

## **Annex 1. Examples of treatment for disorders, including their pharmacological effectiveness<sup>1</sup>**

Interventions for the management of mental and behavioural disorders can be classified into three major categories: prevention, treatment and rehabilitation. For most disorders, the best treatment is one that combines psychosocial interventions with appropriate application of medicines. This section is based on treatment recommendations presented in the World Health Report 2001 (WHO, 2001a). While it focuses on effectiveness of medicines, it is not intended to imply that this should be the sole treatment for mental disorders.

- Prevention (primary prevention or specific protection) comprises measures applicable to a particular disease or group of diseases in order to intercept their causes before they affect the individual; in other words, to avoid the occurrence of the condition.
- Treatment (secondary prevention) refers to measures to arrest a disease process already initiated, in order to prevent further complications and sequelae, limit disability and prevent death.
- Rehabilitation (tertiary prevention) involves measures aimed at disabled individuals, for restoring them to their previous situation or maximizing the use of their remaining capacities. It comprises both interventions at the level of the individual and modifications to the environment.

The following examples present a range of effective interventions of public health importance. For some of these disorders, the most effective intervention is preventive action, whereas for others treatment or rehabilitation is the most efficient approach.

As treatment options for mental disorders change rapidly, these recommendations cannot replace a comprehensive study of the most recent literature on management of mental disorders when designing treatment schedules.

### *Depression*

Antidepressants are effective across the full range of severity of major depressive episodes. With mild depressive episodes, the overall response rate is about 70%. With severe depressive episodes, the overall response rate is lower, and medication is more effective than the placebo. Studies have shown that the older antidepressants (tricyclics) are as effective as the newer medicines and less expensive: the cost of the older antidepressants is about US\$ 2-3 per month in many developing countries. New antidepressants offer more effective treatments for severe depressive episodes, with fewer unwanted effects and greater patient acceptance, but their availability remains limited in many developing countries. These medicines may offer advantages to older age groups.

The phase known as “maintenance pharmacotherapy” is intended to prevent recurrences of mood disorders, and is typically recommended for individuals with a history of three or more depressive episodes, chronic depression, or persistent depressive symptoms. This phase may last for years, and typically requires monthly or quarterly visits to health care facilities.

Some people prefer psychotherapy or counselling to medication for the treatment of depression. Evidence from 20 years of research has revealed that several forms of time-limited psychotherapy are as effective as medicines in mild to moderate depressions. These depression-specific therapies include cognitive behavioural therapy and interpersonal psychotherapy, and emphasize active collaboration and patient education.

<sup>1</sup>: adapted from WHO, 2001a

A number of studies from Afghanistan, India, the Netherlands, Pakistan, Sri Lanka, Sweden, the United Kingdom and the United States show the feasibility of training general practitioners to provide this care, and its cost-effectiveness (Sriram et al., 1990; Mubbashar 1999; Mohit et al., 1999; Tansella & Thornicroft 1999; Ward et al., 2000; Bower et al., 2000).

Even in industrialized countries, only a minority of people suffering from depression seek or receive treatment. Part of the explanation lies in the symptoms themselves. Feelings of worthlessness, excessive guilt and lack of motivation deter individuals from seeking help. In addition, such individuals are unlikely to appreciate the potential benefits of treatment. Financial difficulties and the fear of stigmatization are also deterrents. Beyond the individuals themselves, health care providers may fail to recognize symptoms and to follow best practice recommendations, because they may not have the time or the resources to provide evidence-based treatment in primary care settings.

#### *Alcohol dependence*

The prevention of alcohol dependence needs to be seen within the context of the broader goal of preventing and reducing alcohol-related problems at the population level (e.g. alcohol-related accidents, injuries, suicide and violence). The goals of therapy are reduction of alcohol-related morbidity and mortality, and reduction of other social and economic problems related to chronic and excessive alcohol consumption.

The main strategies that have proved to be effective for the treatment of alcohol-related problems and dependence are: early recognition of problem drinking and early intervention, psychological interventions, treatment of the harmful effects of alcohol (including withdrawal and other medical consequences), teaching new coping skills in situations associated with the risk of drinking and relapse, family education and rehabilitation. Epidemiological research has shown that most problems arise among those who are not significantly dependent, such as individuals who get intoxicated and drive or engage in risky behaviours, or those who drink at high-risk levels but continue to have jobs or go to school and maintain relationships and relatively stable lifestyles. Among patients drinking at hazardous levels who attend primary health care clinics, only 25% are alcohol dependent.

