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International Difference of Tobacco Related COVID-19 Severity

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This study aimed to analyze the correlation between smoking and coronavirus disease 2019 (COVID-19) severity by region and gross domestic product (GDP). The regions were categorized by continent and GDP rankings. Studies conducted between June 3, 2020 and March 27, 2023 were searched to compare the severity of COVID-19 between smokers and non-smokers according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. Compared with never-smokers, the smokers' COVID-19 severity scores were 1.48 (confidence interval [CI]: 1.25-1.75) in Asia, 1.24 (CI: 1.05-1.46) in the Middle East, 1.32 (1.21-1.45) in Europe, 1.39 (1.30-1.49) in North America, 1.69 (1.22-2.34) in South America, and 2.87 (1.82-4.53) in Africa. By GDP, the smokers' COVID-19 severity scores were higher than those of never-smokers: 1.42 (1.32-1.53) in high-GDP countries, 1.33 (1.25-1.41) in middle-GDP countries (11th-50th), and 1.53 (0.85-2.76) in low-GDP countries. The COVID-19 severity in smokers was significantly higher in low-GDP countries than in high- and middle-income countries. The high COVID-19 death rate among smokers in the African continent and low-GDP countries is thought to stem from the lack of medical management systems compared with other countries. In addition to medical treatment, environmental or socioeconomic factors can increase the severity.

Keywords: Cigarette smoking, COVID-19, Socioeconomic factor

Introduction

Coronavirus disease 2019 (COVID-19) has affected more than 700 million people, resulting in more than 6.9 million deaths worldwide [1]. Based on previous studies, the risk factors for developing COVID-19 encompass demographic factors (such as old age, male sex, and ethnicity) and the presence of underlying diseases (such as cardiovascular diseases, hypertension, and chronic obstructive pulmonary disease [COPD]) [2]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection may initially progress without symptoms, but can subsequently trigger manifestations including fever, cough, shortness of breath, severe pneumonia, dyspnea, organ dysfunction, and even death [3,4]. Individuals with comorbidities such as hypertension, diabetes, or older age have a poorer prognosis [5]. A previous study established age as the strongest determinant of mortality risk, with a more than 30-fold difference between the oldest and youngest groups. Moreover, smoking and obesity are associated with a higher mortality risk [6].

The World Health Organization (WHO) has reported approximately 1.1 billion current cigarette smokers worldwide [7]. The global prevalence of cigarette smoking among women has increased in recent years, posing a significant public health concern [8]. Smoking is one of the most prevalent causes of death

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due to non-communicable diseases [9].

Several studies have explored the correlation between smoking and COVID-19 severity, yielding inconsistent results. One study showed no significant difference between smoking rates and mortality from COVID-19 (p = 0.21) [10]. Zhang et al. [11] observed that among the participants in the severe COVID-19 outcome group, 3.4% were current smokers, and 6.9% were former smokers (n = 58). In the non-severe patient group (n = 82), none were current smokers, while 3.7% were former smokers (odds ratio: 2.23, 95% confidence interval [CI]: 0.65-7.63; p = 0.2). Huang et al. [12] found no significant differences between the intensive care unit (ICU) and non-ICU groups (p = 0.31). Another meta-analysis did not find an association between current smoking status and disease severity [13].

A few studies have analyzed the correlation between smoking and COVID-19 severity by region. One study showed that the severity of COVID-19 differs in various geographical locations, with mortality rates of 0.7 deaths per 100,000 in South Korea and 86.8 per 100,000 in Belgium [14]. Another study found that countries with a high prevalence of male smokers had low COVID-19 mortality and SARS-CoV-2 infection rates within each continent, implying a potential protective effect of active smoking against COVID-19. From the results of this study, COVID-19 mortality was reported in 13 (5-24) per million inhabitants in countries with a male smoking rate of > 45% and 33 (4-133) per million inhabitants in countries with a male smoking rate of < 25% [15].

As a result, the relationship between COVID-19 severity and smoking and the differences between regions remain unclear. This study aimed to analyze the correlation between smoking and COVID-19 severity by region and gross domestic product (GDP). The regions were categorized according to continent and GDP rankings.

Methods

Search strategy and selection criteria

A systematic literature survey was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The PubMed, Cochrane Library, and Embase databases were searched to find studies published between June 3, 2020, and March 27, 2023. The search terms used were COVID-19, smoking, and synonyms.

(1) Clinical trials, observational studies, and randomized controlled trials, including published or unpublished studies;
(2) studies published in English; (3) in vivo studies; (4) stud-

ies conducted in patients infected with coronavirus; (5) studies conducted among smokers; (6) studies that examined non-smoking patients; and (7) studies that reported the mortality rates, severe outcomes, hospitalization rates, or the use of oxygen supply were included in the final analysis. Patients without available data were excluded.

Randomized and observational studies reporting the smoking status of COVID-19 patients with different degrees of COVID-19 severity and studies examining individuals using all types of smoke, such as cigarettes, tobacco, or e-cigarettes, were also included in this study.

The literature search, study identification, and data extraction were performed between March 2023 and July 2023. Disagreements were resolved through discussion with all reviewers. The relevant data were extracted by one reviewer using the prepared form and verified for accuracy by another reviewer. The data extracted from the eligible studies included participant characteristics, sample sizes, study designs, data collection period, comorbidities, race, country, participant's age, underlying diseases, type of cigarette used, and criteria for determining severe outcomes.

The clinical endpoints in our study were death, ICU admission, O_2 level, and ventilation outcome. Studies reporting other diseases or topics, reviews, editorials, and nonclinical studies were excluded.

After the initial screening, the four authors independently reviewed the titles and abstracts, and a second screening was conducted by reviewing the full-text records. All discrepancies were resolved by six authors.

Data analysis

A meta-analysis was performed using SPSS Statistic 27.0 (IBM Corp., Chicago, Illinois, USA), and statistical significance was defined as a two-sided p-value of < 0.05. The pooled effects were calculated using fixed- and random-effects models. Statistical heterogeneity among the included studies was assessed using an χ^2 test and a Higgins I² value, with an I² value of > 75% suggesting high statistical heterogeneity. Publication bias was assessed using funnel plots.

Results

The initial search yielded 5,309 studies, of which 1,114 were unique articles. After screening the titles and abstracts of the remaining 1,114 studies, the full text of 140 articles was reviewed. Overall, 140 studies met the inclusion criteria (Fig. 1). The 140 included studies were conducted in COVID-19 patients, of



Fig. 1. Flow chart for the process of selecting eligible publications.

whom 16,121,336 reported any smoking history. Among these patients, 5,608,207 were smokers, while 10,513,129 were non-smokers.

A total of 59 multicenter studies (12 prospective cohort, 37 retrospective cohort, 8 cross-sectional, and 2 case-control studies) and 81 single-center studies (14 prospective cohort, 49 retrospective cohort, 14 cross-sectional, 3 case-control, and 1 randomized control trial) were analyzed. We evaluated the effect of smoking on the rates of COVID-19, death, ICU admission, and O_2 and ventilation use.

Continent

The results were compared by continent. A total of 29 studies performed in Asia evaluated the rates of death, ICU admission, and O_2 or ventilation use between smokers (current or former) and never-smokers (Fig. 2A). Similarly, 30 studies conducted in the Middle East (Fig. 2B), 36 in Europe (Fig. 2C), 25 in North America (Fig. 2D), 9 in South America (Fig.

GDP

The results were compared based on the national GDP. A total of 59 studies were performed in high-GDP income (1st-10th GDP) countries (Fig. 3A), 52 in middle-GDP countries (11th-50th) (Fig. 3B), and 12 in low-GDP countries (GDP 51th and below) (Fig. 3C). The COVID-19 severity in smokers was significantly higher in low-GDP countries than high-and middle-income countries.

