

# Research article

## Ερευνητική εργασία

### **Epidemiology of panic disorder and subthreshold panic symptoms in the Greek general population**

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Psychiatriki 2020, 31:201–215

**P**anic disorder (PD) is a common anxiety disorder with severe social and health consequences in the lives of individuals who suffer from it. General population studies that attempt to measure the prevalence of this disorder across the world suggest that a 1.7% to 4.7 % of adults and adolescents suffer from Panic Disorder. In Greece, research analyzing the abovementioned matters is limited, and previous studies were put forward in small samples. The aim of the present study was to describe the prevalence and sociodemographic associations of panic disorder (PD) and related subthreshold panic symptoms in the general population of Greece and to appraise the comorbidity, use of services and impact on quality of life of these syndromes. This was a secondary analysis of the 2009–2010 psychiatric morbidity survey carried out in a representative sample of the Greek general population (4894 participants living in private households, 18–70 years, response rate 54%). Psychiatric disorders were assessed with the computerized version of the revised Clinical Interview Schedule (CIS-R). Quality of life was assessed with the EuroQoL EQ-5D generic instrument. The utilization of health services was examined by making relevant questions. Finally, direct questions were used to assess sociodemographic and socioeconomic factors. According to our findings, 1.87% of the participants (95% confidence interval [CI]: 1.50–2.26%) met criteria for PD and 1.61% met criteria for subclinical PD (95% CI: 1.26–1.96%). There was a clear female preponderance for both PD ( $p=0.001$ ) and Sub-PD ( $p=0.01$ ). In addition, 3.48% of the participants reported having experienced panic attacks during the past week (95% confidence interval [CI]: 2.98–4.01%). PD or subclinical PD was independently associated with a limited number of sociodemographic and socioeconomic variables especially after the adjusted analysis. Both panic related conditions involved significant reductions in quality of life and elevated utilization of health services for both medical and psychological reasons in

comparison to healthy participants. In conclusion, PD and subclinical panic symptoms were common in the general Greek population with substantial comorbidity and impaired quality of life. The observed use of the general and psychological health services among adults with panic symptoms and its temporal and economic consequences calls for more efficient diagnostic and treatment policies.

**Key words:** Epidemiology, panic disorder, adults, comorbidity, quality of life, Greece.

## Introduction

Panic disorder (PD) is a common anxiety disorder with severe social and health consequences in the lives of individuals who suffer from it.<sup>1</sup> In the most severe cases such consequences can be similar or even greater than the ones linked with major depression.<sup>2,3</sup> PD is related, among others, with poor social functioning,<sup>4</sup> heightened possibility of suicide attempts,<sup>5</sup> and drug and alcohol abuse.<sup>6</sup> PD is rare before the age of fourteen<sup>7</sup> and has a typical age of onset in late adolescence and the early twenties.<sup>8,9</sup>

General population studies that attempt to measure the prevalence of this disorder across the world suggest that a 1.7% to 4.7 % of adults and adolescents suffer from panic disorder.<sup>10–12</sup> In particular, according to most recent studies, the 12-month prevalence estimation for this disorder in the United States is as high as 4.7%<sup>12</sup> whereas in Europe it has been observed to be 1.8% (ranging from 0.7–2.2% across studies).<sup>13</sup> In a cross-national epidemiological study, using data collected in 25 countries between 2001 and 2012, researchers reported a lifetime prevalence for PD of approximately 1.7%.<sup>10</sup> In addition, more recent studies begin to look into subthreshold forms of panic regarding its prevalence and impact<sup>14,15</sup> and some report considerable disability associated even with subthreshold panic symptoms.<sup>16</sup>

Sociodemographic and socioeconomic associations have also been examined in community studies. Contemporary research findings show considerable gender differences (i.e. stronger associations with female gender), in the prevalence of PD and subthreshold panic.<sup>10,11,15</sup> Age is another sociodemographic variable positively associated with panic syndromes and its course in many community studies.<sup>10,13,15</sup> Regarding other socioeconomic variables, such as urbanicity, marital status and education, no significant associations have been observed in the majority of previous studies.<sup>13,17</sup> However, some researchers have

suggested that variables such as unemployment, being divorced, widowed or separated, lower education and low household income were associated with PD and subthreshold panic symptoms.<sup>6,13</sup>

Individuals suffering from PD as well as subthreshold panic symptoms often struggle with comorbid psychiatric conditions.<sup>10,15–18</sup> PD is often comorbid with anxiety, mood and other psychiatric disorders<sup>10,17,19,20</sup> as well as with a number of medical conditions such as migraine,<sup>21</sup> and cardiovascular illness.<sup>22</sup> Similar comorbidities, although in a milder form, have been also observed for subthreshold panic.<sup>15,18</sup> PD is also associated with suicidal ideation and suicidal behaviour<sup>5,23</sup> and drug and alcohol abuse.<sup>6</sup> It is also noteworthy that individuals with panic syndromes display increased utilization of health care services and hospital emergency divisions<sup>15,24</sup> leading to financial strain, elevated stress and increased number of days absent from work.<sup>1,25</sup>

In Greece, research analyzing the abovementioned matters is limited, and previous studies were put forward in small samples.<sup>26–28</sup> To our knowledge there is no other epidemiological research in this country assessing exclusively the abovementioned disorder and its subthreshold forms in large samples of the community. This makes apparent the need for further research in this topic using a representative sample of the Greek general population. Thus, the assessment of PD and of subthreshold forms of panic in relation to its epidemiology, comorbidity, quality of life, as well as its association with several socioeconomic and sociodemographic characteristics were the main aim of this study.

