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# Factors associated with gender and sex differences in anxiety prevalence and comorbidity: A systematic review

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## Abstract

**Background:** The prevalence and comorbidity of anxiety disorders are significantly different between women and men, with research showing a greater impact on women. The aim of this review was to identify the psychosocial and biological factors that have been considered to explain this gender and sex difference in prevalence and determine whether these factors are related to any anxiety comorbidity differences between men and women. **Methods:** Following the PRISMA guidelines, we carried out a systematic review of studies published between 2008 and 2021 in PsycINFO and PubMed databases. Empirical and review studies evaluating psychosocial and biological factors that could influence the difference in prevalence and comorbidity between men and women were included. A qualitative narrative synthesis was performed to describe the results. **Results:** From 1012 studies, 44 studies were included. Retrieved articles were categorized depending on their object of study: psychosocial factors (n = 21), biological factors (n = 16), or comorbidity (n = 7). Results showed that differences in anxiety between women and men have been analyzed by psychosocial and biological factors but rarely together. Among the psychosocial factors analyzed, masculinity may be a protective factor for anxiety development, while femininity can be a risk factor. In the studies that took biological factors into account, the potential influence of brain structures, genetic factors, and fluctuations in sexual hormones are pointed out as causes of greater anxiety in women. Concerning comorbidity, the results noted that women tend to develop other internalizing disorders (e.g. depression), while men tend to develop externalizing

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disorders (e.g. substance abuse). **Conclusions:** For an accurate understanding of differences between women and men in anxiety, both biological and psychosocial factors should be considered. This review highlights the need to apply the biopsychosocial model of health and the gender perspective to address differences in anxiety between sexes.

**Keywords**
Anxiety, sex differences, gender differences, women's mental health, systematic review

## Introduction

The prevalence of anxiety disorders is significantly higher in women than in men.[1] This difference occurs not only in adults but also in children and teenagers.[2,3] To better understand this issue, it is necessary to identify the protective and risk factors that may influence the vulnerability of each sex to present anxiety and related comorbidities. The biopsychosocial model of health[4] already raised the need to adopt a holistic perspective. From this model, biological, psychological, and social factors must be accounted for to respond to health-related issues. However, some authors have pointed out that despite the great relevance of this approach, the sex-gender gap is not yet fully explained in the health sciences.[5] According to them, a gender-feminist perspective is required to accurately address the reasons for the considerable differences between women and men in health conditions such as anxiety disorders.[6,7]

A gender perspective allows the identification of the influence of sociocultural factors in women's mental health so that these factors are also considered when establishing a treatment. The incorporation of this perspective into the study of sex-gender differences in anxiety implies much more than the simple task of "adding" women to the data as a simple item of statistical information. It requires delving deeper into what it means to be a woman or a man in health research, especially when sex-gender differences are a central analytical category.[8–10] In other words, it is necessary to include a gender/feminist-specific vision of the vulnerability of each sex to present an anxiety disorder. This relies on the requirement of differentiating two concepts, sex and gender, both of which need to be clarified to understand the further analysis of this article. Sex is commonly understood as a biological variable, an immutable inherent condition that classifies individuals as women and men according to biological factors (i.e. hormones, chromosomes, etc.).[11] Gender, on the other hand, refers to the sociocultural construction that takes place through a process of constant gender socialization in which the person is influenced by the norms, rules, roles, stereotypes, and expectations of their culture based on their biological sex.[12,13] Adopting the gender perspective involves the analysis of how this different gender socialization might affect this mental health condition in terms of diagnosis, prognosis, treatment, and comorbidity. Gender socialization has a great impact on the psychosocial factors involved in mental health.[14] In this way, this socialization might influence the acquisition and development of certain behaviors, as well as the patterns of thought and feelings related to anxiety. For example, throughout their socialization process, girls are more likely to ask for help; they are allowed and encouraged to express their fears and worries and are more frequently oriented towards

dependence, fearfulness, passivity, and obedience, which leads to an education according to the feminine role or the expressivity dimension.[15,16] In contrast, boys are more likely to be taught to contain feelings of fear and insecurity and are more frequently prepared for action, problem-solving, goal achievement, and success, that is, attitudes and behavior typically associated with a masculine role or instrumental dimension.[17,18]

As a consequence of this gender socialization, anxiety levels could differ between sexes,[14] experiencing certain feelings, such as anxiety and fear, is normalized for women, and it is expected that they express them. In the case of men, the reinforcement of the suppression of certain emotions and the social expectation that they should be strong and brave might facilitate their development of useful resources to cope with those feelings.[18] However, despite this clear connection between gender socialization and anxiety, this gender perspective is seldom taken into account to explain the differences observed between women and men in its diagnosis and prognosis and, even less, to establish its treatment.[19,20] Therefore, data on the prevalence of anxiety disorders may reflect a patriarchally biased explanation that places women in a situation of greater mental health vulnerability.

In any case, the literature consistently indicates that anxiety disorders are more prevalent in women than in men. However, research on the origin of these differences between women and men in the expression of anxiety is rather inconsistent. Evidence addressing this issue is generally focused on biological factors.[21] Many of them are even centralized on animal studies,[22] which precludes the analysis of gender and other psychosocial factors. Other studies do not distinguish between gender and sex differences,[23] which may lead to ambiguity in the analysis. These studies, while offering valuable information on the mechanisms underlying this difference, still fail to provide a panoramic insight into the specific roles of the sex and gender variables (i.e. they refer to gender or sex but rarely together). In addition, despite the existence of recommendations and guidelines in this field,[24] the frequent confusion between these two terms makes it difficult to identify and understand previous research findings on anxiety in both sexes.[5]

Furthermore, another relevant aspect for mental health and, specifically, for anxiety disorders is that comorbidity is the rule rather than the exception.[25,26] However, little is known about how these gender and sex differences have been studied regarding anxiety and related mental health comorbidities. This makes it necessary to examine whether, along with biological influences, psychosocial factors also have an impact on any differences in anxiety comorbidity between women and men. Thus, an integrative overview of this issue seems to be required.

Given this context, the present study was designed to systematically identify and synthesize the contributions made by empirical and review studies concerning anxiety and sex/gender differences in the last decades. To this end, the framework of the biopsychosocial model of health and the feminist perspective were considered. In particular, the aim was to, firstly, identify what specific factors, both psychosocial and biological, have been considered so far to explain the difference in anxiety between women and men and, secondly, explore whether these factors are able to explain any differences in anxiety comorbidity. To the best of our knowledge, an updated systematic review of the differences observed in the manifestation of anxiety between women and men and its comorbidity has not been provided to date.

## Methods

### Eligibility criteria

The inclusion criteria were documents that analyzed (a) the prevalence of anxiety disorders in men and women and (b) the psychological, social, and/or biological factors that explained the difference in the prevalence of various anxiety disorders or in the anxious symptomatology between the sexes or (c) the difference in the comorbidity of anxiety disorders in men and women. Eligible articles could include (d) empirical or review studies, (e) published between 2008 and 2021, (f) in either Spanish or English. Exclusion criteria were (a) research studying anxiety in clinical populations of other mental disorders, (b) studies that addressed the gender or sexual difference of anxiety from a single anxiety disorder, and (c) articles whose object of study did not answer the research question (those that match the search terms but are out of our scope).

