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Quality of life in Brazilian medical students: A systematic review and meta-analysis

Carolina Kakiuthi Martins, Jonas Carneiro Cruz, Renata Dellalibera-Joviliano

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Quality of life in Brazilian medical students: A systematic review and meta-analysis

Running title: Quality of life in Brazilian medical students

Carolina Kakiuthi Martins\textsuperscript{a}, Jonas Carneiro Cruz\textsuperscript{b,*}, Renata Dellalibera-Joviliano\textsuperscript{a,c}

\textsuperscript{a}Medical School of University of Ribeirão Preto, Ribeirão Preto, 14040-901, Brazil.
\textsuperscript{b}University of Sao Paulo, Ribeirão Preto, 14040-901, Brazil.
\textsuperscript{c}Department of Biomedical and Health Sciences. State University of Minas Gerais, Campus Passos, Brazil

*Corresponding author: Cruz, J. C, email: jonas-cruz@hotmail.com; phone number: +5535988556308

ABSTRACT

Introduction: Medical training negatively impacts the quality of life of students. Assessing the well-being of medical students might guide academic policies and future research for improving mental and physical health status of the population at risk. Objectives: This study aimed to identify the influence of medical training on the quality of life of Brazilian medical students. Method: A systematic review and meta-analysis was conducted according to the Cochrane criteria and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol. The search was performed by two independent investigators using a predefined protocol registered in PROSPERO (CRD42021237926). Data were extracted from PubMed, EMBASE, and Biblioteca Virtual de Saúde. For quantitative synthesis, a meta-analysis was...
conducted to assess the mean difference in the quality of life between medical students of different academic cycles stratified by sex. All data were analyzed using the random-effects model, with a confidence interval of 95%. **Results:** After evaluating the eligibility criteria, five studies were included in the meta-analysis. The data revealed that students in the pre-clinical cycle of the course exhibited higher quality of life scores in the physical (3.05 [1.48, 4.62], p < 0.0001) and psychological (3.05 [0.80, 5.30], p < 0.0001) domains than students in the clerkship cycle. No statistically significant difference was observed in the environmental (0.78 [-2.92, 4.49], p = 0.68) and social domains (1.41 [-0.52, 3.34], p = 0.15). **Conclusion:** Our analysis revealed that the medical course is associated with a decreased quality of life in the physical and psychological domains of medical students. This finding was observed in both men and women. However, these findings should be interpreted with caution given the limitations of this study.

**Keywords:** Medical students, Quality of life, Meta-analysis,

**INTRODUCTION**

The World Health Organization (WHO) has defined quality of life (QoL) as "the individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns." It is a broad term that is used to describe an individual's health, making this assessment more comprehensive.

Many observational studies have been conducted worldwide to assess the QoL of medical students using various indices. These studies showed that future physicians were more likely to have poorer scores on QoL, anxiety, and depression indices.

Medical students have stressful and overloaded academic lives. The constant proximity to diseases, exhausting medical curriculum, and highly competitive environment appear to negatively impact the well-being of students.
A recent study conducted by Pagnin et al.,\textsuperscript{7} showed that Brazilian medical students exhibited lower QoL scores in psychological and social domains than the general young population. Similar results were found for medical students in New Zealand,\textsuperscript{8} Italy,\textsuperscript{9} and South Korea.\textsuperscript{10} In addition, some of these studies showed that gender has a considerable effect on the QoL of students, but its exact influence is not clear.\textsuperscript{7,9}

In this context, assessing the well-being of students might guide academic policies in improving the mental and physical health status of the population at risk.\textsuperscript{11} Therefore, this systematic review and meta-analysis aimed to investigate the available evidence on the influence of academic training on the well-being of Brazilian medical students. We stratified our analysis by sex to obtain more accurate and reliable results. This strategy was also important for controlling the analysis of this potential confounder and reducing the sources of heterogeneity.

**MATERIALS AND METHODS**

This study has been reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines\textsuperscript{12} and designed according to the Cochrane\textsuperscript{13} criteria for systematic review and meta-analysis. The PRISMA-P checklist for reporting this systematic review\textsuperscript{14} is presented in Supplementary File 1.

**Eligibility criteria**

The search strategy for this systematic review was to find answers to the following guiding questions structured according to the generic Patient, Exposure, Control, Outcome (PECO) framework.
1. Population: Brazilian medical students in the last academic cycle (fifth and sixth years)

2. Exposure: Medical training

3. Comparison: Brazilian medical students in the first academic cycle (first and second years)

4. Outcomes: QoL evaluated using the abbreviated World Health Organization Quality of Life (WHOQOL-bref) questionnaire assessing four domains: physical, social, psychological, and environmental.

The inclusion criteria were as follows: 1) studies comparing only medical students, 2) studies comparing students only in the first and last academic cycles, 3) studies using the WHOQOL-bref questionnaire, and 4) studies that included indices stratified by sex for assessing the QoL. No restrictions concerning the study year, design, or location were applied.

The exclusion criteria included: 1) studies involving students of disciples other than medicine, 2) studies comparing medical interns, 3) studies that did not involve any comparator, 4) studies that did not use the WHOQOL questionnaire as the instrument to assess the QoL, 5) studies that were not peer-reviewed, 6) studies conducted outside Brazil, 7) studies with incomplete or missing data (mean and standard deviation), 8) reviews, letters to the editors, conference summaries, or expert opinions, and 9) studies that assessed QoL using indices not stratified by sex.
Information sources and search strategy

The PubMed and Embase databases were searched for articles in English. Additionally, Biblioteca Virtual de Saúde (BVS) was searched for articles in Portuguese. The BVS is a space for the integration of health information sources (mostly in Portuguese and Spanish) comprising Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS), Index Psicologia – Periódicos, and BDENF - Enfermagem. Word combinations and truncations were specifically designed and tailored for each electronic database. The reference list of a previous meta-analysis conducted by Solis and Lotufo-Neto was also explored. The complete search strategy used in the databases is presented in Supplementary File 2. The investigation was conducted on March 1, 2021. No effort was made to contact a subject-matter expert to verify the indication of any pertinent articles that could be included.

Selection process

All articles extracted from the databases were imported into an Endnote library as bibliographic citation files. Endnote was used to manage citations and identify the duplicates. All titles, abstracts, and full texts extracted from the databases were screened by two independent reviewers (JCC and CKM). The full texts of potentially relevant studies were assessed. The reasons for excluding studies from the meta-analysis were divided into four categories: (i) lack of data (standard deviation or of the total number of participants in each sex group), (ii) studies that did not compare the influence of academic cycles on the QoL, (iii) studies that did not use the WHOQOL-bref as the instrument measure (including the 36-Item Short Form Survey [SF-36] and Vida de Estudante e Residente na
Área de Saúde (VERAS-Q) as questionnaires), and (iv) studies that did not compare the last and first academic cycles. Only articles that met all the eligibility criteria were included in the meta-analysis. All excluded studies (with reasons) have been appraised in Supplementary File 3. Any disagreement regarding study inclusion was resolved by consensus between the investigators.

Data collection process and data items

The extracted data were entered into an Excel spreadsheet (Excel, Microsoft, Washington, USA) by one reviewer (JCC). All data were verified by the second reviewer (CKM). Any conflicts in data were verified again and resolved by consensus between the investigators. The following information was extracted from the included studies: authorship, data collection date, location of study, name of university, type of university (public or private), population (number of students enrolled), proportion of the analyzed population, instrument used to assess the QoL, investigated parameters, and predictor factors. No efforts were made to contact the authors regarding incomplete or missing data.

The mean and standard deviation of the WHOQOL scores were obtained for all four domains (physical, social, psychological, and environmental). When results in the studies were provided in the form of crude scores (without transformation into percentage), they were converted into a normalized scale according to the guidelines of the WHO.

The WHOQOL-bref is the most widely used questionnaire for research purposes. This tool is a valid and reliable short version of the WHOQOL-100 version. The WHOQOL-bref comprises 26 questions, which are divided into four domains (physical, psychological, social, and environmental). This instrument
was developed to measure individuals’ perceptions of all facets of their QoL.\textsuperscript{15}

The Brazilian-Portuguese translated version was developed in 2000.\textsuperscript{16}

According to Brazilian medical training guidelines, the academic curriculum is divided into three cycles: pre-clinical, clinical, and clerkship. When the included studies presented the QoL scores by academic year, the first two years were considered in the pre-clinical cycle, the third and fourth years were categorized in the clinical cycle, and the last two years in the clerkship cycle.

