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Accepted: Available online: Published:	2022.12.01 2023.01.19 2023.02.09	and Mental Health in 72 Indonesia During the CC	29 Medical Students in OVID-19 Pandemic			
Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G BE 1,2 BE 1,		<ul> <li>David Nugraha (b)</li> <li>Sovia Salamah (b)</li> <li>Kevin Luke</li> <li>Zefo Kiyosi Wibowo</li> <li>Andro Pramana Witarto (b)</li> <li>Caesariska Deswima</li> <li>Nabila Ananda Kloping (b)</li> <li>Bendix Samarta Witarto (b)</li> <li>Adila Taufik Syamlan (b)</li> <li>Abyan Irzaldy (b)</li> <li>Abyan Irzaldy (b)</li> <li>Maftuchah Rochmanti</li> <li>Dewi Ratna Sari</li> <li>Sakina Sakina</li> </ul>				
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_	Background: Material/Methods:	The coronavirus disease 2019 (COVID-19) pandemic and mental health worldwide. However, its impact or mented. This study aimed to evaluate HRQoL and m the COVID-19 pandemic. We conducted a cross-sectional study from 31 August line questionnaire that was distributed via social mer	has impacted the health-related quality of life (HRQoL) n medical students in Indonesia has not been well docu- ental health in 729 Indonesian medical students during to 30 September 2021. The study instrument was an on-			
	Results:	was used to measure HRQoL, and the 21-item Depre measure mental health. From 729 Indonesian medical students included in the 66.9% had impaired mental component of HRQoL. T dence, history of hospitalization, and family member?	e analyses, 37.3% had impaired physical component and The determinants were medical students' island of resi- s hospitalization and death due to COVID-19. Concerning			
	Conclusions:	mental health, the prevalence of reported symptoms and 60.9%, respectively. Sex, study method, grade, p ous learning experience, and history of family isolatic This study highlights the adverse effects of COVID-19 dents. The results identified key associations, includi by the students, the health of their families, includin isolation during the pandemic.	s of depression, anxiety, and stress were 45.4%, 65.2%, previous COVID-19 disease severity, comorbidities, previ- on were identified as the determinants of mental health. on HRQoL and mental health in Indonesian medical stu- ng SARS-CoV-2 infection and comorbidities experienced og grief following bereavement, and the effects of social			
	Keywords:	COVID-19 • Indonesia • Mental Health • Quality of	f Life • Students, Medical			
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**Evaluation of Health-Related Quality of Life** 



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# Background

On 11 March 2020, the World Health Organization declared coronavirus disease 2019 (COVID-19) to be a pandemic due to its alarming levels of spread and severity [1]. To date, this disease has infected more than 600 million people, and caused the deaths of more than 6 million people worldwide [2]. In addition to the clinical consequences, this disease also causes a substantial impact on the mental health of the global population [3]. A previous meta-analysis and review showed that the prevalence of depression and anxiety during the COVID-19 pandemic in the general population was 26.93% and 27.77%, respectively [4]. However, healthcare workers (HCWs) are at higher risk of having mental health problems compared to the general population [5], as HCWs are more exposed to COVID-19 [6]. Previously, we have shown that the prevalence of depression, anxiety, and stress among HCWs was 29.4%, 44.9%, and 31.8%, respectively, when evaluated using 21-item depression, anxiety, and stress scale (DASS-21) [7].

Other than HCWs, there is another vulnerable group for developing mental health problems during the COVID-19 pandemic, that is, medical students. A recent systematic review and metaanalysis study concluded that the prevalence of mental health problems among medical students during the COVID-19 pandemic was relatively higher than among HCWs and the general population [8]. It was already known that medical students were susceptible to mental health problems, which is associated with and closely related to Health-Related Quality of Life (HRQoL) [9]. Previous studies conducted before the COVID-19 pandemic have demonstrated that medical students are highly susceptible to developing an extremely high level of depression, stress, and other deterioration of mental health compared to the general population [10-12]. During this unprecedented COVID-19 pandemic, these conditions worsened, as shown by the increasing prevalence of mental health problems among medical students compared to the pre-pandemic era [13]. Furthermore, compared to the early period, the prevalence of mental health problems was reported to be worsened in the later period of the COVID-19 pandemic [14,15].

Reflecting on the severe acute respiratory syndrome (SARS) outbreak in 2003, emotional distress conditions could persist 1-2 years after the outbreak has ended, which was marked by an increased incidence of burnout, anxiety, depression, and posttraumatic stress disorder [16]. Medical students are the future medical doctors who will become the backbone of the nation's healthcare personnel. Therefore, mental health problems that can decrease the HRQoL of medical students, which may persist 1-2 years after the outbreak, will plausibly disturb the future of the health care system [16]. However, to the best of our knowledge, only 1 previous study has evaluated both the HRQoL and mental health of Indonesian medical

students [17], and the study participants were from only 1 university. Therefore, the present study aimed to evaluate HRQoL and mental health in 729 Indonesian medical students during the COVID-19 pandemic.

