

# The Prevalence of patients with panic attacks (PAs) and panic disorder (PD) visiting Emergency Departments of the Verona Hospital

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*Key words: Panic attacks (PAs), panic disorder (PD), anxiety, panic, emergency department*

*Parole chiave: Attacchi di panico (PA), disturbo da attacchi di panico (DAP), ansia, panico, pronto soccorso*

## Abstract

**Background.** Panic Attacks (PAs) and Panic Disorder (PD) represent a heavy burden not only because of the difficulty in distinguishing them from other pathologies and in treating them appropriately but also because of their impact on public health worldwide. In Europe, PD constitutes one of the five most common mental disorders adversely affecting quality of life.

**Study design.** The aim of this study is to evaluate the period prevalence of visits to the Emergency Departments of the University Hospital of Verona (North East of Italy) over the period between 2012-2016 because of symptoms of PAs or PD in order to quantify the burden of the disorder.

**Methods.** This study was carried out by retrospectively collecting data from the medical records of all the patients assessed at the Emergency Departments (EDs) of the Verona Hospital because of symptoms of PAs or PD over a 5-year period (1 January 2012 - 31 December 2016). The search words used in reviewing the medical records registered in the hospital discharge reports from the Gynecological, Pediatric and General Medicine Emergency Departments were: "Anxiety" and/or "Panic". A multiple logistic regression model was also created to evaluate the predictors of ED visits for PAs or PD over the period that was investigated.

**Results.** The study identified 3,771 cases of PAs or PD; 62.3% were females and 37.7% were males. The female-to-male ratio was 1.7:1. The mean age was 44 years (46 for the females and 41 for the males). The majority of the patients fell into two age categories: 30 to 39 (20.6%) and 40 to 49 (23.8%). The proportion of visits to the EDs for PAs or PD was approximately 20% per year, with an average of approximately 754 patients visiting the EDs every year. The period prevalence of accesses for PAs or PD over the five year period studied in the mean resident population (1.4%) and the mean visits to the EDs (2.5%) were calculated. Study results showed that the majority of the patients (80.9%) were referred to their general practitioner (GP) at the end of the assessment protocol at the EDs. According to the regression logistic model, the following variables were significant ( $p < 0.05$ ) risk factors for PAs or PD: being female vs. male (OR 1.899; 95% CI 1.785-2.020), being Italian vs. Foreigner (OR 1.292; 95% CI 1.174-1.421), having a white or green priority code at arrival (low urgency) vs. the other ones (OR 1.195; 95% CI 1.100-1.297), and being aged  $\leq 42$  years old (OR 1.091; 95% CI 1.024-1.161).

**Conclusions.** The role of the GP is crucial in the management of PD and PAs. Given the difficulty of implementing primary and secondary prevention programs for these conditions, public health officials should make every effort to promote tertiary prevention in order to reduce the burden of the ailment and societal cost.

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## Introduction

Accounting for about 1% of all Disability Adjusted-Life years worldwide in 2010, anxiety disorders are the mental disorders that rank second only to depressive ones (1, 2). Panic attacks (PAs), defined as an uncontrollable sudden fear or anxiety, and Panic Disorder (PD), defined as the presence of recurrent, unexpected panic attacks, are two independent diagnostic entities (3-6). Although the etiology of PD is not entirely clear, it seems to be multifactorial and heterogeneous. A variety of hypotheses have been proposed in the light of different mechanisms underlying the development of panic (5, 7-22). New approaches to defining activity in the human brain such as Functional Magnetic Resonance Imaging (fMRI) and biochemical analyses have uncovered that panic attacks occur when an individual interprets a previously neutral stimuli or symptom as a signal of danger (5, 11-17). There appears to be an anomalous connection in subjects with the disorder between the prefrontal cortex and the limbic system (18) on functional grounds and an imbalance in noradrenaline (NA), serotonin and GABA neurotransmitter concentrations (19-21).

Data collected between 2001 and 2012 by the World Mental Health Surveys uncovered that the worldwide lifetime prevalence (the proportion of the population that has ever experienced a PA or PD) was respectively 13.2% and 1.7% (23, 24), with the highest prevalence rates registered in high-income countries. More specifically, according to an important cross-national epidemiological analysis, PA and PD prevalence in the Americas resulted respectively 16.8% and 2.2%; it was 15.6% and 2.0% respectively in the Western Pacific and 13.6% and 1.9% respectively in Western Europe (24). In Italy, the lifetime prevalence of PAs was found to be 8.0%; that of PD was 1.6% (24). The female gender (24-26), being younger than 60 (24), belonging to an ethnic minority (27,

28), a low educational level (24), limited economic resources (26), being unemployed or unmarried (24), an early age at onset of PA or PD (24), a parental history of mental disorder (26), having smoking and/or alcohol problems or other anxiety and mental disorders (26) are all risk factors for the onset of PA and/or PD.

In 2004 the WHO World Mental Health (WMH) conducted the 'European Study on the Epidemiology of Mental Disorders' (ESEMeD) in six European countries (Italy, France, Belgium, Holland, Germany and Spain) (29). The study reported that approximately 20 million people had experienced a mental disorder over the previous year's time, more than 12 million had experienced an anxiety disorder, and more than 9 million a mood disorder (29).

