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Observational Study

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Observational Study

Medical student depression and its correlates across three international medical schools

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Abstract

BACKGROUND
Medical students have high rates of depression, anxiety, and burnout that have been found to affect their empathy, professional behaviors, and performance as a physician. While studies have examined predictors for burnout and depression in the United States (US), no study, to our knowledge, has compared depression in medical students cross-culturally, or has attempted to examine the effect of factors influencing rates including burnout, exercise, stress, unmet mental health needs, and region.

AIM
To examine rates of depression in three international cohorts of medical students, and determine variables that may explain these differences.

METHODS
Convenience samples of medical students from three countries (US, China, and a Middle Eastern country whose name remains anonymous per request from the school) were surveyed in this observational study. Using the Patient Health Questionnaire-2 (PHQ-2) and a modified Maslach Burnout Inventory, depression and burnout were examined among medical students from the three cohorts (*n* = 473). Chi-square test and analysis of variance were used to examine differences in demographics, behavioral, and psychological variables across these three schools

to identify potentially confounding descriptive characteristics. Analysis of covariance compared depression and the emotional exhaustion component of burnout identified through Principal Component Analysis across countries. Multiple linear regression was used to analyze the impact of demographic, behavioral, and psychological variables on screening positive for depression.

RESULTS
Medical students from the Middle Eastern country had the highest rates of positive depression screens (41.1%), defined as a PHQ-2 score of ≥ 3, followed by China (14.1 %), and then the US (3.8%). More students in the Middle Eastern school had unmet mental health needs (50.8%) than at the medical school in China (34.8%) or the school in the US (32.8%) (Pearson chi-square significance < 0.05). Thus, PHQ-2 scores were adjusted for unmet mental health needs; however, the Middle Eastern country continued to have the highest depression. Adjusting for PHQ-2 score, medical students from the US scored the highest on emotional exhaustion (a measure of burnout). Demographic variables did not significantly predict medical student depression; however, lack of exercise, unmet mental health needs, stress, and emotional exhaustion predicted nearly half of depression in these cohorts. In comparison to the US, coming from the Middle Eastern country and China predicted higher levels of depression.

CONCLUSION
Depression rates differ in three international cohorts of medical students. Measured factors contributed to some observed differences. Identifying site-specific prevention and intervention strategies in medical student mental health is warranted.

Key words: Medical students; Wellness; Burnout; Depression; International

Core tip: Depression among medical students places them at increased risk for suicide, and impacts many aspects of professional performance. Medical students around the world share common stressors, including competitive selection processes, intense coursework, and pressure for high achievement. However, differences in depression rates are influenced, in part, by burnout, exercise, stress, unmet mental health needs, and region.

INTRODUCTION

Medical students have high rates of depression, anxiety, and burnout, significantly higher than age-matched samples and the general population[1,2]. In fact, a recent meta-analysis found depression or depressive symptoms among medical students to be 27.2%, with a prevalence of suicidal ideation of 11.1%[3]. Burnout and depression affect both the student and their future patients, as they are associated with lowered academic performance[4], decreased empathy[5], increased suicidal ideation[6], unprofessional behaviors, and lack of altruistic goals for their future careers[7]. Despite the risk for suicidality, most depressed and burned out students go untreated: Only 12.9% of depressed students in one study sought treatment[8], and only one-third of students with high burnout seek help[9].

Many studies have examined explanations for high rates of burnout in this population. The overall learning environment[2] seems to be the most cited reason, with higher rates of burnout associated with lack of support from faculty and staff, working with cynical residents[10], lack of supportive resources and time off[11], and being mistreated or bullied[12]. Specific grading schemes have been independently

associated with burnout; students were found to be more likely burned out and with high stress in schools with letter grading as opposed to pass/fail[13]. Other studies have found associations with perfectionism, low academic self-efficacy[14], more advanced year of training, negative personal life events in the last 12 mo[15], alcohol abuse and dependence[16], and decreased social intimacy[17]. Sleep quality[17], pathological sleepiness, and sleeping less than seven hours a night also seem to independently predict burnout, however exercise does not[18].

Depression also correlates with high levels of burnout[18]. Studies on predictors of depression in medical students suggest that mistreatment, poor role modeling[19], low optimism[20], gender (females with higher rates) and year of study[8] seem to correlate with higher rates of depression. Resilience and hope are negatively correlated with depression[21].

Studies looking at depression and burnout among medical students in Asia[22] and the Middle East[23-25] report high rates of burnout and depression. To our knowledge, no study has compared depression in medical students cross-culturally, or has attempted to examine the effect of factors influencing rates including burnout, exercise, stress, unmet mental health needs, and region. The purpose of this study is to examine rates of positive screening for depression in three different groups of medical students, each from an internationally distinct medical school: Yale University School of Medicine in the United States (US), Central South University Xiangya School of Medicine in China, and a School of Medicine in the Middle East whose research collaborators chose to remain anonymous. A secondary aim is to examine whether there are differences in other variables across these sites, including age, gender, sleep, exercise, unmet mental health needs, emotional exhaustion, stress, as well as nationality, that may explain any differences in depression.