Brief interventions comprise a variety of activities directed at persons who engage in hazardous drinking, but who are not alcohol dependent. These interventions are of low intensity and short duration: typically no more than three to five sessions comprising 5-60 minutes of counselling and education. They are intended to prevent the onset of alcohol-related problems. The content of such brief interventions varies, but most are instructional and motivational, designed to address the specific behaviour of drinking, with feedback from screening, education, skill-building, encouragement and practical advice, rather than intensive psychological analysis or extended treatment techniques (Gomel et al. 1995).

For early drinking problems, the effectiveness of brief interventions by primary care professionals has been demonstrated in numerous studies (WHO, 1996b; Wilk, Jensen & Haviighurst, 1997). Such interventions have reduced alcohol consumption and heavy drinking by as much as 30% over periods of 6 to 12 months or longer. Studies have also demonstrated that these interventions are cost-effective (Gomel et al., 1995).

For patients with more severe alcohol dependence, both outpatient and inpatient treatment options are available and have been shown to be effective, although outpatient treatment is substantially less costly. Several psychological treatments have proved to be equally effective, including cognitive behavioural treatment, motivational interviewing and the "Twelve Steps" approach associated with professional treatment. Community

reinforcement approaches, such as that of Alcoholics Anonymous, during and following professional treatment are consistently associated with better outcomes than treatment alone.

Therapy for spouses and family members, or simply their involvement, has benefits for both initiation and maintenance of alcohol-dependence treatment.

Detoxification (treatment of alcohol withdrawal) within the community is preferable, except for those with severe dependence, a history of delirium tremens or withdrawal seizures, an unsupportive home environment, or previous failed attempts at detoxification (Edwards et al., 1997). Inpatient care remains a choice for patients with serious comorbid medical or psychiatric conditions. Psychosocial ancillary and family interventions are also important elements in the recovery process, particularly when other problems occur along with alcohol dependence. There is no evidence to indicate that coercive treatment is effective. It is unlikely that such treatment (whether it follows civil commitment, a decision of the criminal justice system, or any other intervention) will be beneficial (Heather, 1995). Medication cannot replace psychological treatment for people with alcohol dependence, but a few drugs have proved to be effective as complementary treatment for reducing relapse rates (NIDA, 2000).

#### *Drug dependence*

The prevention of drug dependence needs to be considered within the context of the broader goal of preventing and reducing drug-related problems at the population level.

The goals of therapy are to reduce morbidity and mortality caused by or associated with the use of psychoactive substances, until patients can achieve a drug-free life. Strategies include early diagnosis, identification and management of risk of infectious diseases as well as other medical and social problems, stabilization and maintenance with pharmacotherapy (for opioid dependence), counselling, access to services and support to achieve social integration.

Persons with drug dependence often have complex needs. They are at risk of HIV and other blood-borne pathogens, comorbid physical and mental disorders, problems with multiple psychoactive substances, involvement in criminal activities, and problems with personal relationships, employment and housing. Their needs demand links between health professionals, social services, voluntary agencies and the criminal justice system.

Shared care and integration of services are examples of good practices in caring for substance dependents. General practitioners can identify and treat acute episodes of intoxication and withdrawal, and provide brief counselling as well as immunization, HIV testing, cervical screening, family planning advice and referral. Counselling and other behavioural therapies are critical components of effective treatment of dependence, as they can deal with motivation, coping skills, problem-solving abilities and difficult interpersonal relationships. Particularly for opioid dependents, substitution pharmacotherapies are effective adjuncts to counselling. As the majority of drug dependents smoke, tobacco cessation counselling and nicotine replacement therapies should be provided. Self-help groups can also complement and improve the effectiveness of treatment by health professionals.

Medical detoxification is only the first stage of treatment for dependence, and by itself does not change long-term drug use. Long-term care needs to be provided along with treatment of comorbid psychiatric disorders, in order to decrease rates of relapse. Most patients require a minimum of three months of treatment to obtain any significant improvement.

