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## Key Words

Smoking Nicotine dependence Comorbidity Epidemiology Eur Addict Res 1998;4:42-49

# **Smoking and Nicotine Dependence**

**Results from a Sample of 14- to 24-Year-Olds in Germany** 

### Abstract

Ths paper describes the distribution of dependence criteria and diagnoses in a sample of 14to 24-year-olds from Munich, Germany (n = 3,021; 71% response rate), evaluates differences between nondependent and dependent smokers and examines associations of smoking with other substances, affective and anxiety disorders. Assessment was made using the M-CIDI. The lifetime prevalence of DSM-IV nicotine dependence in the total sample is 19%, rising to 52% among regular smokers. No gender differences were seen in the progression from regular smoking to nicotine dependence, although men were more likely than women to initiate regular use. Analysis of daily cigarette use identified a significant dose-response relationship with the number of endorsed DSM-IV dependence criteria with unsuccessful cut-backs being the most prevalent criterion. As compared to nondependent smokers, dependent smokers were more likely to associate negative health effects with smoking and to have a desire to change and attempt a change in their pattern of use. Regular use of nicotine was found to be significantly associated with other substance and nonsubstance disorders, although dependent regular use was more strongly associated with these disorders than nondependent regular use. These results indicate that daily smoking is a behavior which is resistant to change despite an expressed desire and repeated cut-back attempts. Although initiation of regular smoking among nonsmokers does not occur frequently after the early twenties, the risk for dependent smoking among regular users persists into adulthood and is associated with a range of mental disorders.

## Introduction

Among other major policy statements, the publication of the 1988 US Surgeon Generals report on smoking [1], the testimony before the US Congress by the Director of the US Food and Drug Administration [2] and the recent classification of nicotine as a drug of abuse in the United States have marked the alignment of the medical and public health establishment against smoking and the use of tobacco. Adding to this awareness have been a series of reviews which summarize the evidence for classifying nicotine as a drug of abuse [3–7] as well as the medical [8] and economic costs of smoking [9]. Consistent with these

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This article is also accessible online at: http://BioMedNet.com/karger reports, nicotine dependence is now included as one form of substance use disorder in the 10th International Classification of Diseases (ICD-10) [10] and the Diagnostic and Statistical Manual of Mental Disorders (DSM) [11].

Although the association between regular smoking and mental disorders has been investigated using data from the St. Louis [12] and Durham sites of the Epidemiologic Catchment Area Study [13], the assessment of DSMdefined nicotine dependence and its association with these disorders has been initiated only recently. The first reports in nonclinical populations are provided by Breslau et al. [14, 15] who assessed DSM-III-R diagnoses among 21- to 30-year-old members of a Detroit area health maintenance organization. These authors reported that 51% of lifetime smokers met the criteria for a DSM-III-R diagnosis and that while dependent smoking was significantly related to other DSM-defined substance, af-

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fective and anxiety disorders, nondependent smoking was significantly related to only substance disorder [14]. A subsequent report by this group [15] showed that compulsive use is reported by about two-thirds and that withdrawal symptoms and tolerance are reported by about one-third of lifetime smokers, findings which are consistent with those from a US general population survey of symptoms among 12-month smokers [16].

Recently, we assessed the prevalence of various DSM-IV substance and nonsubstance disorders in a population of 14- to 24-year-olds in Munich, Germany, and found that nicotine dependence was equally prevalent among men and women and one of the most prevalent DSMdefined disorders in the population [17]. In a further elaboration of these findings, this paper reports on the characteristics of nondependent and dependent regular smoking exploring age of onset, progression, the distribution of dependence criteria at increasing levels of use, and their association with other substance and nonsubstance disorders. These analyses were prompted by: (a) the lack of epidemiological data about strictly defined nicotine dependence in general population samples, and (b) interest in the development of nicotine dependence and its association with other forms of mental disorder.

## Methods

#### Sample

This sample was drawn from 1994 government registries of residents in metropolitan Munich (1990 population 2.6 million [18]) expected to be 14-24 years of age at the time of interview during the first half of 1995. Because the study is designed as a panel with special interest in the development of substance disorders, 14- to 15year-olds were sampled at twice the probability of persons 16-21 years of age and 22- to 24-year-olds were sampled at half this probability. Among the sampled individuals, a total of 3,021 interviews were completed resulting in a response rate of 71% (for further details, see Wittchen et al. [17]). To account for the different sampling probabilities, noncontact and nonresponse, a relative weight [19] is used in all analyses which adjusts the data by age, sex and geographic location to match the distribution of the sampling frame. Almost three-quarters of the population were students, 36% at the secondary level and 35% at university, nearly two-thirds (64%) were living with their parents and 23% were living alone.

