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ARTICLE A systematic review and meta-analysis on the prevalence of stigma in infectious diseases, including COVID-19: a call to action

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Infectious diseases, including COVID-19, are crucial public health issues and may lead to considerable fear among the general public and stigmatization of, and discrimination against, specific populations. This meta-analysis aimed to estimate the pooled prevalence of stigma in infectious disease epidemics. We systematically searched PubMed, PsycINFO, Embase, MEDLINE, Web of Science, and Cochrane databases since inception to June 08, 2021, and reported the prevalence of stigma towards people with infectious diseases including SARS, H1N1, MERS, Zika, Ebola, and COVID-19. A total of 50 eligible articles were included that contributed 51 estimates of prevalence in 92722 participants. The overall pooled prevalence of stigma across all populations was 34% [95% CI: 28-40%], including enacted stigma (36% [95% CI: 28-44%]) and perceived stigma (31% [95% CI: 22-40%]). The prevalence of stigma in patients, community population, and health care workers, was 38% [95% Cl: 12-65%], 36% [95% Cl: 28-45%], and 30% [95% CI: 20-40%], respectively. The prevalence of stigma in participants from low- and middle-income countries was 37% [95% CI: 29–45%], which is higher than that from high-income countries (27% [95% CI: 18–36%]) though this difference was not statistically significant. A similar trend of prevalence of stigma was also observed in individuals with lower education (47% [95% Cl: 23-71%]) compared to higher education level (33% [95% CI: 23-4%]). These findings indicate that stigma is a significant public health concern, and effective and comprehensive interventions are needed to counteract the damaging effects of the infodemics during infectious disease epidemics, including COVID-19, and reduce infectious disease-related stigma.

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INTRODUCTION

The outbreak of the coronavirus disease 2019 (COVID-19) around the world has brought public attention to infectious disease epidemics again [1]. In fact, infectious diseases have become more frequent and more complex in recent years, with notable examples such as severe acute respiratory syndrome (SARS), influenza A subtype H5N1, Zika, Ebola, and Middle East respiratory syndrome coronavirus (MERS-CoV) [2], which pose a health threat to the general public and are issues of concern for public health professionals in terms of preventing their spread, promoting public awareness, and educating the public about the diseases [3-5].

In view of the possibility of the rapid spread of infectious diseases, infodemics (the rapid and far-reaching dissemination of information of questionable quality) during epidemics and subsequent protracted physical and psychological morbidity and mortality, epidemic-related stigma emerges consequently [6-9]. Stigma is described as an attribute that is deeply discreditable or undesirable [10] and is further conceptualized as a social process of labeling, stereotyping, and prejudices that lead to segregation, devaluation, and discrimination [10]. Various layers of stigma are explored, including enacted (experienced) stigma and perceived public (anticipated) stigma. Enacted stigma refers to actual negative actions taken against someone due to their infection status [11]. Perceived public stigma refers to the perception of being stigmatized and the anticipation of being discriminated against [12].

Populations vulnerable to stigma during infectious disease epidemics involve both infected individuals and health care

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workers, especially frontline medical staff [9]. Substantial incidents of stigmatization of healthcare workers and patients have come up during the COVID-19 pandemic across the world [13]. Some patients were fearful of being shamed and accused by others [14], which will bring extra psychological burden to patients and can hinder their social adaptation after recovery. As for frontline medical workers, they were at higher risk of being exposed to COVID-19 virus when working in the hospitals or clinics. Stigma from their families and friends might increase their psychological stress and interfere with their normal work [9]. It was even reported that patients recovered from COVID-19 infection and medical workers were denied access to public transportation, assaulted on the street or in the ordinary course of work, and forced to move out of their rented houses [15, 16]. However, these over-generalized applications of stereotypes should be differentiated from realistic fear caused by epidemics. In this case, negative reactions to involved populations does not necessarily mean stigmatization. Some kind of avoidance or social distancing measures during epidemics (e.g., imposing shelter-inplace orders, restricting dining-in at restaurants, home isolation) are required and have been shown effective in containing the spread of the virus [17].

Stigma and discrimination may cause mental stress, physical harm, and loss of jobs and educational opportunities for involved populations, and further pose a serious threat to the control of epidemics and the recovery and development of the economy and society [13, 18, 19]. Evidence has suggested that stigma contributed to psychological distress and acute and posttraumatic stress (PTSD) of affected patients and healthcare workers during SARS, H1N1, MERS, Ebola, and COVID-19 outbreaks [20-23]. A cross-sectional study also found that higher level of depression and anxiety were significantly associated with the experience of health facility-related stigma among Ebola survivors [24]. Therefore, stigma can be a hindrance for the public to have an accurate understanding of the disease and can act as a barrier for them to adopt health promoting behavior, seek health care and adhere to treatment, which may lead to suboptimal control of epidemics [25, 26].

As COVID-19 might be a continuing threat for the human society, stigma related to this pandemic would be a long-term concern for wellbeing, social recovery, and development in a long time [27]. The rapid spread of the pandemic was associated with high levels of fear [28, 29]. From a public health perspective, fear and its associated stigma constituted the high impact of the pandemic [30]. Stigma is a barrier to help-seeking. That means people may not use services (diagnostics, prevention, and/or treatment) in order to avoid labeling/stigma. Therefore, fear associated with stigma and discrimination has significantly compromised the public health efforts [31, 32]. Identifying the influence of stigma during the pandemic would be helpful not only for the mental health of affected patients, but also for policy making and social support services globally. However, there is a lack of quantitative estimate of stigma profiles and risk factors among affected individuals during infectious disease epidemics. Therefore, this systematic review and meta-analysis aimed to evaluate the prevalence of stigma during infectious disease epidemics, including COVID-19, to raise public health concern and call for actions to promote the development of effective and comprehensive interventions to reduce infectious disease-related stigma.