The clerkships are regulated by the Ministry of Education (Brazil) through the National Curricular Guidelines for Medical Courses. This cycle has a minimum duration of 2700 hours and is performed under professional supervision. The mandatory curriculum includes activities at the first, second, and third levels of attention in the following areas: Internal Medicine, Surgery, Obstetrics-Gynecology, Pediatrics, and Public Health.\textsuperscript{17}

Assessment of quality and risk of bias for the studies included in the meta-analysis

The quality of the studies was appraised using the Joanna Briggs Institute’s Critical Appraisal Tools in eight domains. The study domains were classified (yes or no) by two independent reviewers (JCC and CKM) to determine the extent to which a study addressed the possibility of bias in its design. Any disagreements were resolved by consensus. No contact was made with the authors of the included studies regarding any unclear information. Publication bias was not assessed because of the small number of included studies.
Effect measures and quantitative synthesis

The primary outcome was the mean difference in the QoL between Brazilian medical students in the last academic cycle (clerkship) and those in the first cycle (pre-clinical) of medical training. Forest plots were created using the Review Manager 5.2.7 software (Cochrane Collaboration, Oxford, United Kingdom). The means and standard deviations of the WHOQOL scores were obtained for four domains (physical, social, psychological, and environmental). Data were stratified according to sex. This strategy was used to reduce potential heterogeneity across studies, as the baseline QoL scores of women might have been considerably lower. Weighted mean difference was calculated using generic inverse variance in the random-effects model. Heterogeneity in the subgroups was estimated using the inconsistency index ($I^2$) statistic test. Sensitivity analysis was not conducted.

Certainty assessment

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)18 system was used to evaluate the quality of evidence. The quality of evidence was classified into four levels (high, moderate, low, and very low) according to the following parameters: risk of bias, inconsistency, indirectness, imprecision, publication bias, magnitude of effect, dose-response gradient, and residual confounding. This assessment was performed by two independent investigators (JCC and CKM). Any disagreements were resolved by consensus.
RESULTS

Study selection

We identified 592 articles through our search strategy, of which 97 were duplicates. After evaluating the titles and abstracts, the full texts of 32 studies were assessed. Finally, for quantitative synthesis, five studies (including 1819 students) were included in the meta-analysis. Figure 1 illustrates the PRISMA flowchart for the summarized results. Supplementary File 3 shows the detailed characteristics of the studies not included in the meta-analysis, including the reasons for exclusion. The main characteristics of each study are summarized in Table 1.
Figure 1 - PRISMA flow chart

Figure 1 – Prisma flow chart for the summarized results
Table 1 – Characteristics of the studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Autorship</th>
<th>Data collection date</th>
<th>Location</th>
<th>University (abbreviation) (type of institution)</th>
<th>Population (N) -</th>
<th>Percentage of enrolled population</th>
<th>Comparisons</th>
<th>Negative predictor factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alves19</td>
<td>Aug-2006 - Apr 2007</td>
<td>Recife-PE</td>
<td>Multicentric: Universidade Federal de Pernambuco (UFPE) (public), Universidade Estadual de Pernambuco (UPE) (public) and Escola Pernambucana de Medicina (EPM) (private).</td>
<td>First and last semester (370)</td>
<td>83.2% (First year) 90.9% (Last year)</td>
<td>First and last semester</td>
<td>Last semester</td>
</tr>
<tr>
<td>Pagnin7</td>
<td>Not informed</td>
<td>Niterói-RJ</td>
<td>Universidade Federal Fluminense (UFF) (public)</td>
<td>2nd, 4th and 6th year (206)</td>
<td>86.4%</td>
<td>Academic year Gender Young general population</td>
<td>Females Being a medical student</td>
</tr>
<tr>
<td>Serinolli22</td>
<td>Oct 2014 – Nov 2014.</td>
<td>São Paulo-SP</td>
<td>Universidade Nove de Julho (Uninove) (private)</td>
<td>All-students (405)</td>
<td>65.3%</td>
<td>Academic year Body mass index Gender Daily traveling time Housing conditions Parents’ education background Religiosity Smoking</td>
<td>Absence of religious beliefs High BMI Females Long traveling time Lack of a physician in the Family</td>
</tr>
<tr>
<td>Study</td>
<td>Time Period</td>
<td>Location</td>
<td>Institution</td>
<td>Sample Size</td>
<td>Proportion</td>
<td>Gender</td>
<td>Academic Cycle</td>
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<tr>
<td>Cazolari</td>
<td>Aug 2017 – Oct 2017</td>
<td>São Paulo-SP</td>
<td>Universidade Federal de São Paulo (UNIFESP) (public)</td>
<td>All-students (302)</td>
<td>42%</td>
<td></td>
<td>Academic Cycle</td>
</tr>
<tr>
<td>Paro</td>
<td>Aug 2011 – Aug 2012</td>
<td>Multicentric (14 states; BA, SP, PB, PR, RO, RS, PI, CE, RS, GO, MS, RJ, TO, MG)</td>
<td>Multicenter (10 public; 12 privates)</td>
<td>All-students (1350)</td>
<td>81.8%</td>
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<td>Academic cycle Empathy Gender</td>
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</table>

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Study characteristics

We included five studies,\textsuperscript{7, 19-22} which were performed in 1819 students. Data collection in the included studies was performed from February 2006\textsuperscript{19} to October 2017.\textsuperscript{20} The study locations included all five macroregions of Brazil (South, North, Northeast, Southeast, and Midwest). A single multicenter study\textsuperscript{21} evaluated medical students in 14 of 27 states, including BA, SP, PB, PR, RO, RS, PI, CE, RS, GO, MS, RJ, TO, and MG. Other unicenter studies were performed in three states (PE,\textsuperscript{19} SP,\textsuperscript{20, 22} and RJ\textsuperscript{7}). Thirteen states were not included in any study (ES, MT, AC, SE, PB, RN, MA, PA, AP, RR, AM, SC, and AL). In contrast, SP (the most populated state) was the most common region included in research.

Other investigated parameters included sex, lack of a physician in the family, low education environment, absence of religious beliefs, lack of physical activity, burnout, sleep difficulty, stress, body mass index, presence of comorbidities, low resilience, low levels of physical activity, depression, and anxiety. Among the evaluated institutions, 13 were public and 15 were private. The percentage of students enrolled in the study ranged from 42\%\textsuperscript{20} to 90.9\%\textsuperscript{19} (Table 1).

Synthesis of results

The meta-analysis revealed that medical students in the last academic cycle presented lower QoL scores in the social and psychological domains than those in the first academic cycle. The mean difference in the social domain scores was 2.19 [0.11, 4.27] (p=0.04) for men, 4.18 [1.79, 6.57] (p= 0.006) for women, and 3.05 [1.48, 4.62] (p<0.0001) for the global effect (Figure 2A). The
heterogeneity for this outcome was considerably low for both subgroups and the global effect \( (\tau^2 = 0.00; \chi^2 = 4.41, df = 9, p = 0.88; I^2 = 0\%) \).

![Figure 2](http://doi.org/10.47626/2237-6089-2022-0497)

**Figure 2** – Forest plots (stratified by gender) for the difference in the quality of life scores in Brazilian medical students in the (a) social, (b) psychological, (c) environmental and (d) physical domain.

The mean difference in the psychological domain scores was 4.52 [1.36, 7.69] \( (p = 0.005) \) for women and 3.05 [0.80, 5.30] \( (p = 0.008) \) for the global effect.

No statistically significant difference was observed when only men were included: 1.42 [1.80, 4.64] \( (p = 0.39) \). Moderate heterogeneity was identified for men \( (\tau^2 = 5.56; \chi^2 = 7.25, df = 4, p = 0.12; I^2 = 45\%) \), women \( (\tau^2 = 6.42; \chi^2 = 8.40, df = 4, p = 0.08; I^2 = 52\%) \), and the global effect \( \tau^2 = 5.92; \chi^2 = 18.29, df = 9, p = 0.03; I^2 = 51\% \) (Figure 2B).
The mean difference in the environmental domain scores was 3.24 [1.20, 5.27] (p=0.002) for women. However, no statistically significant difference was observed in the scores for men (-0.74 [-2.83, 1.36]; p=0.49) or the global effect (1.41 [-0.52, 3.34]; p=0.15). Heterogeneity was considerably low for subgroup analyses (I² = 0) but remained at a moderate level for the global estimative (τ² = 2.49; Chi² = 11.60, df = 8, p = 0.17; I² = 31%) (Figure 2C).
Finally, no difference was observed in the physical domain scores for men (-0.92 [-3.55, 1.70], p=0.22), women (1.93 [-4.83, 8.69], p=0.58), or the global estimate (0.78 [-2.92, 4.49] p=0.68). Although the heterogeneity was moderate in men (τ² = 2.65; χ² = 5.75, df = 4, p = 0.22; I² = 30%), it was high for women (τ² = 51.20; χ² = 43.76, df = 4, p < 0.00001; I² = 91%) and the global estimate (τ² = 26.96; χ² = 57.27, df = 9, p < 0.00001; I² = 84%) (Figure 2D).

