, a person identified by **genetic screening** as vulnerable or at risk of becoming drug-dependent may suffer from reduced self-esteem. If this information is available to others, it may disadvantage the person by reducing chances of finding a job, a company prepared to offer insurance, or a partner.

Clinical trials compare the effects of different drug or behavioural treatments, and sometimes placebos, on the drug use, health, social adjustment, and well-being of persons with drug dependence. Thus, a person participating in a clinical trial might benefit from it. Because drug companies pay for many clinical trials, it is important to ensure that the public can trust the results. The criteria for good clinical trials agree in requiring that a representative sample of the population at risk is recruited into such studies. Independent monitoring of compliance with the study protocol is recommended.

Other ethical issues include ensuring equal access to treatment for all those who may need it. Questions are raised as to what extent public money should fund drug dependence

treatments and whether someone should be forced to accept medical treatment for drug dependence.

7. Conclusions

Drug use and addiction cause a lot of disease and disability in the world. Recent advances in neuroscience may help improve policies to reduce the harm that the use of tobacco, alcohol, and other psychoactive drugs impose on society.

Effective action should take into account the following:

1. Since the effects of drugs on health vary greatly depending on the type of drug and on the way it is used, the public health response to drug use should be proportional to the health-related harm it causes.
2. Use of psychoactive substances is to be expected because of their pleasurable effects as well as social influences. The greater the frequency and amount of drug used, the higher the risk of becoming dependent.
3. Effective public health policies and programmes that address not only drug dependence but also other forms of harmful drug use could lead to a significant reduction in the overall health burden of drug use.
4. The risk of becoming dependent on drugs is determined by a combination of biological, genetic, psychological, social, cultural, and environmental factors. Currently, it is impossible to predict who will become drug dependent.
5. Drug dependence is a medical disorder, not a lack of willpower or strength of character.
6. Drug dependence and mental illnesses often affect the same individuals. Therefore, it would be useful to integrate research, assessments, and treatments for both types of disorders.
7. The cost-effective treatment and management of drug dependence can save lives, improve health, and reduce costs to society. Beyond stopping drug use, effective treatment requires changes in the behaviour of users and often the use of substitute drugs.
8. Treatment must be accessible to all in need and the health care sector should provide the most cost-effective treatments.
9. Prejudice and discrimination against drug dependent people is one of the main barriers to their treatment. Everyone has the same rights to health care, education, work opportunities and integration into society.
10. Investment in brain research on drug dependence must continue and expand to cover social science, prevention, treatment and policy research. The results of research should be used to devise evidence-based policies to reducing the burden from drug use.

Recent advances in the treatment of drug dependence raise difficult ethical issues that must be addressed by scientific and policy communities as a priority.

Annex

Annex 1:

Depressants – overview of effects

Substance	How it works	Tolerance	Withdrawal	Effects of prolonged use
Ethanol (alcohol)	Alters the effects of the neurotransmitters glutamate and GABA. Probably increases activity in the dopamine system involved in motivation and learning.	Develops due to increased processing in the liver and changes to receptors in the brain.	Withdrawal from long-term use can include shaking, sweating, weakness, agitation, headache, nausea, vomiting, seizures, and <i>delirium tremens</i> .	Changed brain function and structure, reduced mental capacity, decreased brain volume.
Hypnotics and sedatives	Enhances the effects of some neurotransmitters (e.g. GABA).	Develops quickly due to changes in brain receptors.	Anxiety, alertness, restlessness, insomnia, excitability, seizures.	Memory problems.
Inhalants (volatile solvents)	Like other sedatives and hypnotics, probably affect specific transmitters. Increases activity in the dopamine system involved in motivation and learning.	Some tolerance develops, but is difficult to estimate.	Increased susceptibility to seizures during withdrawal	Changes in how dopamine works in the body, problems in the nervous system, reduced mental capacity; psychiatric problems.

Stimulants - overview of effects

Substance	How it works	Toleranc	Withdrawal	Effects of prolonged use
Nicotine	Activates specific receptors. Increases the production and release of dopamine.	Develops through metabolic factors, as well as receptor changes.	Irritability, hostility, anxiety, unease, discomfort, depressed mood, decreased heart rate, increased appetite.	It is difficult to separate the health effects due to nicotine from the effects due to other components of tobacco.
Cocaine	Prolongs the effects of transmitters such as dopamine.	Perhaps short-term tolerance.	There is not much evidence of withdrawal. Depression is common among dependent people who stop using the drug	Abnormalities in specific regions of the brain, loss of some mental capacity, problems with movement, decreased reaction times.
Amphetamines	Increase the release and prolong the effects of dopamine and related transmitters.	Develops quickly	Fatigue, depression, anxiety and intense craving for the drug.	Sleep disturbances, anxiety, decreased appetite; changes in dopamine brain receptors, changes in metabolism in some parts of the body, reduction of mental capacity and deterioration of movement.
Ecstasy	Increases the release and prolongs the effects of the neurotransmitter serotonin.	May develop in some individuals.	Depression and insomnia	Damages some brain systems, leads to physical changes and to changes in behaviour. Long-term psychiatric and physical problems such as loss of memory, problems with decision-making and self-control, paranoia, depression and panic attacks.