METHODS

Search strategy and selection criteria

We performed a systematic review and meta-analysis in accordance with preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines (Table S1) [33]. The protocol was registered in International Prospective Register of Systematic Reviews (PROSPERO

CRD42020206287 at www.crd.york.ac.uk/PROSPERO). We searched the PubMed, PsycINFO, Embase, MEDLINE, Web of Science, and Cochrane databases to identify studies that reported the prevalence of stigma during infectious disease epidemics, including SARS, MERS, H1N1, H5N1, Zika, Yellow fever, Ebola, Viral Haemorrhagic fevers, and COVID-19, since inception to June 8, 2021. However, other infectious diseases like tuberculosis were not included in our study, as we focused on the infectious diseases that cause a sudden increase in the number of infected cases in a short period of time, of which the outbreak has posed serious public health threats and has been associated with stigma and discrimination against related populations. The search terms were shown in the Appendix. The literature search was limited to English. We also checked the reference lists and review articles for additional studies that might meet the inclusion criteria.

Three researchers (Huang XL, Zhang YX, and Huang YT) independently assessed the articles for their eligibility for inclusion. The studies that met the following criteria were included: (1) cross-sectional or cohort studies on the epidemics of infectious diseases including SARS, MERS, H1N1, H5N1, Zika, Yellow fever, Ebola, Viral Haemorrhagic fevers, and COVID-19; (2) defining stigma via self-reported perception or questionnaires; and (3) directly providing prevalence of stigma or sufficient data to calculate the prevalence. Exclusion criteria were as follows: (1) guidelines, book sections, case-reports, commentaries, and conference abstracts; and (2) studies that measured stigma as a numerical variable without cut-off value and the prevalence could not be calculated. If the same population was used in more than one publication, only one publication with the most comprehensive information would be included. The process of identifying eligible studies and the reasons for exclusion are shown in Fig. 1 and eTable 1 in Appendix.

Data extraction

The data were independently extracted from eligible papers by researchers (Huang XL, Huang YT, Zhong Y, and Wang YJ) and the extracted data were subsequently cross-checked. Discrepancies were discussed until a consensus was reached. The following information was extracted from each study: (1) first author, (2) year of publication, (3) study design, (4) research site (country), (5) total sample size, (6) type of epidemics of infectious diseases, (7) sex proportion of participants, (8) type of study population (patients, community population, and health care workers), and (9) measurement of stigma (question or scale), classification of stigma (enacted stigma, and perceived stigma), etc. (see Table 1).

Assessment of study quality

Two researchers (Huang XL and Su SZ) assessed the quality of the studies using the Australia's Joanna Briggs Institute (JBI) critical appraisal checklist for prevalence studies [34]. It consists of nine items, and four options (yes, no, unclear, and not applicable) were used for evaluating items (see eTable 2 in Appendix). Disagreements were discussed with and resolved by a third author (Zhang YX).



Fig. 1 Study selection flow diagram. We systematically searched the PubMed, PsycINFO, Embase, MEDLINE, Web of Science, and Cochrane databases to identify studies that reported the prevalence of stigma during infectious disease epidemics. A total of 112,556 articles were identified. After screening, 50 eligible studies were included in this meta-analysis.

Table 1. Chara	acteristics of the	studies included i	n the meta-analysis.							
Study	Country	Study design	Type of epidemics	Type of stigma	Total sample size	Effective sample size	Participants	Female (%)	Prevalence of stigma (%)	Measurement of stigma
Abdelhafiz et al., 2020 [79]	Egypt	Cross sectional	COVID-19	Enacted stigma	559	559	Community population	62.3	22.7	Items: Infection with the virus is associated with stigma
Abdel Wahed et al., 2020 [78]	Egypt	Cross sectional	COVID-19	Enacted stigma	407	407	Health care workers	49.4	66.3	Items: Those who get infection is the public stigmatizers
Abuhammad et al., 2020 [80]	Jordan	Cross sectional	COVID-19	Enacted stigma	2000	1655	Community population	63.8	46.1*	Scale: A self- administered questionnaire
Alzoubi et al., 2020 [74]	Jordan	Cross sectional	COVID-19	Perceived stigma	592	592	Undergraduate students	65.5	5.4	ltems: Infection is a stigma
Aqeel et al., 2020 [81]	India	Cross sectional	COVID-19	Enacted stigma	1050	823	Community population	43.01	73.34	Items: COVID-19 infection has become a social stigma; Therefore, the patients are reluctant to disclose their symptoms at the early stage
Badi et al., 2021 [88]	Sudan	Cross sectional	COVID-19	Enacted stigma	657	657	Community population	60.4	5.2	Items: Do you agree that the infection with the virus is associated with stigma
Bai et al., 2004 [60]	China	Cross sectional	SARS	Enacted stigma	338	338	Hospital staff	51.0	20.0*	Items: Stigmatization and rejection in the neighborhood because of hospital work
Cassiani- Miranda et al., 2020 [82]	Colombia	Cross sectional	COVID-19	Enacted stigma	1687	1687	Community population/ health care workers	59.0	4.1*	Scale: Questionnaire on COVID-19 Stigma- Discrimination
Chen et al., 2020 [<mark>83</mark>]	China	Cross sectional	COVID-19	Perceived stigma	5239	1902	Community population	43.89	44.34	ltems: Perceived discrimination
Chong et al., 2004 [6 1]	China	Cross sectional	SARS	Perceived stigma	1257	1007	Health care workers	81.1	59.6	Items: People avoid my family because of my work
De Roo et al., 1998 [14]	Congo	Cross sectional	Ebola	Perceived stigma	¥.	34	Ebola survivors	76.0	35.0	Items: They tried to escape from their family or immediate neighborhood during their illness because haemorrhagic fever was a very stigmatizing disease
Elhadi et al., 2020 [84]	Libyan	Cross sectional	COVID-19	Perceived stigma	800	745	Health care workers	51.9	31.0	ltems: Feeling stigmatized
Etard et al., 2017 [6 8]	Guinea	Cohort	Ebola		802	786	Ebola survivors	55.0	26.0	Items: Your situation is predominantly one of the stigma's effects
Etokidem et al., 2018 [<mark>72</mark>]	Nigeria	Cross sectional	Ebola	Enacted stigma	177	177	Nursing students	94.4	22.0*	Item: (1) If your friend who had EVD has been certified cured of the disease, would you be

