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# Prevalence of self-medication with vitamin or mineral supplements in the prevention and treatment of COVID-19: a systematic review and meta-analysis

Shideh Rafati<sup>1</sup>, Foozieh Rafati<sup>2\*</sup>, Nahid Shahabi<sup>1</sup>, Neda Dastyar<sup>2</sup>, Fatemeh Arjmand<sup>1</sup> and Seyedeh Masoumeh Mousavi Nejad<sup>3</sup>

## **Abstract**

**Background** Self-medication, as a self-care practice, increased dramatically during the COVID-19 pandemic. Among the most prevalent medications used for self-medication were vitamins and minerals. Accordingly, this study aimed to estimate the prevalence of self-medication with vitamins or minerals for preventing and treating COVID-19 and its related factors.

**Material and method** A comprehensive search was performed in four electronic databases (PubMed, Web of Science, Scopus, and ProQuest), two preprint repositories (MedRxiv and SciELO), two grey literature sources (Google and Google Scholar), and the reference lists of eligible studies in January 2024. The search strategy was built on two core concepts: "self-medication" and "COVID-19". No language, place, and time restrictions were applied. Risk of bias assessment tool was adapted from Hoy checklist. The protocol of this study was registered under the code CRD42023434567 in the open-access online database of the International Prospective Register of Systematic Reviews (PROSPERO). A random effect model was applied to estimate the pooled prevalence of self-medication. Statistical heterogeneity among the studies was assessed using both the  $I^2$  statistic and the  $\chi 2$  test. Moreover, subgroup analysis and meta-regression model were used to identify the potential sources of methodological heterogeneity of the studies. A two-sided P-value < 0.05 was considered statistically significant.

**Results** Out of 1424 non-duplicate studies, 56 were included in the meta-analysis. Vitamin C, vitamin D, B complex, multivitamins, and zinc were most commonly used for self-medication. The pooled prevalence of self-medication with vitamins was 29% (95% Cl: 22%,37%;  $I^2 = 99.62\%$ ), with minerals 15% (95% Cl: 8%, 23%;  $I^2 = 99.68\%$ ), and the corresponding value for the concomitant use of minerals and vitamins was 34% (95% Cl: 27%, 42%;  $I^2 = 98.72\%$ ). The subgroup analysis showed people who lived in the American continent practiced self-medication with vitamins less (Pooled prevalence: 12%, 95% Cl: 8%,16%;  $I^2 = 91.39\%$ ), and self-medication with vitamins and minerals was most

\*Correspondence: Foozieh Rafati foozieh1384@yahoo.com

Full list of author information is available at the end of the article



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prevalent in Asia. Besides; according to I<sup>2</sup> values, the continents in which the studies were conducted could be the reason for the statistical heterogeneity.

**Conclusion** The reported prevalence of self-medication with vitamins and minerals to prevent and treat COVID-19, especially in Asia, is concerning and needs more public health action. In addition, people should be educated about the possibility of poisoning with vitamins and minerals because awareness of the risks of supplements can reduce self-medication practices at present and even in future pandemics.

Keywords Self-medication, COVID-19, Pandemic, Prevalence, Systematic review, Meta-analysis

# **Background**

According to the World Health Organization (WHO), "Self-medication involves the use of medicinal products by the consumer to treat self-recognized disorders or symptoms, or the intermittent or continued use of a medication prescribed by a physician for chronic or recurring diseases or symptoms" [1, 2].

With the outbreak of COVID-19 in Wuhan, China, in December 2019 and its spread to other areas of Asia, and then worldwide in early 2020, everyone in the endless virtual world and the Internet was advised to use a variety of herbal and industrial medicines and medicinal supplements to prevent or treat the COVID-19 disease since at that time, there were no definitive treatments with confirmed evidence for this disease [3].

People resorted to self-medication (SM) for reasons such as fear of infection or contact with an infected person, fear of quarantine, fear of stigmatization or discrimination, low access to healthcare facilities, misinformation, advice of others, and lack of financial ability [4]. In this regard, SM increased dramatically, with COVID-19-related self-medication prevalence ranging from 3.4 to 96% [5]; however, evidence showed that many of the SM practices had little or no benefit for the patients, or were even known to be harmful [6].

Among the medications that met with public favor for the prevention or treatment of this disease, vitamin and mineral supplements were most prevalent because consumers believed these medications were useful for improving and strengthening the immune system [7–14]. Nevertheless, arbitrary use of these medications can have negative side effects, hence doctors and experts warn about the irreparable side effects of excessive use of vitamins and minerals without a physician's supervision [15].

The COVID-19 pandemic has generated considerable interest in self-medication practices, especially regarding the use of vitamin and mineral supplements. Based on our knowledge, despite numerous studies investigating this phenomenon, there remains a significant gap in the literature concerning the prevalence of self-medication specifically with these supplements for COVID-19 prevention and treatment. One notable systematic review, which did not include a meta-analysis, analyzed 11 observational studies from PubMed and Scopus to

investigate the relationship between vitamin D and COVID-19 among the elderly [13]. Furthermore, three narrative reviews assessed the role of vitamins and minerals as immunity boosters in COVID-19 [10, 11, 14]. A systematic review with a meta-analysis of 8 randomized trial studies was published in October 2022 indicating that vitamin D supplementation did not improve the clinical outcomes in COVID-19 patients [12]. Furthermore, other existing systematic literature reviews have often focused broadly on all medications rather than specifically on vitamins and minerals, underscoring the need for a more targeted investigation [4, 5].

The relative advantage of our systematic review and meta-analysis lies in its focused approach. By narrowing the review question specifically to vitamin and mineral supplements, expanding the search to include a broader range of sources, and performing subgroup analyses, our study aims to provide more precise insights into self-medication practices.

The primary objective of this study was to conduct a systematic review with meta-analysis to synthesize the previous primary studies related to the prevalence of self-medication with vitamin or mineral supplements in the prevention and treatment of COVID-19. The secondary objectives were to assess the factors associated with self-medication including age and education of the participants, reasons for self-medication, and the type of vitamin or mineral taken, and to find potential reasons for heterogeneity. Therefore, the present study was conducted to estimate the overall prevalence of self-medication with vitamins and minerals in order to prevention or treatment of COVID-19, related factors, self-medication reasons and determining the types of consumed vitamins and minerals. This detailed analysis will contribute valuable insights into public health strategies and inform healthcare providers about patient behaviors during health crises.

# **Methods**

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16] was followed in conducting and reporting this systematic review and meta-analysis which sought to estimate the pooled prevalence of self-medication with vitamin or mineral

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supplements in the prevention and treatment of COVID-19. The protocol of this study was registered under the code CRD42023434567 in the open-access online database of the International Prospective Register of Systematic Reviews (PROSPERO).