#### General Assessment

Diagnostic assessment was based on the Munich version of the Composite International Diagnostic Interview (M-CIDI) [20]. The M-CIDI is an updated version of the World Health Organisation's CIDI version 1.2 (WHO-CIDI) [21] which incorporated questions assessing DSM-IV and ICD-10 criteria. The reliability and procedural validity of the CIDI [20, 22] have been reported previously and are reported for the M-CIDI elsewhere in this issue.

#### Definition of Use, Regular Use and Nicotine Dependence

For the purpose of this survey tobacco products were defined as cigarettes, cigars, pipes, snuff or chew and regular use of one of these tobacco products was defined as daily use for a period of at least 4 weeks. Using these criteria, almost the entire population of regular users reported regular cigarette use (99%) with the balance reporting exclusive regular use of chew or snuff. It should be noted that in Germany the legal age for the purchase of tobacco products is 16 years, although enforcement of this age limit is negligible since vending machines are present in most public places.

DSM-IV criteria [11] were used to assess dependence among all respondents indicating regular use of a tobacco product at some time in their life. In DSM-IV, three of seven criteria must be endorsed as occurring within the same 12-month time frame for a diagnosis to be assigned and include: (1) tolerance; (2) withdrawal; (3) use in larger amounts or for longer periods of time than intended; (4) a persistent desire or unsuccessful cut-down or unsuccessful attempts at controlling use; (5) a great deal of time using the substance; (6) giving up important social, occupational, or recreational activities because of use; (7) use despite knowledge of recurrent physical or psychological problems that are likely to have been caused or exacerbated by use. In addition, DSM-IV specifies a diagnosis of physiologic dependence when the criteria for tolerance or withdrawal are fulfilled.

#### Statistical Analysis

To account for the bias introduced by the differing lengths of follow-up time for each respondent, i.e. they have different ages, survival analysis was used in analyzing the data where appropriate [23–26]. Cumulative incidence curves for age at first use, regular use and nicotine dependence were calculated using life table methods and the comparison of curves was done using the log-rank test.

Using lifetime diagnoses and logistic regression models, prevalence odds ratios and their 95% confidence intervals (POR and 95% CI) [24] were used to estimate the association of nondependent and dependent regular use with co-occurring diagnoses.

For each row variable three associations were tested: the first was between non-regular and regular use (†); the second was between dependent and nondependent use (†); and the third simultaneously estimates the magnitude of association with non-dependent regular use and dependent regular use (\*). Results from the first model indicate whether regular use in general is associated with the row variable and from the second model indicate whether the association of the row variable with dependent regular use is significantly stronger than that with nondependent regular use. All models were adjusted for gender and birth-cohort and the associations with affective and anxiety disorders were additionally adjusted for substance disorders.

All data management and analyses were conducted using SAS software (SAS, 1996) and relative weights (the sum of the weights equals the number of respondents) [19].

## Results

# *Use, Regular Use and Dependence: Incidence and Prevalence*

As shown in table 1, the cumulative incidence (CI) of ever using tobacco is greater for men than women and increases with age reaching 85% of men and 78% of wom**Table 1.** Tobacco<sup>1</sup> use and regular use (%) in the total population

Age	Ever use <sup>2</sup>			Lifetime	Lifetime regular use <sup>3</sup>			12-month regular use <sup>3</sup>		
(years)	men		women	men		women		men		women
14–24	79.9	*	72.8	36.5		35.2		32.8		31.3
14–15 16–17 18–21 22–24	64.5 79.1 80.3 85.3	* *	61.4 70.1 72.5 77.5	12.7 31.9 43.3 43.1	*	17.8 30.0 34.6 43.1		12.5 31.0 40.6 36.5	*	17.4 27.7 32.6 36.0

Men: n = 1,493; women: n = 1,528.

\*  $\chi^2_1$ , p < 0.05.

<sup>1</sup> Tobacco products were described as: cigarettes, cigars, pipes, snuff or chew.

