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Tobacco Addiction

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1. Introduction

"Tobacco is the single most preventable cause of death in the world today. This year, tobacco will kill more than five million people – more than tuberculosis, HIV/AIDS and malaria combined. By 2030, the death toll will exceed eight million a year. Unless urgent action is taken tobacco could kill one billion people during this century. Tobacco is the only legal consumer product that can harm everyone exposed to it – and it kills up to half of those who use it as intended." (WHO Report on the global tobacco epidemic, 2008, p. 8)

Although nearly all smokers are aware of the outstanding healthy risks of cigarette smoking and the majority of them is willing to quit, only a small proportion of regular smokers is able to stop smoking successfully. Within 12 months after a stop smoking trial, only 2-6% of quitters remain abstinent. This high relapse rate can only be explained by mechanisms of addiction. The term "*tobabacco addiction*" refers to the definition of substance use disorders, which includes harmful substance use as well as physiological and psychological dependence. This chapter aims to summarize the current state of knowledge regarding to the phenomenon of tobacco addiction and tobacco use related disorder.

2. Classification, epidemiology, etiology, and treatment of tobacco addiction

2.1 Diagnostic classification

Tobacco addiction states a mental disorder with severe somatic and mental symptoms and consequences. The term '*addiction*' was, due to its terminological vagueness, discarded as an official name for a diagnostic category by the WHO in 1964, however it is still used today in everyday speech and as part of the technical language. Within the current clinical classification systems DSM-IV and ICD-10 the phenomene of addiction caused by psychotropic substances is classified in two different diagnostic categories: DSM-IV differenciates '*substance dependence*' (303.xx) and '*substance abuse*' (305.xx) whereas ICD-10 refers to 'dependence' and '*harmful use*' (F1x.1). According to DSM, drug dependence is defined by seven diagnostic core criteria of which three must be met along with clinically important suffering in order to confirm the diagnosis. In contrast, abuse is determined by repeated, maladjusted substance use and psychosocial impairments (e.g., interpersonal problems, legal problems, high risk behaviour) over a period of at least 12 months (cf. Tab. 1).

There is a clinical and neurobiological distinction between somatic and mental addiction. *Somatic addiction* is primarily defined by development of tolerance and physiological withdrawal symptoms. That means, the organism "gets used" to the regular dose of the

DSM-IV-TR		DSM-V
Nicotine Abuse	**Nicotine Dependence**	**Tobacco Use Disorder**
at least one of the following *criteria* within the same 12 months period: (1) Severe problems regarding family, home, profession or school due to substance use (2) Substance use in dangerous situations (3)Legal problems due to substance use (4) Social and/or interpersonal problems due to substance use The symptoms have never fulfilled the criteria for substance addiction of the respective substance class.	*at least three* of the following *criteria* within the same 12 months period: (1) Development of tolerance (2) Withdrawal symptoms (3) Substance use longer or in larger quantities than intended (4) Permanent wish or failure to control substance use (5) Time-consuming procurement, use and recovery from substance (6) Important social, professional or recreational activities are given up or limited due to substance use (7) Continued substance use despite physical or psychic problems	*maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by 2 (or more) of the following, occurring within a 12-month period:* 1. recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home 2. recurrent substance use in situations in which it is physically hazardous 3. continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance 4. tolerance, as defined by either of the following: a need for markedly increased amounts of the substance to achieve intoxication or desired effect b) markedly diminished effect with continued use of the same amount of the substance 5. withdrawal, as manifested by either of the following: a) the characteristic withdrawal syndrome for the substance; b) the same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms 6. the substance is often taken in larger amounts or over a longer period than was intended 7. there is a persistent desire or unsuccessful efforts to cut down or control substance use 8. a great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects 9. important social, occupational, or recreational activities are given up or reduced because of substance use 10. the substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance 11. Craving or a strong desire or urge to use a specific substance.

Table 1. Tobacco-related Disorders according to DSM-IV-TR vs. DSM-V.

substance and thus needs ever increasing amounts to reach the desired state of intoxication (dose increase), however, also can tolerate higher doses than at the beginning of drug use (tolerance). In contrast, the *mental addiction* is characterized by behavioral patterns such as compulsive use, loss of control, addiction memory, craving and coping deficits. The term "addiction" refers more to the mental aspect of the dependency, i.e. to the continuing compulsive consumption of the drug despite negative effects and/or despite the wish to stop drug use. Whereas the somatic dependency syndrome is generally gone some weeks after the withdrawal, the addiction memory may remain active for years and decades and continue to trigger periodical craving or even relapses from time to time. Thus, a dependent smoker may have stopped to be dependent on tobacco after successful withdrawal therapy but he/she may remain addicted, possibly for his/her whole life.

Within the process for revising the Diagnostic and Statistical Manual of Mental Disorders *(DSM-V)* the work group which is responsible for addressing substance use disorders currently developed new recommendations to redefine these diagnostic categories. Among the work group's proposals are the following recommendations:

i. To move the categories of 'abuse' and 'dependence' in one common diagnosis category named 'Substance-Related Disorders';
ii. To include both substance use disorders and non-substance addictions (Gambling disorder, Internet addiction) in this new diagnostic category
iii. To tentatively re-title the category into the term 'Addiction and Related Disorders'.

In consequence, the diagnosis 'Nicotine Dependence' (305.1) should be replaced by *'Tobacco Use Disorder'* which includes 11 diagnostic criteria (s. table 1).

2.2 Epidemiology

2.2.1 Prevalence of cigarette smoking and nicotine dependence

The epidemiology of addictive smoking can be demonstrated by international *point prevalence* as well as *life-time prevalence* data of representative population-based health surveys. The rates of current smokers in adult population (> 14 years) are extremely varying by country and gender (figure 2).

Approximately one half of the smoking men and one-third of the women are classified as heavy smokers (>20 cig./day). However, not every chronic cigarette smoker will necessarily become addicted to nicotine or tobacco. A number of international epidemiological studies found that only a minority of persistent smokers become dependent according the diagnostic criteria for substance use disorders described above. In a currently conducted, well controlled population survey on nearly 8,000 representative participants in Germany, 6.3% participants among the total sample and 29.9% of all current smokers (smoking rate: 29,6%) met the DSM-IV criteria for a *nicotine dependence disorder* (Papst et al., 2010). Nevertheless, nicotine dependence has an outstanding significance from an epidemiological perspective since, with a lifetime prevalence of 17% and 21% (cf. Tab. 2), it is one of the most common mental disorders, compared to affective disorders (lifetime prevalence: 12-19%) or anxiety disorders (LT prevalence: 15%). By trend, nicotine dependence occurred more often in female smokers and in younger age groups compared with older cohorts. In Lifetime, 50% of all smokers succeed to quit, mostly after 5-10 ineffective attempts.

Approximately every second smoker who has tried to quit smoking reports somatic withdrawal symptoms that manifest themselves in psycho-vegetative conditions or

cognitive-emotional adverse effects (cf. table 3). The *nicotine withdrawal syndrome* starts 2-4 hours after the last cigarette, reaches its intensity peak after 24-48 hours and gradually passes after 1-4 weeks. However, the primarily mental symptoms (craving, feeling of hunger, dysphoria) may persist for months.