### Risk of bias

Overall, all articles included in the meta-analysis presented a moderate risk of bias. All studies had a low risk of bias in terms of exposure to medical training and the application of statistical analysis. The studies conducted by Paro et al.,²¹ Alves et al.,¹⁹ and Pagnin et al.,⁷ included a large sample of enrolled students and had a low risk of bias in terms of participant selection. In contrast, the studies by Serinolli and Novaretti²² and Cazolari et al.,²⁰ had a moderate risk of bias. In addition, all studies were highly biased in terms of assessing the outcome because questionnaires are subjective forms of evaluation (Table 2).
Table 2 – Risk of bias of the included studies

<table>
<thead>
<tr>
<th>Reference</th>
<th>Were the criteria for inclusion in the sample clearly defined?</th>
<th>Were the study subjects and the setting described in detail?</th>
<th>Was the exposure measured in a valid and reliable way?</th>
<th>Were objective, standard criteria used for measurement of the condition?</th>
<th>Were confounding factors identified?</th>
<th>Were strategies to deal with confounding factors stated?</th>
<th>Were the outcomes measured in a valid and reliable way?</th>
<th>Was appropriate statistical analysis used?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alves19</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Pagnin7</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Serinolli22</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Cazolari20</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>Paro21</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Confidence in cumulative evidence

According to the GRADE tool, the overall quality of evidence was very low. Methodological limitations (lack of randomization), inconsistency (lack of controlling confounding factors such as economic class and ethnicity), and inaccuracy (subjectiveness of questionnaires) were the main factors responsible for decreasing the level of evidence. In addition, the magnitude of this effect was not substantial.

DISCUSSION

This systematic review and meta-analysis investigated the available evidence on the reduction in the QoL of Brazilian medical students during their graduation period. Based on the available literature and eligibility criteria, our data revealed that medical training was a negative predictor of the well-being of students. The meta-analysis revealed that medical students in the clerkship (fifth and sixth years) had an average of 3.05% lower QoL scores in both psychological and social domains than students in the pre-clinical cycle.

In part, these results might be explained by the stressful and competitive environment faced by medical students. In this context, the overwhelming burden of educational information, extensive workload, and the demand for high academic performance can lead to the development of mental disorders such as burnout, anxiety, and depression. In addition, other causes of student distress include personal events, ethical conflicts, exposure to death and human suffering, student abuse (verbal, physical, or sexual), and educational debt. Although these sources of stress may vary widely across training years, they tend to become more intense by the end of medical training.
Although the heterogeneity ($I^2$) scores in the environmental and social domains were reduced to 0% after controlling for sex, those in the physical and psychological domains remained moderate. However, the variations in analyses could be explained by the designs of the studies and the academic curriculum. In this regard, some studies categorized their data among years of medical training (first to sixth), while others stratified their results according to academic cycle (pre-clinical, clinical, and clerkship). In addition, curricular differences between courses, especially problem-based learning (PBL) and lecture-based learning (LBL), are a potential source of heterogeneity. Some Brazilian medical schools employ a PBL methodology based on the application of acquired knowledge and integration of new information. At the same time, other universities use the traditional LBL approach, in which the students adopt the role of a passive learner.

Although not investigated in this review, the difference in the QoL between genders could be explained by sex differences in socioeconomic status. In this context, gender disparities appear to have a significant effect on the well-being of women. Women are more likely to suffer from mental disorders (such as depression, anxiety, or stress), while men experience social issues such as substance abuse. Additionally, men are physically more active, less prone to suffer from chronic pain, and have higher self-esteem than women. In this scenario, mental status could be a confounder, as recent studies have shown that female medical students exhibited higher risks of developing mental disorders, such as depression and anxiety, than male students.
Comparison with other studies

Although the influence of medical training on the QoL of Brazilian medical students has already been investigated by Solis and Lotufo-Neto in a previous meta-analysis, they presented their results in terms of effect sizes (Hedges g). This approach can lead to spurious results and the magnitude of effects is difficult to interpret, as the results are presented as standard deviations. By contrast, our analysis was performed using weighted mean difference. This strategy yields an objective estimative (expressed in percentage), which is easier for clinicians and researchers to understand.

However, the results of our analysis corroborate with those of a previous meta-analysis conducted by Solis and Lotufo-Neto, which revealed that medical training is associated with decreased QoL scores in Brazilian students. However, our data provided more accurate results as we performed the meta-analysis after stratification by sex. This variable may act as a confounder, explaining some part of the heterogeneity between the overall estimates.

We also found similarities of our results with those of two cross-sectional studies conducted in China and Saudi Arabia. Both studies showed lower QoL scores in the psychological and social domains in clerkship students than in those in the pre-clinical cycle.

Limitations

There are significant limitations to our data. First, the QoL assessment through questionnaires is based on a subjective interpretation, which each respondent perceives and expresses differently. In addition, controlling for potential confounding factors in observational studies is difficult, and our analysis
did not allow the insertion of adjusted scores. Further, socio-demographics of medical studies could be different, which could affect the results and cause problems in interpreting the results. Although a better strategy would be to include longitudinal studies, only Moutinho et al.,\textsuperscript{40} utilized this study design. However, follow-up was performed only for two years.

We also found that the number of clerkship students enrolled was lower than that of students in the first academic cycle. However, this finding could be explained by the academic routine, which makes it challenging to obtain responses to questionnaires from these students.

In addition, not all medical students were included in the meta-analysis because of differences in the instruments used to assess QoL. We identified studies in which the VERAS-Q and the SF-36 questionnaires were used for data extraction. The SF-36 is being increasingly used in the scientific literature, but its validity as a measure of overall QoL is questionable.\textsuperscript{41} The VERAS-Q is a specific questionnaire developed in Brazil to appraise the QoL of medical students. The instrument contains 90 items in a Likert-scale response format. This tool was validated in 2009 in 800 medical students from 75 Brazilian medical schools. However, this instrument has not been widely applied or approved worldwide.\textsuperscript{42}

Although these questionnaires are valid instruments for assessing the QoL, they are not interchangeable. Therefore, mixing the constructs could significantly increase the sources of heterogeneity.\textsuperscript{43}

In many studies assessed in the full-text form during the extraction process, controlling for sex differences was not performed or the recorded data were insufficient. Therefore, the differences in the QoL across the course cycles could be directly affected by the imbalance between number of male and female
participants in the studies. Therefore, these articles were not included in the final synthesis.

Future directions

Although several studies have been conducted to estimate the impact of medical training on the QoL of Brazilian medical students, most studies concerning these outcomes were not well replicated, did not control for potential confounders, or used low-quality/nuclear-quality instruments of measurements. Therefore, we recommend that studies should apply the WHOQOL-bref questionnaire in future investigations.

We strongly recommend that controlling for the variable of sex should be performed in studies while determining the QoL index. This is possible by stratifying the data according to sex (reporting standard deviation for each subgroup) or performing analysis of covariance including gender as a covariable.

New research should address the influence of mental disorders, economic status, ethnicity, and social class on student well-being. These variables could act as confounders, explaining the differences in the QoL scores evident in other studies. Further studies should focus on whether the PBL or LBL academic curriculum influences the student well-being. Furthermore, since affirmative action policies have widely changed in Brazil in the last decade, new studies should be conducted to investigate the impact of medical training on the QoL of this specific class of students.
**Contribution of this study**

We believe that these findings will be a valuable tool to guide future research and design specific academic policies for improving the well-being of particular students. Therefore, we recommend that the psychological health of medical students should be monitored, and support should be provided within the educational institution. In addition, we maintain that the workload can be revised.

**OTHER INFORMATION**

The registration was carried out in the PROSPERO database under the two following submissions: CRD42021234363 "Is medical school associated with decreased quality of life in Brazilian students? A systematic review and meta-analysis over a decade". (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=234363).

**ACKNOWLEDGMENTS**

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**DISCLOSURE**

The authors declare no conflict of interest.
REFERENCES

PRISMA 2020 expanded checklist

Note: This expanded checklist details elements recommended for reporting for each PRISMA 2020 item. Non-italicized elements are considered ‘essential’ and should be reported in the main report or as supplementary material for all systematic reviews (except for those preceded by “If…”, which should only be reported where applicable). Elements written in italics are ‘additional’, and while not essential, provide supplementary information that may enhance the completeness and usability of systematic review reports. Note that elements presented here are an abridged version of those presented in the explanation and elaboration paper, with references and some examples removed. Consulting the explanation and elaboration paper is recommended if further clarity or information is required (doi:10.1136/bmj.n160).

