

# Risk of suicidality in mental and neurological disorders in low and middle-income countries: A systematic review and meta-analysis

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## ABSTRACT

**Background:** Both fatal and nonfatal suicidal behaviours are important complications of mental, neurological, and substance use disorders (MNSDs) worldwide. We aimed at quantifying the association of suicidal behaviour with MNSDs in Low and Middle Income Countries (LMICs) where varying environmental and socio-cultural factors may impact outcome.

**Methods:** We conducted a systematic review and meta-analysis to report the associations between MNSDs and suicidality in LMICs and the study-level factors of these associations. We searched the following electronic databases: PUBMED, PsycINFO, MEDLINE, CINAHL, World Cat, and Cochrane library for studies on suicide risk in MNSDs, with a comparison/control group of persons without MNSDs, published from January 1, 1995 to September 3, 2020. Median estimates were calculated for relative risks for suicide behaviour and MNSDs, and when appropriate, these were pooled using random effects metanalytic model. This study was registered with PROSPERO, CRD42020178772.

**Results:** The search identified 73 eligible studies: 28 were used for quantitative synthesis of estimates and 45 for description of risk factors. Studies included came from low and upper middle-income countries with a majority of these from Asia and South America and none from a low-income country. The sample size was 13,759 for MNSD cases and 11,792 hospital or community controls without MNSD. The most common MNSD exposure for suicidal behaviour was depressive disorders (47 studies (64%)), followed by schizophrenia spectrum, and other psychotic disorders (28 studies (38%)). Pooled estimates from the meta-analysis were statistically significant for suicidal behaviour with any MNSDs (odds ratios (OR) = 1.98 (95%CI = 1.80–2.16)) and depressive disorder (OR = 3.26 (95%CI = 2.88–3.63)), with both remaining significant after inclusion of high-quality studies only. Meta-regression identified only hospital-based studies (ratio of OR = 2.85, CI:1.24–6.55) and sample size (OR = 1.00, CI:0.99–1.00) as possible sources of variability in estimates. Risk for suicidal behaviour in MNSDs was increased by demographic factors (e.g., male sex, and unemployment), family history, psychosocial context and physical illness.

**Interpretation:** There is an association between suicidal behaviour and MNSDs in LMICs, the association is greater for depressive disorder in LMICs than what has been reported in High Income Countries (HICs). There is urgent need to improve access for MNSDs care in LMICs.

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## 1. Introduction

### Panel: Research in Context

#### Evidence before this study

Over 79% of suicides worldwide occur in LMICs with MNSDs contributing the highest risk for suicidality. The association between suicidal behaviour and MNSDs is not fully understood. Previous reviews and meta-analysis reported on prevalence studies, surprisingly reporting higher estimates in HICs (80%) compared to LMICs (45–58%), which often lacked a comparison group with community or healthy controls. Studies designed with a comparison group can more accurately estimate this risk by accounting for the distorting effects of extraneous and confounding variables. Therefore, we report on the associations (e.g. odds ratios (OR)) between MNSDs and suicidality in LMICs and examine the study-level factors that affected the reported associations. We systematically searched the following electronic databases; PUBMED, PsycINFO, MEDLINE, CINAHL, World Cat, and Cochrane library for studies reporting on suicide risk in MNSDs. We focused on studies that had a comparison group.

#### Added value of this study

We found that the association for suicidality with any MNSDs was high especially for depressive disorders and personality disorders and that size of associations differed by region, economic class, and study setting. We identified risk factors that can be used to prioritise MNSD care and triage those at risk of suicide in LMIC. To our knowledge, this is the first systematic review and meta-analysis that reports on the associations between MNSDs and suicidality in LMICs. In addition, we included both fatal and non-fatal suicidal behaviour which provides a clearer picture of progression of suicidal behaviour in MNSDs. Further, the inclusion of all MNSDs highlighted the need for more research on the association of neurological disorders such as epilepsy, with suicidal behaviour which is common in many LMICs.

#### Implications of all the available evidence

This study confirms an association between suicide and MNSDs in LMICs, which for depressive disorders, is stronger than reports from HICs. This underscores the importance of improving access for care for those with MNSD. Well-powered empirical studies are required in many LMIC, especially Africa, which generated fewest studies despite available reports that these problems may be common in these countries.

