Original Article

I|J|S|P

International Journal of
Social Psychiatry
2015, Vol. 61(7) 693–699

DOI: 10.1177/0020764015573848
isp.sagepub.com
SAGE

The attributable burden of panic disorder in the impairment of quality of life in a national survey in Italy

Mauro Giovanni Carta[1], Maria Francesca Moro[1], Eugenio Aguglia[2], Matteo Balestrieri[3], Filippo Caraci[2], Liliana Dell'Osso[4], Guido Di Sciascio[5], Filippo Drago[2], Maria Carolina Hardoy[1], Ernesto D'Aloja[1], Sergio Machado[6], Rita Roncone[7] and Carlo Faravelli[8]

Abstract

Introduction/Objective: The aim was to measure the lifetime prevalence of panic disorder (PD) in an Italian community sample, and to estimate the burden attributable to PD in compromising the quality of life (QoL) of people diagnosed with it.

Methods: Community survey was conducted on a sample of 4,999 randomly selected adult subjects. Instruments used were semi-structured clinical interview Advanced Neuropsychiatric Tools and Assessment Schedule (ANTAS), administered by clinicians and allowing diagnosis according to *Diagnostic and Statistical Manual of Mental Disorder* (4th ed.; DSM-IV); Short Form Health Survey (SF-12).

Results: The lifetime prevalence of PD was 3.6% (4.4% in females, 2.5% in males; $p = .002$). People with PD had a lower SF-12 score than the standardized community sample (35.5 ± 6.5 vs. 38.4 ± 5.9; $p < .0001$) with a mean difference (attributable burden) of 2.9 ± 0.7, that is, lower than PD with agoraphobia (AP; 4.2 ± 2.4). Wilson Disease (WD), Multiple Sclerosis, Major Depressive Disorder and Eating Disorders (ED) show a higher attributable burden in impaired QoL than PD, while the attributable burden of PD with AP is not lower than in ED and WD.

Conclusions: The burden attributable to the impairment of QoL following a lifetime diagnosis of PD was found to be not so great compared to the impairment caused by Major Depressive Disorder (MDD) or neurological conditions. The comorbidity of PD with AP worsens QoL significantly.

Keywords

Panic disorder, quality of life, community survey, Italy

Introduction

Panic disorder (PD) is an anxiety disorder characterized by unexpected recurring severe panic attacks, accompanied by autonomic symptoms PD is frequently associated with agoraphobia (AP) as a comorbid factor (according to the new *Diagnostic and Statistical Manual of Mental Disorder* (5th ed.; DSM-5) perspective), or as a component that aggravates its course according to a more traditional approach (Wittchen, Heinig, & Beesdo-Baum, 2014).

The 2000 Global Burden of Disease Report by the World Health Organization reveals that the rates of point prevalence for PD are quite similar around the world: 5 per 1,000 in the adult population, 4 among males and 6 among females (Mathers et al., 2002).

Olesen, Gustavsson, Svensson, Wittchen and Jonsson (2012) have estimated approximately 7.9 million people in the world suffering from PD; each of these would cost 840 EurosPPP for the direct health-care costs and 661 EurosPPP

[1]University of Cagliari, Cagliari, Italy
[2]University of Catania, Catania, Italy
[3]University of Udine, Udine, Italy
[4]University of Pisa, Pisa, Italy
[5]University of Bari, Bari, Italy
[6]Panic and Respiration Laboratory, Institute of Psychiatry, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
[7]University of L'Aquila, L'Aquila, Italy
[8]University of Florence, Florence, Italy

Corresponding author:
Mauro Giovanni Carta, University of Cagliari, Cittadella Universitaria, SS 554, Monserrato, Cagliari 09042, Italy.
Email: mgcarta@tiscali.it

for the indirect costs. The total cost due to the disorder in 2010 has been calculated as 11,894 million of EurosPPP by the same authors.

