A comparison of DSM-5 and DSM-IV agoraphobia in the World Mental Health Surveys

Annelieke M. Roest (PhD)[1], Ymkje Anna de Vries (PhD)[1], Carmen C. W. Lim (MSc)[2], Hans-Ulrich Wittchen (PhD)[3,4], Dan J. Stein (MD, PhD)[5], Tomasz Adamowski (MD, PHD)[6], Ali Al-Hamzawi (MD)[7], Evelyn J. Bromet (PhD)[8], Maria Carmen Viana (MD, PhD)[9], Giovanni de Girolamo (MD)[10], Koen Demyttenaere (MD, PhD) [11], Silvia Florescu (MD, PhD)[12], Oye Gureje (MD, PhD)[13], Josep Maria Haro (MD, PhD)[14], Chiyi Hu (MD, PhD)[15], Elie G. Karam (MD)[16], José Miguel Caldas-de-Almeida (MD, PhD)[17], Norito Kawakami (MD, DMSc)[18], Jean Pierre Lépine (MD, HDR)[19], Daphna Levinson (PhD)[20], Maria E. Medina-Mora (PhD) [21], Fernando Navarro-Mateu (MD, PhD)[22], Siobhan O'Neill (PhD)[23], Maria Piazza (ScD, MPH)[24], José A. Posada-Villa (MD)[25], Tim Slade (PhD)[26], Yolanda Torres (MPH, Dra.HC)[27], Ronald C. Kessler (PhD)[28], Kate M Scott (PhD) [29], Peter de Jonge (PhD)[1].

[1]Department of Developmental Psychology, University of Groningen, Groningen, The Netherlands.
[2]Queensland Centre for Mental Health Research, and Queensland Brain Institute, University of Queensland, St. Lucia, Queensland, Australia
[3]Institute of Clinical Psychology and Psychotherapy, Technische Universität Dresden, Dresden, Germany.
[4]Department of Psychiatry and Psychotherapy, Ludwig-Maximilans-University Munich, Germany.
[5]Department of Psychiatry and Mental Health, University of Cape Town, Cape Town, Republic of South Africa.
[6]Department of Psychiatry, Medical University of Wroclaw, Wroclaw, Poland.
[7]College of Medicine, Al-Qadisiya University, Diwania governorate, Iraq.
[8]Department of Psychiatry, Stony Brook University School of Medicine, New York, NY, United States.
[9]Department of Social Medicine and Post-Graduate Program in Public Health. Psychiatric Epidemiology Research Center (CEPEP), Federal University of Espírito Santo (UFES), Vitória, Brazil.
[10]IRCCS St John of God Clinical Research Centre, IRCCS Centro S. Giovanni di Dio Fatebenefratelli, Brescia, Italy.
[11]Department of Psychiatry, University Hospital Gasthuisberg, Katholieke Universiteit Leuven, Leuven, Belgium.
[12]National School of Public Health, Management and Professional Development, Bucharest, Romania.
[13]Department of Psychiatry, University College Hospital, Ibadan, Nigeria.
[14]Parc Sanitari Sant Joan de Déu, CIBERSAM, Universitat de Barcelona, Barcelona, Spain.
[15]Shenzhen Insitute of Mental Health & Shenzhen Kangning Hospital, Shenzhen, China.
[16]Department of Psychiatry and Clinical Psychology, Faculty of Medicine, Balamand University; Department of Psychiatry and Clinical Psychology, St George Hospital University Medical Center; Institute for Development Research Advocacy and Applied Care (IDRAAC), Beirut, Lebanon.

[17]Lisbon Institute of Global Mental Health and Chronic Diseases Research Center (CEDOC) and Department of Mental Health, Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisbon, Portugal.

[18]Department of Mental Health, School of Public Health, The University of Tokyo, Tokyo, Japan.

[19]Hôpital Lariboisière Fernand Widal, Assistance Publique Hôpitaux de Paris, University Paris Diderot and Paris Descartes, Paris, France.

[20]Ministry of Health Israel, Mental Health Services, Israel.

[21]National Institute of Psychiatry Ramon de la Fuente, Mexico.

[22]IMIB-Arrixaca;CIBERESP-Murcia; UDIF-SM, Subdirección General de Salud Mental y Asistencia Psiquiátrica, Servicio Murciano de Salud, El Palmar (Murcia), Spain.

[23]School of Psychology, Ulster University, Northern Ireland.

[24]National Institute of Health, Peru, Universidad Cayetano Hereidia, Peru.

[25]Colegio Mayor de Cundinamarca University, Bogota, Colombia.

[26]National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia.

[27]Center for Excellence on Research in Mental Health, CES University, Medellin, Colombia.

[28]Department of Health Care Policy, Harvard University Medical School, Boston, MA, United States.

[29] Department of Psychological Medicine, University of Otago, Dunedin, Otago, New Zealand.