1 continu	Country	Study design	Tvne of enidemics	Tvne of stiama	Total	Effective	Particinants	Female (%)	Prevalence	Measurement
		ufican Annic			sample size	sample size			of stigma (%)	of stigma weilling to continue to be his/ her friend? (2) If
										a food vendor in the school cafeteria is known to have had EVD but is now certified cured, would you still eat the food she prepares? (3) If you know that your patient had EVD but has been certified cured, would you take part in his or her surgical operation as the theater nurse? (4) If you know that your patient who has come in labor had EVD but has been certified cured, would you deliver her of her baby?
al.,	Greece	Cross sectional	A/H1N1 influenza	Perceived stigma	469	469	Health care workers	68.4	3.8	ttems: I felt that family members and friends avoided them because of their hospital work
al,	Canada	Cross sectional	SARS	Perceived stigma	193	193	Health care workers	32.1	35.8	ttems: Physicians felt that they had been treated differently because others knew they had potentially been exposed to a SARS pattent (i.e., stigmatization)
t al.,	ž	Cross sectional	COVID-19	Perceived stigma	1194	1194	Health care workers	92.4	36.5	ltems: Feeling moderately to extremely stigmatized
<u>0</u>	Philippines	Cross sectional	Zika	Perceived stigma	609	609	Teaching staffs	68.5	42.2*	ttems: (1) If a person gets Zika, he/she is discriminated or stigmatized because of it; (2) If a person gets Zika, his/ her family is discriminated or stigmatized because of fir; (3) If somebody in my family were to get Zika, I would want it to remain private or a secret.
t al.,	Indonesia	Cross sectional	COVID-19	Perceived stigma	335	335	Community population	19.4	53.43	Items: Items about social support, social trust, perceived stigma, and experience on the COVID-19 test and quarantine were also

	easurement stigma	dopted from previous udies	ems: Would not elcome survivor sclared to be cured of ola back into the immunity	irrivied Ebola puts thers in the class at thers in the class at sould not buy ould not buy getables from a ould not welcome mmunity;(4) pressed at least one scriminatory attitude wards Ebola	ale: Ebola-related gma Questionnaire	ale: The Stigma Scale S) 20	ale: Seven-item EVD- lated stigma index	ems: Experiences igma from the ammunity: perceived oidance by family embers or their annunity owing to igma and fear of mitracting COVID-19 on them (e.g., oidance from family embers, friends, ighbors, and taxi ivers)	ems: (1) I thought that eeople avoid me ecause of my job"; (2) I It that "people avoid y family members :cause of my job."	ems: The Stigma Scale 5) 20	ems: These items were ainly modified from
	Prevalence M. of of stigma (%)	ac	20.8* Ke de Eb Co Co	71.7* 7. 7: 7: 7: 7: 7: 7: 7: 7: 7: 7: 7: 7: 7:	71.8* Sc sti	53.4 Sc (5	16.2* Sc rel	23.3 4 7 7 6 2 1 6 7 7 7 7 1 4 7 6 7 7 1 4 7 6 7 7 1 4 7 7 6 7 1 4 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	39.3* tre fei fei be	32.3 Ité (S	10.1 Ité m
	Female (%)		49.0	23.0	62.3	50.2	56.0	85 25 20	82.0	62.8	54.7
	Participants		Community population	Community population	Ebola survivors	Community population	Ebola survivors	Health care workers	Health care workers	Community population	Community population
	Effective sample size		5029	1413	358	502	859	430	10511	124	457
	Total sample size		5733	1413	400	502	859	430	10511	124	457
	Type of stigma		Enacted stigma	Enacted stigma	Enacted stigma	Perceived stigma	Perceived stigma	Perceived stigma	Perceived stigma	Perceived stigma	Enacted stigma
	Type of epidemics		Ebola	Ebola	Ebola	COVID-19	Ebola	COVID-19	SARS	SARS	SARS
	Study design		Cross sectional	Cross sectional	Cross sectional	Cross sectional	Cohort	Cross sectional	Cross sectional	Cross sectional	Cross sectional
ned	Country		Guinea	Sierra Leone	Sierra leone	Bahrain	Liberia	Singapore	Singapore	HongKong, China	China
Table 1 contin	Study		Jalloh et al., 2017a [69]	Jalloh et al., 2017b [70]	James et al., 2020 [<mark>75</mark>]	Jassim et al., 2021 [<mark>9</mark> 1]	Kelly et al., 2019 [<mark>73</mark>]	Kirk et al., 2021 [92]	Koh et al., 2005 [64]	Lam et al., 2009 [<mark>93</mark>]	Lau et al., 2006 [66]