## Material method

### *Description of the data set*

The data analyzed in this study were obtained within the framework of the “Greek Psychiatric Morbidity Survey” arranged by the Department of Psychiatry

– University of Ioannina School of Medicine in 2009–2010. The main report of the study<sup>3</sup> offers a thorough description of the survey. In brief, the prevalence and associations of common mental disorders in the Greek general population have been examined. For this a nationally representative sample of the Greek adult general population (18–70 years) has been employed and a cross-sectional survey was carried out. The total rate of response was 54%, consequently 4,902 adults participated, living in private residences encompassing small insular and rural/semirural Greek areas. The study was ethically confirmed by the Greek Ministry of Health and inclusion in it required verbal informed consent by all the participants.<sup>3</sup>

### **Assessment of psychiatric disorders**

We examined psychiatric disorders and symptoms by employing the computerized version of the revised Clinical Interview Schedule (CIS-R).<sup>29</sup> The CIS-R is a systematic psychiatric interview used in a large scale of epidemiological studies in many countries<sup>30–32</sup> as well as in Greece.<sup>3,26</sup> This structured psychiatric interview assesses the presence, seriousness and course of 14 psychiatric symptoms over the previous month period. A general psychiatric morbidity dimension emerges with the calculation of the total score on the CIS-R, by summing up all the symptom sections. The aforementioned dimension has been employed previously by a number of researchers.<sup>3,29</sup> A number of further question items in the interview permit the appliance of the ICD-10 research diagnostic criteria<sup>33</sup> to make a diagnosis for specific psychiatric disorders with the use of specially developed algorithms.<sup>3,17</sup> Specifications on the formulation of the Greek version of the interview are presented elsewhere.<sup>3,26</sup> Reliability was very good with an overall Cronbach's alpha for the whole CIS-R of 0.86 and CIS-R test-retest reliability at 0.84.<sup>3</sup>

### **Assessment of panic symptoms and PD**

For the definition of panic related symptoms, we used the anxiety and panic sections of the CIS-R. We asked the participants two questions concerning whether anxiety was present during the past month. Furthermore the participants who responded positively in the aforementioned question were asked a screening question for panic at-

tack i.e. "Thinking about the past month, did your anxiety or tension ever get so bad that you got in a panic, for instance make you feel that you might collapse or lose control unless you did something about it?" Subsequently the participants who experienced panic attacks in the previous month were presented with an additional question about experiencing panic attacks during the past week. Finally the participants who gave positive answers (i.e. experienced at least one panic attack during that week's period) were required to answer a number of further questions regarding the characteristics, the severity, the duration and the frequency of the panic attacks, in order to obtain the criteria of panic disorder as described in the ICD-10. On that basis we defined two mutually exclusive definitions of panic:

1. *Panic disorder*: Defined as having a score of two or more on the panic scale and impairment  $\geq 1$  where the experience of panic symptoms described in the ICD-10 caused clinically significant distress and disability regarding the individuals social, interpersonal and occupational aspects of life.
2. *Subclinical panic disorder* (Sub-PD): Subjects had a score of two or more on the panic scale but did not meet distress/impairment criteria.

### **Comorbidity and use of health services**

We assessed the comorbidity of PD and subclinical PD with depressive episode, obsessive compulsive disorder, generalized anxiety disorder and all phobias combined. In order to define the aforementioned mental disorders according to the ICD-10 criteria we employed the standard diagnostic algorithms as elaborated previously.<sup>3</sup> Suicidal ideation was assumed to be present when the respondents answered positively in questions involving current death wishes, or had reported continuous and intense ideas that life was not worth living, or reported a history of any suicide attempts during the past month. Current smoking status and current cannabis use (past month) was attained through self-reports [see Skapinakis et al (2013) for details].<sup>3</sup> Harmful alcohol use was assessed using AUDIT and adopting the method detailed in Aalto et al (2009)<sup>34</sup> and our original report.<sup>3</sup>

We assessed Quality of life using the EuroQoL EQ-5D generic instrument which was validated in Greece.<sup>35</sup> Both, the EQ-5D utility index and the EQ-5D Visual Analog Scale (VAS),<sup>3</sup> have been employed.

The utilization of health services was examined by making questions about whether the participants had visited a general practitioner (including internists or other specialist doctors who practice family medicine in Greece in the private sector) or a mental health professional (either a psychiatrist or clinical psychologist) during the past 12 months for any reason concerning their general health or mental health correspondingly.

### **Other variables**

We used direct questions to assess all remaining sociodemographic and socio-economic factors. The following variables have been examined: age, gender, marital status, educational qualifications and employment status, presence of subjective financial difficulties and type of locality. Participants were also asked to report the presence of any chronic physical diseases (from a list of common chronic diseases). Details on the methodology we have used to assess these variables are given elsewhere.<sup>3</sup>

### **Statistical analysis**

All analyses were performed using STATA/SE Version 12.0 (StataCorp, College Station, Texas) and the "svy" family of commands to consider the complex sampling design. Descriptive statistics were elicited for the examined variables, whereas chi-square tests were employed for the prevalence proportions' comparisons. The association between the PD syndromes and the sociodemographic variables were reviewed through the calculations of crude and adjusted odds ratios using logistic regression models. Regarding comorbidity analyses, the dependent variable was the comorbid condition (e.g. depression) and the panic-related condition (e.g. subthreshold panic) was entered as an independent binary variable. The use of health services was also assessed with the employment of similar models. Common doctor visits was the dependent variable and was defined as having visited a general practitioner (including internists or other specialist doctors who practice

family medicine in Greece in the private sector) or a mental health professional (either a psychiatrist or clinical psychologist) during the past 12 months for any reason concerning their general health or mental health correspondingly.

## **Results**

### **Description of the sample**

Four thousand eight hundred and ninety-four (4894) adults took part in this study (54.2% response rate, see method for details). 50.4% of the final sample were women, the participants' mean age were 42 years, 61% were married, 59.6% were employed and 54.8% were living in an urban environment. Table 1 gives full details of the characteristics of the participants.