# **Material and Methods**

### L2 Ethics Statement

This study was conducted according to the principles of the Declaration of Helsinki. Ethics clearance from the Faculty of Medicine Universitas Airlangga Ethical Reviewer Board was obtained prior to data collection (Ethical approval number 164/EC/KEPK/FKUA/2021, approval date 30 August 2021). Participation in this study was voluntary, and all details that might disclose the identity of the respondents were omitted prior to data analyses to ensure respondents' privacy. Informed consent was obtained from each respondent prior to their participation in the study.

#### **Study Design and Population**

This was a cross-sectional study using an open online questionnaire. The study population was Indonesian medical students. Inclusion criteria were active medical students and agreed to participate as respondents in this study. All participants were recruited using the snowball sampling technique, and the questionnaire was distributed through the most popular and accessible social media platforms in Indonesia: LINE®, WhatsApp®, and Instagram®. Data collection was from 31 August to 30 September 2021. During this period, Indonesia has experienced the peak of the second wave that was caused by the Delta variant outbreak, which placed Indonesia in the epicentrum of the pandemic in Asia [18,19].

The minimum required sample size was estimated using Raosoft software version 2.3 (Raosoft, Inc., Seattle, USA). As there are no precise data on the actual number of undergraduate medical students in Indonesia, we referred to a previous study that also involved medical students in Indonesia as their population [20]. A minimum of 382 participants were required to obtain sufficient statistical power with a 5% of margin error and 95% confidence interval.

#### **Study Instrument**

The online questionnaire was constructed according to the CHERRIES checklist [21], and SurveyMonkey<sup>®</sup> was used as the survey platform. Each participant could fill out the questionnaire only once because the IP address was used to detect potential duplicate entries from the same respondent. The time required to complete all questionnaires was approximately 10-15 min.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] The questionnaire consisted of the following 3 sections: 1) sociodemographic background, 2) HRQoL, and 3) mental health. The sociodemographic characteristics comprised questions concerning the participant's gender, age, institution, education batch and semester, education status (preclinical or clinical), place of residence, study method before and during the pandemic, class duration before and during the pandemic, grade point average (GPA) before and during the pandemic, history of self and family COVID-19 infection history, comorbidities, vaccination status, and stigma from society.

HRQoL was measured using the 12-item-short-form version 2 (SF12v2) health survey (license number: QM054173) [22]. This survey had previously been translated into Bahasa Indonesia and demonstrated good validity and reliability [23]. The SF12v2 measures both mental and physical components, which are divided into 8 health domain scales: general health (GH), social functioning (SF), role physical (RP), physical functioning (PF), bodily pain (BP), role emotional (RE), vitality (VT), and mental health (MH). These domain scales have been described in a previous study [23]. Vitality, social functioning, role emotional, and mental health have the greatest mental factor content, whereas physical functioning, role physical, bodily pain, and general health have the greatest physical factor content among the health domains [22]. The Optum® PROCoRE software (Optum PROCoRE 1.3 Smart Measurement System. Optum Inc., USA) was used to perform the scoring of SF12v2. This software calculates the score for each health domain, physical component summary (PCS), and mental component summary (MCS). Scores of less than 47 indicate significant impairment in the associated health domain [22].

Mental health was evaluated using the DASS-21. This is a selfadministered instrument widely used to assess the full range of depression, anxiety, and stress disorders' core symptoms [24]. This instrument is chosen because it can evaluate depression, anxiety, and stress with the fewest questions [5]. DASS-21 has been translated into Bahasa Indonesia with good validity and reliability [25]. It has 3 subscales (depression, anxiety, and stress) composed of 7 questions each (21 questions in total). The score of each question ranges from 0, indicating the lack of symptoms in the past week, to 3, indicating the presence of symptoms almost every day in the past week. Each subscale score must be multiplied by 2 to obtain the final score. The total score is then categorized into normal, mild, moderate, severe, and extremely severe, with the cut off values as follows: normal (0-9), mild (10-12), moderate (13-20), severe (21-27), and extremely severe (28-42) for depression; normal (0-6), mild (7-9), moderate (10-14), severe (15-19), and extremely severe (20-42) for anxiety; and normal (0-10), mild (11-18), moderate (19-26), severe (27-34), and extremely severe (25-42) for stress subscales [24].

### **Statistical Analyses**

All collected data were processed for data cleaning, coding, and tabulation to simplify the visualization. Data analysis was conducted using IBM SPSS Statistics for Windows version 25.0. (IBM Corp., Armonk, NY, USA). Respondents who filled out only the first part of the questionnaire (the sociodemographic background section) were excluded from the analyses. Respondents who also filled out the HRQoL but not the mental health section were included for sociodemographic and HRQoL analyses but not for the mental health analyses. Nominal variables are expressed as frequency (valid percentage), whereas continuous variables are expressed as mean±standard deviation (SD) for normally distributed data and median (interquartile range [IQR]) for skewed data. Data distribution was evaluated using the one-sample Kolmogorov–Smirnov test.

For identification of determinants for impaired HRQoL and mental health condition, 2-step logistic regression analysis was performed. In the first phase, univariate regression analyses were used to identify independent variables associated with impaired HRQoL and mental health. Variables with a *P* of <0.1 were included in the second phase, where a multivariate regression analysis was conducted using backward selection. Variables with a *P* of <0.05 from the multivariate analysis were considered as the determinants [7]. During the analyses to identify the determinants, mental health variables were recategorized into dichotomous (normal or impaired) with the cut off values as follows: >9 for depression, >6 for anxiety, and >10 for stress [24].