Mental, Neurological and Substance use Disorders (MNSDs) are an important cause of all disability-adjusted life years (DALYs) worldwide (10% for all diseases and conditions) [1]. Suicidal behaviour both fatal and nonfatal is an important complication of MNSDs, with about 800,000 people dying by suicide each year, most of whom (79%) are in low- and middle-income countries (LMIC) [2]. Studies have indicated that over 80% of the reported suicides occur in people with MNSDs in high income countries (HIC) [2], but these estimates are surprisingly lower (45–58%) in LMIC [3]. Therefore, studies addressing this discrepancy of suicide in MNSDs are required.

Studies have found a higher risk of death (three-fold) from suicide in people with common neurological disorders such as epilepsy compared to the general population [4], with psychiatric comorbidity aggravating this risk [5,6]. Some studies report that MNSDs such as depression and psychosis are the key risk factors for suicide and suicidal behaviour [7–9]. In HICs, psychiatric disorders have been reported to be present in 90% of completed suicide deaths [10,11] and as the strongest observed risk factor for attempted suicide in all age groups [12,13]. Unfortunately, the risk of suicidality in neuropsychiatric disorders remains largely unexplored in LMICs, where globally the majority of deaths by suicide are reported [3,14].

The extent of association between suicidality and MNSDs is still unclear because most studies report prevalence, without determining the risk factors, or lack comparison against controls without MNSD. The determination and establishment of MNSDs as risk factors for suicide is pivotal, given that there are possibly many other non-psychiatric/non-neurological causes of suicides, whose confounding effect would be accounted for in case-comparison studies. Furthermore, most evidence is based on studies from HIC, where the situation of suicide may be different from LMIC, because of differences in health systems, legal status, health-seeking behaviour, economic factors, and cultural perceptions [15]. For example, the most common method of suicide in LMIC is poisoning with agricultural pesticides, whilst in HIC it is hanging and firearms [16]. The World Health Organization (WHO) has called on culturally sensitive evidence to inform and develop tailored suicide

prevention interventions [2].

There are few systematic reviews on suicidality in MNSDs in LMIC. One such review explored the prevalence of suicidal behaviour in persons with psychiatric morbidity [3]. However, the effect of psychiatry morbidity in suicidality cannot be assessed without comparison with other conditions or healthy controls, especially when the studies have small sample sizes. Also, there could be other important causes of suicide in communities or those seeking health care for non-MNSD reasons. Sources of heterogeneity in the same study was addressed through stratified analysis, although these were not formally or statistically examined. Additionally, it is three years since that review was published, necessitating a recent update of the subject.

Thus, to investigate the effect of MNSDs in suicidality in LMICs, we conducted a systematic review and meta-analysis to synthesize evidence for the associations (as robustly measured from odds ratios, risk ratios or hazard ratios) for both fatal and non-fatal suicidal behaviour with multiple MNSDs. We further statistically examined the study-level factors that affected the reported associations.

## 2. Methods

### 2.1. Protocol and registration

We developed and registered a review protocol with PROSPERO (PROSPERO 2020 CRD42020178772). We conducted this systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines [17]. Definition of mental disorders was as per the diagnostic and statistical manual of mental disorders (DSM) and ICD classifications. We focused on common mental and neurological disorders captured in the World Health Organization (WHO) Mental Health Gap Action Programme (MhGAP). We excluded studies on participants without a confirmed mental/neurological diagnosis and with no history of suicidal behaviour. Our main outcome was suicidal behaviour encompassing all aspects of the suicide continuum i.e. suicide thoughts or suicide ideation, suicide plans, suicide attempts and completed suicide.

### 2.2. Eligibility criteria

#### 2.2.1. Inclusion criteria

We included studies on participants from all age groups with MNSDs who died from fatal suicidal behaviour and who were alive with a history of non-fatal suicidal behaviour.

We focused on studies on MNSDs with a comparison group of persons without MNSDs. The comparison groups in the included studies mainly comprised of the general population or hospital staff. The majority did not have any physical illness while persons with chronic illnesses such as hypertension, cancer, and obesity as control group were included. Included studies were case control studies, controlled trials, cross-sectional and cohort studies (whether prospective or retrospective). Systematic reviews were used as secondary sources of data for relevant articles.