#### Study design and search strategy

A comprehensive search was performed in four electronic databases (PubMed/MEDLINE, Web of Science, Scopus, and ProQuest) in January 2024. Additionally, two preprint repositories (MedRxiv and SciELO), and grey literature sources (Google and Google Scholar) were used to access more records. Moreover, the reference lists of studies that were considered eligible were checked by hand searching to identify additional references. In this study, MEDLINE's thesaurus (The Medical Subject Headings (MeSH)), Embase's thesaurus (Emtree), and free text methods including contact to expert and considering the previous systematic review studies were used to find the synonyms of the keywords. The search strategy was built on two core concepts: "selfmedication" and "COVID-19". All the searched results based on these two concepts, after passing the screening stage, were selected if the frequency of consumption of vitamins and minerals was reported. No language, place, and time restrictions were applied. The steps for formulating the search query for the PubMed database are shown in Table 1. The syntax was then customized to the other databases.

### Inclusion and exclusion criteria

The descriptive or analytical cross-sectional studies, either published in scientific journals or with full text available in preprint repositories, which reported original

Table 1 PubMed search guery

Step	Search strategy	Results
#1	("COVID-19" [Mesh] OR "COVID19" [tiab] OR "COVID-19" [tiab] OR "coronavirus disease 2019" [tiab] OR "2019nCoV" [tiab] OR "2019nCoV" [tiab] OR "novel coronavirus" [tiab] OR "novel corona virus" [tiab] OR "SARS-CoV-2" [tiab] OR "SARS-CoV-2" [tiab] OR "sars2" [tiab] OR "novel coronavirus" [tiab] OR "coronavirus" [tiab]	387,214
#2	("Self Medication" [MeSH] OR "Self Medication" [tiab] OR "Self Medication" [tw] OR "Self-Medication" [tiab] OR "Self-Medication" [tiab] OR "Self-treatment" [tiab] OR "Self-curing" [tiab] OR "Self-management" [tiab] OR "Nonprescription Drugs" [tw] OR "Nonprescription Drugs" [tiab] OR "Nonprescription Drugs" [tiab] OR "Non prescription Drugs" [tw] OR "Non prescription Drugs" [tw] OR "over-the-counter drugs" [tiab] OR "Over-the-counter drugs" [tw] OR "OTC drugs" [tw] OR "OTC drugs" [tw] OR "drug utilization" [tw] OR "drug utilization" [tw] OR "medication utilization" [tiab] OR "medication utilization" [tiab] OR "medication utilization" [tw] OR "medication [tw] OR "medication utilization" [tw] OR "medication utilization"	56,627
#3	#1 AND #2	964

data and evaluated the prevalence of self-medication with vitamins or supplements during the COVID-19 with at least one primary or secondary outcome, were included in this systematic review. Moreover, all research articles or reports from the baseline phase of cohort studies that have been published in the form of separate articles or conventional articles to the cohort profile were included in the study. Besides, primary studies with or without a definition for self-medication were included. In this systematic review, no age, gender, racial, ethnic, or language restrictions on the population were taken into account.

All unrelated studies, review articles, duplicate studies, articles or reports from case report studies, case series, and all types of interventional studies including randomized clinical trials, studies with an unclear method, and those with no access to the full text were excluded. In addition, primary studies with a sample size of less than 30 were not eligible for inclusion in this systematic review.

# Study selection

Hand searching and electronic searching were performed by one author (NS). Searched articles were imported into the EndNote reference management software. After the removal of duplicate records, based on the inclusion criteria, two independent researchers (FA and ND) screened papers by reading the title and abstract of all articles and separated the relevant ones. In this stage, to assess the level of agreement between two authors, Cohen's Kappa coefficient was calculated and its value was 59%. Two authors (FA and MM) independently read the full text of the relevant studies to determine whether they were suitable for inclusion. The discordance between the two authors was resolved through consensus or judgment by the third expert person (FR).

#### **Data extraction**

Two authors (FA and MM) independently extracted the data from the articles selected in the previous step. Cohen's kappa coefficient of 68% indicated that there was acceptable agreement between the two authors. Again, disagreements between the two authors were resolved through consensus or judgment by the third expert person (FR).

The essential information such as first author name, year of publication, country, type of study, sample size, sampling technique (random/nonrandom sampling methods), mean (range) age, sex, education, the definition of self-medication, the frequency of self-medication with vitamins and minerals, period of self-medication, type of medications, and the reason for self-medication were recorded on Microsoft Excel version 2019.

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#### Risk of bias assessment

The appraisal checklist for prevalence studies (adapted from the study by Hoy et al.) [17] was used to assess the quality of primary studies by two reviewers (FA and MM) independently. This checklist includes 9 items each answered with yes (zero value) or no (1 value). Finally, a study with a numerical value between 0 and 3 is considered low risk, 4–6 is moderate risk, and 7–9 is high risk. Inter-rater reliability was used to assess the agreement between two reviewers in the process of assessing the quality of primary studies based on Cohen's kappa. The proper agreement between the two reviewers was confirmed by a Cohen's kappa value of 74%. The discordance between the two authors was resolved through consensus or judgment by the third expert person (FR). All studies with low, middle, and high quality were included in the main analysis.

#### Definition of self-medication

Based on the World Health Organization (WHO), self-medication is when individuals use medicines on their own to treat recognized symptoms or continue using previously prescribed medications [1, 2, 18]. In this systematic review, the number of primary studies that used the definition of self-medication based on WHO guidelines was not adequate, i.e., different definitions of self-medication were presented or many studies did not provide a clear definition of self-medication. Therefore, primary studies with or without a definition for self-medication were also included.

## Data synthesis and statistical analysis

The characteristics and findings of included studies were summarized using structured tables, presenting key variables such as research quality, sample size, population characteristics, type of supplements used, self-medication reason, and reported prevalence of self-medication. Forest plots were used to visualize the individual and pooled estimates of self-medication prevalence along with 95% confidence intervals. For studies not eligible for meta-analysis, findings were described narratively and included in summary tables.

The  $I^2$  statistic and the Cochran's Q ( $\chi 2$ ) test were used to assess statistical heterogeneity between the primary studies. We interpreted  $I^2$  values according to commonly accepted thresholds: 25% as low, 50% as moderate, and 75% or more as high heterogeneity. The  $\chi^2$  test was also conducted, with a p-value less than 0.10 considered indicative of statistically significant heterogeneity, due to its low power in meta-analyses with a small number of studies [19]. Because of significant methodological heterogeneity between primary studies, a random effect meta-analysis was performed to combine the selected studies. The metaprop command was used to calculate

the pooled point estimate and 95% CI of self-medication prevalence. Publication bias was not evaluated because prevalence is always a positive number between zero and one, and cannot be negative. Therefore, an inherent asymmetry can be created in the funnel plot which is not related to publication bias but may mislead the reader.

To investigate the potential sources of heterogeneity, subgroup analysis was performed based on the gender of participants in primary studies (male/female/both), publication year of primary studies (2020-2023), continent (Asia and Pacific/Africa/Europe/America), economic level of the country (low/middle/high income), sampling technique (random or non-random sampling methods), having/not having a definition for self-medication, and quality assessment of primary studies (low risk/moderate risk/high risk). Furthermore, to investigate the relationship between the prevalence of self-medication with sample size and the mean age of the participants, a metaregression model was performed using STATA metareg command. STATA software (version 17.0) was used for data analysis. A two-sided P-value < 0.05 was considered statistically significant.