# Results

A total of 819 medical students across Indonesia filled out the questionnaire. Of them, only 90 participants filled out the sociodemographic section, leaving 729 respondents to be included in the sociodemographic and HRQoL analyses (89% response rate). Eleven participants did not complete the mental health section, leaving 718 respondents to be included in the analyses for mental health (88% response rate). **Figure 1** depicts the flowchart of study participant selection.

### **Baseline Characteristics**

The mean age of participants was 20±1.5 years, with a predominance of females (76%). The majority of participants were preclinical medical students (85.6%) and primarily resided in the main island (65.8%). Approximately one-fourth of the participants never experienced a direct face-to-face class before the pandemic. There were 158 (21.7%) participants who had ever been infected with COVID-19. Most participants have been fully vaccinated, and 125 (17.1%) respondents had at least 1 comorbidity. **Table 1** shows the detailed characteristics of the study participants.



Figure 1. Flowchart of the study participants selection.

Table 1. Characteristics of the study participants.

Variables	N=729
<b>Sex, n (%)</b> Male Female	174 (23.9) 555 (76.1)
Age in years, mean±SD	20±1.5
<b>Island of residence, n (%)</b> Java Island (main island) Other than Java Island	479 (65.8) 249 (34.2)
<b>Status, n (%)</b> Preclinical student Clinical student	624 (85.6) 105 (14.4)
<b>Type of university, n (%)</b> Public university Private university	531 (72.8) 198 (27.2)
<b>University accreditation, n (%)</b> Excellent Good or fair	473 (64.9) 256 (35.1)
Experience of normal teaching method before the COVID-19 pandemic, n (%) Yes No	539 (73.9) 190 (26.1)
Duration of lectures during the COVID-19 pandemic, n (%) >8 hours/day 6-8 hours/day <6 hours/day	188 (25.8) 466 (63.9) 75 (10.3)
Most frequently used learning methods during the COVID-19 pandemic, n (%) Full online Hybrid Full offline	492 (67.5) 227 (31.1) 10 (1.4)
Grade point average during COVID-19 the pandemic, n (%) <3.0/4 3-3.5/4 >3.5/4	61 (8.4) 349 (47.9) 319 (43.8)

# HRQoL

The median [IQR] scores of PCS and MCS were 48.65 [45.63-51.53] and 42.67 [36.49-49.27], respectively. RE health domain had the lowest score compared with other health domain scales. **Figure 2** shows the detailed scores of physical and mental health components and each health domain scale. A total of 272 (37.3%) medical students had an impairment in the physical component, and 488 (66.9%) students had an impairment in the mental component. PF was the most impaired health domain, followed by RE (**Figure 3**).

Variables	N=729
Isolation during COVID-19 infection, n (%) Never infected Self-isolation Hospital	571 (78.3) 138 (18.9) 20 (2.7)
COVID-19 infection severity, n (%) Never infected Asymptomatic-mild Moderate-severe	571 (78.3) 132 (18.1) 26 (3.6)
COVID-19 vaccination status, n (%) Vaccinated Unvaccinated	695 (95.3) 34 (4.7)
Having one or more comorbidities, n (%) Yes No	125 (17.1) 604 (82.9)
Isolation during COVID-19 infection among family members, n (%) Never infected Self-isolation Hospital	304 (41.7) 294 (40.3) 131 (18)
COVID-19 infection severity among family members, n (%) Never infected Asymptomatic-mild Moderate-severe	304 (41.7) 248 (34) 177 (24.3)
Family member death due to COVID-19, n (%) Yes No	125 (17.1) 604 (82.9)

COVID-19 – coronavirus disease 2019.







Figure 3. Prevalence of impaired health-related quality of life in physical and mental components in general and each health domain scale among 729 medical students in Indonesia. BP – bodily pain; GH – general health; MCS – mental component summary; MH – mental health; PCS – physical component summary; PF – physical-function; RP – role-physical; SF – social functioning; SF12v2 – 12-item Short Form version 2; RE – role-emotional; VT – vitality. Health-related quality of life is evaluated using 12-item short form version 2.

Table 2. Univariate logistic regression analysis for impaired health-related quality of life.