### **Prevalence and associations with gender**

Prevalence rates of PD and subclinical PD (Sub-PD) by gender and clinical type of PD are shown in table 2. In total, 1.87% of the participants (95% confidence interval [CI]: 1.50–2.26%) met criteria for PD and 1.61% met criteria for Sub-PD (95% CI: 1.26–1.96%). There was a clear female preponderance for both PD ( $p=0.001$ ) and Sub-PD ( $p=0.01$ ). In addition, 3.48% of the participants reported having experienced panic attacks during the past week (95% confidence interval [CI]: 2.98–4.01%).

Additionally, in figure 1 we present the complete psychopathological profile that the participants with PD and Sub-PD experience in comparison to the general population, as measured by the CIS-R. It can be seen that such symptoms are quite prevalent, as high percentages of the participants with PD experience fatigue (80%), irritability (77%), worry (78%), depressive ideas (73%) and depressive mood (68%). Moreover, similar symptoms of psychopathology are also present in participants with Sub-PD, but their observed prevalence rates are quite lower (i.e. fatigue 52%, irritability 52%, and worry 42%).

### **Sociodemographic and socioeconomic associations**

The associations of PD and Sub-PD with sociodemographic and socioeconomic characteristics are shown in table 3. We present two series of odds ra-

**Table 1.** Characteristics of the Sample.

	(%)
<i>Sex</i>	
Male	2425 (49.6%)
Female	2469 (50.4%)
<i>Age group</i>	
18–29	1226 (25.1%)
30–39	1032 (21.1%)
40–49	934 (19.1%)
50–59	802 (16.4%)
60–70	900 (18.4%)
<i>Marital status</i>	
Married	2995 (61.2%)
Never-married	1446 (29.6%)
Divorced	240 (4.9%)
Widowed	213 (4.3%)
<i>Education</i>	
None/primary	926 (18.9%)
Lower secondary	797 (16.3%)
Upper secondary	2348 (48.0%)
Technical	439 (9%)
University	384 (7.8%)
<i>Employment status</i>	
Fully employed	2917 (59.6%)
Looks after home	691 (14.1%)
Unemployed	184 (3.8%)
Retired	577 (11.8%)
Other	525 (10.7%)
<i>Urbanicity</i>	
Urban	2682 (54.8%)
Semi-urban	607 (12.4%)
Rural	1605 (32.8%)
<i>Presence of financial difficulties</i>	
No	3283 (67.1%)
Yes	1611 (32.9%)
<i>Chronic diseases</i>	
No	4234 (86.5%)
Yes	659 (13.5%)
<i>Smoking</i>	
No	2955 (60.4%)
Yes	1937 (39.6%)

*Continues*

**Table 1.** Characteristics of the Sample (*Continued*).

	(%)
<i>Mental health disorders</i>	
Depression	142 (2.9%)
GAD	201 (4.1)
Panic disorder	92 (1.9%)
OCD	83 (1.7%)
Phobic disorders	137 (2.8%)
Mixed anxiety depressive disorder	131 (2.7%)
<i>CIS-R score</i>	
0–5	3484 (71.1%)
6–11	722 (14.7%)
12–17	332 (6.7%)
≥18	356 (7.2%)

tios, the first adjusted for all other sociodemographic and socioeconomic variables of the table (Model 1) and the second (Model 2) additionally adjusted for the presence of psychiatric comorbidity (as measured by the total CIS-R score excluding the panic related sections).

As seen in the table, statistically significant associations were very few. For PD a robust association was found for female gender, i.e. female participants were more likely to meet criteria for PD independently of general psychiatric morbidity. In addition, the presence of chronic physical diseases and the presence of financial difficulties were also significantly associated with PD independently of general psychiatric morbidity. Finally, significant associations that were noted between PD and age (age groups of 30–39, 40–49 and 60–70), upper secondary educational qualifications and having two or more children were not specific to PD as they became non-significant after adjustment for general psychiatric morbidity (CIS-R scores).

Additionally, significant associations were observed between subclinical panic symptoms (Sub-PD) and unemployment, the presence of chronic physical diseases and the presence of financial difficulties. Significant associations with female gender, being single, having two or more children, lower or upper secondary educational qualifications and



**Table 2.** Prevalence of panic attacks, panic disorder and subclinical panic disorder in a representative sample of the general population of Greece 18–70 (N=4894).

	Male		Female		Total
	Prevalence % (95% CI <sup>1</sup> )		Prevalence % (95% CI <sup>1</sup> )		
Panic Disorder	1.19% (0.76–1.62%)	$p^2 < 0.001$	2.55% (1.93–3.17%)		1.87% (1.50–2.26%)
Subclinical Panic Disorder	1.15% (0.73–1.58)	$p^2 = 0.01$	2.06% (1.50–2.62%)		1.61% (1.26–1.96%)
Panic Attacks (Past week)	2.35% (1.75–2.95%)	$p^2 < 0.001$	4.62% (3.79–5.44%)		3.48% (2.98–4.01%)

\*CI: Confidence Interval; <sup>2</sup> p-values for the comparison between male – female;