MATERIALS AND METHODS

Study participants
Convenience samples of medical students from three countries: US, China, and a Middle Eastern country (whose name remains anonymous per request from the school) were surveyed in this exploratory study. The US sample (*n* = 205) was made up of medical students at the Yale School of Medicine, one of the leading medical schools in the US. Students completed surveys in the fall of 2013 *via* anonymous online distribution with electronic consent. The Chinese sample (*n* = 142), surveyed in November and December 2015, consisted of third- to sixth-year students from an 8-year Doctor of Medicine (MD) program at Xiangya School of Medicine, a leading medical school in China whose curriculum closely resembles that of a US medical school; third and fourth years are preclinical years (equivalent to MS1 and MS2 in the US) and fifth and sixth year are clinical years (equivalent to MS3 and MS4 in the US). The Middle Eastern sample (*n* = 126), surveyed in Fall 2014, consisted of fifth year medical students enrolled at a medical school in the Middle East, one of the top five medical schools in the region. These students completed surveys anonymously *via* paper/pencil after a one-time seminar on mental health, self-care, and help-seeking behaviors, and left their responses in a box near the seminar exit.

The Yale and Middle Eastern School's IRBs deemed this study exempt. The Ethics Committee of Xiangya approved the study. All students were assured of both confidentiality and anonymity, and participation was voluntary. Paper questionnaires were preserved, and data were typed into the computer using anonymous identifiers by investigators. No incentives were offered at Xiangya or the Middle Eastern School for participation; a gift card raffle was offered at Yale.

Survey measures
The survey questionnaire consisted of the following parts: (1) Self-reported questions on demographics, health-seeking behaviors, and personal health behaviors such as sleep and exercise patterns; (2) Patient Health Questionnaire-2 (PHQ-2)[26] screening for depression; (3) A modified version of the Maslach Burnout Inventory (MBI)[27] assessing burnout; (4) Attitudes toward Mental Illness Questionnaire assessing stigma[28]; and (5) Six questions related to comfort with feedback, admitting mistakes, and help-seeking. A detailed description of the survey and its sections can also be found in a previous study[29].

The original survey was translated into both Mandarin and a language native to the Middle Eastern country by contributing authors. The translations were then re-translated back to English by colleagues in the US who were fluent in both languages to assure that the surveys administered to all cohorts of students were comparable. Specific wording was changed in a few questions to more accurately reflect culture

and each country's curriculum of medical education. Ethnicity questions were country-specific to include relevant ethnic groups. No questions about drug or alcohol use were included in the Middle Eastern survey, as consuming alcohol is against Islamic law and religion. The country is officially not at war with another country.

Analyses

Principal components analysis was used to analyze the six items of the modified MBI. One component explained 44.0% of variance, and the second component explained 20.5%. Analysis of eigenvalues, a scree plot, and subjective content of individual items suggested that two components be retained. The first component, which we will call "emotional exhaustion" (*i.e.*, the "emotional exhaustion" portion of the MBI) had high component loadings (> 0.65) on the four questions about being drained, used up, burned out, and uninterested. The second component had high component loadings (> 0.56) on the two questions about personal accomplishment. Of these two components, emotional exhaustion is most relevant to the current study. We created a scale using the four emotional exhaustion items, and computed scale scores by calculating the mean item score across the four items (as long as at least 66% of the questions were answered by the student). Missing data imputation methods applied to less than 5% of students, suggesting any potential bias would be inconsequential. Cronbach's alpha for the four item emotional exhaustion scale was 0.74.

Chi-square test and analysis of variance were used to examine differences in demographics, behavioral, and psychological variables across these three schools. The purpose of these statistics was to identify potentially confounding descriptive characteristics. Analysis of covariance (ANCOVA) was then used to compare depression among these three countries adjusted for differences in "unmet mental health needs". Unmet mental health need was defined as agreeing to the Likert scale question "there are times I have a mental health need for which I do not seek care", where agree and strongly agree were collapsed into one response. Bonferroni type corrections were applied for multiple comparisons. Adjusting for the total PHQ-2 score, Emotional exhaustion was compared between student populations. For each relevant item on the questionnaire, adjusted means of the answers were examined among regions in pairwise comparisons.

To determine the possible predicative variables for medical student depression, multiple linear regression analysis was performed. The analysis included: Demographic variables (age and gender), behavioral variables (sleep, exercise, unmet mental health needs), and psychological variables (stress, emotional exhaustion). The possibility of multicollinearity was ruled out. All analyses were done using SPSS version 25, and statistical significance was evaluated at the $P < 0.05$ level.