#### Results

#### Study selection

Based on the search strategy, first, a total of 4281 records were found through electronic searching and hand searching in PubMed/MEDLINE, Web of Science, Scopus, ProQuest, preprint repositories (MedRxiv and SciELO), grey literature sources (Google and Google Scholar), and the reference lists of eligible studies. After the duplicates were eliminated, the abstract and title of 1424 records were screened based on the inclusion criteria, of which 429 documents remained for the next step of investigation. The full text of 14 records could not be retrieved. This time, the full texts of 415 documents were assessed. Finally, 56 articles were included in the qualitative synthesis and meta-analysis. The process of study selection is shown in Fig. 1.

# Characteristics of the studies

A total of 58,477 participants were identified in 56 studies. In 13 studies, random sampling methods were used to select participants and the sample size ranged from 54 to 15,830. For further consideration, the studies were equally divided into two groups based on their sample size, including less than or equal to 500 participants and more than 500 participants. In the first group, there were 28 studies with 8262 participants, with a sample size between 54 and 489, and in the second group, there were 28 studies with 50,215 participants, with a sample size between 512 and 15,830. Of the 56 studies, one was published in 2020, 15 in 2021, 28 in 2022, and 12 studies have been published after this date. Except for 18 studies

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# Identification of studies via databases and registers

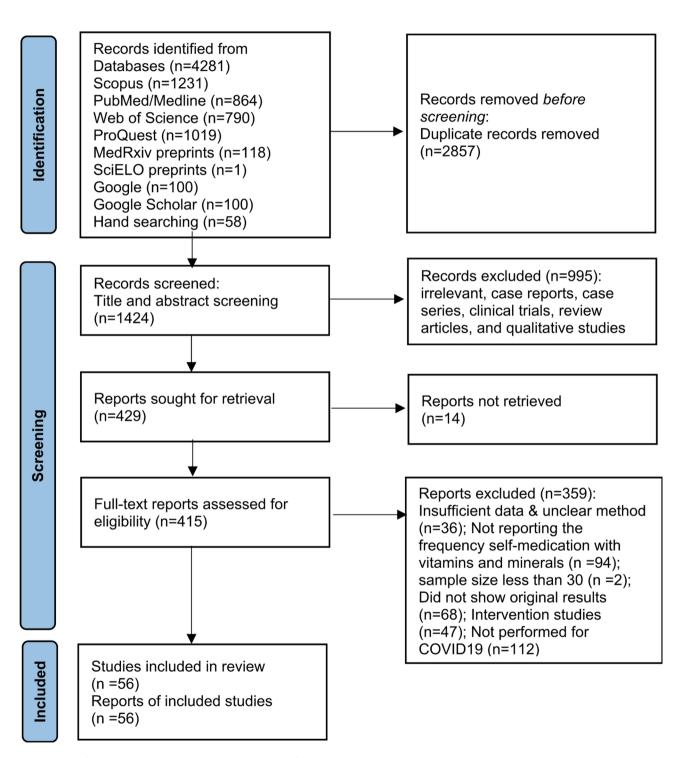


Fig. 1 PRISMA flowchart for study selection at different phases of the systematic review

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[3, 20–36], the rest were population-based. Eleven studies were specifically conducted among medical students, physicians, and other healthcare professionals [3, 20, 22, 25–27, 29–31, 34, 35]. The majority of the studies were conducted in the Asian continent (n=37): 9 studies in India [22, 31, 37–43], 5 studies in Pakistan [3, 27, 29, 33, 44], 5 studies in Iran [28, 34, 45–47], 3 studies in Jordan [20, 48, 49], 2 studies in Turkey [36, 50], 2 studies in Saudi Arabia [51, 52], 2 studies in Indonesia [21, 25], and the rest were conducted in other countries of this continent [53–61]. Eight studies were conducted in Africa [7, 30, 62-67], six studies in Europe [23, 26, 32, 68-70], and the remaining were carried out in America (n=5) [24, 35, 71–73]. Based on the World Bank classification [74], one study was conducted in seven Arab countries with different economic levels [56], two studies were conducted in low-income countries [63, 67], 14 studies in high-income countries [23, 26, 51-53, 55, 57, 59, 60, 68-70, 72, 73], and other studies were done in lower-middle-income countries to upper-middle-income countries. Four studies considered only females [21, 23, 28, 36], while the others included both males and females. According to our evaluations, of the 56 studies, the methodological quality of 23 studies was high, in other words, they had a low risk of bias. Besides, 33 studies had a moderate risk of bias and no study had a high risk of bias. A description of the main characteristics of the included studies is shown in Table 2.

Table 3 provides information on self-medication as reported in the studies included in the systematic review, such as the prevalence of self-medication with minerals and vitamins for the prevention and treatment of COVID-19, the type of vitamins and minerals used, and the reasons for self-medication. Based on 56 studies, the overall prevalence of self-medication for prevention and treatment of COVID-19 varied from 3.7 to 96.9%. Moreover, 41 studies reported the prevalence of selfmedication with vitamins for the prevention and treatment of COVID-19, and 19 studies were found with the prevalence of self-medication with minerals. In addition, in 15 studies, the prevalence of self-medication with simultaneous consumption of vitamins and minerals has been reported. The prevalence of self-medication with vitamins for prevention and treatment of COVID-19 varied from 0.96 to 77.2%, with a mean prevalence of 32.4% across all studies. The prevalence of self-medication with minerals ranged from 0.5 to 69.4%, with a mean prevalence of 18.1% across all studies. The prevalence of selfmedication with both vitamins and minerals ranged from 15.7 to 61.2%, with a mean prevalence of 34.8% across all studies. Among the types of vitamins and minerals used, vitamin C, vitamin D, B complex, multivitamins, and zinc were the most commonly used ones for selfmedication. Based on the results of 32 retrieved studies that reported the reasons for self-medication, the most important reasons for self-medication were time-saving, being influenced by family members, friends, and media, unavailability of the physician, lack of effectiveness of medicines prescribed by the physician, fear of stigma, discrimination, or being infected with COVID-19, convenience and easy accessibility, and financial issues.

# Pooled prevalence and heterogeneity

A total of 41 eligible papers, including 45,572 participants were included in the meta-analysis to estimate the pooled prevalence of self-medication with vitamins for the prevention and treatment of COVID-19. The pooled prevalence of self-medication with vitamins was 29% (95% CI: 22%,37%). For 19 articles, with 33,863 participants, reporting the prevalence of self-medication with minerals for the prevention and treatment of Covid-19, the pooled prevalence of self-medication with minerals was 15% (95% CI: 8%, 23%). For 15 articles, with 13,033 participants, reporting the prevalence of concomitant use of minerals and vitamins for self-medication, the pooled prevalence of self-medication was 34% (95% CI: 27%, 42%). The result of the  $\chi^2$  test and the I2 index (P < 0.001, I2 > 98%) indicated notable statistical heterogeneity among the included studies in three meta-analyses [Figs. 2, 3 and 4]. The weights in Figs. 2 and 3 and figure are from the randomeffect analysis.