PD is a potentially disabling disease. The European Study of the Epidemiology of Mental Disorders (ESEMeD) study ranked (12-month prevalence) PD among the top 10 disorders with the highest independent impact on workday loss (Alonso et al., 2004a). The same study listed PDs at the fourth place in the ranking of disorders that compromise the physical component of quality of life (QoL), and ninth in the list of disorders that could affect psychological QoL. Neurological Problems, Heart Diseases, posttraumatic stress disorder (PTSD), Dysthymia, Arthritis/Rheumatism, Diabetes and Lung disease were found to be associated with a poorer physical QoL than PD; by contrast, only Dysthymia, generalized anxiety disorder (GAD) and Major Depression Episodes have a poorer psychological QoL than PDs (Alonso et al., 2004a).

The subjective perception of QoL is a construct that rises of relevance in today's clinical practice and public health field (Mantovani et al., 1996a; Mura, Bhat, Pisano, Licci, & Carta, 2012) becoming a useful outcomes measure in diseases that impact heavily in the daily life of patients and with high burden on caregivers and families (Carta, Sorbello, et al., 2012; Mantovani et al., 1996b).

The impact of QoL of a disease diagnosed in the past 12 months is a measure that allows an estimation of the impact of a disorder in its active phase, or in recent remission. It may be interesting to measure how much suffering or have suffered from a disorder may jeopardize the entire life of a person.

This can be achieved if we measure the impairment of QoL among those who have had the PD during their lifetime. If this is measured in a sample of people, representative of a community, this produces an estimate as PD may compromise the QoL of this community.

The score of a tool like the Short Form Health Survey-12 (SF-12) measures QoL in the past month; when considering the average of all the subjects who have a lifetime diagnosis of a specific disorder in a given sample, the average score of the SF-12 is determined by those who have been diagnosed, for example, 10 years before and have healed, as well as by those who had the first episode a month before the interview. The more a disease has a chronic course or frequent relapses, the more likely that the person suffering from this disorder will experience a degradation of the QoL at some point in their life.

This study was aimed at measuring the lifetime prevalence of PD in a community sample from six Italian regions, by means of a standardized diagnostic instrument based on DSM-IV criteria. The study was also aimed at measuring the QoL of people with a lifetime diagnosis of PDs and at comparing it both with the standardized average QoL in the community and with the QoL of cases suffering from other brain disorders.

This study has two peculiarities: (a) it uses clinical interviewers and the semi-structured tool 'Advanced Neuropsychiatric Tools and Assessment Schedule' (ANTAS)-SCID, rather than the usual method adopting a structured tool administered by lay interviewers and (b) while the other studies assess the QoL during psychopathology, we measure the present (last month) QoL in relationship with lifetime PD, thus evaluating whether the psychopathology occurred even several years earlier still affects the life of the subject.

Methods

Design

Community survey was carried out by trained clinicians (medical doctors or clinical psychologists) with face-to-face interviews in the house of the participating subjects.

Recruitment and study sample

The sample was randomly selected from the municipal records (18-year-old people) of seven different areas to include a wide array of socioeconomic settings. Sampling and recruitment methods have been described in detail in previously published papers (Carta et al., 2010; Carta, Aguglia, et al., 2012).

Tools and assessment

The interview included the following tools:

1. Demographic data were collected by means of an ad-hoc form previously utilized and validated in a regional survey (Carta et al., 2010).
2. The semi-structured clinical interview ANTAS to assess the presence of psychiatric disorders was derived from the non-patient version of the SCID interview for DSM-IV (SCID/NP; First, Spitzer, Gibbon, & Williams, 1997). The reliability against SCID was found equal to Cohen's K mean value = .85 (Carta et al., 2010).
3. QoL was evaluated with the SF-12 (Ware, Kosinski, & Keller, 1996). The SF-12 includes seven dimensions: physical activity, physical health limitations on role or activities, emotional state, physical pain, self-evaluation of general state of health, vitality, social activity and mental health. SF-12 measures the previous month: the higher the score, the better the QoL.
4. Bipolar Spectrum Symptoms were measured by means of the Mood Disorder Questionnaire (MDQ), Italian version (Hardoy et al., 2005).

