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Review

# Anxiety and Depression Disorders in Undergraduate Medical Students during the COVID-19 Pandemic: An Integrative Literature Review

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**Abstract:** *Introduction:* The COVID-19 pandemic has triggered several challenges on the mental health worldwide. Undergraduate medical students face considerable stress in their academic routines. Thus, there is a need to explore the implications of the mental health of undergraduate medical students during the COVID-19 pandemic. *Objective:* To review the global literature about anxiety and depression disorders in undergraduate medical students during the COVID-19 pandemic. *Method:* we developed an integrative literature review on the occurrence of anxiety and depression symptoms in undergraduate medical students during the COVID-19 pandemic. We assessed the results on the occurrence of anxiety and depression and the severity of symptoms in medical students during the COVID-19 pandemic using quantitative studies applying GAD-7 questionnaire for anxiety or PHQ-9 for depression. *Results:* We reviewed 85 selected studies, and the results showed a significant prevalence of moderate and severe symptoms of anxiety and depression with 28.2% of participants presenting scores  $\geq 10$  on the GAD-7 and 38.9% on the PHQ-9. Statistical analyses revealed associations between higher rates of anxiety symptoms in developing countries and data collected after the lockdown period, in 2020, at the Pandemic lockdown. *Conclusion:* Our findings highlight the need for specific interventions to support the mental health of undergraduate medical students, critically in the female students from developing countries during a Pandemic crisis.

**Keywords:** anxiety; depression; medical students; pandemic; COVID-19; GAD-7; PHQ-9; mental health.

## 1. Introduction

In December 2019, in Wuhan, the first case of a new respiratory disease caused by the SARS-CoV-2 virus was documented. (1). On March 11, 2020, the World Health Organization (WHO) executive director officially categorized COVID-19 as a pandemic. (2) In May 2023, the WHO declared the end of the Public Health Emergency of International Concern regarding this disease. (3)(4) Therefore, in response to the global health crisis, the most widely used approach was social isolation, which resulted in the transition of in-person educational activities to an online format. (5)

COVID-19 not only causes physical health problems but can also lead to a series of mental disorders. (6) Fear of death and the impacts on physical health, isolation, social distancing, the loss of family members, financial difficulties, misinformation, rumors, and uncertainty about the future are sources of distress. According to surveys conducted by the WHO, the COVID-19 pandemic triggered a 25% increase in the prevalence of depression and anxiety worldwide. (7) Thus, the effects of the COVID-19 pandemic provide an opportunity to reflect on the state of mental health and highlight the imminent need to implement fundamental preventive measures for collective well-being. (8) Hence, concerns arise regarding the mental health of undergraduate medical students, who represent a population that already suffers from the daily pressures of academic life, which can

compromise mental, social, and physical health. (9) Furthermore, according to a research developed at our Brazilian medical institution in 2020, there was a higher prevalence of symptoms of anxiety and depression in medical students related to the COVID-19 pandemic. (10) Besides, the mental health of medical students is vital to analyze whether depression and anxiety symptoms represent obstacles to the academic career of medical students. (11)

Many studies have evaluated scales such as GAD-7 and PHQ-9 in medical students during the COVID-19 pandemic. The Generalized Anxiety Disorder (GAD-7) scale is a seven-item diagnostic tool that shows probable cases of generalized anxiety disorder, and assesses symptom severity. It has been confirmed in remote health surveys, epidemiological studies, and primary care settings. (12) This questionnaire is reliable and has a criterion validity. (13) However, this scale only provides probable diagnoses, which need to be confirmed through further assessment. (14) The Patient Health Questionnaire-9 (PHQ-9) is a nine-item questionnaire that screens for depression in primary care and other medical settings. (13) It is a quick, effective, simple, and reliable tool for screening and assessing the severity of depression symptoms. (15) However, this questionnaire does not necessarily match the lived experience of depression. (16) Thus, the PHQ-9 is not considered an instrument to confirm a depression diagnosis. (17)

Therefore, a literature review that analyzes the rates and severity of depression and anxiety symptoms in undergraduate medical students during the COVID-19 pandemic is essential. Although the emergency phase of this pandemic has already ended, it is essential to analyze the psychological effects on medical students, aiming to provide data that guide the development of strategies for future interventions in similar crises. We hypothesize that there is an increase in the occurrence and the severity of symptoms of anxiety and depression in medical students during the COVID-19 pandemic. Hence, we aimed primarily to review the global literature on anxiety and depression disorders with studies that used the PHQ-9 and GAD-7 questionnaires in undergraduate medical students during the COVID-19 pandemic. Moreover, the specific objectives were to analyze the predictive variables for increased symptoms of anxiety and depression in the medical educational institutions.