RESULTS

Response rates differed by cohort. At Yale, 205 out of 519 students (39.5%) responded to the survey. At the Middle Eastern school, 172 out of 203 students (84.7%) and at Xiangya, 142 out of 150 (94.7%) responded to the survey. Responses to specific questions were included in the analyses, even if the survey was not fully completed.

Descriptive statistics

A positive screen for depression was defined as a PHQ-2 score of ≥ 3. According to that definition, students in the Middle Eastern country were significantly more likely to screen positive for depression (41.1% of students screened positive) than students in China (14.1% screened positive). Both cohorts were more likely to be depressed than the US cohort (3.8% screened positive) (Table 1). Other characteristics were also significantly different between schools. For example, in all three cohorts, students in China slept the least number of hours, and students in the Middle East exercised the least. More students in the Middle Eastern school had unmet mental health needs (50.8%) than in China (34.8%) or the US (32.8%) (Pearson chi-square significance < 0.05).

ANCOVA analysis

ANCOVA, with adjustment for differences in unmet mental health needs, showed that on scores from question 1 of the PHQ-2 [F (2.435) = 54.60, $P < 0.001$], a measure of anhedonia, students from the Middle Eastern country reported significantly higher scores than those from the other two cohorts. Students from China also had scores that were significantly higher than those reported from the US. Scores from question 2 of PHQ-2 [F (2.434) = 49.79, $P < 0.001$], a measure of depressed mood, followed the same pattern, with students from the Middle Eastern country having the highest scores, followed by China, then the US. On the total score of PHQ-2 [F (2.434) = 71.48,

Table 1 Chi-square and analysis of variance comparisons of group characteristics

Variable	Yale University School of Medicine, *n* = 205	Middle Eastern Medical School, *n* = 126	Xiangya School of Medicine, *n* = 142	Entire population, *n* = 473	Statistics
Age, mean (SD[1])	25.3 (2.4)	22.1 (1.0)	22.0 (1.5)	23.4 (2.5)	$F = 174.7$[a]
Gender	43.4% Male (M) 56.6% Female (F)	37.3% M 62.7% F	43.7% M 56.3% F	41.8% M 58.2% F	$\chi^2 = 0.5$
Sleep[2] in hr, mean (SD)	6.6 (1.0)	6.6 (1.0)	6.5 (0.9)	6.5 (1.0)	$F = 5.6$[a]
Exercise[3], mean (SD)	2.5 (1.8)	1.4 (1.7)	1.6 (1.8)	1.9 (1.8)	$F = 18.1$[a]
Depression screening by PHQ-2[4] category	Not depressed: 62.8% Mild depression: 33.3% Depressed: 3.8% (*n* = 7)	Not depressed:10.5% Mild depression: 48.8% Depressed: 41.1% (*n* = 51)	Not depressed: 16.2 % Mild depression: 69.7% Depressed: 14.1% (*n* = 20)	Not depressed: 33.6% Mild depression: 49.0% Depressed: 17.4% (*n* = 78)	$\chi^2 = 161.1$[a]
Stress[5]	Yes: 58.4% (*n* = 108)	Yes: 75.4% (*n* = 95)	Yes: 82.9% (*n* = 116)	Yes=70.9% (*n* = 319)	$\chi^2 = 25.3$[a]
Unmet mental health need[6]	Disagree: 49.5% Neutral: 17.7% Agree: 32.8%	Disagree: 32.5% Neutral: 16.7% Agree: 50.8%	Disagree: 47.1% Neutral: 18.1% Agree: 34.8%	Disagree: 44.1% Neutral: 17.6% Agree: 38.3%	$\chi^2 = 12.1$[b]

[a]$P < 0.01$;
[b]$P < 0.05$;
[1]SD: Standard deviation;
[2]For the purposes of scale measurement, if a participant answered < 4 h a night, 3.5 was the number coded, 4-5 h a night = 4.5; 6-7 h a night = 6.5, and > 8 h a night was coded as 8.5;
[3]Mean number of days per week spent exercising at least 30 consecutive minutes;
[4]PHQ-2: Patient Health Questionnaire-2; where not depressed = 0, mild depression is 1-2, depressed is ≥ 3;
[5]Response to question "Are you stressed?";
[6]Answer of agreement to Likert scale question "there are times I have a mental health need for which I do not seek care". Agree and Strongly Disagree were collapsed into one category; Agree and Strongly Agree were collapsed into another.

$P < 0.001$], a screen for depression, students from the Middle Eastern country reported significantly higher scores than those from each of the other countries. Again, students from China also had scores that were significantly higher than those from the US (Table 2).