### Search strategies, data sources, and selection process

A systematic database search was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) methodological framework (see Supplementary File 1).[27] Suggestions from Siddaway et al.[28] were also considered for reporting this research. The search was carried out between December 2021 and February 2022 in the PsycINFO and PubMed databases. The search terms were "gender differences" AND anxiety AND prevalence; "sex differences" AND anxiety AND prevalence; "gender differences" AND anxiety AND comorbidity; and "sex differences" AND anxiety AND comorbidity. The selection process, including the search, screening, and evaluation of the studies, was conducted by two independent researchers. In case of disagreement between reviewers, the article was preselected and fully analyzed by a third researcher.

### Data collection

Regarding data collection, selected studies were examined and classified by two independent researchers following a template that was developed to compile the information related to factors analyzed, method and/or study design, sex sample representation, instruments, etc., in order to facilitate the synthesis of the results. Then, we performed a narrative synthesis of the findings of the included articles, classifying the documents according to their object of study.

### Quality assessment of the studies included

An adaptation of the QualSyst[29] was used to analyze the quality of the studies included in this review considering seven categories (see Supplementary File 2). Specifically, this assessment addressed information related to the objectives, inclusion/exclusion criteria, sample size and participants' sex representation, instruments, and results of the studies analyzed. Most of the studies showed a high quality according to these standards. Quality assessment was also performed by two independent reviewers.

## Results

### Study selection

The initial search generated 1012 results, 607 in psycINFO and 405 in PubMED. Eliminating duplicated documents between both databases, 515 articles were obtained and screened. After screening, 362 articles were excluded and 153 were analyzed in depth. After reading the full text, 109 were discarded using the aforementioned criteria, leaving 44 articles for final inclusion in this systematic review (Figure 1).

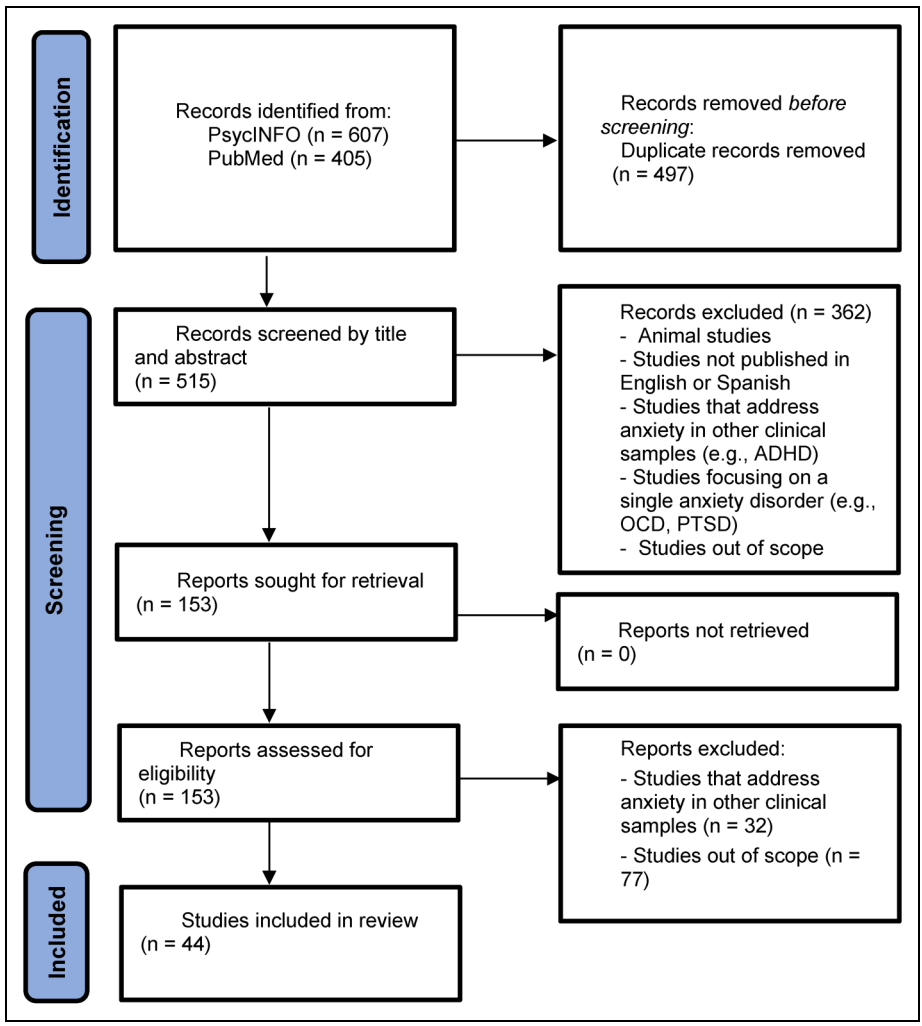


**Figure 1.** PRISMA flow chart of the selection process. *Note.* ADHD = Attention Deficit Hyperactivity Disorder; OCD = Obsessive-Compulsive Disorder; PTSD = Post-traumatic Stress Disorder.

## Characteristics of the studies included

Of the 44 documents, 31 were empirical/quantitative studies[30–60] and 13 were reviews.[61–73] With respect to their objectives, most articles analyzed the difference in the prevalence of anxiety in men and women considering psychosocial (n = 21) or biological (n = 16) factors, and seven articles analyzed the difference in the comorbidity of anxiety with other disorders based on psychosocial factors. Out of the 31 empirical studies, 25 were conducted in western countries; 11 were performed in North America (10 in the United States of America and 1 in Canada), 10 in Europe, and 4 in Australia. Five were conducted in Asia: Pakistan (n = 1), Mongolia (n = 1), Hong Kong (n = 1), and China (n = 2). The remaining study was conducted with a cross-national sample that included different continents.

Tables 1 and 2 present the data and characteristics of the studies analyzed, including their objectives, key findings, and conclusions, classified according to their object of study.

## Qualitative narrative synthesis

*Psychosocial factors.* These documents focused their analysis on the difference in the prevalence of anxiety disorders as well as in the morphology and severity of those symptoms. Their results concluded that women experience higher rates of anxious-depressive symptoms compared to men, with these symptoms also being more severe.[41,42,45] According to these studies, this difference must be understood as an important factor to take into account for treatments in the clinical population, as well as in other areas of life, such as in academia.[38,41,42]

The results from other studies also showed that women generally identified themselves with expressive or feminine traits such as kindness and sweetness, while men identified themselves with instrumental or masculine traits such as competitiveness, assertiveness, and self-confidence.[59,64] These studies found a relationship between gender roles and anxiety.[54] Instrumentality was positively correlated with protective traits for mental health, such as subjective well-being, perceived control, independence, and self-confidence. Masculinity, therefore, seems to act as a buffer between gender and anxiety.[44,54,56,59,70] Importantly, women who scored higher on instrumentality reported lower subjective anxiety and less fear.[64] Therefore, instrumentality mediates between anxiety and gender, not biological sex.