Short title: Epidemiology of DSM-5 agoraphobia

Word count: 3726

Corresponding author:

Annelieke M. Roest, PhD,
Assistant Professor
Faculty of Behavioural and Social Sciences, Department Developmental Psychology
University of Groningen
Grote Kruisstraat 2/1
9712 TS Groningen
The Netherlands

Conflict of interest

In the past 3 years, Dr. Stein has received research grants and/or consultancy honoraria from AMBRF/Foundation for Alcohol Research, Biocodex, Cipla, Lundbeck, National Responsible Gambling Foundation, Novartis, Servier, and Sun. Dr. Demyttenaere has served on advisory boards for, for Eli Lilly, Lundbeck, Johnson&Johnson, Servier, Boehringer Ingelheim, Livanova and has research grants from Eli Lilly, foundation 'ga voor geluk', Fonds voor Wetenschappelijk Onderzoek Vlaanderen.

 In the past 3 years, Dr. Kessler received support for his epidemiological studies from Sanofi Aventis; was a consultant for Johnson & Johnson Wellness and Prevention, Sage Pharmaceuticals, Shire, Takeda; and served on an advisory board for the Johnson & Johnson Services Inc. Lake Nona Life Project. Kessler is a co-owner of DataStat, Inc., a market research firm that carries out healthcare research.

Authors Roest, de Vries, de Jonge, Wittchen, Lim, Adamowski, Carmen Viana, Florescu, Kawakami, Slade, Torres, Posada-Villa, Lépine, Al-Hamzawi, Levinson, de Girolamo, Karam, Elena Medina Mora, Gureje, O'Neill, Hu, Piazza, Miguel Caldas-de-Almeida, Maria Haro, Navarro-Mateu, Bromet, and Scott do not have conflicts of interest to report.

Abstract

Background: The DSM-5 definition of agoraphobia (AG) as an independent diagnostic entity makes it timely to re-examine the epidemiology of AG. Study objective was to present representative data on the characteristics of individuals who meet DSM-IV criteria for AG (AG without a history of panic disorder [PD] and PD with AG) but not DSM-5 criteria, DSM-5 but not DSM-IV criteria, or both sets of criteria.

Methods: Population-based surveys from the World Mental Health Survey Initiative including adult respondents (n=136,357) from 27 countries across the world. The Composite International Diagnostic Interview was used to assess AG and other disorders.

Results: Lifetime and 12-month prevalence estimates of DSM-5 AG (1.5% and 1.0%) were comparable to DSM-IV (1.4% and 0.9%). Of respondents meeting criteria in either system, 57.1% met criteria in both, while 24.2% met criteria for DSM-5 only and 18.8% for DSM-IV only. Severe role impairment due to AG was reported by a lower proportion of respondents who met criteria only for DSM-IV AG (30.4%) than those with both DSM-5 and DSM-IV AG (44.0%) (χ^2_1=4.7;p=.031). The proportion of cases with any comorbidity was lower among respondents who met criteria only for DSM-IV AG (78.7%) than those who met both sets (92.9%) (χ^2_1=14.5;p<.001).

Conclusions: This first large survey shows that, compared to the DSM-IV, the DSM-5 identifies a substantial group of new cases with AG, while the prevalence rate remains stable at 1.5%. Severity and comorbidity are higher in individuals meeting DSM-5 AG criteria compared with individuals meeting DSM-IV AG criteria only.

Introduction

Anxiety disorders are highly prevalent and are major contributors to the burden of disease worldwide (Craske et al., 2017; Murray et al., 2012; Whiteford et al., 2013). Agoraphobia (AG) is one of the least studied anxiety disorders (Asmundson & Asmundson, 2018), and, especially with the introduction of the Diagnostic and Statistical Manual of mental disorders version 5 (DSM-5), there is a lack of research focusing on AG including the cross-national epidemiology of AG.

In the DSM-IV, unlike the International Classification of Diseases (ICD-10), AG was not defined as an independent disorder with specific diagnostic criteria, but instead was described as a residual group only to be coded in the presence or absence of panic disorder (PD) (i.e. PD with AG (300.21), or AG without a history of PD (300.22)) (American Psychiatric Association, 2000). AG was defined as anxiety about being in places or situations from which escape might be difficult (or embarrassing) or in which help may not be available in the event of having a panic attack or panic-like symptoms. These situations had to be avoided, endured with marked distress or with anxiety about having a panic attack or panic-like symptoms, or require the presence of a companion (American Psychiatric Association, 2000).

In DSM-5, which was introduced in 2013, AG is defined as a phobic disorder cued by exposure to agoraphobic situations. As a result, PD (300.01) and AG (300.22) are unlinked, (American Psychiatric Association, 2013; Asmundson, Taylor, & Smits, 2014) consistent with the ICD-10 criteria for AG (F40.0) and PD (F41.0) (World Health Organization, 2016). The decision to classify AG as a disorder that exists separately from PD was based on studies indicating that a substantial proportion of individuals with AG do not have PD (Kessler et al., 2006; Wittchen, Gloster, Beesdo-Baum, Fava, & Craske, 2010), and/or PD or panic attacks do not precede AG (as implied in DSM-IV) (Wittchen, Reed, & Kessler, 1998; Wittchen et al., 2008; Wittchen et al., 2010). As a result, individuals with AG, but without panic-like symptoms, received no formal diagnosis while they showed substantial impairment and disability (Wittchen et al., 2010). Further, DSM-5 criterion A is broadened to a fear or

avoidance of situations because of thoughts that escape might be difficult or help might not be available in the event of developing panic-like symptoms *or other incapacitating or embarrassing symptoms (e.g., fear of falling in the elderly; fear of incontinence)*.(American Psychiatric Association, 2013) This is in line with the ICD criteria, in which AG is understood to be the consequence of a broader range of fears (Kogan et al., 2016; Stein, 2012; Wittchen et al., 2010). In order to make a better distinction from specific phobia (SP), endorsement of fears from two or more *distinct* situational domains is required in DSM-5. Finally, the DSM-5 criteria for AG are extended compared to the DSM-IV criteria to make them more comparable to other (anxiety) disorders, for instance by adding persistence and severity requirements (American Psychiatric Association, 2013; Asmundson et al., 2014).