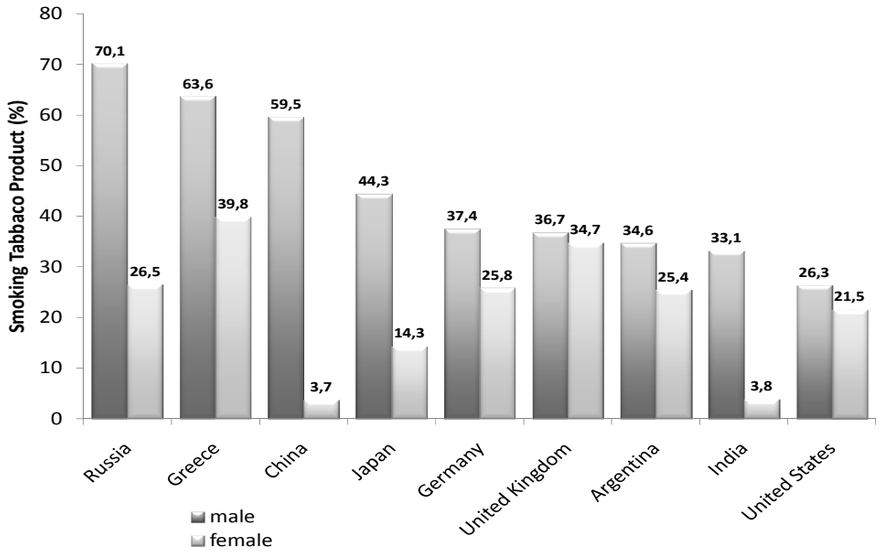

Fig. 1. WHO Report on the Global Tabacco Epidemic (2008)

	Total		Gender	
			Men	Women
Consumption prevalence (30 d)[1]	7,983		3,542	4,441
Non-Smokers	44.8%	(3,858)	38.8%	51.0%
Ex-smokers	26.0%	(1,771)	28.5%	23.6%
Smokers	29.2%	(2,354)	32.8%	25.5%
Consumption frequency (30 d)[2]	2,238		1,096	1,142
Not daily	29.6%	(714)	28.4%	31.0%
Daily up to 10	21.7%	(530)	17.4%	27.1%
Daily 11-19	23.5%	(517)	25.7%	20.9%
Daily more than 20	25.2%	(477)	28.5%	21.1%
DSM-IV (12M)[3]	7,984		3,521	4,427
Total sample	6.3%	(531)	6.8%	5.8%
Consumers[4]	19.9%	(531)	19.2%	20.9%

[1] Non-Smokers: have smoked a total of maximum 100 cigarettes; ex-smoker: have smoked more than 100 cigarettes, but not in the previous 30 days; smokers: smoked cigarettes in the previous 30 days.
[2] Referring to cigarette smokers during the previous 30 days.
[3] Nicotine dependence according to DSM-IV: unweighted number of cases regarding to total sample
[4] Referring to 12 months prevalence of smoking.

Table 2. Prevalence of smoking, of smoke frequency and nicotine dependence according to DSM-IV (Papst e al., 2010, p. 332)

- craving
- increased appetite, sensation of hunger, weight gain
- concentration problems
- nervousness, irritability, restlessness, insomnia
- feeling of frustration, unhappiness, depressive moods, depression, states of anxiety, anxieties
- circulation problems, sweating, digestive disorders

Table 3. Withdrawal symptoms during the smoke stop

The strength of the nicotine dependency can best be measured through specific withdrawal symptoms. The *Fagerstrom Test for Nicotine Dependence (FTND*; Heatherton et al., 1991; cf. table 4), which consists of six items, is recommended worldwide as a dimensional research tool for the measurement of nicotine dependency. This test has been validated in international studies and represents one of the best predictors for abstinence success.

Questions	Answers	Points
1 . How soon after you wake up do you smoke your first cigarette?	Within 5 minutes	3
	6 – 30 minutes	2
	31 – 60 minutes	1
	After 60 minutes	0
2. Do you find it difficult to refrain from smoking in places where it is forbidden, e.g., in church, at the library, in the cinema, etc.?	Yes	1
	No	0
3. Which cigarette would you hate most to give up?	The first one in the morning.	1
	Any other.	0
4. How many cigarettes/day do you smoke?	10 or less	0
	11 – 20	1
	21 – 30	2
	31 or more	3
5. Do you smoke more frequently during the first hours after awakening than during the rest of the day?	Yes	1
	No	0
6. Do you smoke if you are so ill that you are in bed most of the day?	Yes	1
	No	0
Score: Possible range is 0 – 10: Scores of 4 and greater indicating nicotine dependence Scores of 4 and greater indicating severe nicotine dependence		

Table 4. Fagerstrom Test for Nicotine Dependence (FTND; Heatherton et al., 1991)

2.2.2 Addiction and risk potential of the drug tobacco

The '*addiction potential*' of a drug describes the risk for developing a mental or physical dependence when using a drug and the subsequent failure to quit the use and to master a withdrawal. This addiction risk results from a) the pharmacological effects of the substance

on the organism, b) the quality and intensity of the evoked subjective states of intoxication or well-being and c) the learned stimulus-response association between the drug use on the one hand and the 'kick' or flush response (positive reinforcement) and/or the avoidance of withdrawal symptoms on the other (negative reinforcement). The addiction potential of a psychotropic substance is not exclusively determined by its pharmacological characteristics and its potency for physical dependence but essentially, among other things, by the type of the substance intake (addiction potential decreasing with types of applications: injecting, sniffing, smoking and swallowing). This explains that smoked nicotine has a high addiction potential compared to nicotine patches at the same dose.

Alongside heroin, nicotine is seen as the substance with the highest *'pure addiction potential'*. This finding has been determined in animal studies wherein different substances are applied in standardised form (e.g. as an oral application). The measure for the addiction potential is typical addiction behaviour shown by the laboratory animals after a number of applications (e.g. number of lever actions or toleration of pain stimuli in order to get to the drug). However, the approaches for the determination of the addiction potential that are based on complex expert judgements on the addiction risk of persons under real using conditions seem to be more adequate. In a study conducted by the Swiss Institute for the Prevention of Alcohol and Drug Problems (SIPA), renowned addiction experts evaluated the addiction potential of seven different substances in direct comparison according to five evaluation criteria (cf., tab. 5). In the resulting ranking list heroin reached the highest addiction potential, followed by cocaine, alcohol and nicotine, whereby for nicotine especially a very high value for (mental) 'addiction' was declared (Fahrenkrug & Gmel, 1996).

Substance	Overall Evaluation	With-drawal Symptoms	Reinforce-ment	Increase of Tolerance	Addiction	Intoxication
Heroin	1	1	1	1	1	2
Cocaine	2	3	2	3	3	1
Alcohol	3	2	4	2	4	3
Nicotine	**4**	**4**	**3**	**4**	**2**	**6**
Caffeine	7	7	7	6	7	7
Ecstasy	5	5	5	5	5	4
Marihuana	6	6	6	7	6	5

1= highest addiction potential; 7= lowest addiction potential

Table 5. Addiction Potential of Different Psychotropic Substances (quoted in Fahrenkrug & Gmel, 1996).