Discussion

The COVID-19 severity among smokers differs by region and national income. When region is classified by continent, the COVID-19 severity scores of ever-smokers were 1.48 (CI: 1.25–1.75) in Asia, 1.24 (CI: 1.05–1.46) in the Middle East, 1.32 (1.21–1.45) in Europe, 1.39 (1.30–1.49) in North America, 1.69 (1.22–2.34) in South America, and 2.87 (1.82–4.53) in Africa compared with never-smokers. Meanwhile, the COVID-19 severity was lower in Middle Eastern countries but higher in African countries. The high prevalence of smokeless (chewing) tobacco and waterpipe smoking in the Middle Eastern countries [16]. Conversely, the increasing prevalence of smoking due to the low tobacco tax could explain the higher severity in the African continent [17].

COVID severity in smokers differed according to the GDP ranking. The smokers' COVID-19 severity scores were higher compared with never-smokers: 1.42 (1.32–1.53) in high-GDP countries, 1.33 (1.25–1.41) in middle-GDP countries (11th–50th), and 1.53 (0.85–2.76) in low-GDP countries. The COVID-19 severity among smokers was significantly higher in low-GDP countries than in high- and middle-income countries.

This study suggests that smoking increases the severity of COVID-19, with minimal disparity observed between continental and national GDP levels. To date, several studies have demonstrated the risk of respiratory infections from smoking. For instance, smokers are more susceptible to respiratory infections, such as invasive pneumococcal disease [18], community-acquired pneumonia [19], influenza [20], and common colds [21]. Smoking has significant effects on the respiratory tract, immune system, skin, and soft tissues, both locally and systemically. These effects can influence susceptibil-

