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- **Master Thesis –**

Comorbidity of Axis I disorders in a sample of at-risk, problem, and pathological gamblers

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by:

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0. Abstract

Background. Pathological gambling has – as the first behavioral addiction –recently been added to the substance-related disorders in the Diagnostic and Statistical Manual, fifth edition (DSM-5). There are a variety of factors that are associated with pathological gambling as age, gender, impulsivity, and mental disorders. The present study aims to highlight a specific aspect of problematic gambling: the comorbidity of psychiatric conditions in at-risk, problem, and pathological gamblers.

Methods. Based on a general population based sample of 15,023 participants of the study "Pathological Gambling and Epidemiology" (PAGE), the present study analyzed comorbid Axis-I disorders among 164 adult gamblers. Data of this survey were compared with the distribution of psychiatric conditions in a general population sample.

Results. Results are displayed in the published article "Comorbid Axis I-disorders among subjects with pathological, problem, or at-risk gambling recruited from the general population in Germany" (Journal: Psychiatry Research, E-pub ahead of print). Lifetime prevalence of any psychiatric disorder was 93.6% among pathological (5-10 DSM-IV criteria), 83.5% among problem (3-4 DSM-IV criteria), and 81.0% among at-risk gamblers (1-2 DSM-IV criteria). Conditional Odds Ratios (COR) for having a comorbid disorder were 3.5 (95%-Confidence interval, CI 2.6-4.6) in at-risk gamblers, 4.9 (CI 3.3-7.3) in problem gamblers, and 4.6 (CI 3.0-6.9) in pathological gamblers compared to the general population.

Conclusions. The present study was the first one to compare subgroups of gamblers (at-risk, problem, and pathological gamblers) to a sample of the general population regarding Axis I-disorders. The results showed that prevalence proportions of psychiatric conditions were extraordinary high in all three groups of gamblers compared to the general population. These data can help to understand the complexity of problematic gambling and might help to foster a treatment service that reaches gamblers at an early stage of the disorder. Early interventions and prevention programs addressing subthreshold gambling problems appear to be necessary. Longitudinal research concerning the persistence of problematic gambling is required.

1. Introduction

Traditionally, addiction was associated with substance use. In the past few years, the understanding of addiction and dependence in research developed to a more comprehensive concept of addiction that includes also behavioral dependencies like sex addiction, compulsive buying, excessive internet use, and pathological gambling (Mann, Fauth-Bühler, Seiferth et al., 2013). According to the ongoing debate, findings in research about behavioral addictions, their clinical relevance and courses of the disease are still not satisfactory although the cooccurence between substance-related addictions and behavioral addictions are striking (Böning, Meyer, and Hayer, 2013; Kiefer, Fauth-Buhler, Heinz et al., 2013; Mann et al., 2013). In the fifth edition of the DSM (American Psychiatric Association, 2013), the behavioral addiction pathological gambling has been subsumed under "Substance-Related and Addictive Disorders", and the Internet Gaming Disorder is subsumed under "Proposed disorders for further study". Launching a taskforce of experts by the German Association of Psychiatry, Psychotherapy and Psychosomatics (Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde, DGPPN) for behavioral addictions marks a syllogism to the ongoing debate.

The present study aims at highlighting a specific aspect of pathological gambling: the comorbidity of Axis I-disorders by means of data from a large epidemiological survey: "Pathological gambling and Epidemiology (PAGE)". After a description of the phenomenon of pathological gambling and the legal framework in Germany, prevalence estimates and findings concerning psychiatric comorbidity will be presented. This is followed by a detailed presentation of the PAGE-study. Core element of the thesis is the published article "Comorbidity of Axis I disorders in a sample of at-risk, problem, and pathological gamblers" in which the main findings are displayed. Findings are discussed and put into perspective of Public Health aspects.

2. Pathological gambling – a behavioural addiction

Data from international epidemiological studies suggest an increase in the number of pathological gamblers. While most of the gambling individuals never have problems with gambling, an increasing number of gamblers struggle with negative consequences due to their gambling behaviour (Hodgins, Stea, and Grant, 2011). Especially men and socially disadvantaged individuals suffer from adverse consequences in financial, social and personal aspects (Johansson, Grant, Kim et al., 2009).

2.1 Definition

Since 1980, pathological gambling has been included in the international classifications of psychiatric disorders, the Diagnostic and Statistical Manual of Mental Disorders (DSM) and later on in the International Statistical Classification of Diseases, 10th revision (ICD-10; WHO, 1991). In the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV, American Psychiatric Association, 1995), pathological gambling is subsumed under impulse-control disorders. The following ten criteria are used for diagnosing gambling disorders.

2.1.1 DSM-IV criteria

A: Persistent and recurrent maladaptive gambling behavior.
The person concerned

1. is preoccupied with gambling
2. needs to gamble with increasing amounts of money in order to achieve the desired excitement
3. has repeated unsuccessful efforts to control, cut back, or stop gambling
4. is restless or irritable when attempting to cut down or stop gambling
5. gambles as a way of escaping from problems or of relieving a dysphoric mood
6. after losing money gambling, often returns another day to get even ("chasing")
7. lies to family members, therapist, or others to conceal the extent of involvement with gambling
8. has committed illegal acts such as forgery, fraud, theft, or embezzlement to finance gambling
9. has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling

10. relies on others to provide money to relieve a desperate financial situation caused by gambling

B: The gambling behaviour is not better accounted for by a manic episode.

(American Psychiatric Association, 1995)

At least five of these ten criteria have to be fulfilled for a diagnosis of pathological gambling. To date, subthreshold gambling or problem gambling (i.e. 1 to 4 DSM-IV criteria) is not formally defined (Hodgins et al., 2011).

2.1.2 Changes in the DSM-5

Traditionally, the term "addiction" is associated with the dependence of different substances as alcohol, tobacco or drugs. However, recent developments in addiction research show an increasing number of similarities between substance-related addictions and behaviours like gambling, internet use, eating, and compulsive buying in terms of withdrawal, craving, development of tolerance, or even neuropsychological processes (Mann et al., 2013).

In the 5th revision of the DSM, pathological gambling is reclassified as an addictive behavior in the section "Substance-Related and Addictive Disorders" (American Psychiatric Association, 2013). Additionally, criterion 8 (commitment of illegal acts) has been eliminated. Accordingly, diagnosis of pathological gambling is fulfilled with 4 out of 9 DSM-5 criteria. Severity is classified in "mild" (4-5 criteria), "moderate" (6-7 criteria), and "severe" (8-9 criteria).

Since the DSM-5 was released in May 2013, the present study is based on DSM-IV criteria.

2.1.3 Subthreshold gambling problems

Until now, there is no clear definition of „problem gambling" or „subthreshold gambling" in the sense of milder forms of gambling problems that do not reach the threshold of pathological gambling. In the DSM-IV (as well as in the DSM-5) the disorder can be diagnosed if at least 5 of the 10 criteria (DSM-5: 4 out of 9) are fulfilled. Nevertheless, it can be hypothesized that subclinical gambling has an impact on the social, occupational, and mental well-being of the affected individuals (Lorains, Cowlishaw, and Thomas, 2011). Most of the previous studies have defined "problem gambling" as meeting 3 or 4 criteria (Brewer, Potenza, and Desai, 2010; Hodgins, 2004; Lorains et al., 2011), nevertheless, this cut-off has not been empirically validated. Although

prevalence studies used the threshold of 3 criteria for defining problem gambling, only few studies have investigated subthreshold gambling in terms of an impact of increasing numbers of criteria and associations with other factors that might inhibit or enhance the development of pathological gambling and courses of the disorder. One aim of the present study is to examine these possible associations.

2.2 Legal framework in Germany

In Germany, gambling is under governmental control. In 2006, an amendment of the governmental legal framework for gambling (Glücksspielstaatsvertrag) was set, which came into force in 2008. It aimed at regulating the gambling market in the sense of preventing adverse consequences for gamblers (Deutsche Hauptstelle für Suchtfragen e.V. (DHS), 2013). In 2012, a revised version of the gambling regulation (Glücksspieländerungsstaatsvertrag) was set with a less clear focus on prevention and more loose restrictions for internet gambling and betting on sports (Deutsche Hauptstelle für Suchtfragen e.V. (DHS), 2013).