With respect to femininity, the results showed contradictory information. While there are studies that have not found a relationship between femininity and anxiety,[64] other studies revealed that femininity accompanied by low self-esteem favored the development of anxiety.[49,70] This latter finding relates to studies that examined the relationship between anxiety and gender based on psychological factors. Such studies showed that rumination, neuroticism, behavioral inhibition, worry, anxiety sensitivity, trauma, and low self-esteem correlated positively with anxiety, with all variables being typical of the female stereotype.[33,44,51,55,65,73]

Derdikman-Eiron et al.[36] compared the psychosocial functioning, subjective well-being, and self-esteem of adolescents with and without anxiety and found that girls

**Table 1.** Characteristics, main aim(s), and key findings of the studies included in the systematic review (empirical studies).

| Authors (year) | Country | Factors analyzed | Sample (%W/M) | Instruments* | Study aim(s) | Key findings |
|---|---|---|---|---|---|---|
| Ask et al.[30] | Norway | Biological factors | 2788 (54.9/45.1) | SCARED | To evaluate the influence of genetics and environment on the variability of anxiety symptoms in twin adolescents. | - Higher levels of anxiety in girls were mainly due to genetic factors.<br>- Heritability explained 74% of the variance in anxiety in girls and 65% in boys. Environmental factors explained the rest of the variance in anxiety between sexes.<br>- Environment might decrease boys' but not girls' anxious tendencies. |
| Burton et al.[31] | Australia | Biological factors | 1500** | DASS- 42 | To estimate if sex differences in self-reported depression and anxiety are caused by genetic and/or environmental factors. | - Genetic factors played a different role in anxiety, depression, and their comorbidity between the sexes. Men only had genetic risk factors for anxiety-depression co-occurrence, and women for both depression, anxiety, and their comorbidity.<br>- The higher prevalence of internalizing symptoms in women could be due to sex-related biological vulnerability and the type of environmental exposure. |
| Cerasa et al.[32] | Italy | Biological factors | 138 (55.1/44.9) | SCID-I, SCID-II, HAM-A | To identify interactions between gender, anxiety, and 5-HTTLPR genotype and to determine whether these connections would be reflected in the neuroanatomy of anxiety-related brain structures (e.g. amygdala). | - An interaction effect was found between the 5-HTTLPR, anxiety, and the right amygdala in females.<br>- An association between subclinical anxiety and higher right amygdala volume was found in short allele homozygous female.<br>- Sex influences the relationship between the 5-HTTLPR and anxiety given its effect on the amygdala. |
| Chan et al.[33] | Hong Kong | Psychosocial factors | 2802 (55.1/44.9) | SCARED, CERQ, CNCEQ | To describe the prevalence of anxiety symptoms in adolescents and to explore their relationship with rumination, catastrophizing, or daily hassles. | - There was a direct effect of catastrophizing on anxiety in girls and boys.<br>- Rumination was found to have an impact only on girls' anxiety.<br>- Girls' tendency to ruminate and catastrophize increases their vulnerability to anxiety disorders. |

*(Continued)*

**Table 1.** (continued)

| Authors (year) | Country | Factors analyzed | Sample (%W/M) | Instruments* | Study aim(s) | Key findings |
|---|---|---|---|---|---|---|
| Chen et al.[34] | Mongolia | Comorbidity | 4528 (53.9/46.1) | WMH-CIDI (CIDI 3.0) | To explore gender differences in the prevalence and patterns of anxiety-depression comorbidity and related risk factors. | - The comorbidity pattern of anxiety and depression is different between sexes, being more prevalent in women.<br>- There is a need to address comorbidity from a symptom-based approach. |
| Curran et al.[35] | Ireland | Psychosocial factors | 8504 (55.6/44.4) | HADS-A | To study gender differences in anxiety and depression prevalence among older adults considering the social and health characteristics and conditions. | - Women presented more anxiety-depressive symptoms.<br>- The comorbidity pattern of anxiety in women is related to psychosocial variables (e.g. partner support, relationship stress) and to alcohol concern in men.<br>- When considering only anxiety, men reported supportive marital relationships and women reported quality social networks, which could act as a bulwark to combat loneliness. |
| Derdikman-Eiron et al.[36] | Norway | Psychosocial factors | 8704 (49.1/50.1) | SCL 5 | To explore gender differences in psychosocial functioning (e.g. subjective well-being – SWB) of adolescents with and without anxiety-depressive symptoms (ADS). | - Sex moderated the associations between SWB and functioning with ADS. Girls presented more ADS, but boys with ADS showed lower psychosocial functioning, poorer SWB and self-esteem than girls.<br>- Gender socialization favors girls' emotional expression when experiencing ADS, reinforcing their social network, while emotionally blocking boys, which explains these differences. |
| Eaton et al.[37] | USA | Comorbidity | 43,093 (57.1/42.9) | DIS, WMH-CIDI | To examine sex differences in the prevalence of common mental health disorders. To explore the pattern of comorbidity through sex differences in the prevalence of internalizing and externalizing disorders. | - Women exhibited higher prevalence of internalizing disorders (e.g. depression), while men exhibited externalizing ones (e.g. antisocial personality).<br>- The comorbidity pattern in women (anxiety-depression) may be explained by the connection between internalizing dimensions (e.g. rumination). |

*(Continued)*

**Table 1.** (continued)

| Authors (year) | Country | Factors analyzed | Sample (%W/M) | Instruments* | Study aim(s) | Key findings |
|---|---|---|---|---|---|---|
| Gao et al.[38] | China | Psychosocial factors | 1892 (47.5/52.5) | DASS-21 | To study gender differences among university students in the prevalence of depression, anxiety, and stress, considering the influence of socio-demographic variables. | - Genetics could explain this association, but environmental factors (e.g. stressful events in women) need to be explored.<br>- Women showed higher anxiety than men.<br>- Higher levels of anxiety were related to drinking habits, poorer academic progress, and an unhealthy body mass index only in females.<br>- Social pressures (e.g. body image stereotypes) are risk factors for women's mental health. |
| Gardener et al.[39] | Australia | Biological factors | 43 (53.5/46.5) | DASS-42 | To examine sex differences in emotional reactivity and emotional regulation measuring the brain response to negative stimuli. | - Women showed higher emotional reactivity to negative stimuli. Sex differences in emotion regulation were found too.<br>- The greater activity in brain structures (limbic, amygdala) in response to negative stimuli in women supports the hypothesis of a negativity bias in them.<br>- This bias could contribute to sex differences in the prevalence of affective disorders. |
| Gili et al.[40] | Spain | Psychosocial factors | 13,816 (59.7/40.3) | PRIME-MD | To evaluate gender differences in the prevalence of mental disorders during the Spain economic crisis (2006–2010). | - The prevalence of affective disorders during the economic crisis increased in men.<br>- Men who assume traditional masculine gender roles are more likely to suffer, in economic recessions, higher rates of anxiety and depression, among other somatic symptoms. |
| Gitay et al.[41] | Pakistan | Psychosocial factors | 300 (61.7/38.3) | GAD-7 | To assess gender differences in the prevalence of mental health conditions in health science students. | - Women were more prevalent in anxiety, depression, and phobia.<br>- Cognitive variables (e.g. metaworry) and sex hormonal fluctuations (estrogen) play an important role in this vulnerability of women in anxiety. |