According to some studies, after appropriate long-term treatment between 17% and 70% of patients continued to have panic attacks, between 36% and 82% had phobic avoidance, and only one third maintained a disease free condition over time (30, 31). According to others, approximately 50% of patients had a relapse after remission and one third continued to experience PAs or PD; approximately half showed phobic avoidance and about 30% experienced difficulties in participating in social life (31-34).

According to the data of a systematic epidemiological study carried out in Italy examining the prevalence of mental illnesses, 8 million adults suffered from mental disorders during their lifetime, with a lifetime prevalence of panic disorder of 1.6% (95 CI% 1.2%-1.9%) (35). The economic burden of Panic Disorder is exceedingly high as it is responsible for the largest percentage of the overall burden with respect to other mental disorders (36). It is, in fact, one of the five mental disorders with the strongest impact on quality of life (29), work days missed (29, 37) and production loss (36). Interest in its impact and the treatments that are presently available to help reduce

symptoms has increased because of the variety of its physical manifestations and the inappropriate use of medical care service that is frequently associated to them (38). About 80% of patients with panic disorder have sought medical help during their lifetimes (39, 40) and Emergency Departments (EDs) are frequently overflowing with people experiencing panic attacks.

The current study set out to evaluate the period prevalence of individuals with PAs or PD who sought assistance at the Emergency Departments of the Verona Hospital (a city located in North-east Italy) over a five year period (between 2012 and 2016) to calculate the burden of these pathologies on the Italian Health Care System.

## Materials and methods

### *Study Design*

This study was carried out by retrospectively collecting data from the medical records of all the patients admitted for panic symptoms to the General Medicine, Gynecologic and Pediatric Emergency Departments (EDs) of the Hospital of Verona over a 5-year period (1 January 2012 - 31 December 2016) in order to estimate the period prevalence of accesses for PAs or PD over this time period.

The search terms used in reviewing the medical records registered in the hospital discharge reports from the EDs were: "Anxiety" and/or "Panic". The diagnosis of PA was made in accordance with the diagnostic criteria outlined in the Diagnostic and Statistical Manual version-5 (DSM-5) according to which:

- A PA is characterized by 4 or more of the following 13 symptoms not related to any medical condition or substances effects that develop abruptly and peak rapidly in less than 10 minutes: palpitations, sweating, dizziness, numbness or tingling sensations (paresthesias), chills, feelings of unreality

(derealisation), a feeling of choking, chest pain, dyspnea, nausea or abdominal distress, fear of losing control, of going crazy or of dying (4, 5).

- Panic Disorder (PD) is defined as the occurrence of recurrent, unexpected panic attacks. In addition, at least one attack is followed by one month or more of the person fearing that they will have more attacks. The fear is often associated to changes in behavior frequently leading to phobic avoidance.

### *Patients' Information*

The patient-related data that were collected included: identification code, sociodemographic information, the date of access to the ED, the admission and discharge triage color tags (white, green, yellow, red) and the referral made by the ED provider.

More specifically, the following data were registered and analyzed:

- The type of ED the patient approached (General Medicine, Gynecologic, and Pediatric);

- The number of patients with PAs who approached the EDs: the total number for each year and the average proportion per year;

- The time of year the patient approached the ED: the month and period [the year was divided into four trimesters (January to March; April to June; July to September; October to December)], the day of the week and the time of day (the local time using a 24 hour clock);

- The patient's gender, age group, nationality (Italians/Foreigners). The age groups were defined as ages between: 0-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79 and older than 80.

- The patients' triage codes at arrival and at discharge.

The data were also analyzed in relation to the patients' gender, age groups and clinical outcomes.

The patients were classified according to the referral registered by the emergency department provider when the assessment was concluded. These were classified in the following way: the protocol was closed at the time of triage; the patient was discharged; the patient was referred to the general practitioner (GP); the patient was referred to the state agency monitoring work-related accidents (INAIL) or to other Institutions; the patient was hospitalized by ED; the patient refused to be admitted to the hospital; the patient refused to be placed under observation or to receive other care; the patient left the ED before the protocol was concluded; the patient was transferred to a psychiatric facility.

Data concerning the resident population were obtained from the city of Verona's general registry office; the average resident population during the study period was the one that was registered for June 30, 2014 (at the study's halfway point).

The Italian "privacy" law and the Helsinki Declaration on human subjects were fully respected; and the protocols were approved by the local ethical committee.

### *Statistical analysis*

The data collected were registered and analyzed using the Microsoft Excel 2016 and STATA 13.

To calculate the burden of PAs or PD in this geographical area, the patients' distributions by gender and age groups were determined as proportions of both the local resident population of Verona and of the total number of persons accessing the EDs over the five year period studied. Moreover, the overall periodic prevalence of PAs or PD over the 5-year period studied was calculated with respect to both the general population and to the total number of patients accessing the EDs. A 95% confidence interval (CI) for the females and males with PAs or PD was also determined for the entire study period.

The proportions of the number of visits to EDs because of PAs or PD was calculated for each of the five years investigated.

The numbers and percentages of the patients in the various age groups, their gender, and nationality as well as in the type of ED they accessed, the time (recorded as seasons/months/ days of the year), admission and discharge codes and the patient's referrals were registered and analyzed, as well as the numbers and percentages of the patients who were given one triage code at admission but switched to another one at the time of their discharge.