Table 1 contin	ued									
Study	Country	Study design	Type of epidemics	Type of stigma	Total sample size	Effective sample size	Participants	Female (%)	Prevalence of stigma (%)	Measurement of stigma
										stigmatization towards PLWHA
Lau et al., 2021 [<mark>94</mark>]	Singapore	Cross sectional	COVID-19	Perceived stigma	172	166	Health care workers	48	24.7	Items: Felt that people would avoid their family members
Lee et al., 2005 [65]	China	Cross sectional	SARS	Enacted stigma	668	668	Residents of the first outbreak community	59.0	17.2	Items: (1) SARS deeply affected their daily life; (2) Those employed perceived discriminating discriminating employers.
Li et al., 2021 [<mark>95</mark>]	China	Cross sectional	COVID-19	Enacted stigma	2377	2377	Community population	51.4	62.3	Items: Discrimination against Recovered COVID-19 Patients
Misery et al., 2021 [<mark>96</mark>]	France	Cross sectional	COVID-19	Perceived stigma	800	800	Health care workers	80.2	24.9	ltems: Felt stigmatization
Moideen et al., 2021 [<mark>97</mark>]	India	Cross sectional	COVID-19	Perceived stigma	56	56	Patients	58.9	7.1	Scale: COVID-19 related stigma based on Berger-HIV stigma scale (12 items short version)
Nickell et al., 2004 [62]	Canada	Cross sectional	SARS	Enacted stigma	2001	1952	Hospital staffs	78.8	27.8	Items: Being treated differently because of working in hospital
Overholt et al., 2018 [<mark>59</mark>]	Liberia	Cohort	Ebola		299	299	Ebola survivors	43.0	98.0	Scale: The Ebola-related stigma questionnaire
Poyraz et al., 2021 [98]	Turkey	Cross sectional	COVID-19	Perceived stigma	284	284	Patients	49.8	40.7	Items: The patients rated how much they felt they were stigmatized and discriminated against, on a scale of 0 (never), 1 (very little), 2 (moderately), or 3 (considerably)
Raab et al., 2020 [<mark>77</mark>]	Guinea	Cross sectional	Viral Haemorrhagic fevers	Enacted stigma	102	102	Health care workers	52.0	2.9	Items: Not welcome survivor in community
Rahim et al., 2020 [<mark>99</mark>]	Iraq	Cross sectional	COVID-19	Enacted stigma	270	270	Community population	53.3	6.7	Items: Infection with the virus is associated with stigma (1 item)
Robinson et al., 2021 [100]	SU	Cross sectional	COVID-19	Perceived stigma	7138	5549	Community population	51.2	4.8	Items: Four items adapted from the Perceived Everyday Experiences with Discrimination Scale
Secor et al., 2020 [24]	Liberia and Guinea	Cross sectional	Ebola	Perceived stigma	744	744	Patients	53.1	30.4*	Items: (1) Refusal of service due to survivor status, (2) longer wait times for services than non-survivors, (3) receiving less care or attention than non-

	Ŧ	providers out us, (5) and ing ceat them survivor hey had elayed due to fear	lified e	0-19 Igma fic people	in Survey	g of being I by other e to the COVID-19.	uld you meone ur family/ d after the ecovered with with o has n Ebola? m Ebola? m Ebola?	n against ses	ting makes na	hat COVID- țmatized	ence of m: adapted sryday an Scale indicate indicate proceived: eared with or respect
	Measuremer of stigma	survivors, (4) gossiping ab survivor statt providers be nervous to ti due to their due to their status (6) if t avoided or d seeking care of stigma.	Scale: A moc questionnaire	Items: COVIC generates sti against speci	Scale: HCW Stigmatizatio	Items: Feelin discriminated countries due outbreak of 6	ttems: (1) WK welcome sor back into yo community/ neighborhoc person has r you socialize someone wh recovered frc (3) Would yo someone wh	Items: Public discriminatio COVID-19 ca:	ltems: Repor me feel stign	ltems: I felt t 19 was a stig disease	ttems: Experi discriminatio from the Eve Discriminatic Responses we averaged to the overall e of discrimina participants I (1) you are tr less courtesy than other py
	Prevalence of stigma (%)		19.5	39.2	33.2*	15.5	32.4	62.0	57.4	83.8	7.6*
	Female (%)		49.8	48.9	42.0	69.0	27.7	61.0	60.1	23.5	47.9
	Participants		Patients	Community population	Community population	Community population	Community population	Community population	Community population	Community population	Community population
	Effective sample size		751	485	3551	1879	OC 8	4191	1344	247	235
	Total sample size		751	485	3551	2700	008	4191	1344	247	235
	Type of stigma		Perceived stigma	Enacted stigma	Enacted stigma	Perceived stigma	Enacted stigma	Enacted stigma	Perceived stigma	Enacted stigma	Perceived stigma
	Type of epidemics		Ebola	COVID-19	COVID-19	COVID-19	bola	COVID-19	COVID-19	COVID-19	COVID-19
	Study design 7		Cross sectional E	Cross sectional (Cross sectional (Cross sectional (Cross sectional E	Cross sectional (cross sectional (Cross sectional (Cross sectional (
ed	Country		Sierra Leone	India	United States and Canada	Philippines	Ghana	China	China	Ethiopia	United States
Table 1 continu	Study		Secor et al., 2020 [24]	Singh et al., 2021 [101]	Taylor et al., 2020 [85]	Tee et al., 2020 [86]	Tenkorang et al., 2017 [71]	Wang et al., 2021 [102]	Wei et al., 2020 [<mark>87</mark>]	Yohannes et al., 2020 [76]	Yu et al., 2020 [103]

Fable 1 continu	per									
Study	Country	Study design	Type of epidemics	Type of stigma	Total sample size	Effective sample size	Participants	Female (%)	Prevalence of stigma (%)	Measurement of stigma
										people act as if they think you are dangerous
Yu et al., 2021 [104]	China	Cross sectional	COVID-19	Perceived stigma	23863	23863	Community population	68.1	58.1	Items: Perceived discrimination due to COVID-19
Yufika et al., 2021 [105]	Indonesia	Cross sectional	COVID-19	Enacted stigma	288	288	Health care workers	65.3	21.9	Scale: A six-item questionnaire
[*Note]: Studies	with combined pr	evalence of stigma.								

Statistical analysis

The primary outcomes of interest were the overall prevalence estimates of stigma which were calculated across all studies by using a random-effects model. Subgroups and meta-regression analyses were conducted to explore the potential sources of heterogeneity, including the following variables: study population, region, the levels of economic development, sex, and the proportion of tertiary education. *Q* and *I* [2] were calculated to assess heterogeneity across all studies and within subgroups, with $I^2 \ge 50\%$ indicating significant heterogeneity. Egger's test and the funnel plot were used to evaluate publication bias. A bilateral significance level less than 0.05 was considered to be statistically significant. All analyses were calculated with Stata version 15.