*(Continued)*

**Table 1.** (continued)

| Authors (year) | Country | Factors analyzed | Sample (%W/M) | Instruments* | Study aim(s) | Key findings |
|---|---|---|---|---|---|---|
| Höglund et al.[42] | Sweden | Biological factors | 3406 (55.7/44.3) | HADS-A | To compare different types of mental health disorders and its prevalence considering groups of age and sex. | - The prevalence of anxiety and other internalizing disorders and symptoms (i.e. somatization, burnout, insomnia) were higher in women, especially for the youngest cohort.<br>- In men, the middle-aged cohort was the one with higher vulnerability and with higher depression levels compared to other age groups. |
| Kramer et al.[43] | USA | Comorbidity | 2992 (62.8/37.2) | PDSQ, MPQ | To explore if comorbidity between the most common psychopathological disorders is explained by gender differences in the presence of internalizing and externalizing factors. | - Sex differences were found in the prevalence and comorbidity of internalizing and externalizing syndromes.<br>- Women have more internalizing risk factors (e.g. neuroticism) associated with internalizing spectrum disorders, while men have more externalizing risk factors (e.g. aggressive personality trait) associated with externalizing syndromes. |
| Leach et al.[44] | Australia | Psychosocial factors | 7485 (50.9/49.1) | SF-12. EPQ, BIS-BAS, RSQ, GADS | To examine if gender differences in anxiety and depression are mediated by psychosocial factors. | - Women had more anxiety and depression than men at all ages.<br>- Some health-psychosocial variables explained the effect between gender and anxiety (e.g. physical activity, mastery, interpersonal relationship), all of them lower in women.<br>- Higher anxiety in women may be due to different lifestyles, types of stressors, and their coping strategies for them. |
| Liu et al.[45] | China | Psychosocial factors | 1563 (82.7/17.3) | GAD-7, IES-R | To assess gender differences in the prevalence of mental health conditions among healthcare workers (HCW) in China during the Covid-19 pandemic. | - The prevalence of anxiety symptoms, depression, stress, and insomnia was higher in women than in men.<br>- This greater psychological impact in female HCW can be explained by biological (e.g. hormonal fluctuation), psychological (e.g. unhealthy stress |

*(Continued)*

**Table 1.** (continued)

| Authors (year) | Country | Factors analyzed | Sample (%W/M) | Instruments* | Study aim(s) | Key findings |
|---|---|---|---|---|---|---|
| | | | | | | coping strategies: avoidance, self-blame), and social (e.g. social roles, economic and social support) factors. |
| Lungu et al.[46] | Canada | Biological factors | 46 (54.3/45.7) | M/FGRS | To examine if there are sex differences in fronto-limbic connections when processing negative emotions. To explore the effect of sex hormones and other gender connected factors on these connections. | - Sex differences in the prevalence of anxiety and depression may be explained by different fronto-limbic connections when processing negative emotions.<br>- Men showed more activation in the dorso-medial prefrontal cortex, area related to action planning, associated with testosterone and negatively correlated with femininity.<br>- Gender roles may contribute to sex differences in brain connectivity in emotion processing. |
| McLaughlin et al.[47] | USA | Comorbidity | 1065 (48.8/51.2) | MASC | To examine sex differences in the bidirectional association between rumination, externalizing symptoms and anxiety, and depression in adolescents. | - Girls presented more anxiety symptoms and rumination.<br>- Rumination played an important role in the transition between anxiety symptoms (internalizing) and aggressive behavior (externalizing) and vice versa only for boys.<br>- Gender roles make boys exhibit more aggressive behavior as a coping mechanism for distress, especially when adjusting to traditional masculinity. |
| McLean and Hope[48] | USA | Psychosocial factors | 109 (54.1/45.9) | BAT, PAQ | To examine if gender and gender roles influenced subjective anxiety (SA) and behavioral avoidance (BA) during a fear task. | - Women scored higher on expressivity (feminine gender role) and men on instrumentality (masculine role).<br>- Women had greater SA and BA.<br>- Sex but not gender roles predict SA and BA. However, higher expressivity was related to higher BA in men and instrumentality to less BA in both sexes. |
| McLean et al.[49] | USA | Comorbidity | 20,013 (57.3/42.7) | WMH-CIDI | To describe the prevalence of anxiety | |

*(Continued)*

**Table 1.** (continued)

| Authors (year) | Country | Factors analyzed | Sample (%W/M) | Instruments* | Study aim(s) | Key findings |
|---|---|---|---|---|---|---|
| | | | | | disorders and to analyze differences in onset, prognosis, comorbidity, and rates of impaired functioning between men and women. | - The prevalence and chronicity of anxiety disorders were higher in women.<br>- The presence of internalizing risk factors (negative affect, neuroticism) in women facilitate their comorbidity with other internalizing disorders.<br>- Gender socialization moderates these factors, supporting the expression of certain symptoms, favoring these sex differences in anxiety and its comorbidity. |
| Mwinyi et al.[50] | Switzerland | Psychosocial factors | 3695 (52.9/47.1) | SADS-LA | To examine whether there are gender differences in the prevalence of anxiety disorders and how these differences are related to negative economic changes. | - Women were more likely to have lower socio-economic status, alcohol consumption and substance abuse disorder, and higher depression than men.<br>- Compared to anxious men, anxious women reported a greater income reduction.<br>- Anxiety has a more negative impact in women, worsening their already poorer economic situation. |
| Norr et al.[51] | USA | Psychosocial factors | 106 (53.8/46.2) | ASI-3, BAI | To assess if anxiety sensitivity (AS) mediates between gender and anxiety-depression symptomatology. | - AS was found to be a mediating factor between gender and symptoms of anxiety and depression.<br>- The influence of biological and environmental factors contributes to a higher AS in women.<br>- AS is a relevant risk factor for women and a possible explanation for its higher anxiety and other internalizing disorders prevalence. |
| Palma-Gudiel et al.[52] | Spain | Biological factors | 148 (60.8/39.2) | SCID-I/BSI | To study the potential influence of SLC6A4 methylation on anxiety and depression disorders and other | - Sex was significantly associated with SLC6A4 methylation. |

with

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**Table 1.** (continued)

| Authors (year) | Country | Factors analyzed | Sample (%W/M) | Instruments* | Study aim(s) | Key findings |
|---|---|---|---|---|---|---|
| | | | | | psychopathological dimensions (e.g. somatization, hostility). | - Higher SLC6A4 methylation correlated with higher somatization scores.<br>- This hypermethylation of SLC6A4 in women could explain sex differences in SERT expression, with women having a higher vulnerability to certain psychopathological conditions. |
| Rees et al.[53] | Australia | Comorbidity | 4451 (100/0) | WMH-CIDI | To analyze how gender-based violence (GBV) influences women's mental health. | - GBV increases the prevalence of suffering any mental health disorder, especially anxiety.<br>- GBV was related to higher physical problems, disability, and suicide attempts and poorer prognosis, comorbidity, and quality of life.<br>- These findings highlight the importance of addressing GBV as a public health problem due to its consequences for women's mental health. |
| Seedat et al.[54] | Colombia, Lebanon, Mexico, South Africa, Ukraine, Belgium, France, Germany, Israel, Italy, Japan, Netherlands, New Zealand, Spain, USA | Psychosocial factors | 72,933** | WMH-CIDI | To study gender differences in the mental health of men and women in four cohorts of 15 countries and explore if they are determined by psychosocial factors (e.g. gender roles). | - Females had a higher risk of developing an affective disorder; for males, it was externalizing disorders (e.g. substance abuse).<br>- The gender role of traditionality predicted this sex difference. Higher traditionality, higher prevalence of internalizing disorders in women. Lower traditionality, lower sex differences in substance abuse. |
| Stassart et al.[55] | Belgium | Psychosocial factors | 200 (52.5/47.5) | CASI, CPAQ | To explore the identification of gender roles among adolescents and to assess whether these gender roles explain the association between sex and anxiety sensitivity (AS). | - AS correlated with femininity and negatively correlated with masculinity.<br>- Biological sex mediated between gender roles and anxiety. Boys (higher masculinity) were associated with lower AS, whereas girls (higher femininity) were associated with greater AS.<br>- Gender roles explain sex differences in |