Problematically, electronic gambling machines in bars and restaurants or in gambling halls are not subsumed under "gambling" but come under the trade control (Gewerbeaufsicht). At the same time, electronic gambling machines are the gambling offer with the highest Odds Ratio for developing pathological gambling (Meyer, Rumpf, Kreuzer et al., 2011). Of the gross profit of this market section, 56% is made with gambling addicts (Böning et al., 2013). The regulation for commercial gambling (Spielverordnung) from 2006 allowed more flexibility to the providers of electronic gambling machines (Gebhardt and Postel, 2008). In consequence, an increase of commercial gambling halls was registered. Additionally, and according to the legal framework, the number of slot machines in gambling halls increased from 10 to 12 machines per licence, and the net-squaremeter area per slot machine was lowered from 15 sq m to 12 sq m (Trümper and Heimann, 2010). From 2008 to 2010, 1,691 new licences in 587 gambling locations were allocated (Trümper and Heimann, 2010). The total turnover in 2010 was 31,5 billion Euro, compared to 24,9 billion in 2008 (Meyer and Hayer, 2010). At the same time, an increase in turnover of 6.5% to 17.2 billion Euro was registered in the providers of electronic gambling machines (Meyer, 2012).

The costs of these economic profits are high: Aside from long-term debts and bankruptcy as a result of excessive gambling, the social costs of pathological gambling – loss in productivity, delinquency to get money for gambling, and psychological distress in gamblers and their families up to psychiatric disorders – are increased

(Deutsche Hauptstelle für Suchtfragen e.V. (DHS), 2013). In 2010, 18.2% of the pathological gamblers registered in outpatient treatment (n=3,897) had more than 25,000 Euro debts, and 7.4% had more than 50,000 Euro debts (Meyer, 2012). Given that only a minority of gamblers enters treatment (Slutske, 2006), it is likely that these numbers are underestimated.

Factors that facilitate the development of a gambling disorders are:
- rapid frequency of games (as in electronic gambling machines or live sport betting)
- variation of wagers and winnings
- frequent "almost winnings"
- illusion of controlling the game (via pushing a key)
- high density of gambling halls with low entrance restrictions
- extended opening hours (often 24 hours).

(Hayer, 2010)

3. Prevalence estimates

3.1 Prevalence of pathological gambling in international population-based surveys

To date, a number of epidemiological studies giving estimates for the prevalence of pathological in the general population exists. Prevalence rates vary between countries and according to study design, methodology and regional gambling opportunities (Abbott, 2007; Hodgins et al., 2011; Williams and Volberg, 2009). A review of 2007 summarizes 33 prevalence surveys conducted from 2000 to 2005 (Stucki and Rihs-Middel, 2007). It focused on the 12-month-prevalence, i.e. symptoms for pathological gambling were found in the past 12 months before assessment. Studies analysing lifetime prevalence were excluded from this review as well as surveys focussing on specific groups (e.g. inhabitants of prisons), studies with less than 500 interviewees or studies with methodological uncertainties. Of the studies, 88% (n=29) conducted a telephone survey with a random sample of interviewees. Only five studies also interviewed adolescents. Studies used different measurements for diagnosing pathological gambling: 20 of them used the "South Oaks Gambling Screen" (SOGS, Lesieur and Blume, 1987), whereas in 9 studies the "Canadian Problem Gambling Index" (CPGI, Ferris and Wynne, 2001) was conducted. Four studies requested solely the DSM-IV criteria.

In their review, Stucki & Rihs-Middel (2007) show that the 12-month-prevalence for problem gambling (3 to 4 criteria) and pathological gambling (5 to 10 criteria) together sum up to 3%. Prevalence estimates in Europe are lower (0.4-2.2% for problem and 0.2-0.8% for pathological gambling) than in US-American studies (0.7-4.7% for problem and 0.5-3.5% for pathological gambling). Two studies from Asia showed extremely high prevalences (2.0/4.0% for problem and 2.1/1.8% for pathological gambling). These results probably have been influenced by the fact that the studies were conducted in a metropolitan area.

3.2 Prevalence of pathological gambling in Germany

Since 2006, seven population based studies have been conducted in Germany (Bühringer, Kraus, Sonntag et al., 2007; Buth and Stöver, 2008; BZGA, 2008, 2010, 2012; Meyer et al., 2011; Sassen, Kraus, Bühringer et al., 2011) with a broad range of methodological variability cf. Table 1).

Table 1: population-based studies in Germany – prevalence proportions

Study	N	Measurement	Past-year-prevalence subthreshold gambling (3-4 crit.)	Past-year-prevalence pathological gambling (5-10 crit.)
ESA Bühringer et al. (2007)	7,817	DSM-IV-questionnaire by Stinchfield (2002)	0.3%	0.2%
Buth & Stöver (2008)	7,980	DSM-IV-questionnaire by Stinchfield (2002)	0,64%	0.56%
BZgA (2007)	10,000	SOGS	0.41%	0.19%
BZgA (2009)	10,001	SOGS	0,64%	0.45%
Meyer et al. (2011)	15,023	CIDI-Gambling (DSM-IV-based; WHO (2009))	0.31%	0.35%
Sassen et al. (2011)	8,006	DSM-IV-questionnaire by Stinchfield (2002)	0.24%	0.30%
BZgA (2012)	10,002	SOGS	0.51%	0.49%

Prevalence proportions of pathological gambling range from 0.19% to 0.56%. The differences in prevalences are likely to depend on the assessment. The South Oaks Gambling Screen (SOGS; Lesieur and Blume, 1987), a screening instrument for problematic and pathological gambling which is not based on DSM-IV criteria, was originally developed for clinical populations and is known to lead to false-positive results (Lorains et al., 2011; Stucki and Rihs-Middel, 2007). Additionally, it does not assess the more comprehensive negative consequences that can occur with pathological gambling (Petry, Stinson, and Grant, 2005) that are covered by the DSM-IV criteria.

4. Comorbidity

4.1 Psychiatric comorbidity among pathological gamblers – Findings from international studies

There are several risk factors for pathological gambling as younger age, male gender, cognitive distortions as illusion of control and "magic thinking", impulsivity, and comorbid mental diseases (Johansson et al., 2009). Especially depressive symptoms, substance use disorders, and anxiety have shown to be factors associated with pathological gambling behavior in several studies (Brewer et al., 2010; Hodgins, Peden, and Cassidy, 2005; Hodgins et al., 2011; Johansson et al., 2009; McGrath and Barrett, 2009; Park, Cho, Jeon et al., 2010; Rush, Bassani, Urbanoski et al., 2008; Zimmerman, Chelminski, and Young, 2006). These findings are comparable to findings from substance use disorders where an elevated risk of psychiatric comorbidity is known to be common (Crockford and el-Guebaly, 1998). A recent systematic review analysed studies from general population samples that assessed comorbid disorders in problem and pathological gambling from 1998 to 2010 (Lorains et al., 2011). The meta-analysis included 11 studies with adult samples that used a random sample methodology and validated screening instruments for gambling disorders. Most of the studies used the DSM-IV criteria for pathological gambling, or the South Oaks Gambling Screen. Results of the meta-analysis show nicotine dependence to be the most prevalent comorbid disorder followed by other substance disorders, mood disorders, and anxiety disorders (Lorains et al., 2011). Since most of the studies followed a cross-sectional design, causal relations could not be drawn.

The worldwide largest representative study that also assessed pathological gambling was the National Epidemiological Survey on Alcohol and Related Conditions (NESARC; Petry et al., 2005) in the United States. The study was conducted by the

National Institute on Alcohol Abuse and Alcoholism and the sample consisted of 43,093 participants. Interviews were face-to-face with a response rate of 81%. Pathological gambling was assessed with the Alcohol Use Disorder and Associated Disabilities Interview Schedue-DSM-IV (AUDADIS-IV; Grant, Dawson, Stinson et al., 2003), as well as alcohol and drug use, mood and anxiety disorders, and personality disorders. Lifetime prevalence of pathological gambling was estimated with 0.42% (problem gamblers were not included). Of the lifetime pathological gamblers, 73.2% have had also an alcohol use disorder (lifetime), 49.6% suffered from a mood disorder during their lifetime, and 41.3% had an anxiety disorder. 28.5% were diagnosed with an obsessive-compulsive personality disorder, and 23.3% had an antisocial personality disorder. A three-year-follow-up showed that 53.8% of the population with gambling disorders had developed an incident Axis I disorder (Chou and Afifi, 2011). One study analyzed sex differences among participants of the NESARC study with 1 to 4 DSM-IV criteria (Blanco, Hasin, Petry et al., 2006). Participants with subthreshold gambling showed high prevalence proportions of lifetime mood disorders (men: 28.1%, females: 40.1%), and alcohol use disorders (men: 64.8%, females: 38.9%). However, these analyses were not subdivided in 1-2 and 3-4 DSM-IV criteria. Thus, no conclusions could be drawn concerning the impact of varying levels of non-clinical gambling on comorbid Axis-I disorders.