Additionally, we included studies from LMICs as per the World Bank country and lending groups 2019–2020 country classification [18], from both rural and urban settings and from both clinical and community settings. We included all peer reviewed studies published from 1st January 1995 to 3rd September 2020, regardless of the suicidality data collection techniques e.g. record linkage or psychological autopsy data provided they had a comparison group of persons without MNSDs. The initial search was not restricted by language of publication, but only articles written in English or translated were included in the final analysis.

#### 2.2.2. Exclusion criteria

We excluded articles published prior to 1995 owing to changes in the global understanding of suicide especially regarding presentation,

diagnosis, treatment, and suicide prevention strategies [19]. Studies without a comparison group were also excluded from the review. All duplicate records, animal studies and studies on self-harm were not included. Studies on self-harm were excluded because it was not clear whether there was intention to die by suicide. We also excluded qualitative studies, case reports, and studies in a non-English language that lacked an English translation. Prevalence studies where associations between MNSDs and suicidal behaviour were not clearly established were also excluded. Additionally, studies on MNSDs with other comorbidities were excluded.

### 2.3. Information sources

We systematically searched the following electronic databases; PUBMED, PsycINFO, MEDLINE, CINAHL, World Cat and Cochrane library. Additionally, we visually scanned reference lists from relevant systematic reviews.

### 2.4. Search

Search terms were constructed following recommendations by the National Health Service Centre for Reviews and Dissemination [20]. In addition to the main search terms (suicide, mental disorders, and neurological disorders), we used medical subject headings (MeSH) terminology in the search. Boolean operators such as “AND” and “OR,” were used to combine the search terms as necessary. Supplementary table 2 shows the search strategy used in PUBMED.

### 2.5. Study Selection

References were managed using EndNote X9® software. Two independent reviewers (MN and CT in consultation with LO and SK) conducted an initial screening of titles and abstracts against the inclusion criteria to identify potentially relevant articles. The reasons for which excluded studies failed to meet the inclusion criteria were stated. Discrepancies were resolved by discussion and consultation with all the researchers.

Screening of full texts of articles identified as possibly relevant in the initial screening was then conducted by two independent members of the research team (MN and CT in consultation with LO and SK). The reasons for which excluded studies failed to meet the inclusion criteria were also stated. Percentage agreement was used to measure inter-rater reliability. The percentage agreement after the screening was 84.7% which was considered good [21]. Discrepancies were resolved through consultation and discussion between all the researchers until the final number of articles to be included was agreed.

### 2.6. Data extraction process

Data from included studies were extracted into a Microsoft Excel® spreadsheet with a list of variables determined a priori by the investigators. Supplementary Table 3, outlines the data items, which included the year of publication, study design, type of mental or neurological disorder, suicide assessment method/tool, and the quality score of the study.

### 2.7. Risk of bias in individual studies

The quality of the eligible articles was assessed by two independent reviewers (MN and CT in consultation with LO and SK) using the Joanna Briggs Institute critical appraisal tools for case control and cross-sectional studies [22].

For case-control studies, rigorous appraisal was conducted addressing aspects of the comparison groups other than the presence of disease in cases or the absence of disease in controls, whether cases and controls were matched appropriately, and same criteria used for their

identification, whether exposure was measured in a standard, valid and reliable way and in the same way for cases and controls, whether confounding factors were identified and strategies to deal with them stated, whether outcomes were assessed in a standard, valid and reliable way for cases and controls, whether the exposure period of interest was long enough to be meaningful and whether appropriate statistical analysis was used.

For case-comparison group studies nested in cross-sectional studies, the two independent reviewers assessed whether the criteria for inclusion in the sample was clearly defined, whether the study subjects and the setting was described in detail, whether the exposure was measured in a valid and reliable way, whether objective and standard criteria was used for measurement of the condition, whether confounding factors were identified and strategies to deal with confounding factors stated, whether the outcomes were measured in a valid and reliable way and whether appropriate statistical analysis was used.

Answers to items in the checklists were given as “yes”, “no”, “unclear” and “not applicable”. Any discrepancies between the two independent reviewers were resolved through discussion and consultation and the final quality appraisal score was arrived at through mutual consent. Quality scores were generated from the checklist responses and classified as low ( $\leq 49\%$ ), moderate (50–74%), high/excellent ( $\geq 75\%$ ).

### 2.8. Data analysis

Data analysis was conducted using Stata software v15. We performed a descriptive analysis of the general characteristics of included studies by study design, continent/region, economic class, source of sample (hospital/community) and settings (rural vs urban). Odds ratios (OR) were calculated for studies where they were not provided, using the raw number of cases and controls exposed and unexposed. Distribution of OR and relative risks (RR) for significant associations of MNSDs and suicide was analysed by continent, economic class, study design, source of sample, and setting.