## 2. Methods

We performed an integrative literature review from February to July 2024 at FEMA (Educational Foundation of the Municipality of Assis) at the Faculty of Medicine. Regarding the eligibility and search criteria, we included the medical literature in English, Portuguese, and Spanish, using the following keywords: (COVID-19) and (Medical Students) and (anxiety) or (depression) or (mental health). We searched the indexed journals database from PubMed and Bvsalud and selected the manuscripts with data collection from December 2019 to July 2024. We included the manuscripts that used the PHQ-9 and/or GAD-7 questionnaires in their methodology. We excluded systematic reviews, narrative reviews, integrative reviews, meta-analyses, and qualitative analytical studies. We also excluded manuscripts from non-indexed and pre-printed journals.

To outline the search strategy, we followed the PICO strategy, obtaining several studies that were used to conduct the integrative literature review. We used the following variables: studies with data collected in 2020, during the lockdown period, and studies conducted after 2020, post lockdown period. Continent in which the institution was located: Europe, Asia, North America, Latin America, Oceania, and Africa. The actualized Human Development Index (HDI) of the country. Number of study participants, gender, percentile of women, average age of participants. Categorization of the GAD-7 questionnaire into: score 0-4; 5-9; 10-14; 15-21 and categorization into GAD 7 <10 or  $\geq 10$ . Categorization of the PHQ-9 questionnaire into: score 0-4; 5-9; 10-14; 15-19 >19 and categorization into PHQ9 <10 or  $\geq 10$ . The primary outcome was the prevalence of moderate or higher symptoms of anxiety and depression in medical students during the COVID-19 pandemic. The secondary outcome was the search for predictive variables about the severity of symptoms, in studies which GAD-7 and PHQ-9 scores  $\geq 10$ .

We adjusted multiple linear regression models with normal response to explain the GAD-7 percentage greater than or equal to 10 points and the PHQ-9 percentage greater than or equal to 10

points, including, in the deterministic component, only the variables that presented  $p < .20$  in the bivariate investigation. The GAD-7 and PHQ-9 indexes equal or more than ten are a critical instrument for denote the moderate and high severity of the symptoms. (14) The quality of the adjustment of the multiple regression models was analysed by investigating the behavior of the residuals with the Shapiro-Wilk normality test, scatter plot between residuals and predicted values of the models to investigate homoscedasticity, and Cook’s distance measure to investigate the influence of atypical points on the estimates of the model parameters.

The final models considered the associations statistically significant if  $p < .05$ . All analyses were performed with the SPSS 21 software by IBM trademark.

We searched the databases of manuscripts selected by the eligibility criteria. We evaluated the results regarding the occurrence of anxiety and depression through the PHQ-9 and GAD-7 questionnaires during the COVID-19 pandemic. Finally, we created a table summarizing identification data, objectives, and results of each study evaluated.

We collected studies from the literature using secondary data sources. We were concerned about bias risks in the analysis and interpretation of research data, as well as indirect risks to the physical, mental, spiritual, and social dimensions associated with human beings in any research. Regarding the benefits, we considered the manuscript vital for promoting a positive impact on medical practice in mental health.

3. Results

We identified 1.768 studies in the Pubmed database and 60 articles in Bvsalud. Applying the eligibility criteria, we selected 88 articles from the literature. Of these, 43 contained at least one of the questionnaires (GAD-7 or PHQ-9), while in 42 articles, both questionnaires were used. Figure 1 represents the flowchart of the selection process.