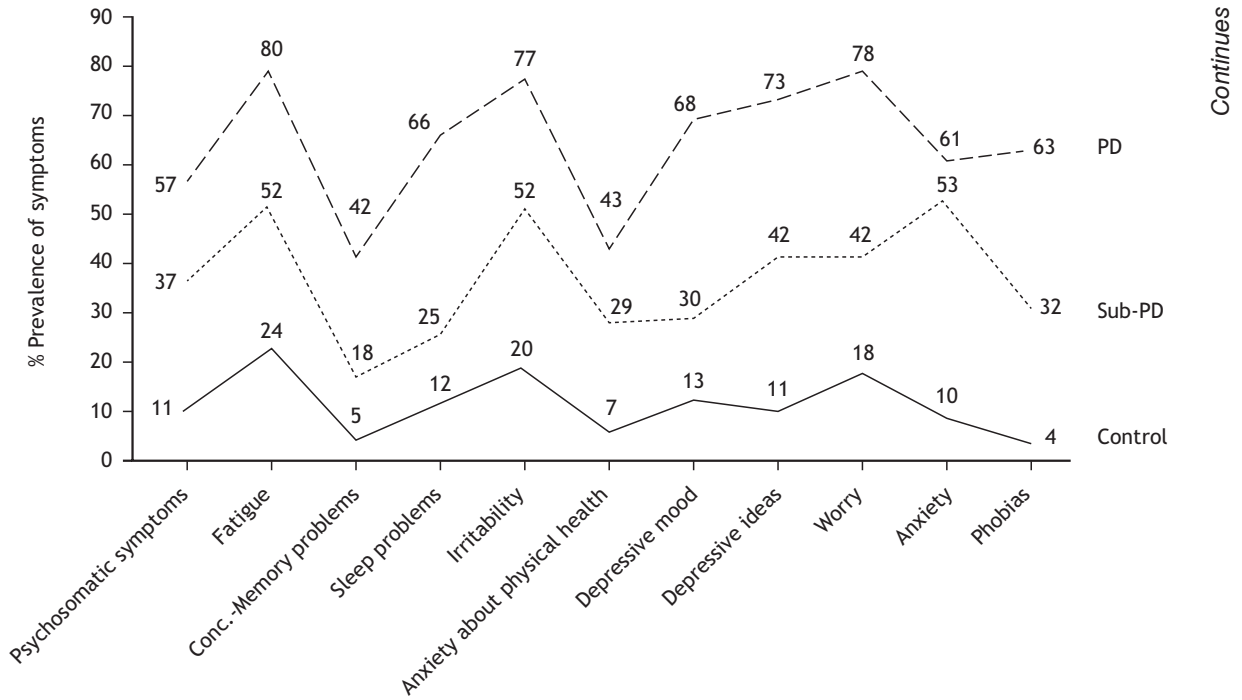
looking after the house were not specific to Sub-PD as they became non-significant after adjustment for psychiatric comorbidity.

### **Comorbidity, quality of life and use of health services**

In table 4 we present the comorbidity patterns of the two PD syndromes. It can be seen that participants with PD or Sub-PD were more likely to report other common mental disorders compared to healthy controls and that this association was more common and higher in those with the full-blown syndrome. Regarding PD, we noted significant comorbidity with all psychiatric conditions (i.e. depressive episode was present in 33.70% of participants with PD, generalised anxiety disorder in 58.70%, OCD in 29.35% and phobias in 63.04%), current suicidal ideation (15.22%) and current cigarette smoking (48.91%). For Sub-PD there was milder but significant associations only with the psychiatric conditions of generalized anxiety disorder (it was present in 15.19% of participants with subclinical PD symptoms) and phobias (11.39%), as well as with the variable current suicidal ideation (11.39%). Moreover, dissimilarly to the clinical condition, the Sub-PD significantly comorbid with frequent alcohol consumption and current cannabis use.

Quality of life is shown in figure 2, where PD and Sub-PD are presented according to their comorbidity with depression. PD is associated with a significant reduction in quality of life compared to controls (and that comorbidity with depression is associated with further reductions ( $p < 0.001$  in comparison with the controls). Overall, both PD and sub-PD had significant reductions in quality of life compared to controls: for PD, the mean score on the EQ-5D utility index was 0.52 versus 0.89 ( $p < 0.001$ ), while for sub-PD was 0.64 versus 0.89 ( $p < 0.001$ ). The difference between PD and sub-PD was also significant (0.52 versus 0.64,  $p = 0.03$ ), as it was the difference between depression and the two syndromes (0.47 versus 0.52 and 0.64 respectively). Finally, the most significant impact in the quality of life involved the comorbidity of PD with Depression (0.43,  $p < 0.001$  compared to controls).

The use of health services is shown in table 5 Compared to healthy participants, either PD or Sub-



**Figure 1.** Presence (%) of symptoms of psychopathology in participants with Panic Disorder (PD) and subclinical PD (Sub-PD) compared to the general population (control).

PD are both significantly associated with increased visits to GPs for medical reasons, or to mental health professionals for psychological reasons. More specifically, 53.26% of adults with PD visited a GP for medical reasons during the past 12 months, as did 37.97% of adults with sub clinical PD symptoms versus 15.56% of the control group. In addition, 44.57% of the participants suffering from PD and 18.99% of participants with sub clinical PD symptoms visited a mental health professional for psychological reasons during the past 12 months, versus 5.35% of healthy adults.

It is noted that the pattern of visits to GP (“medical reason”) as well as the pattern of visits to a mental health professional (“psychological reason”) is more likely in PD compared to subclinical symptoms.

**Discussion**

**Main findings**

In the current cross-sectional study we looked for associations between panic related syndromes and several sociodemographic and socioeconomic characteristics, their comorbidity patterns with

other common mental disorders, suicidal ideation, cigarette smoking, alcohol consumption and cannabis, as well as for associations of these disorders with the frequency of the use of health services among a nationally representative sample of the Greek adult general population. We found that panic syndromes are relatively common conditions and comorbid with other psychiatric disorders, such as depression, general anxiety disorder and phobias, although PD was more severe in terms of psychiatric comorbidity and suicidal ideation in comparison to Sub-PD.

In addition, there was evidence that having PD or Sub-PD was independently associated with a number of sociodemographic and socioeconomic variables such as female gender, the presence of chronic physical diseases and having financial difficulties for the first condition, and with unemployment, financial difficulties and suffering from chronic physical diseases, for the latter. Both panic related conditions involved elevated utilization of health services for both medical and psychological reasons in comparison to healthy participants.

Continues

**Table 3.** Sociodemographic associations of panic disorder (PD) and subclinical panic disorder (Sub-PD) in a representative sample of the general population of Greece 18–70 (N=4894).