We used *metan* command to estimate the heterogeneity between studies this was assessed using  $I^2$  statistic. An  $I^2$  value of 25% was considered low heterogeneity, 50% moderate and 75% substantial [23]. We pooled the overall OR and/or RR for suicidal behaviour and MNSDs for all available studies using the DerSimonian and Laird random-effects model [24], a method for meta-analysis whereby the standard errors of the study-specific estimates are adjusted to incorporate a measure of the extent of variation, or heterogeneity, among the effects sizes observed in different studies it incorporates an assumption that the different studies are estimating different, yet related, effect sizes. This was done for all eligible studies initially and then separately for studies with moderate quality and those with high quality as we did not have a study with low quality score. The random effects model was chosen as it assumes varying effect sizes between studies, because of differences in study characteristics, explored in the descriptive analysis above. Disorders which had less than five studies were not included in this meta-analysis. When metaanalysis was not possible because of few studies or significant study differences, use of medians and ranges were used when reporting summaries for sub-groups e.g., low-income countries vs high income countries or rural versus urban settings. Where only one study had point estimates for a particular disorder, confidence interval from that study was used to represent the range. MNSDs for which point estimates were not available and could not be calculated were not included in this analysis.

Univariate and multivariate regression was done using *metareg* command to assess factors contributing to variability of OR or RR of suicidality in MNSDs. Forest plots were used to visualize the data. We assessed for publication bias and used funnel plot to visualize this data.

## 3. Results

The initial search generated 10,215 records from the electronic

database search and 6 additional records from references of systematic reviews. Of which 6880 articles were included in the review following removal of duplicates. Screening the titles and abstracts of these articles to remove those that did not address the topic of interest retained 171 articles, whose full texts were retrieved and examined for eligibility. A further 98 articles were excluded as they did not meet the inclusion criteria, leaving 73 eligible studies. Of the 73 eligible studies, 28 had data on both association of suicide with MNDSs and risk factors for suicide in MNDSs, while the remainder 45 contained data on risk factors for suicide in MNDSs only. Reasons for exclusion of the articles are outlined in the PRISMA flow diagram in Fig. 2.

Most eligible studies were from Asia, specifically East, South and Southeast Asia ( $n = 51$  (70%)), and South America 18 (25%) (Table 1). The eligible studies represented a total sample size of 25,551 participants, most of whom were from Asia ( $n = 19,767$  (77%)). The sample size was 13,759 for MNDS cases and 11,792 hospital or community controls without MNDSs. Similarly, majority of the reported studies were from upper middle-income countries ( $n = 62$  (85%)) and lower middle-income countries ( $n = 11$  (15%)) (Table 1). All studies used case-control design, with some case-control studies nested in cross-sectional

surveys ( $n = 13$  (18%)). Most studies were conducted in adults ( $n = 52$  (71%)) with fewest included adolescents ( $n = 2$  (3%)). The median proportion of female cases was 54% (Inter Quartile Range (IQR) 41%–66%) and that of female controls was 51% (IQR, 36%–57%).

Majority of eligible studies were conducted in a hospital setting 48 (66%), whereas 25 (34%) were conducted in a community setting. Additionally, majority 51 (70%) were conducted in urban settings whereas 22 (30%) were conducted in rural settings (Table 2).

The median (25–75 IQR) quality score of eligible studies was 90% (80%–90%). The median quality score was lower for the classical case-control studies (90% (80%–90%)) than was for the nested case-control studies (100% (90%–100%)). Of the 73 studies, none had low quality scores, while 11 studies (15%) had moderate scores and 62 (85%) had high quality scores (Supplementary Table 1).