Simple linear regression tests were performed to evaluate if there were any statistically significant patterns in the patients' genders or nationalities (Italian/Foreigner) or in the type of ED that was accessed (General Medicine, Gynecologic and Pediatric) that was approached over the five-year time period investigated (Table 1).

The Anova Oneway Test was performed to verify if the median age of the PA patients changed over the five-year period investigated  $\alpha=0.05$ .

The Kruskal-Wallis non-parametric statistical test was performed to verify if there were any differences in the numbers of patients accessing the EDs on different days of the week.

The Chi-square test was used to analyze the categorical variables, comparing subgroups such as Italians and Foreigners (Table 1) and females and males in every age group (Figures 1A and 1B). A P value of  $<0.05$  was considered significant.

A multiple logistic regression model was fitted to the data using PAs or PD as the dependent variable and gender, nationality, age, the year of access to the ED, the type of ED accessed and the type of priority code at arrival as the independent variables (Table 2).

Multivariate associations of potential determinants with PAs or PD were expressed using ORs and the 95% CI.

Table 1 - Proportions of patients with panic attacks or Panic Disorder classified according to their gender and nationality who visited the three types of emergency departments over the five year period studied.

Variables	Proportions (%)					Overall
	2012	2013	2014	2015	2016	
Panic attack (ratio) $\diamond$	20.7%	19.8%	20.9%	20.6%	18.0%	100.0%
Hospitals						
General Medicine ED $\diamond$	99.4%	99.5%	98.7%	97.3%	97.8%	98.6%
Gynecologic ED *	0.0%	0.1%	0.4%	0.5%	0.7%	0.3%
Pediatric ED $\diamond$	0.6%	0.4%	0.9%	2.2%	1.5%	1.1%
Gender						
Female $\diamond$	65.5%	63.2%	63.9%	55.7%	63.5%	62.3% #
Male $\diamond$	34.5%	36.8%	36.1%	44.3%	36.5%	37.7% #
Nationality						
Italians $\diamond$	89.6%	89.2%	86.7%	87.6%	84.2%	87.5% &
Foreigners $\diamond$	10.0%	10.3%	13.1%	12.1%	14.3%	11.9% &
Non responders	0.4%	0.5%	0.3%	0.3%	1.5%	0.6%

p value for year trend: simple linear regression test

\* = p value < 0.05;  $\diamond$  = p ns

p value for group: Chi-squared test #, & = p value < 0.05

Table 2 - Multiple Logistic Regression Model: Predictors of visits to the Emergency Department (ED) for PAs or PD over the 5 year period that was investigated

Predictors of ED visits for PAs or PD: (Pseudo-R <sup>2</sup> = 0.0305, p = 0.0000)	Odds Ratio (95% CI)
Being female vs. male	1.899* (1.785-2.020)
Age (years)	Being aged $\leq$ 42 years old § 1.091* (1.024-1.161)
ED visits occurring in 2012 compared to:	
visits occurring in 2013	0.624* (0.569-0.684)
visits occurring in 2014	0.644* (0.588-0.706)
visits occurring in 2015	0.618* (0.562-0.680)
visits occurring in 2016	0.525* (0.475-0.580)
Nationality	Being Italian: 1.292* (1.174-1.421)
Access to the Pediatric ED compared to:	
Access to the Gynecologic ED	0.036* (0.009-0.148)
Access to the General Medicine ED	7.568* (5.531-10.355)
Triage priority code at arrival	Low urgency (white or green triage priority code): 1.195* (1.100-1.297)