	SF12v2 N=729						
Variables	MCS		PCS				
	COR (95%CI)	p value	COR (95%CI)	p value			
<b>Sex</b> Male Female	Ref. 1.02 (0.71-1.46)	Ref. 0.923	Ref. 0.91 (0.64-1.30)	Ref. 0.600			
Age in years	1.09 (0.97-1.21)	0.139	2.27 (0.89-1.09)	0.779			
<b>Island of residence</b> Java Island (main island) Other than Java Island	Ref. 1.30 (0.94-1.79)	Ref. 0.112	Ref. 0.75 (0.55-1.03)	Ref. 0.077			
<b>Status</b> Preclinical student Clinical student	Ref. 0.87 (0.56-1.36)	Ref. 0.543	Ref. 1.23 (0.79-1.90)	Ref. 0.363			
<b>Type of university</b> Public university Private university	Ref. 0.93 (0.65-1.31)	Ref. 0.664	Ref. 1.12 (0.80-1.58)	Ref. 0.505			
<b>University accreditation</b> Excellent Good or fair	Ref. 0.91 (0.65-1.25)	Ref. 0.549	Ref. 1.28 (0.93-1.76)	Ref. 0.127			
Experience of normal teaching method before the COVID-19 pandemic No Yes	Ref. 1.43 (1.0-2.06)	Ref. 0.053	Ref. 1.00 (0.71-1.41)	Ref. 0.985			
Duration of lectures during the COVID-19 pandemic <6 h/day 6-8 h/day >8 h/day	Ref. 0.83 (0.50-1.38) 0.96 (0.5-1.68)	Ref. 0.467 0.891	Ref. 0.75 (0.45-1.26) 0.83 (0.47-1.47)	Ref. 0.273 0.522			
Most frequently used learning methods during the COVID-19 pandemic Full online Hybrid Full offline	Ref. 1.31 (0.95-1.83) 0.55 (0.12-2.61)	Ref. 0.104 0.451	Ref. 0.92 (0.67-1.27) 0.38 (0.11-1.37)	Ref. 0.616 0.139			
Grade point average during the COVID-19 pandemic <3.0/4 3-3.54 >3.5/4	0.77 (0.42-1.40) Ref. 1.00 (0.73-1.38)	0.386 Ref. 0.996	1.19 (0.67-2.10) Ref. 1.08 (0.79-1.47)	0.556 Ref. 0.647			
Isolation during COVID-19 infection Never infected Self-isolation Hospital	Ref. 1.40 (0.95-2.05) 1.27 (0.49-3.27)	Ref. 0.089 0.625	Ref. 1.33 (0.90-1.98) 5.49 (1.26-23.98)	Ref. 0.151 <b>0.024</b>			
<b>COVID-19 infection severity</b> Never infected Asymptomatic-mild Moderate-severe	Ref. 1.50 (1.02-2.22) 0.85 (0.35-2.06)	Ref. <b>0.040</b> 0.710	Ref. 1.43 (0.96-2.15) 2.04 (0.80-5.20)	Ref. 0.082 0.133			
<b>COVID-19 vaccination status</b> Unvaccinated Vaccinated	Ref. 1.39 (0.64-3.03)	Ref. 0.405	Ref. 1.20 (0.59-2.39)	Ref. 0.634			

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Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] Table 2 continued. Univariate logistic regression analysis for impaired health-related quality of life.

	SF12v2 N=729						
Variables	MCS		PCS				
	COR (95%CI)	p value	COR (95%CI) p value				
Having one or more comorbidities No Yes	Ref. 0.90 (0.60-1.37)	Ref. 0.627	Ref. Ref. 1.03 (0.69-1.53) 0.897				
Isolation during COVID-19 infection among family members Never infected Self-isolation Hospital	Ref. 1.00 (0.71-1.42) 1.54 (1.01-2.36)	Ref. 0.991 <b>0.045</b>	Ref.Ref.1.22 (0.88-1.70)0.2341.46 (0.95-2.25)0.086				
COVID-19 infection severity among family members Never infected Asymptomatic-mild Moderate-severe	Ref. 1.11 (0.77-1.58) 1.22 (0.82-1.80)	Ref. 0.579 0.328	Ref. Ref. 1.28 (0.90-1.80) 0.170 1.31 (0.89-1.93) 0.169				
Family member death due to COVID-19 No Yes	Ref. 1.46 (0.95-2.26)	Ref. 0.083	Ref. Ref. 0.82 (0.55-1.24) 0.346				

95% CI – 95% confidence interval; COR – crude odds ratio; COVID-19 – coronavirus disease 2019; MCS – mental component summary; PCS – physical component summary; SF12v2 – 12-item short-form version 2. p<0.05 is considered to be statistically significant.

 Table 3. Multivariate logistic regression analysis for impaired health-related quality of life.

	SF12v2 N=729						
Variables	MCS		PCS				
	AOR (95%CI)	p value	AOR (95%CI)	p value			
<b>Island of residence</b> Java Island (main island) Other than Java Island			Ref. 0.71 (0.52-0.98)	Ref. <b>0.039</b>			
<b>Isolation during COVID-19 infection</b> Never infected Self-isolation Hospital			Ref. 1.31 (0.88-1.95) 5.15 (1.17-22.68)	Ref. 0.183 0.030			
Isolation during COVID-19 infection among family members Never infected Self-isolation Hospital	Ref. 0.96 (0.67-1.38) 1.64 (1.04-2.60)	Ref. 0.846 0.034					
Family member death due to COVID-19 No Yes	Ref. 1.71 (1.07-2.72)	Ref. <b>0.024</b>					

95% CI – 95% confidence interval; AOR – adjusted odds ratio; COVID-19 – coronavirus disease 2019; MCS – mental component summary; PCS – physical component summary; SF12v2 – 12-item-short-form version 2. *p*<0.05 is considered to be statistically significant.



Figure 4. OPrevalence of depression, anxiety, and stress among 718 medical students in Indonesia evaluated using 21-item Depression, Anxiety, and Stress Scale.

The univariate logistic regression analyses showed that medical students who experienced asymptomatic COVID-19 infection were more likely to have impaired MCS, as were medical students who had a family member hospitalized because of COVID-19. Regarding PCS, medical students with a history of hospitalization due to COVID-19 were more likely to have impaired PCS (**Table 2**).