In the National Comorbidity Survey Replication (NCS-R; Kessler, Hwang, LaBrie et al., 2008), an US-American representative household sample with 3,435 face-to-face interviews, lifetime prevalence estimates were 0.6 for pathological gambling and 2.3% for problem gambling (defined as at least 1 DSM-IV criterion). The results showed that 96.3% of the pathological gamblers had also suffered of at least one Axis-I disorder during their lifetime. The Odds Ratios were 3.7 for any mood disorder, 3.1 for any anxiety disorder, and 5.5 for any substance disorder. For having three or more disorders, the Odds Ratio was 30.0. The NCS-R also analyzed subclinical gambling (1 to 4 DSM-IV criteria), but only in terms of age onset of comorbid disorders and gambling problems.

Despite the increasing number of studies based on general population based samples, most of the data gathered for prevalence estimations for comorbidity are still drawn from clinical samples (Crockford and el-Guebaly, 1998; Lorains et al., 2011). However, these data are not meaningful for prevalence estimation, since only 7-12% of pathological gamblers ever seek treatment for gambling problems (Slutske 2006).

4.2 Comorbid mental diseases among pathological gamblers in Germany

Until now, data for comorbidity of mental diseases in pathological gamblers were only available via patients in in- and outpatient treatment (Erbas and Buchner, 2012). One of the first published studies in Germany conducted diagnoses in a group of 48 treatment seeking excessive casino and slot machine gamblers (Kröber, 1991). Only one of the participants did not fulfill criteria for a psychiatric disorder. A multicenter study of the nationwide "Task Force Pathological Gambling" (Arbeitskreis Glücksspielsucht), an affiliation of 13 in- and outpatient facilities, assessed descriptive data from 558 pathological gamblers seeking treatment in these facilities in 1993. Results showed that 27.6% of the pathological gamblers suffered from at least one other addiction, 18.5% from an alcohol dependence (Denzer, Petry, Baulig et al., 1995).

A recent clinical study assessed psychiatric comorbidity in a sample of 101 pathological gamblers in a specialised inpatient treatment (Premper and Schulz, 2008). Of these patients, 87% had pathological gambling as primary diagnosis, 11.9% had the primary diagnosis alcohol dependence. Results show that 91.1% of the participants had at least one additional mental disorder over their lifetime. Especially, affective disorders (61.4%), anxiety disorders (57.4%), and substance related disorders (60.4%) showed to be highly prevalent among pathological gamblers.

Unfortunately, the general population-based studies in Germany did not assess comorbid disorders. The study "Pathological Gambling and Epidemiology" (PAGE) was the first study that conducted clinical interviews with a subsample to assess comorbidity for pathological gambling. Results of these data are presented in this paper.

5. The study "Pathological Gambling and Epidemiology (PAGE)"

In 2009, the Federal States of Germany initiated funding for the study Pathological Gambling and Epidemiology (PAGE)" to provide population-based data on pathological gambling. Aim of PAGE was not only to estimate 12-months prevalence proportions as previous studies in Germany but also to assess data for lifetime prevalence, data concerning treatment seeking, recovery, comorbidity, and a wide range of other factors that might be associated with pathological gambling. Because previous studies suffered often from different limitations (postal or online assessment, selection bias of participants, diagnostic assessment), the study design of PAGE included a

comprehensive sampling procedure with different recruitment strategies and a variety of validated measures described in the following.

The PAGE-study (December 2009 to February 2011) was a cooperation project between the Institute for Social Medicine and Prevention, University of Greifswald, and the research group S:TEP (Substance Abuse and related disorders: Treatment, Epidemiology, and Prevention), University of Luebeck. The study was approved by the ethics boards of both universities. The recruitment of the population based sample and the telephone interviews were conducted partly by the Institute for Applied Social Sciences ("Institut für angewandte Sozialwissenschaft", infas).

5.1 Sampling design of the PAGE-study

The cross-sectional study PAGE used a "patched-up" sampling design which included four different subsamples:

1) a random stratified and clustered telephone sample, that included
   a) a random selection of the 14- to 16-year old individuals of the general population
   b) a random selection of individuals that are only available via cell phones
2) a sample of actual gamblers recruited in gambling locations
3) a sample of participants recruited via a project telephone hotline. The number of this hotline was spread via media announcements (newspapers, radio), and via a flyer in facilities where pathological gamblers were expected to be seen more often (addiction counseling centers, self-help groups, debt counselors)
4) a sample of pathological gamblers currently in inpatient treatment facilities.

The study used a two-step approach: First, all of the participants were diagnosed with a diagnostic interview on telephone for the assessment of pathological gambling based on the DSM-IV criteria, and second, an in-depth face-to-face clinical interview was conducted with a subsample of all eligible participants (described in chapter 5.2). For more detailed informations on the study design of the PAGE-study see Meyer et al. (submitted) and the project report (Meyer et al., 2011).

5.1.1 The general population sample

PAGE used three steps for gaining the stratified and clustered general population sample:

Primary sampling unit: Based on the official statistics of the Federal States, 53 German communities were selected. To guarantee representativeness, states, communities, geographic region and the density of slot machines were included in the stratification. The selected sample points are displayed in Figure 1.

Figure 1: Sample points (shown in blue. Pink markers show inpatient treatment facilities in Germany)

Secondary sampling unit: Individual households were determined via a random digit dialing procedure using the prefix number of the selected sample points.

Third sampling unit: Because more than one eligible person could be available in one household, the last selection was done by the "last-birthday" method.

Fieldwork period was between June 2010 and October 2010. Of 26,736 households with eligible individuals aged 14 to 64, the telephone interview could be conducted with 14,022 (52.4%) of the target persons (refuse rate: 38.9%).

Since the proportion of people who are only available via cell phones but not via landline telephones is increasing (European Commission, 2011), an additional sample was drawn. A random digit dialing procedure generated cell phone numbers. Individuals were only included if they had no landline telephone. Since cell phone numbers are not bound to community prefix numbers, the clustering of the sample points could not be conducted in this subsample.

Fieldwork period was between November 2010 and February 2011. Of the 1,767 identified eligible individuals, the telephone interview could be conducted with 1,001 (56.6%) of the target persons (refusal rate: 42.3%).

5.1.2 The non-representative samples

In the selected sample points, attendees of 431 gambling locations were asked to take part in the study. From October 2010 to January 2011, 303 telephone interviews were conducted. Additionally, a free telephone hotline number for study participation was provided via two press releases and flyers that layed out in self-help groups, addiction counseling centers, probation assistants, and debt counseling services. In this subsample, 398 diagnostic interviews could be realized. Finally, participants were recruited in eight clinics that offered specialized treatment for pathological gamblers. In total, 52 diagnostic and clinical interviews were made with participants from inpatient facilities. For more information about recruitment of study participants in the non-representative subsamples, see the project report (Meyer et al., 2011).

5.2 Measures

5.2.1 Diagnostic telephone interview

The computer assisted telephone interview (CATI) assessed gambling behavior and criteria for pathological gambling according to DSM-IV. The diagnostic interview included the Gambling Section of the Composite International Diagnostic Interview (CIDI) by the World Health Organization (WHO, 2009). The English version was translated by a psychologist and back-translated by a specialized translation service. DSM-IV criteria were assessed with multiple questions, as displayed in Table 2.