The 'addiction potential' relates to the addiction risk, but does not state anything about the *overall biopsychosocial risk potential* of a drug. Nutt et al. (2007) determined three main factors of potential damage by a psychotropic substance: 1) physical damage, 2) addiction potential and 3) social effects. A three-dimensional risk categories matrix was derived from this, by means of which the different substances were evaluated by two independent expert groups regarding their overall risk potential. In this multi-dimensional evaluation of the biopsychosocial overall risks, tobacco smoking is positioned in the upper middle field (place 9).

2.2.3 Comorbidity: Tobacco smoking and mental disorders

Tobacco addiction is closely associated with the occurrence of *mental disorders* and their course of disease. Cigarette smoking is disproportionately prevalent amongst persons with mental disorders (population) and/or psychiatric patients (clinical populations; Breslau, 1995; Degenhardt & Hall, 2001; John et al., 2004; Meyer et al, 2004; Haug et al., Heinberg & Guarda, 2001; Kordon & Kahl, 2004). On the whole, prevalence of smoking in mentally comorbid persons is approximately twice as high (50%) when compared to the general population (25-30%) (Grant et al., 2004; Lasser et al., 2000). It even amounts to 71-90% in patients with addictions to other substances (Ker et al., 1996; Patten et al., 1996; Martin et al., 1997; Williams & Ziedonis, 2004); for other *severe types of disorders* such as schizophrenia and bipolar disorders prevalence is on average 80% (Hughes, 1993; Leon & Diaz, 2005). In the US, the market share of the overall cigarette consumption by persons with psychiatric diagnoses is currently between 44 and 46% (Lasser et al., 2000; Grant et al., 2004).

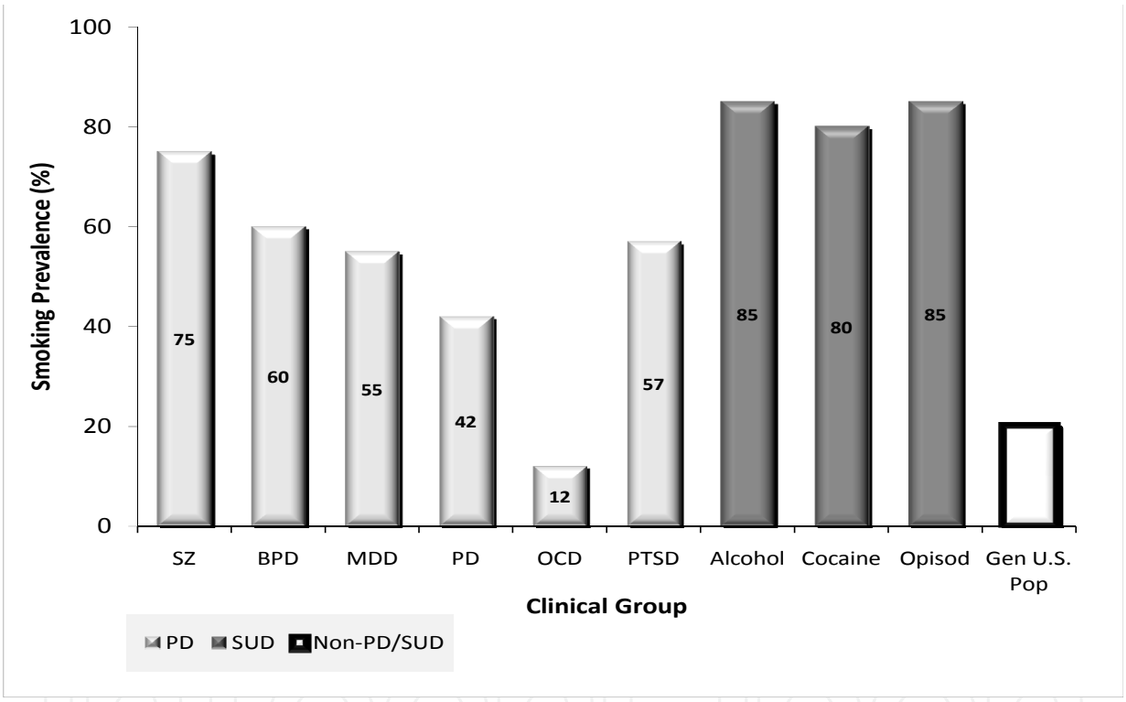

Fig. 2. Co-Morbidity of Smoking in Patients with Psychiatric and Substance Use Disorders (Kalman et al., 2005, p. 107)

Smokers with *mental comorbidity* mostly are heavy smokers, that means they are prone to smoke more cigarettes per day (days pack) and to smoke each cigagette more intensively (e.g. draws per cigarette, draw frequency, inhalation depth) (Lasser et al., 2000; Tidey et al., 2005). As a result, they do not only show increased physic long-term morbidity and mortality rates due to organic diseases associated with tobacco (Williams & Ziedonis, 2004), but they also have, amongst other things, a worse prognosis in relation to their mental disorder, a higher psychiatric lifetime-co-/multimorbidity, a more unfavourable course of disease (e.g. episodes in MDE that are more often, longer and more intensive), less successful therapy outcomes, a higher burden of disease, severe impairment of psychosocial functioning (Brown et al. 2000) as well as a lower *quality of life* (Schmitz et al., 2003). Smokers

suffering from a mental disorder also show a lower self-efficacy and more negative attitudes towards a smoke stop (Carossella et al., 1999; Esterberg & Compton, 2005) as well as below average success rates for tobacco withdrawal that are often <15% (Glassman et al., 1993; Hall, Munoz, Reus, & Sees, 1993; Rohde et al., 2004; Ziedonis & George, 1997; Ziedonis et al., 1994). Moreover, smoking tobacco is a significant predictor for a *lifetime-suicidal tendency*, even when monitoring possible confounders (Breslau et al., 2005; Oquendo et al., 2004; Bronisch et al., 2009; Miller et al., 2000; figure 4).