ANCOVA, with adjustment for differences in PHQ-2 total scores, measured differences in burnout (Table 3). On the burnout item "I feel emotionally drained by my studies" [F (2.430) = 33.31, $P < 0.001$], students from the US reported significantly higher scores than those from each of the other regions, followed by China where scores were significantly higher than those reported from the Middle Eastern country. On the item "I feel used up at the end of a day in medical school" [F (2.438) = 13.41, $P < 0.001$], students from the US reported significantly higher scores than those from each of the other countries. However, on this item, the other schools scores were not significantly different from each other.

Examining answers to the item "I feel burned out from my studies" [F (2.445) = 10.06, $P < 0.001$], students from the US and the Middle Eastern country reported significantly higher scores than China, but the scores from the students in the Middle Eastern country and China were not significantly different from one another. On the final item "I have become less interested in my studies since my enrollment in medical school" [F (2.445) = 7.27, $P = 0.001$], students from the US and the Middle Eastern country again reported significantly higher scores than China, but the scores were not significantly different from one another. For the overall emotional exhaustion component measurement [F (2.444) = 19.26, $P < 0.001$], students from the US reported significantly higher scores than those from each of the other countries. The scores from the students in China and the Middle East were not significantly different from each other.

Multiple linear regression

Results from the multiple linear regression analyses on medical student depression (as measured by total PHQ-2 score) are listed in Table 4. Demographic variables did not significantly predict medical student depression. Among behavioral variables, exercise and unmet mental health needs significantly predicted medical student depression, but amount of sleep did not. Both unmet mental health needs and emotional exhaustion were positively related to medical student depression, while the amount of exercise had a negative impact on depression (*i.e.*, more time exercising, lower depression score). Both psychological variables, stress as well as the emotional exhaustion component of burnout, were predictors of medical student depression. Stress was measured by answering "yes" to the question "are you stressed?".

Table 2 Comparison of samples of medical students on depression (ANCOVA)[1]

Over the past 2 wk, how often have you been bothered by any of the following problems? (PHQ-2[2])	a United States	b Middle Eastern country	c China	
	LS mean (SE)	LS mean (SE)	LS mean (SE)	Paired comparison
1 Little interest or pleasure in doing things	0.37 (0.05)	1.18 (0.06)	0.92 (0.06)	b > a, c; c > a
2 Feeling down, depressed or hopeless	0.36 (0.05)	1.07 (0.06)	0.76 (0.05)	b > a, c; c > a
Total Score	0.73 (0.08)	2.25 (0.10)	1.68 (0.09)	b > a, c; c > a

[1]Adjusted for differences in unmet mental health needs;
[2]PHQ-2: Patient Health Questionnaire-2; where not depressed = 0, mild depression is 1-2, depressed is ≥ 3. LS mean: Least square mean; SE: Standard error.

Admitting stress at the interview was negatively related to depression (*i.e.*, more stress, less depression). In comparison to the US, coming from the Middle Eastern country and China predicted higher levels of depression. The total model explained 47% of the variance of medical student depression (F = 41.621; df = 9,418; *P* < 0.001). The effect size (*i.e.*, Cohen's f[2] = 0.90) was large.

DISCUSSION

Medical students are known to be at increased risk of depression, stress, and burnout. While previous studies have examined depression and burnout at individual medical schools in the US and abroad[24-25,29-30], to our knowledge this is the first study to compare depression and its correlates across three very different cohorts of international medical students. A recent meta-analysis[8] reported a global prevalence of depression among medical students of 28%. In comparison, our study revealed significantly lower rates of positive depression screens among medical students attending Yale in the US (3.8%) and Xiangya in China (14.1%), and higher rates of positive depression screens among students attending medical school at the site in the Middle East (41.1%). These rates were significantly different from one another, and even when controlling for the differences in unmet mental health needs between the groups, the school in the Middle East had consistently and significantly higher scores.

The high rate of depression in Middle Eastern students is consistent with data from previous studies[23-25]. Possible hypotheses for this high rate vary in the literature. Assadi *et al*[25] surmised that increased depression in Middle Eastern medical students compared to interns and general practitioners may be due to psychosocial factors such as the state of campus conditions, extensive exams, and limited employment opportunities. They also reported an association between psychiatric distress and high levels of indifference and cynicism, factors like those described in the literature on burnout. Farahangiz *et al*[23] reported an association between satisfaction with the field of study and mental health, with higher satisfaction being associated with better mean scores on the General Health Questionnaire-28. In our study, however, students in the Middle East were not the most emotionally exhausted after adjusting for the influence of depression. Our data instead suggest that unmet mental health needs (which is largest in this cohort) is associated with increased depression. Even though this was assessed only with a single question and therefore does not provide a full picture of what is meant by unmet needs, this may be a potential target for intervention in the future.