§= age median value; OR=Odds Ratio; \*p<0.05

Figure 1A

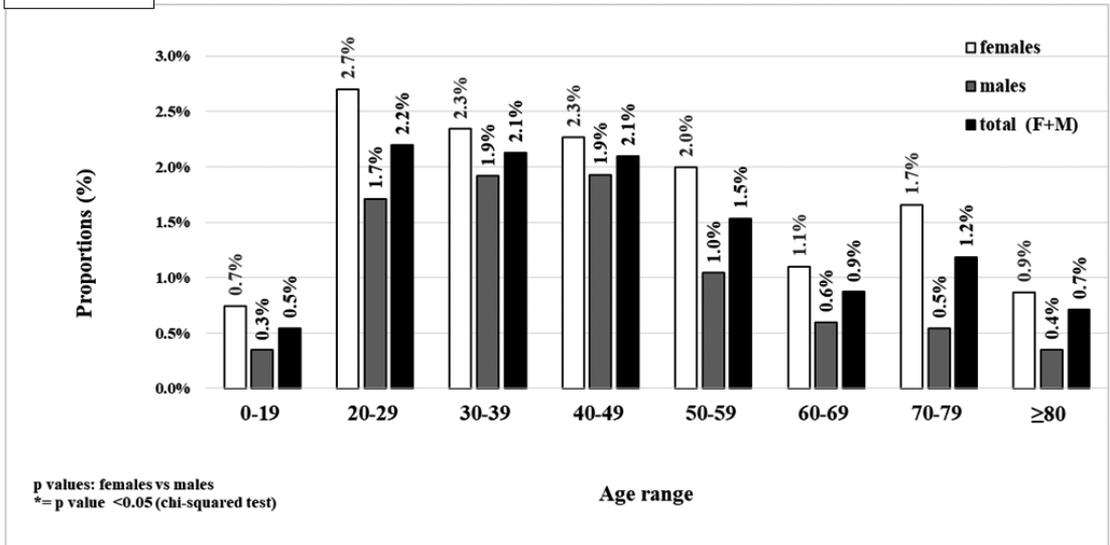


Figure 1B

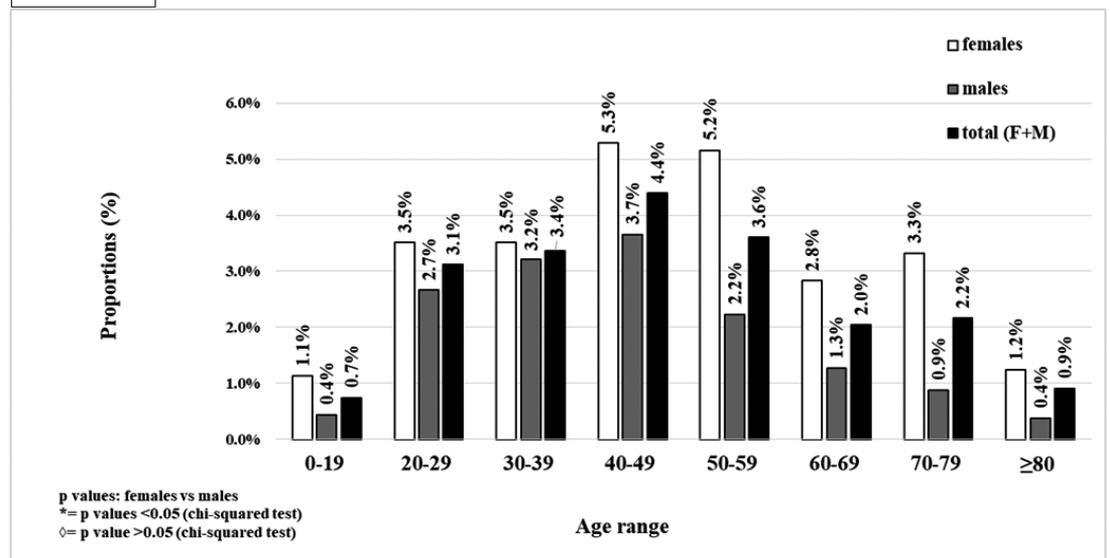


Figure 1A and B - Proportions of PAs or PD by age classes and gender, related to the mean of the resident population (1A) and related to the mean of the total ED accesses for all causes (1B).

More specifically, dichotomous variables were created for age using the patients' median age as the cut-off, and for the priority triage codes, which were distinguished as low urgency (white and green codes) or as high urgency (red or yellow codes). Moreover, to investigate the impact of the period of access, we created dummy variables and calculated the ORs for all the years with reference to the first year of observation. Lastly, to investigate the role of the type of Emergency Department, we used the Pediatric ED as the reference group and calculated the OR for the accesses to General Medicine ED and Gynecologic ED.

## Results

The study identified 3,771 cases of panic attacks or panic disorder; 62.3% were in females (95% CI 61.0%-64.0%; 2,350 cases) and 37.7% were in males (95% CI 36.0%-39.0%; 1,421 cases), with a female-to-male ratio of 1.7:1.

The mean age was 44 years; 46 for the females (range 5-95 years) and 41 for the males (range 7-90 years). The majority of the patients fell into the 30 - 39 age range (20.6%) and the 40 - 49 age range (23.8%). Twenty-two point one percent of the patients were younger than 30; 13.9% and 19.6% of the patients respectively fell into the 50 - 59 age range and the 60 and over age range.

Table 1 shows the proportions of visits to EDs over the five-year period that was investigated (2012-2016). The proportion of accesses with PAs or PD was approximately 20% every year with an average of approximately 754 patients accessing the EDs every year. The slight fall in numbers over the five-year period studied (from 20.7% in 2012 to 18.0% in 2016) was not significant ( $p=ns$ , simple linear regression test).

Ninety-eight point six percent of the patients accessed the General Medicine ED; the highest percentages were female (42.3%) and Italians (87.5%).

The only significant trend over the five year period was found for the number of cases accessing the Gynecologic ED ( $p<0.05$ , simple linear regression test).

The proportions of visits to the ED by gender were substantially constant both in the female and male populations without significant differences ( $p=ns$ , simple linear regression test).

The proportions were always significantly higher in the females than in the males when the figures for the overall sample were analyzed (females 62.3%, males 37.7%), both when the data were calculated with reference to the resident population (females 1.7%, males 1.1%) and with reference to the total population admitted to the EDs (females 3.3%, males 1.9%) (in all cases:  $p<0.05$ , Chi-square test).

Eleven point nine percent of the visits to the EDs were made by foreigners from various geographical areas: 6.0% from Asia, 24.3% from Africa, 59.7% from other European countries, 9.8% from America and 0.2% from Oceania. The proportion of foreign patients was substantially constant over the five-year time period.

There was a statistically significant difference in the number of visits in the overall sample population between the Italians (87.5%) and non-Italians (11.9%); this was seen in both the mean percentage (1.3% of Italians vs 0.2% of Foreigners) and in the mean percentage of the total number of visits to the EDs (2.1% of Italians vs 0.3% of Foreigners), (in all cases:  $p<0.05$ , Chi-square test).