These changes in DSM-5 call for a re-examination of epidemiological data on AG. The available information is difficult to evaluate because most studies have examined AG only in individuals without a history of PD (Goodwin et al., 2005). As a result, the prevalence of AG (Goodwin et al., 2005) and the impairment due to AG has likely been underestimated. Furthermore, there is a lack of information on age of onset (AOO) (Wittchen et al., 2010), sociodemographic correlates, and comorbidity patterns of AG.(Goodwin et al., 2005). Therefore, the aim of the current study is to present and compare data on characteristics of AG according to DSM-5 and DSM-IV criteria (AG without a history of PD and PD with AG) from countries in the World Health Organization (WHO) World Mental Health (WMH) Survey Initiative.

Methods

Survey samples

Data came from 27 surveys administered in low/lower-middle income countries, upper-middle income countries, and high-income countries. A total of 136,357 respondents participated. Interviews were conducted face-to-face in respondent homes. Adults were selected based on multi-stage clustered area probability sampling designs designed to generate samples that were

representative of the household populations in the countries. The details of within-country sampling methods are described in detail elsewhere (Heeringa et al., 2008; Pennell et al., 2008).

Ethics, consent and permissions

Informed consent was obtained according to protocols endorsed by local Institutional Review Boards.

Measures

Mental disorders

Mental disorders were assessed with the WHO Composite International Diagnostic Interview (CIDI), a fully-structured interview administered by trained lay interviewers, which generates diagnoses according to the criteria of the DSM-IV (Kessler & Ustün, 2004). To reduce respondent burden, interviews were administered in 2 parts. All respondents completed Part I of the CIDI, assessing core mental disorders. Part II, which assessed other disorders and correlates, was administered to all respondents with any lifetime Part I diagnosis and a probability subsample of other Part I respondents. The Part II data were weighted to adjust for the under-sampling of Part I non-cases so that weighted prevalence estimates in the Part II sample are identical to those in the Part I sample.

The disorders include anxiety disorders (PD, AG, generalized anxiety disorder [GAD], social anxiety disorder, SP, posttraumatic stress disorder [PTSD][1], separation anxiety disorder), mood disorders (major depressive episode and/or dysthymia, bipolar disorder [I, II or subthreshold]), disruptive behavior disorders (intermittent explosive disorder, bulimia nervosa, binge eating disorder, oppositional defiant disorder, conduct disorder, attention deficit disorder), and substance use disorders (alcohol abuse and drug abuse, both with or without dependence). These diagnoses have shown generally good concordance with clinical diagnoses based on blinded Structured Clinical

---

[1] In DSM-5 PTSD is no longer listed as an anxiety disorder but instead falls under "trauma- and stressor-related disorders".

Interview (SCID) reappraisal (Haro et al., 2006). The AOO of AG was assessed using special recall probes that have been shown to yield more plausible distributions of AOO of disorders than conventional recall questions (Knäuper, Cannell, Schwarz, Bruce, & Kessler, 1999).

For purposes of the current analysis, DSM-5 AG diagnoses were generated retrospectively; a series of questions were used to operationalize DSM-5 AG criteria (see supplemental table 1 for the DSM-IV and DSM-5 criteria and corresponding CIDI algorithms). We defined three diagnostic groups: respondents who only met DSM-IV criteria (AG without a history of PD and PD with AG) ("DSM-IV only AG"), respondents who only met DSM-5 criteria ("DSM-5 only AG"), and respondents who met both DSM-5 and DSM-IV criteria ("DSM-5 with DSM-IV AG").

Impairment

Severe role impairment in home management, ability to work, ability to form and maintain close relationships, and social life was assessed with a modified version of the Sheehan Disability Scale (SDS) in respondents with 12-month AG (Leon, Olfson, Portera, Farber, & Sheehan, 1997). The response scale for each role domain is from 0-10. Severe impairment was defined as a score ≥7 in at least one specific role domain. Respondents with 12-month AG were also asked how many days in the past year they were totally unable to work or carry out their normal activities due to their AG (Ormel et al., 2008). Additionally, all Part II respondents were asked how many days in the past 30 days they were totally unable to work or carry out their normal activities because of any physical or mental health problems. Finally, all Part I respondents were asked whether they seriously thought about committing suicide in the past 12 months.

 Treatment

Respondents were asked whether they ever saw each of a long list of professionals. Responses were aggregated into treatment in the specialty mental health sector (e.g.

psychiatrist/psychologist), general medical sector (e.g. general practitioner), human services sector (e.g. social worker), and complementary and alternative medicine (CAM) sector (e.g. herbalist).