Injection of illicit drugs poses a particular threat to public health. Sharing of injection equipment is associated with transmission of blood-borne pathogens (especially HIV and hepatitis B and C), and has been responsible for the spread of HIV/AIDS in many countries, wherever injecting drug use is widespread. People who inject drugs and who do not get treatment are up to six times more likely to become infected with HIV than those who enter and remain in treatment. Treatment services should therefore provide assessment for HIV/AIDS, hepatitis B and C, tuberculosis and other infectious diseases and, whenever possible, provide treatment for these conditions and counselling to help patients stop unsafe injecting practices.

Drug dependence treatment is cost-effective in reducing drug use (40%-60%), and the associated health and social consequences, such as HIV infection and criminal activity. The effectiveness of drug dependence treatment is comparable to the success rates for the treatment of other chronic diseases such as diabetes, hypertension and asthma (NIDA, 2000). Treatment has been shown to be less expensive than alternatives, such as not treating dependents or simply incarcerating them. For example, in the United States, the average cost for one full year of methadone maintenance treatment is approximately US\$ 4,700 per patient, whereas one full year of imprisonment costs approximately US\$18,400 per person.

### *Schizophrenia*

The treatment of schizophrenia has three main components. First, there are medications to relieve symptoms and prevent relapse. Second, education and psychosocial interventions help patients and families cope with the illness and its complications, and also help prevent relapse. Third, rehabilitation helps patients reintegrate into the community and regain a place in the educational or occupational world. The real challenge in the care of people suffering from schizophrenia is the need to organize services that lead seamlessly from early identification to regular treatment and rehabilitation.

Two groups of medicines are currently used to treat schizophrenia: standard antipsychotics (previously referred to as neuroleptics), and novel antipsychotics (also referred to as second-generation or “atypical” antipsychotics). The first standard antipsychotic medicines were introduced 50 years ago and have proved useful in reducing, and sometimes eliminating, such symptoms of schizophrenia as thought disorder, hallucinations and delusions. They can also reduce associated symptoms such as agitation, impulsiveness and aggressiveness. This can be achieved in a matter of days or weeks in about 70% of patients. If taken consistently, these medicines can also reduce the risk of relapse by half. Currently available medicines appear to be less effective in alleviating such symptoms as apathy, social withdrawal and poverty of ideas. First-generation medicines are inexpensive, costing no more than US\$ 5 per month of treatment in developing countries. Some of them can be administered in the form of long-acting injections at 1-4 week intervals.

Antipsychotic medicines can help sufferers benefit from psychosocial forms of treatment. The newer ones are less likely to induce some side-effects while improving certain symptoms. There is no clear evidence that these newer antipsychotic medications differ appreciably from the older ones in their effectiveness, although there are differences in their most common side-effects.

The average duration of treatment is 3-6 months. Maintenance treatment continues for at least one year after the first episode of illness, for 2-5 years after the second episode, and for longer periods in patients with multiple episodes. In developing countries, response to treatment tends to be more positive, medicine dosages lower and duration of treatment shorter.

In the total care of the patients, the support of the families is important. Some studies have shown that a combination of regular medication, family education and support can reduce relapses from 50% to less than 10% (Leff & Gamble, 1995; Dixon, Adams & Lucksted, 2000; Pharaoh, Marij & Streiner, 2000).

### *Epilepsy*

Effective actions for the prevention of epilepsy are adequate prenatal and postnatal care, safe delivery, control of fever in children, control of parasitic and infectious diseases, and prevention of brain injury (for example, control of blood pressure and the use of safety belts and helmets). The goals of therapy are to control fits by preventing them for at least two years, and to reintegrate people with epilepsy into educational and community life. Early diagnosis and the steady provision of maintenance medicines are fundamental for a positive outcome.