<sup>2</sup> Use = Ever used a nicotine product at least once.

<sup>3</sup> Regular use = Ever used a nicotine product daily for 4 weeks or more.

**Table 2.** Lifetime cumulative incidence (%) and 12-month prevalence (%) of DSM-IV nicotine dependence in the total population and among regular users

Age (years)	Lifetim	e cumulative in	ncidence		12-month prevalence					
	total po	total population <sup>1</sup>		lifetime regular users <sup>2</sup>		total population		12-month regular users <sup>3</sup>		
	men	women	men	women	men	women	men	women		
14–24	19.1	18.5	52.2	52.6	15.8	14.1	47.0	44.1		
14-15	6.5	8.9	50.9	50.1	6.0	8.7	48.0	49.9		
16–17	16.2	18.9	50.7	63.1	14.8	16.8	47.6	58.7		
18-21	22.1	17.5	51.2	50.7	18.5	14.0	45.6	42.9		
22–24	23.0	22.1	53.3	51.4	18.1	15.1	47.5	40.2		

<sup>1</sup> Total population – men: n = 1,493; women: n = 1,528.

<sup>2</sup> Lifetime regular users = Ever used a nicotine product daily for 4 weeks or more: men: n = 545; women: n = 538.

<sup>3</sup> 12-Month regular users = Used a nicotine product daily for 4 weeks or more in the past 12 months: men: n = 489; women: n = 478.

en by 22–24 years. Overall, the lifetime CI of regular use is about half that of ever using, but this masks important gender and age effects which show that women are more likely to make the transition from ever use to regular use and that the proportion of ever users making this transition increases sharply in the mid to late teens. The relatively high prevalence of 12-month regular use reflects this teen trend of recent incidence by remaining at 95% of lifetime regular use through 21 years of age and then falling to 85% in the oldest age group reflecting an increasing rate of remission.

Table 2 shows the lifetime CI and 12-month prevalence of nicotine dependence in the total population and among regular users. Overall, about 19% of the population meets criteria for lifetime and 15% for 12-month nicotine dependence. For lifetime CI there were no significant gender differences, although a strong age effect (p < 0.05) resulted in a CI of 22–23% by 22–24 years of age. However, this age effect can be attributed to that of the transition to regular use (table 1) since the distribution of dependence among regular users is generally consistent across age groups at slightly more than 50%.

## Criteria Prevalence by Level of Use

Table 3 shows the distribution of DSM-IV nicotine dependence criteria among regular users and stratified by the number of cigarettes smoked per day at peak use. (For comparison purposes, cut points for the number of ciga**Table 3.** Distribution (%) of DSM-IVnicotine dependence criteria, diagnosis andother indicators among regular users bynumber of cigarettes smoked at the time ofpeak use

DSM-IV criteria, diagnosis	Total		n cigarett	n cigarettes/day at peak use1			
and other indicators			1–14	15–24	25+		
Number							
Just one criterion	16.0		25.5	16.8	2.6		
Just two criteria	23.7		28.8	26.0	14.2		
Three or more criteria	53.5	*	34.3	49.9	83.2		
Clustering of 3+ criteria <sup>2</sup>	98.0		96.6	96.8	99.6		
Туре							
1 tolerance	23.8		20.4	25.3	25.2		
2 withdrawal	36.9	*	23.2	39.8	50.3		
3 more/longer than intended	47.8	*	43.0	45.6	57.7		
4 unsuccessful cut-down	81.9		79.5	83.0	83.2		
5 a lot of time using	27.5	*	0.0	2.1	100.0		
6 activities given up	7.1		6.1	6.3	9.9		
7 continued use despite problems	49.6	*	32.0	50.9	70.8		
DSM-IV nicotine dependence	52.4	*	33.2	48.3	82.9		
Craving	36.0	*	21.1	35.9	54.8		
Reported dependence	55.0	*	36.6	59.0	72.9		

\*  $\chi^2$ , p < 0.05 test of differences in prevalence between levels of use.

<sup>1</sup> Among regular users (n = 1,084): 34% reported 1-14/day; 39% reported 15-24/day; 27% reported 25+/day.

<sup>2</sup> 12-month clustering among those with 3 or more criteria.

rettes smoked daily at peak use were based on those used by the US National Centers for Disease Control in their report Surveillance for Tobacco-Use Behaviors [27].)