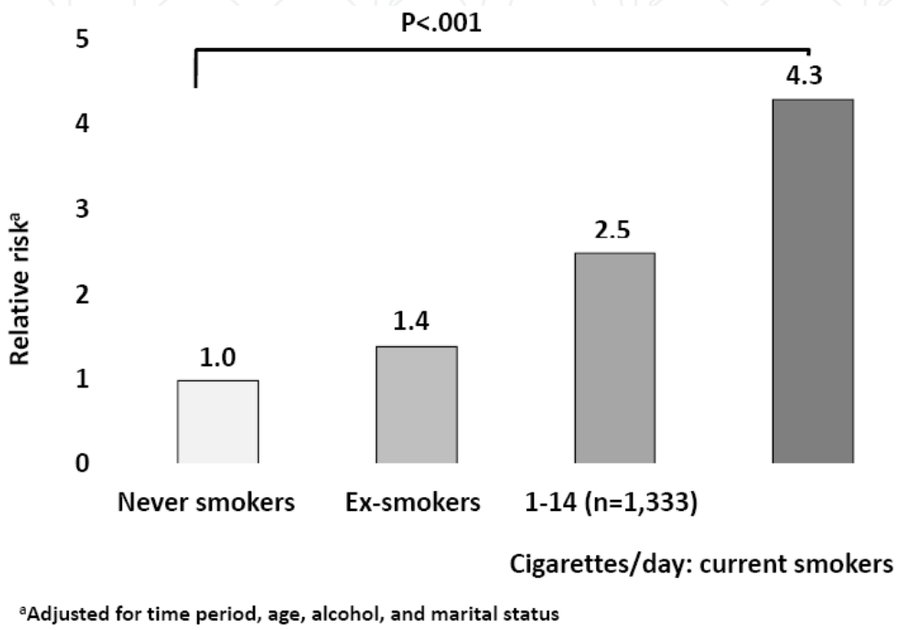

Fig. 3. Smoking and suicide risk (Miller et al., 2000)

The *etiological causality* of this coincidence between smoking tobacco and mental disorders is largely unresolved. Three competing theoretical models are being discussed: 1) According to the '*primary disorder model*' smoking is a reaction to the mental disorder (Guidelines of the American Psychiatric Association, 1996; Kendler et al., 1993; Pomerleau et al., 1997). In the sense of the '*self treatment hypothesis*', persons suffering from mental strain use nicotine for stress reduction (easing effect of nicotine) and for alleviating their subjective mental symptoms (effect of nicotine to soothe, enhance moods and improve the well-being of smokers) (Kendler et al., 1993; Hughes, 2004; Breslau, 2001). It is true that nicotine has specific anti-depressive effects (Tizabi et al., 1999; Balfour et al., 2000), since the serotonergic system is activated by nicotine similar to antidepressants (Vazquez-Palacios et al., 2005), and it is often used by psychiatric patients to specifically enhance their mood. According to this model, initial manifestation of the mental disorder would have to precede chronological tobacco smoking. 2) In contrast, the '*primary smoking model*' states that smoking can contribute to the development of a mental disorder. According to that, exposition to nicotine is a risk factor making individuals vulnerable to mental disorders due to the chronic impact on diverse transmitter systems that are involved in the development of mental disorders. This hypothesis is supported by the observation that the initial manifestation of mental symptoms often follows a longer break of regular smoking. Furthermore, for example, prenatal exposition to smoking is associated with the later occurrence of ADHD and

depression in infancy and adolescence. 3) The '*bidirectional model*' assumes a long lasting interaction effect between smoking and mental disorders. Therefore, smoking triggers the development of mental symptoms in genetically disposed persons first and is later used for easing symptoms. In this way, regular nicotine consumption contributes to the chronification of the disorders in the long term (Mueser et al., 1998). It could be possible that smokers with mental disorders shy away from smoke stop because nicotine withdrawal symptoms contribute to an exacerbation of psychiatric symptoms and an increase of the relapse risk (Glassman, 2001; Balfour et al., 2000). Finally, it has been proven that e.g. schizophrenic patients often use nicotine to specifically counter regulate the effect of neuroleptics (Barnes et al., 2006; Glassman, 1994; Haring, Barnas, Saria, Humpel, & Fleischhaker, 1989; Hughes, 1993). 4) Finally, the '*common-factor model*' assumes a common etiology of nicotine dependence and other mental disorders (Breslau et al., 1998; Dierker, 2002; Covey, 1998). Since nicotine dependence itself is a mental disorder with manifold commonalities in terms of neurobiological, cognitive personal or social risk factors and mechanisms with a) other substance disorders (e.g. dopaminergic system) and also b) with other mental disorders (e.g. serotonergic system in MD), a common genetic disposition for e.g. depressions and susceptibility for the effects of nicotine positive seems likely (Kendler et al., 1993; Breslau et al., 1998).

2.3 Etiology: Neurobiological and psychological addiction mechanisms

2.3.1 Vulnerability and risk factors

Today, the average age of onset for smoking cigarettes ranges between eleven to thirteen years (Silagy et al., 1994; Nelson et al., 1998). The development of a tobacco addiction is dependent on a number of factors or causes. In addition to a *genetic disposition* (e.g. number of receptors, availability of specific enzymes, and function of transmitter systems), multiple acquired vulnerabilities and risk factors have been identified that comprise individual characteristics as well as specific environmental conditions (Brown et al., 1992; US Department of Health and Human Services, 1990). In the stage of initial or experimental use, despite of *availability of tobacco products* and *advertising influences*, *social factors like family models and the peer group* that are decisive for the start of one's smoking (Silagy et al., 1994). There are significant differences in *social classes* with the highest smoking rates in the lower social class, in unemployed people and social groups with lower educational achievement. Furthermore, an existing *psychiatric comorbidity* and unfavourable influences of the *family milieu* (parental psychopathology) primarily count towards the individual risk factors for the development of a tobacco addiction (WHO, 2001). Moreover, tobacco addiction and health risks towards smoking-related disorders correlate with the *early onset of smoking*. The physical addiction phenomena seem to develop especially rapidly in children and adolescents. In the stage of regular and dependent use, smokers try to manage their *psycho-social stress* or *daily hassles* by using nicotine ('self treatment'). In the long term run, the most important condition to maintain dependency is *negative reinforcement*, because every cigarette acts more and more to reduce withdrawal symptoms in the first line.

2.3.2 Neurobiological mechanisms

Like all psychotropic substances, nicotine stimulates the *mesolimbic dopamine system ('desire and reward system')* whose neurones are located in the area tegmentalis ventralis and project to the nucleus accumbens as well as the corpus striatum, among others. In contrast to other

drugs, nicotine exposition initiates a particular long term potentiation of specific neurons in this area of the brain, which causes a persistent increase of the dopamine level even after short term nicotine exposition.
In order to compensate for the artificial biochemical flooding and to maintain the normal functions, the brain reacts on two levels: 1) with a neuroanatomical change of the number and responsiveness of specific receptors (*neuroplastic down or up regulation*) and 2) with an inhibiting feedback on the level of transmitters, restricting the effect of nicotine by releasing *counter-regulative molecules* (Kunze et al., 1998). Both reactions lead to a weakening of the effect of nicotine. If the smoker subsequently tries to compensate the diminishing effect by means of more intensive smoking, the brain respectively produce more inhibiting molecules in that ever-increasing doses of nicotine are necessary to achieve 'intoxication' (*tolerance*). If the organism is then suddenly deprived of the substance (*withdrawal*), the balance of the system is forcefully disturbed. On the one hand, too few bodily-owned transmitters are available since the body has limited its own production and, on the other hand, a surplus of compensatorily released inhibitory molecules, which further inhibit the normal remaining functions of the transmitter balance, exist for a number of weeks. A strong *state of deprivation* results thereof and causes torturing mental and physical acute withdrawal conditions (withdrawal syndrome). The body is now not able to exist without tobacco any more and, therefore, an *addiction* has formed.