Epilepsy is almost always treated with anti-epileptic medicines. Recent studies in both developed and developing countries have shown that up to 70% of newly diagnosed cases of children and adults with epilepsy can be successfully treated with such medicines, making them seizure-free, provided they take their medicines regularly. After 2-5 years of such successful treatment (cessation of epileptic fits), the treatment can be withdrawn in 60%-70% of cases. The remainder have to continue on medication for the rest of their lives, but provided that they take the medication regularly, many are likely to remain free of seizures; in others the frequency or severity of seizures can be considerably reduced. For some patients with intractable epilepsy, neurosurgical treatment may be successful. Psychological and social support are also valuable (ILAE/IBE/WHO, 2000).

Phenobarbitone has become the front-line antiepileptic medicine in developing countries, perhaps because the cost of other medicines is 5-20 times higher. A study in rural India found that 65% of those who received phenobarbitone were successfully treated, with the same proportion responding to phenytoin; adverse events were similar in both groups (Mani et al., 2001). A study in Indonesia concluded that, despite some disadvantages, phenobarbitone should still be used as the first-line medicine in the treatment of epilepsy in developing countries. Studies in Ecuador and Kenya compared phenobarbitone to carbamazepine and found that there were no significant differences between them in terms of efficacy and safety (Scott, Lhatoo & Sander, 2001). In most countries, the cost of treatment with phenobarbitone can be as low as US\$ 5 per patient per year.

### *Alzheimer's disease*

Cholinergic receptor agonists (AChEs) have generally been beneficial in ameliorating global cognitive dysfunction, and are most effective in improving attention. Treatment with these AChE inhibitors also appears to benefit non-cognitive symptoms in Alzheimer's disease, such as delusions and behavioural symptoms. However findings concerning amelioration of learning and memory impairment, the most prominent cognitive deficits in Alzheimer's disease, have been less consistent. Treatment of depression in Alzheimer's disease patients has the potential to improve functional ability.

### *Mental retardation*

Because of the severity of mental retardation and the heavy burden that it imposes on affected individuals, their families and the health services, prevention is extremely important. In view of the variety of different aetiologies of mental retardation, preventive action must be targeted at specific causative factors. Examples include the iodization of water or salt to prevent iodine-deficiency mental retardation (cretinism) (Mubbashar,

1999), abstinence from alcohol consumption by pregnant women to avoid foetal alcohol syndrome, dietary control to prevent mental retardation in people with phenylketonuria, genetic counselling to prevent certain forms of mental retardation (such as Down's syndrome), adequate prenatal and postnatal care, and environmental control to prevent mental retardation caused by intoxication from heavy metals such as lead.

The treatment goals are early recognition and optimal utilization of the intellectual capacities of the individual through training, behaviour modification, family education and support, vocational training and opportunities for work in protected settings. Early intervention comprises planned efforts to promote development through a series of manipulations of environmental or experimental factors, and is initiated during the first five years of life. The objectives are to accelerate the rate of acquisition and development of new behaviours and skills, to enhance independent functioning, and to minimize the impact of impairment. Typically, a child is given sensory motor training within an infant stimulation programme, along with supportive psychosocial interventions. The training of parents to act as trainers in the skills of daily living has become central to the care of persons with mental retardation, especially in developing countries. This means that parents have to be aware of the learning principles and to be educated in behaviour modification and vocational training techniques. In addition, parents can support each other through self-help groups.

The majority of children with mental retardation experience difficulties in following regular school curricula. They need additional help, and some need to attend special schools where the emphasis is on daily activities such as feeding, dressing, social skills and understanding the concept of numbers and letters. Behaviour modification techniques play an important role in developing many of these skills, as well as in increasing desirable behaviours while reducing undesirable behaviours. Vocational training in sheltered settings and using behavioural skills has led to a large number of people with mental retardation leading active lives.

#### *Hyperkinetic disorders*

The precise aetiology of hyperkinetic disorders and hyperactivity in children, often with involuntary muscular spasms, is unknown. Thus, primary prevention is currently not possible. It is possible, however, to prevent the onset of symptoms that are often misdiagnosed as hyperkinetic disorders through interventions with families and schools. The treatment of these disorders cannot be considered without first addressing the adequacy and appropriateness of diagnosis. All too often, hyperkinetic disorders are diagnosed even though the patient does not meet the objective diagnostic criteria. Failure to make an appropriate diagnosis leads to difficulties in establishing the patient's response to therapeutic interventions. Hyperkinetic symptoms can be seen in a range of disorders for which there are specific treatments that are more appropriate than the treatment for hyperkinetic disorder. For instance, some children and adolescents with symptoms of hyperkinetic disorder are in fact suffering from psychosis, or may be manifesting obsessive compulsive disorder. Others may have specific learning disorders. Still others may be within the normal range of behaviour but live in environments with a reduced tolerance for the behaviours that are reported. Some children manifest hyperkinetic symptoms as a response to acute stress in the school or home. A thorough diagnostic process is thus essential, for which specialist help is often needed.