	Study	Experi Events	mental Total	Events	Control Total	Risk Ratio	RR	95%-CI	Weight
	Rui 2021	2	17	6	74		1 4 5 1	10 320: 6 5751	10%
	Akiyama 2022	397	7672	427	10312	+	1 250	[1 094: 1 428]	5 3%
	Vumi 2022	215	6038	103	8107		1 3 16	[1 087: 1 50/]	5 1%
	Vue 2022	215	30	40	549		2 1 1 2	[0.054: 4.672]	2.5%
	Fang 2022	109	172	250	1216		0.990	[0.799: 1.002]	5 496
	Faily 2022	100	701	009	5000	10 March 10	0.009	[0.700; 1.003]	1.470
	They 2022	40	/91	203	5098	Time	0.900	[0.709, 1.300]	4.0%
	21100 2021	12	20	24	83		2.075	[1.209, 3.393]	3.8%
	Tugade 2023	2	20	21	146		0.695	[0.1/6; 2./44]	1.2%
	Yamini 2022	3	4	45	196		3.267	[1.755; 6.080]	3.2%
	Islam 2021	1	59	4	268		1.136	[0.129; 9.977]	0.5%
	Kittu 2022	18	63	17	357		6.000	[3.272; 11.002]	3.2%
	Cen 2020	16	88	206	919		0.811	[0.512; 1.284]	3.9%
	Wang 2020	4	11	7	45		2.338	[0.829; 6.591]	1.8%
	Hu 2020	22	38	124	285		1.331	[0.984; 1.799]	4.7%
	Zheng 2020	2	8	28	65		0.580	[0.169; 1.990]	1.4%
	Ni 2021	72	123	454	710		0.915	[0.781; 1.073]	5.3%
	Zhan 2020	25	46	123	359	-	1.586	[1.174: 2.144]	4.7%
	Chen 2020	25	111	183	1748	· · · ·	2.151	[1.484: 3.119]	4.4%
	Ye 2021	10	29	34	167		1.694	[0.944: 3.039]	3.3%
	7hou 2022	20	223	9	38		0.379	IO 187 0 7681	2.8%
	Tomoki 2022	42	57	27	60		1 637	[1 189: 2 255]	4.6%
	Mohsin 2021	147	567	153	933	一番	1 581	[1 293: 1 933]	5 1%
	Wang 2020	14/	507	20	50		1.501	[1.255, 1.555]	5 104
	Schoren 2022	9	9	32	50		0.556	[1.200, 1.900]	1.60/
	Saberon 2022	4	00	9	15		0.000		1.0%
	Kishaba 2020	0	3	3	4		0.184	[0.013, 2.500]	0.4%
	Fumihiro 2022	35	11	15	64	1	1.939	[1.169; 3.216]	3.7%
	Misako 2023	334	570	88	380	1 100	2.530	[2.081; 3.077]	5.1%
	Mohsin 2021	121	594	182	1428		1.598	[1.297; 1.970]	5.1%
	Kumar 2021	16	18	2	22		9.778	[2.582; 37.024]	1.2%
	Random effects model		18427		33848	\$	1.478	[1.248; 1.750]	100.0%
	Heterogeneity: $l^2 = 86\% \tau^2$	= 0.1347	p < 0.0	1					
						0.1 0.51 2 10			
3)		Experi	mental		Control				
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	Study	Evenus	Total	Events	lotal	RISK Ratio	RR	95%-C	l Weight
	Study	Events	Total	Events	Total	RISK Ratio	RR	95%-C	l Weight
	Meisam 2022	events 2	Total 52	Events 45	413		0.353	95%-C [0.088; 1.413	Weight] 1.1%
	Meisam 2022 Ebrahim 2022	2 3	Total 52 4	45 12	413 46		0.353 2.875	95%-C 0.088; 1.413 1.363; 6.063	I Weight] 1.1%] 2.5%
	Meisam 2022 Ebrahim 2022 Imad 2021	2 3 30	Total 52 4 110	45 12 85	413 46 145		0.353 2.875 0.465	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650]	I Weight] 1.1%] 2.5%] 4.1%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022	2 3 30 12	Total 52 4 110 35	45 12 85 80	413 46 145 159		0.353 2.875 0.465 0.681	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106]	I Weight 1.1% 2.5% 4.1% 3.5%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021	2 3 30 12 18	Total 52 4 110 35 33	45 12 85 80 40	413 46 145 159 150		0.353 2.875 0.465 0.681 2.045	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080	Weight 1.1% 2.5% 4.1% 3.5% 3.8%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022	2 3 30 12 18 713	52 4 110 35 33 2986	45 12 85 80 40 1611	413 46 145 159 150 7081		RR 0.353 2.875 0.465 0.681 2.045 1.050	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134	1.1% 2.5% 4.1% 3.5% 3.8% 5.0%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022	2 3 30 12 18 713 104	Total 52 4 110 35 33 2986 134	45 12 85 80 40 1611 59	413 46 145 159 150 7081 98		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551	1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022	2 3 30 12 18 713 104 29	Total 52 4 110 35 33 2986 134 43	45 12 85 80 40 1611 59 78	413 46 145 159 150 7081 98 81		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023	2 3 30 12 18 713 104 29 3532	Total 52 4 110 35 33 2986 134 43 34213	45 12 85 80 40 1611 59 78 10556	413 46 145 159 150 7081 98 81 146546		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433	95%-C 0.088; 1.413 1.363; 6.063 0.333; 0.650 0.420; 1.106 1.359; 3.080 0.972; 1.134 0.972; 1.51 0.567; 0.866 1.389; 1.486	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022	2 3 30 12 18 713 104 29 3532 40	Total 52 4 110 35 33 2986 134 43 34213 298	45 12 85 80 40 1611 59 78 10556 98	413 46 145 159 150 7081 98 81 146546 420		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641	95%-C 0.088; 1.413 1.363; 6.063 0.333; 0.650 0.420; 1.106 1.359; 3.080 0.972; 1.134 1.072; 1.551 0.567; 0.866 1.382; 1.486 1.482	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.4%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yaðid 2022	2 3 30 12 18 713 104 29 3532 49 19	Total 52 4 110 35 33 2986 134 43 34213 128 52	45 12 85 80 40 1611 59 78 10556 98	413 46 145 159 150 7081 98 81 146546 420 68		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.382; 1.486 [1.240; 2.171] [1.834; 11.620	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.4% 1.9%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağıc 2022 Amanat 2021	2 3 30 12 18 713 104 29 3532 49 18	Total 52 4 110 35 33 2986 134 43 34213 34213 128 53 127	45 12 85 80 40 1611 59 78 10556 98 5 220	413 46 145 159 150 7081 98 81 146546 420 68 736		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.634 [1.245; 1.675	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.6% 1.9%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Yağcı 2022 Amanat 2021 Abdule alam 2022	2 3 30 12 18 713 104 29 3532 49 18 60	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7	45 12 85 80 40 1611 59 78 10556 98 5 239 60	413 46 145 159 150 7081 98 81 146546 420 68 736 94		RR 0.353 2.875 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.674	95%-C 0.088; 1.413 1.363; 6.063 0.420; 1.106 1.359; 3.080 0.972; 1.134 1.072; 1.551 0.557; 0.866 1.382; 1.486 1.240; 2.171 1.834; 11.630 1.086; 1.672 1.824 1.834; 11.630 1.086; 1.672 1.834 1.834; 11.630 1.834; 11.630; 11.630 1.834; 11.630 1.834; 11.630 1.834; 11.630; 11.	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.6% 1.9% 2.1%
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	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022	2 3 30 12 18 713 104 29 3532 49 18 60 3 190	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436	413 46 145 159 150 7081 98 81 146546 420 68 736 94 678		RR 0.353 2.875 0.465 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [0.420]	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 5.0% 4.6% 1.9% 4.6% 2.1%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022	2 3 30 12 18 713 104 29 3532 49 18 60 0 3 190 21	Total 52 4 110 35 33 2986 134 43 34213 137 7 342 291	45 122 85 80 40 1611 59 78 10556 98 5 239 60 436 24	413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443		RR 0.353 2.875 0.681 2.045 1.209 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 1.9% 2.1% 3.1%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağıc 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022	2 3 30 12 18 713 104 29 3532 49 18 60 3 190 3 12 0 21 0	Total 52 4 1100 35 33 2986 134 43 34213 128 53 137 7 342 291 4	45 12 85 80 40 1611 599 78 10556 98 5 239 60 436 24 31	413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 61 -		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217	95%-C 0.088; 1.413 1.363; 6.063 0.420; 1.106 1.359; 3.080 0.972; 1.134 1.072; 1.551 0.567; 0.866 1.382; 1.486 1.240; 2.171 1.834; 11.630 (1.086; 1.675 0.282; 1.601 1.074; 0.965 2.449; 7.687 0.016; 2.994	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 1.9% 4.6% 2.1% 4.9% 3.1% 0.4%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022	2 3 30 12 18 713 104 29 3532 49 3532 49 18 60 3 190 21 0 77	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342 291 4 521	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 436 24 31 61	413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 678 1443 678		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921	95%-C 0.088; 1.413 1.363; 6.063 0.333; 0.650 0.420; 1.106 1.359; 3.080 0.972; 1.134 1.072; 1.551 0.567; 0.866 1.382; 1.486 1.240; 2.171 1.834; 11.630 1.086; 1.675 0.282; 1.601 0.774; 0.965 12.449; 7.687 10.016; 2.994 10.676; 1.254	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.4% 1.9% 4.6% 1.9% 4.6% 3.1% 0.4% 4.3%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021	2 3 30 12 18 713 104 29 3532 49 3532 49 3532 49 3532 190 21 0 77 76	Total 52 4 110 35 33 2986 134 43 34213 137 7 342 291 4 521 77	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222	413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 04 678 1443 61 - 380 259		RR 0.353 2.875 0.465 0.681 2.045 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.271 0.921 0.242	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.156; 0.376	Weight 1.1% 2.5% 4.1% 3.5% 5.0% 4.7% 4.6% 5.0% 4.6% 2.1% 4.6% 3.1% 4.9% 3.1% 3.7%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Abbas 2022 Surme 2021 Ayhan 2021	2 3 30 12 18 713 104 29 3532 49 3532 49 18 60 3 3 190 21 0 77 16 6	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342 291 4 521 77 77 716	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5	413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 617 380 259 40		RR 0.353 2.875 0.465 0.681 2.045 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.242 3.000	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.1711 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.165; 8.450	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 1.9% 2.1% 3.1% 0.4% 3.7% 3.7%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020	2 3 30 12 18 713 104 29 3532 49 18 60 3 190 21 0 777 16 6 56	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342 291 4 521 77 166 197	45 12 85 80 40 1611 59 98 5 239 60 436 24 31 61 222 5 35	413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 61 - 380 259 40 368		RR 0.353 2.875 0.465 0.681 2.045 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.921 0.921 0.929	95%-C 0.088; 1.413 1.363; 6.063 0.333; 0.650 0.420; 1.106 1.359; 3.0800 0.972; 1.134 1.072; 1.551 10.567; 0.866 1.382; 1.486 1.240; 2.171 1.834; 11.630 1.086; 1.675 0.282; 1.601 10.776; 0.965 2.449; 7.687 0.016; 2.994 10.676; 1.254 10.65; 8.450 1.055; 8.450 1.203; 4.394	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.4% 1.9% 2.1% 3.1% 0.4% 3.7% 1.7% 3.9%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abbhamr 2020	2 3 30 12 18 713 104 29 3532 49 3532 49 18 60 3 190 21 0 77 16 6 56 16	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 3422 291 4 521 77 16 197 65	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 436 436 436 436 5 222 5 355 2 355 2 355 2	413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 678 678 64 678 1443 61 678 1443 61 380 259 40 368 43		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.242 3.000 2.989 5.292	95%-C 0.088; 1.413 1.363; 6.063 0.420; 1.106 1.359; 3.080 0.420; 1.106 1.359; 3.080 0.972; 1.134 1.072; 1.551 0.567; 0.866 1.382; 1.486 1.240; 2.171 1.834; 11.630 1.086; 1.675 0.282; 1.601 0.774; 0.965 12.449; 7.687 10.016; 2.994 10.676; 1.254 10.156; 0.376 1.065; 8.450 1.023; 4.394 1.281; 21.864	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.7% 3.8% 5.0% 4.6% 1.9% 4.6% 1.9% 4.6% 1.9% 3.1% 0.4% 3.7% 3.7% 3.9% 1.1%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020	2 3 30 12 18 713 104 29 3532 49 3532 49 3532 49 3532 49 18 60 3 190 21 0 0 777 16 6 566 16 11	Total 52 4 110 35 33 2986 134 43 34213 137 7 342 291 4 521 77 16 197 65 14	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 2 78	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 04 678 1443 61 - 380 259 40 368 43 109		RR 0.353 2.875 0.465 0.681 2.045 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.242 3.000 2.989 5.292 1.098	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.65; 8.450 [2.033; 4.394 [1.281; 21.864 [1.281; 21.864	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.6% 2.1% 4.6% 3.1% 4.9% 3.1% 4.3% 3.7% 1.7% 3.9% 1.1% 4.3%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020	2 3 30 12 18 713 104 29 3532 49 3532 49 18 60 3 3 190 21 0 777 16 6 56 16 11 107	Total 52 4 110 35 33 2986 133 4213 34213 128 53 137 7 342 291 4 521 77 16 197 65 14 160	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 2 78 245	413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 61 - 380 259 40 368 43 109 608		RR 0.353 2.875 0.465 0.681 2.045 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.242 3.000 2.989 5.292 1.098 1.669	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.165; 8.450 [2.033; 4.394 [1.281; 21.864 [1.281; 21.864 [1.281; 21.864 [0.815; 1.479	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 1.9% 2.1% 3.1% 0.4% 3.7% 3.7% 1.7% 3.9% 1.1% 4.3% 4.3% 4.3% 4.3% 4.3% 4.3% 4.3%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020 Abohamr 2020 Eliesar 2022	2 3 30 12 18 713 104 29 3532 49 3532 49 18 60 3 3 190 21 0 77 16 6 56 16 11 11 27 2	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342 291 4 521 77 16 197 65 14 160 437	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 25 35 2 35 2 278 245 5 56	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 61 - 380 259 40 368 43 109 608 615		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.921 0.921 0.922 3.000 2.989 5.292 1.098 1.660 0.579	95%-C 0.088; 1.413 1.363; 6.063 0.333; 0.650 0.420; 1.106 1.359; 3.080 0.972; 1.134 1.072; 1.551 0.567; 0.866 1.382; 1.486 1.240; 2.171 1.834; 11.630 1.086; 1.675 0.282; 1.601 0.774; 0.965 2.449; 7.687 0.016; 2.994 1.056; 8.450 1.056; 8.450 1.033; 4.394 1.281; 21.864 0.815; 1.479 1.434; 1.920 1.381; 0.924 1.381; 0.925; 0.924 1.381; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925; 0.925;	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 5.0% 4.6% 1.9% 4.6% 2.1% 3.1% 0.4% 3.1% 1.1% 3.1% 1.1% 3.1% 1.1% 3.1% 3.1% 3.1% 3.1% 3.1% 3.1% 3.1% 3.1% 3.1% 3.1% 3.1% 3.1% 3.5%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Addulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020 Abohamr 2020 Elissar 2022 Kofabi 2022	2 3 30 12 18 713 104 29 3532 49 18 60 3 190 21 0 77 16 6 56 16 11 107 23 374	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342 291 4 521 77 16 197 65 14 160 437 282	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 2 78 245 5 2 78	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 678 1443 678 1443 678 1443 61 259 40 368 43 109 608 615 51796		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.242 3.000 2.989 5.292 1.098 1.660 0.575	95%-C 0.088; 1.413 0.33; 0.650 0.420; 1.106 1.359; 3.080 0.972; 1.134 1.072; 1.551 0.567; 0.866 1.382; 1.486 1.240; 2.171 1.834; 11.630 1.086; 1.675 0.282; 1.601 1.076; 1.254 1.0.676; 1.254 1.0.676; 1.254 1.0.65; 8.450 1.065; 8.450 1.065; 8.450 1.0815; 1.479 1.434; 1.920 1.434; 1.920 1.4	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 5.0% 4.7% 5.0% 4.7% 3.8% 5.0% 4.7% 3.8% 5.0% 4.7% 3.1% 0.4% 3.1% 0.4% 1.7% 3.7% 1.1% 3.9% 1.1% 4.8% 3.5%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020 Abohamr 2020 Elissar 2022 Kofahi 2022	2 3 30 12 18 713 104 29 3532 49 3532 49 3532 49 3532 49 18 60 3 190 21 0 0 777 16 6 566 16 11 107 23 77	Total 52 4 110 35 33 2986 134 43 34213 137 7 342 291 4 521 77 16 197 65 144 160 437 362	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 22 78 245 56 408	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 61 - 380 259 40 368 43 109 608 615 1786		RR 0.353 2.875 0.465 0.681 2.045 1.050 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.242 3.000 2.989 5.292 1.098 1.660 0.578 0.657	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.65; 8.450 [2.033; 4.394 [1.281; 21.864 [0.815; 1.479 [1.434; 1.920 [0.361; 0.924 [0.685; 1.076	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 2.1% 4.6% 3.1% 4.6% 3.1% 4.3% 3.7% 1.7% 3.9% 1.7% 3.9% 1.1% 4.8% 3.5% 4.6% 3.7% 4.8% 3.5% 4.6%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020 Abohamr 2020 Elissar 2022 Kofahi 2022 Golnar 2022	2 3 30 12 18 713 104 29 3532 49 18 60 3 3 190 21 0 777 16 6 56 16 11 107 23 71	Total 52 4 110 35 33 2986 4 34213 34213 34213 128 53 137 7 342 291 4 521 77 16 197 65 14 160 437 362 13	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 2 2 78 245 56 408 80 436 24 35 25 35 25 80 40 40 1611 59 78 50 80 40 1611 59 78 50 80 40 1611 59 78 50 80 78 50 80 98 50 78 50 50 78 50 78 50 78 50 78 50 78 50 78 50 78 50 78 50 78 78 78 78 78 78 78 78 78 78 78 78 78	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 61 - 380 259 40 368 43 109 608 615 1786 471		RR 0.353 2.875 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.242 3.000 2.989 5.292 1.098 1.660 0.578 0.859 4.982	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.165; 8.450 [2.033; 4.394 [1.281; 21.864 [1.281; 21.864 [1.281; 21.864 [0.815; 1.479 [1.434; 1.920 [0.361; 0.924 [0.685; 1.076 [3.669; 6.765	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 1.9% 2.1% 3.1% 0.4% 3.7% 1.7% 3.9% 1.7% 3.9% 1.1% 4.8% 3.5% 4.6% 3.5% 4.6% 3.5% 4.6% 3.5% 4.6% 3.5% 4.6%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020 Abohamr 2020 Elissar 