<table>
<thead>
<tr>
<th>Section and Topic</th>
<th>Item #</th>
<th>Elements recommended for reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>TITLE</td>
<td>1</td>
<td>- Identify the report as a systematic review in the title.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Report an informative title that provides key information about the main objective or question the review addresses (e.g. the population(s) and intervention(s) the review addresses).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Consider providing additional information in the title, such as the method of analysis used, the designs of included studies, or an indication that the review is an update of an existing review, or a continually updated (“living”) systematic review.</td>
</tr>
<tr>
<td>ABSTRACT</td>
<td>2</td>
<td>- Report an abstract addressing each item in the PRISMA 2020 for Abstracts checklist.</td>
</tr>
<tr>
<td>INTRODUCTION</td>
<td>3</td>
<td>- Describe the current state of knowledge and its uncertainties.</td>
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<td></td>
<td>- Articulate why it is important to do the review.</td>
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<tr>
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<td></td>
<td>- If other systematic reviews addressing the same (or a largely similar) question are available, explain why the current review was considered necessary. If the review is an update or replication of a particular systematic review, indicate this and cite the previous review.</td>
</tr>
<tr>
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<td></td>
<td>- If the review examines the effects of interventions, also briefly describe how the intervention(s) examined might work.</td>
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<tr>
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<td></td>
<td>- If there is complexity in the intervention or context of its delivery (or both) (e.g. multi-component interventions, equity considerations), consider presenting a logic model to visually display the hypothesised relationship between intervention components and outcomes.</td>
</tr>
<tr>
<td>OBJECTIVES</td>
<td>4</td>
<td>- Provide an explicit statement of all objective(s) or question(s) the review addresses, expressed in terms of a relevant question formulation framework.</td>
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<tr>
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<td></td>
<td>- If the purpose is to evaluate the effects of interventions, use the Population, Intervention, Comparator, Outcome (PICO) framework or one of its variants, to state the comparisons that will be made.</td>
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</table>

METHODS

Introduction: “Therefore, this systematic review and meta-analysis aimed to investigate the available evidence on the the influence of academic training in the Brazilian medical student’s well-being.

• “Not applicable
ELIGIBILITY CRITERIA

- Specify all study characteristics used to decide whether a study was eligible for inclusion in the review, that is, components described in the PICO framework or one of its variants, and other characteristics, such as eligible study design(s) and setting(s), and minimum duration of follow-up.
- Specify eligibility criteria with regard to report characteristics, such as year of dissemination, language, and report status (e.g. whether reports, such as unpublished manuscripts and conference abstracts, were eligible for inclusion).
- Clearly indicate if studies were ineligible because the outcomes of interest were not measured, or ineligible because the results for the outcome of interest were not reported.
- Specify any groups used in the synthesis (e.g. intervention, outcome and population groups) and link these to the comparisons specified in the objectives (item #4).
- Consider providing rationales for any notable restrictions to study eligibility.

INFORMATION SOURCES

- Specify the date when each source (e.g. database, register, website, organisation) was last searched or consulted.
- If bibliographic databases were searched, specify for each database its name (e.g. MEDLINE, CINAHL), the interface or platform through which the database was searched (e.g. Ovid, EBSCOhost), and the dates of coverage (where this information is provided).
- If study registers, regulatory databases and other online repositories were searched, specify the name of each source and any date restrictions that were applied.

Section and Topic Item # Elements recommended for reporting

- If websites, search engines or other online sources were browsed or searched, specify the name and URL of each source.
- If organisations or manufacturers were contacted to identify studies, specify the name of each source.
- If individuals were contacted to identify studies, specify the types of individuals contacted (e.g. authors of studies included in the review or researchers with expertise in the area).
- If reference lists were examined, specify the types of references examined (e.g. references cited in study reports included in the systematic review, or references cited in systematic review reports on the same or similar topic).
- If cited or citing reference searches (also called backward and forward citation searching) were conducted, specify the bibliographic details of the reports to which citation searching was applied, the citation index or platform used (e.g. Web of Science), and the date the citation searching was done.
- If journals or conference proceedings were consulted, specify of the names of each source, the dates covered and how they were searched (e.g. handsearching or browsing online).
SEARCH STRATEGY

7. Provide the full line by line search strategy as run in each database with a sophisticated interface (such as Ovid), or the sequence of terms that were used to search simpler interfaces, such as search engines or websites.

7. Describe any limits applied to the search strategy (e.g. date or language) and justify these by linking back to the review’s eligibility criteria.

7. If published approaches, including search filters designed to retrieve specific types of records or search strategies from other systematic reviews, were used, cite them. If published approaches were adapted, for example if search filters are amended, note the changes made.

7. If natural language processing or text frequency analysis tools were used to identify or refine keywords, synonyms or subject indexing terms to use in the search strategy, specify the tool(s) used.

7. If a tool was used to automatically translate search strings for one database to another, specify the tool used.

7. If the search strategy was validated, for example by evaluating whether it could identify a set of clearly eligible studies, report the validation process used and specify which studies were included in the validation set.

7. If the search strategy was peer reviewed, report the peer review process used and specify any tool used such as the Peer Review of Electronic Search Strategies (PRESS) checklist.

7. If the search strategy structure adopted was not based on a PICO-style approach, describe the final conceptual structure and any explorations that were undertaken to achieve it.

• The complete search strategy carried out in the databases are presented in supplementary file 2

• Inclusion: Studies conducted in Portuguese and English.

• Not applicable

• Not applicable

• Not applicable

• Not applicable

• Not applicable

• Not applicable

• Not applicable

SELECTION PROCESS

8. Recommendations for reporting regardless of the selection processes used:

8. Report how many reviewers screened each record (title/abstract) and each report retrieved, whether multiple reviewers worked independently at each stage of screening or not, and any processes used to resolve disagreements between screeners.

8. Report any processes used to obtain or confirm relevant information from study investigators.

8. If abstracts or articles required translation into another language to determine their eligibility, report how these were translated.

8. All articles extracted from the databases were imported to an Endnote library as bibliographic citation files. The software was also used to manage citations and identify duplicates. All titles, abstracts, and full texts extracted from the databases were screened by two independent reviewers (JCC and CKM). The potentially relevant studies were assessed in the full-text form. Only the articles that met all eligibility criteria were included in the meta-analysis.

8. Recommendations for reporting in systematic reviews using automation tools in the selection process:

8. Report how automation tools were integrated within the overall study selection process.

8. If an externally derived machine learning classifier was applied (e.g. Cochrane RCT Classifier), either to eliminate records or to replace a single screener, include a reference or URL to the version used. If the classifier was used to eliminate records before screening, report the number eliminated in the PRISMA flow diagram as ‘Records marked as ineligible by automation tools’.

8. If an internally derived machine learning classifier was used to assist with the screening process, identify the software/classifier and version, describe how it was used (e.g. to remove records or replace a single screener) and trained (if relevant), and what internal or external validation was done to understand the risk of missed studies or incorrect classifications.

8. If machine learning algorithms were used to prioritise screening (whereby unscreened records are continually re-ordered based on screening decisions), state the software used and provide details of any screening rules applied.

8. Not applicable

8. Not applicable

8. Not applicable
Recommendations for reporting in systematic reviews using crowdsourcing or previous ‘known’ assessments in the selection process:

<table>
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<tr>
<th>Section and Topic</th>
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<tbody>
<tr>
<td><strong>DATA COLLECTION</strong></td>
<td>9</td>
<td>• If crowdsourcing was used to screen records, provide details of the platform used and specify how it was integrated within the overall study selection process.</td>
</tr>
<tr>
<td>PROCESS</td>
<td></td>
<td>• If datasets of already-screened records were used to eliminate records retrieved by the search from further consideration, briefly describe the derivation of these datasets.</td>
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<td>• If decision rules were used to select data from multiple reports corresponding to a study, and any steps were taken to resolve inconsistencies across reports, report the rules and steps used.</td>
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<td>• The extracted data were gathered in an orderly fashion in an Excel spreadsheet (Excel, Microsoft, Washington, USA) by one reviewer (JCC). All information was verified by a second reviewer (CKM). Any conflicting information was verified again and solved by consensus between the investigators.</td>
</tr>
<tr>
<td><strong>DATA ITEMS (outcomes)</strong></td>
<td>10a</td>
<td>• List and define the outcome domains and time frame of measurement for which data were sought.</td>
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<td>• Specify whether all results that were compatible with each outcome domain in each study were sought, and if not, what process was used to select results within eligible domains.</td>
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<td>• If any changes were made to the inclusion or definition of the outcome domains, or to the importance given to them in the review, specify the changes, along with a rationale.</td>
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<td>• If any changes were made to the processes used to select results within eligible outcome domains, specify the changes, along with a rationale.</td>
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<td></td>
<td>• Consider specifying which outcome domains were considered the most important for interpreting the review’s conclusions and provide rationale for the labelling (e.g. “a recent core outcome set identified the outcomes labelled ‘critical’ as being the most important to patients”).</td>
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<tr>
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<td>• The scores and standard deviation of the whoqol questionnaire were assessed in the four domains (physical, social, psychological and environmental).</td>
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<td>• The academic cycle was divided in three groups according to Brazilian medical training guidelines: pre-clinical, clinical, and clerkship. When the articles described the quality of life scores by year of study, the first two years were placed in the pre-clinical step, the 3rd and 4th years were categorized as clinical and the last two years as clerkship.</td>
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<td>• Not applicable</td>
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<tr>
<td><strong>DATA ITEMS (other variables)</strong></td>
<td>10b</td>
<td>• List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources).</td>
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<td>• Describe any assumptions made about any missing or unclear information from the studies.</td>
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<td>• If a tool was used to inform which data items to collect, cite the tool used.</td>
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<td>• Not applicable</td>
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<td>• Not applicable</td>
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</tbody>
</table>
### STUDY RISK OF BIAS ASSESSMENT