2.3.3 Psychological and neuropsychological mechanisms

Addicted ex-smokers are still at *risk to relapse* in face of any smoking-associated cues which trigger an irresistible desire (craving) for nicotine, even many years and decades after the withdrawal, probably for their whole lifetime. This long time active '*addiction memory*' cannot be explained by mechanism of physical dependence, which normalise within a few weeks after quitting. In the first line, complex *learned conditioning processes* are responsible for the continuing sensitisation to nicotine and the ongoing high relapse rates.
Simultaneously to dopamine release in the '*desire and reward system*' nicotine stimulates specific *areas in the brain which are involved in association learning processes*. That is why smoking tobacco has a particularly strong link to *situational* (smoking break, coffee drinking, after work beer), *behavioural* (reaching for the box of cigarettes), *sensory* (smell, taste) or *affective* (mood) *cues* that are associated with smoking. Insofar, persistent addiction can be primarily traced back to *respondent* and *operant conditioning*. In the case of smoking *positive reinforcement* is generated by the fateful association between the inhalation (stimulus) and the subsequent state of well-being (response) that permanently becomes engraved in memory ('*addiction memory*') within a short time. Despite the missing intensive intoxication, the high addiction potential of tobacco smoking results from the brain of a regular smoker being flooded with nicotine 200 to 400 times per day (per year: 73,000 to 146,000 times) — and the stimulus-response connection is thereby continuously enforced.
The high *risk of a relapse* and the actual *relapse process* after a smoke stop can be explained by means of *neuropsychological* and *cognitivepsychological models*. However, one of the main - questions, why the addiction behaviour and craving is not extinguished after a certain time was not resolved satisfactorily. The latest research in cognitive learning shows that the *extinction* of a respondent conditioning is, in a neurobiological sense, no unlearning in terms of a decoupling of synaptic links but a *new learning and/or re-learning* where new stimulus-reaction-links are generated while the old ones are principally still available (Conklin &

Tiffany, 2002). That is why old addiction conditionings can, if certain triggers emerge, be reactivated even after a long time (e.g. by reinstatement or spontaneous recovery).
Furthermore, the hypersensitivity to the addiction cues (*cue reactivity*), which is profoundly resistant against extinction and overwriting, can be explained with *neuroplastic changes* in the dopamine system. In the case of chronic substance intake a neurobiological hyper reactivity to the drug and their trigger cues develops in the mesolimbic dopamine system (*subcortical dysfunction*) and, at the same time, the areas that are responsible for executive control (*frontal cortical dysfunction*) are weakened. Finally, the relapse can be described by the different levels of information processing of addiction-related cues on the one hand, and by the intentional control of action on the other (Tiffany und Conklin, 2000). The addicts' reaction to drug-associated cues is an example of '*automatic processing*', i.e. it is made unconsciously quick, linked to certain trigger situations, with a low use of cognitive capacity and can only be influenced to a small degree. In contrast, abstinence demands an intentional regulation of action with conscious information processing and executive control functions ('*controlled processing'*), which is consciously, intention controlled and flexible, but relatively slow, cognitively demanding and limited by the processing capacity. In case of chronic substance abuse an increasing disequilibrium between the growing influence of automatic stimulus processing ('*implicit cognitions'*), as well as a weakening of executive control and regulation of emotions that makes the person trying to quit increasingly vulnerable to addiction triggers and, finally, relapse.

2.4 Treatment

Almost all smokes are aware of the smoke-related health risks and a majority of them repeatedly tries to stop smoking. The *willingness to quit* depends on the individual stage of motivation. According to the widely known *transtheoretical model* (Prochaska & DiClimente, *1993)* smokers move through a discrete series of five motivational stages before they quit successfully: (i) *precontemplation* (no thoughts of quitting), (ii) *contemplation* (thinking about quitting), (iii) *preparation* (planning to quit in the next 30 days), (iv) *action* (quitting successfully for up to six months), and (v) *maintenance* (no smoking for more than six months). The transtheoretical theory has not been empirically supported, and some authors cast doubt its practical value (Etter & Sutton, 2002; Sutton, 2001).
However, most smokers will succeed to quit at one point in their life: There are more ex-smokers than current smokers to be found in the age cohort over 50 years old. However, tobacco withdrawal often requires a multitude of stop smoking trials to be successful when no professional help is sought. The success rate of unassisted smoke stop trials is at a mere 3-6% during the 12-months period. However, less than 5 % of all smokers willing to stop make use of professional help, despite the availability of effective smoking cessation therapies (WHO, 2001; Nelson & Wittchen, 1998).
Professional smoking cessation treatments include a wide range of interventions, from medical advice through to brief motivational interventions to complex withdrawal programs. In practice, less effective methods such as hypnosis and acupuncture are used alongside motivational interviewing, cognitive-behavioural therapy interventions (CBT) and medicinal approaches in withdrawal and substitution treatment. Professional smoking cessation treatment is first and foremost based on behavioural group interventions (cf. Box 1) and approaches of motivational interviewing, and often offered in combination with medicinal support (e.g. nicotine substitutes).

1. Psychoeducation: education, information and attitude change
2. Analysis of problem and behaviour: Analysis and documentation of smoking behaviour and the maintaining cognitive and situational or social conditions
3. Strengthening of motivation to change (motivational interview): Clear decision to quit smoking, determination of a deadline to stop smoking
4. Systematic preparation for abstinence, execution of smoke stop and modification of behaviour: Control of conditioning stimuli, development and training of alternative behaviour, contract management, self-reward, teaching of strategies of self-control
5. Activation of a supporting social network and teaching of health promotional behaviour
6. Relapse prevention: Dealing with risk situations, strategies against relapse risks (role play exercises)

Box 1. Components of complex behavioural therapy programmes for smoking cessation.

Primary goal in smoking cessation treatment is *total abstinence*. Controlled tobacco use leading to harm reduction is only aimed for in exceptional cases (in cases of severe disease or pregnancy with simultaneous inability to remain abstinent; Stead & Lancaster, 2007; Lumley et al., 2009). The medicinal treatment in smoking cessation primarily aims to soothe the somatic withdrawal symptoms and associated craving. The *pharmacological treatment* options are based on three different modes of action:

i. In *nicotine replacement therapy* a patient is given nicotine doses, which substitute the nicotine the patient does not take in anymore by smoking, by means of drugs containing nicotine (nicotine patch, gum, inhaler, lozenge, nasal spray, sublingual tablet). By means of retaining an equal level of nicotine withdrawal symptoms are soothed and the withdrawal is made easier by stepwise downdosing the pharmacological nicotine.
ii. The nicotine-free drug *bupropion (Zyban®)*, originally developed as *anti-depressant*, inhibits the synaptic absorption of catecholamines (adrenalin, dopamine) in the mesolimbic dopamine system, thereby compensating the dopamine lack caused by the nicotine withdrawal and, in this way, soothes the withdrawal symptoms without supplying nicotine. Due to serious contra-indications, side-effects and pharmaceutical risks, bupropion may only be applied under medical supervision.
iii. The *partial agonist varenicline (Chantix®)* binds to specific nicotine receptors of the subtype that is responsible for one of the addictive effects of the nicotine. The active agent stimulates the receptors and thereby eases withdrawal symptoms. At the same time, it inhibits the effect of externally supplied nicotine by blocking the receptors. Also due to the serious side-effects and risks (nausea, headache, insomnia, abnormal dreams, suicidal ideation and occasional suicidal behavior, erratic behavior and drowsiness) there are similarly strict regulations for varenicline in terms of prescription and medical supervision.