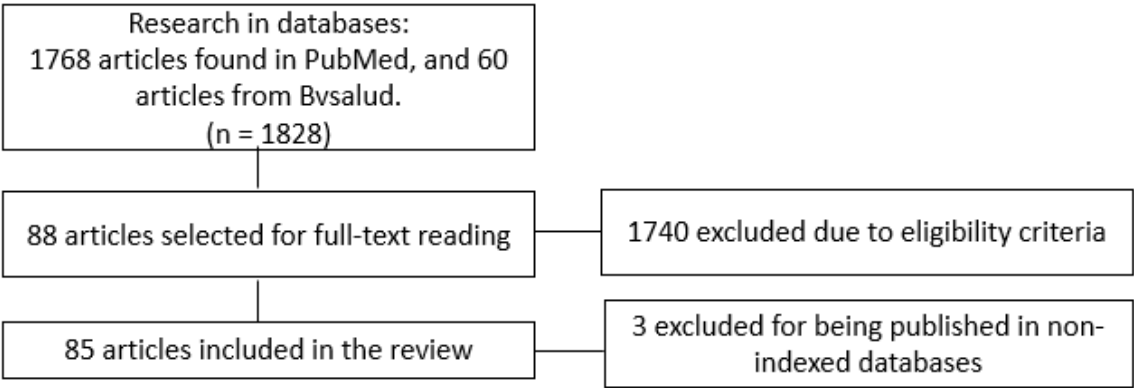


Figure 1. Flowchart of the selection process of the studies included in the review.

Table 1 contains the list of selected studies. Three manuscripts were excluded because they were published in non-indexed databases. Thus, the study was based on data from 85 manuscripts in the literature.

Table 1. List of the eligible studies and the percentiles of GAD-7 and / or PHQ-9 scores  $\geq 10$ .

	Author	Country	N	GAD-7 $\geq 10$ (%)	PHQ-9 $\geq 10$ (%)
1	Zheng (28)	China	468	11.30	20.70
2	Coico-Lama (29)	Peru	431	29.50	28.50
3	Bhongade (30)	Emirates	107	25.30	
4	Din (31)	Pakistan	444	46.17	64.41
5	Reddy (32)	India	164	20.00	
6	Ortega-Moreno (33)	Mexico	384	24.50	43.00

7	Shahzad (34)	Pakistan	585	41.00	
8	Iqbal (35)	India	261	51.70	58.70
9	Gomez-Duran (36)	Spain	175	34.70	26.60
10	Wiguna (37)	Indonesia	1023		77.40
11	Tanuseriawan (38)	Indonesia	635		63.40
12	Purnomo (39)	Indonesia	161		8.70
13	Yuryeva (40)	Ukraine	154	27.90	44.80
14	Arshad I (41)	India	261	65.50	67.80
15	Lakshmi (42)	India	200	83.00	
16	Ernst J (43)	Swiss	574	22.60	
17	Cao W (44)	China	7143	3.60	27.20
18	Chistophers B (45)	USA	1139	20.00	
19	Sartorao (10,46)	Brazil	340	a	a
20	Lin S (47)	USA	154		24.00
21	Huarccaya Victoria (48)	Colombia	1238	19.00	34.00
22	Pinsai (49)	Tailandia	37	51.35	
23	Verma (50)	India	267	28.50	
24	Alkwai (51)	Saudi Arabia	55	17.00	26.42
25	Bartra (52)	Peru	57	22.80	
26	Guralwar(52)	India	604	54.14	
27	Almarri(53)	India	7116	40.50	
28	Kamran(52)	Pakistan	324	44.50	
29	Porwal (55)	Saudi Arabia	22	13.60	40.90
30	Primatanti(56)	Indonesia	7949	13.90	
31	AbuDujain(57)	Saudi Arabia	345	13.90	
32	Imran(58)	Pakistan	1100	40.40	48.10
33	Rafsanjanipoor (59)	Iran	83	24.20	
34	Srivastava (60)	India	97	24.74	48.10
35	Pedraz-Petrozzi (61)	Colombia	125	12.80	34.40
36	Vajpeyi (62)	Emirates	798	39.10	
37	Alshehri (63)	Saudi Arabia	182	30.80	
38	Paz D (64)	USA	152	36.70	40.90
39	Schindler (65)	Germany	63		44.00
40	Lu (66)	China	519		41.50
41	Chakeyanunn(67)	Thailand	437		27.00
42	Huarcaya victoria (48)	Colombia	1238	19.00	
43	Camelier-Mascarenhas (68)	Brazil	310	33.50	42.60
44	Dziedzic (69)	Brazil	162	29.60	34.00
45	Eleftheriou (70)	Greece	559	67.60	43.70
46	Cheng(71)	China	947	37.80	39.30
47	Santander (72)	Peru	370	38.38	
48	Çimen (73)	Turkey	2778	44.50	46.21
49	Vlillalon López (74)	Chile	359	41.50	60.10
50	Villagomes-Lopez (74)	Ecuador	1528	30.30	
51	Harries(75)	USA	741	25.60	
52	Liu (76)	China	29663	46.00	37.80
53	Pattanaseri (77)	Thailand	224	a	a
54	Teh(78)	Malaysia	371	37.00	35.70
55	Adhikari (79)	Nepal	223	a	a
56	Chalise (80)	Nepal	315	12.90	
57	Romic (81)	Croatia	280	32.50	52.20
58	Nguyen (82)	Vietnan	747	7.90	20.63