Table 1. Lifetime prevalence of panic disorder by sex and age.

	N (%)	χ^2	*P*	OR	95% CI
<25 males	4 (2.1)	–			
25–44	13 (2.6)	0.01*	.99	1.26	0.38–4.63
45–64	13 (2.8)	0.24*	.92	1.28	0.38–4.71
>64	6 (2.1)	0.01*	.99	1.01	0.25–4.31
Total males	36 (2.5)	–			
<25 females	13 (5.4)	–			
25–44	29 (4.7)	0.17	.68	0.87	0.43–1.80
45–64	35 (4.9)	0.07	.79	0.91	0.46–1.94
>64	10 (2.5)	3.86	.048	0.44	0.18–1.09
Total females	87 (4.4)	9.53	.002	1.84°	1.22–2.79

OR: odds ratio; CI: confidence interval.
*Yates corrected OR females vs. males.

Data analysis

Lifetime prevalence for DSM-IV-TR PD (APA, 2000) was calculated in the whole sample and in specific age groups, as was comorbidity with PD and the main Psychiatric DSM-IV Disorders. The odds ratios (ORs) of specific age groups (univariate analysis) for PD (dependent variable) were calculated using the age < 25 as a pivot. Statistical significance was calculated using the χ^2 test in 2×2 tables.

The 'attributable burden' due to PD was calculated as the difference between the QoL of those suffering from PDs and the QoL level in the community sample (Carta, Aguglia et al., 2012) with an indirect standardization method (by age and sex). The attributable burden due to PD was compared to the attributable burden calculated for other diseases in previous studies from the same database, or in case-control studies adopting the same database from which the controls were drawn (Carta, Moro, et al., 2014; Carta, Preti, et al., 2014).

Ethical aspects

The study was approved by the ethical committee of the Italian National Health Institute ('Istituto Superiore della Sanità'), Rome. Each candidate signed the informed consent form.

Results

Data on the enrolled sample characteristics by Age, Sex and the non-interviewed rate have been published elsewhere in details (Carta et al., 2010; Carta, Aguglia, et al., 2012). A sample of 1,437 males (59.3% of the randomized sample) and 1,961 females (75.2%) was interviewed.

The lifetime prevalence of PD in the overall sample was 3.6%. The lifetime prevalence of PD by sex and age is shown in Table 1. Females were found to be at risk (4.4% vs. 2.5%, $\chi^2 = 9.53$; $p = .002$; OR = 1.84, 95% CI = [01.22–2.79]). No differences were found regarding age and sex with the exception of a trend toward a lower frequency in older women with borderline statistical significance (2.5% vs. 5.4%, in younger age class,; $\chi^2 = 3.86$; $p = .048$; OR = .44, 95% CI = [0.18–1.09]). PD was associated with several psychiatric disorders (Table 2) namely, ranked by decreasing odd ratios: AP, Social Phobia, PTSD and Binge Eating Disorder (ED), Bipolar II Disorder, Obsessive Compulsive Disorders and Major Depressive Disorder. Also MDQ-positive subjects were at risk of receiving a co-diagnosis of PD.

The SF-12 mean score in the overall sample of the community survey was standardized by sex and age according to the distribution of the sub-sample of people with PD: the resulting standardized mean was 38.4 ± 5.9. People with Panic Disorder Diagnosis had a poorer SF-12 score than the standardized community sample ($F = 19.93$, DF 1,3481,3482, $p < .0001$) with a mean difference (attributable burden) of 2.9 ± 0.7.

Table 3 compares the burden attributable to PD with the burden caused by other diseases, as found in previous studies made with the same database, or in case-control studies adopting the same database from which the controls were drawn. Both neurological diseases (as Wilson Disease and Multiple Sclerosis) and psychiatric diseases (Major Depressive Disorders and EDs) show a higher attributable burden than PD, but the attributable burden of PD with AP is not lower than that of EDs and Wilson Disease.