There were 17 broad domains of MNDSs reported as exposures of suicidality. The most common MNDS studied was depressive disorders (47 studies (64%)), followed by schizophrenia spectrum and other psychotic disorders (28 studies (38%)), with the least reported MNDS being epilepsy (one study (1%)) (Table 4). In 29 (40%) studies, two or more MNDSs were reported. The most common MNDS i.e., depression

**Table 1**  
General characteristics of included studies.

Classification	Categories	Number of studies (N = 73)	Cases sample size (N = 13,759)	Control sample size (N = 11,792)	Total sample size (N = 25,551)
<b>Continent</b>	Africa	2 (2•74%)	288 (2•09%)	282 (2•39%)	570 (2•23%)
	Asia	51 (69•86%)	10,519 (76•45%)	9248 (78•43%)	19,767 (77•36%)
	Europe	2 (2•74%)	428 (3•11%)	213 (1•81%)	641 (2•51%)
	South America	18 (24•66%)	2524 (18•34%)	2049 (17•38%)	4573 (17•90%)
<b>Country income</b>	Upper middle income	62 (84•93%)	12,436 (90•38%)	10,619 (90•05%)	23,055 (90•23%)
	Lower middle income	11 (15•07%)	1323 (9•62%)	1173 (9•95%)	2496 (9•77%)
<b>Study design</b>	Case-control	60 (82•19%)	12,617 (91•70%)	11,045 (93•67%)	23,662 (92•61%)
	Nested Case-control	13 (17•81%)	1142 (8•30%)	747 (6•33%)	1889 (7•39%)
<b>Age of participants</b>	Adults	52 (71•23%)	8950 (65•05%)	6975 (59•15%)	15,925 (62•33%)
	Children/Adolescents	2 (2•74%)	349 (2•54%)	233 (1•98%)	582 (2•28%)
	Mixed	19 (26•03%)	4460 (32•42%)	4584 (38•87%)	9044 (35•40%)
<b>Sex distribution (Males %)</b>	Males	46•71%*	6546** (47•58%)	5390** (45•71%)	11,936 (46•71%)
<b>Setting</b>	Community	25 (34•25%)	5521 (40•13%)	5706 (48•39%)	11,227 (43•94%)
	Hospital	48 (65•75%)	8238 (59•87%)	6086 (51•61%)	14,324 (56•06%)
<b>MNDSs</b>	Schizophrenia spectrum and Psychotic Disorders	28 (38•36%)	2776 (20•18%)	19 (0•16%)	2795 (10•94%)
	Bipolar and related Disorders	24 (32•88%)	1418 (10•31%)	6 (0•05%)	1424 (5•57%)
	Depressive Disorders	47 (64•38%)	3795 (27•58%)	114 (0•97%)	3909 (15•30%)
	Anxiety Disorders	18 (24•66%)	416 (3•02%)	51 (0•43%)	467 (1•83%)
	Obsessive-Compulsive and Related Disorders	8 (10•96%)	181 (4•82%)	0 (0%)	181 (0•71%)
	Substance-Related and Addictive Disorders	22 (30•14%)	415 (3•02%)	118 (1•00%)	533 (4•52%)
	Personality Disorders	11 (15•07%)	100 (0•73%)	27 (0•23%)	127 (0•50%)
	Trauma and Stressor Related	16 (21•92%)	275 (2•00%)	20 (0•17%)	295 (1•15%)
	Disruptive, impulse control and conduct disorders	6 (8•23%)	2 (0•02%)	0 (0%)	2 (0•01%)
	Feeding and eating disorders	4 (5•48%)	3 (0•02%)	0 (0%)	3 (0•01%)
	Neurodevelopmental disorders	4 (5•48%)	30 (0•23%)	0 (0%)	30 (0•12%)
	Dissociative disorders	5 (6•85%)	27 (0•20%)	1 (0•01%)	28 (0•12%)
	Sexual dysfunctions	4 (5•48%)	1 (0•01%)	0 (0%)	1 (0•01%)
	Somatic symptom and related disorders	7 (9•59%)	39 (0•28%)	18 (0•15%)	57 (0•22%)
	Epilepsy	1 (1•37%)	153 (1•11%)	0 (0%)	153 (0•60%)
	Dementia	2 (2•74%)	14 (0•10%)	4 (0•03%)	18 (0•07%)
	Unspecified MNDSs***	14 (19•18%)	1891 (13•74%)	145 (1•23%)	2036 (7•97%)
	Before 2000	1 (1•37%)	100 (0•73%)	100 (0•85%)	200 (0•78%)
	After 2000	72 (98•63%)	13,659 (99•27%)	11,692 (99•15%)	25,351 (99•22%)
	Low	0	NA	NA	NA
	Moderate	11 (15•07%)	2305 (16•75%)	1625 (13•78%)	3930 (15•38%)
	Excellent/High	62 (84•93%)	11,454 (83•25%)	10,167 (86•22%)	21,621 (84•62%)

Studies from Europe were done in Serbia and Bosnia and Herzegovina.