- Specify the tool(s) (and version) used to assess risk of bias in the included studies.
- Specify the methodological domains/components/items of the risk of bias tool(s) used.
- Report whether an overall risk of bias judgement that summarised across domains/components/items was made, and if so, what rules were used to reach an overall judgement.
- If any adaptations to an existing tool to assess risk of bias in studies were made, specify the adaptations.
- If a new risk of bias tool was developed for use in the review, describe the content of the tool and make it publicly accessible.
- Report how many reviewers assessed risk of bias in each study, whether multiple reviewers worked independently, and any processes used to resolve disagreements between assessors.
- Report any processes used to obtain or confirm relevant information from study investigators.
- If an automation tool was used to assess risk of bias, report how the automation tool was used, how the tool was trained, and details on the tool’s performance and internal validation.

The quality of the studies was appraised by the Joanna Briggs institute tool.
- Not applicable
- Not applicable
- Not applicable
- These classifications were made by two independent reviewers (JCC and CKM) and any disagreements were addressed to a third reviewer (CMA).
- No contact was made with the authors regarding unclear information.
- Not applicable

### EFFECT MEASURES

- Specify for each outcome (or type of outcome [e.g. binary, continuous]), the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.
- State any thresholds (or ranges) used to interpret the size of effect (e.g. minimally important difference; ranges for no/trivial, small, moderate and large effects) and the rationale for these thresholds.

The primary outcome was the mean difference in the quality of life between Brazilian medical students in the last academic cycle (clerkship) compared to those in the begging of the medical training (pre-clinical stage).
- Not applicable

<table>
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<tr>
<th>Section and Topic</th>
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</tr>
</thead>
<tbody>
<tr>
<td>SYNTHESIS METHODS (eligibility for synthesis)</td>
<td>13a</td>
<td>Describe the processes used to decide which studies were eligible for each synthesis.</td>
</tr>
<tr>
<td>SYNTHESIS METHODS (preparing for synthesis)</td>
<td>13b</td>
<td>Report any methods required to prepare the data collected from studies for presentation or synthesis, such as handling of missing summary statistics, or data conversions.</td>
</tr>
<tr>
<td>SYNTHESIS METHODS (tabulation and graphical methods)</td>
<td>13c</td>
<td>Report chosen tabular structure(s) used to display results of individual studies and syntheses, along with details of the data presented.</td>
</tr>
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</table>

Results: The main characteristics of each study are summarized in Table 1.
- When the results were given in the crude scores (without transforming into a percentage scale), they were converted in the normalized scale according to the WHO normative.
- Forest plots were created with the aim of the Review Manager 5.2.7 software (Cochrane Collaboration, Oxford, United Kingdom).
SYNTHESIS METHODS (statistical synthesis methods) 13d

- If statistical synthesis methods were used, reference the software, packages and version numbers used to implement synthesis methods.
- If it was not possible to conduct a meta-analysis, describe and justify the synthesis methods or summary approach used.
- If meta-analysis was done, specify: o the meta-analysis model (fixed-effect, fixed-effects or random-effects) and provide rationale for the selected model. o the method used (e.g. Mantel-Haenszel, inverse-variance).
  - any methods used to identify or quantify statistical heterogeneity (e.g. visual inspection of results, a formal statistical test for heterogeneity, heterogeneity variance (τ), inconsistency (e.g. F), and prediction intervals).
- If a random-effects meta-analysis model was used: o specify the between-study (heterogeneity) variance estimator used (e.g. DerSimonian and Laird, restricted maximum likelihood (REML)).
  - specify the method used to calculate the confidence interval for the summary effect (e.g. Wald-type confidence interval, Hartung-Knapp-SidikJonkman).
  - consider specifying other details about the methods used, such as the method for calculating confidence limits for the heterogeneity variance.
- If a Bayesian approach to meta-analysis was used, describe the prior distributions about quantities of interest (e.g. intervention effect being analysed, amount of heterogeneity in results across studies).
- If multiple effect estimates from a study were included in a meta-analysis, describe the method(s) used to model or account for the statistical dependency (e.g. multivariate meta-analysis, multilevel models or robust variance estimation).
- If a planned synthesis was not considered possible or appropriate, report this and the reason for that decision.

- The data was stratified according to sex. This strategy was performed to reduce potential heterogeneity across studies as the baseline QoL index might be considerably different between these groups.
- Forest plots were created with the aim of the Review Manager 5.2.7 software (Cochrane Collaboration, Oxford, United Kingdom).
  - Not applicable
- The weighted mean difference was calculated using the generic inverse variance model in the random effects model
  - Heterogeneity in the sub-groups was estimated by the I² statistic test.
  - I²
  - Not applicable
  - Not applicable
  - Not applicable
  - Not applicable
  - Not applicable
  - Not applicable
SYNTHESIS METHODS
(methods to explore heterogeneity)

- If methods were used to explore possible causes of statistical heterogeneity, specify the method used (e.g. subgroup analysis, meta-regression).
- If subgroup analysis or meta-regression was performed, specify for each: which factors were explored, levels of those factors, and which direction of effect modification was expected and why (where possible).
  - whether analyses were conducted using study-level variables (i.e. where each study is included in one subgroup only), within-study contrasts (i.e. where data on subsets of participants within a study are available, allowing the study to be included in more than one subgroup), or some combination of the above.
  - how subgroup effects were compared (e.g. statistical test for interaction for subgroup analyses).
- If other methods were used to explore heterogeneity because data were not amenable to meta-analysis of effect estimates (e.g. structuring tables to examine variation in results across studies based on subpopulation), describe the methods used, along with the factors and levels.
- If any analyses used to explore heterogeneity were not pre-specified, identify them as such.

The data was stratified according to sex.
This strategy was performed to reduce potential heterogeneity across studies as the baseline QoL index might be considerably lower in women.

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<tr>
<td>SYNTHESIS METHODS (sensitivity analyses)</td>
<td>13f</td>
<td>If sensitivity analyses were performed, provide details of each analysis (e.g. removal of studies at high risk of bias, use of an alternative meta-analysis model). If any sensitivity analyses were not pre-specified, identify them as such.</td>
</tr>
<tr>
<td>REPORTING ASSESSMENT BIAS</td>
<td>14</td>
<td>Specify the methods (tool, graphical, statistical or other) used to assess the risk of bias due to missing results in a synthesis (arising from reporting biases). If risk of bias due to missing results was assessed using an existing tool, specify the methodological components/domains/items of the tool, and the process used to reach a judgement of overall risk of bias. If any adaptations to an existing tool to assess risk of bias due to missing results were made, specify the adaptations. If a new tool to assess risk of bias due to missing results was developed for use in the review, describe the content of the tool and make it publicly accessible. Report how many reviewers assessed risk of bias due to missing results in a synthesis, whether multiple reviewers worked independently, and any processes used to resolve disagreements between assessors. Report any processes used to obtain or confirm relevant information from study investigators. If an automation tool was used to assess risk of bias due to missing results, report how the automation tool was used, how the tool was trained, and details on the tool’s performance and internal validation. Not applicable</td>
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Not applicable
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Not applicable
Not applicable
CERTAINTY ASSESSMENT

15 - Specify the tool or system (and version) used to assess certainty (or confidence) in the body of evidence.

- Report the factors considered (e.g. precision of the effect estimate, consistency of findings across studies) and the criteria used to assess each factor when assessing certainty in the body of evidence.

- Describe the decision rules used to arrive at an overall judgement of the level of certainty, together with the intended interpretation (or definition) of each level of certainty.

- If applicable, report any review-specific considerations for assessing certainty, such as thresholds used to assess imprecision and ranges of magnitude of effect that might be considered trivial, moderate or large, and the rationale for these thresholds and ranges (item #12).