The proportion of visits over the five-year period (2012-2016) calculated with reference to the mean resident population and the total number of visits to the EDs were respectively 1.4% (95% CI 1.4%-1.5%) and 2.5% (95% CI 2.5%-2.6%).

Table 2 shows the predictors of ED visits for PAs or PD over the 5 years that were investigated.

According to the regression logistic model, the following variables were significant ( $p < 0.05$ ) risk factors for PAs or PD: being female vs. male (OR 1.899; 95% CI 1.785-2.020), being Italian vs. Foreigner (OR 1.292; 95% CI 1.174-1.421), having a white or green priority code at arrival (low urgency) vs. the other ones (OR 1.195; 95% CI 1.100-1.297), and being aged  $\leq 42$  years old (OR 1.091; 95% CI 1.024-1.161).

The model also suggests that there was a statistically significant ( $p < 0.05$ ) negative association between the outcomes and the ED visits that took place each year following the first year of observation (2012), which was used as a reference year. The type of ED was also significantly associated ( $p < 0.05$ ) to the PAs or PD with respect to the reference point (Pediatric ED visits). In fact, the Gynecologic ED visits were negatively (OR 0.036; 95% CI 0.009-0.148) associated, while the General Medicine visits were positively (OR 7.568; 95% CI 1.100-1.297) associated to the outcomes.

Figures 1A and 1B show the proportions of visits to the EDs by patients classified according to their age classes and gender in relation to the mean resident population (1A) and the mean of the total number of ED visits for all causes (1B).

When the proportions of visits to the EDs were calculated in relation to the mean resident population (Figure 1A), it became clear that:

- when both sexes were considered (total: females plus males) the highest proportion was found in the patients between 20 and 49; there was a modest increase (2.2%) in the 20-29 age range and a peak in the youngest (0.5%) and oldest (0.7%) age groups;

- the highest proportion was detected in the females (2.7%) in the 20-29 age range and in the males (1.9%) in the 30-49 age range.

When the proportions of visits to the EDs were calculated in relation to the mean of all ED visits for all causes (Figure 1B), it became clear that:

- when both sexes were considered, the highest proportion (4.4%) in both sexes was found in a slightly older age range (30-59 years old) with respect to the data of the resident population, and there was a similar lower level in the younger and older age classes;

- when sexes were considered separately, in females the highest proportion was detected between 40-59 years (5.3% in 40-49, 5.2% in 50-59) while in males it was detected between 40-49 (3.7%). In this case as well, the age classes with a higher prevalence were older than the ones of the resident population.

In Figures 1A and 1B the Chi-squared tests showed that the difference in the proportions between the females and males was statistically significant for each year's group, with the exception of the 30-39 age range (Figure 1B). The Kruskal-Wallis test showed that the age medians of both sexes evaluated together were significantly different over the years that were sampled ( $p < 0.05$ ).

Over the five year period, the percentage and number of visits to the EDs differed depending on the day of the week; the percentages ranged from 11.9% on Sundays to 16.0% on Thursdays. There were significant differences in the median number of visits on different days of the week: the mean number of visits was distributed as follows: 117.4 on Monday, 111.2 on Tuesday, 112.0 on Wednesday, 120.4 on Thursday, 106.6 on Friday, 97 on Saturday and 89.9 on Sunday;  $p < 0.05$ , Kruskal-Wallis test).

Figure 1A and B. Proportions of PAs or PD by age classes and gender, related to the mean of the resident population (1A) and related to the mean of the total ED accesses for all causes (1B).

The Anova Oneway test used to compare the mean number of visits to the ED during

different seasons of the year did not uncover statistically significant differences ( $p=ns$ ). If all five years are considered, the distribution of the patients admitted to EDs by month was fairly constant (mean prevalence 8.3%), with only a slightly rising pattern between June (9.1%) and August (8.9%) and with a minimum prevalence recorded for February (7.2%).

The distribution of the triage codes in patients approaching the EDs classified

according to age, sex and final referrals are outlined in Table 3. The majority were assigned a green code (78.2%; of these 61.9% were females and 38.1% were males), the second most numerous code was yellow (15.2%; of these 60.8% were females and 39.2% were males), then white (6.3%; of these 71.3% were females and 28.7% were males) and finally red (0.3%; of these 70% were females and 30% were males).

Table 3 - Triage codes at admission to the Emergency Departments in the patients with PA or PD symptoms classified according to gender, age group and final referral.