Quality of the study: Low =  $\leq 49\%$ , Moderate =  $50\text{--}74\%$ , High =  $\geq 75\%$  (Quality determined using the Joanna Briggs Institute Critical Appraisal Tools).

\* Proportion of males in the whole study population.

\*\* Represents the total sample size for males in studies that provided number of males and females. Studies that did not specify number of males and females are not included.

\*\*\* Represents studies where sample sizes were not specified for each mental disorder.

**Table 2**

Percentage distribution of studies with significant associations of MNSDs with suicidality by study design, setting and income level.

	Study design		Hospital/Community Studies		Setting		Income Level	
	Case-control (N = 60)	Nested Case-control (N = 13)	Hospital (N = 48)	Community (N = 25)	Urban (N = 51)	Rural (N = 22)	Lower middle income (N = 11)	Upper middle income (N = 62)
Depressive disorders	41 (68•33%)	6 (46•15%)	27 (56•25%)	20 (80%)	31 (60•78%)	16 (72•73%)	8 (72•73%)	39 (62•90%)
Schizophrenia spectrum and related disorders	25 (41•67%)	3 (23•08%)	14 (29•17%)	14 (56%)	18 (35•29%)	10 (45•45%)	8 (72•73%)	20 (32•36%)
Bipolar and related disorders	17 (28•33%)	6 (46•15%)	16 (33•33%)	7 (28%)	17 (33•33%)	7 (31•82%)	5 (45•45%)	18 (29•03%)
Anxiety disorders	18 (30%)	0 (0%)	5 (10•42%)	13 (52%)	10 (19•61%)	8 (36•36%)	2 (18•18%)	16 (25•81%)
Obsessive compulsive and related disorders	5 (8•33%)	3 (23•08%)	6 (12•50%)	2 (8%)	6 (11•76%)	2 (9•09%)	2 (18•18%)	6 (9•68%)
Personality disorders	9 (15%)	2 (15•38%)	6 (12•50%)	5 (20%)	7 (13•73%)	4 (18•18%)	4 (36•36%)	7 (11•29%)
Substance related and addictive disorders	20 (33•33%)	2 (15•38%)	7 (14•58%)	15 (60%)	11 (21•57%)	11 (50%)	7 (63•64%)	15 (24•19%)
Trauma and stressor related disorders	14 (23•33%)	2 (15•38%)	6 (12•50%)	10 (40%)	10 (19•61%)	7 (31•82%)	6 (54•55%)	10 (16•13%)
Disruptive impulse control and conduct disorders	6 (10%)	0 (0%)	3 (6•25%)	3 (12%)	4 (7•84%)	2 (9•09%)	1 (9•09%)	5 (8•06%)
Somatic symptom and related disorders	5 (8•33%)	2 (15•38%)	3 (6•25%)	4 (16%)	5 (9•80%)	2 (9•09%)	3 (27•27%)	4 (6•45%)
Dissociative disorders	4 (6•67%)	1 (7•69%)	3 (6•25%)	2 (8%)	3 (5•88%)	2 (9•09%)	2 (18•18%)	3 (4•84%)
Neurodevelopmental disorders	4 (6•67%)	0 (0%)	2 (4•17%)	2 (8%)	2 (3•92%)	2 (9•09%)	1 (9•09%)	3 (4•84%)
Elimination disorders	4 (6•67%)	0 (0%)	2 (4•17%)	2 (8%)	2 (3•92%)	2 (9•09%)	1 (9•09%)	3 (4•84%)
Sexual dysfunctions	4 (6•67%)	0 (0%)	1 (2•08%)	3 (12%)	1 (1•96%)	3 (13•64%)	2 (18•18%)	2 (3•23%)
Feeding and eating disorders	4 (6•67%)	0 (0%)	2 (4•17%)	2 (8%)	2 (3•92%)	2 (9•09%)	1 (9•09%)	3 (4•84%)
Epilepsy	1 (1•67%)	0 (0%)	0 (0%)	1 (4%)	1 (1•96%)	a	0 (0%)	1 (1•61%)
Dementia	2 (3•33%)	0 (0%)	0 (0%)	2 (8%)	2 (3•92%)	a	0 (0%)	2 (3•23%)
Unspecified MNSDs	14 (23•33%)	0 (0%)	2 (4•17%)	12 (48%)	2 (3•92%)	12 (54•55%)	2 (18•18%)	12 (19•35%)

a: no observations.

was mainly contributed by studies from Asia ( $n = 35$  (69%)), while the least common MNSD i.e., epilepsy was reported in a study from South America ( $n = 1$  (6%)) (Table 1).