- If any adaptations to an existing tool or system to assess certainty were made, specify the adaptations.

- Report how many reviewers assessed certainty in the body of evidence for an outcome, whether multiple reviewers worked independently, and any processes used to resolve disagreements between assessors.

- Report any processes used to obtain or confirm relevant information from investigators.

- If an automation tool was used to support the assessment of certainty, report how the automation tool was used, how the tool was trained, and details on the tool’s performance and internal validation.

- Describe methods for reporting the results of an assessment of certainty, such as the use of Summary of Findings tables.

- If standard phrases that incorporate the certainty of evidence were used (e.g. “hip protectors probably reduce the risk of hip fracture slightly”), report the intended interpretation of each phrase and the reference for the source guidance.

- The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) [17] system was used to evaluate the quality of evidence.

- according to the following parameters: risk of bias, inconsistency, indirectness, imprecision, and publication bias.

- The quality of the evidence was classified into four levels (high, moderate, low, and very low)

- This assessment was assessed by two independent authors (JCC and CKM). Any disagreement was solved by consensus

RESULTS

STUDY SELECTION (flow of studies)

16a - Report, ideally using a flow diagram, the number of: records identified; records excluded before screening; records screened; records excluded after screening titles or titles and abstracts; reports retrieved for detailed evaluation; potentially eligible reports that were not retrievable; retrieved reports that did not meet inclusion criteria and the primary reasons for exclusion; and the number of studies and reports included in the review. If applicable, also report the number of ongoing studies and associated reports identified.

- If the review is an update of a previous review, report results of the search and selection process for the current review and specify the number of studies included in the previous review.

- If applicable, indicate in the PRISMA flow diagram how many records were excluded by a human and how many by automation tools.

- Figure 1 shows the PRISMA flowchart for the summarized results. The main characteristics of each study are summarized in Table 1.

- Not applicable

STUDY SELECTION (excluded studies)

16b - Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.

- Table 2 shows the characteristics of the studies not included in the meta-analysis including the reasons for exclusion.
<table>
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<tr>
<th>Section and Topic</th>
<th>Item #</th>
<th>Elements recommended for reporting</th>
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</thead>
</table>
| STUDY CHARACTERISTICS                  | 17     | • Cite each included study.  
• Present the key characteristics of each study in a table or figure (considering a format that will facilitate comparison of characteristics across the studies).  
• If the review examines the effects of interventions, consider presenting an additional table that summarises the intervention details for each study. |
| RISK OF BIAS IN STUDIES                | 18     | • Present tables or figures indicating for each study the risk of bias in each domain/component/item assessed (e.g. blinding of outcome assessors, missing outcome data) and overall study-level risk of bias.  
• Present justification for each risk of bias judgement, for example in the form of relevant quotations from reports of included studies.  
• If assessments of risk of bias were done for specific outcomes or results in each study, consider displaying risk of bias judgements on a forest plot, next to the study results. |
| RESULTS OF INDIVIDUAL STUDIES          | 19     | • For all outcomes, irrespective of whether statistical synthesis was undertaken, present for each study summary statistics for each group (where appropriate). For dichotomous outcomes, report the number of participants with and without the events for each group; or the number with the event and the total for each group (e.g. 12/45). For continuous outcomes, report the mean, standard deviation and sample size of each group.  
• For all outcomes, irrespective of whether statistical synthesis was undertaken, present for each study an effect estimate and its precision (e.g. standard error or 95% confidence/credible interval). For example, for time-to-event outcomes, present a hazard ratio and its confidence interval.  
• If study-level data is presented visually or reported in the text (or both), also present a tabular display of the results.  
• If results were obtained from multiple data sources (e.g. journal article, study register entry, clinical study report, correspondence with authors), report the source of the data.  
• If applicable, indicate which results were not reported directly and had to be computed or estimated from other information. |
| RESULTS OF SYNTHESSES                  | 20a    | • Provide a brief summary of the characteristics and risk of bias among studies contributing to each synthesis (meta-analysis or other). The summary should focus only on study characteristics that help in interpreting the results (especially those that suggest the evidence addresses only a restricted part of the review question, or indirectly addresses the question).  
• Indicate which studies were included in each synthesis (e.g. by listing each study in a forest plot or table or citing studies in the text). |

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<td>Risk of bias section</td>
<td>Sup file 3</td>
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RESULTS OF SYNTHESSES (results of statistical syntheses)

• Report results of all statistical syntheses described in the protocol and all syntheses conducted that were not pre-specified.
• If meta-analysis was conducted, report for each: o the summary estimate and its precision (e.g. standard error or 95% confidence/credible interval) o measures of statistical heterogeneity (e.g. \( \tau^2 \), \( I^2 \), prediction interval)
• If other statistical synthesis methods were used (e.g. summarising effect estimates, combining P values), report the synthesized result and a measure of precision (or equivalent information, for example, the number of studies and total sample size).
• If the statistical synthesis method does not yield an estimate of effect (e.g. as is the case when P values are combined), report the relevant statistics (e.g. P value from the statistical test), along with an interpretation of the result that is consistent with the question addressed by the synthesis method.
• If comparing groups, describe the direction of effect (e.g. fewer events in the intervention group, or higher pain in the comparator group).
• If synthesising mean differences, specify for each synthesis, where applicable, the unit of measurement (e.g. kilograms or pounds for weight), the upper and lower limits of the measurement scale (e.g. anchors range from 0 to 10), direction of benefit (e.g. higher scores denote higher severity of pain), and the minimally important difference, if known. If synthesising standardised mean differences, and the effect estimate is being re-expressed to a particular instrument, specify details of the instrument, as per the mean difference.

RESULTS OF SYNTHESSES (results of investigations of heterogeneity)

• If investigations of possible causes of heterogeneity were conducted: o present results regardless of the statistical significance, magnitude, or direction of effect modification.
  o identify the studies contributing to each subgroup.
  o report results with due consideration to the observational nature of the analysis and risk of confounding due to other factors.
• If subgroup analysis was conducted:
  o report for each analysis the exact P value for a test for interaction, as well as, within each subgroup, the summary estimates, their precision (e.g. standard error or 95% confidence/credible interval) and measures of heterogeneity.
  o consider presenting the estimate for the difference between subgroups and its precision.

If meta-regression was conducted: o report for each analysis the exact P value for the regression coefficient and its precision.
• consider presenting a meta-regression scatterplot with the study effect estimates plotted against the potential effect modifier.

  • If informal methods (i.e., those that do not involve a formal statistical test) were used to investigate heterogeneity, describe the results observed.

RESULTS OF SYNTHESSES (results of sensitivity analyses)

  • If any sensitivity analyses were conducted: o report the results for each sensitivity analysis. o comment on how robust the main analysis was given the results of all corresponding sensitivity analyses.

  o consider presenting results in tables that indicate: (i) the summary effect estimate, a measure of precision (and potentially other relevant statistics, for example, I² statistic) and contributing studies for the original meta-analysis; (ii) the same information for the sensitivity analysis; and (iii) details of the original and sensitivity analysis assumptions.

  o consider presenting results of sensitivity analyses visually using forest plots.

REPORTING BIASES

  • Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.

  • If a tool was used to assess risk of bias due to missing results in a synthesis, present responses to questions in the tool, judgements about risk of bias and any information used to support such judgements.

  • If a funnel plot was generated to evaluate small-study effects (one cause of which is reporting biases), present the plot and specify the effect estimate and measure of precision used in the plot. If a contour-enhanced funnel plot was generated, specify the ‘milestones’ of statistical significance that the plotted contour lines represent (P = 0.01, 0.05, 0.1, etc.)

  • If a test for funnel plot asymmetry was used, report the exact P value observed for the test, and potentially other relevant statistics, for example the standardised normal deviate, from which the P value is derived.

  • If any sensitivity analyses seeking to explore the potential impact of missing results on the synthesis were conducted, present results of each analysis (see item #20d), compare them with results of the primary analysis, and report results with due consideration of the limitations of the statistical method.

  • If studies were assessed for selective non-reporting of results by comparing outcomes and analyses pre-specified in study registers, protocols, and statistical analysis plans with results that were available in study reports, consider presenting a matrix (with rows as studies and columns as syntheses) to present the availability of study results.
TRENDS PSYCHIATRY PSYCHOLOGICAL TREATMENT

CERTAINTY OF EVIDENCE
22
- Report the overall level of certainty (or confidence) in the body of evidence for each important outcome.
- Provide an explanation of reasons for rating down (or rating up) the certainty of evidence (e.g. in footnotes to an evidence summary table).
- Communicate certainty in the evidence wherever results are reported (i.e. abstract, evidence summary tables, results, conclusions), using a format appropriate for the section of the review.
- Consider including evidence summary tables, such as GRADE Summary of Findings tables.