Opioids – overview of effects

Substance	How it works	Tolerance	Withdrawal	Effects of prolonged use
Opioids	Activate specific receptors that are abundant in an area of the brain that is involved in motivation and learning.	Due to short-term and long-term receptor changes, and to changes in the way some cells communicate.	Can be severe. Watery eyes, runny nose, yawning, sweating, restlessness, chills, cramps, muscle aches.	Long-term changes in certain receptors. Changes in learning and in the response to stress.

Hallucinogens – overview of effects

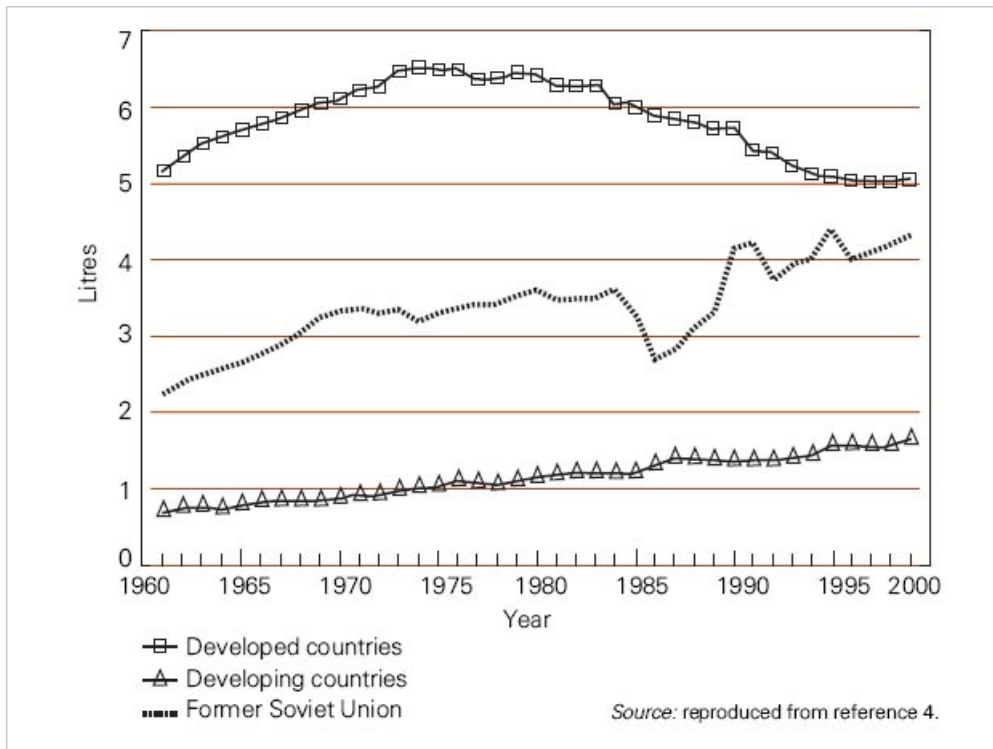
Substance	How it works	Tolerance	Withdrawal	Effects of prolonged use
Cannabis	Activates specific receptors. Affects the dopamine system involved in motivation and learning.	Develops quickly.	Withdrawal is rare perhaps because cannabis remains in the body for a long time.	Long-term exposure may produce long-lasting reduction of mental capacity. May make mental illness worse.
Hallucinogens (such as LSD and PCP)	Different substances in this class act on different brain receptors.	Develops quickly.	There is no evidence of withdrawal.	Short or long term disturbed mental state in which a person experiences hallucinations, delusions, personality changes and loss of contact with reality. Flashbacks or re-experiencing of drug effects, long after drug use.

Source: WHO: GreenFacts based on Table 4

*Neuroscience of Psychoactive Substance Use and Dependence, Summary (2004), [see http://www.who.int/substance_abuse/publications/en/Neuroscience_E.pdf]
Global use of psychoactive substances and burden to health, p 18-19*

Annex 2:

Figure 1. Adult (15+) Per Capita Alcohol Consumption by Development Status



*Source: WHO Neuroscience of Psychoactive Substance Use and Dependence, Summary (2004), [see http://www.who.int/substance_abuse/publications/en/Neuroscience_E.pdf]
Global use of psychoactive substances and burden to health, p.9*

Annex 3:

Table 1. Prevalence of smoking among adults and youths in selected countries

Country	Annual per capita consumption of cigarettes	Prevalence of smoking (%)			
		Adults		Youths	
		Males	Females	Males	Females
Argentina	1495	46.8	34.4	25.7	30
Bolivia	274	42.7	18.1	31	22
Chile	1202	26	18.3	34	43.4
China	1791	66.9	4.2	14	7
Ghana	161	28.4	3.5	16.2	17.3
Indonesia	1742	59	3.7	38	5.3
Jordan	1832	48	10	27	13.4
Kenya	200	66.8	31.9	16	10
Malawi	123	20	9	18	15
Mexico	754	51.2	18.4	27.9	16
Nepal	619	48	29	12	6
Peru	1849	41.5	15.7	22	15
Poland	2061	44	25	29	20
Singapore	1230	26.9	3.1	10.5	7.5
Sri Lanka	374	25.7	1.7	13.7	5.8
USA	2255	25.7	21.5	27.5	24.2