2022 Kofahi 2022 Golnar 2022 Ozturk 2021 Liad 2022	2 3 30 12 18 713 104 29 3532 49 18 60 3 3 190 21 0 77 16 6 56 16 11 11 107 23 71 11	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342 291 4 521 77 166 197 65 14 160 437 362 13 61	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 2 2 78 245 5 60 408 80 49 9 8 9 8 9 8 9 8 9 8 9 8 9 8 9 8 9 8	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 61 - 380 259 40 368 43 109 608 615 1786 471 386		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.242 3.000 2.989 5.292 1.098 1.660 0.578 4.982 0.517	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.165; 8.450 [2.033; 4.394 [1.281; 21.864 [0.815; 1.479 [1.434; 1.920 [0.361; 0.924 [0.685; 1.076 [3.669; 6.765 [0.193; 1.380 [0.924] [0.934] [0.934] [0.934] [0.934] [0.944] [0.685; 1.076 [0.193; 1.380 [0.944] [0.944] [0.944] [0.685; 1.076 [0.193; 1.380 [0.944] [0.944] [0.944] [0.685; 1.076 [0.193; 1.380 [0.944] [0.944] [0.944] [0.685; 1.076 [0.193; 1.380 [0.944] [0.944	Weight 1.1% 2.5% 4.1% 3.5% 5.0% 4.7% 5.0% 4.7% 1.1% 3.8% 5.0% 4.6% 1.9% 4.6% 2.1% 3.1% 0.4% 3.7% 1.7% 3.9% 1.1% 4.3% 3.5% 4.6% 3.5% 3.5% 4.3% 3.5% 4.3% 3.5% 3.5%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Addulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020 Abohamr 2020 Abohamr 2020 Elissar 2022 Kofahi 2022 Golnar 2022 Öztürk 2021 Hadi 2022	2 3 30 12 18 713 104 29 3532 49 18 60 3 190 21 0 77 16 6 56 16 11 107 23 71 11 107 23 71 14 6 6	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 342 291 4 521 77 165 14 160 437 361 437 361 8 8	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 2 78 245 56 408 8 99 40 40 40 40 40 40 40 40 40 40 40 40 40	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 678 1443 61 - 380 259 40 368 43 109 608 615 1786 471 386 74		RR 0.353 2.875 0.465 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.217 0.921 0.242 3.000 2.989 5.292 1.098 1.660 0.578 0.858 0.859 2.922 1.098	95%-C 0.088; 1.413 0.33; 0.650 0.420; 1.106 1.359; 3.080 0.972; 1.134 1.072; 1.551 0.567; 0.866 1.382; 1.486 1.240; 2.171 1.834; 11.630 1.086; 1.675 0.282; 1.601 1.0776; 1.254 1.0.776; 0.965 1.2449; 7.687 0.016; 2.994 10.676; 1.254 1.055; 8.450 1.065; 8.450 1.065; 8.450 1.065; 8.450 1.085; 1.479 1.434; 1.920 0.361; 0.924 1.380; 6.765 0.193; 1.380 1.883; 2.180 1.883; 2.180 1.885; 1.95	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.7% 4.6% 5.0% 4.4% 1.9% 4.6% 1.9% 4.6% 3.7% 3.7% 1.1% 3.7% 1.1% 3.7% 1.1% 3.7% 1.1% 3.7% 3.7% 1.1% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.7% 3.5% 4.6% 3.6%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağc 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Abbamr 2020 Abohamr 2020 Abohamr 2020 Abohamr 2020 Elissar 2022 Kofahi 2022 Golnar 2022 Goturk 2021 Hadi 2022 San 2021	2 3 30 12 18 713 104 29 3532 49 3532 49 3532 49 3532 49 3532 49 18 60 3 190 21 0 0 777 16 6 566 16 11 107 23 71 114 46 4	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342 291 4 521 77 16 197 65 144 160 437 362 13 65 14 160 437 362 13 8 21	45 12 85 80 40 1611 59 78 10556 98 5239 60 436 24 31 61 222 535 227 8 245 56 408 80 40 40 40 40 40 40 40 40 40 40 40 40 40	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 678 1443 678 1443 678 1443 678 40 368 43 109 608 615 1786 471 386 74 396		RR 0.353 2.875 0.661 2.045 1.050 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.671 0.864 4.339 0.217 0.921 0.864 4.339 0.242 3.000 2.989 5.292 1.098 1.660 0.578 0.859 4.982 0.517 1.387	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.033; 4.394 [1.281; 21.864 [0.815; 1.479 [1.434; 1.920 [0.361; 0.924 [0.685; 1.076 [3.669; 6.765 [0.193; 1.380 [0.883; 2.180 [0.711; 4.538	Weight 1.1% 2.5% 4.1% 3.5% 3.5% 3.8% 5.0% 4.7% 4.6% 5.0% 4.6% 2.1% 4.6% 3.1% 4.9% 3.1% 4.3% 3.7% 1.7% 3.9% 1.1% 4.8% 3.5% 4.6% 1.1% 4.8% 3.5% 4.8% 3.5% 4.8% 3.6% 1.8%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağcı 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Amir 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020 Abohamr 2020 Abohamr 2020 Elissar 2022 Kofahi 2022 Golnar 2022 Goturk 2021 Hadi 2022 San 2021 Al-Baka 2021	2 3 30 12 18 713 104 29 3532 49 3532 49 3532 49 3532 49 3532 49 18 60 3 190 21 0 0 777 16 6 566 16 11 107 23 71 107 4 6 6 56 4 6 6 56 6 16 56 6 16 11 104 21 104 104 104 105 105 105 105 105 105 105 105 105 105	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342 291 4 521 77 16 197 65 144 160 437 362 13 61 18 21 104	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 2 78 245 56 408 80 40 40 42 2	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 678 1443 678 1443 678 1443 678 40 368 43 109 608 615 1786 471 386 74 396 94		RR 0.353 2.875 0.681 2.045 1.050 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.671 0.864 4.339 0.217 0.921 0.242 3.000 2.989 5.292 1.098 1.660 0.578 0.859 4.982 0.517 1.387 1.796 2.712	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.033; 4.394 [1.281; 21.864 [1.281; 21.864 [0.815; 1.479 [1.434; 1.920 [0.361; 0.924 [0.685; 1.076 [3.669; 6.765 [0.193; 1.380 [0.711; 4.538 [0.561; 13.109	Weight 1.1% 2.5% 4.1% 3.5% 3.5% 4.7% 4.6% 4.6% 4.6% 4.6% 4.6% 4.4% 3.1% 4.6% 3.1% 4.3% 3.7% 1.7% 3.9% 1.7% 3.9% 1.1% 4.8% 3.5% 4.6% 1.1% 4.8% 3.5% 4.6% 1.8% 3.5% 1.8% 3.6% 1.9% 0.9%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağci 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020 Abohamr 2020 Abohamr 2020 Elissar 2022 Kofahi 2022 Golnar 2022 Öztürk 2021 Hadi 2022 San 2021 Al-Baka 2021	2 3 30 12 18 713 104 29 3532 49 3532 49 3532 49 3532 49 18 60 3 190 21 0 0 777 16 6 566 16 11 11 107 23 71 114 4 6 4 4 6	Total 52 4 110 35 33 2986 134 43 34213 137 7 342 291 4 521 77 16 197 65 144 160 437 362 13 61 18 21 104	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 22 78 245 56 408 80 40 42 27 8	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 61 - 380 259 40 368 43 109 608 615 1786 471 386 74 396 94 163848		RR 0.353 2.875 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.671 0.864 4.339 0.217 0.921 0.869 1.089 5.292 1.098 5.292 1.098 5.678 0.859 4.982 0.578 0.859 4.982 0.577 1.387	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.655; 4.450 [2.033; 4.394 [1.281; 21.864 [0.855; 1.479 [1.434; 1.920 [0.361; 0.924 [0.685; 1.076 [3.669; 6.765 [0.193; 1.380 [0.711; 4.538 [0.561; 13.109 [1.054; 1.462]	Weight 1.1% 2.5% 4.1% 3.5% 3.5% 4.7% 4.6% 4.6% 4.6% 4.6% 4.6% 4.6% 3.1% 4.6% 3.1% 4.3% 3.7% 1.7% 3.9% 4.3% 3.5% 4.6% 1.1% 4.3% 3.5% 1.1% 4.8% 3.5% 4.6% 1.8% 3.6% 1.9% 0.9%
	Meisam 2022 Ebrahim 2022 Imad 2021 Hamed 2022 Aumann 2021 Ahmad 2022 Hulya 2022 Suleyman 2022 Lilac 2023 Ahmed 2022 Yağci 2022 Amanat 2021 Abdulsalam 2022 Gosadi 2022 Telmesani 2022 Amir 2022 Abbas 2022 Surme 2021 Ayhan 2021 Caliskan 2020 Abohamr 2020 Abohamr 2020 Abohamr 2020 Elissar 2022 Kofahi 2022 Golnar 2022 Oztürk 2021 Hadi 2022 San 2021 Al-Baka 2021 Random effects model Heterogeneity: / ² = 93%. T ²	2 3 30 12 18 713 104 29 3532 49 3532 49 3532 49 3532 49 3532 190 21 0 0 777 16 6 566 16 11 11 107 23 71 11 4 4 6 4 6	Total 52 4 110 35 33 2986 134 43 34213 128 53 137 7 342 291 4 521 77 16 197 65 144 160 437 362 13 65 14 160 437 362 13 65 14 197 65 14 197 65 14 197 65 14 197 65 14 197 65 14 197 65 14 197 65 14 197 65 14 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 16 197 17 197 17 197 197 197 197 197 197 1	45 12 85 80 40 1611 59 78 10556 98 5 239 60 436 24 31 61 222 5 35 2 78 245 56 408 80 40 42 25 78 245 56 408 80 40 40 40 40 1611 12 22 2 78 245 23 2 78 245 20 27 27 8 20 27 20 20 20 20 20 20 20 20 20 20 20 20 20	10tal 413 46 145 159 150 7081 98 81 146546 420 68 736 94 678 1443 61 - 380 259 40 368 43 109 608 615 1786 471 386 74 396 94 163848		RR 0.353 2.875 0.681 2.045 1.050 1.289 0.700 1.433 1.641 4.619 1.349 0.671 0.864 4.339 0.671 0.864 4.339 0.217 0.921 0.869 4.989 5.292 1.098 1.660 0.578 0.859 4.982 0.517 1.387 1.796 2.712 1.241	95%-C [0.088; 1.413 [1.363; 6.063 [0.333; 0.650 [0.420; 1.106 [1.359; 3.080 [0.972; 1.134 [1.072; 1.551 [0.567; 0.866 [1.382; 1.486 [1.240; 2.171 [1.834; 11.630 [1.086; 1.675 [0.282; 1.601 [0.774; 0.965 [2.449; 7.687 [0.016; 2.994 [0.676; 1.254 [0.016; 2.994 [0.676; 1.254 [0.033; 4.394 [1.281; 21.864 [0.855; 1.479 [1.434; 1.920 [0.361; 0.924 [0.685; 1.076 [3.669; 6.765 [0.193; 1.380 [0.711; 4.538 [0.561; 13.109 [1.054; 1.462]	Weight 1.1% 2.5% 4.1% 3.5% 3.8% 5.0% 4.7% 4.6% 4.6% 2.1% 4.6% 3.1% 4.6% 3.1% 4.3% 3.7% 1.7% 3.9% 1.7% 3.9% 1.7% 3.5% 4.8% 3.5% 4.6% 1.8% 3.6% 1.9% 0.9%