## Subgroup analysis

Table 4 presents the results of the subgroup analysis. Concerning the continents in which the studies were conducted (Asia and Pacific/Africa/Europe/America), the results of the subgroup analysis showed people who lived in the American continent practiced self-medication with vitamins less for the prevention and treatment of COVID-19 (Pooled prevalence: 12%, 95% CI: 8%,16%); furthermore, the test for heterogeneity between subgroups indicated a statistically significant difference (Q = 35.40, df = 3, p < 0.001), suggesting that the continent may significantly contribute to the overall heterogeneity across studies. Gender of participants (male/female/ both), the income level of countries (low, middle, high), year of publication, sampling technique (random or non-random sampling methods), having or not having a definition for self-medication, and quality assessment of primary studies (low, moderate, high) were not identified as the reasons for the statistical heterogeneity of the individual studies because there was no significant difference between the subgroups(P for heterogeneity between sub-groups > 0.1).

Besides, based on Table 5, the prevalence of self-medication with minerals was higher in studies conducted in Asia (24%, 95% CI: 11%, 39%) than in studies done in other continents. The prevalence of self-medication

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**Table 2** Summary of the results of studies included in systematic review

First author	Publica- tion year	Country	Sample size	Mean age (SD)	Female proportion	Education*	Research quality
Roganovic [32]	2020	Montenegro	101	39.4 (8.7)	NR	NR	Moderate
Amna Abdullah Alotiby [51]	2021	Saudi Arabia	1054	35.1 (12.9)	0.77	0.75	High
Annette d'Argom [21]	2021	Indonesia	610	NR	1.00	0.80	Moderate
Anthony Ike Wegbom [62]	2021	Nigeria	461	42.2 (10.7)	0.57	0.88	High
Arnold J. Sadio [63]	2021	Togo	955	36 (NR)	0.28	0.51	Moderate
Chun Sing Lam [53]	2021	Hong Kong	632	NR	0.63	0.82	Moderate
Deepti Chopra [37]	2021	India	1100	NR	0.48	NR	High
Eman Elayeh [48]	2021	Jordan	1179	32.0 (12.5)	0.56	0.60	High
Hamna Azhar [38]	2021	India	290	38 (NR)	0.62	NR	Moderate
Irene A. Kretchy [64]	2021	Ghana	1195	25 (NR)	0.54	0.94	Moderate
Mahlagha Dehghan [45]	2021	Iran	782	31.0 (9.1)	0.66	0.77	High
Narjes Heshmatifar [46]	2021	Iran	342	66.2 (5.6)	0.55	NR	High
Rana Talha Saleem [33]	2021	Pakistan	520	21.7 (1.9)	0.53	NR	High
T.J Ainsy Goldlin [39]	2021	India	323	NR	0.65	0.40	Moderate
V.D. Tran [54]	2021	Vietnam	787	26.0 (NR)	0.64	0.90	Moderate
Zainab Nazneen [29]	2021	Pakistan	400	NR	0.45	NR	Moderate
Abdoulaye Toure [7]	2022	Guinea	975	33.5 (NR)	0.52	NR	High
Agnete Egilsdatter Kristof- fersen [68]	2022	Norway	1008	46.4 (18.7)	0.48	0.53	High
Andrés Gaviria-Mendoza [71]	2022	Colombia	397	31.0 (NR)	0.58	0.67	High
Anna Merwid-L [26]	2022	Poland	624	NR	0.74	NR	Moderate
Bakhtawar Chaudhry [44]	2022	Pakistan	460	38.0 (NR)	0.41	NR	High
Chidinma Ihuoma Amuzie [65]	2022	Nigeria	469	39.9 (13.5)	0.57	0.71	High
Eva Amenta [72]	2022	USA	150	57.8 (14.6)	0.14	0.71	Moderate
Eva Gerbier [23]	2022	Five European countries (Norway, Belgium, the United Kingdom, Switzerland, The Netherlands)	5210	NR	NR	0.73	Moderate
Faiqah Batrisyia Syaza Bahrin Dzulkharnain [55]	2022	Bahrain	364	23.0 (NR)	0.78	0.51	Moderate
Farah Yasmin [3]	2022	Pakistan	489	NR	0.78	NR	Moderate
Feras Jirjeesa [56]	2022	Algeria, Egypt, Iraq, Lebanon, Libya, Tu- nisia, and the United Arab of Emirates	3519	NR	0.68	0.75	Moderate
Gayathri Kothawar [40]	2022	India	210	NR	0.42	NR	Moderate
Ghalia Shamlan [52]	2022	Saudi Arabia	2368	NR	0.66	0.76	Moderate
Hadia Radwan [57]	2022	United Arab Emirates	2060	36.2 (10.1)	0.75	0.76	Moderate

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Table 2 (continued)

First author	Publica- tion year	Country	Sample size	Mean age (SD)	Female proportion	Education*	Research quality
Ibukunoluwa Busayo Bello [66]	2022	Nigeria	356	20.3 (NR)	0.54	NR	High
J. Corbin Norton [73]	2022	United States of America	15,830	NR	0.35	NR	Moderate
Jahan Sharmila [58]	2022	Bangladesh	54	42.0 (14.9)	0.26	0.33	Moderate
Lin Ang [59]	2022	South Korea	2177	32.2 (8.5)	0.55	NR	Moderate
Louise T. C. Mulder [69]	2022	Netherlands	1004	NR	0.51	0.50	Moderate
Malak M. Angor [49]	2022	Jordan	1252	NR	0.54	NR	Moderate
María DR González- González [24]	2022	Mexico	284	NR	0.66	NR	Moderate
Nailya Bulatova [20]	2022	Jordan	560	26.8 (8.4)	0.66	1.0	Moderate
Nitin Joseph [41]	2022	India	294	36.6 (12.1)	0.54	0.58	High
Ogochukwu Chinedum Okoye [30]	2022	Nigeria	669	35.6 (8.7)	0.56	0.97	High
Putri Salisa Maulida [25]	2022	Indonesia	336	NR	0.78	NR	Moderate
Siddhartha Krishna Deka [22]	2022	India	104	NR	0.59	NR	High
Samaneh Naseri [28]	2022	Iran	228	30.5 (5.7)	1.00	0.49	Moderate
Yo-Yu Liu [60]	2022	Taiwan	351	57.0 (7.6)	0.54	0.65	High
Anita Michael [42]	2023	India	328	NR	049	0.74	Moderate
Ayan Aden Moussa [67]	2023	Somalia	350	NR	0.39	NR	High
Fatma Uslu-Sahan [36]	2023	Turkey	177	53.7 (10.1)	1.00	0.17	Moderate
Hamide Arslan Tarus [50]	2023	Turkey	547	30.1 (10.2)	0.74	0.76	Moderate
Maria Letícia Carnielli Tebet [35]	2023	Brazil	396	NR	0.75	NR	Moderate
Maryam Janatolmakan [47]	2023	Iran	147	39.5 (1.1)	0.33	0.39	High
Michael Jeitler [70]	2023	Germany	1138	49.2 (13.7)	0.81	0.55	Moderate
Michelle L Tan [61]	2023	Malaysia	160	41.0 (NR)	0.75	0.26	High
Patel Princy Alpesh [31]	2023	India	512	21.9 (2.2)	0.59	NR	High
Roghayeh Salmani [34]	2023	Iran	241	24.3 (7.3)	0.67	1.0	High
Toral Gohil [43]	2023	India	775	NR	0.61	0.73	Moderate
Zia Ul Mustafa [27]	2023	Pakistan	1173	NR	0.52	0.53	High

<sup>\*</sup>Proportion of people with university education; Abbreviations: NR = not reported; SD = standard deviation

with minerals was lower in studies conducted in high-income countries (6%, 95% CI: 2%, 12%) than in others. Moreover, due to the limited number of studies that have investigated the concomitant use of vitamins and minerals, the subgroup analysis to examine the pooled prevalence of self-medication for the concomitant use of vitamins and minerals was not performed.