The independent determinants of MCS and PCS were then analyzed using multivariate logistic regression analysis. Medical students who had a family member hospitalized (adjusted odds ratio [AOR]=1.64, P=0.034) and who died because of COVID-19 (AOR=1.71, P=0.024) were more likely to have impaired MCS. Students with a history of hospitalization were more likely to have impaired PCS (AOR=5.15, P=0.030), whereas medical students who resided outside main island were less likely to have impaired PCS (AOR=0.71, P=0.039) (**Table 3**).

### Mental Health

The median (IQR) score for depression was 8 [4-14], for anxiety it was 10 [6-16], and for stress it was 14 [8-18]. Of 718 respondents, 326 (45.4%) reported symptoms of depression, 468 (65.2%) reported symptoms of anxiety, and 437 (60.9%) reported symptoms of stress. Data on the severity of each mental health component are presented in **Figure 4**.

The univariate logistic regression analyses revealed that medical students who had a history of moderate-severe COVID-19 infection, a comorbidity, and a family member with moderate-severe COVID-19 infection were more likely to report symptoms of depression, whereas medical students who had a high GPA were less likely to report symptoms of depression. Regarding anxiety, female medical students, those who had ever undergone self-isolation, those who had moderate-severe COVID-19 infection, those who had a comorbidity, and those who had a family member who underwent self-isolation or had moderate-severe COVID-19 infection were more likely to report symptoms of anxiety. In contrast, older medical students, medical students in their clinical year, those who learned in the hybrid method, and those who had ever experienced the normal (face-to-face) teaching method before the pandemic were less likely to report symptoms of anxiety. For stress, female medical students, those who had moderate-severe COVID-19 infection, those who had a comorbidity, and those who had a family member who underwent self-isolation or had moderate-severe COVID-19 infection were more likely to report symptoms of stress. However, older medical students, medical students in their clinical year, and those who learned in the hybrid method were less likely to report symptoms of stress (Table 4).

The independent determinants of depression, stress, and anxiety were then analyzed using multivariate logistic regression analysis. Those who had a comorbidity were more likely to report symptoms of depression (AOR=1.72, P=0.009), whereas those who had high GPAs were less likely to report symptoms of depression (AOR=0.43, P=0.004). Female medical students (AOR=1.75, P=0.003) and those who had a comorbidity (AOR=2.06, P=0.003) were more likely to report symptoms of anxiety. However, medical students who learned in the hybrid method (AOR=0.67, P=0.022) and had ever experienced offline

### Table 4. Univariate logistic regression analysis for mental health problems.

	DASS-21 N=718					
Variables	Depressio	on	Anxiety		Stress	
	COR (95%CI)	<i>p</i> value	COR (95%CI)	p value	COR (95%CI)	p value
<b>Sex</b> Male Female	Ref. 1.07 (0.76-1.51)	Ref. 0.713	Ref. 1.64 (1.15-2.33)	Ref. <b>0.006</b>	Ref. 1.49 (1.06-2.11)	Ref. <b>0.023</b>
Age in years	1.03 (0.92-1.15)	0.617	0.84 (0.75-0.95)	0.003	0.89 (0.80-1.0)	0.043
<b>Island of residence</b> Java Island (main island) Other than Java Island	Ref. 0.96 (0.71-1.31)	Ref. 0.812	Ref. 1.35 (0.97-1.87)	Ref. 0.076	Ref. 1.28 (0.93-1.76)	Ref. 0.130
Status Preclinical student Clinical student	Ref. 0.82 (0.54-1.26)	Ref. 0.369	Ref. 0.60 (0.39-0.91)	Ref. 0.017	Ref. 0.59 (0.37-0.86)	Ref. <b>0.008</b>
<b>Type of university</b> Public university Private university	Ref. 0.96 (0.69-1.33)	Ref. 0.796	Ref. 1.0 (0.71-1.41)	Ref. 0.986	Ref. 0.82 (0.59-1.15)	Ref. 0.251
University accreditation Excellent Good or fair	Ref. 0.98 (0.72-1.33)	Ref. 0.880	Ref. 1.29 (0.93-1.79)	Ref. 0.123	Ref. 1.03 (0.75-1.41)	Ref. 0.843
Experience of normal teaching method before the COVID-19 pandemic No Yes	Ref. 1.11 (0.79-1.55)	Ref. 0.555	Ref. 0.59 (0.41-0.85)	Ref. <b>0.005</b>	Ref. 0.76 (0.54-1.08)	Ref. 0.125
Duration of lectures during the COVID-19 pandemic <6 h/day 6-8 h/day >8 h/day	Ref. 0.89 (0.55-1.46) 0.99 (0.58-1.70)	Ref. 0.650 0.965	Ref. 1.32 (0.80-2.17) 1.64 (0.94-2.86)	Ref. 0.279 0.085	Ref. 1.18 (0.72-1.93) 1.61 (0.93-2.80)	Ref. 0.513 0.091
Most frequently used learning methods during the COVID-19 pandemic Full online Hybrid Full offline	Ref. 0.86 (0.62-1.18) 0.76 (0.21-2.73)	Ref. 0.340 0.675	Ref. 0.64 (0.46-0.89) 1.08 (0.28-4.23)	Ref. <b>0.007</b> 0.914	Ref. 0.64 (0.46-0.88) 0.55 (0.16-1.93)	Ref. <b>0.006</b> 0.352
Grade point average during the COVID-19 pandemic <3.0/4 3-3.5/4 >3.5/4	0.63 (0.36-1.09) Ref. 0.40 (0.23-0.71)	0.099 <b>0.002</b>	0.71 (0.38-1.31) Ref. 0.58 (0.31-1.07)	0.270 0.082	0.66 (0.37-1.20) Ref. 0.59 (0.30-1.07)	0.175 0.081
<b>Isolation during COVID-19 infection</b> Never infected Self-isolation Hospital	Ref. 0.98 (0.67-1.43) 1.21 (0.47-3.09)	Ref. 0.926 0.693	Ref. 1.51 (1.00-2.28) 2.05 (0.67-6.31)	Ref. 0.049 0.211	Ref. 1.05 (0.72-1.55) 1.30 (0.48-3.52)	Ref. 0.798 0.603
<b>COVID-19 infection severity</b> Never infected Asymptomatic-mild Moderate-severe	Ref. 0.83 (0.56-1.22) 2.93 (1.20-7.18)	Ref. 0.350 <b>0.019</b>	Ref. 1.37 (0.91-2.61) 4.10 (1.21-3.92)	Ref. 0.137 <b>0.024</b>	Ref. 0.86 (0.59-1.27) 7.16 (1.67-0.76)	Ref. 0.445 <b>0.008</b>
<b>COVID-19 vaccination status</b> Unvaccinated Vaccinated	Ref. 0.68 (0.34-1.37)	Ref. 0.283	Ref. 0.93 (0.45-1.96)	Ref. 0.855	Ref. 0.88 (0.43-1.83)	Ref. 0.738