DISCUSSION
23a
- Provide a general interpretation of the results in the context of other evidence.

DISCUSSION (limitations of evidence)
23b
- Discuss any limitations of the evidence included in the review.

DISCUSSION (limitations of review processes)
23c
- Discuss any limitations of the review processes used, and comment on the potential impact of each limitation.

DISCUSSION (implications)
23d
- Discuss implications of the results for practice and policy.
- Make explicit recommendations for future research.

OTHER INFORMATION
24a
- Provide registration information for the review, including register name and registration number, or state that the review was not registered.

REGISTRATION AND PROTOCOL (registration)
24b
- Indicate where the review protocol can be accessed (e.g. by providing a citation, DOI or link), or state that a protocol was not prepared.

REGISTRATION AND PROTOCOL (amendments)
24c
- Report details of any amendments to information provided at registration or in the protocol, noting: (a) the amendment itself; (b) the reason for the amendment; and (c) the stage of the review process at which the amendment was implemented.

The registration was carried out in the PROSPERO database under the two following submissions: CRD42021234363 “Is medical school associated with decreased quality of life in Brazilian students? A systematic review and meta-analysis over a decade”...
### SUPPORT
25
- Describe sources of financial or non-financial support for the review, specifying relevant grant ID numbers for each funder. If no specific financial or nonfinancial support was received, this should be stated.
- Describe the role of the funders or sponsors (or both) in the review. If funders or sponsors had no role in the review, this should be declared.
- This work was supported financially by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq, Brasília, Brazil). The funding sources had no impact in the design, conduct, or reporting of the article or the decision to publish the study. The authors declare no conflict of interest.

### COMPETING INTERESTS
26
- Disclose any of the authors’ relationships or activities that readers could consider pertinent or to have influenced the review.
- If any authors had competing interests, report how they were managed for particular review processes.
- The author declare no conflict of interest

### AVAILABILITY OF DATA, CODE, AND OTHER MATERIALS
27
- Report which of the following are publicly available: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.
- If any of the above materials are publicly available, report where they can be found (e.g. provide a link to files deposited in a public repository).
- If data, analytic code, or other materials will be made available upon request, provide the contact details of the author responsible for sharing the materials and describe the circumstances under which such materials will be shared.
- Not applicable
- Not applicable
- Not applicable
Supplementary table 1. Detailed search strategy containing the databases and the number of extracted references.

<table>
<thead>
<tr>
<th>Search filters</th>
<th>Records</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PUBMED – Search filters</strong></td>
<td></td>
</tr>
<tr>
<td>#1 Population [Mesh]: (Students, medical)</td>
<td>38,171</td>
</tr>
<tr>
<td>#2 Outcome [Mesh]: (quality of life)</td>
<td>220,359</td>
</tr>
<tr>
<td>#3 Combined search: (#1 AND #2)</td>
<td>270</td>
</tr>
<tr>
<td><strong>EMBASE – Search filters</strong></td>
<td></td>
</tr>
<tr>
<td>#1 Population [tittle, abstract, keyword]: medical student</td>
<td>79,660</td>
</tr>
<tr>
<td>#2 Outcome [All fields]: (quality of life)</td>
<td>560,012</td>
</tr>
<tr>
<td>#3 Combined search: (#1 AND #2)</td>
<td>176</td>
</tr>
<tr>
<td><strong>BVS database – Search filters</strong></td>
<td></td>
</tr>
<tr>
<td>#1 Population [title, abstract, subject]: estudantes de medicina</td>
<td>4,197</td>
</tr>
<tr>
<td>#2 Outcome [title, abstract, subject]: Qualidade de vida</td>
<td>23,458</td>
</tr>
<tr>
<td>#3 Combined search: (#1 AND #2)</td>
<td>146</td>
</tr>
</tbody>
</table>
Supplementary file 3 – Characteristics of studies not included in the meta-analysis (with reasons)