59	Biswas (83)	Bangladesh	425		31.80
60	Song (84)	China	666	17.80	15.20
61	Guo (85)	USA	929	31.10	48.80
62	Essangri (86)	Morocco	549	25.70	45.70
63	Saali(87)	USA	108	32.40	
64	Nishimura (88)	Japan	473	7.20	74.70
65	Sserunkuuma (89)	Uganda	269		24.10
66	Batais (90)	Saudi Arabia	332	13.70	15.90
67	Crisol-deza (91)	Peru	1238	19.00	34.00
68	Tsiouris (92)	Germany	1438		34.00
69	Sudi(93)	Malaysia	196		38.90
70	Wercelens (94)	Brazil	150		40.70
71	Yin (95)	China	5982	4.20	9.90
72	Chwa (96)	USA	87	27.40	
73	Pandey (97)	India	83	9.80	24.70
74	Elhadi(99)	Libya	2430	27.00	
75	Xiao (100)	China	933	4.60	7.30
76	Essadek (101)	France	668		42.80
77	Liu (102)	China	217	7.40	
78	Chootong (103)	Thailand	325	12.90	7.60
79	Saeed (104)	Pakistan	234	62.40	64.10
80	Huang (105)	China	1021	10.98	38.17
81	Wang(106)	Korea	454	18.50	11.10
82	Halperin (107)	USA	1428	30.60	31.00
83	Bilgi (108)	Turkey	178	37.10	20.10
84	Alsairafi (109)	Kuwait	298	85.20	93.00
85	Allah (110)	Saudi Arabia	1591	19.20	
86	Khidri (111)	Pakistan	864		40.80
87	Shreevastava (112)	India	1208	40.30	
88	Afzal (113)	Pakistan	433		40.65

<sup>a</sup> The manuscripts referenced as 19, 53, and 55 were excluded due to non-indexed publication. .

Table 2 shows the manuscripts sample characteristics. Of the selected manuscripts, 28 collected information after 2020. About the institution continent area, 49 papers were from Asian institutions. On the HDI (Human Development Index), 35 were from countries with a very high HDI.Third-one from countries with a high HDI, and 22 from countries with a medium or low HDI.

Table 2. Manuscripts description variables.

<i>Variable</i>	<i>n</i>	<i>%</i>
<b>Data collection time</b>		
After 2020	28	31.8
In 2020	60	68.2
<b>Continent</b>		
Europe	9	10.2
North America	8	9.1
Asia	49	55.7
Oceania	5	5.7
Latin America	14	15.9
Africa	3	3.4
<b>Human Development Index (HDI)</b>		
Very high	35	39.8
High	31	35.2

Medium or low	22	25.0
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Table 3 provides the variable range list and the interquarles. Concerning the HDI variable, the median of the countries was 0.79 (0.70-0.88). The median age of the participants was 22.0 years (20.0–23.0). The percentile of women who answered the questionnaires was 63.0% (52.3–68.7). Regarding the GAD-7 questionnaire, we observed a median of 28.2% (18.3 – 39.4) with a score ≥ 10. About the PHQ-9 questionnaire, the median score ≥10 was 38.9% (26.8 – 47.2).