#### Meta-regression analysis

The sample size and the age of participants in primary studies were assessed as other explanatory factors to explore possible sources of heterogeneity among studies and inconsistency in the results of the studies. The results of the multivariable meta-regression model showed there was no significant association between sample size and the age of participants with the prevalence of self-medication with vitamins or minerals or both (P value > 0.05).

 Table 3
 Information on self-medication in studies included in systematic review

First author	Overall SM prevalence*	SM preva- lence with vitamins	SM preva- lence with	SM preva- lence with minerals and	Type of vitamins or minerals	Self-medication reason
Roganovic [32]	0.772	0.772	W W	Z.Z	N.	<u>~~</u>
Amna Abdullah Alotiby [51]	NR	0.160	Z Z	E W	Vitamin C	N. N
Annette d'Arqom [21]	0.751	Z Z	Z Z	0.313	NR	NR N
Anthony Ike Weg- bom [62]	0.410	0.213	æ Z	N N	Vitamin C and multivitamin	Fear of stigma or discrimination, fear of being quarantined or self-isolation, delay in receiving treatment at health facilities, the influence of friends to use self-medication to prevent COVID-19, the effect of television, radio, newspaper, and social media, non-availability of drugs for COVID-19 treatment in the health facilities
Arnold J. Sadio [63]	0.342	0.276	N N	NR	Vitamin C	The long delay in finding an appropriate treatment for COVID-19, the influence of social media, the influence of leaders, the stigmatization of people infected with COVID-19
Chun Sing Lam [53]	0.440	Υ Z	ZZ Z	0.253	Vitamin C and vitamin B were the most commonly used vitamins	NR Company of the Com
Deepti Chopra [37]	0.242	0.07	W.	ZZ	Multivitamins	NR NR
Eman Elayeh [48]	0.804	0.330	0.233	Z Z	Zinc, magnesium, iron, vitamin C, vitamin B, vitamin D, multivitamins, omega-3, immune boosters	Being in contact with an infected person, having a positive coronavirus test, preventing COVID-19 infection despite having no symptoms
Hamna Azhar [38]	0.493	0.252	N N	N.	Vitamin D, vitamin C	Being a habit, the unavailability of a doctor required, financial issues, lack of effectiveness of doctor's medicine, fear of getting the virus, bad experience with the doctor
Irene A. Kretchy [64]	0.825	0.727	0.184	NN N	NR	Being influenced by health practitioners, family, friends, colleagues, medicines retail outlets (pharmacy and chemical shops), social media
Mahlagha Deh- ghan [45]	0.840	W.	Ϋ́ Z	0.612	Vitamin D, vitamin C, multivitamin, vitamin B6, vitamin B complex, vitamin E, zinc, calcium, iron, omega 3, folic acid or a combination of supplements	Preventing infection with COVID-19, reducing The anxiety of COVID-19
Narjes Heshmatifar [46]	0.564	N R	N R	0.471	NR	NR
Rana Talha Saleem [33]	0.581	0.102	N.	NR	Vitamins	Save money, save time, symptoms are minor, doctor prescribed me the same medication, past experience, pharmacist advice
T.J Ainsy Goldlin [39]	0.396	0.189	0.074	Z Z	Z.	Fear of visiting hospitals, time-saving, lack of easy access to hospitals, easy availability of drugs in local pharmacies, being familiar with the drugs, trusting online information, getting advice from medical shops, being influenced by family members, friends, TV, newspaper, social media, Internet, and medical websites
V.D. Tran [54]	0.468	NR R	NR	0.354	NR	NR

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First author	Overall SM prevalence*	SM preva- lence with vitamins	SM preva- lence with minerals	SM preva- lence with minerals and vitamins	Type of vitamins or minerals	Self-medication reason
Zainab Nazneen [29]	0.815	0.057	N.	NR	Multivitamins	Lack of resources like shortage of time and money, flaws in healthcare delivery, mild illness, drug accessibility
Abdoulaye Toure [7]	0.151	0.042	N.	Z.	Vitamin C	NR
Agnete Egilsdatter Kristoffersen [68]	0.570	N N	N.	0.430	NR	Improving well-being, preventing COVID-19, treating COVID-19-related symptoms
Andrés Gaviria- Mendoza [71]	0.343	0.073	£	œ Z	Vitamins	Having knowledge about the treatment for their discomfort, fear of being infected by coronavirus, difficult access to services due to administrative procedures, little time availability, fear of being penalized for leaving home, mistrust in health personnel or institutions, economic difficulties, difficulty in transportation, health system affiliation problem, fear of getting the COVID-19
Anna Merwid-L [26]	0.700	0.553	0.189	œ Z	Magnesium, vitamin B6, vitamin B-group complex, vitamin D, vitamin C, vitamin B12, multivitamin, iron, zinc, vitamin E, vitamin A+E, folic acid, calcium, vitaminized beverages, biotin	improving immunity and willingness to stay healthy
Bakhtawar Chaudhry [44]	0.343	0.391	0.235	Z Z	Vitamin D, vitamin C, folic acid, calcium	Already existing habits, unavailability of the physician, financial issues, difficulty in traveling, reaching healthcare professionals, lack of effectiveness of medicines prescribed by a physician, fear of contracting the virus, bad experience with the physician
Chidinma Ihuoma Amuzie [65]	0.266	0.085	0.026	X Z	Vitamin supplement, calcium supplement	Fear of being isolated due to COVID-19, fear of being infected through a fear of stigmatization due to COVID-19 disease, fear of being infected through a confirmed case of COVID-19, poor services of the health system, death of a colleague/family member due to COVID-19, anticipated delay in laboratory test results, being influenced by friends and the media
Eva Amenta [72]	0.273	0.267	N N	W W	Vitamin C	Supporting the immune system, ensuring getting enough vitamin C to prevent COVID-19
Eva Gerbier [23]	0.148	0.145	0.111	NR	NR	NR
Faiqah Batri- syia Syaza Bahrin Dzulkharnain [55]	0.882	0.593	N N	æ Z	W.	Using OTC medicines due to the convenience and easy accessibility, consulting with family members beforehand, time-saving, low cost, being safe and tolerable, easy accessibility, effectiveness
Farah Yasmin [3]	0.830	0.560	NR N	NR	Multi-vitamin	Preventive measures for COVID-19 symptoms
Feras Jirjeesa [56]	0.399	Z Z	N N	0.245	Vitamins and dietary supplements	Prophylaxis before infection with COMD-19
Gayathri Kothawar [40]	0.490	0.395	0.148	N N	Vitamin C, multivitamin, B	To prevent the COVID-19
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continued)	
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Table	