Socio-demographic correlates

Factors considered include gender, age cohorts (18-34, 35-49, 50-64, 65+), education level (low, low-average, high-average, high), marital status (married, never married, previously married), and employment status (employed, student, homemaker, retired, other).

Statistical analysis

The actuarial method was used to generate AOO survival curves, and differences in age of onset between DSM-IV only AG, DSM-5 only AG, and DSM-5 with DSM-IV AG were tested using discrete-time logistic regression in the subsample with DSM-IV or DSM-5 AG. Logistic regression analysis was used to evaluate the significance of differences in role impairment, suicidality, comorbidity, and treatment between DSM-IV only AG, DSM-5 only AG, and DSM-5 with DSM-IV AG cases, and between AG cases and non-cases (where applicable). Logistic regression was also used to compare socio-demographic correlates of DSM-IV only AG, DSM-5 only AG, and DSM-5 with DSM-IV AG. All analyses were carried out in SAS (9.4). Because the data were clustered and weighted to account for unequal selection probabilities, standard errors were estimated using the Taylor series linearization method (Wolter, 1985) implemented in SUDAAN (11.0.1) (Research Triangle Institute, 2002). Significance tests were evaluated using 0.05-level two-sided tests.

Results

Prevalence and course of AG

Lifetime and 12-month prevalence estimates of DSM-IV AG were 1.4% and 0.9%, while those of DSM-5 AG were 1.5% and 1.0% (table 1). Consistent with DSM-IV criteria, 100% of cases with DSM-IV AG experienced fear of panic attacks, compared to 70.2% of cases with DSM-5 AG. Of all

respondents with lifetime PD (prevalence of 1.7%), 19.7% met criteria for DSM-IV AG and 18.2% for DSM-5 AG (supplemental table 2).

Of all respondents with lifetime AG, 57.1% (SE=1.3) met criteria for both DSM-5 and DSM-IV AG, 18.8% (SE=1.0) only met criteria for DSM-IV, and 24.2% (SE=1.1) only met criteria for DSM-5. DSM-5 only lifetime cases had a significantly lower lifetime proportion with PD (9.3%) than DSM-5 with DSM-IV cases (26.5%) (χ^2_1=54.3;p<.001) and DSM-IV only cases (19.3%) (χ^2_1=20.9;p<.001). Respondents with DSM-5 with DSM-IV AG had higher persistence (i.e.12-month prevalence among lifetime cases; 71.2%) than DSM-IV only (51.9%) (χ^2_1=47.1;p<.001) and DSM-5 only (64.1%) (χ^2_1=6.2;p=.012) cases. DSM-5 only cases also had a significantly higher persistence than DSM-IV only cases (χ^2_1=18.6;p<.001).

(Table 1)

The median AOO of DSM-5 only AG was 14 years old (interquartile range [IQR] = 9-25), which was significantly lower than the median AOO of DSM-IV only AG (median=23, IQR=13-41) and of DSM-5 with DSM-IV AG (median=21, IQR=13-39 (χ^2=21.8-24.4;p<.001) (supplemental figure 1). The AOO of DSM-IV only AG and DSM-5 with DSM-IV AG did not differ significantly (χ^2=0.3, p=0.55).

Impairment

Severe role impairment in the past 12 months was reported by 30.4% of respondents with DSM-IV only AG, 43.3% of respondents with DSM-5 only AG, and 44.0% of respondents with DSM-5 with DSM-IV AG, with a significant difference between DSM-IV only and DSM-5 with DSM-IV AG (χ^2_1=4.7;p=.031). Mean number of days out of role in the past year due to AG was also significantly lower among respondents with DSM-IV only AG (29.9) compared with DSM-5 with DSM-IV AG (55.8) (χ^2_1=8.0;p=.005), while that for DSM-5 only AG (40.2) did not differ from DSM-IV only AG (χ^2_1=2.1;p=0.147) or DSM-5 with DSM-IV AG (χ^2_1=1.7;p=0.190). Although suicidal ideation rates were higher for all AG subgroups compared to respondents without AG (1.7%), there were no significant

differences in suicidal ideation rates among respondents with DSM-IV only (10.0%), DSM-5 only (15.7%), or DSM-5 with DSM-IV (15.8%) AG (table 2).

(Table 2)

Comorbidity

Respondents in all AG subgroups reported higher rates of lifetime and 12-month mental disorder comorbidity compared to respondents without AG, except for 12-month substance use disorders in the DSM-IV only AG subgroup (χ^2_1=0.7;p=0.39) (table 3). Comorbidity rates were significantly lower for respondents with DSM-IV only (3.5–78.7%) than for respondents with DSM-5 with DSM-IV AG (8.1–92.9%), except for 12-month disruptive behavior disorders and 12-month and lifetime substance use disorders. Respondents with DSM-5 only AG did not have a significantly lower rate of comorbidity (12.6–88.7%) than respondents with DSM-5 with DSM-IV AG for any disorder category except any lifetime disorder (χ^2_1=4.4;p=0.036). Also, they reported a significantly higher rate of comorbidity than respondents with DSM-IV only AG for 12-month anxiety disorder (χ^2_1=6.9;p=0.009) and lifetime anxiety disorders (χ^2_1=7.1;p=0.008).