Variables		Triage code				
		White	Green	Yellow	Red	Total
Gender	males	4.8%	79.2%	15.8%	0.2%	100.0%
	Females	7.2%	77.7%	14.9%	0.3%	100.0%
Age	0-19	7.2%	78.9%	13.1%	0.8%	100.0%
	20-29	3.0%	78.5%	18.0%	0.5%	100.0%
	30-39	5.4%	79.5%	14.7%	0.4%	100.0%
	40-49	7.4%	77.8%	14.8%	0.0%	100.0%
	50-59	7.2%	80.4%	12.2%	0.2%	100.0%
	60-69	5.8%	74.2%	19.6%	0.4%	100.0%
	70-79	10.9%	74.5%	14.6%	0.0%	100.0%
	>=80	3.0%	80.0%	17.0%	0.0%	100.0%
Referral	the patient left the ED before the protocol was concluded	13.1%	81.9%	4.7%	0.3%	100.0%
	The patient refused to be placed under observation or to receive other care	1.5%	76.9%	21.5%	0.0%	100.0%
	The patient refused to be admitted to the hospital	0.0%	60.0%	40.0%	0.0%	100.0%
	The patient was hospitalized by ED	3.3%	76.2%	20.5%	0.0%	100.0%
	The patient was referred to a state agency or other institution	0.0%	100.0%	0.0%	0.0%	100.0%
	The patient was referred to the general practitioner	5.2%	78.4%	16.2%	0.3%	100.0%
	The patient was discharged	8.7%	78.3%	12.4%	0.6%	100.0%
	The protocol was closed at the time of triage	0.0%	100.0%	0.0%	0.0%	100.0%
	The patient was transferred to a psychiatric facility	0.0%	60.0%	40.0%	0.0%	100.0%

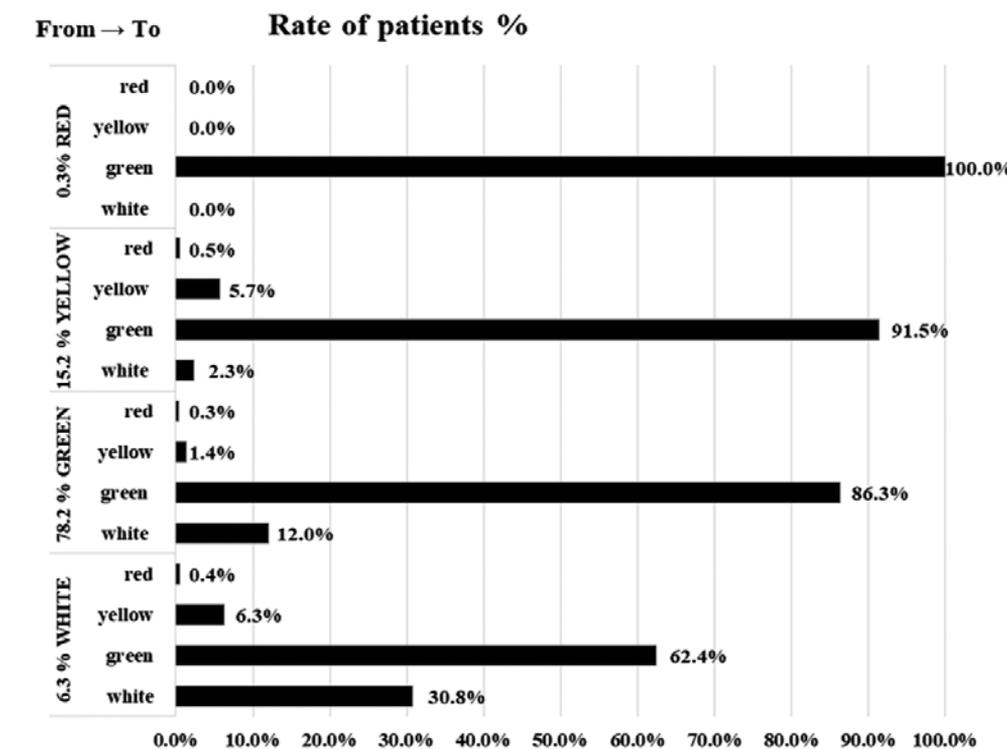


Figure 2 - Transition from triage code to discharge code for each patient with PAs or PD

“Leaving the ED before the assessment was concluded” and “Refusing to be placed under observation or to receive other treatment” were the most frequent referrals in the green coded patients (respectively 81.9% and 76.9%). “Refusing hospitalization” and “Hospitalization” were found more frequently in the patients assigned a green code at admission (respectively 60.0% and 76.2%) but also in the yellow one (respectively 40.0% and 20.5%). None of the patients who were assigned a red code were hospitalized: the diagnosis of PA was confirmed meaning that they were not in any danger.

With regard to switches in the triage code from the one assigned at admission to the one assigned at the end of the protocol (Figure 2), a green code assigned at admission was most frequently (86.3%) confirmed

at discharge. In most cases a red code at admission was switched to a green one at the end of the assessment protocol (100%). Most of the red, yellow and white triage codes at admission were switched to green at the end of the protocol.

When the different referrals following the examination/interview with the emergency department provider (Figure 3) were analyzed, it was found that the majority of the patients (80.9%) were referred to their GP, 9.1% left the ED before the assessment was concluded, 3.6% were hospitalized and the 4.0% were discharged.