Discussion

Our study showed that the lifetime frequency of PD is not dissimilar from the results of other recent studies conducted in Western countries, in terms of both the general frequency in the overall sample and the specific distribution by gender and age. However, our study is the only one that used an instrument derived from the semi-structured interview SCID carried out by clinical interviewers, while the majority of the other studies used the

Table 2. Comorbidity of panic disorder with other psychiatric disorders.

	Number of cases (% in PD)	χ^2	*P*	OR	95% CI
Major depressive disorder	28 (22.8)	33.34	<.0001	3.30	2.13–5.39
Bipolar disorders	4 (3.2)	16.24*	<.0001	9.14	2.45–31.09
Bipolar II disorders	4 (3.2)	18.42*	<.0001	10.97	2.85–38.70
MDQ+	13(10.6)	24.67	<.0001	4.18	.15–7.96
Agoraphobia	32 (26.0)	500.1	<.0001	58.38	30.6–112.1
Obsessive compulsive disorder	10 (8.1)	40.78	<.0001	10.84	3.86–26.65
Social phobia	5 (4)	49.96*	<.0001	19.78	5.37–70.59
PTSD	10 (8.1)	39.62*	<.0001	19.76	5.36–50.79
Binge eating disorder	5 (4.1)	39.62*	<.0001	19.76	5.36–50.79
Anorexia	1 (0.8)	0.01*	.999	1.15	0.06–8.14
Bulimia	2 (1.6)	1.52*	.217	3.85	0.59–17.99

OR: odds ratio; CI: confidence interval.
The mean average of SF-12 scores in people with panic disorder was 35.5 ± 6.5.

Table 3. Attributable burden due to panic disorder in decreasing quality of life and comparison with other disorders.

Disorders	SF-12 (Mean ± *SD*)	Attributable impairment of QoL due to disorder (SF-12 score in a community sample without disorder – SF-12 score of a given disorder)	Comparison with panic disorders (ANOVA 1 way)	Comparison with panic disorder with agoraphobia
Major depressive disorders	33.8 ± 9.2	5.6 ± 3.6 (*n* = 37)*	DF 1,158,159; *F* = 62.245; *p* < .0001	DF 1,66,67; *F* = 5.341; *p* < .024
Multiple sclerosis	29.5 ± 7.3	7.0 ± 3.5 (*n* = 201)*	DF 1,322,323; *F* = 164.56; *p* < .000	DF 1,231,232; *F* = 19.02; *p* > .0001
Wilson disease	33.8 ± 9.0	4.4 ± 1.7 (*n* = 23)***	DF 1,144,145; *F* = 50.892; *p* < .000	DF 1,53,54; *F* = 0.12; *p* = .733
Eating disorders	34.9 ± 6.2	4.4 ± 6.6 (*n* = 60)°	DF 1,181,182; *F* = 6.245; *p* < .013	DF 1,90,91; *F* = 0.03; *p* = .869
Panic disorders	35.5 ± 4.6	2.9 ± 0.9 (*n* = 123)		
Panic disorders with agoraphobia		4.2 ± 2.4 (*n* = 32)		

ANOVA: analysis of variance.

interview Composite International Diagnostic Interview (CIDI)-DSM-IV (Kessler et al., 2004) or other structured interviews conducted by lay interviewers.

The National Comorbidity Survey Replication found a lifetime prevalence of 3.7% for PD without AG (PD only), and 1.1% for PD with AG (Kessler et al., 2005, 2006) as against 2.7% and 0.9%, respectively, in this survey. The US National Epidemiologic Survey on Alcohol and Related Conditions found, quite differently, 1.1% of Lifetime Prevalence of PD without AG and 1.6% of PD with AG (Grant et al., 2006). All these studies, as well as almost all the studies carried out in Western countries, found a higher prevalence in females and in younger age classes (Joyce, Bushnell, Oakley-Browne, Wells, & Hornblow, 1989).