Table 2: Items for assessing DSM-IV criteria in the CIDI Gambling Section

DSM-IV criteria for pathological gambling	Corresponding items in the CIDI gambling section	
(1) is preoccupied with gambling	GM10a	Did you ever have periods when you would spend lots of time thinking about your gambling when you should have been thinking about other things?
	GM10b	Did you ever have periods when you would spend lots of time planning your bets or studying the odds when you should have been doing other things?
(2) needs to gamble with increasing amounts of money in order to achieve the desired excitement	GM10c	Over time, did you have to increase the amount you bet or gambled in order to keep it exciting?
(3) has repeated unsuccessful efforts to control, cut back, or stop gambling	GM10k	Did you ever have times when you gambled even though you promised yourself you wouldn't, or when you bet a lot more or for a longer period of time than you intended?
	GM10l	How many times did you ever make a serious attempt to cut down or stop gambling?
(4) is restless or irritable when attempting to cut down or stop gambling	GM13	Did trying to quit or cut down on gambling make you feel restless or irritable?
(5) gambles as a way of escaping from problems or of relieving a dysphoric mood	GM10d	Did you ever have a time in your life when you would often use betting or gambling as a way to get out of a bad mood or to improve your mood?
	GM10e	Did you often gamble in order to escape or stop thinking from personal problems?
(6) after losing money gambling, often returns another day to get even ("chasing")	GM10f	After losing money gambling, did you often return another day soon to win back your losses?
	GM10g	When you had a big gambling debt, did you gamble more and more in the hope of winning back the losses?
(7) lies to family members, therapist, or others to conceal the extent of involvement with gambling	GM8c	Was there a time when you often tried to keep your family or friends from knowing how much you gambled?
	GM8d	Did you sometimes claim to be winning when you were actually losing?
(8) has committed illegal acts such as forgery, fraud, theft, or embezzlement to finance gambling	GM10h	Did you ever try to raise gambling money by writing a bad check, stealing, or doing something else that was illegal?
(9) has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling	GM8a	Was there ever a time when your betting or gambling often interfered with your work or responsibilities at school, on a job, or at home?
	GM8b	Was there ever a time when your betting or gambling caused repeated arguments or other serious problems with your family, friends, neighbors, or coworkers?
(10) relies on others to provide money to relieve a desperate financial situation caused by gambling	GM10i	Did you repeatedly borrow money from your family or friends to support your gambling or to pay back gambling debts?

The assessment of gambling behavior was adapted to gambling types available in Germany. It included the following gambling types (listed in German due to specification of the German gambling types), assessed for lifetime and for the 12 months prior to the interview:

- Lotto 6 aus 49
- Spiel 77 und/oder Super 6
- KENO
- Bingo
- Quicky
- Klassenlotterien
- Fernsehlotterien
- andere Lotterien (other lotteries; Glücksspirale, Soziallotterie, Prämienlos, Lotterie-Sparen, Gewinnsparen)
- Sofortlotterien (Rubbel- und Aufreißlose)
- Oddset
- Toto
- Pferdewetten (horse betting)
- andere Sportwetten (other betting on sports)
- riskante Börsenspekulationen (gambling on stock exchange)
- großes Spiel im Casino (Roulette, Baccara, Black Jack)
- Poker
- kleines Spiel im Casino (Automatenspiel)
- Spielautomaten in Spielhallen und Gastronomie (electronic gambling machines)
- Unterhaltungsspielgeräte mit Token (Fun Games)
- Dauer Quizsendungen im Fernsehen (permanent quiz shows on TV)
- privat organisiertes oder illegales Glücksspiel (private or illegal gambling)

Additionally, screening questions for Bipolar I disorder were included to cover criterion B of the DSM-IV. Finally, participants were asked (when affirming a Bipolar I disorder) if they also gambled beyond manic episodes for assessment of overlapping of gambling disorder and manic episodes.

At the beginning of the CATI, questions not related to gambling were asked to provide a convenient start and avoid resistance or refusal. For this purpose, the Social Capital questionnaire (Hanson, Ostergren, Elmstahl et al., 1997) was assessed. Subsequently, the Compulsive Internet Use Scale (CIUS; Meerkerk, Van Den Eijnden, Vermulst et al.,

2009) was assessed for Internet addiction. The CATI ended with basic sociodemographic questions. The CATI lasted ca. 20 minutes.

When the interviewee fulfilled at least one DSM-IV criterion for pathological gambling, he or she was asked to participate in the clinical interview. In total, 1,744 participants of the telephone samples, the gambling location sample, and the hotline sample were eligible for the clinical interview, plus all of the 52 patients of the inpatient facilities.

5.2.2 Clinical in-depth interview

The computer assisted personal interview (CAPI) covered a variety of topics: problems arising from gambling behavior, comorbid psychiatric disorders, personality disorders, individual risk factors, recovery of gambling problems, willingness to change gambling behavior, treatment utilization of professional help, and health related characteristics. A list of all measures assessed in the CAPI is provided in Meyer et al. (submitted) and the project report (Meyer et al., 2011).

One of the core instruments of the CAPI was the Munich Composite International Diagnostic Interview (M-CIDI; Wittchen, Beloch, Garczynski et al., 1995), which assesses DSM-IV Axis I disorders. The following disorders were assessed: Tobacco dependence, alcohol abuse and dependence, anxiety disorders (excl. specific phobias) posttraumatic stress disorder, depression, dysthymia, manic episodes, illicit drug abuse and dependence, and legal drug abuse and dependence.

The CAPI was conducted by trained academics, and lasted on average 121.6 minutes (SD 47.57). Because of the length of the interview, an additional paper-pencil questionnaire was provided with a stamped addressed envelope. The CAPI was mostly conducted face-to-face at participant's homes or another place if participants requested, like cafés or restaurants. For participation in the CAPI, participants received an incentive of 100 €. The topic of relapse to pathological gambling due to the incentive was discussed with the participants.

Because of limited project budget and a restricted time period for the field work, not all of the eligible participants of the diagnostic CATI could be included in the in-depth interview. Therefore, a subsample was selected. Participants were prioritized for this selection with respect to the following aspects: All pathological gamblers were preferred, as well as participants from the general population sample; a minimum of 50 participants with problem gambling (i.e. 3-4 DSM-IV criteria) and 50 participants with at-risk gambling (i.e. 1-2 DSM-IV criteria) were targeted. In total, 594 clinical in-depth interviews were conducted. Of these, 444 participants fulfilled the diagnosis for pathological gambling (i.e. ≥ 5 DSM-IV criteria).

6. Aim of the study

Aim of the present study "Comorbid Axis I-disorders among subjects with pathological, problem, or at-risk gambling recruited from the general population in Germany – results of the PAGE study" was to examine lifetime comorbidity among individuals with a history of gambling problems and compare it to a sample of the general population of the project "Transitions in Alcohol Consumption and Smoking" (Meyer, Rumpf, Hapke et al., 2000; Meyer, Rumpf, Hapke et al., 2001). Therefore, the sample of the present analyses is limited to the adult general population sample of PAGE for representativeness and comparability of the data.

In addition to the analysis of comorbidity of pathological gamblers, the present study is the first to compare subgroups with different levels of subclinical gamblers (at-risk gamblers, problem gamblers) with a general population sample and with pathological gamblers in terms of comorbidity of Axis I-disorders. Hypothesis of the present study was that Axis I-disorders were strongly related to the number of fulfilled DSM-IV criteria for pathological gambling.

7. Results – The article "Comorbid Axis I-disorders among subjects with pathological, problem, or at-risk gambling recruited from the general population in Germany – results of the PAGE study"

Results are presented in the following article.

The article "Comorbid Axis I-disorders among subjects with pathological, problem, or at-risk gambling recruited from the general population in Germany – results of the PAGE study" was written during the Master-Program and submitted on the 12th October 2012 to "Psychiatry Research" (Impact Factor 2.456). After two revisions, the paper was published as an Epub ahead of print on the 17th August 2013 (available on: http://www.sciencedirect.com/science/article/pii/S0165178113004010. Accessed: 2013-10-16. (Archived by WebCite® at http://www.webcitation.org/6KPnECBEi), DOI:10.1016/j.psychres.2013.07.026).

Comorbid Axis I-disorders among subjects with pathological, problem, or at-risk gambling recruited from the general population in Germany – results of the PAGE study

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Abstract

The aim of the present study was to analyze comorbid Axis I-disorders in a sample of individuals with at-risk, problem, and pathological gambling. 164 adult gamblers derived from a random sample of 15,023 individuals were compared with a general population sample. The lifetime prevalence of any psychiatric disorder was 93.6% among pathological (5-10 criteria), 83.5% among problem (3-4 criteria), and 81.0% among at-risk gamblers (1-2 criteria). Substance use disorders were the most common comorbid disorders in gamblers. Logistic regression analyses revealed elevated odds ratios for having a comorbid disorder in at-risk (Conditional Odds Ratio, COR 3.5, Confidence Interval, CI 2.6-4.6), problem (COR 4.9, CI 3.3-7.3), and pathological gamblers (COR 4.6, CI 3.0-6.9) compared to the general population. No significant differences were found between at-risk and problem gamblers or problem and pathological gamblers. Compared to at-risk gamblers, pathological gamblers showed elevated rates of comorbid substance use disorders. The data suggest a linear association between gambling disorder severity and comorbid Axis I-disorders. In conclusion, comorbid disorders are very prevalent in individuals with gambling problems. Even at-risk gamblers with 1 to 2 DSM-IV criteria show high rates of Axis I-disorders. Therefore, this group should be included in further studies on problematic gambling.