RESULTS

A total of 112,556 articles were identified, of which 225 studies with full text were assessed for eligibility. We excluded 151 articles without stigma prevalence, 20 articles identifying stigma as continuous variables [35–54], two articles not meeting quality assessment [55, 56], and two articles with data from social media platforms [57, 58]. Ultimately, 50 eligible studies were included in this meta-analysis. The complete PRISMA flow chart is shown in Fig. 1.

A total of 50 articles [14, 22, 24, 59-105] were included that contributed 51 estimates of prevalence in 92,722 participants. The basic characteristics of the studies are shown in Table 1. Overall, 10 studies focused on Ebola [14, 24, 59, 68-73, 75], eight studies on SARS [60-66, 93], 29 studies on COVID-19 [74, 76, 78-92, 94-105], and the remaining three studies focused on H1N1 influenza [67], Zika [22], and Viral Haemorrhadic fevers [77], respectively. There was also a broad geographical and population distribution of included studies. There were 16 studies from Africa [14, 24, 59, 68-73, 75-79, 84, 88], 25 studies from Asia [22, 60, 61, 64-66, 74, 80, 81, 83, 86, 87, 90-95, 97-99, 101, 102, 104, 105], and others were conducted in Europe [67, 89, 96], North America [62, 63, 85, 100, 103] and South America [82]. More than half (27 studies) of the studies were conducted within community populations [22, 60, 66, 69-72, 74, 76, 79–81, 83, 85–88, 90, 91, 93, 95, 99–104], while others (13 consisted of health care workers studies) [60, 61, 63, 64, 67, 77, 78, 84, 89, 92, 94, 96, 105] and patients (eight studies) [14, 24, 59, 68, 73, 75, 97, 98]. Of the 50 articles, 10 studies [24, 59, 73, 75, 80, 82, 85, 91, 97, 105] used modified scales for measuring stigma, while other studies measured the stigma by using one or more questions [14, 22, 60-72, 74, 76-79, 81, 83, 84, 86-90, 92-96, 98-104] (Table 1).

The pooled estimate of the prevalence of stigma across all studies was 34% [95% CI: 28–40%, $l^2 = 99.9\%$]. We further analyzed the pooled prevalence based on the different populations. Three studies [62, 65, 82] were not included in this subgroup analysis because of the lack of clear description of population type. Among the 47 articles that included 48 estimates of the prevalence of stigma in the population subgroups, the estimated prevalence was 38% [95% CI: 12–65%], 36% [95% CI: 28–45%], and 30% [95% CI: 20–40%], in patients, community population, and health care workers, respectively (Fig. 2). The meta-regression analysis indicated that the pooled prevalence of stigma based on population had no significant difference (p = 0.684).

Subgroup analyses were performed with regard to stigma type, countries, type of infectious outbreak, gender, education level, and measurement tools (Fig. 3). In terms of stigma type, two studies [59, 68] were excluded because of no clear description of stigma types. Among the included 48 studies, 23 focused on enacted stigma (36% [95% Cl: 28–44%]) and 25 on perceived stigma (31% [95% Cl: 22–40%]) (Figs. 3 and S1). Meta-regression showed that the estimated prevalence based on types of stigma had no significant difference (p = 0.655).

Among health care workers, pooled prevalence of enacted stigma was 28% [95% CI: 0-57%], while pooled prevalence of

Study ID	ES (95% CI)	% Weight
Health care workers Abdel Wahed et al., 2020 ⁷⁹ Bai et al., 200460 Chong., 200461 Elhadi et al., 2020 ⁸⁴ Goulia., 2010 ⁶⁷ Grace., 2005 ⁶³ Greene et al., 2021 ⁸⁹ Kirk et al., 2021 ⁹² Koh et al., 2021 ⁹⁴ Misery et al., 2021 ⁹⁶ Raab., 2020 ⁷⁷ Yufika et al., 2021 ¹⁰⁵ Subtotal (I-squared = 99.5%, p = 0.000)	$\begin{array}{c} 0.66 \ (0.62, 0.71) \\ 0.22 \ (0.16, 0.28) \\ 0.60 \ (0.57, 0.63) \\ 0.31 \ (0.28, 0.34) \\ 0.04 \ (0.02, 0.05) \\ 0.36 \ (0.29, 0.43) \\ 0.37 \ (0.34, 0.39) \\ 0.23 \ (0.19, 0.27) \\ 0.39 \ (0.39, 0.40) \\ 0.25 \ (0.18, 0.31) \\ 0.25 \ (0.22, 0.28) \\ 0.03 \ (-0.00, 0.06) \\ 0.22 \ (0.17, 0.27) \\ 0.30 \ (0.20, 0.40) \end{array}$	2.04 2.03 2.05 2.06 2.01 2.05 2.04 2.01 2.05 2.04 2.05 2.05 2.04 2.05 2.04 26.54
Community population Abdelhafiz et al., 2020 78 Abuhammad et al., 202080 Alzoubi., 202074 Aqeel et al., 202081 Badi et al., 202188 Bai et al., 202083 Etokidem et al., 201872 Gregorio et al., 201922 Harjana et al., 201992 Harjana et al., 20176 69 Jalloh et al., 2017b 70 Jassimet al., 202191 Lam et al., 200993 Lau et al., 200993 Lau et al., 202099 Robinson et al., 2021100 Singh et al., 2021101 Taylor et al., 2020 85 Tee et al., 2020 87 Yohannes., 202076 Yu et al., 2021104 Subtotal (I-squared = 99.9%, p = 0.000)	$\begin{array}{c} 0.23 \ (0.19, 0.26) \\ 0.46 \ (0.45, 0.47) \\ 0.05 \ (0.04, 0.07) \\ 0.73 \ (0.70, 0.76) \\ 0.05 \ (0.04, 0.07) \\ 0.19 \ (0.10, 0.28) \\ 0.44 \ (0.42, 0.47) \\ 0.22 \ (0.19, 0.25) \\ 0.42 \ (0.40, 0.44) \\ 0.53 \ (0.48, 0.59) \\ 0.21 \ (0.20, 0.22) \\ 0.72 \ (0.70, 0.73) \\ 0.53 \ (0.49, 0.58) \\ 0.32 \ (0.24, 0.41) \\ 0.10 \ (0.09, 0.11) \\ 0.62 \ (0.60, 0.64) \\ 0.07 \ (0.04, 0.10) \\ 0.05 \ (0.04, 0.05) \\ 0.39 \ (0.35, 0.44) \\ 0.33 \ (0.33, 0.34) \\ 0.16 \ (0.14, 0.17) \\ 0.32 \ (0.29, 0.36) \\ 0.62 \ (0.61, 0.63) \\ 0.57 \ (0.55, 0.60) \\ 0.84 \ (0.79, 0.88) \\ 0.08 \ (0.06, 0.09) \\ 0.58 \ (0.57, 0.59) \\ 0.36 \ (0.28, 0.45) \\ \end{array}$	2.05 2.06 2.06 2.05 2.06 2.06 2.05 2.06 2.05 2.06 2.06 2.05 2.06 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.05 2.06 2.06 2.06 2.06 2.06 2.06 2.05 2.06
Patients De Roo et al., 1998 ¹⁴ Etard et al., 2017 ⁶⁸ James et al., 2020 ⁷⁵ Kelly et al., 2019 ⁷³ Moideen et al., 2021 ⁹⁷ Overholt., 2018 ⁵⁹ Poyraz et al., 2021 ⁹⁸ Secor et al., 2020 ²⁴ Secor et al., 2020 ²⁴ Subtotal (I-squared = 99.9%, p = 0.000)	0.35 (0.19, 0.51) 0.26 (0.23, 0.29) 0.72 (0.70, 0.74) 0.16 (0.15, 0.17) 0.07 (0.00, 0.14) 0.98 (0.96, 1.00) 0.41 (0.35, 0.46) 0.30 (0.27, 0.34) 0.19 (0.17, 0.22) 0.38 (0.12, 0.65)	1.80 2.05 2.06 2.06 2.01 2.06 2.02 2.05 2.05 18.16
Overall (I-squared = 99.9%, p = 0.000) NOTE: Weights are from random effects analysis	0.35 (0.29, 0.41)	100.00
996 0	996	