	PD <sup>1</sup>						Sub-PD <sup>2</sup>					
	Odds Ratios–Model 1 <sup>3</sup>		Odds Ratios–Model 2		Odds Ratios <sup>3</sup>		Odds Ratios <sup>4</sup>		Odds Ratios <sup>5</sup>		Odds Ratios <sup>6</sup>	
	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>
<i>Gender</i>												
Men	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Women	2.16	1.39–3.37	1.98	1.21–3.23	1.81	1.13–2.87	1.52	0.89–2.58	1.52	0.89–2.58	1.52	0.89–2.58
<i>Age</i>												
18–29	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
30–39	2.03	1.02–4.06	1.44	0.64–3.26	1.62	0.81–3.26	1.18	0.52–2.70	1.18	0.52–2.70	1.18	0.52–2.70
40–49	2.25	1.13–4.50	1.20	0.50–2.87	1.32	0.62–2.78	0.78	0.31–1.98	0.78	0.31–1.98	0.78	0.31–1.98
50–59	1.66	0.77–3.54	0.65	0.25–1.73	1.65	0.79–3.44	0.77	0.29–2.03	0.77	0.29–2.03	0.77	0.29–2.03
60–70	2.23	1.11–4.49	0.57	0.19–1.69	1.67	0.82–3.41	0.58	0.19–1.77	0.58	0.19–1.77	0.58	0.19–1.77
<i>Marital status</i>												
Married	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Single	0.42	0.23–0.77	0.57	0.25–1.31	0.45	0.25–0.82	0.51	0.21–1.20	0.51	0.21–1.20	0.51	0.21–1.20
Divorced/Separated	1.60	0.76–3.39	1.32	0.60–2.93	0.63	0.19–2.02	0.51	0.15–1.72	0.51	0.15–1.72	0.51	0.15–1.72
Widowed	1.82	0.86–3.84	1.30	0.55–3.09	0.95	0.34–2.65	0.69	0.23–2.12	0.69	0.23–2.12	0.69	0.23–2.12
<i>Number of children</i>												
None/One	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Two or more	1.81	1.18–2.79	1.26	0.73–2.19	1.65	1.04–2.61	1.08	0.59–1.98	1.08	0.59–1.98	1.08	0.59–1.98
<i>Educational Qualifications</i>												
None/Primary education	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Lower secondary	0.80	0.43–1.47	0.93	0.48–1.81	1.05	0.57–1.95	1.17	0.59–2.29	1.17	0.59–2.29	1.17	0.59–2.29
Upper secondary	0.55	0.33–0.92	0.77	0.40–1.48	0.49	0.28–0.87	0.66	0.32–1.33	0.66	0.32–1.33	0.66	0.32–1.33
Technical vocational	0.48	0.19–1.17	0.68	0.25–1.86	0.19	0.04–0.80	0.27	0.06–1.27	0.27	0.06–1.27	0.27	0.06–1.27
Tertiary education	0.46	0.17–1.20	0.66	0.22–1.92	0.76	0.32–1.80	1.27	0.47–3.44	1.27	0.47–3.44	1.27	0.47–3.44
<i>Employment status</i>												
Full-time/part-time	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Looking after house	1.63	0.94–2.83	0.84	0.44–1.62	2.33	1.32–4.09	1.25	0.63–2.47	1.25	0.63–2.47	1.25	0.63–2.47
Unemployed	1.70	0.67–4.34	1.31	0.49–3.47	3.26	1.43–7.43	2.79	1.15–6.74	2.79	1.15–6.74	2.79	1.15–6.74
Retired	1.41	0.76–2.62	0.84	0.36–1.97	1.45	0.71–2.95	1.03	0.41–2.61	1.03	0.41–2.61	1.03	0.41–2.61
Other/Economically Inactive	1.07	0.52–2.19	1.14	0.53–2.48	1.28	0.59–2.77	1.53	0.66–3.53	1.53	0.66–3.53	1.53	0.66–3.53
<i>Presence of chronic physical diseases</i>												
No	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Yes	3.38	2.17–5.24	3.58	2.14–5.98	2.37	1.43–3.93	2.21	1.23–3.96	2.21	1.23–3.96	2.21	1.23–3.96



**Table 3.** Sociodemographic associations of panic disorder (PD) and subclinical panic disorder (Sub-PD) in a representative sample of the general population of Greece 18–70 (N=4894) (Continued).

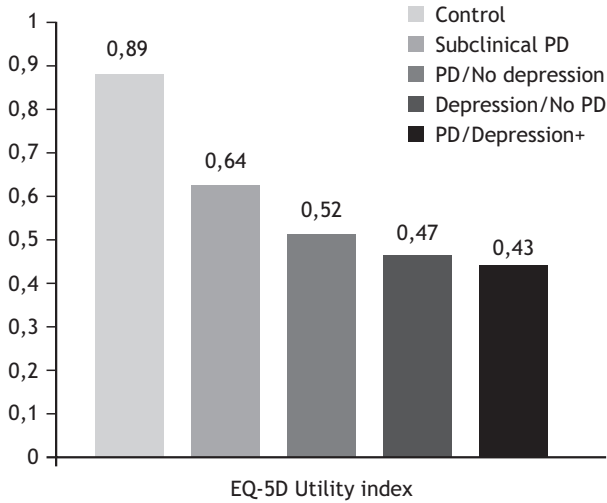
	PD <sup>1</sup>						Sub-PD <sup>2</sup>					
	Odds Ratios–Model 1 <sup>3</sup>			Odds Ratios–Model 2			Odds Ratios <sup>3</sup>			Odds Ratios <sup>4</sup>		
	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>	OR <sup>5</sup>	95% CI <sup>6</sup>
Type of locality												
Urban	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Semi-rural	0.95	0.49–1.83	0.91	0.47–1.78	1.56	0.82–2.96	1.48	0.77–2.83	1.56	0.82–2.96	1.48	0.77–2.83
Rural	0.98	0.62–1.55	0.91	0.57–1.46	1.31	0.81–2.15	1.15	0.69–1.91	1.31	0.81–2.15	1.15	0.69–1.91
Financial difficulties												
No	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref	1.00	Ref
Yes	2.74	1.65–4.54	1.89	1.09–3.26	2.69	1.56–4.64	2.05	1.14–3.68	2.69	1.56–4.64	2.05	1.14–3.68