(Table 3)

Treatment

Respondents in all AG subgroups were more likely to receive any lifetime treatment (31.0-52.8%) than respondents without AG (8.4%), but respondents with DSM-IV only AG were significantly less likely than respondents with DSM-5 with DSM-IV AG to receive any lifetime treatment (table 4). They were also less likely than respondents with DSM-5 with DSM-IV AG to receive 12-month specialty mental health care or any 12-month treatment but not less likely to receive 12-month general medical care, human services, or CAM treatment. Respondents with DSM-5 only AG were significantly less likely to receive any type of treatment than respondents with DSM-5 with DSM-IV AG with the exception of human services or CAM treatment. There were no significant differences in

treatment rates between respondents with DSM-IV only AG and those with DSM-5 only AG, with the exception of lifetime human services (χ^2_1=5.5,p=.019).

(Table 4)

Sociodemographic correlates

Younger age, female gender, lower education, not being married, and unemployment were associated with 12 month- and lifetime AG, although some associations did not reach statistical significance for one or more of the diagnostic groups (table 5). As a group, the ORs for age cohort for DSM-5 only AG differed from the ORs for DSM-5 with DSM-IV AG, yet p-values for comparing ORs between specific age groups were not statistically significant. Compared to high education, odds for respondents with low, low-average, and high-average education, were particularly high for DSM-IV only AG.

(Table 5)

Discussion

This study is the first to present representative data for DSM-5 compared to DSM-IV AG (AG without a history of PD and PD with AG) from countries across the world. Lifetime and 12-month prevalence estimates of DSM-5 AG were 1.5% and 1.0%, while those of DSM-IV AG were 1.4% and 0.9%. Hence, there was no marked shift in AG prevalence from DSM-IV to DSM-5. However, only 57.1% of respondents with AG met criteria in both diagnostic systems, with 18.8% of AG cases meeting criteria only for DSM-IV and 24.2% meeting criteria only for DSM-5. Compared to DSM-IV AG, DSM-5 AG was characterized by a higher persistence of AG and higher rates of severe role impairments, treatment-seeking, and mental disorder comorbidity.

Several sociodemographic correlates of AG were identified, consistent with other studies of AG and PD (Andrews & Slade, 2002; Jonge et al., 2016). Although some quantitative differences were

13

found for associations between sociodemographic factors and diagnostic subgroups, the general patterns were comparable, with younger age, female gender, lower education, not being married, and unemployment being associated with AG.

Although our prevalence rates are comparable to the reported prevalence of 12-month DSM-IV AG without a history of PD across European countries (1.3%) (Goodwin et al., 2005), they are in contrast with the extremely low prevalence rate of 0.05% for 12-month DSM-IV AG without a history of PD found in a nationally representative study in the US, which may (partly) result from the exclusion of lifetime PD cases and a clinical significance criterion used in that study (Grant et al., 2006). Although our 12-month prevalence rate of DSM-IV AG increased by including AG with PD, it is interesting to note that 75% of respondents with 12-month DSM-IV AG did not have a history of PD. This percentage is comparable to that found for 12-month AG in an Australian survey, in which 64% did not have a history of PD (Andrews & Slade, 2002), and clearly supports the decision made in DSM-5 to separate AG from PD.

The relatively stable prevalence rates for DSM-IV and DSM-5 AG may result from a broadening of the range of fears beyond a fear of panic attacks or panic-like symptoms in DSM-5 on the one hand, while increasing the strictness of the (severity) criteria on the other hand. None of the respondents with DSM-5 only AG reported fear of panic attacks in the feared situations. In addition, the percentage of respondents reporting severe role impairment, and the mean number of days out of role in the past year due to AG, were significantly lower for respondents with DSM-IV only compared to respondents with 12-month DSM-5 with DSM-IV AG. However, the mean number of days out of role in the past 30 days for any health reason, and 12-month suicidal ideation, were increased for all AG subgroups compared to respondents without AG. In addition, respondents with DSM-IV only AG also had increased treatment and mental comorbidity rates compared to respondents without AG. Although these results indicate that individuals who meet DSM-IV but not DSM-5 AG criteria also suffer from clinically significant symptoms including impairment, this suffering

may for a large part be the result of comorbid mental disorders. However, we cannot exclude the possibility that a small group of individuals who experience severe distress or impairment are left without a diagnosis as a result of the changes in DSM-5, but the population prevalence rate of lifetime DSM-IV only AG without mental disorder comorbidity is very low, namely 0.08%.

We found a particularly low median AOO for DSM-5 only AG. This result adds to previous studies that showed that AG is not a mere consequence of PD (Wittchen et al., 1998; Wittchen et al., 2008) and that the median AOO of AG appears to be lower than the AOO of PD (Wittchen et al., 1998). The current study therefore confirms that DSM-5 AG is more comparable to other phobic disorders, which have early onsets as well (Kessler et al., 2005; Stein et al., 2017). Identifying individuals who suffer from AG at a younger age may lead to earlier AG focused treatment and thereby has the potential to prevent disorder progression and development of comorbidity (Jones, 2013; Kessler et al., 2005).