Concerning the previous research works made in Italy, the ESEMeD Survey found a lifetime prevalence of 0.9% in the Italian sample, 2.2% in females and 1.6% in males. Surprisingly (since the Italian population does not differ greatly from the other participating countries), the same study shows a weighted lifetime prevalence of 1.6%, lower than in Belgium (2.7%), France (3.0%) and the Netherlands (3.9%) and has no statistically significant difference against Germany (1.8%) and Spain (1.7%; Alonso et al., 2004b; de Girolamo et al., 2005).

In two regions where this survey was carried out, researchers made one local survey and a regional one. A study conducted in Florence on a representative sample of the population (Faravelli, Guerrini Degl'Innocenti, & Giardinelli, 1989) showed a lifetime prevalence of 1.35% of DSM-III PD, and 0.9% of PD with AP. A previous survey made in Sardinia found a prevalence rate of only 1.7% (Carta et al., 2002). Earlier Italian studies had found lower rates of PD. These differences could be due to the different

methodologies adopted, or to an increase of the disorders over time, or to both factors. It is interesting to note that the study made in Sardinia observed a higher frequency of PDs in the Sardinians who had migrated to Paris. This suggests an influence of environmental conditions and the likelihood of an increase in the rates of PD.

The high comorbidity of PD with other psychiatric disorders is not surprising. A recent survey shows a strict comorbidity between obsessive compulsive disorders and PD, indicating even an association between PD, PTSDs and Binge EDs (Torres et al., 2014). Similarly, it is not astonishing that our study has found a higher risk of Panic in Bipolar Disorder, and Bipolar II disorder markedly, than in Major Depressive Disorder even though the latter, due to its elevated frequency, still remains the disorder with the highest percentage of comorbidity with PD (22.8%). The strict association between PD and Bipolar II Disorders was shown by both epidemiological (Schaffer, Cairney, Cheung, Veldhuizen, & Levitt, 2006) and clinical studies (Sugaya et al., 2013).

The reliability and validity of the diagnosis of Bipolar Disorders made with standardized interviews and self-administered questionnaires (like the MDQ or HCL-32) were the targets of discussions and may raise some problems. This remains a general limitation of the epidemiological research about bipolar disorders (Angst et al., 2010; Carta & Angst, 2005; Karam et al., 2014). We have tried to address this limitation, at least partially, by using a clinician for the interview in the epidemiological survey and by applying both methodologies (interviews and self-reporting tools). Both methodologies have shown an association between PDs and DSM-IV Bipolar Disorder Diagnosis (by ANTAS) and the whole Bipolar Spectrum (by MDQ).

The innovative finding of our study relates to the impairment of QoL that is associated with a lifetime diagnosis of PD. This form of impairment was found relevant with reference to the average QoL of the people in the community, but it was not so great when compared to the impairment caused by other diagnoses, at least according to the expectations based on the data of the above-cited ESEMeD study (Alonso et al., 2004a). When adding the two physical and psychological components of the SF-12, which are presented separately in ESEMeD, PD results to be compromising the QoL (PCS −4.59; MCS −9.43) as much as neurological disorders (PCS −15.30; MCS +0.96) and Major Depressive Disorder (respectively −4.02; −9.62). In our study, the attributable burden in terms of impaired QoL, following diagnosis, is lower in PD than in Major Depressive Disorder and in two Neurological Diseases, notably Multiple Sclerosis and Wilson's Disease. This result is quite in agreement with the data from a recent UK survey extracted from the Adult Psychiatric Morbidity Surveys carried out in 2000 and 2007 on a representative sample of the general population in England (Roberts, Lenton, Keetharuth, & Brazier, 2014). This study measured the impairment of QoL due to different diagnoses by two specifically structured sub-scales of SF-12 named SF-6D – the health utility index measuring general health – and the EQ-5D questionnaire consisting of five questions on mobility, self-care, usual activities, pain and discomfort. In SF-6D, people with PDs reached an average score of 0.645 ± 0.134 (against 0.551 ± 0.105 in depression and 0.513 ± 0.324 in Long Term Depression) and of 0.664 ± 0.274 in EQ-5D (against 0.537 ± 0.311 in Depression and 0.532 ± 0.104 in Long Term depression). By contrast, the people with no Physical Health problems showed 0.829 ± 0.114 and 0.851 ± 0.165, respectively, and the people with no Mental Health problems -0.827 ± 0.114 and 0.842 ± 0.170. The two Italian and English studies agree that PD can impair the QoL of those affected, but this disorder does not cause as significant an impact as depressive disorder.