Multi-modal smoking cessation programmes can be divided into three stages: (i) reinforcement of the abstinence motivation and the patient's commitment to quit smoking, (ii) preparation and realisation of smoke stop, (iii) maintenance of abstinence and using new coping strategies to avoid a return to use.

i. Regular smokers generally are ambivalent towards quitting. Although almost every smoker is aware of the health risks and further disadvantages of smoking, most of them dread the burdens associated with smoke stop (fear of withdrawal symptoms and loss of positive reinforcement) and continually postpone their withdrawal, often for years. This is why it is necessary to make an explicit decision pro tobacco withdrawal at the beginning of the *withdrawal stage* (in case of smokers willing to stop) and/or to motivate in favor of a smoke stop (in case of smokers not yet willing to stop). For this purpose, *motivational interviewing* is a suitable approach (Miller & Rollnick, 2002 by which the motivation to quit smoking and the confidence to change can be analysed and systematically strengthened during the preparation stage. In smoking cessation practice, behavioural-therapeutic techniques (smoking diaries, behavioural analysis, CO-measurement, reinforcement plans, pros-cons lists, target hierarchies, aim in life analysis, short and long term benefits, strengthening of self-efficacy) as well as cognitive techniques (disputation of irrational ideas, worst case scenarios, development of rational alternatives) are applied for the preparation of the smoke stop. The explicit commitment of the smoker to his/her desire to quit smoking (importance) and his belief to being able to reach this goal (realisability) proves to be decisive in this stage.
ii. During the *quitting stage* the smoker is systematically prepared for the smoke stop and the time of abstinence. For this purpose, it is important, not only to create adequate commitment but also to enhance the optimism about one's ability to change and to strengthen self efficacy. Using the 'cold turkey method', a certain quit day is determined. In the sense of a stimulus control, all triggers (smoke utensils such as ashtray, cigarette boxes, lighter etc.) are removed from the immediate surrounding and/or typical smoke situations (e.g. local pub) are temporarily avoided for the time of the smoke stop preparation stage. The smoke stop can be supported by means of aversion therapy (excessive inhaling, retain smoke in lung, smelling of containers with cigarette butts and cold ash) or counter conditioning (presentation of unpleasant stimuli such as deterring photos of smoke-related diseases contingent to smoking).
iii. The treatment stage most important to keep long term abstinence is the *maintenance and relapse prevention*. The ex-smoker is supported in his/her self control management (response control) and self instruction in order for him/her to master craving and withdrawal symptoms and to successfully cope with high risky situation (refusal training). At the same time, positive alternatives to smoking (relaxation exercise, physical exercise, easy breathing, water drinking, pleasant activities and attentional distraction) are proposed and trained. Positive stimuli (e.g. appraisal, material rewards, amount of money saved, improvement of lung function, duration of abstinence) or contracting (written commitment, rewards vs punishment) are used to support abstinence and social resources are mobilised (workshop assistants, supporters). During abstinence a cognitive reframing shall be triggered in which the smokefree life comes to be seen as less unpleasant condition of withdrawal and loss but increasingly as an awarding situation in which a positive physical well-being and independence dominates. Finally, an individual emergency plan is drafted and structured relapse prevention management is trained (what to do when having a relapse).

2.5 Empirical evidence

Up to date, a large amount of professional and more or less *evidence-based smoking cessation treatments* have been developed, that range from minimal interventions (physician's advice to quit smoking) and medicinal withdrawal treatment (nicotine replacement therapy, psychotropic drugs such as bupropion or varenicline) to telephone counselling ('quit-line') and online quitting programmes as well as to multi-modal smoking cessation in behavioural group therapy described above. The efficacy of professional smoking cessation treatments is well determined. An impressive number of RCTs as well as several meta-analyses and *Systematic Cochrane Reviews* clearly proved the high efficacy of several cessation treatments towards the primary outcome of long-term abstinence.

In particular, *group behaviour therapy* programmes for smoking cessation yielded high effect sizes in many randomised controlled trials (RCT) and were found to be superior to self help, and other less intensive interventions (Stead & Lancaster, 2005). However, there is not enough evidence to evaluate whether groups are more effective, or cost-effective, than intensive individual counselling and only limited evidence that the addition of group therapy to other forms of treatment, such as advice from a health professional or nicotine replacement, produced extra benefit (Stead & Lancaster, 2005, p 2). *Individual behavioural counselling interventions* for smoking cessation have been well-proven, too (Lancaster & Stead, 2005). Individual counselling was more effective than control, but a greater effect of intensive counselling compared to brief counseling could not be found. *Aversion therapy*, which pairs the pleasurable stimulus of smoking a cigarette with some unpleasant stimulus in order to extinguish the urge to smoke, has been evaluated in a smaller number of RCT's that provide insufficient evidence to determine the efficacy of rapid smoking (Hajek & Stead, 2001).

Pharmaceutical treatment in smoking cessation is high efficient as well. All of the commercially available forms of *nicotine replacement therapy* (gum, transdermal patch, nasal spray, inhaler and sublingual tablets/lozenges) can help people who make a quit attempt to increase their chances of successfully stopping smoking by 50-70%, regardless of setting Stead et al., 2008). The empirical evidence show that the *antidepressants* bupropion and nortriptyline are equally effective and of similar efficacy to nicotine replacement therapy, but there is insufficient evidence that adding bupropion to nicotine replacement therapy provides an additional long-term benefit (Hughes et al., 2007, p 2). Also *varenicline* at standard dose increases the chances of successful long-term smoking cessation between two- and threefold compared with pharmacologically unassisted quit attempts (Cahill et al., 2011, p 2).

The trials to *internet-based interventions* for smoking cessation did not show consistent effects, but for some interventions there is evidence that online counselling can assist smoking cessation, especially if the information is appropriately tailored to the users and frequent automated contacts with the users are ensured (Civljak, Sheikh, Stead & Car, 2010, p 2). Similarly, proactive *telephone counselling* for smoking cessation can efficiently help smokers in quitting, but a minimum of three or more calls are required to increase the chances of quitting compared to a minimal intervention (providing standard self-help materials, brief advice), or compared to pharmacotherapy alone (Stead et al., 2006). *Motivational interviewing* for smoking cessation yielded a modest but significant increase in quitting compared to brief advice or usual care and was more effective, when delivered by primary care physicians and by counselors and when conducted in longer and multiple sessions (Lai et al., 2010).