Fig. 2. Evaluation of the rate of death, intensive care unit admission, and O_2 or ventilation use between smokers (current or former) and never-smokers by Asian (A), Middle Eastern (B), European (C), North American (D), South American (E), and African (F). RR, risk ratio; 95% Cl, confidence interval. (Continued to the next page)

95%-CI Weight

4.0%

3.9%

3.5%

3.8%

4.2%

3.9%

2.4%

2.7%

4.3%

3.2%

4.0%

1.9%

4.2%

3.6%

2.9%

1.9%

17%

3.6%

2.9%

3.0%

3.3%

3 6%

4.2%

1.7%

2.6%

1.6%

0.1%

1.1%

1.6%

2.2%

2.5%

3.9%

1.4% 3.7%

0.6%

0.2%

2		Exp	erimental		Control			
	Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI
	Mitra 2021	152	241	279	404		0.913	[0.813; 1.026]
	Hamer 2020	406	172281	354	214828	(a)	1.430	[1.240; 1.649]
	Ho 2020	224	107053	173	128865		1.559	[1.278; 1.900]
	Johanna 2022	254	34875	572	79191	di la constante	1.008	[0.870; 1.168]
	Holman 2020	5293	1479950	5678	1642360		1.034	[0.997; 1.074]
	Stuart 2021	790	204705	287	111579	+	1.500	[1.311; 1.717]
	Natanov 2022	9	11	33	74		1.835	[1.259; 2.675]
	Elin 2021	23	48	115	637		2.654	[1.893; 3.722]
	Min 2022	6237	3220571	8133	4718435		1.124	[1.087; 1.161]
	Pinato 2021	109	583	86	732	- E	1.591	[1.226; 2.066]
	Tenreiro 2022	129	184	209	286	+	0.959	[0.853; 1.079]
	Gisli 2022	57	90	14	74		3.348	[2.036; 5.504]
	Silvano 2023	567	913	562	907		1.002	[0.933; 1.077]
	Atanasov 2022	199	521	133	1552		4.457	[3.665; 5.421]
	Tenreiro 2022	28	80	7727	38465	三	1.742	[1.292; 2.350]
	Antoine 2021	15	57	62	171		0.726	[0.450; 1.170]
	Jose 2022	21	61	15	45	- <u>+</u> -	1.033	[0.602; 1.771]
	Carolin 2022	101	259	191	605		1.235	[1.019; 1.497]
	Richard 2023	39	65	49	134	<u></u>	1.641	[1.217; 2.212]
	Richard 2022	38	54	47	120) (E) (E) (E) (E) (E) (E) (E) (E) (E) (E	1.797	[1.355; 2.383]
	Philomène 2022	12	14	65	74		0.976	[0.775; 1.228]
	Ramillon 2022	88	317	628	3044	C3	1.346	[1.112; 1.628]
	Beatriz 2021	290	433	1595	2229		0.936	[0.872; 1.005]
	Aurélie 2022	14	43	29	243		2.728	[1.575; 4.725]
	Thông 2022	25	51	53	118		1.091	[0.774; 1.539]
	Wallis 2021	19	35	13	66		2.756	[1.552; 4.894]
	Marina 2022	0	5	43	83 -		0.175	[0.012; 2.472]
	Balfanz 2021	7	34	31	91		0.604	[0.294; 1.241]
	Veloz 2020	7	16	219	431		0.861	[0.490; 1.512]
	Talavera 2020	20	118	126	458		0.616	[0.402; 0.943]
	Bellan 2020	24	54	67	258	<u></u>	1.711	[1.191; 2.459]
	Polverino 2020	251	800	526	1963		1.171	[1.032; 1.328]
	Jourdes 2020	7	18	44	196		1.732	[0.918; 3.269]
	Hewitt 2020	211	724	205	814		1.157	[0.982; 1.364]
	Margalida 2022	5	22	6	35		1.326	[0.459; 3.828]
	Nataliya 2022	1	15	36	126		0.233	[0.034; 1.581]
	Random effects model		5225301		6949693	4	1.324	[1.210; 1.449]
		2						25 N N N N N N N N N N N N N N N N N N N

Heterogeneity: $l^2 = 92\%$, $\tau^2 = 0.0495$, p < 0.01

Г 0.1 0.512

4 [1.210; 1.449] 100.0% ٦ 10

	Expe	rimental		Control					
Study	Events Total		Events	Total	Risk Ratio	RR	95%-CI	Weight	
Padilla 2020	2423	17495	25154	207722	10	1.144	[1.100; 1.189]	6.9%	
Aldin 2023	4	24	8	225	i	4.688	[1.523; 14.424]	0.4%	
Wadhwa 2022	40	348	7	33		0.542	[0.264; 1.112]	0.8%	
Puebla 2021	114	636	510	5102	-	1.793	[1.489; 2.159]	4.7%	
Ram 2022	356	2239	536	4478		1.328	[1.173; 1.504]	5.7%	
Thomas 2023	9025	40865	10668	57454		1.189	[1.160; 1.220]	7.0%	
Imad 2023	17	47	14	42		1.085	[0.612; 1.923]	1.2%	
Trung 2022	4	11	4	15		1.364	[0.433; 4.293]	0.3%	
Jennifer 2021	274	3012	200	6916		3.146	[2.635; 3.756]	4.8%	
Luis 2022	205	1167	384	3703	·	1.694	[1.449; 1.980]	5.2%	
Yeh 2022	287	1201	323	1612		1.193	[1.036; 1.372]	5.5%	
Moschovis 2021	91	506	64	777		2.183	[1.618; 2.946]	3.0%	
Estiri 2021	137	1441	693	15268		2.095	[1.758; 2.495]	4.8%	
Jacqueline 2022	7864	18910	88529	223132		1.048	[1.030; 1.067]	7.0%	
Kelly 2023	1474	10479	2540	33791		1.871	[1.762; 1.988]	6.7%	
Gaspar 2020	3215	24484	35095	306814		1.148	[1.110; 1.187]	7.0%	
Claire 2023	170	687	152	869	1 <u>+</u>	1.415	[1.165; 1.719]	4.5%	
Kuderer 2020	124	369	99	469		1.592	[1.270; 1.996]	4.0%	
Marco 2022	35351	177712	441161	2256850		1.018	[1.008; 1.028]	7.1%	
Hernández 2022	5372	16445	60123	194558		1.057	[1.033; 1.082]	7.0%	
Nicolás 2022	2	264	148	13615	·	0.697	[0.174; 2.798]	0.2%	
Ozer 2021	13	24	12	44		1.986	[1.083; 3.644]	1.1%	
Monteiro 2020	10	27	14	77		2.037	[1.029; 4.033]	0.9%	
Zhao 2020	52	139	143	454	HE I	1.188	[0.921; 1.532]	3.6%	
Esposito 2020	8	27	7	19		0.804	[0.352; 1.839]	0.6%	
Random effects model	1	318559		3334039		1.392	[1.300; 1.490]	100.0%	
Heterogeneity: $I^2 = 97\%$, τ^2	= 0.0172	2, p < 0.01			1 I I I I				

0.1

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Fig. 2. Continued.