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	DASS-21 N=718					
Variables	Depression		Anxiety		Stress	
	COR (95%CI)	<i>p</i> value	COR (95%CI)	p value	COR (95%CI)	<i>p</i> value
Having one or more comorbidities No Yes	Ref. 1.86 (1.26-2.76)	Ref. <b>0.002</b>	Ref. 1.89 (1.21-2.96)	Ref. <b>0.005</b>	Ref. 1.52 (1.00-2.31)	Ref. <b>0.048</b>
Isolation during COVID-19 infection among family members Never infected Self-isolation Hospital	Ref. 1.18 (0.85-1.63) 1.44 (0.95-2.18)	Ref. 0.321 0.086	Ref. 1.79 (1.23-2.45) 1.49 (0.95-2.27)	Ref. <b>0.002</b> 0.083	Ref. 1.50 (1.08-2.10) 1.29 (0.85-1.97)	Ref. <b>0.017</b> 0.237
COVID-19 infection severity among family members Never infected Asymptomatic-mild Moderate-severe	Ref. 1.12 (0.80-1.57) 1.47 (1.01-2.14)	Ref. 0.519 <b>0.044</b>	Ref. 1.38 (0.97-1.96) 2.16 (1.43-3.27)	Ref. 0.070 <b>&lt;0.001</b>	Ref. 3.28 (1.07-10.04) 1.62 (1.10-2.40)	Ref. 0.120 <b>0.015</b>
Family member death due to COVID-19 No Yes	Ref. 1.07 (0.72-1.58)	Ref. 0.748	Ref. 1.12 (0.74-1.69)	Ref. 0.605	Ref. 1.22 (0.81-1.83)	Ref. 0.334

 Table 4 continued.
 Univariate logistic regression analysis for mental health problems.

95% CI – 95% confidence interval; COR – crude odds ratio; COVID-19 – coronavirus disease 2019; DASS-21 – 21-item Depression, Anxiety, and Stress Scale. p<0.05 is considered to be statistically significant.

classes before the pandemic (AOR=0.65, P=0.029) were less likely to report symptoms of anxiety. Female medical students (AOR=1.58, P=0.014), those who had moderate-severe COVID-19 infection (AOR=5.87, P=0.019), those who had a comorbidity (AOR=1.60, P=0.035), and those who had a family member who underwent self-isolation (AOR=1.47, P=0.031) were more likely to report symptoms of stress. In contrast, medical students who learned in the hybrid method (AOR=0.69, P=0.033) were less likely to report symptoms of stress (**Table 5**).

## Discussion

Our study showed that among 729 Indonesian medicals students, 272 (37.3%) had impaired physical component and 488 (66.9%) had impaired mental component of HRQoL. All respondents had impairment in the PF health domain and 89% of respondents also had impairment in the RE health domain. The determinants of HRQoL in this study were medical students' island of residence, history of hospitalization, and family member's hospitalization and death due to COVID-19. Concerning mental health, 326 (45.4%) reported symptoms of depression, 468 (65.2%) reported symptoms of anxiety, and 437 (60.9%) reported symptoms of stress. Sex, study method, grade, previous COVID-19 disease severity, comorbidities, previous learning experience, and history of family isolation were identified as determinants of mental health problems. Previous studies conducted in India and Brazil also reported that medical students have lower levels of HROoL during the COVID-19 pandemic [26,27]. The deleterious effects of COVID-19 on the HROoL of medical students in other countries are similar to the Indonesian circumstances. However, a previous study in Indonesia reported that low HRQoL, either in physical or psychological components, was only observed in a minority of the respondents [17]. The discrepancy from our findings might be caused by difference in study period, as the previous study was conducted in the earlier period of the pandemic (June-November 2020), when the number of cases and mortality rates were still relative low [28], whereas our study was conducted after the peak of the second wave [18,19]. The discrepancy in findings might also be due to the difference in the instruments used to assess the HRQoL. In the present study, we used SF12v2, while the previous study used a different instrument.