Of the 73 studies, 28 provided associations or adequate information for computation of associations between MNSDs and suicidality. The median associations were variable according to economic class with the OR being 23•98 (range: 1•12–105•20) for depressive disorders in UMIC, 5•04 (range: 3•40–6•68) for trauma and stressor related disorders in LMIC, 2•02 (range: 0•10–170•37) for bipolar and related disorders in LMIC, 2•4 (range: 1•10–3•20) for epilepsy in UMIC, and 6•3, (range: 0•07–68•76) for any MNSD in LMIC. Other associations by economic class are in Table 3 and Table 4.

Stratified according to source of samples, median associations of suicidality with MNSDs ranged from 25•34 (range: 9•3–208•20) for depressive disorders in community studies to 3.90 for bipolar and

**Table 3**

Overall distribution of odds/risk Ratios for associations of MNSDs with suicidality.

Type of MNSD	Median (Range)
Depressive disorders	23•14 (1•12–208•2)
Schizophrenia spectrum and related disorders	4•09 (3•03–27•72)
Bipolar and related disorders	3•05 (2•02–36•9)
Anxiety disorders	2•98 (1•44–11•61)
Obsessive compulsive and related disorders	3•9**
Personality disorders	10•03 (3•43–21•65)
Substance related and addictive disorders	2•77 (0•06–7•37)
Trauma and stressor related disorders	3•4 (3–6•68)
Epilepsy	2•4 (1•1–3•2) *
Dementia	9•9 (2•1–45•8) *
All MNSD	7.81(0.40–68.76)

\* ; confidence interval used instead of range.

\*\* ; confidence interval and range not available.

related disorders in hospital studies. Summarizing associations according to settings showed that OR ranged from 39•37 (range: 1•12–208•20) for depressive disorders in rural settings to 21•45 (range: 9•30–105•20) for depressive disorders in urban settings. Other associations stratified according to study settings are in Table 4.

Univariable analysis for all MNSDs together revealed that, whether a study was conducted in a hospital versus a community population, contributed to variability of suicidality and MNSD associations (OR = 2•85 (95% CI = 1•24–6•55,  $P = 0•015$ ). Sample size showed a trend for significance (OR = 1•001 (95% CI = 0•9999–1•002,  $P = 0•065$ ) while other factors did not reach statistically significant levels (Table 5).

Using a meta-analytic approach, the risk of suicidality was statistically significant for any MNSDs (OR = 1•98 (95%CI = 1•80–2•16)) and for depressive disorders (OR = 3•26 (95%CI = 2•88–3•63)) in all studies. In the meta-analysis of high-quality studies only, the risk of suicidality again was statistically significant for depressive disorders (OR = 3•19 (95%CI = 2•79–3•59)) and for any MNSDs (2•01 (95%CI = 1•82–2•20)) (Table 6). Most studies plotted at the same point outside the funnel plot suggesting precision. (Fig. 1).

All 73 studies reported on risk factors for suicidality. More than one risk factor was reported in >50% of the studies ( $n = 44$  (61%)). Risk factors supported by highest number of studies (the top three highest number of studies) included biomarkers (e.g. O.R 1•40 (range, 0•87–2•26 for all MNSDs combined)), psychosocial factors (e.g. O.R 27•98 (range, 15•02–52•74) for personality disorders)) and measures of poor economic status (e.g. O.R 6•15 (range, 4•43–8•65) for bipolar and related disorders)). For single risk factors, biological factors such as elevated cholesterol levels were the most common mediators of the relationship between suicide and MNSDs, reported in 19 (26%) of the studies, followed by psychological risk factors such as bereavement reported in 7 (10%) of the studies.

For studies assessing individual disorders, biological risk factors such

**Table 4**

Distribution of significant associations of MNSDs with suicidality by setting and Income Level.