One of the reasons for the controversy whether AG can be regarded as a disorder that is independent of PD (Grant et al., 2006; Wittchen et al., 1998; Wittchen et al., 2008) is that AG without a history of PD is not typically seen in clinical studies and it has been suggested that many individuals diagnosed with AG in epidemiological studies actually suffer from SP (Horwath, Lish, Johnson, Hornig, & Weissman, 1993). However, another study validated the existence of AG in the absence of panic attacks in a survey through a re-evaluation with structured interviews (Faravelli, Cosci, Rotella, Faravelli, & Dell'Osso, 2008). A better distinction between SP and AG probably reflects better measurements of AG in recent surveys (Andrews & Slade, 2002; Wittchen et al., 2010). For example, in order to meet criteria for AG in this study, agoraphobic anxiety had to apply to at least two situations. The low percentage of AG cases seen in clinical care might also be the result of these individuals being less likely to seek help (Andrews & Slade, 2002; Wittchen et al., 1998), potentially as a result of avoidance behaviour (Andrews & Slade, 2002). Indeed, the percentage of individuals with

AG seeking treatment was lower compared to rates for individuals with PD in the WMH surveys (de Jonge, Roest, Lim, Levinson, & Scott, 2018; Roest et al., 2018).

A previous review article concluded that AG should be seen as a disorder independent from PD based on data from community samples on prevalence rates, temporal relationships of AG, panic attacks, and PD, and impairment associated with AG without panic attacks (Wittchen et al., 2010). Greene and Eaton (2016) also argued that AG is a diagnostic entity that should be separated from PD. By examining multivariate comorbidity patterns of PD and AG, the authors showed that AG could be categorized as a fear disorder, while PD is more strongly related to distress disorders, such as depression (Greene & Eaton, 2016). Yet, evidence is lacking for specific genetic underpinnings of AG (Wittchen et al., 2010) and for differential treatment effects; the latter may result from a lack of treatment studies focusing on patients with AG without PD (Bandelow, 2017; Wittchen et al., 2010). To our knowledge only one other study examined the effect of changes from DSM-IV to DSM-5 criteria for AG. This study examined the effect of the more stringent criterion A in DSM-5 (endorsement of fears from multiple distinct situational domains) on the prevalence rate of AG in children and adolescents seeking anxiety treatment (Cornacchio, Chou, Sacks, Pincus, & Comer, 2015). Authors concluded that this adaptation may be too strict for youth, because a substantial proportion (25%) of individuals no longer met criteria for AG, despite being more similar regarding symptomatology and impairment, to individuals who met the new AG criteria than to individuals with SP (Cornacchio et al., 2015). Whether and how the changes in DSM-5 criteria will affect clinical treatment is yet unclear (Bandelow, 2017), however additional research into DSM-5 AG in general (Wittchen et al., 2010), and specifically the treatment of DSM-5 AG without PD or panic attacks is warranted, especially given the high persistence of DSM-5 AG shown in the current study.

A strength of the current study is the use of data from the WMH surveys. The WHO WMH Survey Initiative provides a unique opportunity to examine the cross-national epidemiology of AG because it included data from countries with different income ranges. The numbers of respondents

were large enough to examine both lifetime and 12-month AG and compare diagnostic groups based on DSM-IV and DSM-5 criteria, although not large enough to additionally examine differences between countries. Another strength is that the surveys used a common protocol and instrument to assess AG separately from PD. However, this study also has a number of limitations. First, although we examined AG using both DSM-IV and DSM-5 criteria, the algorithm was modified in retrospect, as was the case in other reports on DSM-5 criteria for GAD, PTSD, and substance use disorder in the WMH surveys (Ruscio et al., 2017; Slade et al., 2016; Stein et al., 2014). As a result, the CIDI questions do not match all DSM-5 criteria perfectly. Although this could have caused misclassification in some cases concerning the DSM-5 diagnosis of AG, we do not expect this to have a large impact on the comparisons between results for the AG subgroups, since the criteria based on the CIDI questions were sometimes less and sometimes more strict than original DSM-5 criteria. Second, because the data are cross-sectional, AOO is reported retrospectively and the indicator of AG persistence is a proxy indicator.

In conclusion, this study is the first to investigate and compare the epidemiology of AG according to the DSM-5 and the DSM-IV. Results show that the DSM-5 criteria may be an improvement over the DSM-IV criteria as the DSM-5 identifies individuals with a higher disorder persistence, severity, and comorbidity and help-seeking rates, while the global lifetime and 12-month prevalence rates remained relatively constant.

References

American Psychiatric Association (Ed.). (2000). *Diagnostic and statistical manual of mental disorders.*

4th ed., text revision. Washington DC: American Psychiatric Press.

American Psychiatric Association (Ed.). (2013). *Diagnostic and statistical manual of mental disorders.*

5th ed. Washington DC: American Psychiatric Press.

Andrews, G., & Slade, T. (2002). Agoraphobia without a history of panic disorder may be part of the

panic disorder syndrome. *Journal of Nervous & Mental Disease, 190*(9), 624-630.