Our analysis revealed that residing on the main island was an independent risk factor for the HRQoL of medical students. Consistent with a previous study, medical students who lived in rural areas showed better HRQoL than those living in urban areas, especially for the physical health component [26]. During COVID-19 home quarantine, decreased physical activity and higher screen time or internet usage appeared to be the influential factors contributing to lower HRQoL in urban areas [29]. Moreover, the impacts of COVID-19 in rural areas are still low, as the transmission of COVID-19 in sparsely

#### Table 5. Multivariate logistic regression analysis for mental health problems.

	DASS-21 N=718						
Variables	Depression		Anxiety		Stress		
	AOR (95%CI)	p value	AOR (95%CI)	<i>p</i> value	AOR (95%CI)	p value	
<b>Sex</b> Male Female			Ref. 1.75 (1.21-2.54)	Ref. <b>0.003</b>	Ref. 1.58 (1.10-2.26)	Ref. <b>0.014</b>	
Experience of normal teaching method before the COVID-19 pandemic No Yes			Ref. 0.65 (0.44-0.96)	Ref. <b>0.029</b>			
Most frequently used learning methods during the COVID-19 pandemic Full online Hybrid Full offline			Ref. 0.67 (0.48-0.94) 0.80 (0.19-3.39)	Ref. 0.022 0.763	Ref. 0.69 (0.49-0.97) 0.41(0.11-1.57)	Ref. 0.033 0.191	
Grade point average during COVID-19 pandemic <3.0/4 3-3.5/4 >3.5/4	0.65 (0.37-1.14) Ref. 0.43 (0.24-0.76)	0.133 <b>0.004</b>					
<b>COVID-19 infection severity</b> Never infected Asymptomatic-mild Moderate-severe					Ref. 0.83 (0.55-1.25) 5.87 (1.33-25.88)	Ref. 0.372 <b>0.019</b>	
Having one or more comorbidities No Yes	Ref. 1.72 (1.15-2.57)	Ref. <b>0.009</b>	Ref. 2.06 (1.29-3.29)	Ref. <b>0.003</b>	Ref. 1.60 (1.03-2.47)	Ref. <b>0.035</b>	
Isolation during COVID-19 infection among family members Never infected Self-isolation Hospital					Ref. 1.47 (1.04-2.09) 1.26 (0.81-1.98)	Ref. <b>0.031</b> 0.308	

95% CI – 95% confidence interval; AOR – adjusted odds ratio; COVID-19 – coronavirus disease 2019; DASS-21 – 21-item Depression, Anxiety, and Stress Scale. p<0.05 is considered to be statistically significant.

populated areas is much lower than that in urban areas, and, living close to nature could regenerate the senses and mind, which can improve HRQoL [30,31].

In this study, we found that medical students with a history of hospitalization due to COVID-19 had lower HRQoL. A previous study conducted in Bangladesh also found that patients hospitalized because of COVID-19 had significantly lower HRQoL [32]. Their physical components were also affected, such as difficulty in walking and lifting and carrying things, which are commonly found in hospitalized patients [33]. Additionally, persistence of symptoms, delayed recovery, and stress response in hospitalized patients also increase the risk of distress [32,34]. Experiences of close contact with patients with COVID-19, especially family, could potentially decrease HRQoL because of high rates of depression and fatigue [34]. Moreover, young people had a higher risk of negative psychological conditions caused by the restriction of social activities during the COVID-19 pandemic [35]. This finding was consistent with our study, which showed that medical students whose family members had COVID-19 had lower MCS. The fear of getting infected increased their anxiety and frustration, and the hospitalized family also induced worries and disrupted their concentration [36,37]. Facing the death of family members due to COVID-19 altered the self-efficacy and coping mechanisms of the medical students because the family member was the first-line support and the loss of their presence placed them in more stressful and frustrating situations [38,39].

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The prevalence of depression, anxiety, and stress in our study were 45.4%, 65.2%, and 60.9%, respectively. The prevalence was higher than in previous studies. A study in India reported that the prevalences of depression, anxiety, and stress among undergraduate medical students during the COVID-19 pandemic were 33.5%, 33.2%, and 24.9%, respectively [13]. In a recent systematic review and meta-analysis, the pooled prevalence of depression and anxiety among medical students during the COVID-19 pandemic was 37.9% and 33.7%, respectively [8]. There are 3 previous studies from Indonesia that also evaluated the prevalence of mental health problems among medical students where the DASS-21 was also used as the study instrument; the prevalence of depression, anxiety, and stress was 13.5-18.6%, 15-48.1%, and 7.5-44.6%, respectively [17,30,40]. One of the possible explanations of the high prevalence in our study is because we collected the data shortly after Indonesia faced the peak of the second wave, which was caused by the Delta variant outbreak, and which placed Indonesia as the epicentrum of the pandemic in Asia [18,19].