Other unmeasured environmental variables may also contribute to high rates of depression among medical students at some locations in the Middle East. Nedjat *et al*[31] reported that choosing medicine as a career in many circumstances is based on societal prestige and pressure from family and friends. Education has been described as a major determinant of class mobility[32] and, as entry into medical school is extremely competitive and significantly based on an entrance exam (with < 1% of applicants ultimately accepted), students often face enormous academic pressure during high school. As perfectionism and imposter syndrome have been linked with distress in health professional students[33], it is possible that students who prepare extensively and perform very well on the entrance exam and then face academic challenges in medical school may be at higher risk for emotional distress. However, it also seems plausible that pressure to do well on a high stakes exam [*i.e.*, the Medical

Table 3 Comparison of samples of medical students on emotional exhaustion (ANCOVA)[1]

Survey items	a United States	b Middle Eastern country	c China	Paired comparison[1]
	LS mean (SE)	LS mean (SE)	LS mean (SE)	
I feel emotionally drained by my studies.	2.82 (0.07)	1.92 (0.08)	2.31 (0.07)	a > b, c; c > b
I feel used up at the end of a day in medical school.	3.44 (0.08)	3.05 (0.10)	2.84 (0.08)	a > b, c
I feel burned out from my studies.	2.83 (0.07)	2.81 (0.09)	2.41 (0.08)	a > c, b > c
I have become less interested in my studies since my enrollment in medical school.	2.51 (0.08)	2.40 (0.10)	2.07 (0.09)	a > c, b > c
Emotional exhaustion component	2.90 (0.05)	2.55 (0.07)	2.42 (0.06)	a > b, c

[1]Adjusted for differences in Patient Health Questionnaire-2 total score. LS mean: Least square mean; SE: Standard error.

College Admission Test (MCAT)] and subsequent stress in medical school might predict similar rates of psychological distress in the US, which we did not observe among students enrolled in the US site. This may be due, in part, to the fact that admission to medical school in the US is based on a number of factors in addition to the MCAT, and not on the test alone. It might also highlight the fact that personality and societal variables don't quite account for the significant differences observed. In fact, simply the request for anonymity from the Middle-Eastern school suggests that there is difficulty in acknowledging the reality of depression and burnout among students by the authorities of this school. The behavior of the administration itself could be a key difference in the culture of this institution that may help explain its high rates.

Medical students at Xiangya were also more likely to screen positive for depression than medical students at Yale. While two studies of medical student mental health in China report rates of depression as low as 3-5%[34-35], a number much lower than suggested by our study, another multi-site study of depression among Chinese medical students reported a prevalence rate of 66.8%[21]. This was similar to rates of depression among Chinese physicians in general[36]. One hypothesis for high rates in this region is that stigma is preventing access to care[37]. Alternatively, treatment-seeking may be limited logistically and financially by a lack of continuity of care and access to a range of evidence-based treatments in China, such as Cognitive Behavioral Therapy. This lack of access to and stigma towards mental health treatment may explain why unmet mental health needs are higher in China than the US. This difference, in turn, may predict higher depression in this population. Other hypothesized reasons for higher rates of depression as compared to the US cohort include the effects of academic pressure and stress from grading, professional satisfaction, and family environment on students' mental health[35], as well as lack of social support and negative life events[38]. As these factors may also be seen in the US cohort, there are likely other unmeasured environmental stressors unique to Chinese medical students. One example is that a recent increase in reports of serious doctor-patient conflicts in China may lead to concerns about a future in medicine[36], and therefore could contribute to negative mental health among students.

While we found that emotional exhaustion was lowest in this cohort, stress was significantly higher in China than in other groups. While one might hypothesize high stress would lead to higher rates of depression, and thus this data might explain the high rates in the Chinese cohort, this is not what we found in our regression model. Instead, we found higher stress led to lower depression. This may be because stress is more readily and easily admitted to by students than depression. As such, the students that are stressed are less likely to screen positive for depression. However, this inverse relationship could also be a fault of the binary measurement and/or different interpretations of the term "stress".

It is also worth considering what factors may have contributed to Yale's lower rate of screening positive for depression. Unlike the other two countries, the US has a medical education system so structured that students matriculate after having completed four (or more) years of undergraduate study. Yale is not unique among US medical schools in this regard; yet rates of positive depression screening at Yale are lower than rates reported in other US studies, which are as high as 21%[39-40]. Again,

Table 4 Multiple linear regression on medical student depression measured by patient health questionnaire-2 in response to demographic, behavioral and psychological variables

Predictor variables	R^2	Adjusted R^2	F	Significance	B	Std. Error	β	t
Model	0.473	0.461	41.621	*P* < 0.001				
Age					0.025	0.027	0.043	0.906
Male					-0.089	0.101	-0.032	-0.881
Sleep					0.006	0.105	0.002	0.055
Exercise[a]					-0.120	0.044	-0.103	-2.756
Unmet mental health needs[a]					0.235	0.041	0.228	5.780
Emotional exhaustion[a]					0.496	0.072	0.271	6.903
Stress					-0.264	0.122	-0.086	-2.155
Middle Eastern country[a]					1.477	0.157	0.475	9.439
China[a]					1.005	0.155	0.338	6.492