*(Continued)*

**Table 1.** (continued)

| Authors (year) | Country | Factors analyzed | Sample (%W/M) | Instruments* | Study aim(s) | Key findings |
|---|---|---|---|---|---|---|
| | | | | | | anxiety. Masculinity (related to problem-solving, action-oriented strategies), may help to cope with anxiety. |
| Stoyanova and Hope[56] | USA | Psychosocial factors | 144 (46.5/53.5) | FSQ, PAQ, BAT | To examine the effect of gender on self-reported fear, subjective anxiety, and other anxiety-related variables (e.g. heart rate, avoidance behavior) during an anxiety-inducing task. | - Women had higher anxiety, fear, and phobic avoidance during a spider behavioral avoidance task than men.<br>- Masculinity (i.e. instrumentality) was negatively associated with anticipatory anxiety in women but not in men.<br>- In women, instrumentality would encourage fear coping, while tending and befriending might inhibit an active coping style. |
| Van Dam et al.[57] | USA | Psychosocial factors | 818 (49.9/50.1) | ASI | To explore differences in anxiety sensitivity (AS) between men and women and to analyze if these differences are determined by their response pattern to the ASI. | - Women scored higher on the ASI. However, when items 2 and 4 were removed, sex differences disappeared.<br>- The ASI-scale different pattern response between sexes may be biased by gender roles.<br>- A review of instruments measuring AS and anxiety is needed before assuming sex-gender differences. |
| Van de Velde et al.[58] | Belgium; Bulgaria; France; Germany; Italy; Netherlands; Northern Ireland; Portugal; Romania; Spain | Psychosocial factors | 37,289 (54.4/45.6) | CIDI 3.0 | To assess and study the connection between different European welfare regimes and gender differences in any mental health disorder (AMD). | - Sex differences in the prevalence of AMD depended on the country's welfare regime,<br>- Social factors (e.g. marital status) mediated the effect of sex on the AMD prevalence.<br>- This sex differences could be explained by social factors (e.g. political actions, gender norms in the economic structure of the country). |
| Zalta and Chambless[59] | USA | Psychosocial factors | 398 (60.1/39.9) | SMS, PAQ, | To investigate the mediating influence of | - Women reported higher levels of anxiety, discomfort, and lower instrumentality |

*(Continued)*

**Table 1.** (continued)

| Authors (year) | Country | Factors analyzed | Sample (%W/M) | Instruments* | Study aim(s) | Key findings |
|---|---|---|---|---|---|---|
| | | | | PSWQ, DASS-21 | gender roles on the relationship between anxiety and gender. | and mastery. These latter traits predicted the association between anxiety and gender.<br>- Gender roles related to mastery and instrumentality may place women at greater vulnerability to anxiety.<br>- How biological factors influenced these traits need to be explored. |
| Zlomke and Hahn[60] | USA | Psychosocial factors | 1080 (73.1/26.9) | DASS-42, PSWQ | To explore the different emotional regulation (ER) coping strategies used by men and women and to investigate whether these strategies are related to their different levels of anxiety and worry. | - ER strategies to cope with worry, anxiety, and stress differed between sexes.<br>- In stressful situations, men blamed others, while women ruminated and relativized. Women's lower worry was associated with acceptance and positive reappraisal, while men's lower anxiety, worry, and stress were associated with reorientation toward planning.<br>- Gender socialization may contribute to sex differences in ER and its subsequent consequences. |

*Note.* * Only instruments that assess anxiety or related constructs are included. ** Percentage of women and men non available in the paper. W = Women; M = Men; USA = United States of America; ASI = The 16-item Anxiety Sensitivity Index; ASI-3 = Anxiety Sensitivity Index – 3 ; BAI = Beck Anxiety Inventory; BAT = Self-report measures and a Behavioral Avoidance Task; BIS-BAS = The 24-item Behavioral Inhibition and Activation Scales; BSI = Brief Symptom Inventory; CASI = Childhood Anxiety Sensitivity Index; CIDI 3.0 = Composite International Diagnostic Interview; CPAQ = Children's Personality Attributes Questionnaire; DASS-21 = Depression, Anxiety and Stress Scales-21; DASS-42 = Depression, Anxiety and Stress Scale-42; DIS = Diagnostic Interview Schedule; EPQ = Eysenck Personality Questionnaire; FSQ = The Fear of Spiders Questionnaire; GADS = Goldberg Anxiety and Depression Scales; GAD-7 = Generalized Anxiety Disorder, GAD-7 ; HADS-A = Hospital Anxiety and Depression Scale ; HAM-A = Hamilton Rating Scale for Anxiety; IES-R = Impact of Event Scale Revised; MASC = The Multidimensional Anxiety Scale for Children ; M/FGRS = The Masculine and Feminine Gender Role Stress; MPQ = Multidimensional Personality Questionnaire, PAQ = Personal Attributes Questionnaire; PCL-C = Post Traumatic Stress Disorder; PDSQ = Psychiatric Diagnostic Screening Questionnaire; PRIME-MD = Primary Care Evaluation of Mental Disorder; PSWQ = Penn State Worry Questionnaire; RSQ = Response Styles Questionnaire; SADS-LA = Lifetime and Anxiety disorder version; SCARED = Screen for Child Anxiety-Related Disorders; SCL 5 = Short version of the Symptom Checklist for anxiety and depression; SF-12 = The 12-item Short Form Health Survey; SCID-I, SCID-II = Structured Clinical Interviews for DSM-IV-TR; SMS = Self Mastery Scale; WMH-CIDI = The World Mental Health Survey Initiative Version of the World Health Organization Composite International Interview.