<sup>1</sup>PD: Panic Disorder according to ICD-10 criteria, <sup>2</sup>Sub-PD: Subclinical panic symptoms; experiencing panic attacks but not meeting full criteria for ICD-10 obsessive compulsive disorder. The two conditions are mutually exclusive (see methods), <sup>3</sup>Odds ratios adjusted for all other variables of the table, <sup>4</sup>Odds ratios adjusted for all other variables of the table and psychiatric morbidity (total score on the CIS-R excluding Panic related sections), <sup>5</sup>OR: Odds Ratios, <sup>6</sup>CI: Confidence Interval, <sup>7</sup>Ref: Reference category. Values in bold indicate statistical significance at the 0.05 level.

**Table 4.** Comorbidity of panic disorder (PD) and subclinical panic disorder (Sub-PD) with other psychiatric disorders/use of substances in a representative sample of the general population of Greece 18–70 (N=4894).

Comorbid condition	(%) In total sample	(%) in participants with PD <sup>1</sup>	Odds Ratio <sup>3</sup> (95% CI <sup>3</sup> )	(%) in participants with Sub-PD <sup>2</sup>	Odds Ratio <sup>3</sup> (95% CI <sup>3</sup> )
Depressive episode	2.90%	33.70%	20.35 (12.47–33.22)	3.80%	1.15 (0.36–3.73)
GAD <sup>4</sup>	4.10%	58.70%	43.20 (27.28–68.42)	15.19%	3.93 (2.07–7.45)
OCD	1.69%	29.35%	33.47 (19.61–57.12)	3.80%	2.09 (0.64–6.82)
Phobias	2.79%	63.04%	97.49 (59.97–158.50)	11.39%	4.26 (2.07–8.75)
Current Suicidal ideation	1.68%	15.22%	11.18 (5.94–21.04)	11.39%	7.47 (3.55–15.72)
Frequent Alcohol Consumption	12.69%	15.22%	1.51 (0.84–2.71)	27.85%	3.26 (1.95–5.44)
Current Cigarette Smoking	39.60%	48.91%	1.83 (1.19–2.81)	45.57%	1.52 (0.96–2.43)
Current Cannabis use	2.06%	3.26%	2.68 (0.80–8.93)	2.53 %	1.76 (0.41–7.46)

<sup>1</sup>PD: Panic Disorder according to ICD-10 criteria, <sup>2</sup>Sub-PD: Subclinical panic symptoms; experiencing panic attacks but not meeting full criteria for ICD-10 panic disorder. The two conditions are mutually exclusive (see methods), <sup>3</sup>Odds ratios adjusted for age and sex and calculated from logistic regression models with the comorbid condition as the dependent variable and PD or Sub-PD as the independent variable. The reference group for the reported odds ratios is “participants without PD or Sub-PD respectively”, <sup>4</sup>GAD: Generalized anxiety disorder



**Figure 2.** Quality of life (scores on the EQ-5D index) in participants with Panic Disorder (PD) and subclinical PD (Sub-PD) according to comorbidity with depression

**Prevalence**

The prevalence of panic disorder (PD) among the participants of this study was 1.87% (95% CI: 1.50–2.26). Our findings lay within the range of other general population studies that estimated the prevalence of PD across the world between 1.7% to 4.7%.<sup>10–12</sup> Reports on the prevalence of subclinical panic symptoms in epidemiological studies are rare,<sup>17</sup> in our study the prevalence rates of such symptoms (1.61%, 95% CI: 1.26–1.96) although lower, are also consistent with similar studies available, whose results ranged from 1.90% to 2.73%.<sup>17,15</sup> Discrepancies in the estimation rates of these studies concerning the prevalence of PD and Sub-PD could be explained due to methodological variations in the screening and diagnostic tools, differences in the diagnostic criteria applied, whether or not there was involvement of clinicians in the administration of the interviews<sup>12,36</sup> as well as in differences in characteristics of the samples.<sup>37,38</sup>

**Sociodemographic and socioeconomic associations**

In our study a broad number of sociodemographic variables have been also examined for possible associations with PD and Sub – PD. We observed significant associations for both conditions with financial difficulties and the presence of chronic physical diseases. Significant associations have

**Table 5.** Use of health services use in participants with panic disorder (PD) and subclinical panic disorder (Sub-PD) in a representative sample of the general population in Greece (N=4894).

	Use of health services	
	Visited GP <sup>1</sup> for medical reasons (past 12 months)	Visited Mental Health professional for psychological reasons (past 12 months)
	(%)	OR2 (95% CI <sup>3</sup> )
No PD	15.56%	1.00 (Reference)
Sub-PD	37.97%	2.92 (1.82 – 5.84)
PD	53.26%	5.63 (7.88 – 18.92)

<sup>1</sup>GP: Any doctor in general practice (including internal medicine specialists practicing mainly general medicine in Greece), <sup>2</sup>Odds ratios adjusted for age and sex and calculated from logistic regression models with frequent doctor visits as the dependent variable and PD or Sub-PD as the independent variables (e.g., the odds of frequent doctor visits for a medical reason was 1.70 times higher for participants with Sub-PD compared to participants without Sub-PD). Bold values indicate statistical significance at the 0.05 level, <sup>3</sup>CI: Confidence Interval

been also found for female gender and PD and for unemployment and sub – PD. Our findings are in line with a number of contemporary epidemiological studies whose observations also describe associations between PD and factors such as female gender, the presence of chronic physical diseases and experiencing financial difficulties,<sup>10,11,15</sup> They are also in agreement regarding associations between Sub-PD and factors such as unemployment, the presence of chronic physical diseases and having financial difficulties.<sup>10,15,17</sup>