[a]$P < 0.01$. Associated changes in R^2 for the following independent variable last added into the model, as its unique contribution to the improvement in the model's goodness-of-fit: Exercise: 0.01; Unmet mental health needs: 0.045; Emotional Exhaustion: 0.061; Stress: 0.006; Middle Eastern country: 0.113; China: 0.054

this might be a function of convenience sampling, however this may also be because Yale does not formally grade medical students during the first two years, unlike many other US medical schools. Studies suggest that pass/fail curricula improve student wellness and overall satisfaction with medical education[13,41]. Additionally, Yale does not rank students. At Xiangya and in the Middle East, more traditional numerical grading systems are utilized, and at Xiangya, students are aware of their ranking on exam scores and grades, which may be a source of increased emotional distress in these populations in comparison. Students at Yale also reported the statistically significantly highest number of hours of exercise and least amount of unmet mental health needs between the groups, which may be due to the fact that mental health providers are readily available and free to students. As more exercise correlated with lower depression, and higher unmet needs correlated with higher depression, these factors may contribute to Yale's overall lower rate of depression. Lastly, it is possible that lower rates of positive depression screening at Yale may be explained by the low response rate (39.5%) and students' concerns about survey confidentiality, which may have influenced their likelihood of participating or endorsing depressive symptoms. Yale's low response rate as compared to the other two schools, in fact, might itself suggest an unmeasured "cultural" difference, *i.e.*, conformity and respect for authority, not seen in the US, but very central to the two non-Western schools.

We were also interested in factors that predicted depression rates in medical students. One such factor that is often seen in studies to be correlated with depression[18] is burnout. Our study confirmed this correlation given that in our regression model, emotional exhaustion predicted depression. Yet, emotional exhaustion alone did not account for the differences in depression. We know this because when controlling for PHQ-2 total scores, the US had much higher emotional exhaustion scores than the other cohorts; the US also had much lower overall depression rates. Stress as well as unmet mental health needs contributed to depression in our model, however gender and age did not. Burnout and depression as consequences of inadequate sleep and exercise had been previously reported in a single site in the US[18]. However, here we are reporting findings from a multi-national study, where lack of exercise but not sleep correlated with depression across study sites in three countries. Additionally, given the vastly different rates of depression between cohorts, we hypothesized that region may be predictive of increased depression. The regression model suggested that the effect of internationally distinct medical school sites on overall depression scores was significant. Given that the total model explained 47% of the variance of medical student depression, it is likely that many unmeasured variables, including environmental, cultural, and region-specific ones, were unmeasured in our model and should be points of study in the future.

Our study has several limitations. The study design only involved three medical schools and may not have been broadly representative of medical students in the three countries, or other medical universities in these countries. Due to our research collaborators' request for anonymity, we cannot report the exact country or school of origin for the data in the Middle East. Response rates were much lower in the US (39.5%) compared with other sites (84.7% in the Middle East and 94.7% in China), which attenuates comparability across groups and could explain some portion of the

differences we observe across sites. It is possible that students who are most distressed may be less likely to complete a survey on mental health, which would create significant sampling bias when response rates are low. Although all students were given assurance of anonymity and confidentiality, some students may have felt reluctant to participate in a survey addressing their personal health and behaviors, particularly in cultures that are less comfortable openly discussing mental illness. The survey at the Middle Eastern school was also given to students immediately following a mental health seminar that may have influenced their willingness to participate and/or may have affected their responses to survey questions. Information bias might have also accounted for the differences in depression. Finally, sampling was also done out of convenience and that may have biased the results.

The survey itself also had limitations. For example, the PHQ-2 was used to measure depression screening rates, and not the PHQ-9. Though the PHQ-2 has been validated and is as effective as longer instruments like the Beck Depression Inventory[42,43] for better understanding of depressive symptoms and a higher positive predictive value, those who screen positive should have been given the PHQ-9. "Stress" and "unmet mental health needs" were also both measured with a single question. As evidenced by our results and variance explained by our model, variables that may account for the differences across sites were not identified in the current study. These could include cultural, political, financial, social support, access to evidence-based treatment, and other factors. While these were not included in the surveys or current study, they warrant further investigation. Differences in educational programs may also contribute to the differences in the results. We surveyed the entire school and included all class years in the same group for the US, whereas we surveyed only one class in the others. It is not clear whether results would have been significantly impacted had we surveyed the entire school in all countries and analyzed class groups separately. Additionally, as this study is cross-sectional in nature, it cannot assess cause and effect relationships. Lastly, our results may also be affected by survey translation. Though we made every effort to ensure accurate translation both linguistically and culturally, it is possible that miscommunication occurred.