As can be seen, the number of regular users reporting any criteria and the number of reported criteria increases significantly as peak use increases with the reported clustering of 3 or more criteria remaining high at all levels of use. Dose-response relationships were significant for four of seven criteria: (2) withdrawal; (3) using more or longer than intended (chain smoking); (5) a lot of time spent using, and (7) continued use despite problems, representing symptoms of physiologic adaptation and loss of control. Among those not showing a response to changes in levels of use, (4) unsuccessful cut-down was uniformly high across all levels (82%) possibly indicating a low response-threshold, with (1) tolerance being moderately low (24%) possibly indicating a high response-threshold, and (6) giving up activities being relatively uncommon (7%) most likely reflecting the social acceptance of tobacco use.

The proportion of regular users fulfilling criteria for dependence also increased relative to peak use from 33% among those using the least up to 48% and then to 83% among those using the most. Among regular users, 78% of

dependence diagnoses included the physiologic symptoms of tolerance or withdrawal. Craving was reported by 36% of users overall and also exhibited a significant doseresponse relationship. After controlling for level of peak use, these distributions were not significantly different between older and younger regular users.

## Course

Figure 1 shows the cumulative incidence of nicotine use, regular use and dependence as estimated by survival analyses and shows the significant birth-cohort effects which are apparent for each of these outcomes (no gender differences were found). Investigation of these effects shows that the cohort differences in ever use but not regular use persist even after removing outcomes with onsets in early childhood.

As seen in the data from the most recent birth-cohort, beginning at around 10 years of age the incidence of first use begins to rise with peak incidence seen at 12–15 years. This is followed by peak incidence of regular use at 13–18 years of age and of nicotine dependence beginning at 15 years of age. It is interesting to note that peak incidence of first use ends in the mid-teens followed by regular use in the late teens, while the cumulative incidence of depen-

DSM-IV Nicotine Dependence



Fig. 1. Cumulative incidence of tobacco use, regular use and dependence.

dence appears to continue into adulthood. Gender differences were significant only for ever use with men being significantly more likely than women to ever use a tobacco product with cohort effects being similar for both men and women.

Table 4 shows state stability by comparing the use/ diagnosis status at 13+ months in the past to that of the past 12 months. The table is stratified by gender, with men in the upper panel (I) and women in the lower panel (II). The table is organized with past status on the left margin (r1-r4) and current status across the top margin (c1c4) with the hierarchical status defined as: (1) never used/ quit; (2) ever use; (3) regular use, and (4) dependence. In addition, the diagonal of the matrix is shown in column 5 for clarity.

Focusing on past nondependent (r3) and dependent (r4) regular users, the persistence of regular use in this young population is reflected in the findings that approximately three-quarters of respondents remained in the same nondependence/dependence state when their 12month status was assessed and an even higher proportion remained regular users (89%), with most transitions among regular users being between states of nondependence and dependence. Among transitions out of regular use, nondependent regular users (r3) were more likely to quit or use less-than-regularly than dependent regular users (r4; 15% vs. 6%, p < 0.05).

Table 5 shows differences in attitudes and attempted cut-backs between lifetime nondependent and dependent past-year regular users. As can be seen, dependent regular users are significantly more likely to express an interest in changing their pattern of use and are correspondingly more likely to view their level of use as having a negative health impact. Associated with these attitudes are significantly more dependent users attempting to cut-back and more persistence in these attempts as shown by the number of cut-backs attempted and use of special therapies.

# *Characteristics of Nondependent and Dependent Regular Users*

In table 6 we look at associations between regular smoking and other substance and nonsubstance disorders. Significant associations between regular smoking and a row disorder are represented by (†) and significant differences in the magnitude of association between nondependent and dependent smoking are represented by (‡), with **Table 4.** Diagnosis stability: comparison of past and current nicotine use/diagnosis profiles and estimated 12-month incidence and remission

Status at 13+ months	12-mon	Stability				
population and smoking status <sup>1</sup>	cumulative incidence %	never/ quit (c1)	ever used (c2)	regular use (c3)	depen- dence (c4)	— in a row (%) (c5)
I. Men						
rl Never	24.8	_	15.6	1.5	1.6	81.2
r2 Ever use <sup>2</sup>	41.6	_3	_	2.7	2.4	94.9
r3 Regular use	17.7	9.0	5.6	-	9.7	75.7
r4 Dependent use	16.0	2.6	2.7	15.5	-	79.1
II. Women						
rl Never	31.3	_	10.9	1.2	0.9	87.0
r2 Ever use <sup>2</sup>	36.2	_3	-	3.8	2.0	94.2
r3 Regular use	16.7	10.9	4.3	-	9.0	75.9
r4 Dependent use	15.8	5.2	1.9	19.7	-	73.3

<sup>1</sup> Populations are defined by their past (13+ months) use/diagnosis status.