## Discussion and conclusions

Study results show that the proportions of visits for PAs or PD to the Emergency

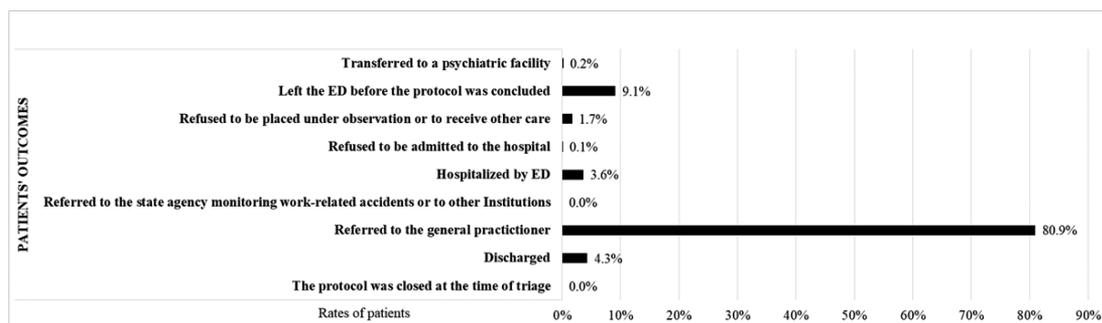


Fig. 3 - Distribution of referrals by the emergency care provider given the patients with panic attacks

Departments of the Hospital of Verona, calculated with reference to the local population and to the total number of visits to the EDs, were respectively 1.4% (95%CI 1.4%-1.5%) and 2.5% (95%CI 2.5%-2.6%), that is 1.78 times higher than what happens in the general population.

Some studies have reported a prevalence of panic disorder in the primary care setting that is approximately double (respectively 4% to 8%) with respect to that in the general population (41-43).

In accordance with other studies (24-26), this survey detected that higher proportions of cases are in females, both with reference to the resident population (1.7% in females vs 1.1% in males) and to ED settings (3.3% in females vs 1.9% in males).

Our results are also in line also with other studies reporting that there is a higher frequency of anxiety spectrum disorders and panic disorders in women than in men, both in school age and in adult Italians (44-45).

A survey carried out in the United States in 2010 reported that the lifetime prevalence of PD ranged between 1 and 3% in the resident population (46); an Italian survey carried out in 2004 found a lifetime prevalence of 1.6% (95% CI 0.4%-0.8%) (35). Although both studies reported similarly higher prevalences in the females with respect to the males, it is important to remember that the two studies

used different methodologies and examined different periods in time.

Our study confirms that the female gender and age <60 years old (24) are two risk factors for the onset of PAs and PD (24-26, 35, 46). Other well-known risk factors are early age at onset of PAs, being unemployed, divorced, separated or widowed, a lower educational level and income status and stressful life events (such as physical illness, disability, pregnancy related problems) (24, 47, 48).

The peak in PAs or PD detected by our study was found at an age when most subjects are working, and there does seem to be a connection between stressful events at work and PD (49). Some studies have reported that 80% of individuals with PD have a comorbid psychiatric diagnosis, including major depressive disorder, anxiety disorders, bipolar disorder, psychosis, alcohol or substance abuse (50-56). This variable was not, however, analyzed by the current study as patients were not asked about comorbidities during the assessment in the ED.

Various life-threatening medical conditions such as angina pectoris, cardiac arrhythmias, neurological diseases, endocrinological problems, severe hypoglycemia, use of stimulants and drug withdrawal may mimic PAs and must, therefore, be considered in the differential

diagnosis of PD or PAs (57, 58). Most green or white code assignments at admission were confirmed in our study population, meaning that they were indeed panic attacks. The same concordance was found for the red code assignments. Conversely, 1.5% of all the green codes (78.2%) and 6.7% of all the white codes (6.3%) at admission were switched to red or yellow codes at discharge, meaning that the patients were probably affected by some organic diseases. The problem of a differential diagnosis between PAs and other medical condition also emerged in the population studied here.

The burden of PD is linked to the difficulty in making a diagnosis and in managing the disorder but also to the exorbitant economic impact on society and on public health. In fact, its monetary costs are higher than those of other mental disorders (36). Indeed, in the United States PD causes 1.7 work days missed per month per capita (37) and 25% of the individuals with PD are unemployed (59). In Europe, PD is one of the five mental disorders that have the most important impact on quality of life and it accounts for a loss of 11% of workdays over the previous 30 days' time (29). Moreover, a study carried out in the Netherlands in 2007 revealed that the annual per capita cost of PD was €10.269, which means that it exceeded the cost of other mental disorders (36). Most of the total costs can be attributed to production losses or to direct medical costs (36). Despite of the lack of information about the occupational status of the patients studied here, the economic impact is without doubt prohibitive in view of the fact that the highest prevalence of the disorder was detected in 20-49 age group which is a crucial age for career improvement and productivity.

The overwhelming majority of individuals suffering with PAs originally turn to their GP or to the hospital emergency department for assistance particularly at their first attack. Many studies have described the heavy economic burden of assessing and treating

patients with PD who turn to Emergency Services for care (60, 61). According to one American study (60) 41.1% of individuals with PD seek help at EDs, while only 5.2% of other psychiatric patients do so. This heavy burden for Emergency Departments could be reduced if patients are provided a precocious diagnosis based on the Diagnostic Criteria for Panic Disorders and are prescribed a specific treatment protocol (60-62). For the time being, the journey is often not a smooth one and patients frequently need to be seen by many physicians before they are diagnosed with PD (63).

Specific, appropriate training for GPs and specialists staffing ED Units to deal with panic attacks and anxiety disorders will help care providers to reach a correct and rapid diagnosis and to provide targeted therapeutic interventions. A coordinated management of this type of patient by specialists, GPs and psychiatrists may be able to provide appropriate and cost-saving care and decrease the burden on EDs. Cognitive Behavioral Therapy (CBT) sometimes associated with symptomatic use of Benzodiazepines (BDZ) and Antidepressants Selective Serotonine Reuptake Inhibitors (SSRIs) is presently considered the first line treatment for PD (64, 65).