Future research might include focus groups to explore site-specific factors associated with depression, stress, and burnout that were not included in our survey. This might allow for a more complete picture of depression and associated factors across internationally-distinct medical school sites. Specifically, future studies might explore the relationship between motivations for entering medicine (*e.g.*, personal desire *vs* family/societal pressures) and emotional distress among medical students. Equally important is to investigate the effectiveness of interventions designed to support student mental health, such as Xiangya's peer psychological support program and Yale's peer advocate program. While a previous study in New Zealand was not able to show a statistically significant change in mental health with the addition of peer support[44], Yale's peer advocate program is known to help lead students towards counseling, as mental health concerns were the most common reason a student reached out to the peer advocate[45]. The Middle Eastern site has recently launched a voluntary faculty mentorship program, wherein students are given the option of having a faculty member assigned to them as a longitudinal mentor for academic and personal support. A similar, though mandatory, program exists at the site in China. As comfort with academic help-seeking and supportive faculty relationships have been found to be possible protective factors in student mental health[29], it would be worthwhile studying the impact of mentoring programs on rates of depression.

In conclusion, this study suggests that mental health concerns affect a significant proportion of medical students worldwide. We compared three internationally distinct groups of medical students which, though individually unique, all share common stressors: The competitive pre-selection into medical school, the academic rigor and significant burden of coursework while in medical school, and pressure for high achievement during and after medical school. Rates of depression using ANCOVA were found to be the highest in the Middle East, then China, then the US. Linear regression suggested that emotional exhaustion, stress, unmet mental health needs, region, and exercise predicted nearly half of depression in these cohorts. Though rates of depression vary among the three groups studied, and response rate differences might have influenced the outcomes, our results suggest that continued efforts toward identifying site-specific prevention and intervention strategies in medical student mental health are warranted, and additional socio-cultural variables should be studied.

ARTICLE HIGHLIGHTS

Research background

Medical students have high rates of depression and burnout. These high rates are also seen internationally, including in populations in Asia and the Middle East. While burnout and depression affect the student's academic performance, decrease empathy, and increase unprofessional behaviors, very few students seek mental health treatment when they need it. Some studies have examined explanations for the high rates of burnout and depression. For depression, predictors included mistreatment, poor role models, low optimism, gender, and year of study. The overall learning environment was most often cited as a reason for burnout, with other explanations ranging from specific grading schemes to sleep. To our knowledge, no study has compared depression in medical students from different international populations. Additionally, we are unaware of other studies that have examined whether there are differences in other variables across international sites, including age, gender, sleep, exercise, unmet mental health needs, emotional exhaustion, stress, as well as nationality, which may explain any differences in depression. This study seeks to add to the literature by examining both of these questions and reporting on the data from three different groups of medical students, each from an internationally distinct medical school: Yale University School of Medicine in the United States (US), Central South University Xiangya School of Medicine in China, and a School of Medicine in the Middle East whose research collaborators chose to remain anonymous.

Research motivation

The motivation behind this research is that depression and burnout in medical students affect patient care outcomes, and also contribute to high suicide rates among medical students and physicians. We have yet to fully understand why medical students have such high rates of depression and burnout, nor do we understand the global scope of the problem. We hope that by looking at these questions, we can better develop interventions to address depression in medical students. Currently, no best-practices exist, so a better understanding of the correlates of depression and need for site-specific interventions is warranted.

Research objectives

The primary aim of this research was to compare depression rates in medical students across three internationally distinct populations. By doing so, we hoped to examine and better understand the universality of depression in medical students. The secondary aim of this research was to examine whether there are differences in other variables across these sites, including age, gender, sleep, exercise, unmet mental health needs, emotional exhaustion, stress, as well as nationality, which may explain any differences in depression. By doing so, we hoped to better understand the correlates of depression in medical students, as well as develop a better understanding of cross-cultural differences. The importance of looking at both of these aims is to better describe depression and its correlates in medical students, which can then help determine intervention strategies or identify additional variables to be studied in the future.

Research methods

Convenience samples of medical students from the US, China, and a Middle Eastern country were surveyed in this exploratory study. Incentives were only offered at Yale (a gift card raffle), and participation was confidential, anonymous, and voluntary at all sites. The authors designed the survey utilizing some previously validated questionnaires for more accurate results. The Patient Health Questionnaire-2 measured depression, and a positive screen was defined as a PHQ-2 score of ≥ 3. A modified version of the Maslach Burnout Inventory (MBI) assessed burnout. Prior to analyzing the survey data, principal components analysis was used to analyze the modified MBI and develop a component called "emotional exhaustion", which had high component loadings on the first four survey items about feeling drained, used up, burned out, or uninterested. Other questions on variables like sleep, exercise, and mental health need were assessed with self-reported multiple-choice questions. The original survey was translated into Mandarin, and by a language native to the Middle Eastern country by contributing authors. The translations were then re-translated back to English by colleagues in the US who were fluent in both languages to assure that the surveys administered to all cohorts of students were comparable. Chi-square test and analysis of variance were used to examine differences in demographics, behavioral, and psychological variables across these three schools. Analysis of covariance (ANCOVA) was then used to compare depression among these three countries adjusted for differences in "unmet mental health needs". Unmet mental health need was defined as rating one's agreement with the Likert scale item "There are times I have a mental health need for which I do not seek care", where agree and strongly agree were collapsed into one response. To determine the possible predictive variables for medical student depression, multiple linear regression analysis was performed. The analysis included: demographic variables (age and gender), behavioral variables (sleep, exercise, unmet mental health needs), and psychological variables (stress, emotional exhaustion). The possibility of multicollinearity was ruled out. All analyses were done using SPSS version 25, and statistical significance was evaluated at the $P < 0.05$ level.