In contrast, there is no consistent, bias-free evidence that *acupuncture*, *acupressure*, *laser therapy* or *electrostimulation* or *exercise interventions* for smoking cessation are effective for

smoking cessation (White et al., 2011; Ussher et al., 2008). Also, the empirical evidence for *hypnotherapy* fails to show a greater effect on six-month quit rates than other interventions or no treatment (Barnes et al., 2010). *Standard self-help materials* may increase quit rates compared to no intervention, but the effect is likely to be small, and no additional benefit has been found alongside other interventions such as advice from a healthcare professional, or nicotine replacement therapy (Lancaster & Stead, 2005, p 2). Materials that are tailored for individual smokers are more effective than untailored materials, although the absolute size of effect is still small.

Smoking *reduction versus abrupt cessation* in smokers who want to quit makes no difference with regard to long-term abstinence (Lindson et al., 2010). According to the *transtheoretical model stage-based* self-help interventions (expert systems and/or tailored materials) and individual counselling were neither more nor less effective than their non-stage-based equivalents (Cahill et al., 2010, p 2).

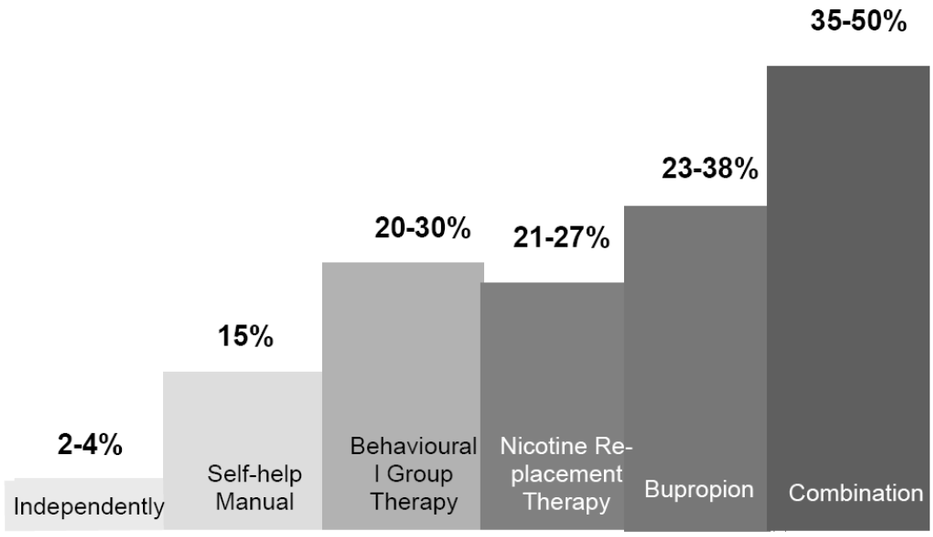

Fig. 4. Success rates (12-months abstinence) of measurements for tobacco withdrawal in clinical studies (efficacy) according to a meta-analysis of the US Department of Health and Human Services (Fiore et al., 2008)

In context of the *US Clinical Practice Guidelines*, sponsored by the U.S. Public Health Service, Guideline Panel conducted 2000 a large mega-metanalysis '*Treating Tobacco Use and Dependence*' which has been updated in 2008 (Fiore et al., 2008). The main results are shown in figure 7. In Detail, the effectiveness and abstinence rates of various interventions and medications in smoking cessation treatment are presented in table 6 and 7. In summary, the most effective smoking cessation treatment is a combination of group behavior therapy or

individual counseling with pharmaceutical treatment, whereas a combination of more than one pharmaceutics has an extra benefit (e.g., NRT patch + NRT gum or NRT patch + oral medication).

Based on the empirical evidence of international trials in the field of smoking, tobacco dependence and smoking cessation in numerous countries specific clinical guidelines for treating tobacco addiction have been developed during the last decade, e.g. :

- The well-known *US 'Clinical Practice Guideline for Treating Tobacco Use and Dependence'* (Fiore et al., 2000, 2008) occurred as a result of an extraordinary partnership among Federal Government and nonprofit organizations;
- in UK the National Institute for Health and Clinical Excellence – NICE created a number of clinical guidelines:
  - Smoking cessation services in primary care, pharmacies, local authorities and workplaces, particularly for manual working groups, pregnant women and hard to reach communities (2008)
  - The Impact of Quitlines on Smoking Cessation (2007)
  - Economic Analysis of Interventions for Smoking Cessation Aimed at Pregnant Women (2007)
  - School-based interventions to prevent the uptake of smoking among children and young people: cost-effectiveness model (2010)
  - The effectiveness of smoking cessation interventions to reduce the rates of premature death in disadvantaged areas through proactive case finding, retention and access to services
  - Mass-media and point-of-sales measures to prevent the uptake of smoking by children and young people (2008)
  - Workplace health promotion: how to help employees to stop smoking (2007)
- *Association of the Scientific Medical Societies* in Germany co-ordinates the national programme of medical guidelines of its member organizations. In cooperation with numerous institutions and non-profit organizations (e.g. German Society of Addiction Research; German Association for Psychiatry and Psychotherapy) two smoking cessation guidelines have been developed:
  - Guidelines for Treating Substance Use Disorders (2004)
  - Smoking Cessation in COPD patients (2008)

These various national guidelines do explicitly consider the different conditions of the social, cultural or health care systems in each country and should be received by the health care professionals in the specific region they are developed for.

Various intensity levels of session length (n = 43 studies)[a]			
Level of contact	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
No contact	30	1.0	10.9
Minimal counseling (< 3 minutes)	19	1.3 (1.01–1.6)	13.4 (10.9–16.1)
Low-intensity counseling (3–10 minutes)	16	1.6 (1.2–2.0)	16.0 (12.8–19.2)

Higher intensity counseling (> 10 minutes)	55	2.3 (2.0–2.7)	22.1 (19.4–24.7)
Total amount of contact time (n = 35 studies) [a]			
Total amount of contact time	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
No minutes	16	1.0	11.0
1–3 minutes	12	1.4 (1.1–1.8)	14.4 (10.3–17.5)
4–30 minutes	20	1.9 (1.5–2.3)	18.8 (15.6–22.0)
31–90 minutes	16	3.0 (2.3–3.8)	26.5 (21.5–31.4)
91–300 minutes	16	3.2 (2.3–4.6)	28.4 (21.3–35.5)
> 300 minutes	15	2.8 (2.0–3.9)	25.5 (19.2–31.7)
Various types of formats (n = 58 studies) [a]			
Format Number	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
No format	20	1.0	10.8
Self-help	93	1.2 (1.02–1.3)	12.3 (10.9–13.6)
Proactive tel. counseling	26	1.2 (1.1–1.4)	13.1 (11.4–14.8)
Group counseling	52	1.3 (1.1–1.6)	13.9 (11.6–16.1)
Individual counseling	67	1.7 (1.4–2.0)	16.8 (14.7–19.1)
Various types of counseling and behavioral therapies (n = 64 studies) [a]			
Type of counseling and behavioral therapy	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
No counseling/ behavioral therapy	35	1.0	11.2
Relaxation/breathing	31	1.0 (0.7–1.3)	10.8 (7.9–13.8)
Contingency contracting	22	1.0 (0.7–1.4)	11.2 (7.8–14.6)
Weight/diet	19	1.0 (0.8–1.3)	11.2 (8.5–14.0)
Cigarette fading	25	1.1 (0.8–1.5)	11.8 (8.4–15.3)
Negative affect	8	1.2 (0.8–1.9)	13.6 (8.7–18.5)
social support	50	1.3 (1.1–1.6)	14.4 (12.3–16.5)
Extratreatment social support	19	1.5 (1.1–2.1)	16.2 (11.8–20.6)
Practical counseling (problem solving/skills)	104	1.5 (1.3–1.8)	16.2 (14.0–18.5)
Other aversive smoking	19	1.7 (1.04–2.8)	17.7 (11.2–24.9)
Rapid smoking	19	2.0 (1.1–3.5)	19.9 (11.2–29.0)

[a] Go to www.surgeongeneral.gov/tobacco/gdinrefs.htm for the articles used in this meta-analysis.