**Table 3.** Variable range list and the interquartile ranges.

<i>Variable</i>	<i>Median</i>	<i>Q1</i>	<i>Q3</i>
Human Development Index	0.79	0.70	0.88
Number of participants	377.5	185,5	912,8
Male	160.0	89.0	322,0
Female	240.0	113,0	597,0
Percentual of women	63.0	52.3	68.7
Age	22.0	20.0	23.0
GAD-7 score 0-4	25.3	0.0	39.2
GAD-7 score 5-9	37.8	30.4	67.2
GAD-7 score 10-14	19.9	12.8	27.5
GAD-7 score 15-21	3.4	0.0	13.9
GAD-7 score ≥ 10	28.2	18.3	39.4
PHQ-9 score 0-4	0.0	0.0	28.4
PHQ-9 score <10	40.0	27.0	60.9
PHQ-9 score 10-14	23.0	19.0	36.8
PHQ-9 score 15-19	4.9	0.0	13.9
PHQ-9 score >19	0.0	0.0	6.2
PHQ-9 score ≥10	38.9	26.8	47.2

Q1: first interquartile range Q3: third interquartile rang.e.

Table 4 presents the bivariate associations by simple linear regression to explain the percentage of GAD-7 with a score ≥ 10 points (p < .20). We observed significant results (p < .20) regarding the variables: data collected in 2020, Latin America, Oceania, Asia (reference: Europe). And medium or low and high HDI (reference: very high HDI).

**Table 4.** Bivariate associations by simple linear regression to explain the percentage of GAD-7 score ≥ 10.

<i>Variable</i>	<i>b</i>	<i>IC95%</i>		<i>p</i>
Data Collection in 2020 (Ref: After 2020)	-15.16	-23.15	-7.17	.000
Africa	-13.48	-40.54	13.58	.329
Latin America	-13.22	-29.79	3.35	.118
Oceania	-25.93	-61.73	9.87	.156
Asia	-9.51	-23.98	4.95	.198
North America	-10.72	-29.16	7.72	.255
Continent (Ref: Europe)	0 <sup>a</sup>			
Human Development Index	-34.12	-68.59	0.35	.052
Medium or low	9.23	-0.12	18.59	.053
High	-10.72	-19.10	-2.35	.012
Human Development Index (Ref: very high)	0 <sup>a</sup>			
Number of participants	0.00	0.00	0.00	.914
Number of women	0.00	0.00	0.00	.963
Percentage of women	0.08	-0.30	0.46	.684

Average age	0.67	-3.82	5.15	.771
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B: beta coefficient; 95%CI: 95% confidence interval; P<.20.

Table 5 shows the data obtained after multiple linear regression to explain the percentage of GAD-7 scores  $\geq 10$  ( $p < .05$ ). Table 5 shows the data obtained after multiple linear regression to explain the percentage of GAD-7 scores  $\geq 10$ . After statistical analysis, we observed that studies with data collected in 2020 –during the lockdown in most of countries worldwide - had a GAD-7 response percentage  $\geq 10$ , that was on average 14% lower compared to collected after 2020 ( $\beta$ : -14.02; 95% CI -21.63 to -6.40;  $p < .001$ ). Countries with medium or low HDI had a GAD-7 response percentage  $\geq 10$  twelve percent higher than from countries with high or very high HDI ( $\beta$ : 12.61; 95%CI 2.93 to 22.29;  $p < .011$ ).

**Table 5.** Multiple Linear Regression to Explain the Percentage of GAD-7 score  $\geq 10$ .

Variable	$\beta$	95%CI		p
Data collection in 2020 (Ref: After 2020)	-14.02	-21.63	-6.40	.000
Africa	-6.26	-30.28	17.76	.610
Latin America	2.63	-13.92	19.18	.755
Oceania	-22.24	-53.37	8.90	.162
Asia	-7.25	-20.49	5.99	.283
North America	-5.38	-20.71	9.96	.492
Continent (Ref: Europe)	0 <sup>a</sup>			
Medium or low	12.61	2.93	22.29	.011
High	-8.37	-18.37	1.63	.101
Human Development Index (Ref: very high)	0 <sup>a</sup>			

p < .05; homoscedasticity; dCook < 1 = 100%; B: beta coefficient; 95%CI: 95% confidence interval.

Regarding studies using PHQ-9, Table 6 shows the bivariate associations by simple linear regression to explain the percentage of PHQ-9 scores  $\geq 10$ . As a result, the percentage of women was the only association presenting a p-value under .20 on the bivariate analysis ( $\beta$ : 0.36; 95%CI -0.04 to 0.75;  $p < .077$ ).