Keywords: pathological gambling, problem gambling, comorbidity, epidemiology.

1. Introduction

Pathological gambling has received increased interest in the last ten years. Comparable to substance use disorders, pathological gamblers show elevated rates of psychiatric comorbidity (Crockford and el-Guebaly, 1998; Lorains et al., 2011). In particular substance use disorders, mood and anxiety disorders have been associated with pathological gambling (Brewer et al., 2010; Hodgins et al., 2005; Hodgins et al., 2011; Park et al., 2010; Rush et al., 2008; Zimmerman et al., 2006). Population-based surveys indicate substantial prevalence rates of lifetime pathological gambling (classified by at least 5 of 10 DSM-IV criteria; American Psychiatric Association, 1995) from 0.4% to 4.2% and high prevalence rates of psychiatric comorbidity in individuals with pathological and problem gambling (Lorains et al., 2011).

In the representative National Epidemiological Survey on Alcohol and Related Conditions (NESARC; Petry et al., 2005), 73.2% of pathological gamblers had an alcohol use disorder, 49.6% suffered from a mood disorder, and 41.3% had an anxiety disorder (Petry et al., 2005). In a follow-up study three years later, 53.8% of the population with disordered gambling had an incident Axis I psychiatric disorder (Chou and Afifi, 2011).

Similarly, the population-based US National Comorbidity Survey Replication (NCS-R) revealed that 74.3% of study participants with a diagnosis of pathological gambling fulfilled the criteria for at least one DSM-IV Axis I lifetime disorder. The strongest association was found for substance use disorders (Kessler et al., 2008).

However, the comorbidity rates are primarily drawn from studies in clinical settings (Crockford and el-Guebaly, 1998; Lorains et al., 2011). Because the majority of pathological gamblers never seek treatment (Slutske, 2006), data from clinical samples may suffer substantially from sample selection bias.

To date, there is no consensus about criteria defining milder forms of gambling problems not reaching the threshold of pathological gambling according to the DSM-IV. In most studies, subthreshold gambling problems have been defined by meeting 3 or 4

criteria (Brewer et al., 2010; Hodgins, 2004; Lorains et al., 2011). However, the cut-off of 3 criteria has not been empirically validated and to date appears rather arbitrary. Recently, lowering the threshold of pathological gambling from 5 to 4 criteria has been discussed (American Psychiatric Association, 2012), which would also imply a shift in the definition of problem gambling.

Only a few studies have investigated problem gamblers with less than 5 DSM-IV criteria. In the NCS-R, subclinical gambling was only analyzed in terms of age onset of comorbid disorders and gambling problems. In a study that examined sex differences among participants in the NESARC study with 1 to 4 criteria, participants showed high prevalence rates of lifetime mood disorders (28.1% of the men and 40.1% of the women) and alcohol use disorders (64.8% of the men and 38.9% of the women, Blanco et al., 2006). However, no analyses were conducted in this study separating different categories of subthreshold diagnoses (e.g., 1-2 and 3-4 criteria). Thus, no conclusions were drawn concerning the impact of varying levels of subthreshold gambling on comorbid disorders.

The aim of the present study was to examine lifetime comorbidity among individuals with a history of gambling problems in comparison to the general population. In addition to pathological gamblers, we compared subgroups with different levels of subclinical gambling problems. We hypothesized that Axis I-disorders were strongly related to the number of fulfilled DSM-IV criteria for pathological gambling.

2. Methods

2.1. Sample

This study was part of the Pathological Gambling and Epidemiology (PAGE; Meyer et al., submitted) project, conducted from December 2009 to February 2011, and is based on a nationwide representative, stratified, and clustered random sample of 15,023 participants. The sampling included a random digit dialing procedure that was adapted

to the German system of allocation of telephone numbers. To maximize coverage, two sampling frames were used comprising landline and mobile phone numbers. The inclusion criterion was an age of 14 to 64 years. In a computer-assisted telephone interview (CATI; see measures section), participants were asked about their gambling behavior and activities in their leisure time. Participants who fulfilled at least 1 criterion for pathological gambling based on the DSM-IV (American Psychiatric Association, 1995) were asked to take part in a comprehensive clinical computer-assisted personal interview (CAPI; see measures section).

According to the classification used by Hodgins (2004) and Brodbeck et al. (2009), we differentiated two subthreshold categories in addition to pathological gambling: at-risk gambling and problem gambling, defined by meeting 1-2 and 3-4 DSM-IV criteria, respectively.

Due to limited resources and a restricted time period for the field work, a subsample was selected for the CAPI. The selection sought to minimize travelling expenses, optimize the exhaustion of personal resources, and ensure sufficient subgroup sizes according to gambling problems. The priority was to reach all pathological gamblers. Additionally, it was the intention of the study to include 50 clinical interviews with problem gamblers and 50 with at-risk gamblers according to the given definition.

In total, 1,129 individuals (7.5%) were eligible for the clinical interview, and 543 persons (48.1%) agreed to take part in the clinical interview. The clinical interview was conducted in 164 adult participants with at-risk (1-2 criteria, n=63), problem (3-4 criteria, n=52), or pathological (5-10 criteria, n=49) gambling (**Figure 1**).

[Insert Figure 1 about here]

To evaluate a possible selection bias, the available characteristics gathered in the telephone interview were compared between eligible adult subjects not participating in the clinical interview and participants included in the final analysis sample. In the first step, we calculated chi-square and t-tests. Because the study design included different priorities to assign subjects for the clinical interview according to the number of DSM-IV

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criteria fulfilled, these analyses were stratified for subjects with at-risk (63 participants vs. 711 non-participants), problem (52 participants vs. 127 non-participants), and pathological gambling (49 participants vs. 58 non-participants). In the second step, we calculated effect sizes (Cohen's *d* and *w*) for significant differences, which were classified according to Cohen (1988; small effect: w=0.1 or d=0.2; medium effect: w=0.3 or d=0.5; large effect w=0.5 or d=0.8). In all three groups, participants did not differ significantly from eligible non-participants with respect to gender, marital status, frequency of gambling, or highest loss of money due to gambling within one year. In the at-risk gambling group, participants reported a significantly higher educational level compared to non-participants (*p*=0.004). However, the effect size was small (Cohen's *w*=0.12). In the group of pathological gamblers, participants were significantly older (age 38.2 [SD 12.7] vs. 32.0 [SD 11.7] years, *p*=0.01) and showed a significantly higher educational level (44.9% vs. 29.8% with more than 10 years of school, *p*=0.028), which represents a medium effect size (age: *d*=0.51; educational level: *w*=0.26). Non-participants in the group of pathological gamblers more often had a migration background (53.4% vs. 31.2%, *p*=0.03, small effect size: Cohen's *w*=0.22) and more often reported symptoms of pathological gambling within the last 12 months (41.4% vs. 20.4%, *p*=0.02, small effect size: Cohen's *w*=0.22). In the group of problem gamblers, no differences between participants and non-participants were identified.

The PAGE study controlled for the DSM-IV-criterion B, specifying that pathological gambling is only to be diagnosed if the gambling disorder cannot be better explained by a manic episode. Three participants (1.7%) reported a manic episode in their lifetime but had also gambled independently of their manic episodes. Therefore, they were not excluded.

In this paper, data from participants in the clinical interview were analyzed in terms of comorbid Axis I-disorders and compared with a sample of the general population of the project Transitions in Alcohol Consumption and Smoking (TACOS; Meyer et al., 2000;

Meyer et al., 2001). The TACOS study was conducted from 1996 to 1997 in Northern Germany. Participants were randomly recruited from resident registration office files in Luebeck and 46 surrounding communities (Hapke, Rumpf, Meyer et al., 1998). The final sample included 4,075 individuals. Because all participants in the TACOS study were at least 18 years old, subjects younger than 18 years were excluded from the PAGE sample when comparing both samples.

2.2. Measures

For the classification of pathological or problem gambling (both lifetime and for the last 12 months) in the CATI, the translated version of the Gambling Section of the Composite Diagnostic Interview (CIDI) was used, which is based on the DSM-IV-criteria (WHO, 2009). Kessler et al. found good internal consistency for the CIDI Gambling Section (Cronbach's alpha 0.90; Kessler et al., 2008). In our study, we could replicate the internal consistency reliability with a Cronbach's alpha of 0.88. In the CATI, demographic characteristics (i.e., gender, age, occupational status, migration background, marital status) were also assessed.