**Table 2.** Characteristics, main aim(s), and conclusions of the studies included in the systematic review (reviews).

| Study Authors (year) | Country | Factors analyzed | Study aim(s) | Conclusions |
|---|---|---|---|---|
| Brivio et al.[61] | Germany | Biological factors | To review how sex influences stress-specific transcriptomic changes and explore how literature discusses how stress affects men and women. | Evidence proves sex as a variable that modulates the process involving response to stress. Differences in the transcriptional signatures of genes related to stress between sexes were found. |
| Cummings et al.[62] | USA | Comorbidity | To review the existing models that explained the anxiety-depression comorbidity and propose new pathways considering several psychosocial variables (e.g. gender differences). | Anxiety-depression comorbidity may be due to the presence of vulnerability factors for both disorders (rumination, exposure to stressors, etc.), with those factors being more present in women. |
| Day and Stevenson[63] | UK | Biological factors | To review the factors involved in sex differences in anxiety disorders. | Sex differences in anxiety disorders could be explained by differences in fear learning, extinction, and inhibition, and how it relates to sex-related hormones and the activation of brain regions involved in learned fear and emotional regulation. |
| Donner and Lowry[64] | Netherlands | Biological factors | To review gender differences in anxiety disorders and to analyze the influence of biological factors involved in this difference. | Sex differences in emotional behavior may be the result of anatomical and functional differences in serotonergic circuits involved in the modulation of anxiety and panic. |
| Hantsoo and Epperson[65] | USA | Psychosocial factors | To provide an overview of anxiety disorders in women defining the biopsychosocial factors that may underlie them. To propose guidelines that consider these differences and the factors involved for better assessment, differential diagnosis, and treatment. | The prevalence of anxiety disorders in women is due to a combination of biological (hormonal fluctuations) and psychosocial (stressors and coping cognitive strategies) factors. The different evolutive phase of women should be considered when establishing a treatment for anxiety. |
| Hodes and Epperson[66] | USA | Biological factors | To review how sex and epigenetic regulation of hormones affect the impact of stress exposure at different periods of life (perinatal, puberty, menopause, andropause) in men and women. | The impact of stress varies according to sex. In men, it affects on a cognitive level; in women, the impact is emotional and sensitive to hormonal changes. The type of stressor, the evolutive period, and sex should be considered when studying the mechanisms that underlie the stress. |
| Holingue et al.[67] | USA | Biological factors | To explore the role of the gut-brain axis to explain sex differences in the prevalence of neurodevelopmental, psychiatric, and neurodegenerative disorders. | Gut-brain axis has an important role in behavior and brain function. Its plasticity and sensitivity to environmental exposures could explain sex differences in mental health. This should be considered to better understand these disorders and to establish accurate treatments. |
| Kaczkurkin et al.[68] | USA | Biological factors | To review sex differences in the development of brain structures, | Related to anxiety, there are sex differences in cerebral blood flow |

*(Continued)*

**Table 2.** (continued)

| Study Authors (year) | Country | Factors analyzed | Study aim(s) | Conclusions |
|---|---|---|---|---|
| | | | cerebral blood flow, and white matter. To describe if these differences are connected to sex differences in psychopathology. | in adults under the same stress conditions. This is also observed in adolescents, where anxiety-depressive symptoms are related to a higher level of perfusion of the amygdala in girls. |
| Li and Graham[69] | Australia | Biological factors | To give an overview of the literature exploring the role of sex hormones in biopsychological factors influencing sex differences in anxiety disorders. | The natural sex hormone fluctuations in women (e.g. menstrual cycle, menopause, pregnancy) could lead to intermittent periods of increased vulnerability to anxiety. |
| McLean and Anderson[70] | USA | Psychosocial factors | To review the relationship between gender, fear, and anxiety considering biological (e.g. genes) psychological (e.g. rumination), and environmental (e.g. gender roles) factors. | Gender socialization seems to have an important role in sex differences in fear and anxiety. This socialization process may facilitate the development of different traits and cognitive factors that are related to a greater anxiety vulnerability, especially on girls and women. |
| Merikangas and Almasy[71] | USA | Biological factors | To review the mechanisms proposed in the literature to explain sex differences in neuropsychiatric disorders. | The studies analyzed proposed sex hormones, genes, and environmental factors as the explanation of differences in prevalence, course, and severity of anxiety disorders in women. |
| Murphy et al.[72] | UK | Biological factors | To deepen the hypothesis of the interoception (focus on the internal state of the body) as the mechanism that underlies sex differences in some mental health disorders. | Atypical interoception (perceptive bias) found in women caused by biological changes (puberty, menstrual cycle) and life experiences (related to socialization) could explain the sex differences in certain mental illnesses, such as anxiety. |
| Smith et al.[73] | USA | Psychosocial factors | To explore which variables have been studied to explain sex differences in the expression of mental health conditions. | Gender socialization, seeking help, coping styles, and socioeconomic status influenced the sex difference tendency to develop any mental health disorder. |

*Note*. USA = United States of America; UK = United Kingdom.

anxiety had more adaptive psychosocial functioning than boys with anxiety. Other studies indicated that although instrumentality was a protective factor in the appearance of anxiety, expressiveness helped in coping strategies, as it was related to seeking help and support in interpersonal relationships.[44,73]

Finally, in relation to the nature of anxiety-related stimuli, gender differences were also found. The main cause of anxiety in men was of a work-related nature,[44] especially for those who identified with the stereotypical male role.[40] In women, anxiety stemmed from problems in interpersonal relationships.[65] However, women had different ways to express anxiety in relation to their social network compared to men. Anxious women tended to maintain contact with their social environment, which may protect them from loneliness and depression.[35] Therefore, women had more positive experiences in their environment and felt more supported by their social network. Thus, it seems that

interpersonal relationships, which can be covered by partners, friends, family, acquaintances, etc., played a dual role in women's anxiety: on the one hand, they constituted the main source of anxiety, and on the other hand, they acted as a protective factor of it.[35,44]

The political, economic, and social situation, individually and globally, may also have a differential effect on women's and men's mental health, both in general terms and in anxiety specifically. Van de Velde et al.[58] analyzed the gender gap in common mental disorders according to the welfare regime of the country and social risk factors. The higher gender gap in the prevalence of any type of anxiety disorder (18.8% women vs 9.4% men) was found in the southern countries of Europe where the female unemployment rates are pretty high. According to social risk factors, in countries with a southern regime, women who stay at home as a housekeeper reported less mental health problems than the employees. Other studies reported the importance of social gender roles in the result of anxiety under struggling economical situations. Men who identified themselves with the traditional male role were more likely to develop anxiety as a result of economic difficulties,[40] while in the presence of an anxiety disorder, women were more likely to have economic difficulties than men.[50] According to the social sphere, it is necessary to highlight the results found by Liu et al.[45] regarding how the Covid-19 pandemic has had a more severe effect on women's mental health than in men's mental health, with higher levels of anxiety and other anxiety-related variables such as insomnia, stress, and depression.

*Biological factors.* These studies indicated that anxiety is determined by genetic, hormonal, and/or neuroanatomical factors. With respect to the latter, it has been pointed out that one of the possible explanations for differences in anxiety between the sexes resides in the brain regions relevant to emotions (i.e. fear) and their regulation, such as the hippocampus, amygdala, and prefrontal cortex.[63,64] The results of several studies have shown that they are dimorphic structures and that they react differently in men and women.[32] Specifically, the left central amygdala is activated by stimuli and negative emotions in women,[39] while in men, it is activated by positive emotions.[64] However, other studies, as exposed in Kaczkurkin et al.,[68] have shown contradictory results regarding the influence of brain structures on sex differences in anxiety. In addition to brain regions, the conclusions of this review highlighted the role of cerebral blood flow as an important brain phenotype for understanding sex differences. Not specifically related to cerebral regions but with neurological communication, Holingue et al.[67] pointed out that a possible explanation of sex differences in mental health is the gut-brain axis, which responds to the bidirectional canal communication between microbiota and the neurological system. This study indicated that there are sex differences in the microbiome associated with childhood temperament. The plasticity and susceptibility to environmental exposures of the microbiome at early ages could be one of the variables associated with these differences in anxiety, trauma, and stressor-related disorders.[67]