First author	Overall SM prevalence*	SM preva- lence with	SM preva-	SM preva- lence with	Type of vitamins or minerals	Self-medication reason
	-	vitamins	lence with minerals	minerals and vitamins		
Ghalia Shamlan [52]	0.231	0.231	NR	NR	Vitamin D	Boost immunity against COVID-19 infection
Hadia Radwan [57]	0.565	0.478	0.056	NR	Vitamin C, vitamin D, multivitamin, calcium, B complex, zinc, iron, folic acid	Preventing or treating COVID-19
Ibukunoluwa Busayo Bello [66]	0.654	0.520	N N	0.157	Vitamin C, multivitamin, minerals	N
J. Corbin Norton [73]	0.125	0.087	0.018	0.030	Vítamin C, vitamin D, multivitamin, zinc, vitamin B, B complex, B12, B6, vitamin E	N. Y.
Jahan Sharmila [58]	0.944	0.611	NR	NN	NR	NR
Lin Ang [59]	0.361	NR	NR M	0.172	NR	NR
Louise T. C. Mulder [69]	0.680	Z Z	N N	0.550	NR	N
Malak M. Angor [49]	0.847	0.738	0.694	Z Z	NR.	N
María DR González- González [24]	0.268	0.144	N N	X Z	NR	N
Nailya Bulatova [20]	0.641	NR	NR	0.484	NR	NR
Nitin Joseph [41]	0.037	0.020	Z Z	Z Z	Vitamin C, multivitamin	AR AN
Ogochukwu Chin- edum Okoye [30]	0.363	0.027	0.007	Z Z	Vitamin C, zinc	Poor access to public health facilities, long waiting time, unavailability of essential medicines at hospitals, the high cost of visiting private health facilities
Putri Salisa Maulida [25]	0.408	Z Z	Z Z	0.375	Vitamin C, vitamin E, vitamin D, multivitamin, vitamin B complex, zinc	COVID-19 Prevention and COVID-19-related symptoms
Siddhartha Krishna Deka [22]	0.510	0.01	N N	NR	Vitamin C	N
Samaneh Naseri [28]	696:0	Z Z	0.061	Z Z	Ferfolic, calcium	EN.
Yo-Yu Liu [60]	699.0	N.	N.	0.225	NR	N.S.
Anita Michael [42]	0.835	Ψ Z	K K	0.308	Vitamins and mineral supplements	Time-saving, money-saving, believing it is not necessary to visit a doctor for minor illnesses, believing some OTC drugs provide faster relief compared to prescribed medications, prior experience, habit, lack of medical support or hospitals nearby, lack of assistance to guide me to the hospital
Ayan Aden Moussa [67]	0.629	0.569	NR	NR	ZZ.	Hospital far from home, high cost, pharmacist advice, old prescription

Table 3 (continued)

	(5.2.1)					
First author	Overall SM	SM preva-	SM	SM preva-	Type of vitamins or	Self-medication reason
	prevalence*	lence with vitamins	preva- lence with minerals	lence with minerals and vitamins	minerals	
Fatma Uslu-Sahan [36]	0.554	0.508	Z Z	N N	Multivitamin	To increase the body's resistance to protect against COVID-19, to boost hope and positive thinking, to reduce stress and relax physically, to reduce the undesirable effects of medical treatment, not to feel pain
Hamide Arslan Tarus [50]	0.720	0.355	N N	N.S.	Vitamin C, E, and D	To prevent the disease before being diagnosed with COVID-19 or to reduce symptoms after being diagnosed with COVID-19
Maria Letícia Carni- elli Tebet [35]	0.136	0.076	0.028	N.	Vitamin D, vitamin E, vita- min C, zinc	NR
Maryam Janatol- makan [47]	0.694	0.592	W Z	Ψ Z	Vitamins (C, D, multivitamins B complex)	Strengthening the immune system, preventing COVID-19, fear of getting COVID-19, death of relatives or acquaintances due to COVID-19, direct contact with persons with COVID-19, treating possible symptoms of COVID-19, fear of hospitalization, fear of being quarantined, unavailability of COVID-19 treatment in the hospitals, crowded medical centers, having information in the field of pharmacology, pressure from family members and friends, existence of healthcare workers among family members and friends, pharmaceutical advertising in mass media, inadequate quality of hospital care, high costs of treatment, lack of access to a doctor, being away from medical centers, not having enough time to see a doctor
Michael Jeitler [70]	NR	0.018	0.005	æ Z	Vitamin D, vitamin B complex or Vitamin B12, magnesium	NR NR
Michelle L Tan [61]	0.706	0.619	0.619	ZZ Z	Vitamin C, vitamin D, zinc, multivitamin supplements	Fear of being infected by COVID-19, difficulty getting to a clinic or hospital, time-saving
Patel Princy Alpesh [31]	0.744	0.310	0.258	N.	Multivitamins, zinc, vitamin C	NR
Roghayeh Salmani [34]	0.510	Z Z	N N	0.278	Multivitamins and mineral supplements	Previous use and effectiveness of the drug in the past, no major illness, no need to see a physician, the existence of a free drug market, lack of insurance
Toral Gohil [43]	0.841	0.720	0.400	N.	Vitamin C, zinc, multivita- mins, Vitamin D	Evidence regarding the effectiveness for COVID-19, popularity, belief, easy to take, more effective, cheaper, fewer side effects
Zia Ul Mustafa [27]	0.660	0.395	0.101	N.	Multivitamins, vitamin C, calcium, zinc supplement	COVID-19 prevention, Suspected COVID symptoms, COVID-19 positive
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\*The overall prevalence of self-medication with any type of medication; Abbreviations: NR= not reported; SM= self-medication

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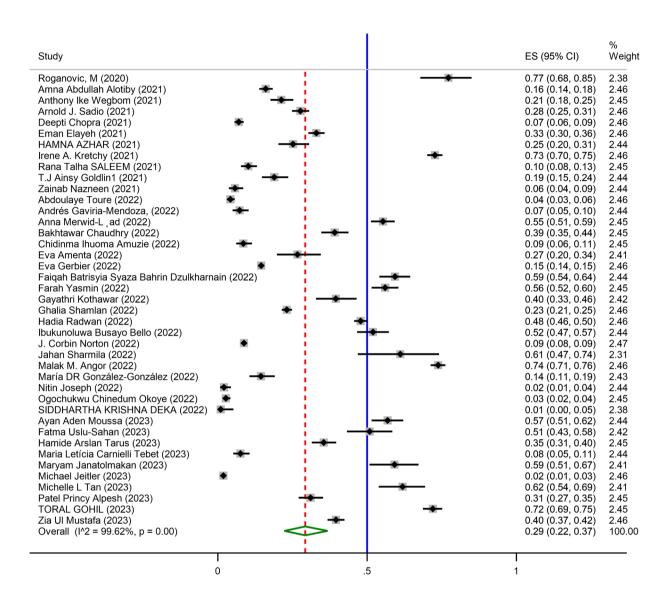


Fig. 2 Forest plot of the pooled prevalence of self-medication with vitamins

Therefore, age and sample size were not the reasons for the variability in the results.