On the other hand, the abovementioned epidemiological studies had also identified significant associations with other sociodemographic factors not observed in our analysis. For instance, De Jonge et al (2016)<sup>10</sup> in his epidemiology study of PD using data from the World Mental Health Surveys<sup>38,39</sup> reported associations for both conditions with age, lower education and being divorced or widowed. Batelaan et al (2006)<sup>15</sup> also described additional SES associations with PD (i.e. lower education, urbanicity, living alone, low household income, low self-esteem) and sub PD (i.e. age, lower education, living alone, low household income). In our study, significant associations were also noted for PD and age, upper secondary educational qualifications and having two or more children, but their statistical power diminished after adjustment for general psychiatric morbidity (CIS-R scores). Similarly, whereas several factors such as female gender, being single, having two or more children, and looking after the house displayed significant associations with Sub-PD in the first analysis section, they became non-significant after adjustment for CIS-R scores.

Considering the abovementioned observations some factors (i.e. gender, age, financial difficulties) appear to be associated with PD and/or subthreshold PD across most epidemiological studies. Most epidemiological studies, despite their inconsistencies,<sup>15</sup> postulate that at least some environmental factors seem to hold an important role in the course and development of PD. Nevertheless, many suggest a process of complex interactions between genetic,<sup>40–42</sup> environmental<sup>43–45</sup> and psychological factors<sup>46</sup> in the development of PD.

Moreover the robust associations of PD and Sub-PD with financial difficulties observed in our analy-

sis, even after adjustment for general psychiatric morbidity (CIS-R scores), and the associations of Sub-PD with unemployment, are of particular interest in the context of the current economic situation in Greece. Further research should shed light on the impact that austerity has in the emergence and prevalence of psychiatric morbidity in Greece examining the role of unemployment and financial strain in the transition from health to subclinical forms of disease and the emergence of full blown psychiatric syndromes.

### ***Comorbidity, quality of life and use of services***

PD is highly comorbid thus people suffering from it often struggle with additional psychiatric disorders,<sup>10,16</sup> and this is noticeable yet in the subthreshold forms of the condition.<sup>15,18</sup> PD involves considerable decline in the quality of patients' lives<sup>1</sup> and comorbidity is associated with further deterioration. For instance, comorbidity of PD and depression involves considerably more incidents of suicide attempts than PD or major depression alone.<sup>47</sup> In our analysis the propositions made above are evident and our results suggest that PD and Sub-PD seriously challenge the health status of the adult general population in Greece. According to our estimations, a little less than two in three of our samples with PD also met criteria for generalized anxiety disorder and phobias, one third of them also suffered from depressive episode and a little less than one in seven also suffered from suicidal ideation. In addition, comorbidity with generalized anxiety disorder and phobias was considerably high (though milder) even in the subthreshold condition. Interestingly suicidal ideation comorbidity with Sub – Pd nearly matched the clinical condition's estimation. Our findings are in agreement with previous studies showing heightened comorbidity between PD and other psychiatric conditions as well as suicidal ideation<sup>5,10,17,19,20,23</sup> and considerable but milder comorbidity associations with Sub-PD.<sup>15–18</sup> PD comorbidity is associated with further deterioration in the quality of patients' lives<sup>48</sup> but more research is necessary to illuminate the impact of such comorbidities in the already depleted quality of life of individuals suffering from it.<sup>1</sup>

The burden of PD described above in combination with its persistent and relapsing course,<sup>17,48</sup> and the impairments in the quality of life,<sup>1</sup> often results to an augmented utilization of health services. This is well observed in many studies,<sup>1,24,49</sup> as well as in ours, where participants suffering from PD or Sub-PD displayed considerably elevated visits to GPs for medical reasons or to mental health professionals for psychological reasons, in comparison with healthy ones. Such visits are fuelled by sudden and intense somatic symptoms associated with PD that mimic medical conditions such as asthma and cardiovascular illness and require further diagnostic, time consuming and expensive processes.<sup>1,25</sup> Considering the complexity of the symptoms and the high comorbidity with other mental disorders, the diagnosis of PD can be a daunting task.<sup>50</sup> According to Vermani et al (2011)<sup>51</sup> misdiagnosis rates for PD among 840 primary care patients were as high as 85.8%, and this indicates an important barrier for the individuals suffering from PD until they receive a correct diagnosis and an optimal treatment.

### **Limitations of the study**

A few limitations characterize our study. Since there was no clinical validation in the structured diagnostic interview, we employed the possibility that there was an overestimation in the prevalence of common psychiatric disorders in the general population<sup>52</sup> cannot be ruled out. What is more the cross-sectional design of our study does not allow us to reject the likelihood of reversed causality in the observed associations therefore we cannot suggest any causal relations. Finally, our data has been derived from a general Greek population survey and there was a rather low response rate (54%), which is typical of surveys of this type in Greece and elsewhere.<sup>3</sup> Hence selection bias cannot be ruled out although it is unlikely since our sample has been representative of the Greek adult population and the sex distribution and age of the participants was comparable to the national data.

### **Implications and conclusions**

This study was the first epidemiological study of a nationally representative sample in Greece exploring the prevalence, comorbidity use of health services

and several SES associations for panic related conditions. According to our observations panic disorder and subthreshold panic are quite common in the general adult Greek population with substantial comorbidity rates for the clinical type and milder but also important comorbidity rates for the subthreshold type. It has been proposed that the emergence of PD, as it happens with other psychiatric disorders, is characterized by continuity,<sup>53</sup> and the severity of the symptoms progress with the passage from benign to more poignant versions of panic,<sup>17</sup> where subthreshold panic holds a transitional space amidst health (or no panic) and PD.<sup>15</sup> We observed milder associations for subthreshold symptoms indicating a moderate impact in the lives of the participants in comparison to PD. These observations could generate questions in relation to the onset and course of this disorder as described above and further research to illuminate the pathway of PD. For instance, new research should investigate if there is an in-between position occupied by subthreshold forms of panic and a transitional process from such forms to the full-blown panic disorder.