Regarding genetic factors, some studies indicated the influence of genes on anxiety. These studies explored the relationship between the alteration of the FMR1 gene on anxiety disorders,[71] as well as the influence of genes on anxiety vulnerability factors, such as anxiety sensitivity and neuroticism.[64] The implication of serotonergic pathways

on mood regulation has also been analyzed, with results indicating that these pathways seem to be damaged in some mental health disorders. The research of Palma-Gudiel et al.[52] aimed to analyze if the serotonin transporter (SERT), encoded by the SLC6A4 gene, was responsible for sex differences in mental health. The results of this study pointed out that in women, the SLC6A4 methylation was higher compared to men, which could underlie the differential SERT expression in women, leading to a higher prevalence of somatic disorders in them. Other studies indicated that the variable sex may modulate the response to the stress process. According to them, the reason for the sex differences in anxiety is due to the transcriptional signatures of genes related to stress.[31] In any case, a biological explanation of anxiety contemplates the possibility of a mutual influence between factors. In this way, the influence of genetic factors, which depend on sex and moderate the risk for anxiety disorders, can affect anxiety-related brain regions such as the amygdala and the hippocampus function.[63] This vulnerability is bi-directionally related to the environment; therefore, environmental factors such as gender socialization could counteract the anxious tendency in men and enhance it in women.[30,71]

Finally, some studies suggest that women's hormonal fluctuations (progesterone, estrogens, and oxytocin) may be the cause of sexual differences in anxiety.[30,49,64,69] According to Murphy et al.,[72] these biological changes could make women exhibit an interoceptive processing pattern characterized by increased interoceptive attention and low objective accuracy of internal sensations. This pattern has been named atypical interoception. In their review, it is discussed that this "disrupted" pattern of perception may explain the difference in anxiety between women and men. This hypothesis leans on the studies that suggest that during the physical change periods, there is more vulnerability to experience this atypical interoception, making women more vulnerable due to their biological condition. Related to this, Hodes and Epperson[66] postulate that stress impacts men and women at different levels. According to these authors, the vulnerability in women resides in periods of hormonal changes and affects their emotional sphere, while stress in men impacts them at a cognitive level. Other studies have analyzed how hormonal periods can affect variables related to anxiety. For example, Day and Stevenson[63] in their review exposed deep literature on fear learning, and even though there are some inconclusive results, the majority of the studies found differences between men and women, reflecting the important role of hormones in this process. Lungu et al.[46] provided another explanation, indicating that differences between men and women in anxiety could be explained by the relationship between sex hormones and the processing of negative information, given that testosterone seems to be related to less frontolimbic activity before negative stimuli and progesterone are related to greater activity. However, the authors did not rule out that this difference between the sexes in emotional regulation might be mediated by sociocultural factors such as gender roles.

*Comorbidity.* The results of the studies revealed differences in the comorbidity of anxiety. Women are more likely to experience a depressive disorder along with anxiety.[34,48] Studies indicated that the relationship between the two disorders is based on the common presence of internalizing factors (i.e. neuroticism, rumination).[47,62] Therefore, other internalizing disorders, such as bulimia nervosa or another anxiety disorder, may

appear alongside anxiety.[37,43] In men, anxiety is often comorbid with disorders characterized by the presence of externalizing traits (i.e. hyperactivity, aggressiveness). Thus, according to the studies reviewed, the most common comorbid anxiety disorders and/or symptoms in men are substance abuse, attention deficit hyperactivity disorder (ADHD), and intermittent explosive disorder.[35,43,47]

## Discussion

The aim of this study was to provide a systematic updated review of the literature that has addressed differences in anxiety between women and men and its comorbidity. Importantly, it also aimed to reflect the necessity of applying the gender perspective in the conceptualization and analysis of the influence of sex and gender factors on health. Our purpose included the exploration of the hypothesis considered, the instruments used, and the principal conclusions of the studies reviewed. To cover every aspect of this issue, we tried to gather as many studies as possible involving both psychosocial and biological factors.

Our results complement and expand the findings of recent reviews that address this topic by focusing only on biological factors,[21,74] those that consider gender-sex differences but only in a specific anxiety disorder,[74,75] or those that do not clearly distinguish between gender and sex differences.[23] A novel contribution of this review is that it provides a broad overview of this subject, considering both studies that support the biological hypothesis and those that address gender roles, social and economic situations, life experiences, discrimination, etc., as significant factors in explaining why men and women experience anxiety differently. This approach contributes to supporting a biopsychosocial model of health, which should be enhanced by a gender/feminist analysis of mental health.

### *Psychosocial factors*

The results seem to indicate that gender socialization is, at least in part, responsible for the development of the psychosocial characteristics that act as risk factors for women and protective factors for men in the onset and course of anxiety.[44,54,56,59,64,70]

The psychosocial factors highlighted in the studies reviewed are aligned with those explored in recent literature. For example, in the Spanish context, Aparicio-García et al.[76] found that greater adjustment to gender norms (i.e. femininity) in women was related to greater anxiety symptoms, especially in the cognitive domain. According to this statement, some of the most salient risk factors for women observed from our review were rumination[33,44,49,65,73] and anxiety sensitivity.[51,55,57,65]

The results also suggest that gender socialization mediates the type of stimuli that are anxiogenic in women and men.[40] Such stressors are congruent with the differential socialization received by each sex found in the literature, centered on the achievement, competitiveness, and attainment of economic resources for men and masculinity and on relationships with others, sociability, and care for women and femininity.[77]

These findings offer further evidence that traditional socialization appears to be more advantageous for men in terms of health, whereas with regard to the expected gender

roles in society, women are more likely to suffer from mental health problems, particularly stress and anxiety.[78] Previous research even reinforces the idea that women's internalization of gender norms, highly connected to anxiety and depression, might be understood as hidden social violence.[79] The studies reviewed also underline that women's poorer living conditions may contribute to anxiety problems. Indeed, other studies have pointed to social conditions such as the sexual division of labor, beauty standards, the market economy, and environmental degradation as major challenges to improve women's health.[80] These factors may worsen with socioeconomic crises, as occurred during the COVID-19 situation,[81] which is also in line with the greater impact of anxiety problems on women noted in this review.