The core element of the CAPI was the clinical assessment of comorbid psychiatric disorders with the Munich Composite International Diagnostic Interview (M-CIDI; Wittchen et al., 1995) for lifetime and current Axis I-disorders. In the CIDI, the following diagnoses were included: substance use disorders, anxiety disorders (specific phobia questions had been skipped), and mood disorders. The M-CIDI has a good to excellent test-retest reliability (kappa values 0.55 to >0.72; Wittchen, Lachner, Wunderlich et al., 1998). The following analyses are based on lifetime Axis I-disorders.

The CAPI was conducted by trained interviewers who visited the participants at home. Identical instruments were used in the TACOS study to assess Axis I-disorders.

2.3. Analysis methods

For comparisons with the general population sample, the two data files of the PAGE and TACOS studies were merged. Therefore, participants in PAGE were grouped as at-risk, problem, and pathological gamblers. In the first step, we separately compared the comorbidity of each psychiatric condition between the four groups comprising the general population and the groups defined by the different levels of gambling problems by computing multinomial multivariate regression analyses, which were adjusted for age, sex, and education level. To analyze independent associations of each Axis I-disorder with the different categories of gambling problems, we computed one multinomial regression model including the covariates of the preceding analyses simultaneously. In all multinomial regression analyses, the regression coefficient (Exp[B]) was interpreted in terms of a conditional odds ratio (COR; Gould, 2000). All analyses were performed using SPSS Statistics 20.

3. Results

Sociodemographic characteristics

Of the 164 interviewed adults, 74.4% (n=122) were male, and the mean age was 37.91 (SD 12.26) years. The level of education was twelve or more school years for 55.1% (n=91) of the participants. Additionally, 28.7% (n=47) of the participants were married, and 10.4% (n=17) were unemployed. Chi-square tests found no significant differences between pathological and problem or at-risk gamblers regarding age, marital status, or unemployment. However, participants meeting fewer DSM-IV criteria had significantly more school education (p=0.017), and the rate of females was significantly higher in the groups with 1-2 criteria compared to the groups with 3 or more criteria (p=0.004).

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Lifetime prevalence of Axis I-disorders

The lifetime prevalence of Axis I-disorders is shown in **Table 1**. Due to small group sizes, rare diagnoses were grouped into main diagnostic categories. The rates of any psychiatric disorder were 93.6% in pathological, 83.5% in problem, and 81.0% in at-risk gamblers and 35.7% in the reference sample from the general population. Among all three groups defined by gambling problems, the most prevalent comorbid diagnoses were tobacco dependence and alcohol use disorders, followed by mood disorders and anxiety disorders.

Table 1. Lifetime prevalence of Axis I-disorders in adult at-risk, problem, and pathological gamblers in comparison with the general population

DSM-IV disorders	general population (N=4.075)		at-risk gamblers 1-2 criteria (N=63)		problem gamblers 3-4 criteria (N=52)		pathological gamblers 5-10 criteria (N=47)	
	%	SD	%	SD	%	SD	%	SD
Substance use disorders total	25.8	0.9	65.1	1.0	75.0	0.9	87.2	0.7
Substance dependence without tobacco dependence	9.0	0.6	44.4	1.0	63.5	1.0	63.8	1.0
Alcohol use disorders	8.3	0.6	44.4	1.0	61.5	1.0	61.7	1.0
Illicit drug use disorders	1.2	0.2	17.5	0.8	11.5	0.6	19.1	0.8
Tobacco dependence	20.9	0.8	54.0	1.0	48.1	1.0	68.1	1.0
Mood disorders total	12.3	0.7	49.2	1.0	46.2	1.0	46.8	1.0
Major depression	10.0	0.6	42.9	1.0	40.4	1.0	36.2	1.0
Anxiety disorders total	6.5	0.5	23.8	0.9	32.7	0.9	38.3	1.0
Psychiatric disorders total	35.7	1.0	81.0	0.8	88.5	0.6	93.6	0.5
Psychiatric disorders without tobacco dependence	22.9	0.8	74.6	0.9	86.5	0.7	85.1	0.7
Psychiatric disorders without substance use disorders	16.1	0.7	57.1	1.0	59.6	1.0	61.7	1.0

SD: Standard deviation.

In the category mood disorders, the most prevalent disorder was major depression (c.f. Table 1), followed by dysthymia (at-risk: 7.6%, problem: 13.8%, pathological: 8.2%). In the category anxiety disorders, 16.3% of the pathological gamblers reported a panic disorder with agoraphobia. The second most common anxiety disorder was social phobia (at-risk: 6.1%, problem: 6.9%, pathological: 6.1%). Posttraumatic stress disorder was diagnosed in 3% of the at-risk gamblers, 8.6% of the problem gamblers, and 6.1% of the pathological gamblers.

Table 2 shows separate analyses for each diagnostic category and regression coefficients (interpreted as conditional odds ratios, CORs), which were adjusted for age, gender, and education. Comparing the general population sample with each of the gambling problem groups revealed significantly increased odds for each of the DSM-IV Axis I-disorders ($p<0.001$; c.f. Table 2, columns 1 to 3) among the gamblers. With regard to the major diagnostic categories, the CORs were highest for substance use disorders, followed by anxiety disorders and mood disorders.

When comparing problem gamblers with at-risk gamblers and pathological gamblers (c.f. columns 4 and 5 of Table 2), no significant group differences were found. Pathological gamblers tended to report higher rates for only tobacco dependence compared to problem gamblers (COR: 1.5, Confidence Interval, CI: 1.0-2.3, $p=0.051$).

Additionally, we compared the two "extreme" groups of at-risk gamblers and pathological gamblers (c.f. column 6). The data revealed a significant difference regarding substance use disorders. However, no significant differences were identified in terms of substance-specific subgroups (alcohol, illicit drugs, and tobacco).

Table 2. Multinomial regression analyses to compare psychiatric comorbidity among at-risk, problem, pathological gamblers and the general population.

DSM-IV disorders	at-risk gamblers vs. general population[1]		problem gamblers vs. general population[1]		pathological gamblers vs. general population[1]		problem gamblers vs. at-risk gamblers[1]			pathological gamblers vs. problem gamblers[1]			pathological gamblers vs. at-risk gamblers[1]		
	Exp (B)[2]	(95%-CI)[3]	OR[2]	(95%-CI)[3]	Exp (B)[2]	(95%-CI)[3]	Exp (B)[2]	(95%-CI)	p-value	Exp (B)[2]	(95%-CI)	p-value	Exp (B)[2]	(95%-CI)	p-value
Substance use disorders total	2.4	(1.8-3.1)	2.8	(2.0-3.8)	4.1	(2.7-6.4)	1.2	(0.8-1.8)	0.422	1.5	(0.9-2.5)	0.152	1.7	(1.1-2.9)	0.030
Substance dependence without tobacco dependence	3.0	(2.2-3.9)	3.9	(2.9-5.3)	3.7	(2.7-5.0)	1.3	(0.9-2.0)	0.192	0.9	(0.6-1.5)	0.799	1.2	(0.8-1.9)	0.314
Alcohol use disorders	3.2	(2.4-4.2)	3.9	(2.9-5.3)	3.7	(2.7-5.0)	1.2	(0.8-1.9)	0.302	0.9	(0.6-1.4)	0.766	1.2	(0.8-1.7)	0.485
Illicit drug use disorders	4.1	(2.8-5.9)	3.0	(1.9-4.7)	3.9	(2.6-5.9)	0.7	(0.4-1.3)	0.260	1.3	(0.8-2.3)	0.326	1.0	(0.6-1.6)	0.906
Tobacco dependence	2.2	(1.7-2.8)	1.9	(1.4-2.4)	2.8	(2.0-3.8)	0.9	(0.6-1.2)	0.404	1.5	(1.0-2.3)	0.051	1.3	(0.9-1.9)	0.214
Mood disorders total	3.0	(2.3-3.9)	3.0	(2.2-3.9)	3.1	(2.3-4.2)	1.0	(0.7-1.4)	0.904	1.0	(0.7-1.6)	0.841	1.0	(0.7-1.5)	0.928
Major depression	3.0	(2.3-3.9)	3.0	(2.2-4.0))	2.8	(2.0-3.8)	1.0	(0.7-1.5)	0.951	0.9	(0.6-1.4)	0.768	0.9	(0.6-1.4)	0.715
Anxiety disorders total	2.6	(1.9-3.5)	3.3	(2.4-4.5)	3.8	(2.8-5.3)	1.3	(0.8-2.0)	0.258	1.2	(0.8-1.8)	0.483	1.5	(1.0-2.3)	0.069
Psychiatric disorders total	2.9	(2.1-4.1)	3.8	(2.5-5.8)	5.2	(2.9-9.4)	1.3	(0.8-2.2)	0.354	1.4	(0.7-2.8)	0.392	1.8	(0.9-3.4)	0.095
Psychiatric disorders without tobacco depen-dence	3.5	(2.6-4.6)	4.9	(3.3-7.3)	4.6	(3.0-6.9)	1.4	(0.9-2.3)	0.171	0.9	(0.5-1.7)	0.937	1.3	(0.8-2.2)	0.270
Psychiatric disorders without substance use disorders	3.2	(2.4-4.2)	3.4	(2.6-4.6)	3.7	(2.7-5.0)	1.1	(0.7-1.6)	0.724	1.1	(0.7-1.6)	0.749	1.1	(0.8-1.7)	0.501

[1]Last category is reference category.
[2]Regression coefficients are interpreted in terms of conditional odds ratios (CORs). CORs are adjusted for age, gender, education.
[3]All comparisons with the general population are significant at p<0.001.