Fig. 2 Prevalence estimates by the study population. The estimated prevalence of stigma in patients, community population, and health care workers was 38%, 36%, and 30%, respectively. ES effect size (proportion), CI confidence interval.

perceived stigma was 31% [95% CI: 19–43%] (p = 0.699). Among community population, the prevalence of enacted stigma was 38% [95% CI: 29–47%], and the prevalence of perceived stigma was 34% [95% CI: 16–52%]) (p = 0.624) (Figs. 3 and S2). The estimated prevalence of stigma in low- and middle-income countries was 37% [95% CI: 29–45%], while the estimated prevalence of stigma from high-income countries was 27% [95% CI: 18–36%]. However, the difference of prevalence of stigma between low- and middle-income countries and high-income countries was not statistically significant (p = 0.237) (Figs. 3 and

S3). The estimated prevalence of stigma in studies during the COVID-19, SARS, Ebola, and other infectious diseases was 35% [95% CI: 26–44%], 30% [95% CI: 20–40%], 40% [95% CI: 22–58%], and 16% [95% CI: 0–43%], respectively (p = 0.737) (Figs. 3 and S4).

The pooled estimated prevalence of stigma in studies with a majority of female participants (\geq 50%) was 30% [95% Cl: 23–37%], lower than those studies with a minority (<50%) of female participants (46% [95% Cl: 34–57%]). However, this difference was not statistically significant (p = 0.062) (Figs. 3 and S5). In terms of the education level of participants, as twenty studies

Subgroup	No. of studies	No. of participants	Prevalence(95% CI)	I ² (%)	P value
Overall	50	84964	0.34 (0.	28-0.40) 99.9	
Stigma type			⊢ ∎ ⊣		0.655
Enacted stigma	23	28702	0.36(0.2	28, 0. 44) 99. 9	
Health care workers	4	1011	0.28(0,0). 57) 99. 4	
Community population	16	22770	0.38(0.2	29, 0. 47) 99. 9	
Perceived stigma	25	55177	0.31(0.2	22, 0. 40) 99. 9	
Health care workers	9	15515	0.31(0.1	.9, 0. 43) 99. 6	
Community population	11	36934	0.34(0.1	.6, 0. 52) 99. 9	
Patients	5	2728	0.24(0.1	7, 0. 31) 99. 6	
Countries					0.237
High-income countries	13	25676	0.27 (0.	18, 0. 36)	
Low- and middle-income countries	34	59288	0.37 (0.	29, 0.45)	
Infections					0.737
COVID-19	29	57073	0.35 (0.	26, 0.44) 99.9	
SARS	8	15461	0.30 (0.	20, 0. 40) 99. 9	
Ebola	10	11250	0.40 (0.	22, 0. 58) 99. 9	
Others (Zika, HIN1, Viral Haemorrhagic fevers)	3	1180	0.16(0,0). 43) 99. 7	
Female sex proportion					0.062
≥50%	37	70257	0.30 (0.	23, 0.37)	
<50%	14	14707		34, 0.57)	
Education level					0.141
Tertiary education proportion >50%	20	44396		23, 0.44) 100.0	
Tertiary education proportion <50%	10	6669	. 47 (0.	23, 0.71) 99.9	
Measurement tools					0.942
Items	41	74958	·-■ 0.34(0.2	27, 0. 40) 99. 9	
Scales	10	10006	· 0. 37 (0. 2	22, 0. 53) 100. 0	
		I			
		0.00	20 00% 40 00% 60 00% 80 00%		

Fig. 3 Subgroup analysis of prevalence estimates across variables. We performed subgroup analyses with regard to stigma type, countries, type of infectious outbreak, gender, education level, and measurement tools. Meta-regression showed that the estimated prevalence based on different characteristics subgroup had no significant difference (p > 0.05).