Our analysis revealed that female gender was a significant independent predictor of anxiety and stress among medical students, which agrees with previous findings in the United Arab Emirates [41], France [42], and Morocco [43]. A worldwide cross-sectional study conducted in the general population has also consistently shown that women had more anxiety than men [44]. Additionally, it is stated that women are twice more likely to develop stress- and anxiety-related psychiatric disorders than men. Men and women have different fear and stress mechanisms because of hormonal influences [45]. Generally, the COVID-19 pandemic has in fact increased the incidence of mental health disorders significantly and being female is one of the risk factors. However, female gender is not the primary risk factor, as other variables such as personality type, lifestyle, and coping mechanisms also influence the levels of depression, anxiety, and stress [46-48].

We found that students with previous moderate or severe COVID-19 infection were more likely to exhibit depressive and stress symptoms than those who had never had the disease. Irrespective of being medical students, previous studies on general COVID-19 survivors have shown a high prevalence of psychiatric sequelae, including posttraumatic stress disorder, major depression, and anxiety [49,50]. Immunological responses to the infection and psychological factors, such as stigma, social isolation, concerns of infecting others, and mental impact due to a novel potentially fatal disease, might contribute to the development of post-COVID-19 psychiatric consequences [49]. Our results also showed that the presence of COVID-19-related medical comorbidities was highly associated with depression, anxiety, and stress. People with existing chronic illnesses were found to have poorer mental health during the COVID-19 pandemic. This association might be caused by the

fact that individuals with comorbidities are more vulnerable to death due to COVID-19 and thus would likely have higher rates of psychiatric symptoms [51]. Our study also showed that some students with a family history of isolation were more susceptible to stress than those without a family history of isolation. Education level was considered to be related to the level of stress, which was higher among university students because of their capability of understanding the risk of SARS-CoV-2 infection and being more cautious of their surroundings [52]. Furthermore, some individuals, including students, were reported to have fears of getting infected from their family members who tested positive for COVID-19 and were extremely concerned about their own health, especially if they experienced any signs and/or symptoms related to any specific diseases during the associated pandemic [53]. The latter statement also well strengthened our finding that students' stress was not significantly increased when the family members who tested positive for COVID-19 had their isolation periods in the hospital. When a family member was diagnosed with COVID-19, there were also some potential disruptions in the family relationship, routines, and rituals, which might further elevate the level of stress of the other family members [54].

In our study, lower rates of anxiety and stress were found in students who had experienced offline classes and had undergone the hybrid or blended learning method during the COVID-19 pandemic. A longer offline learning experience decreased the level of anxiety and stress among the medical students, as there were still more achievable clinical skills than those obtained with full online learning methods [55,56]. Our finding was also affected by the participants as our study sample was predominated by preclinical than clinical students, implying that preclinical students still did not understand the importance of offline classes compared with clinical students who require more offline clinical skill development rather than just discussing it online and will soon become professional medical health teams in the field [56-58]. Additionally, hybrid learning methods were likely to improve self-directed learning of the students as they had more time to learn medical skills and theory [58]. Consistent with our findings, a previous study also reported that students with lower GPAs were more likely to be depressed [59]. Thus, hybrid learning methods might decrease the levels of depression, anxiety, and stress, as there was more time for self-learning in the middle of having offline classes.

Depression is tightly associated with obesity, a phenomenon that was recently introduced as depreobesity (depression in the context of obesity) [60]. During the COVID-19 pandemic, previous studies have shown that depression is more prevalent in people with weight gain than in people with weight loss [61,62]. Compared to old individuals, young individuals are more likely to have increased bodyweight during the COVID-19 pandemic [63], possibly because of the unhealthy eating behaviors to cope with the pandemic, which is common among young people [64]. If no intervention is offered, especially among young people, including medical students, an upcoming epidemic of depreobesity can be expected in the near future [60,65].

This study has 3 important limitations to consider. First, the cross-sectional nature of the study precludes any causal inference or evaluation of longitudinal changes in HRQoL and mental health problems during the COVID-19 pandemic. Second, both instruments used in this study - DASS-21 to evaluate mental health and SF12v2 to evaluate HROoL – are self-reported questionnaires; thus, this may under- or overestimate the prevalence of impaired HRQoL and mental health problems, and may not concur with objective assessment by health professionals. Third, as snowball sampling was used to recruit the respondents, this study was prone to selection bias, as only those with internet access and spare time were able to participate in this study. In addition, although the number of respondents in this study surpassed the minimum required number, the number of respondents was still small compared to the total number of medical students in Indonesia. Therefore, generalization of study findings to all medical students in Indonesia should be done cautiously.

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# Conclusions

This study of Indonesian medical students during the COVID-19 pandemic supports the findings from other studies on the adverse effects on HRQoL and mental health. The results identified key associations, including SARS-CoV-2 infection and comorbidities experienced by the students, the health of their families, including grief following bereavement, and the effects of social isolation during the pandemic. As medical students are essential for advancing the country's health system and become the core of health services, we recommend that higher-learning institutions in Indonesia, in collaboration with the government, provide psychological assistance to medical students, especially to those who are at higher risk.

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#### **Declaration of Figures' Authenticity**

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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