To determine whether the associations found were independent of each other, a multinomial multivariate regression analysis was performed, which included the covariates substance use disorders, mood disorders, and anxiety disorders simultaneously (c.f. **Table 3**). The first three columns of Table 3 display CORs for at-risk, problem, and pathological gambling in comparison with the general population. CORs were adjusted for age, gender, and education. The highest CORs for pathological gamblers were found for substance use disorders, followed by anxiety disorders. This analysis revealed that each of the associations shown in Table 2 remained significant, independent of each other.

Table 3. Multinomial multivariate regression analysis to compare psychiatric comorbidity among at-risk, problem, pathological gamblers and the general population.

DSM-IV disorders	at-risk gamblers vs. general population[1]		problem gamblers vs. general population[1]		pathological gamblers vs. general population[1]		problem gamblers vs. at-risk gamblers[1]			pathological gamblers vs. problem gamblers[1]			pathological gamblers vs. at-risk gamblers[1]		
	Exp (B)[2]	(95%-CI)[3]	Exp (B)[2]	(95%-CI)[3]	Exp (B)[2]	(95%-CI)[3]	Exp (B)[2]	(95%-CI)	p-value	Exp (B)[2]	(95%-CI)	p-value	Exp (B)[2]	(95%-CI)	p-value
Substance use disorders total	2.0	(1.5-2.6)	2.3	(1.7-3.2)	3.4	(2.2-5.2)	1.2	(0.8-1.8)	0.460	1.5	(0.9-2.5)	0.167	1.7	(1.0-2.9)	0.039
Mood disorders total	2.4	(1.8-3.2)	2.1	(1.6-2.9)	2.0	(1.5-2.8)	0.9	(0.6-1.3)	0.540	1.0	(0.6-1.5)	0.837	0.8	(0.6-1.3)	0.420
Anxiety disorders total	1.7	(1.2-2.4)[4]	2.2	(1.6-3.1)	2.5	(1.8-3.6)	1.3	(0.8-2.0)	0.251	1.1	(0.7-1.8)	0.577	1.5	(0.9-2.3)	0.091

[1]Last category is always reference category.
[2]Regression coefficients are interpreted in terms of conditional odds ratios (CORs). CORs are adjusted for age, gender, education.
[3]All comparisons with the general population are significant at p<0.001 unless otherwise indicated.
[4]p=0.002.

Columns 4 and 5 of Table 3 show the comparisons between problem gamblers and at-risk gamblers and pathological and problem gamblers. No significant differences between these pairs were found. As shown in column 6, comparisons between the "extreme" groups of at-risk gamblers and pathological gamblers revealed a significant difference regarding substance use disorders.

4. Discussion

The PAGE study is the first general population-based study comparing at-risk and problem gambling with pathological gambling regarding Axis I comorbidities.

The data revealed that the prevalence rates of comorbid lifetime DSM-IV disorders were significantly elevated compared to the general population. These results are generally consistent with the NCS-R and the NESARC studies. In the NCS-R, 96.3% of pathological gamblers had at least one lifetime comorbid disorder compared to 93.6% in the PAGE study (Kessler et al., 2008). In comparison with the NESARC data (Petry et al., 2005), the lifetime prevalence of alcohol use disorders among pathological gamblers was lower (PAGE: 61.7%, NESARC: 73.2%), whereas the results were similar regarding mood disorders (PAGE: 46.8%, NESARC: 49.6%) and anxiety disorders (PAGE: 38.3%, NESARC: 41.3%). The numeric differences in the prevalence of alcohol use disorders between the PAGE study and the NESARC are most likely explained by national variations or methodological differences. The NESARC used the "Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version" (AUDADIS-IV, Grant et al., 2003) to diagnose pathological gambling and comorbid disorders, whereas the PAGE study used the M-CIDI.

Axis I-disorders in the PAGE study were numerically most prevalent in pathological gamblers (any lifetime psychiatric disorder: 93.6%). Regression analyses revealed an elevated risk for all three groups of gamblers (at-risk gamblers, problem, and pathological gamblers) for having a comorbid lifetime Axis I-disorder in comparison to the general population. In contrast, there were no significant differences concerning the

risk for having a comorbid lifetime Axis I-disorder between at-risk and problem gamblers or problem and pathological gamblers. When comparing at-risk and pathological gamblers, the data revealed a significant difference in univariate and multivariate analyses between the two groups regarding substance use disorders. This significant difference could not be replicated in univariate sub-analyses of alcohol misuse or dependence, tobacco dependence, or illegal drug misuse or dependence. The COR for substance use disorders in the multivariate regression model was elevated for pathological gamblers compared to at-risk gamblers. Nevertheless, the difference was not due to a specific substance use disorder. However, the present study might not have been sufficiently powered to detect such differences.

Additionally, a tendency (not significant) toward mood and anxiety disorders was found in the comparison between the two "extreme" groups. Again, the group sizes may have been too small to find significant differences. Nevertheless, the results suggest that there is a linear association between gambling disorder severity and comorbid Axis I-disorders, at least for substance use disorders, although further investigations with larger sample sizes are necessary.

Surprisingly, the findings indicate that even gamblers with only 1 or 2 DSM-IV criteria can suffer from a burden of psychiatric comorbidity comparable to individuals fulfilling more criteria for pathological gambling. A possible explanation could be that individuals with psychiatric disorders are particularly vulnerable to developing gambling problems. Gambling could function as a coping strategy to handle psychological strains. This possibility is supported by a recent review examining studies on older gamblers, which found that loneliness and low social support served as risk factors for developing a gambling problem (Tse, Hong, Wang et al., 2012). Because the trajectories of gambling disorders are not yet clear, a more intense examination of at-risk gamblers appears necessary. To date, subthreshold gamblers are not the focus of research or treatment options. Given that only a small percentage of pathological gamblers seek treatment for their gambling problems (Bischof, Meyer, Bischof et al., 2012; Erbas and Buchner,

2012; Slutske, 2006), the rate of treatment seeking in at-risk gamblers will be negligible.

The results indicate that gambling problems in general are highly associated with comorbid psychiatric disorders independent of the cut-off value for pathological gambling. In contrast to the common practice in problem gambling research, our data clearly do not support a threshold for problem gambling of 3 criteria with respect to comorbid disorders. The PAGE findings are in line with the modifications to the diagnostic criteria for pathological gambling in the DSM-5 (American Psychiatric Association, 2012). Pathological gambling will no longer be classified as an impulsive control disorder but as a substance-related disorder. The threshold for pathological gambling will be lowered to 4 instead of 5 criteria (and the original 10 criteria in the DSM-IV will be reduced to 9 criteria in the DSM-5), which will also influence the description and handling of "problem gambling" or subthreshold diagnoses of gambling disorders. Our data support these changes.

In a recent review, neuropsychological and biochemical aspects of pathological gambling are discussed in terms of other addictions (Conversano, Marazziti, Carmassi et al., 2012). Results showed that especially impaired decision making and a dysfunctional executive system are associated with pathological gambling. Further research is needed in order to determine the association of neurobiological aspects with subthreshold gambling problems.