The results of some studies have shown that the majority of patients (80.9%) were referred to their GPs at the end of their assessment in the emergency room. That finding is in line with the results presented by other investigators showing that the GP plays a crucial role in managing PD and PAs (46, 63-66). Indeed, an American study reported that patients with PD are more likely to seek primary care treatment and to receive psychiatric medication from their primary care physician. Likewise, their primary care physician is the one who most frequently refers them to a mental/substance abuse specialist (46). A Canadian-French clinic review (63) reported that the GP plays a crucial role in recognizing

and diagnosing PD at an early stage and in prescribing appropriate treatment. In association with the American Academy of Family Physicians, the family doctors of the United States drafted a printable handout explaining anxiety and panic and describing their causes and symptoms as a form of patient education and a prevention measure (67).

Finally, given the difficulty of implementing primary and secondary prevention programs for this condition, public health officials should make every effort to promote tertiary prevention in order to reduce the burden of this ailment and societal costs. Tertiary prevention can be enhanced by organizing training programs for healthcare personnel working in hospitals and in other public facilities and classes or at least some lectures on the subject for medical school students. This would certainly assist health care workers in the challenging job of recognizing and diagnosing the pathology and of treating it in the most opportune manner, thus helping patients to manage the disabilities and comorbidities associated to PD and improving their ability to function, their quality of life and their life expectancy.

Beyond the large numbers that were analyzed over a relatively long time period, one of the study's strengths is its interest in an insufficiently studied condition that has important implications for public health. The facts that it was not designed as a prospective study and that other data would be necessary to perform a multiple logistic regression analysis on the general population can be considered its defects. Generally speaking, the study confirms the relevance of the phenomenon here in Italy and the importance of further studies to identify ways to assist persons with this disorder before they present in emergency departments.

## Riassunto

### *Prevalenza degli accessi per attacchi di panico e disturbo di panico nelle Unità Operative di Pronto Soccorso di Verona*

**Obiettivi.** Gli attacchi di panico (PA) ed il Disturbo da attacchi di panico (DAP) gravano pesantemente sia per la complessità di gestione che per l'impatto economico sulla società e sulla sanità pubblica. In Europa, il DAP è tra i cinque disturbi mentali con maggiore impatto sulla qualità di vita. Lo scopo dello studio è di valutare la prevalenza periodale di accessi per PA e DAP nelle Unità Operative di Pronto Soccorso (UU.OO. PS) di Verona (Nordest Italia) nel periodo 2012-2016, al fine di stimare il peso sanitario e sociale di queste patologie.

**Metodi.** Questo studio è stato condotto raccogliendo retrospettivamente i dati dalle cartelle cliniche dei pazienti ammessi presso le UU.OO. PS (Generale, Ginecologico, Pediatrico) a causa di sintomi di panico nel periodo 1 gennaio 2012- 31 dicembre 2016. I casi sono stati estratti cercando nelle cartelle cliniche le parole chiave "ansia" e "panico" riportate nella diagnosi di dimissione delle UU.OO. PS. Un modello di regressione logistica multipla è stato anche effettuato per valutare i fattori predittivi degli accessi in PS per PA o DAP negli anni indagati.

**Risultati.** Sono stati identificati 3.371 casi di attacchi di PA o DAP, di cui 62,3% nelle femmine e 37,7% nei maschi, con un rapporto femmine: maschi di 1,7: 1. L'età media è risultata essere di 44 anni, 46 nelle femmine e 41 nei maschi. La maggior parte dei pazienti ha un'età compresa nelle fasce di 30-39 anni (20,6%) e 40-49 anni (23,8%). La proporzione degli accessi per PA o PAD per anno campionato è stata pari a circa il 20%, con una media di 754 pazienti per anno. Le prevalenze periodali di casi di PA o PAD nei 5 anni considerati sono state calcolate sulla media della popolazione veronese residente (1,4%) e sulla popolazione media (media degli accessi) afferente alle UU.OO. PS (2,5%). Il nostro studio evidenzia che la maggior parte dei pazienti (80,9%) è stata dimessa ed inviata al Medico di Medicina Generale. Secondo il modello di regressione logistica multipla, sono fattori di rischio significativi per PA e DAP: il genere femminile (OR 1.899; 95% CI 1.785-2.020), essere di nazionalità italiana rispetto agli stranieri (OR 1.292; 95% CI 1.174-1.421), avere un codice triage bianco o verde all'ingresso (bassa urgenza) rispetto agli altri codici (OR 1.195; 95% CI 1.100-1.297), ed avere un'età pari o inferiore ai 42 anni (OR 1.091; 95% CI 1.024-1.161).

**Conclusioni.** Il ruolo del Medico di Medicina Generale risulta cruciale nella gestione degli attacchi di panico e del disturbo da attacchi di panico. Considerando le difficoltà inerenti alla prevenzione primaria e secondaria di queste patologie, gli sforzi della Sanità Pubblica

dovrebbero essere rivolti al potenziamento delle attività di prevenzione terziaria, al fine di ridurre il peso delle stesse sulla società.

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