Fig. 4 Begg's funnel plot and Egger test. There was no publication bias suggested by Begg's funnel plot (left) and Egger test (right). t = 0.86, p = 0.391.

[14, 61, 63–65, 68–70, 72, 73, 77, 84, 89, 92, 94, 97, 99, 100, 102, 105] did not report educational levels or did not indicate tertiary education proportion, 30 studies were included in this subgroup analysis. We divided the studies into two groups according to the proportion of participants with tertiary education (<50% and \geq 50%). The pooled estimated prevalence of stigma in studies with a minority (<50%) of participants with tertiary education was 47% [95% CI: 23–71%], higher than those studies with a majority (\geq 50%) of participants with tertiary education (33% [95% CI: 23–44%]). However, this difference was not statistically significant (p = 0.141) (Figs. 3 and S6).

As some studies included in our studies used items and the left used scales to measure stigma, we further performed subgroup analysis in terms of the measurement tools. Forty studies clearly described stigma items, and 10 studies used modified scales for measuring stigma. One study contributed two estimates of prevalence [24] (Table 1). The estimated prevalence of stigma was 34% [95% Cl: 27–40%] in studies using items and 37% [95% Cl: 22–53%] in studies using scales, respectively. The meta-regression analysis indicated that the pooled prevalence of stigma based on measurement tools had no significant difference (p = 0.942) (Figs. 3 and S7).

The Egger's tests and funnel plots (Fig. 4) did not show a publication bias (p > 0.05). A sensitivity analysis that was used for examining the impact of each study on the overall results showed similar estimates of stigma prevalence after excluding any single study, indicating that any study included in the present metaanalysis was unlikely to have a disproportionate impact on the reported prevalence estimates.

DISCUSSION

To our knowledge, this systematic review and meta-analysis provides the first quantitative estimate of stigma of affected individuals during infectious disease epidemics. We found that over a third of vulnerable populations reported infectious disease epidemic-related stigma, mainly involving infected patients, community members, and health care workers. People from low- and middle-income countries or with lower education are vulnerable populations who may have a greater risk of reporting stigma (enacted stigma or perceived public stigma). The results indicate that stigma is a significant public health concern during infectious disease epidemics, including COVID-19, and calls for actions to raise public health concern and develop effective and comprehensive interventions to reduce infectious disease-related stigma.

The rapid spread of an epidemic is typically associated with high levels of fear, which is manifested as stigma of and discrimination against affected individuals. Stigma can be a hindrance for the public to have an accurate understanding of the disease and can impose an adverse effect on the control of infectious disease epidemics. For example, during the COVID-19 epidemic, patients were reluctant to disclose their symptoms and see doctors at the early stage when COVID-19 became a social stigma [81]. Patients recovered from COVID-19 infections were even denied to take public transportation, assaulted on the street, or interfered with in their normal work [15, 16], which might increase their psychological stress and negatively affect the control of the pandemic. Although there is limited information in the extant literature, effective and accurate educational interventions and protecting policies of affected individuals are needed to counteract the damaging effects of infectious diseaserelated stigma, promote the control of infectious diseases, improve public mental and physical health, and facilitate the social stability and development ultimately.

Stigma was commonly reported by patients, community population, and health care workers during the epidemics, which can have a long-term adverse impact on their well-being and willingness to engage with health care. In the general population, enacted stigma (36%) was a little higher than their perceived stigma (31%). This could mean that perceptions were optimistic, underestimating the prevalence of enacted stigma that actually occurred. In community populations, the prevalence was 38% for enacted stigma, and 34% for perceived stigma, respectively. Residents living in places where the outbreak first occurred would be accused of spreading the virus, considered infectious, and thus further subjected to discrimination and stigmatization [83, 106]. On the other hand, people may endorse stigma when accepting survivors back into communities. However, variance in epidemicrelated stigma across communities exists and some communitylevel factors may account for this. For example, communities with higher knowledge of the disease and high mobilization efforts were less likely to endorse stigma, while communities that were concerned about providing assistance and care during the epidemics were more likely to endorse stigma (i.e., enacted stigma) [71, 107]. Community-level interventions are needed to increase awareness and knowledge of the epidemics among community populations.

The high prevalence of enacted stigma (28%) and perceived stigma (31%) among health care workers also indicated that they not only expressed discrimination against some particular groups related to infectious diseases, but also were discriminated more seriously by the general public. During the epidemic of infectious diseases, health care workers are at high risk of infection. Physical and mental exhaustion, fear of infection, worries about passing the infection to their friends and families, as well as medical violence (the conflicting doctor-patient relationship, especially in China) during the pandemic of COVID-19 were main complaints of medical workers [108–110]. Moreover, an increasing proportion of medical staffs reported suffering from isolation and avoidance from the community population. They described the feelings of rejection in their neighborhood because of hospital work or the feelings of being treated differently because others knew they might have contacted patients with infectious diseases [60, 64]. The stigma they experienced had adverse effects on their mental health. Therefore, more social support policies and mental health services are urgently needed for health care workers to protect their wellbeing and effectively control the epidemics.

The finding that individuals with higher levels of education had a lower prevalence of stigma is consistent with our expectations, though no significant difference was observed possibly due to the limited number and heterogeneity of studies included. An overabundance of news and mixed messages is a key driver of stigma in our time, especially during large-scale disasters like COVID-19 [111–113]. With a higher level of education, individuals may have better access to accurate knowledge about infectious diseases and have a better understanding of the situation, so that they could distinguish between factual information and misinformation. This may be more difficult for those with lower education level, who may be more easily misled by biased or false information provided by traditional media, social media, and self-proclaimed experts [114]. As previous studies reported, education, clear and correct communication have the potential to significantly improve the knowledge, attitudes, and behaviors related to infectious diseases, such as Ebola and COVID-19, and reduce infectious disease-related stigma [115, 116]. Therefore, it is important to improve public awareness of the nature of the disease to reduce fear and anxiety, and subsequently reduce the stigma [117]. In addition, the higher educational level is always associated with high socio-economic status, which could explain the fact that people with higher income level may be less worried and less likely to stigmatize others, especially in high-income countries [118]. However, there were few studies on infectious

disease-related stigma from high-income countries, and more

studies are needed in the future.