Some limitations of the study have to be noted. We were only able to include a limited subsample of individuals for the clinical interview. Differences between study participants and eligible non-participants were found primarily among pathological gamblers with regard to the number of symptoms, migration background, education level, and age. Differences between participants with at-risk gambling and eligible non-participants with 1-2 criteria were found regarding education level. The sample sizes of all three groups were rather small, restricting the statistical power of our analyses. Thus, smaller differences are likely to have been overlooked. Additionally, the analysis

of gender differences in terms of patterns of Axis I-disorders was precluded due to the small sample size. The timeframes of the two surveys (PAGE and TACOS) also differed. Changes in psychiatric morbidity in the general population over the last 14 years cannot be excluded. However, it is rather unlikely that this would reach such a magnitude that the findings of this study would be affected. Furthermore, the TACOS project represents the general population of a distinct region of Germany, and the possibility of an influence of regional differences cannot be completely discarded. One nationwide study, the German Health Interview and Examination Survey (GHS), showed slightly higher prevalence rates than the TACOS project (Jacobi, Wittchen, Holting et al., 2004). However, this study primarily covered 12-month diagnoses, and lifetime data were not available for all diagnostic groups analyzed in the PAGE study. Thus, we have to consider that the national rates of psychiatric morbidity are slightly underestimated in the TACOS sample. However, given the size of the CORs identified in the present analysis, we assume that elevated psychiatric comorbidity in the PG groups cannot be attributed to the varied time frames of the two studies.

In conclusion, the data from the PAGE study provide important information regarding Axis I-disorder comorbidity in persons with at-risk, problem, and pathological gambling. Subthreshold diagnoses are highly related to psychiatric comorbidity, even if just 1 or 2 DSM-IV criteria are fulfilled. These data are necessary for considering clinical implications, particularly in terms of highly comorbid at-risk gamblers. The findings should be discussed in terms of treatment necessities. Further research should focus on at-risk gambling, the trajectories of gambling problems with associated comorbid disorders, and the influence of comorbidity on brief intervention and treatment in problem gambling.

Acknowledgments

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8. Discussion

The PAGE-study was the first study in Germany that assessed comorbid Axis I-disorders among at-risk, problem, and pathological gamblers from a general population sample. These data can be seen as representative, although only a subsample of eligible gamblers could be analyzed in this study. The present study was the first one to compare subgroups of gamblers (at-risk, problem, and pathological gamblers) to a sample of the general population regarding Axis I-disorders. The results showed that prevalence proportions of psychiatric conditions were extraordinary high in all three groups of gamblers compared to the general population.

Data revealed that rates of Axis I-disorders among pathological gamblers in the PAGE-study were in accordance with rates of previous international population-based studies as NESARC and the NCS-R-study (Kessler et al., 2008; Petry et al., 2005).

When comparing pathological gamblers with problem gamblers, no significant differences regarding Axis I-disorders could be found. The same results were found to be valid for the comparison of problem gamblers with at-risk gamblers. Tendencies of difference were found between at-risk gamblers and pathological gamblers regarding substance use disorders and mood and anxiety disorders. However, these differences were not found to be significant, probably due to small sample sizes. Nevertheless, these results indicate a linear association between gambling problems and psychiatric conditions.

All comparisons between PAGE and the general population sample were significant, even in the group with only 1-2 DSM-IV criteria for pathological gambling. Data suggest that gamblers in general might be a highly vulnerable group that suffers from a heavy burden even if clinical symptoms of pathological gambling are not fulfilled. The recently published DSM-5 has partially taken this problem into account when lowering the threshold of pathological gambling from 5 to 4 criteria. However, the classification of the disorder in "mild" (4-5 criteria), "moderate" (6-7 criteria), and "severe" (8-9 criteria) gambling disorder (American Psychiatric Association, 2013) does not take into account subthreshold gambling with 1-3 criteria. Our data would clearly support further considerations of observing subclinical gambling.

Some limitations of the presented data have to be mentioned. Since PAGE was a cross-sectional study, no causal conclusions can be drawn. The analyzed data were lifetime data, onset of gambling disorder and/or Axis I-disorder were not topic of the analysis. The coincidence of gambling problems and psychiatric disorder was not analyzed. Nevertheless, it can be assumed that the extraordinary high prevalence rates

of Axis I-disorders are associated with the gambling behavior and the development of problematic gambling. Further studies are necessary to examine trajectories of gambling behavior. The examined subsamples of gamblers were rather small, so the statistical power of the analysis was restricted. Therefore, gender differences could not be taken into account. Moreover, smaller differences are likely to have been overlooked. Additionally, there were differences between study participants and non-participants, explained in the article. Finally, the timeframes of the two compared studies (PAGE and TACOS) differ. Therefore, changes in psychiatric morbidity of the general population of today cannot be excluded.

Nevertheless, data of the present study provide important results regarding the burden of psychiatric morbidity among different subsamples of individuals with gambling problems from the general population. These data can help to understand the complexity of problematic gambling, the psychological strains that distress the affected persons and might help to foster treatment services that reach gamblers at an early stage of the disorder.

The adverse consequences that come along with pathological gambling as financial strains, social stress, and the oppressiveness of keeping the gambling addiction secret (American Psychiatric Association, 1995; Hodgins et al., 2011; Johansson et al., 2009), are intensified by the burden of psychiatric disorders. The finding that even gamblers with just few criteria suffer from this burden makes pathological gambling to a disorder with special public health concern, even if the prevalences are – in general – low. As discussed in the paper, gambling could be a coping strategy for handling psychological strains as loneliness and low social support (Tse, Hong, Wang et al 2012). Concerning neuropsychological and biochemical aspects of pathological gambling, results of recent studies showed that impaired decision making and a dysfunctional executive system are associated with gambling disorders (Conversano et al., 2012). To what extent these neuropsychological characteristics are associated with additional comorbid psychiatric disorders and how these aspects have an influence on subthreshold gambling problems needs further research.

Given that gamblers especially on electronic gambling machines have a high chance (OR 6.3; Meyer et al., 2011) to develop an addiction, further actions concerning the legal framework, the protection of gamblers, and restrictions of profit and advertising of the gambling industry are coercively required. Highway rest areas with 24 hours openings of slot machine halls, advertising addressing young adults, television advertising of poker events with celebrities are of special concern and should be restricted.

To date, gamblers with less than five criteria (DSM-IV) are not in the focus of the treatment system and only very few studies have analyzed individuals with non-clinical gambling problems. Our data suggest that this group of gamblers should "enter the stage" in both research and help system. We know that only a minority of pathological gamblers seek treatment for their gambling problems (Bischof et al., 2012; Erbas and Buchner, 2012; Slutske, 2006), and it seems unlikely that individuals with less severe gambling problems can be reached more easily. At the same time, data from the PAGE study revealed that comorbid axis I-disorders were significantly associated with treatment seeking behavior among pathological gamblers (Bischof, Meyer, Bischof et al., in press; Bischof, Meyer, Bischof et al., submitted). Early interventions and prevention programs addressing subthreshold gambling problems appear to be necessary. However, longitudinal research concerning the persistence of problematic gambling is required.

To date, several barriers to treatment are recognized among pathological gamblers: insufficient availability of treatment services, shame and worry about stigmatization, lacking knowledge of treatment services, one's own lacking problem awareness, and the belief that the problems can be resolved by (Hodgins and El-Guebaly, 2000; Laging, 2009; Rockloff and Schofield, 2004; Suurvali, Cordingley, Hodgins et al., 2009). It can be assumed that these barriers are much more present in at-risk and problem gamblers, since adverse consequences might not yet be as apparent as in pathological gamblers, and problem awareness is likely to be perceived less. Thus, proactive low-threshold treatment offers are needed that can reach this special population of gamblers. One opportunity is to use short screening questionnaires in the anamnesis in treatment facilities like psychiatries, counseling services, or among psychologists in private practice to detect gambling problems among help-seeking individuals. Because of the association of problematic gambling with comorbid psychiatric disorders, it is likely that concerned individuals will enter treatment during lifetime regarding other Axis I-disorders. Validated short screenings like the Lie and Bet Questionnaire (Johnson, Hamer, and Nora, 1998) or the NODS-Clip (to date only in English; Toce-Gerstein, Gerstein, and Volberg, 2009) could be appropriate measurements.

Moreover, appropriate brief interventions for subthreshold gambling problems have to be tested and implemented. International studies have shown that brief motivational treatment is effective in pathological gamblers (Hodgins, 2005; Larimer, Neighbors, Lostutter et al., 2011; Petry, Weinstock, Ledgerwood et al., 2008; Petry, Weinstock, Morasco et al., 2009). Further research is needed to see, if these interventions can also reach a broader target population.

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10. Statutory Declaration

I declare that I have developed and written the enclosed Master Thesis completely by myself, and have not used sources or means without declaration in the text. Any thoughts from others are clearly marked. The Master Thesis was not used in the same or in a similar version to achieve an academic grading or is being published elsewhere.

Lübeck,

(Anja Bischof)