 $^2$  Snuff and chew users are considered to have initiated >12 months ago, with no assessment of recency.

<sup>3</sup> Nonuse in the past 12 months was assessed only among subgroups with past 'regular use' or 'dependence'.

all tests of associations controlling for age, gender and cooccurring alcohol and illicit drug disorders.

As can be seen in the first section of columns in the table, the prevalence of these outcomes increases consistently from nonsmokers to nondependent smokers and again for dependent smokers. These positive associations are reflected in the prevalence odds ratios (POR) presented in the second section of columns in the table which are consistently greater than 1.0. By focusing on the associations with smoking we can also see that most of these are significant (†) and are consistently stronger for dependent smokers as compared to nondependent smokers (‡) with most differences between smokers and nonsmokers being accounted for by the dependent smokers, the exception being for substance disorders.

## Discussion

Consistent with the results of Breslau et al. [15] for young adults in the United States, these results have shown that slightly more than half of regular smokers will meet criteria for nicotine dependence with the earliest cases appearing in the mid-teens. Extending these findings, our results show that, as compared to nondependent smokers, dependent smokers were shown to be more persistent smokers despite a higher recognition of the nega-

DSM-IV Nicotine Dependence

**Table 5.** Attitudes and attempted cut-backs among past-year regular smokers

	Lt dependence diagnosis (n = 966)				
	no (45.3%)		yes (54.7%)		
Health effects, %					
	10.2	*	15.7		
_	17.0		26.3		
+/-	65.9		53.2		
+	7.0		4.8		
Would like to change pattern of use, %	56.0	*	74.0		
Ever attempted a cut-back, %	67.2	*	92.0		
Number of attempts, median (max.)	2 (40)		3 (30)		
Use of special therapy to aid cut-back, %	1.6	*	4.6		
$\chi^2, p < 0.05.$					

tive health effects associated with smoking, their greater interest in changing their smoking practices and their increased number of attempts at cutting-back. This is perhaps not so surprising since over 90% of regular smokers report at least one criterion of DSM-defined substance dependence with symptoms of compulsive use

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Table 6. Lifetime association of regular use	e and nicotine dependence wi	ith selected psychiatric disorders1
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Co-occurring disorders	Row d	Row diagnosis, %			Smoker	Smokers <sup>2</sup>				
	no	smokers	smokers		nondep	nondependent		ent		
	use	no dx	dx	_	POR	95% CI	POR	95% CI		
Substance disorders		16.8	30.7	†‡	1.80	(1.33-2.44)*	3.98	(3.04-5.22)*		
Alcohol abuse	7.9									
Alcohol dependence	2.4	7.7	17.9	†‡	2.52	(1.59-3.98)*	6.14	(4.14-9.11)*		
Illicit abuse	0.5	8.1	11.9	Ť	13.78	(6.84-27.75)*	15.41	(7.76-30.62)*		
Illicit dependence <sup>3</sup>	0.0	3.0	8.1				7.68	(4.13–14.29)*		
Affective disorders, any	12.2	19.7	30.0	†‡	1.58	(1.21-2.06)*	2.63	(2.06-3.35)*		
Hypomania	1.1	2.0	2.7	†	1.86	(0.86 - 4.03)	2.21	(1.72-4.56)*		
Mania, single episode	0.0	0.2	0.1		10.85	(0.35 - 339.6)	3.21	(0.05 - 195.6)		
Bipolar I or II	1.3	1.2	4.1	‡	0.88	(0.36 - 2.14)	2.55	(1.36-4.78)*		
Major depression	8.8	14.7	19.3	†‡	1.57	(1.17-2.11)*	2.18	(1.65-2.89)*		
Dysthymia	2.0	2.8	6.7	†‡	1.28	(0.68–2.40)	2.86	(1.73-4.75)*		
Anxiety disorders, any	11.5	13.4	23.0	†‡	1.10	(0.81-1.48)	1.94	(1.49-2.53)*		
Panic attack	2.4	4.0	11.3	†‡	1.48	(0.86 - 2.54)	3.71	(2.41-5.70)*		
Panic disorder	0.7	1.8	2.2	_	2.12	(0.83 - 5.45)	2.07	(0.78 - 5.45)		
Agoraphobia	1.6	2.5	6.4	†‡	1.50	(0.71 - 3.15)	3.06	(1.64-5.70)*		
Social phobia	1.9	2.3	5.1	_	1.11	(0.53 - 2.31)	2.20	(1.19-4.07)*		
Simple phobia, any	1.0	1.4	4.3	†‡	1.34	(0.52 - 3.47)	3.74	(1.80-7.77)*		
Blood/injection phobia	0.1	0.7	1.5	†	6.09	(0.94-39.62)	10.05	(1.72-58.76)*		
Phobia NOS	4.4	2.4	6.9	‡	0.58	(0.30 - 1.14)	1.63	(1.00-2.66)*		
Generalized anxiety	0.1	1.2	2.1	†	14.55	(1.76-120.2)*	14.53	(1.74–121.4)*		
Obsessive-compulsive	0.3	1.2	0.9	-	3.90	(1.07-14.19)*	2.19	(0.49-9.83)		
Posttraumatic stress	0.3	0.4	2.8	†‡	1.06	(0.18-6.29)	5.78	(1.86–17.98)		