In addition, although men appear to exhibit lower levels of anxiety, some authors warn of a bias in this interpretation. A recent systematic review focused on anxiety in men suggested that when following the masculine gender norms, men have a general preference for self-reliance over help-seeking when dealing with anxiety problems.[82] A lack of awareness of anxiety, limited resources available for help-seeking, as well as a distrust of being helped, are other possible risk variables found to be relevant when considering anxiety in men.[83] Even so, the different presentation of anxiety in men would still be linked to gender norms. In brief, awareness of such evidence provides further support for the need to integrate the gender-feminist perspective in health, not only in research but also in its translation into real practical implications.[84]

## *Biological factors*

Conversely, other studies show that differences in anxiety disorders between sexes may be due to (a) differences in the brain structures involved in emotional regulation, which explain the difference in the processing of negative information,[32,39,68] (b) the fluctuations of sexual hormones that affect the anxious state of women,[46,49,63,64,66,69] and (c) genetic factors.[30,31,52,61,64,71]

The biological factors reported in this review are consistent with factors analyzed in recent research. Several studies exploring this direction include the impact of the menstrual cycle on anxiety,[85] the sex differences in the activation of brain structures in fear conditioning,[86] and the gen-specific risk in women.[87] Nevertheless, when it comes to biological factors, the still predominant literature of animal studies and their influence on the interpretation of human studies to address this question can be noted. Despite their importance, animal models have obvious limitations for the study of this topic that should not be neglected.[88] Importantly, they hamper the inclusion of other important aspects such as the analysis of gender and other psychosocial factors mentioned above. Also, it has been argued that the results of preclinical or animal studies should be interpreted with caution when generalizing the findings to differences between female and male humans in health-related issues.[89] In addition, some neuroscientists warn of the role of gender socialization in neuroplasticity, so that differences between women and men that have been understood as purely sexual may not be so.[90,91] Therefore, if and how the psychosocial factors, such as life experiences, gender stereotypes, and cultural expectations, could directly influence the differences found in biological factors associated with anxiety in women and men still need to be clarified.

## Comorbidity

Finally, the results relating to comorbidity reveal that considering gender differences in anxiety, comorbidity is the key to understanding discrepancies in the prevalence of anxiety disorders between the sexes. Thus, comorbid disorders may favor the chronicity of anxiety and mediate throughout its prognosis.[53]

In summary, it can be concluded that psychosocial factors related to gender are not only responsible, at least partially, for the difference in the prevalence of anxiety in men and women but also influence its comorbidity.

However, comorbidity results should be carefully considered. Just as a diagnosis bias has been demonstrated in anxiety stemming from gender norms,[92] there is also a vast literature supporting a similar bias in concomitant disorders. Depression, for instance, is known to be underdiagnosed in men. Several studies have explained this fact by the high presence of externalizing symptoms (e.g. avoidance, angriness) as well as the lack of help-seeking followed by masculinity, which makes depression more difficult to be diagnosed in men.[93] Conversely, several authors defend that depression criteria are similar to femininity roles and stereotypes, facilitating this diagnosis in women.[94] Another example of this phenomenon can be seen in ADHD. It has been widely documented that it is underdiagnosed in women and girls due to a more prevalence of internalizing symptoms (i.e. low self-esteem, inattention) compared to men and boys.[95] This presentation of internalizing symptoms tends to be mistaken for other mental health conditions, such as depression.[96]

Moreover, it is important to highlight that regarding affective and anxiety disorder diagnosis, several studies have reported the need to conceptualize, examine, and treat them as a continuum rather than discrete categories.[97,98] From this perspective, it would be difficult to delimitate, for example, the diagnosis between anxiety and depression, as both disorders share risk and maintaining factors and symptoms.[97] This spectrum approach is scarcely acknowledged in the studies reviewed, which may lead to a misinterpretation of the anxiety expression, implying an inadequate diagnostic response affecting men and women differently. The continuum perspective would act as an artifact to the theoretical concept of comorbidity and could help to better address the differential clinical symptomatology in men and women, mitigating the sex-gender diagnostic bias.

## Practical implications and future lines of research

This systematic review reflects the heterogeneity and complexity of the factors that have been analyzed to explain sex and gender differences in anxiety. This fact supports the need to apply the biopsychosocial model of health and the gender perspective to conceptualize, research, and intervene on this issue. However, several studies have documented the difficulty of implementing these approaches clinically.[99] For instance, some authors explicitly argue that due to the inherent characteristics of the biopsychosocial model (e.g. subjectivity and individuality in the patient's approach), its applicability in clinical practice is difficult and should, therefore, be understood only as a theoretical model.[99] Other authors doubt the scientific view of the gender/feminist perspective and its implementation in health.[6] The belief that the consideration of gender in health sciences is far from

neutrality, together with other prejudices such as sexism or androcentrism that persist in science, could act as barriers to an effective application of this perspective in clinical research and practice.[6] The medicalization of women with anxiety is a good example of an inadequate, or at least insufficient, treatment, as it continues to focus on a predominant biomedical model despite the strong evidence of the contribution of psychosocial factors.[100]

Consequently, future studies should focus on how to effectively implement the combination of biological, psychosocial, and social factors to address anxiety, and overcome the obstacles mentioned above. This main challenge could be approached by incorporating new treatment strategies such as person-centered care interventions. This perspective would allow consideration of not only the biological aspects but also the psychosocial context of patients, as it takes subjectivity and individuality as the heart of the intervention. It is clear that exploring the extent to which it would be beneficial for women's health to apply such health care strategies to intervene in anxiety and its comorbidities remains an interesting research question.[101] Furthermore, it is important to consider other essential factors that may have a great influence on health issues, such as the patient-professional relationship, the existence of implicit and explicit gender stereotypes in health care providers, the training of health professionals on gender perspectives, and so on.[102]

Overall, the results of this review indicate that it is necessary to reformulate the explanation of the occurrence, symptomatology, or treatment orientation for anxiety disorders. In doing so, therapeutic models that pathologize and medicate women's experiences should be left behind[103,104] because it is necessary to assume a new approach that considers any political, social, and developmental inequalities that contribute to and harm women's health.[105,106]

## Limitations

This study presents some limitations that need to be pointed out. First, the number of databases consulted was limited. Nevertheless, databases were selected for their suitability to address our subject of study given their broad scope in the literature related to the topic. Second, even if both empirical studies and reviews were included, the absence of qualitative studies could pose another limitation, reducing the variety of results obtained. Therefore, studies examining the experience of men and women facing anxiety from a qualitative analysis could complement the findings of this review. Thirdly, some studies aimed at analyzing gender differences in anxiety did not use specific instruments to assess psychosocial factors involved (e.g. identification with gender roles, gender stereotypes). They reduced their evaluation to the measurement of anxiety in both men and women, which could limit their conclusions and can affect the quality of their findings. To overcome this issue, it should be clear for future studies addressing this topic that sex disaggregation alone is insufficient to make gender-based assumptions.[10] Another limitation is related to a potential language bias, given that the review was targeted at English and/or Spanish written studies only. Although both languages are widely used throughout the world and in the scientific community, it is likely that this linguistic restriction has led to the sample of studies coming mainly from Western countries.

Considering the potential influence of culture on psychosocial factors (e.g. gender), it would be interesting for future research to analyze whether such factors have the same influence on anxiety in different countries and backgrounds.[14] Finally, concerning the review process, our systematic review protocol was not registered publicly; however, our methods are fully and systematically described in the present article.

The results of this review are relevant because they highlight the importance of explaining the onset and course of anxiety from a gender perspective. Considering that health is framed within a biopsychosocial model, psychosocial factors, in addition to biological factors, must be calculated during the evaluation and treatment process. These results indicate the need to implement new therapeutic models that consider how gender inequalities at different levels place women in a position of greater vulnerability to experience anxiety. In this way, women would be depathologized and the focus would be placed on how to pay attention to the patriarchal culture and how this affects their mental health.[94,100,103,104]

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## Authors' contributions

All authors have a substantial contribution in the study design, data interpretation and writing, reviewing, and approving the final manuscript.

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## Ethical statement

Ethical approval and informed consent were not required for this systematic review.

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## Supplemental material

Supplemental material for this article is available online.

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