**Table 6.** Bivariate associations by simple linear regression to explain the percentage of PHQ-9 score  $\geq 10$ .

Variable	$\beta$	95%CI		p
<b>Data Collection in 2020 (Ref: After 2020)</b>	1.42	-8.71	11.54	.784
Africa	-8.59	-35.82	18.64	.536
Latin America	-4.46	-21.19	12.28	.602
Oceania	3.61	-17.48	24.70	.737
Asia	-6.21	-19.92	7.49	.374
North America	-7.31	-28.40	13.78	.497
Continent (Ref: Europe)	0 <sup>a</sup>			
Human Development Index	-22.58	-62.59	17.42	.269
Medium or Low	6.67	-5.34	18.68	.276
High	-6.14	-16.19	3.92	.232
Human Development Index (Ref: Very High)	0 <sup>a</sup>			
Number of Participants	0.00	0.00	0.00	.625
Number of Women	0.00	0.00	0.00	.665
Percentage of Women	0.36	-0.04	0.75	.077
Average age	4.78	-5.13	14.70	.344

B: beta coefficient; 95%CI: 95% confidence interval; P<.20.



#### 4. Discussion

We found evidence that studies performed in 2020 showed students with an average 14% lower percentage of responses to the GAD-7 anxiety symptoms score  $\geq 10$  compared to studies after 2020. This may be explained by the lockdown period and the beginning of the Pandemic, a period of uncertainty. (18,19)

Furthermore, we observed that students from countries with medium or low HDI had a significant average 12% higher percentage of responses to the anxiety GAD-7 score  $\geq 10$  than those from countries with high or very high HDI. Finally, the higher percentage of female students was the only significant association found concerning the PHQ-9 depression symptoms score  $\geq 10$ . It is known that female gender is related to be more affected during pandemic related stressors. (20,21) Moreover, it is important to highlight that low- and middle-income countries are also associated with a high burden of mental health disorders (22) with some studies suggesting that lower-income countries have a reduced capacity to provide access to depression treatment (23,24).

A study conducted at our Brazilian institution in 2020 applied the GAD-7 and PHQ-9 questionnaires to medical students during the beginning of the COVID-19 pandemic. The study found a higher prevalence of moderate and severe symptoms of anxiety and depression in students, especially in women. (10). Using a cut-off score of 10 for GAD-7 anxiety questionnaire, 46.17% of the students were identified with moderate or severe symptoms of anxiety, and 64.41% with PHQ-9 score  $\geq 10$ . Sartorao-Filho et al. also observed after multivariate analysis, a positive significant relationship between GAD-7 total score and female students;  $r(340) = 0.130$ ,  $p = .016$ , and a positive significant relationship between PHQ-9 total score and female students;  $r(340) = 0.128$ ,  $p = .018$  (10). The prevalence of symptoms of anxiety and depression observed in this previous study has results similar to those of this review.

A meta-analysis published by Jia et al in 2022 demonstrated the pooled prevalence of depression in 37.9% of medical students (95%CI: 30.7-45.4%), and pooled anxiety prevalence of 33.7% (95%CI: 26.8-41.1%). In addition, their results varied by gender, country and continent. (25)

Another study, in 2024, from Lin et al. (26) reported the pooled prevalence for anxiety of 45% (95%CI: 40-49%) and for depression of 48% (95%CI:43-52%). For moderate and severe anxiety, 28% (95%CI 24-32%) and for moderate and severe depression, 30% (95%CI: 26-35%). After the meta-regression, medical students in Asia had a lower prevalence of anxiety and depression than from other regions. (27)

The critical limitations on the current review is that the study analyzed global data based on observational studies that used the questionnaires GAD-7 and PHQ-9, recognized as screening instruments for anxiety and depression symptoms. However, the diagnosis of depression and anxiety is not based solely on the application of the questionnaires and requires a detailed clinical evaluation. In addition, the results cannot be generalized due to the consideration of limitations inherent to observational studies, such as difficulty in controlling variables, potential confounders, temporal ambiguity, and the location where the studies were conducted, in addition to selection and information biases.

#### 5. Conclusions

We found in the worldwide literature studies that demonstrated a high occurrence of symptoms of depression and anxiety in the population of undergraduate medical students. We observed a higher occurrence of anxiety symptoms in studies performed after the lockdown period, and studies in developing countries. We also described a higher occurrence of depression symptoms in the female population. These findings highlight the urgency of developing targeted intervention strategies to mitigate these symptoms in populations that demonstrate high susceptibility to mental disorders during pandemic periods.

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