While treatment with amphetamine-like stimulants is now common, there is support for the use of behavioural therapy and environmental manipulation to reduce hyperkinetic symptoms. Therapies should be evaluated for their appropriateness as first-line treatments, especially where the diagnosis of hyperkinetic disorder is questionable. In the absence of universally accepted guidelines for the use of psycho-stimulants in children and adolescents, it is important to start with low dosages and only gradually

increase to an appropriate dose, under continuous observation. Sustained-action medications are now available, but the same caution regarding appropriate dosage applies. Tricyclic antidepressants and other medications have been reported to be of use, but are not currently seen as first-line medications. The diagnosis of hyperkinetic disorder is often not made until children reach school age, when they may benefit from a more structured school environment or more individualized instruction. In the home environment, parental support and avoidance of unrealistic expectations or conflicts can help reduce hyperkinetic symptoms. Once thought to be a disorder that children outgrew, it is now known that for some people hyperkinetic disorder can persist into adulthood. Recognition of this by the patient can help him (rarely her) to find life situations that are better adapted to limiting the debilitating effects of the untreated disorder.

### *Suicide prevention*

There is compelling evidence indicating that adequate prevention and treatment of some mental and behavioural disorders can reduce suicide rates, whether such interventions are directed towards individuals, families, schools or other sections of the general community. Early recognition and treatment of depression, alcohol dependence and schizophrenia are important strategies in the primary prevention of suicide. Educational programmes to train practitioners and primary care personnel in the diagnosis and treatment of depressed patients are particularly important. In one study of such a programme on the island of Gotland, Sweden (Rutz, Knorrning & Walinder, 1995), the suicide rate, particularly among women, dropped significantly in the year after an educational programme for general practitioners was introduced, but increased once the programme was discontinued.

Ingestion of toxic substances, such as pesticides, herbicides or medication, is the preferred method for committing suicide in many places, particularly in rural areas of developing countries. For example, in Western Samoa in 1982, the ingestion of paraquat, a herbicide, had become the predominant method of suicide. By reducing the availability of this herbicide to the general population a significant reduction in the number of suicides was achieved, without a corresponding increase in suicide by other methods (Bowles, 1995). Similar successful examples relate to the control of other toxic substances and the detoxification of others, such as domestic gas and car exhaust. In many countries, the lack of easily accessible emergency care results in deaths from the ingestion of toxic substances which in most industrialized countries would be suicide attempts that are saved.

In the Russian Federation and its neighbouring countries, alcohol consumption has risen sharply in recent years, and has been linked to an increase in rates of suicide and alcohol poisoning (Vroublevsky & Harwin, 1998), and to a decline in male life expectancy (Notzon et al., 1998; Leon & Shkolnikov, 1998).

Several studies have shown an association between the possession of handguns at home and suicide rates (Kellerman et al., 1992; Lester & Murrell 1980). Legislation restricting access to handguns may have a beneficial effect. This is suggested by studies in the United States, where a restriction on the sale and purchase of handguns was associated with lower rates of suicide using firearms. States with the strictest handgun control laws had the lowest firearm suicide rates, and there was no switching to an alternative method of suicide (Lester, 1995).

As well as interventions that involve restricting access to common methods of suicide, school-based interventions involving crisis management, enhancement of self-esteem, and the development of coping skills and healthy decision-making have been shown to lower the risk of suicide among young people (Mishara & Ystgaard, 2000). It is believed that glamorizing suicide may lead to imitation. Thus the media can assist in prevention

by limiting graphic and unnecessary depictions of suicide and by deglamorizing news reports of suicides. In a number of countries, a decrease in suicide rates coincided with the media's consent to minimize the reporting of suicides and to follow proposed guidelines.