<table>
<thead>
<tr>
<th>Authorship</th>
<th>Data collection date</th>
<th>Location</th>
<th>University (abbreviation) (type of institution)</th>
<th>Population (N)</th>
<th>Percentage of enrolled population</th>
<th>QOL Evaluation instrument</th>
<th>Comparisons</th>
<th>Negative predictor factors</th>
<th>Reasons for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paro, Morales (1)</td>
<td>Feb 2006 - Feb 2007</td>
<td>Uberlandia-MG</td>
<td>Universidade Federal de Uberlandia (UFU) (public)</td>
<td>All-students (352)</td>
<td>78.2%</td>
<td>SF-36</td>
<td>Academic year, Depression, Gender, Living arrangements</td>
<td>3rd year, Depression, Females</td>
<td>Not using the WHOQOL-bref as the instrument measure (SF-36 as the questionnaire), Lack of data (scores given as median and percentiles)</td>
</tr>
<tr>
<td>Ramos-Dias, Libardi (2)</td>
<td>Not informed</td>
<td>Sorocaba-SP</td>
<td>Pontifício Universidade católica (PUC) (private)</td>
<td>First and last year (100)</td>
<td>Not informed</td>
<td>WHOQOL-Bref</td>
<td>Academic year</td>
<td>First-year</td>
<td>Not controlling for gender</td>
</tr>
<tr>
<td>Authors</td>
<td>Dates</td>
<td>Location</td>
<td>Institution/Program (Public/Private)</td>
<td>Sample Size</td>
<td>Gender</td>
<td>Academic Year</td>
<td>Comorbidities</td>
<td>Gender</td>
<td>Social Class</td>
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</tr>
<tr>
<td>Bampi, Baraldi (3)</td>
<td>Aug 2010 - Aug 2011</td>
<td>Brasilia-DF</td>
<td>Universidade de Brasilia (UnB) (public)</td>
<td>All-students (84)</td>
<td>18 %</td>
<td>WHOQOL-Bref</td>
<td>Questionnaire domains</td>
<td>Psychological domain</td>
<td>Not comparing the influence of the academic cycle in the QoL index</td>
</tr>
<tr>
<td>César, de Pádua Paz (4)</td>
<td>Aug 2009 - Nov 2009</td>
<td>Brasilia-DF</td>
<td>Not informed</td>
<td>All-students (345)</td>
<td>70%</td>
<td>WHOQOL-Bref</td>
<td>Academic year</td>
<td>4th year</td>
<td>Lack of data (standard deviation)</td>
</tr>
<tr>
<td>Chazan and Campos (5), Chazan, Campos (6)</td>
<td>Apr 2010 - May 2010</td>
<td>Rio de Janeiro – RJ</td>
<td>Universidade Estadual do Rio de janeiro (UERJ) (public)</td>
<td>All-students (394)</td>
<td>72 %</td>
<td>WHOQOL-Bref</td>
<td>Academic year</td>
<td>Third and sixth year</td>
<td>Refered chronic morbidity Females Quota students Social class C</td>
</tr>
<tr>
<td>Meyer, Guimarães (7)</td>
<td>June 2011 - Sept 2011</td>
<td>Multicenter-SC</td>
<td>Multicenter (1 public; 11 private)</td>
<td>Last year students (302)</td>
<td>Not informed</td>
<td>WHOQOL-Bref</td>
<td>Gender Occupational stress (Job stress scale)</td>
<td>None</td>
<td>Not comparing the influence of the academic cycle in the QoL index</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Location and Institution</td>
<td>Population</td>
<td>Year</td>
<td>Outcome Measure</td>
<td>Academic Year</td>
<td>Comparison</td>
<td>Notes</td>
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<tr>
<td>Olmo, Ferreira (8)</td>
<td>Not informed</td>
<td>Universidade Metropolitana de Santos (Unimes) (private)</td>
<td>First and last year (108)</td>
<td>75% First year, 57% last year</td>
<td>WHOQOL-Bref, Academic year</td>
<td>Last-year</td>
<td>Not comparing the influence of the academic cycle in the QoL index</td>
<td></td>
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</tr>
<tr>
<td>Paro and Bittencourt (9)</td>
<td>Not informed</td>
<td>Universidade Estadual de Campinas (UNICAMP) (public)</td>
<td>All-students (309)</td>
<td>47%</td>
<td>SF-36, Academic year</td>
<td>5th year</td>
<td>Not using the WHOQOL-bref as the instrument measure (SF-36 as the questionnaire)</td>
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<tr>
<td>Hickel, Fabro (10)</td>
<td>Dec 2012 - Mar 2013</td>
<td>Universidade Federal de Pelotas (UFPel) (public)</td>
<td>First to 7th semester (95%)</td>
<td>WHOQOL-Bref, Academic year</td>
<td>Distance from hometown</td>
<td>Not comparing the last academic cycle (The comparison was established between the first and 7th semester)</td>
<td></td>
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<tr>
<td>Study Authors</td>
<td>Study Period</td>
<td>Location</td>
<td>Sample Description</td>
<td>Data Collection</td>
<td>Measurement Instruments</td>
<td>Results</td>
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<tr>
<td>Lins, Carvalho (11), Lins, Carvalho (12)</td>
<td>Oct 2013 – Nov 2013</td>
<td>Salvador, BA, Escola Bahiana de Medicina e Saúde pública (EBMSP)(private)</td>
<td>All-students (180)</td>
<td>Not informed</td>
<td>SF-36</td>
<td>Academic year, Age (17-22/ 23-33), Gender, Headaches, Loan program, Living arrangements, Physical activity, Sleepiness, Suffering from headaches, Not using the WHOQOL-bref as the instrument measure (SF-36 as the questionnaire)</td>
<td></td>
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<tr>
<td>Serinolli and El-Mafarjeh (13)</td>
<td>Feb 2014 - Apr 2014</td>
<td>São Paulo, SP, Universidade Nove de Julho (Uninove) (private)</td>
<td>All-students (405)</td>
<td>Not informed</td>
<td>WHOQOL-Bref</td>
<td>Mental diseases, Physical activity, Religiosity, Previous diagnosis of mental diseases, Lack of physical activity, Absence of religious beliefs</td>
<td>Not comparing the influence of academic cycle in the contr</td>
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<tr>
<td>Chagas, Sanches (14)</td>
<td>Oct 2015 - Dec 2015</td>
<td>São Carlos-SP</td>
<td>Universidade Federal de São Carlos (UFSCar) (public)</td>
<td>First to 4th year</td>
<td>Not informed</td>
<td>WHOQOL-100</td>
<td>Academic year</td>
<td>3rd year</td>
<td>Not academicnder</td>
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<tr>
<td>Cunha, Moraes (15)</td>
<td>Aug 2011 - Dec 2011</td>
<td>São Paulo-SP</td>
<td>Universidade Federal de São Paulo (UNIFESP) (public)</td>
<td>All-students (607)</td>
<td>82,5%</td>
<td>WHOQOL-100</td>
<td>Academic cycle</td>
<td>Academic year</td>
<td>Gender</td>
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<tr>
<td>Pereira, Ribeiro (16)</td>
<td>Not informed</td>
<td>Patos-PB</td>
<td>Faculdade integrada de Patos (FIP) – (private)</td>
<td>First to the fifth semester (138)</td>
<td>76,7%</td>
<td>WHOQOL-Brief</td>
<td>Academic semester</td>
<td>Age</td>
<td>Burnout</td>
</tr>
<tr>
<td>dos Santos, Ribeiro (17)</td>
<td>2016</td>
<td>Jequié-BA</td>
<td>Universidade Estadual do Sudoeste da Bahia (UESB) (public)</td>
<td>Not informed</td>
<td>Not informed</td>
<td>WHOQOL-Brief</td>
<td>Common Mental Disorders</td>
<td>Presence of psychiatric symptoms</td>
<td>Not comparing the influence of the academic cycle in the QoL index</td>
</tr>
<tr>
<td>Antunes, Silva Menezes (18)</td>
<td>2014</td>
<td>Salvador-Ba</td>
<td>Escola Bahiana de Medicina e Saúde pública (EBMSP)(private)</td>
<td>All-students (291)</td>
<td>Not informed</td>
<td>VERAS-Q</td>
<td>Academic cycle Gender</td>
<td>Last academic cycle Females</td>
<td>WHOQOL-bref as the instrument measure (VERAS-Q as the questionnaire)</td>
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<tr>
<td>Cavalcante, Cazolari (19)</td>
<td>Aug 2017 - Dec 2018</td>
<td>São Paulo-SP</td>
<td>Universidade Federal de São Paulo (UNIFESP) (public)</td>
<td>First and last-year</td>
<td>Not informed</td>
<td>WHOQOL-Bref</td>
<td>Academic year</td>
<td>Last-year</td>
<td>Not controlling for gender</td>
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<tr>
<td>Andrade, Caetano (20)</td>
<td>June 2018 – not informed</td>
<td>Franca-SP</td>
<td>Universidade de Franca (UNIFRAN) (private)</td>
<td>First to 4th year (n=310)</td>
<td>Not informed</td>
<td>WHOQOL-Bref</td>
<td>Academic year Gender Studying hours</td>
<td>First-year Females</td>
<td>Not comparing the last academic cycle (The comparison was established between the first to the 4th year)</td>
</tr>
<tr>
<td>Study</td>
<td>Location</td>
<td>Institution</td>
<td>Year/Type</td>
<td>Sample Size</td>
<td>Measure</td>
<td>Workload</td>
<td>Control for Gender</td>
<td>Comparison</td>
<td></td>
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<tr>
<td>Durán and Dunningham (21)</td>
<td>Salvador-BA</td>
<td>Centro Universitário Faculdades de Tecnologia e Ciências (UniFTC) (private)</td>
<td>First to 8th semester (80)</td>
<td>Not informed</td>
<td>SF-36</td>
<td>High workloads</td>
<td>Not controlling for gender</td>
<td>Not using the WHOQOL-bref as the instrument measure (SF-36 as the questionnaire)</td>
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<tr>
<td>Meyer, Barbosa (22)</td>
<td>Multicenter-SC</td>
<td>Multicenter (1 public; 8 private)</td>
<td>Last year students (508)</td>
<td>Not informed</td>
<td>WHOQOL-Bref</td>
<td>The difficulty of conciliating clerkship and studies</td>
<td>Not comparing the influence of the academic cycle in the QoL index</td>
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<td></td>
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<tr>
<td>Moutinho, Lucchetti (23)</td>
<td>Juiz de Fora-MG</td>
<td>Universidade Federal de Juiz de fora (UFJF) (public)</td>
<td>Students were included if they could be followed for two years (312)</td>
<td>54.2%</td>
<td>WHOQOL-Bref</td>
<td>Anxiety, Depression, Ethnicity, Gender, Religiosity, Social class, Stress</td>
<td>Not comparing the last academic cycle (The comparison was established between the first to the 4th semester)</td>
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<tr>
<td>Rocha 2019</td>
<td>Jan 2018 - June 2018</td>
<td>Franca-SP</td>
<td>Universidade de Franca (UNIFRAN) (private)</td>
<td>All-students</td>
<td>Not informed</td>
<td>WHOQOL-Bref</td>
<td>VERAS</td>
<td>Academic year</td>
<td>3rd and 5th year</td>
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<tr>
<td>Cangussu, Ezequiel (24)</td>
<td>2015</td>
<td>Juiz de fora-MG</td>
<td>Universidade Federal de Juiz de Fora (UFJF) (public)</td>
<td>All-students (776)</td>
<td>77%</td>
<td>WHOQOL-Bref</td>
<td>Academic cycle Gender</td>
<td>First cycle Females</td>
<td>Lack of data (the authors gave the standard error instead of the standard deviation and the total number of participants was not available for each group)</td>
</tr>
<tr>
<td>Miranda, Tavares (25)</td>
<td>Not informed</td>
<td>Aparecida de goiânia-GO</td>
<td>Universidade de Rio Verde (UniRV) (private)</td>
<td>Second to 8th semester (419)</td>
<td>Not informed</td>
<td>WHOQOL-Bref</td>
<td>Comorbidities Food consumption Gender Practicing physical activity</td>
<td>Presence of comorbidities. Females Use of stimulants,</td>
<td>Not comparing the first academic cycle in the QoL index</td>
</tr>
<tr>
<td>Pires, Gusmão (26)</td>
<td>Aug 2017 - Dec 2017</td>
<td>Maceió-AL</td>
<td>Universidade Estadual de Ciências da Saúde de Alagoas (Uncisal) (public)</td>
<td>All-students (190)</td>
<td>63%</td>
<td>WHOQOL-Bref</td>
<td>Academic cycle Gender</td>
<td>Last academic cycle</td>
<td>Females</td>
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<tr>
<td>Silva, Pereira (27)</td>
<td>Not informed</td>
<td>Caratinga-MG</td>
<td>Centro universitário de Caratinga (UNEC) (private)</td>
<td>First, third and fifth year (n=94)</td>
<td>64% First year 50% Second year 51.1% Fifth year</td>
<td>WHOQOL-Bref</td>
<td>Minor mental disorders</td>
<td>Prevalence of minor mental disorders</td>
<td>Not comparing the influence of the academic cycle in the QoL index</td>
</tr>
</tbody>
</table>


21. Durán FC, Dunningham WA. Relação entre a carga horária e a qualidade de vida dos alunos do curso de medicina de uma faculdade de salvador. Revista Brasileira de Neurologia e Psiquiatria. 2019;23(3).