#### Discussion

This study reviewed self-medication with vitamin or mineral supplements during the COVID-19 pandemic. To the best of the researchers' knowledge, this is currently the most up-to-date systematic review of the prevalence of vitamin or mineral supplements self-medication during the pandemic. The findings reveal a significant prevalence of self-treatment with vitamins and minerals, particularly in Asian countries. Although there is no accurate basis for comparing this study's results with the prevalence of self-medication with vitamins and minerals

before the COVID-19 pandemic, it is possible that due to the anxiety induced by COVID-19, paying more attention to health during the pandemic, and the increased misinformation in virtual space, this prevalence has been increased compared to the pre-COVID period. Easy access to vitamins and supplements may be the reason for self-medication. This aligns with findings of Zheng et al. indicating high rates of self-medication during the pandemic, where individuals often relied on personal knowledge rather than professional medical advice for their health decisions [75]. Therefore, there is a need to monitor the use of vitamins and supplements without a physician's prescription.

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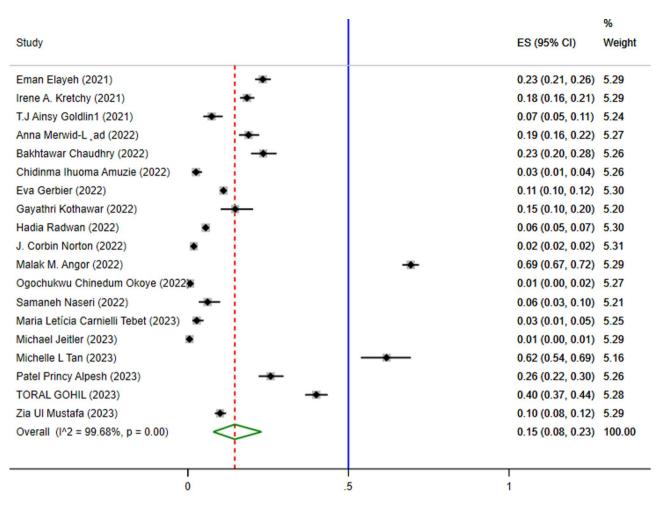


Fig. 3 Forest plot of the pooled prevalence of self-medication with minerals

The prevalence of self-medication with vitamins and minerals for the prevention and treatment of COVID-19 varied widely in the primary studies included in this systematic review and meta-analysis. The difference in methodology or socioeconomic and cultural differences, differences on definitions of self-medication, the pharmaceutical laws and regulations of the place where the research was conducted may be the reasons related to this wide variation in the prevalence of vitamin and mineral self-mediation of reviewed studies.

In the study by Ayosanmi et al. [5], the prevalence of self-medication with vitamins and minerals was reported higher than in the present study. The difference between the results of this study and our study about the prevalence of self-medication with vitamins and minerals may be related to the period of extracting the articles of the two studies.

Our results indicate that Time-saving, being influenced by family members, friends, and media, unavailability of the physician, lack of effectiveness of medicines prescribed by the physician, fear of stigma, discrimination, or being infected with COVID-19, convenience and easy accessibility, and financial issues were the reasons for self-medication, as reported in other systematic review studies on self-medication during COVID-19 pandemic [6, 10–14]. Many individuals turned to self-medication as a way to save time, especially when faced with long waiting periods at healthcare facilities. Additionally, the fear of infectious COVID-19 in medical settings intensified this trend, prompting people to seek quick relief through self-medication instead of waiting for professional help [75, 76]. Furthermore, due to stigma, some individuals were afraid of being judged or treated differently if they wanted help from healthcare facilities for symptoms related to COVID-19 [76]. Influences from family, friends, and the media significantly shaped their views and spread misinformation about self-medication. Consequently, people often relied on these sources for advice on medications, frequently without sufficient medical guidance.

According to the results, the highest prevalence of self-medication was in Asia, which is in line with Kazemioula et al.'s study results on self-medication practice during the COVID-19 pandemic [4]. The higher prevalence

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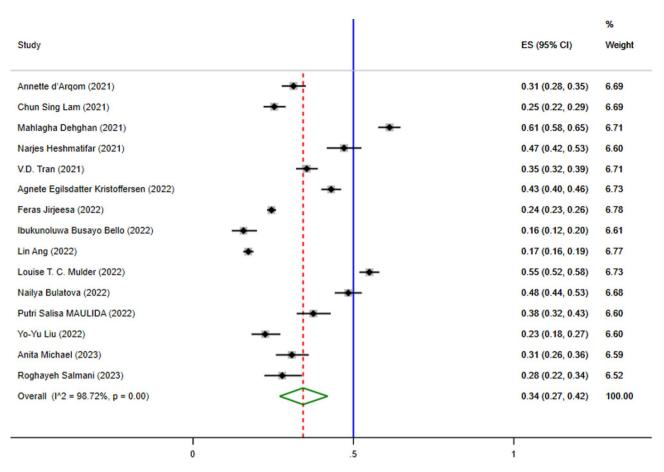


Fig. 4 Forest plot of the pooled prevalence of concomitant use of minerals and vitamins

of self-medication in Asia may be related to a complex interplay of cultural beliefs, economic constraints, vaccine availability, fear-driven behaviors, and regulatory challenges associated with selling vitamins and minerals. In many Asian countries, cultural attitudes towards health often prioritize self-care and the use of traditional remedies. Economic factors also play a significant role, as limited access to healthcare services and the high costs of medical consultations lead many people to turn to selfmedication [77]. As a result, individuals often view selfmedication as a quicker and more affordable option than seeking professional medical advice. Moreover, the early unavailability or doubts about their effectiveness in some countries likely contributed to the public's reliance on alternative preventive measures, including vitamin and mineral use.

In contrast, high-income countries revealed the lowest rates of self-medication, likely due to stronger health-care systems, effective public health communication, and severer regulations on the marketing and availability of supplements. Napolitano et al. mentioned that in high-income countries, law enforcement, awareness campaigns, and effective supervision contribute to a decrease in the prevalence of self-medication [78]. In addition, the

concern about the adequacy of mineral intake such as iron through daily food may be greater in people of low-income countries. In these regions, where nutritional deficiencies are common, it's crucial to implement public health initiatives that focus on improving food intake rather than relying on supplements. Educating people about balanced diets and increasing access to fortified foods could help reduce the reliance on self-medication with vitamins and minerals.