Research results

Response rates differed by cohort. At Yale, 205 out of 519 students (39.5%) responded to the survey. At the Middle Eastern school, 172 out of 203 students (84.7%) and at Xiangya, 142 out of 150 (94.7%) responded to the survey. Students in the Middle Eastern country were significantly more likely to screen positive for depression (41.1% of students screened positive) than students in China (14.1% screened positive). Both cohorts were more likely to be depressed than the US cohort (3.8% screened positive). Students in China slept the least number of hours, and students

in the Middle East exercised the least. More students in the Middle Eastern school had unmet mental health needs. When ANCOVA was used to adjust for unmet mental health needs, the students from the Middle Eastern country continued to have significantly higher rates of screening positive for depression, followed by China, and then the US. ANCOVA was also used to adjust rates of emotional exhaustion by PHQ-2 scores, and students from the US reported significantly higher scores than those from each of the other countries. The scores from the students in China and the Middle East were not significantly different from each other. Results from the multiple linear regression analysis on medical student depression found that demographic variables did not significantly predict medical student depression. Among behavioral variables, exercise and unmet mental health needs significantly predicted medical student depression, but amount of sleep did not. Both psychological variables, stress, as well as the emotional exhaustion component of burnout, were predictors of medical student depression. Stress was measured by answering "yes" to the question "are you stressed?". Admitting stress was negatively related to depression (*i.e.*, more stress, less depression). In comparison to the US, coming from the Middle Eastern country and China predicted higher levels of depression. The total model explained 47% of the variance of medical student depression (F = 41.621; df = 9,418; $P < 0.001$). The effect size (*i.e.*, Cohen's $f^2 = 0.90$) was large. Our results contribute to the field, as we found statistically significant differences in depre-ssion across our three international cohorts, and differences in other correlates, like emotional exhaustion, sleep, and unmet mental health needs, which had not previously been described. We also found that our model only predicted 47% of depression, with region as the greatest predictor. While this identified some of the potential correlates for depression, including unmet needs that could be better targeted in each program, our results also show that there are inherent differences by region that need to be further assessed. For example, future studies might explore the relationship between motivations for entering medicine (*e.g.*, personal desire *vs* family/societal pressures) and emotional distress among medical students. Equally important is to investigate the effectiveness of interventions designed to support student mental health to better understand ways to improve these high rates internationally.

Research conclusions

This study found that depression, as measured by the PHQ-2, was highest among students in the Middle East, followed by China, and then the US. Emotional exhaustion was highest, however, in the US. Linear regression suggested emotional exhaustion, stress, unmet mental health need, region, and exercise predicted nearly half of depression in these cohorts. Even though the study design only involved three medical schools and may not have been broadly representative of medical students in the three countries, or other medical universities in these countries, we know that depression is a key problem in medical students internationally, it varies between groups and region, and other site-specific factors are important reasons for these high rates. We also know that unmet mental health needs must be addressed. Although rates of depression vary among the three groups studied, and response rate differences might have influenced the outcomes, our results suggest that continued efforts toward identifying site-specific prevention and intervention strategies in medical student mental health are warranted, and that additional socio-cultural variables should be studied.

Research perspectives

In carrying out this research, the authors learned that while specific curricula are unique at each individual medical school, medical students in three countries share common experiences and stressors: Competitive entry to medical school, and the pressure and academic rigor of studying to be a physician. For some students, these experiences can lead to depression and burnout. The reasons behind this are complex, and further research is warranted to fully elucidate them. In this study, the authors also learned a great deal about international collaboration. This was a rich experience, yet came with some unplanned challenges. For example, one important lesson learned is that when translating surveys, they should always be translated back into the original language before administration to assure the questions read as originally intended. Additionally, with the request by one collaborating institution for anonymity in publication, we learned that sometimes there is difficulty in acknowledging the reality of depression and burnout among students by the authorities of schools. This can limit research studies in their dissemination. Future research should further explore site-specific factors associated with depression. One way to do this would be to include focus groups that help inform survey design. This might allow for a more complete picture of depression and associated factors across internationally distinct medical school sites.

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