Source: WHO Neuroscience of Psychoactive Substance Use and Dependence, Summary (2004), [see http://www.who.int/substance_abuse/publications/en/Neuroscience_E.pdf]
Global use of psychoactive substances and burden to health, p.8

Annex 4:

Table 3. Percentage of total global mortality and DALYs attributable to tobacco, alcohol and illicit substances

Risk factor	High mortality developing countries		Low mortality developing countries		Developed countries		World-wide
	Males	Females	Males	Females	Males	Females	
Mortality							
Tobacco	7.5	1.5	12.2	2.9	26.3	9.3	8.8
Alcohol	2.6	0.6	8.5	1.6	8	-0.3	3.2
Illicit drugs	0.5	0.1	0.6	0.1	0.6	0.3	0.4
DALYs							
Tobacco	3.4	0.6	6.2	1.3	17.1	6.2	4.1
Alcohol	2.6	0.5	9.8	2	14	3.3	4
Illicit drugs	0.8	0.2	1.2	0.3	2.3	1.2	0.8

Source: WHO Neuroscience of Psychoactive Substance Use and Dependence, Summary (2004), [see http://www.who.int/substance_abuse/publications/en/Neuroscience_E.pdf]
Global use of psychoactive substances and burden to health, p.11

Annex 5:

Table 5. Pharmacological treatments for substance dependence

Substance	Treatment	Efficacy
Alcohol	Acamprosate is a synthetic substance with structural similarity to a naturally occurring amino acid. Restores the normal activity of neurons, which become hyperexcited as a result of chronic exposure to alcohol.	Overall, patients treated with acamprosate exhibit a significant increase in rate of completion of treatment, time to first drink, abstinence rate and/or cumulative duration of abstinence, compared with patients treated with placebo.
	Naltrexone : Blocks opioid receptors.	Naltrexone is effective in reducing relapse and in helping people to remain abstinent and to decrease alcohol consumption.
	Disulfiram interferes with the normal metabolism of acetaldehyde, a metabolite of alcohol. High acetaldehyde levels produce an unpleasant reaction that is intended to render the consumption of alcohol aversive.	The efficacy of disulfiram is variable, and is confounded by the need to carefully titrate the dose, and by the need for a high degree of compliance.
Nicotine	Nicotine substitution with nicotine patch or gum .	All nicotine-replacement therapies are equally effective in helping people to quit smoking, and, combined with increased public service announcements in the media about the dangers of smoking, have produced a marked increase in successful quitting
	Bupropion : A weak norepinephrine and dopamine reuptake inhibitor, and a nicotinic receptor blocker.	Bupropion improves the abstinence rates of smokers, especially if combined with nicotine replacement therapy .
	Immunotherapy: Vaccines that can prevent nicotine from acting on the brain have been proposed.	Vaccines are not yet ready for clinical trials. Trials with mice show promising results.
Heroin	Methadone (synthetic opioid agonist).	Methadone maintenance treatment is safe, and very effective in helping people to stop taking heroin, especially when combined with behavioural therapies or counseling and other supportive services.
	Buprenorphine : Partial agonist at the mu opioid receptor and a weak antagonist at the kappa opioid receptor.	Relatively long duration of action and good safety profile.
	Levo-alpha-acetyl-methadol (LAAM): a synthetic opioid.	Long-acting synthetic opioid that can be used to treat heroin dependence, but it needs only be taken three times per week, thus making it even easier for people to use this therapy.
	Naltrexone blocks the effects of morphine, heroin and other opioids by acting as antagonist at the opioid receptors.	This therapy begins after medically supervised detoxification, because naltrexone does not protect against the effects of withdrawal, and can in fact precipitate withdrawal symptoms in dependent people. Naltrexone itself has no subjective effects or potential for the development of dependence. Patient noncompliance is a common problem. Therefore, a favourable treatment outcome requires that there also be a positive therapeutic relationship, effective counselling or therapy, and careful monitoring of medication compliance.
Cocaine	GBR 12909 is an inhibitor of dopamine uptake that antagonizes the effects of cocaine on mesolimbic dopamine neurons in rats, and blocks self-administration of cocaine in rhesus monkeys.	Clinical trials of this substance were at the planning stage in 2004.
	Immunotherapies : cocaine is sequestered in the bloodstream by cocaine specific antibodies that prevent its entry into the brain.	Clinical trials are underway.
Sedatives/hypnotics	Slow tapering of substance dose combined with behavioural therapy.	Effective.

Source: WHO Neuroscience of Psychoactive Substance Use and Dependence, Summary (2004), [see http://www.who.int/substance_abuse/publications/en/Neuroscience_E.pdf]

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