Our study has also shown that the comorbidity of PD with AP worsens QoL significantly. PD with AP is in fact associated with an impairment of the QoL at similar levels as ED, or Wilson's disease, although it does not reach the levels of Major Depression or Multiple Sclerosis.

This potential impairment associated with PD with AP is not currently recognized at the decision-making level in the public health-care system. The new Italian Guidelines that define the levels of disability assign a score of 15 (fixed score) to PD and a score of 35 (fixed score) to AP with PD; a person with a disability has the right to be paid the invalidity pension when they reach a minimum disability score of 75 (Istituto Nazionale della Previdenza Sociale (INPS), 2014). In our study, PD with AP is associated with an impaired QoL that is similar to the impact caused by EDs; significantly enough, the guidelines assign to anorexia, a score ranging from 35 to 100. Another truly problematic aspect, even on the basis of our findings, is that PD with AP has a fixed disability score, while our study reveals a wide distribution around the average values, due probably to the fact that important factors such as non-response to treatment can change the level of disability widely.

Limitations

This research is a corollary of a community survey that had other main objectives. The levels of disability produced by psychiatric disorders should be measured taking into account important co-factors, such as comorbidity with other medical diseases and response to treatments. Those variables can be studied best in case-control studies. The findings of this research are therefore preliminary and of a heuristic value.

Conclusion

The attributable burden in the impairment of the QoL following a lifetime diagnosis of PD was found relevant with

reference to the average QoL of people in the community, but not so great compared to the impairment caused by other diagnoses like Major Depressive Disorder or neurological conditions. Our study has also shown that the comorbidity of PD with AP worsens QoL significantly. PD with AP is in fact associated with impaired QoL at similar levels as ED, or Wilson's disease, although it does not reach the levels of Major Depression or Multiple Sclerosis. This impairment must be studied in case-control design studies in order to better understand the role of determinants, for example, response to treatments and comorbidity.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S., Bryson, H., … Vollebergh, W. A.; ESEMeD/MHEDEA 2000 Investigators, European Study of the Epidemiology of Mental Disorders (ESEMeD) Project. (2004a). Disability and quality of life impact of mental disorders in Europe: Results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatrica Scandinavica, 420*(Suppl.), 38–46.

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S., Bryson, H., … Vollebergh, W. A.; ESEMeD/MHEDEA 2000 Investigators, European Study of the Epidemiology of Mental Disorders (ESEMeD) Project. (2004b). Prevalence of mental disorders in Europe: Results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatrica Scandinavica, 420*(Suppl.), 21–27.

Angst, J., Meyer, T. D., Adolfsson, R., Skeppar, P., Carta, M., Benazzi, F., … Gamma, A. (2010). Hypomania: A transcultural perspective. *World Psychiatry, 9*(1), 41–49.

APA - American Psychichiatric Association. (2000). *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition, Text Revision (DSM-IV-TR) Wahsington DC: American Psychiatric Association.