Differences in infectious disease-related stigma hinge on the features related to infectious diseases. Among various infectious diseases, stigma related to human immunodeficiency virus/ acquired immunodeficiency syndrome (HIV/AIDS) has been the most salient and widely studied [119]. However, in our present study, we excluded the infectious diseases like HIV/AIDS that do not cause an outbreak. Compared with infectious diseases like SARS and COVID-19, the means of infection and disease course of HIV/AIDS differ substantially [120]. HIV/AIDS has been perceived as a fatal condition with little hope of recovery since the infection [8], while epidemic-related infectious diseases may be cured by antiviral medications or controlled just by physical distancing. Therefore, the disease course of HIV/AIDS is chronic, while that of epidemic-related infectious diseases is usually acute and timelimited. Furthermore, HIV/AIDS is always being stigmatized with negative connotations such as drug abuse, sex work, poverty, or incarceration, which are considered to be deviant and disapproved by the society [121]. In contrast, epidemic-related diseases such as SARS and COVID-19 are caused mainly by external factors that are not considered as morally reprehensible. Therefore, stigmatization of these infectious diseases is mainly driven by the fear of the disease itself, and will be reduced as the perceived threat level decreases [26, 65].

To tackle social stigma derived from infectious disease epidemics, many health authorities and academic associations across the world have appealed to stop stigmatizing and discriminating against certain populations, such as survivors and those from high-risk areas [122, 123], highlighting the negative consequences of stigma that compromise efforts to treat the disease and reduce its further transmission. As COVID-19 is still a continuing threat for the human society, several crucial actions are needed to reduce COVID-19-related stigma. First, governments and authorities need to work closely to stop racism and xenophobia toward specific countries and areas at high epidemic level [124]. Evidence shows that disease outbreaks have always been accompanied by an increase in xenophobic or racist sentiment [125]. The COVID-19 is a global public health issue and united efforts are crucial to win the worldwide battle against it. Second, proper public health education with scientific-based information and an anti-stigma campaign appear to be the most effective ways to prevent social harassment of at-risk groups [13, 126]. This would also help create an appropriate environment to work together to contain this pandemic. Third, the government and health authorities should appeal for the public to access COVID-19 information from reliable sources like the Centers for

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Disease Control and Prevention (CDC) and the World Health Organization (WHO). Fourth, community leaders and public health officials should maintain the privacy and confidentiality of survivors, avoid using negative languages that may cause stigmatization, and provide community and social support to challenge stereotypes and stigmatization [123]. Fifth, more research using scales to estimate the prevalence of stigma are needed and more standardized scales should be developed for routine assessment of infectious disease-related stigma in at-risk groups and necessary support should be provided for those who may feel stigmatized [127]. Last but not least, the long-term impact of COVID-19 on stigma should be examined and the effectiveness of protection measures and interventions should be explored in further studies.

This study had several limitations that compromise the interpretation of the findings. First, the lack of reliable and valid instruments of infectious disease-related stigma used in the populations studied is a major limitation for both research and practice. Only 10 studies [24, 59, 73, 75, 80, 82, 85, 91, 97, 105] used modified scales for measuring stigma. And these measure tools, such as the Ebola-related stigma Questionnaire, seven-item EVDrelated stigma index, varied widely in terms of measurement development, the groups surveyed and the domains assessed (i.e., knowledge, attitude, and behavior). Moreover, other studies without valid scales measured the prevalence of infectious disease-related stigma by using one or more items. We defined the (combined) proportion of "Yes" of one item or several items in studies as the (combined) prevalence of stigma in these studies. Standardized scales should be developed to assess infectious disease-related stigma in further studies. Second, although we initially searched for all major infectious disease epidemics, the majority of eligible studies (47 out of 50) mainly focused on Ebola, SARS, and COVID-19, resulting in insufficient data to allow subgroup analysis of the prevalence of stigma in other infectious diseases. Furthermore, the literature search in the present study was limited to English, which may omit some useful studies related to the stigmatization of infectious diseases in other languages. Finally, there was high heterogeneity in the estimated prevalence of stigma with an l^2 of more than 99%, possibly because of the vastly diverse and non-standardized scales used in the included studies as mentioned above. Furthermore, we also took measures to find out other sources of heterogeneity, including using random-effect models, subgroup analysis, and meta-regression analysis. Sensitivity analyses were also conducted to identify the influence of individual studies on the pooled estimates by excluding each of the studies from the pooled estimate. Nonetheless, the remaining unexplained heterogeneity was still substantial. More research is needed to provide us with more accurate information about the prevalence of infectious disease-related stigma.

CONCLUSIONS

In conclusion, individuals reported infectious disease-related stigma, including enacted stigma and perceived stigma, exceeded one-third, with the highest prevalence of stigma observed in infected patients, followed by community populations and health care workers. Our findings indicate that infectious disease-related stigma is a significant public health concern during infectious disease epidemics, including COVID-19. Governments and public health authorities need to pay more attention to take comprehensive and effective measures and strategies to eliminate or reduce threats of infectious disease-related stigma.

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AUTHOR CONTRIBUTIONS

LL, BYP, SL, and YK proposed the topic and main idea. YK, HXL, and YW contributed equally to this article. HXL and ZYX were responsible for the literature search and study selection. HXL, GYM, SSZ, HYT, ZY, WYJ, YZ, TSS, ZYB, FTT, ZYJ, and YW were responsible for the data extraction and quality assessment. HXL and YK wrote the initial draft. YK, HXL, SSZ, WY, ZYJ, MSQ, SYK, LX, ZTM, RMS, WSYSW, RN, SL, BYP, and LL commented on and revised the paper. LL, BYP, and SL made the final version. All authors contributed to the final draft of the paper.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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