 $\dagger$  Indicates a significant difference (p < 0.05) between nonregular use and regular use, regardless of dependence.

 $\ddagger$  Indicates a significant difference (p < 0.05) between nondependent and dependent regular use.

\*  $\chi^2$ , p < 0.05.

<sup>1</sup> Dx = dependence; POR = prevalence odds ratio; CI = confidence interval. Lifetime cumulative incidence of no use (less than regular use) = 64.1%, of regular use = 17.1%, and of dependence = 18.8%. Reported ORs reflect the association with nondependent regular use (regular use) and dependent regular use (dependence), modeled simultaneously.

<sup>2</sup> Controls for alcohol and illicit substance disorders in addition to gender and birth-cohort.

<sup>3</sup> All persons reporting illicit substance dependence were also regular users.

and physiologic adaptation being among the most often reported.

Our analysis of the association between regular smoking and other psychopathology showed that, consistent with earlier findings from the ECA [12], regular smoking is strongly associated with other substance, affective and anxiety disorders. However, we also showed that the cumulative incidence of these disorders is significantly higher among dependent smokers than nondependent smokers, even for disorders with a relatively high prevalence among nonsmokers such as major depression, dysthymia, panic attacks, agoraphobia, posttraumatic stress disorder (PTSD) and the alcohol disorders. With few exceptions, it appears that dependent regular smoking is responsible for the previously reported association between regular smoking and nonsubstance psychopathology.

These results should be interpreted with the knowledge that they are based on retrospective reports collected using fully structured diagnostic instruments administered by lay interviewers. Despite the proven reliability and validity of these instruments, it is unrealistic to expect that such data will match the accuracy of information collected in the context of a clinical evaluation over time using multiple informants. In addition, some respondents may underreport their level of symptomatology leading to the underestimation of prevalence and strength

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of association between diagnoses. However, the basic findings from this report would not be changed if it were the case that symptomatology is underreported. In fact, in the absence of this information bias we would expect a confirmation of these findings in the form of stronger associations.

This report is among the few that have been published to date examining differences between nondependent and dependent smokers and of the co-occurrence dependence with other substance and nonsubstance disorders. In addition, it is the only general population study we are aware of which shows associations with specific substance, affective and anxiety disorders. The pattern of strong association which was identified indicates a common liability for these substance disorder outcomes may exist in the form of a coping strategy or biologic susceptibility and deserves further investigation. Although it remains to be seen, it can be hypothesized that comorbid dependent smokers are more persistent smokers and may not respond successfully to intervention therapy without recognition of the underlying psychopathology. Whether this is related to more severe withdrawal symptoms [28] and/or the triggering of depressive episodes [29, 30] has yet to be investigated.

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