Carta, M. G., Aguglia, E., Balestrieri, M., Calabrese, J. R., Caraci, F., Dell'osso, L., … Hardoy, M. C. (2012). The lifetime prevalence of bipolar disorders and the use of antidepressant drugs in bipolar depression in Italy. *Journal of Affective Disorders, 136*, 775–780.

Carta, M. G., Aguglia, E., Bocchetta, A., Balestrieri, M., Caraci, F., Casacchia, M., … Hardoy, M. C. (2010). The use of antidepressant drugs and the lifetime prevalence of major depressive disorders in Italy. *Clinical Practice and Epidemiology in Mental Health, 6*, 94–100.

Carta, M. G., Kovess, V., Hardoy, M. C., Morosini, P. L., Murgia, S., & Carpiniello, B. (2002). Psychiatric disorders in Sardinian immigrants in Paris: A comparison with Parisians and Sardinians resident in Sardinia. *Social Psychiatry and Psychiatric Epidemiology, 37*, 112–117.

Carta, M. G., Moro, M. F., Lorefice, L., Picardi, A., Trincas, G., Fenu, G., … Marrosu, M. G. (2014). Multiple sclerosis and bipolar disorders: The burden of comorbidity and its consequences on quality of life. *Journal of Affective Disorders, 167*, 192–197.

Carta, M. G., Preti, A., Moro, M. F., Aguglia, E., Balestrieri, M., Caraci, F., … Bhugra, D. (2014). Eating disorders as a public health issue: Prevalence and attributable impairment of quality of life in an Italian community sample. *International Review of Psychiatry, 26*, 486–492.

Carta, M. G., Sorbello, O., Moro, M. F., Bhat, K. M., Demelia, E., Serra, A., … Demelia, L. (2012). Bipolar disorders and Wilson's disease. *BMC Psychiatry, 12*, Article 52.

Carta, M.G. & Angst, J. (2005). Epidemiological and clinical aspects of bipolar disorders: controversies or a common need to redefine the aims and methodological aspects of surveys. *Clin Pract Epidemol Ment Health.;1*:4.

de Girolamo, G., Polidori, G., Morosini, P., Mazzi, F., Serra, G., Visonà, G., … Reda, V. (2005). *La prevalenza dei disturbi mentali in Italia. Il Progetto ESEMED-WMH. Una sintesi*. [The prevalence of mental disorders in Italy. The Project ESEMED-WMH. A summary]. Roma: ISS. Retrieved from http://www.epicentro.iss.it/ temi/mentale/esemed.pdf

Faravelli, C., Guerrini Degl'Innocenti, B., & Giardinelli, I. (1989). Epidemiology of anxiety disorders in Florence. *Acta Psychiatrica Scandinavica, 79*, 308–312.

First, M., Spitzer, R., Gibbon, M., & Williams, J. (1997). *Structured clinical interview for DSM-IV axis I disorders, research version, non-patient edition (SCID-I/NP)*. New York: Biometrics Research, New York State Psychiatric Institute.

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. *Journal of Clinical Psychiatry, 67*, 363–374.

Hardoy, M. C., Cadeddu, M., Murru, A., Dell'Osso, B., Carpiniello, B., Morosini, P. L., … Carta, M. G. (2005). Validation of the Italian version of the 'Mood Disorder Questionnaire' for the screening of bipolar disorders. *Clinical Practice and Epidemiology in Mental Health, 1*, 8.

Istituto Nazionale della Previdenza Sociale. (2014). *Linee Guida INPS per l'accertamento degli stati invalidanti*. Retrieved from http://www.inps.it/docallegati/Informazioni/ approfondimenti/pensioni/prestazioniassistenziali/provvideneeconomicheinfavoredeiminoraticivili/Documents/Linee_Guida_INPS_Accertamenti_Stati_Invalidanti.pdf

Joyce, P. R., Bushnell, J. A., Oakley-Browne, M. A., Wells, J. E., & Hornblow, A. R. (1989). The epidemiology of panic symptomatology and agoraphobic avoidance. *Comprehensive Psychiatry, 30*, 303–312.