Table 6. Meta-analysis (2000): Effectiveness and abstinence rates of various interventions in smoking cessation treatment

Various medications and medication compared to placebo at 6-months post quit (n = 83 studies) [a]			
Medication	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Placebo	80	1.0	13.8
Monotherapies			
Varenicline (2mg/day)	5	3.1 (2.5–3.8)	33.2 (28.9–37.8)
Nicotine Nasal Spray	4	2.3 (1.7–3.0)	26.7 (21.5–32.7)
Hig-Dose Nicotine Patch (> 25mg) (These include both standard or ling-term-duration)	4	2.3 (1.7–3.0)	26.5 (21.3–32.5)
Long-Term Nicotine Gum (>14 weeks)	6	2.2 (1.5–3.2)	26.1 (19.7–33.6)
Varenicline (1mg/day)	3	2.1 (1.5–3.0)	25.4 (19.6–32.2)
Nicotine Inhaler	6	2.1 (1.5–2.9)	24.8 (19.1–31.6)
Clonidine	3	2.1 (1.2–3.7)	25.0 (15.7–37.3)
Bupropion SR	226	2.0 (1.8–2.2)	24.2 (22.2–26.4)
Nicotine Patch (6–14 weeks)	632	1.9 (1.7–2.2)	23.4 (21.3–25.8)
Long-Term Nicotine Patch (> 14 weeks)	3102	1.9 (1.7–2.3)	23.7 (21.0–26.6)
Nortriptyline	5	1.8 (1.3–2.6)	22.5 (16.8–29.4)
Nicotine Gum (6–14 weeks)	15	1.5 (1.2–1.7)	19.0 (16.5–21.9)
Combination therapies			
Patch (long-term; > 14 weeks) + ad llb NRT (gum or spray)	3	3.6 (2.5–5.2)	36.5 (28.6–45.3)
Patch + Bupropion SR	3	2.5 (1.9–3.4)	28.9 (23.5–35.1)
Patch + Nortriptyline	2	2.3 (1.3–4.2)	27.3 (17.2–40.4)
Patch + Inhaler	2	2.2 (1.3–3.6)	25.8 (17.4–36.5)
Patch + Second generation antidepressants (paroxetine, venlafaxine)	3	2.0 (1.2–3.4)	24.3 (16.1–35.0)
Medications not shown to be effective			
Selective Serotonin Re-uptake Inhibitors (SSRIs)	3	1.0 (0.7–1.4)	13.7 (10.2–18.0)
Naltrexone	2	0.5 (0.2–1.2)	7.3 (3.1–16.2)

[a] Go to www.surgeongeneral.gov/tobacco/gdinrefs.htm for the articles used in this meta-analysis.

Table 7. Meta-analysis (2000): Effectiveness and abstinence rates of various medications in smoking cessation treatment

3. Conclusion

The *smoking rates* in the population vary from country to country with a range between approximately 25-60% of adult population. Although only every third smoker meets the diagnostic criteria for *nicotine dependence*, tobacco addiction is the *most prevalent mental disorder* worldwide. Besides the well-known impact of tobacco smoking on physical health, there is a growing body of evidence that smoking increases the *vulnerability for mental disorders*, too. Point prevalence of tobacco smoking amongst persons with mental disorders (MD) is 40-50% and thus, on average, twice as high as amongst the general population. Smokers with psychiatric comorbidity do not only show increased somatic morbidity and mortality rates, but also a significantly worse prognosis in relation to their MD, up to a significant increase of lifetime *suicide risks*.

The *addiction potential of tobacco smoking* as well as the difficulty to quit and to permanently remain abstinent is often highly underestimated by smokers themselves, but by many health care professionals as well. The high failure and relapse rates in smoking cessation, even in patients with life threatening smoking-associated disorders (e.g. myocardial infarction, pulmonary emphysema or lung transplantation) demonstrates that nicotine dependence is a serious mental disorder and an addiction comparable harmful like in case of illicit drugs. Overcoming smoking as a serious 'substance use disorder' in many cases calls for *professional cessation treatment*. Although every second smoker succeeds to quit at some point in his/her life without professional help, however, this is only achieved after many years and after a number of failed trials. During this long lasting period since smokers are successful in quitting, in many cases serious harm to their physical or mental health has already been caused. Therefore, in *routine care*, smokers should be *encouraged to quit smoking* at an *early stage* and they should be tested on a routine basis for a *tobacco addiction* and, if necessary, be referred to a *smoking cessation specialist* or an outpatient cessation clinic.

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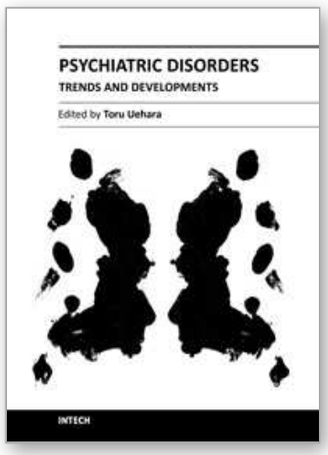

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Due to their prevalence, pervasiveness and burden inflicted on men and women of today, psychiatric disorders are considered as one of the most important, sever and painful illnesses. This impairment of cognitive, emotional, or behavioural functioning is in some cases tragic. Aside from knowing the physical organic factors, such as infections, endocrinal illnesses or head injuries, the aetiology of psychiatric disorders has remained a mystery. However, recent advances in psychiatry and neuroscience have been successful in discovering subsequent pathophysiology and reaching associated bio-psycho-social factors. This book consists of recent trends and developments in psychiatry from all over the world, presented in the form of multifarious and comprehensive articles. The first two sections of the book are reserved for articles on schizophrenia and depression, two major illnesses present in this field. The third section of the book is reserved for addiction psychiatry, related not only to socio-cultural but also biological alterations. The last section of the book, titled Biological Neuropsychiatry, consists of three topics - updated molecular biology, fundamental neuroscience and clinical neuropsychiatric conditions. Doubtlessly, this book will be fruitful for future developments and collaboration in world psychiatry.

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