Asmundson, G. J. G., & Asmundson, A. J. N. (2018). Are anxiety disorders publications continuing on a

trajectory of growth? A look at boschen's (2008) predictions and beyond. *Journal of Anxiety*

Disorders, 56, 1-4. doi:10.1016/j.janxdis.2018.05.003

Asmundson, G. J. G., Taylor, S., & Smits, J. A. J. (2014). Panic disorder and agoraphobia: An overview

and commentary on DSM-5 changes. *Depression and Anxiety, 31*(6), 480-486.

doi:10.1002/da.22277

Bandelow, B. (2017). Comparison of the DSM-5 and ICD-10: Panic and other anxiety disorders. *CNS*

Spectrums, 22(5), 404-406. doi:10.1017/S1092852917000116

Cornacchio, D., Chou, T., Sacks, H., Pincus, D., & Comer, J. (2015). Clinical consequences of the

revised dsm-5 definition of agoraphobia in treatment-seeking anxious youth. *Depression and*

Anxiety, 32(7), 502-508. doi:10.1002/da.22361

Craske, M. G., Stein, M. B., Eley, T. C., Milad, M. R., Holmes, A., Rapee, R. M., & Wittchen, H. (2017).

Anxiety disorders. *Nature Reviews.Disease Primers, 3*, 17024-17024. doi:10.1038/nrdp.2017.24

de Jonge, P., Roest, A. M., Lim, C. C. W., Levinson, D., & Scott, K. M. (2018). Panic disorder and panic

attacks. In K. Scott, P. de Jonge, D. Stein & R. Kessler (Eds.), *Mental disorders around the world.*

facts and figures from the WHO world mental health surveys (pp. 93-105) Cambridge University Press.

de Jonge, P., Roest, A. M., Lim, C. C. W., Florescu, S. E., Bromet, E. J., Stein, D. J., . . . Lee, S. (2016). Cross-national epidemiology of panic disorder and panic attacks in the world mental health surveys. *Depression & Anxiety (1091-4269), 33*(12), 1155-1177. doi:10.1002/da.22572

Faravelli, C., Cosci, F., Rotella, F., Faravelli, L., & Dell'Osso, M. C. (2008). Agoraphobia between panic and phobias: Clinical epidemiology from the sesto fiorentino study. *Comprehensive Psychiatry, 49*(3), 283-287. doi:10.1016/j.comppsych.2007.12.001

Goodwin, R. D., Faravelli, C., Rosi, S., Cosci, F., Truglia, E., de Graaf, R., & Wittchen, H. U. (2005). The epidemiology of panic disorder and agoraphobia in europe. *European Neuropsychopharmacology, 15*(4), 435-443. doi:10.1016/j.euroneuro.2005.04.006

Grant, B. F., Hasin, D. S., Stinson, F. S., Dawson, D. A., Goldstein, R. B., Smith, S., . . . Saha, T. D. (2006). The epidemiology of DSM-IV panic disorder and agoraphobia in the united states: Results from the national epidemiologic survey on alcohol and related conditions. *The Journal of Clinical Psychiatry, 67*(3), 363-374. doi:10.4088/JCP.v67n0305

Greene, A. L., & Eaton, N. R. (2016). Panic disorder and agoraphobia: A direct comparison of their multivariate comorbidity patterns. *Journal of Affective Disorders, 190*, 75-83. doi:10.1016/j.jad.2015.09.060

Haro, J. M., Arbabzadeh-Bouchez, S., Brugha, T. S., De Girolamo, G., Guyer, M. E., Jin, R., . . . Kessler, R. C. (2006). Concordance of the composite international diagnostic interview version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO world mental health surveys. *International Journal of Methods in Psychiatric Research, 15*(4), 167-180. doi:10.1002/mpr.196

Heeringa, S., Wells, J., Hubbard, F., Mneimneh, Z., Chiu, W., & Sampson, N. (2008). Sample designs

    and sampling procedures. In R. Kessler, & T. Ustün (Eds.), *The WHO world mental health surveys:*

    Global perspectives on the epidemiology of mental disorders. (pp. 14-32). New York, NY:

    Cambridge University Press.

Horwath, E., Lish, J. D., Johnson, J., Hornig, C. D., & Weissman, M. M. (1993). Agoraphobia without

    panic: Clinical reappraisal of an epidemiologic finding. *The American Journal of Psychiatry,*

    150(10), 1496-1501. doi:10.1176/ajp.150.10.1496

Jones, P. B. (2013-1). Adult mental health disorders and their age at onset. *The British Journal of*

    Psychiatry.Supplement, 54, 5-10.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime

    prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity

    survey replication. *Archives of General Psychiatry, 62*(6), 593-602.

    doi:10.1001/archpsyc.62.6.593

Kessler, R. C., Chiu, W. T., Jin, R., Ruscio, A. M., Shear, K., & Walters, E. E. (2006). The epidemiology of

    panic attacks, panic disorder, and agoraphobia in the national comorbidity survey replication.

    Archives of General Psychiatry, 63(4), 415-424.

Kessler, R. C., & Ustün, T. B. (2004). The world mental health (WMH) survey initiative version of the

    world health organization (WHO) composite international diagnostic interview (CIDI).

    International Journal of Methods in Psychiatric Research, 13(2), 93-121.

Knäuper, B., Cannell, C. F., Schwarz, N., Bruce, M. L., & Kessler, R. C. (1999). Improving accuracy of

    major depression age-of-onset reports in the US national comorbidity survey. *Int J Methods*

    Psychiatr Res, 8(1), 39-48.