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Fig. 2. Continued.

ity to contracting infection and the progression of infection [22]. Various smoking mechanisms increase the risk of viral infections. These mechanisms include changes in the immune response; changes in airway biology, such as the activation of the epithelium; and significant structural changes in the respiratory tract, such as impaired mucociliary clearance, mucus hypersecretion, fibrosis, and epithelial barrier dysfunction [23-26].

Angiotensin-converting enzyme 2 (ACE2) may be the key factor that links smoking with the progression of COVID-19. The entry of coronaviruses into human cells involves a multifaceted process, encompassing various distinct domains of spike (S) protein that mediate viral attachment to the cell surface, receptor engagement, protease processing, and membrane fusion [27]. ACE2 is abundantly present in the epithelia of the lungs and small intestines and serves as an entry point for SARS-CoV [28]. The binding of S proteins to human cells is facilitated by the ACE2 receptor in several viruses, such as SARS-CoV and SARS-CoV-2 [29-31]. A previous study demonstrated the upregulation of pulmonary ACE2 gene expression in ever-smokers compared with never-smokers, regardless of the tissue subset or COPD status [32]. A recent meta-analysis indicated a heightened risk of COVID-19 progression (30%-50%) among current and ex-smokers com-

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pared with never-smokers. These results suggested that 6.2 million deaths due to COVID-19 worldwide are caused by tobacco smoking [33].

The pooled prevalence rates of smokers in Oceania, Asia, Europe, America, and Africa were 36%, 14%, 38%, 31%, and 32%, respectively [34]. We compared the smokers' COVID severity by continent and GDP level. One study showed that the severity of COVID-19 differs in various geographical locations, with mortality rates of 0.7 deaths per 100,000 in South Korea and 86.8 per 100,000 in Belgium [14]. Another study comparing the COVID-19 severity by region concluded that smoking had a protective effect against COVID-19. The COVID-19 mortality rates were 13 (5-24) per million inhabitants in countries with a high male smoking prevalence (>45%) and 33 (4 COVID-19 133) in countries with a low male smoking prevalence (<25%) [15]. The high COVID-19 death rate among smokers in the African continent and low-GDP countries is attributed to the lack of medical management systems compared with other countries. In addition to medical treatment, environmental or socioeconomic factors can increase the severity. However, no available study has compared the COVID-19 severity according to the type and amount of smoking.

Study	Events	Total	Events	Total	Risk Ratio	RR	95%-CI	We
Aldin 2022	4	24	0	225	1:	4 600	11 502: 14 4041	(
Modbwo 2022	40	24	07	220		4.000	[1.025, 14.424]	-
Wauliwa 2022	40	340	540	5400	100	0.042	[0.204, 1.112]	
Puebla 2021	114	636	510	5102	- Fill	1.793	[1.489; 2.159]	
Ram 2022	356	2239	536	4478	<u></u>	1.328	[1.173; 1.504]	
Thomas 2023	9025	40865	10668	57454	1	1.189	[1.160; 1.220]	
Imad 2023	17	47	14	42		1.085	[0.612; 1.923]	
Trung 2022	4	11	4	15	· · · ·	1.364	[0.433; 4.293]	
Jennifer 2021	274	3012	200	6916		3.146	[2.635: 3.756]	
Luis 2022	205	1167	384	3703	100 M	1.694	[1,449: 1,980]	
Yeh 2022	287	1201	323	1612		1 193	[1036: 1372]	
Moschovis 2021	91	506	64	777	T-F	2 183	[1 618: 2 946]	
Fetiri 2021	137	1441	603	15268		2 0 9 5	[1 758: 2 495]	
Kally 2022	1474	10470	2540	22704	100	1 071	[1.750, 2.400]	
Claira 2023	14/4	10479	2040	33/91	pros.	1.0/1	[1.702, 1.900]	
Cialle 2023	170	00/	152	809	1.00	1.415	[1.100, 1.719]	
Ozer 2021	13	24	12	44		1.980	[1.083, 3.044]	
Monteiro 2020	10	27	14	77	<u>L:</u>	2.037	[1.029; 4.033]	
Zhao 2020	52	139	143	454	- 青	1.188	[0.921; 1.532]	
Esposito 2020	8	27	7	19		0.804	[0.352; 1.839]	
Rui 2021	2	17	6	74		1.451	[0.320; 6.575]	
Yue 2022	6	39	40	549		2.112	[0.954; 4.672]	
Fang 2022	108	172	859	1216		0.889	[0.788: 1.003]	
Zhou 2021	12	20	24	83	÷	2 0 7 5	[1,269: 3,393]	
Cen 2020	16	88	206	919		0.811	[0 512: 1 284]	
Wang 2020	4	11	200	45		2 3 3 8	[0.820: 6.501]	
Hu 2020	22	20	124	295	÷.	1 221	[0.023, 0.331]	
7hana 0000	22	50	00	205		0.500	[0.304, 1.733]	
Zrieng 2020	70	400	28	740		0.580	[0.109, 1.990]	
NI 2021	12	123	454	/10	The second se	0.915	[0.781, 1.073]	
Zhan 2020	25	46	123	359	=	1.586	[1.1/4; 2.144]	
Chen 2020	25	111	183	1748		2.151	[1.484; 3.119]	
Ye 2021	10	29	34	167		1.694	[0.944; 3.039]	
Zhou 2022	20	223	9	38		0.379	[0.187; 0.768]	
Wang 2020	9	9	32	50		1.554	[1.266; 1.908]	
Akivama 2022	397	7672	427	10312	-	1,250	[1.094: 1.428]	
Yumi 2022	215	6938	193	8197		1.316	[1.087: 1.594]	
Tomoki 2022	42	57	27	60	÷	1.637	[1.189: 2.255]	
Kishaha 2020	0	3	3	4 -		0 184	[0 013: 2 506]	
Fumihiro 2022	35	77	15	64		1 939	[1 169: 3 216]	
Miesko 2022	224	570	00	200	100	2.520	[2 091: 2 077]	
Notopov 2023	554	11	22	74		1 9 2 5	[2.001, 3.077]	
Natariov 2022	101	050	101	COE	1 Percenter of the second seco	1.030	[1.209, 2.070]	
Carolin 2022	101	209	191	005		1.230	[1.019, 1.497]	
Balfanz 2021	/	34	31	91		0.604	[0.294; 1.241]	
Hamer 2020	406	1/2281	354	214828		1.430	[1.240; 1.649]	
Ho 2020	224	107053	173	128865	53	1.559	[1.278; 1.900]	
Holman 2020	5293	1479950	5678	1642360		1.034	[0.997; 1.074]	
Stuart 2021	790	204705	287	111579	+	1.500	[1.311; 1.717]	
Min 2022	6237	3220571	8133	4718435	5	1.124	[1.087; 1.161]	
Wallis 2021	19	35	13	66		2.756	[1.552: 4.894]	
Yamini 2022	3	4	45	196		3 267	[1 755: 6 080]	
Kittu 2022	18	63	17	357	· · · · ·	6,000	13 272 11 0021	
Kumar 2021	16	19	2	22		0.779	[2 592: 37 024]	
Mitro 0004	150	044	070	404		0.010	[2.002, 07.024]	
Millia 2021	102	241	2/9	404		0.913	[0.813, 1.020]	
Tenreiro 2022	129	184	209	286		0.959	[0.853; 1.079]	
Antoine 2021	15	57	62	171		0.726	[0.450; 1.170]	
Ramillon 2022	88	317	628	3044		1.346	[1.112; 1.628]	
Thông 2022	25	51	53	118	書	1.091	[0.774; 1.539]	
Jourdes 2020	7	18	44	196	<u>+</u> ;æ—	1.732	[0.918; 3.269]	
Silvano 2023	567	913	562	907	in the second se	1.002	[0.933; 1.077]	
Bellan 2020	24	54	67	258	Tæ	1711	[1.191: 2.459]	
Polverino 2020	251	800	526	1963	-	1 171	[1.032: 1.328]	
			525		Π			
Dandom offacte mo	del	5266750		6981029	10	1 / 17	11 316. 1 5251	10
Hataraaaaat ul ²	2 . 0.0500	0.0.04		0001020		1.411	[1.510, 1.525]	