Karam, E. G., Sampson, N., Itani, L., Andrade, L. H., Borges, G., Chiu, W. T., … Akiskal, H. (2014). Under-reporting bipolar disorder in large-scale epidemiologic studies. *Journal of Affective Disorders, 159*, 147–154. doi:10.1016/j.jad.2014.01.011

Kessler, R. C., Abelson, J., Demler, O., Escobar, J. I., Gibbon, M., Guyer, M. E., … Zheng, H. (2004). Clinical calibration of DSM-IV diagnoses in the World Mental Health (WMH) version of the World Health Organization (WHO) Composite International Diagnostic Interview (WMHCIDI). *International Journal of Methods in Psychiatric Research, 13*, 122–139.

Kessler, R. C., Berglund, P. A., Demler, O., Jin, R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Archives of General Psychiatry, 62*, 593–602.

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*, 415–424.

Mantovani, G., Astara, G., Lampis, B., Bianchi, A., Curreli, L., Orrù, W., … Rudas, N. (1996a). Evaluation by multidimensional instruments of health related quality of life of elderly cancer patients. *Support Cancer in Care, 4*, 129–140.

Mantovani, G., Astara, G., Lampis, B., Bianchi, A., Curreli, L., Orrù, W., … Rudas, N. (1996b). Impact of psychosocial interventions on quality of life of elderly cancer patients. *Psycho-Oncology, 5*, 127–135.

Mathers, C. D., Stein, C., Ma Fat, D., Rao, C., Inoue, M., Tomijima, N., … Murray, C. J. L. (2002). *Global Burden of Disease 2000: Version 2 methods and results* (Global Programme on Evidence for Health Policy, Discussion Paper No. 50). Geneva, Switzerland: World Health Organization.

Mura, G., Bhat, K. M., Pisano, A., Licci, G., & Carta, M. (2012). Psychiatric symptoms and quality of life in systemic sclerosis. *Clinical Practice and Epidemiology in Mental Health, 8*, 30–35. doi:10.2174/1745017901208010030

Olesen, J., Gustavsson, A., Svensson, M., Wittchen, H. U., & Jonsson, B. (2012). The economic cost of brain disorders in Europe. *European Journal of Neurology, 19*, 155–162.

Roberts, J., Lenton, P., Keetharuth, A. D., & Brazier, J. (2014). Quality of life impact of mental health conditions in England: Results from the adult psychiatric morbidity surveys. *Health and Quality of Life Outcomes, 12*, 6. doi:10.1186/1477-7525-12-6

Schaffer, A., Cairney, J., Cheung, A., Veldhuizen, S., & Levitt, A. (2006). Community survey of bipolar disorder in Canada: Lifetime prevalence and illness characteristics. *Canadian Journal of Psychiatry, 51*, 9–16.

Sugaya, N., Yoshida, E., Yasuda, S., Tochigi, M., Takei, K., Otani, T., … Tanii, H. (2013). Prevalence of bipolar disorder in panic disorder patients in the Japanese population. *Journal of Affective Disorders, 147*, 411–415. doi:10.1016/j.jad.2012.10.014

Torres, A. R., Ferrão, Y. A., Shavitt, R. G., Diniz, J. B., Costa, D. L., do Rosário, M. C., … Fontenelle, L. F. (2014). Panic disorder and agoraphobia in OCD patients: Clinical profile and possible treatment implications. *Comprehensive Psychiatry, 55*, 588–597. doi:10.1016/j.comppsych.2013.11.017

Ware, J. Jr., Kosinski, M., & Keller, S. D. (1996). A 12-Item Short-Form Health Survey: Construction of scales and preliminary tests of reliability and validity. *Medical Care, 34*, 220–233.

Wittchen, H. U., Heinig, I., & Beesdo-Baum, K. (2014). Anxiety disorders in DSM-5: An overview on changes in structure and content. *Der Nervenarzt, 85*, 548–552. (In German).