Kogan, C. S., Stein, D. J., Maj, M., First, M. B., Emmelkamp, P. M. G., & Reed, G. M. (2016). The

classification of anxiety and fear-related disorders in the ICD-11. *Depression and Anxiety, 33*(12),

1141-1154. doi:10.1002/da.22530

Leon, A. C., Olfson, M., Portera, L., Farber, L., & Sheehan, D. V. (1997). Assessing psychiatric

impairment in primary care with the sheehan disability scale. *International Journal of Psychiatry

in Medicine, 27*(2), 93-105. doi:10.2190/T8EM-C8YH-373N-1UWD

Murray, C. J. L., Vos, T., Lozano, R., Naghavi, M., Flaxman, A. D., Michaud, C., . . . Memish, Z. A.

(2012). Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-

2010: A systematic analysis for the global burden of disease study 2010. *Lancet (London,

England), 380*(9859), 2197-2223. doi:10.1016/S0140-6736(12)61689-4

Ormel, J., Petukhova, M., Chatterji, S., Aguilar-Gaxiola, S., Alonso, J., Angermeyer, M. C., . . . Kessler,

R. C. (2008). Disability and treatment of specific mental and physical disorders across the world.

The British Journal of Psychiatry, 192(5), 368-375. doi:10.1192/bjp.bp.107.039107

Pennell, B., Mneimneh, Z., Bowers, A., Chardoul, S., Wells, J., Viana, M., . . . Vilagut, G. (2008).

Implementation of the world mental health surveys. In R. Kessler, & T. Ustün (Eds.), *The WHO

world mental health surveys: Global perspectives on the epidemiology of mental disorders.* (pp.

33-57). New York, NY: Cambridge University Press.

Research Triangle Institute. (2002). *SUDAAN: Professional software for survey data analysis.* Research

Triangle Institute: Research Triangle Park.

Roest, A. M., de Jonge, P., Lim, C. C. W., Stein, D. J., Medina-Mora, M. E., & Scott, K. M. (2018).

Agoraphobia. In K. M. Scott, P. de Jonge, D. J. Stein & R. C. Kessler (Eds.), *Mental disorders

around the world. facts and figures form the WHO world mental health surveys* (pp. 106-119)

Cambridge University Press.

Ruscio, A. M., Hallion, L. S., Lim, C. C. W., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., . . . Scott, K.

    M. (2017). Cross-sectional comparison of the epidemiology of DSM-5 generalized anxiety

    disorder across the globe. *JAMA Psychiatry, 74*(5), 465-475.

    doi:10.1001/jamapsychiatry.2017.0056

Slade, T., Chiu, W., Glantz, M., Kessler, R. C., Lago, L., Sampson, N., . . . Degenhardt, L. (2016). A cross-

    national examination of differences in classification of lifetime alcohol use disorder between

    DSM-IV and DSM-5: Findings from the world mental health survey. *Alcoholism: Clinical and*

    Experimental Research, 40(8), 1728-1736. doi:10.1111/acer.13134

Stein, D. J. (2012). Agoraphobia and panic disorder: Options for ICD-11. *World Psychiatry, 11*(Suppl.

    1), 88-92.

Stein, D. J., Lim, C. C. W., Roest, A. M., de Jonge, P., Aguilar-Gaxiola, S., Al-Hamzawi, A., . . . Karam, A.

    (2017). The cross-national epidemiology of social anxiety disorder: Data from the world mental

    health survey initiative. *BMC Medicine, 15*, 1-21. doi:10.1186/s12916-017-0889-2

Stein, D. J., McLaughlin, K. A., Koenen, K. C., Atwoli, L., Friedman, M. J., Hill, E. D., . . . Kessler, R. C.

    (2014). DSM-5 and ICD-11 definitions of posttraumatic stress disorder: Investigating 'narrow'

    and 'broad' approaches. *Depression and Anxiety, 31*(6), 494-505. doi:10.1002/da.22279

Whiteford, H. A., Degenhardt, L., Rehm, J., Baxter, A. J., Ferrari, A. J., Erskine, H. E., . . . Vos, T. (2013).

    Global burden of disease attributable to mental and substance use disorders: Findings from the

    global burden of disease study 2010. *The Lancet, 382*(9904), 1575-1586. doi:10.1016/S0140-

    6736(13)61611-6

Wittchen, H. U., Reed, V., & Kessler, R. C. (1998). The relationship of agoraphobia and panic in a

    community sample of adolescents and young adults. *Archives of General Psychiatry, 55*(11),

    1017-1024.

Wittchen, H. U., Gloster, A. T., Beesdo-Baum, K., Fava, G. A., & Craske, M. G. (2010). Agoraphobia: A review of the diagnostic classificatory position and criteria. *Depression & Anxiety (1091-4269), 27*(2), 113-133. doi:10.1002/da.20646

Wittchen, H. U., Nocon, A., Beesdo, K., Pine, D. S., Hofler, M., Lieb, R., & Gloster, A. T. (2008). Agoraphobia and panic. prospective-longitudinal relations suggest a rethinking of diagnostic concepts. *Psychotherapy and Psychosomatics, 77*(3), 147-157. doi:10.1159/000116608

Wolter, K. M. (1985). *Introduction to variance estimation.* New York: Springer-Verlag.

World Health Organization. (2016). Icd-10. Retrieved from
http://apps.who.int/classifications/icd10/browse/2016/en