Fig. 3. COVID-19 severity in high-income (GDP 10th place or higher) countries (A), middle-income countries (GDP 11th–50th) (B), and low-income countries (GDP 51th and below) (C). RR, risk ratio; 95% Cl, confidence interval. (Continued to the next page)

B	Study	Experi Events	imental Total	Events	Control Total	Risk Ratio	RR	95%-CI	Weight
	Nataliva 2022	1	15	36	126		0.233	[0.034; 1.581]	0.1%
	Lucas 2022	45	68	81	148	<u>i</u>	1,209	[0.966: 1.513]	2.6%
	Isabella 2022	44	62	119	238	E	1.419	[1.158; 1.740]	2.8%
	Juliana 2022	155	332	1730	9474		2.557	[2.262; 2.890]	3.5%
	Fornazieri 2022	11	15	29	58		1.467	[0.984; 2.186]	1.5%
	Menezes 2020	77	209	1075	10504		3.600	[2.988; 4.337]	3.0%
	Ferrari 2021	14	41	19	157		2.822	[1.551; 5.134]	0.8%
	Mauricio 2022	22	32	88	139	五	1.086	[0.833; 1.416]	2.3%
	Jose 2022	21	61	1505	45		1.033	[0.602; 1.771]	1.0%
	Veloz 2020	290	433	210	121		0.930	[0.872, 1.005]	0.0%
	Talavera 2020	20	118	126	458		0.616	[0.402: 0.943]	1 4%
	Margalida 2022	5	22	6	35	_	1.326	[0.459: 3.828]	0.3%
	Padilla 2020	2423	17495	25154	207722	li i	1.144	[1.100; 1.189]	4.0%
	Jacqueline 2022	7864	18910	88529	223132	1	1.048	[1.030; 1.067]	4.1%
	Gaspar 2020	3215	24484	35095	306814		1.148	[1.110; 1.187]	4.1%
	Marco 2022	35351	177712	441161	2256850	÷	1.018	[1.008; 1.028]	4.1%
	Hernández 2022	5372	16445	60123	194558	- 1	1.057	[1.033; 1.082]	4.1%
	NICOIAS 2022	100	264	148	13015		0.697	[0.174; 2.798]	0.2%
	G0S80I 2022	21	342	430	1//2		0.804	[0.774, 0.905]	3.0%
	Abohamr 2020	16	65	24	1445		- 5 202	[2.445, 7.007]	0.3%
	Abohamr 2020	107	160	245	608		1.660	[1.434: 1.920]	3.3%
	Hulya 2022	104	134	59	98	100	1.289	[1.072; 1.551]	3.0%
	Suleyman 2022	29	43	78	81	12	0.700	[0.567; 0.866]	2.7%
	Yağcı 2022	18	53	5	68	_	4.619	[1.834; 11.630]	0.4%
	Surme 2021	16	77	222	259		0.242	[0.156; 0.376]	1.3%
	Aynan 2021 Coliekon 2020	6	107	25	269		3.000	[1.065; 8.450]	0.3%
	Akeu 2020	11	14	70	100	± ~	2.909	[2.035, 4.394]	2 106
	Öztürk 2021	4	61	49	386		0.517	[0.193: 1.380]	0.4%
	San 2021	4	21	42	396		1,796	[0.711: 4.538]	0.4%
	Johanna 2022	254	34875	572	79191	南	1.008	[0.870; 1.168]	3.3%
	Elin 2021	23	48	115	637	-	2.654	[1.893; 3.722]	1.8%
	Philomène 2022	12	14	65	74	二 二	0.976	[0.775; 1.228]	2.6%
	Richard 2023	39	65	49	134		1.641	[1.217; 2.212]	2.1%
	Aumann 2021	38	32	47	120		2.045	[1.300, 2.383]	2.2%
	Lilac 2023	3532	34213	10556	146546		1.433	[1.382: 1.486]	4.0%
	Amir 2022	0	4	31	61		0.217	[0.016; 2.994]	0.1%
	Islam 2021	1	59	4	268	i <u> </u>	1.136	[0.129; 9.977]	0.1%
	Mohsin 2021	147	567	153	933		1.581	[1.293; 1.933]	2.8%
	Mohsin 2021	121	594	182	1428	100	1.598	[1.297; 1.970]	2.8%
	Nassar 2021	8	1/	31	143		2.1/1	[1.200; 3.927]	0.8%
	Found 2021	129	21	94	202	indi	2.034	[1.097, 2.438]	3.0%
	Tugade 2023	2	20	21	146		0.695	[0 176: 2 744]	0.3%
	Saberon 2022	4	60	9	75		0.556	[0.180; 1.716]	0.3%
	Ismail 2022	40	791	263	5098	+	0.980	[0.709; 1.355]	1.9%
	Emily 2023	12	41	23	117		1.489	[0.817; 2.714]	0.8%
	Nancy 2021	16	19	19	25	11111111111111111111111111111111111111	1.108	[0.826; 1.487]	2.1%
	Tenreiro 2022	28	80	1121	38465	1 () () () () () () () () () (1.742	[1.292; 2.350]	2.1%
	Random effects model	1	329953		3505475	6	1.326	[1.248: 1.409]	100.0%
	Heterogeneity: $l^2 = 96\%$. τ^2	= 0.0234.	p < 0.01						
_						0.1 0.5 1 2 10			
C		Experin	nental	Con	trol				
	Study	Events Total Events Total				Risk Ratio	RR	95%-CI Wei	ght
			-						
	Abdulsalam 2022	3	104	60	94		0.6/1 [0.2	82; 1.601] 7.	9%
	AI-Baka 2021	63	104	27	340		2.712 [0.50	15: / 3001 0	3.9%
	Aurélie 2022	14	43	29	243		2 728 [15	75: 4 7251 8	9%
	Atanasov 2022	199	521	133 1	552		4 457 [3.6	65: 5 4211 9	5%
	Marina 2022	0	5	43	83		0.175 [0.0	12; 2.472] 3.	2%
	Kofahi 2022	71	362	408 1	786		0.859 [0.6	85; 1.076] 9.	5%
	Gisli 2022	57	90	14	74		3.348 [2.0	36; 5.504] 9.	0%
	Imad 2021	30	110	85	145		0.465 [0.3	33; 0.650] 9.	3%
	Abbas 2022	77	521	61	380		0.921 [0.6	/6; 1.254] 9.	3%
	Ahmed 2022	23	431	20	228		5 506 14 1	81: 7 2511 0	4%
		2	-				[T.]		

Fig. 3. Continued.

Random effects model

Heterogeneity: l^2 = 96%, τ^2 = 0.9354, p < 0.01

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Т т 0.1 0.51 2 10 1.534 [0.853; 2.760] 100.0%

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Ethics approval

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Conflict of interest

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