Self-medication with vitamins and minerals is a world-wide practice. Although it may be helpful as a self-care practice, it might lead to adverse health consequences as well as a waste of household income. Therefore, it seems necessary to establish rules and regulations for people accessing supplements without a physician's prescription. Furthermore, it is necessary to provide public education to control the self-medication practice. Consumers should be aware that supplements may contain actual pharmaceuticals or nothing of value and have significant toxic potential. In regions with high supplement use, culturally sensitive health education involving community healthcare workers and local media is needed to address misconceptions about supplements. Efforts should focus on enhancing access to healthcare and encouraging

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**Table 4** Subgroup analysis to estimate the pooled prevalence of self-medication with vitamins by gender, publication year, continent, economic level of the country, sampling technique, having a definition for self-medication, and quality assessment

Subgroups		Number of	Prevalence (95%CI)	Heterogene	ity Between studies	Test for
		studies		l <sup>2</sup>	P <sub>heterogeneity</sub>	heterogene- ity between sub-groups
Publication	2020	1	77% (68%,85%)			Q=4.09; Df=3;
year	2021	10	22% (10%,37%)	99.49%	< 0.001	P = 0.252
	2022	20	26% (17%,36%)	99.68%	< 0.001	
	2023	10	39% (21%,59%)	99.53%	< 0.001	
Gender of participants	Female	2	15% (14%,16%)			Q = 2.35; $Df = 1$ ;
	Both	39	29% (22%,37%)	99.63%	< 0.001	P = 0.125
Economic level of the	Low	2	35% (33%,38%)			Q = 3.11; $Df = 2$ ;
country	Moderate	30	30% (20%,40%)	99.49%	< 0.001	P = 0.210
	High	9	25% (15%,37%)	99.73%	< 0.001	
Sampling technique	Random	6	43% (18%,71%)	99.65%	< 0.001	Q = 1.47; $Df = 2$ ;
	Non-random	32	24% (18%,31%)	99.50%	< 0.001	P = 0.480
	Unknown	3	58% (19%,92%)			
Definition for SM	Yes	25	28% (18%,38%)	99.47%	< 0.001	Q = 1.07; $Df = 1$ ;
	No	16	32% (21%,44%)	99.72%	< 0.001	P = 0.300
Continent	Asia	24	35% (25%,43%)	99.35%	< 0.001	Q=35.40; Df=3;
	Africa	8	27% (9%,51%)	99.69%	< 0.001	
	Europe	4	32% (10%,60%)	99.69%	< 0.001	P < 0.001
	America	5	12% (8%,16%)	91.39%	< 0.001	
Risk of bias	Low	18	22% (13%,31%)	99.16%	< 0.001	Q = 2.44; Df = 1;
	Moderate	23	36% (25%,47%)	99.74%	< 0.001	P = 0.118

**Table 5** Subgroup analysis to estimate the pooled prevalence of self-medication with minerals by gender, publication year, continent, economic level of the country, sampling technique, having a definition for self-medication, and quality assessment

Subgroups		Number of	Prevalence (95%CI)	Heterogene	ity Between studies	Test for
		studies		l <sup>2</sup>	P <sub>heterogeneity</sub>	heterogene- ity between sub-groups
Publication	2021	3	16% (8%,25%)			Q=1.61; Df=2;
year	2022	10	15% (9%,21%)	99.73%	< 0.001	P = 0.450
	2023	6	23% (13%,33%)	99.50%	< 0.001	
Gender of participants	Female	2	11% (10%,12%)			Q = 2.04; Df = 1;
	Both	17	19% (15%,23%)	99.64%	< 0.001	P = 0.153
Economic level of the	Moderate	14	22% (13%,31%)	99.65%	< 0.001	Q = 8.80; $Df = 1$ ;
country	High	5	6% (2%,12%)	99.38%	< 0.001	P < 0.001
Sampling technique	Random	4	21% (7%,35%)	99.37%	< 0.001	Q = 2.51;
	Non-random	15	13% (10%,16%)	99.26%	< 0.001	Df = 1; P = 0.113
Definition for SM	Yes	6	25% (8%,42%)	99.83%	< 0.001	Q = 1.35; $Df = 1$ ;
	No	13	15% (11%,18%)	99.36%	< 0.001	P = 0.250
Continent	Asia	11	24% (11%,39%)	99.62%	< 0.001	Q=19.90;
	Africa	3	7% (1%,15%)			Df = 3; P < 0.001
	Europe	3	10% (1%,19%)			
	America	2	2% (1%,3%)			
Risk of bias	Low	8	19% (11%,26%)	99.17%	< 0.001	Q = 3.64; $Df = 2$ ;
	Moderate	10	12% (9%,15%)	99.33%	< 0.001	P = 0.162
	High	1	69% (67%,72%)			

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nutrition from food sources, such as by subsidizing or fortifying staple foods, to decrease dependence on supplements.

# Strengthens, limitations, and recommendations

This study found relative advantage compared to the previous studies by narrowing the review question, expanding the search interval in systematic review and meta-analysis, searching for more sources, including more articles, and performing subgroup analysis and meta-regression. However, this study had some limitations. Lack of access to the Embase database and review of only cross-sectional studies were two of the limitations of the present study. Another limitation of the study was the inclusion of studies with different definitions for selftreatment or even without a clear definition. One of the main limitations of this study was the high heterogeneity observed among the included studies. This could be attributed to differences in population characteristics, definitions of self-medication and the types of supplements used. Although random-effects model was applied and subgroup analyses were conducted to explore potential sources of heterogeneity, the results should still be interpreted with caution. Nevertheless, this heterogeneity may also reflect the real-world diversity in self-medication behaviors across different settings, which is itself an important finding. It is suggested to conduct future review studies on self-medication with herbal medicines and home remedies aimed at preventing and treating COVID-19. The availability or lack of vaccines against this disease, a factor whose data were not available in our selected eligible studies, could be an important factor to investigate in future studies.

# **Conclusions**

The reported prevalence of self-medication with vitamins and minerals to prevent and treat COVID-19, especially in Asia, is concerning and needs more public health action. It is suggested to plan for providing more education about how a vitamin or mineral is ineffective for a person without vitamin or mineral deficiency to prevent or treat a viral disease. In addition, people should be educated about the possibility of poisoning with vitamins and minerals because awareness of the risks of supplements can reduce self-medication practices at present and even in future pandemics.

## **Supplementary Information**

The online version contains supplementary material available at https://doi.or q/10.1186/s40795-025-01083-5.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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#### **Author contributions**

SHR and FR planned and designed the study. ND and NSH and FA wrote the original draft. SFM performed the statistical analysis. SHR and FR performed manuscript preparation and revised the manuscript. All authors reviewed, edited, and/or approved the final manuscript for submission.

#### **Funding**

Not applicable.

#### Data availability

The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

#### **Declarations**

#### Ethics approval and consent to participate

This study was approved by the Ethics Committee of Hormozan University of Medical Sciences, Bandar Abbas, Iran (code: IR.HUMS.REC.1400.278).

#### Consent to participate

Not applicable.

#### Consent for publication

Not applicable.

# **Competing interests**

The authors declare no competing interests.

#### **Author details**

<sup>1</sup>Social Determinants in Health Promotion Research Center, Hormozgan Health Institute, Hormozgan University of Medical Sciences, Bandar Abbas. Iran

<sup>2</sup>Department of Nursing, Nursing and Midwifery School, Shahed Square, Jiroft University of Medical Sciences, Jiroft 7861756447, Iran <sup>3</sup>Fertility and Infertility Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

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