Finally, the observed overuse of the general and psychological health services among adults with panic symptoms and its temporal and economic consequences could be controlled with the development of more efficient diagnostic and treatment plans where the patients will be entitled to timely and to the point care. Such specialized health structures, offering high quality management and treatment of PD and other anxiety disorders are sporadic in the Greek primary health care system. Despite the availability of efficient treatments for the above-mentioned disorders,<sup>50</sup> in many cases in Greece, psychological and psychiatric treatments are very brief and limited in offering common encouragement the first and some standardized psychotropic medication prescription the latter. For that reason emphasis must be given in the promotion and establishment of specialized services and protocols where the patients will receive an optimal treatment, they will have the opportunity to understand the nature of the disorder, to become informed about their treatment options and educated in relation to the personal management of this debilitating syndrome.

# Η επιδημιολογία της διαταραχής πανικού και των υποκλινικών συμπτωμάτων πανικού στον ελληνικό γενικό πληθυσμό

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Ψυχιατρική 2020, 31:201–215

Η Διαταραχή Πανικού (ΔΠ) είναι μια κοινή ψυχιατρική νόσος που ανήκει στην κατηγορία των διαταραχών άγχους και επιφέρει σοβαρή επιβάρυνση στην υγεία και την καθημερινότητα των ατόμων που υποφέρουν από αυτήν. Μελέτες στον γενικό πληθυσμό που επιχειρούν να μετρήσουν τον επιπολασμό αυτής της διαταραχής ανά τον κόσμο υποστηρίζουν ότι περίπου 1,7% με 4,7% του ενηλίκου και εφηβικού πληθυσμού έχουν ΔΠ. Στην Ελλάδα, η σχετική έρευνα, είναι περιορισμένη καθώς προηγούμενες μελέτες έχουν χρησιμοποιήσει μικρά δείγματα πληθυσμού. Σκοπός της μελέτης μας ήταν η περιγραφή του επιπολασμού και των κοινωνικο-δημογραφικών συσχετίσεων της διαταραχής πανικού (ΔΠ) και των σχετιζόμενων υποκλινικών συνδρόμων στον γενικό ενήλικο πληθυσμό της Ελλάδας, καθώς και η εκτίμηση της συννοσηρότητας, της χρήσης των υπηρεσιών υγείας και των επιπτώσεων των παραπάνω συνδρόμων στην ποιότητα ζωής των ατόμων. Η παρούσα μελέτη αποτελεί δευτερογενή ανάλυση της μελέτης ψυχιατρικής νοσηρότητας του γενικού ενήλικου Ελληνικού πληθυσμού που διενεργήθηκε το διάστημα 2009–2010 σε αντιπροσωπευτικό δείγμα της χώρας (4.894 συμμετέχοντες που ζούσαν σε ιδιωτικά νοικοκυριά, ποσοστό συμμετοχής 54%). Για την εκτίμηση της ψυχιατρικής νοσηρότητας χρησιμοποιήθηκε η αναθεωρημένη Κλινική Διαγνωστική Συνέντευξη (CIS-R). Η εξέταση της ποιότητας ζωής έγινε με τη χρήση του εργαλείου EuroQoL EQ-5D και η χρήση των υπηρεσιών υγείας αξιολογήθηκε χρησιμοποιώντας σχετικές ερωτήσεις. Όλοι οι κοινωνικο-δημογραφικοί και κοινωνικο-οικονομικοί δείκτες εξετάστηκαν κάνοντας ευθείες ερωτήσεις στους συμμετέχοντες. Σύμφωνα με τα αποτελέσματά μας το 1,87% των συμμετεχόντων (95% διάστημα εμπιστοσύνης [CI]: 1,50–2,26%) πληρούσαν τα κριτήρια για ΔΠ και 1,61% πληρούσαν τα κριτήρια για τα υποκλινικά συμπτώματα πανικού (95% CI: 1,26–1,96%) και υπήρξε μια ξεκάθαρη υπεροχή του θηλυκού φύλου στη συσχέτιση με τη ΔΠ ( $p=0.001$ ) και με την υποκλινική ΔΠ ( $p=0.01$ ). Η ΔΠ ή τα υποκλινικά συμπτώματα πανικού συσχετίστηκαν μόνο με έναν περιορισμένο αριθμό κοινωνικο-δημογραφικών και κοινωνικο-οικονομικών μεταβλητών, ειδικότερα μετά τη σταθμισμένη ανάλυση. Επίσης και τα δύο αυτά σύνδρομα πανικού σχετίζονται με σημαντικές εκπτώσεις στην ποιότητα ζωής των ασθενών και αυξημένη χρήση των υπηρεσιών υγείας για ψυχολογικά ή παθολογικά αίτια σε σύγκριση με υγιή άτομα. Συμπερασματικά, τόσο η διαταραχή πανικού (ΔΠ) όσο και τα υποκλινικά συμπτώματα πανικού είναι κοινά στο γενικό ενήλικο ελληνικό πληθυσμό με σημαντική συννοσηρότητα και έκπτωση στην ποιότητα ζωής. Η παρατηρηθείσα χρήση των υπηρεσιών υγείας από άτομα που υποφέρουν από συμπτώματα πανικού καλεί για τη σχεδίαση πιο αποτελεσματικών πολιτικών αντιμετώπισης.

**Λέξεις ευρετηρίου:** Επιδημιολογία, διαταραχή πανικού, ενήλικοι, συννοσηρότητα, ποιότητα ζωής, Ελλάδα.



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