	Hospital/Community Studies		Setting		Income Level	
	Hospital (median, range)	Community (median, range)	Urban (median, range)	Rural (median, range)	Lower middle income (median, range)	Upper middle income (median, range)
Depressive disorders	2•7 (1•12–5•54)	25•34 (9•3–208•2)	39•37 (1•12–208•2)	21•45 (9•3–105•2)	14•64 (9•3–208•2)	23•98 (1•12–105•2)
Schizophrenia spectrum and related disorders	3•9 ****	6•23 (3•03–27•72)	15•81 (3•9–27•72)	4•085 (3•03–26•17)	4•27(0•82–42•01)*	3•9 (3•03–27•72)
Bipolar and related disorders	2•7**	4•27 (2•02–36•9)	5•49 (2•7–36•9)	2•84 (2•02–24•68)	2•02 (0•10–170•37)*	4•27 (2•62–36•9)
Anxiety disorders	1•9**	3•57 (1•44–11•61)	1•67 (1•44–1•9)	6•11 (2•39–11•61)	a	2•98 (1•44–11•61)
Obsessive compulsive and related disorders	3•9 **	a	3•9**	a	a	3•9**
Personality disorders	3•43 (1•88–6•28)*	15•84 (10•03–21•65)	3•43 (1•88–6•28)*	15•84 (10•03–21•65)	3•43 (1•88–6•28)*	15•84 (10•03–21•65)
Substance related and addictive disorders	2•1 (1•4–2•8)	2•77 (0•06–7•37)	1•4 (0•06–3•14)	2•79 (1•17–7•37)	2•8 (1•57–6•47)	2•75 (0•06–7•37)
Trauma and stressor related disorders	3•2 (3–3•4)	6•68 (1•42–62•6)*	3**	5•04 (3•4–6•68)	5•04 (3•4–6•68)	3**
Epilepsy	a	2•4 (1•1–3•2)*	2•4 (1•1–32)	a	a	2•4 (1•1–32)*
Dementia	a	9•9 (2•1–45•8)*	9•9 (2•1–458)	a	a	9•9 (2•1–45•8)*
Any MNSDs***	2•68 (0•07–19•12)	13•21 (1•23–68•76)	5•05 (0•63–28•67)	8•81 (0•40–68•76)	6•42(1•63–19•5)	6•3 (0•07–68•76)

a; point estimate not given and could not be calculated.

\* ; confidence interval used instead of range.

\*\* ; confidence interval and range not available.

\*\*\* Any MNSD represents overall odds ratios for all MNSD reported in the study.

**Table 5**

Factors contributing to variability of odds/risk ratio of suicidality in mental disorders.

Factor	Univariable analysis		Multivariable analysis	
	Odds/risk ratio (95% CI)	P-value	Odds/risk ratio (95% CI)	P-value
Year of publication (Unit year 1999–2020 ref = 1999)	0•97 (0•88–1•06)	0•471	1•01 (0•89–1•15)	0•852
Study design (classic case-control versus case-control nested in surveys) (ref = case_control)	0•44 (0•15–1•31)	0•135	0•11 (0•002–5•20)	0•240
Continent	0•86 (0•58–1•26)	0•418	0•97 (0•45–2•09)	0•927
Economic class	0•85 (0•26–2•73)	0•776	0•27 (0•04–1•83)	0•164
Sample size	1•001 (0•9999–1•002)	0•065	1•001 (0•999–1•003)	0•315
Hospital/Community Setting (ref = hospital setting)	2•85 (1•24–6•55)	0•015	6•51 (0•48–88•52)	0•147
Rural/Urban Setting (ref = rural setting)	0•51 (0•22–1•22)	0•125	12•87 (0•31–541•89)	0•166
Age category (adults, adolescents, mixed ref = adults)	1•45 (0•89–2•34)	0•127	0•60 (0•20–1•77)	0•327
Diagnosis/screening method	0•43 (0•13–1•39)	0•154	0•03 (0•0007–1•56)	0•079
Males%	1•02 (0•99–1•05)	0•260	0•97 (0•91–1•03)	0•314
Quality of studies	0•98 (0•92–1•04)	0•467	0•99 (0•89–1•09)	0•758
Types of MNSDs	1•04 (0•99–1•10)	0•132	1•03 (0•90–1•17)	0•636

as serum lipid levels were most common in depressive disorders 8 (40%). Other risk factors reported in fewer studies included childhood trauma in a study focused on obsessive compulsive disorder and

environmental factors in a study on depressive disorders. Other risk factors are reported in Table 7.

#### 4. Discussion

Findings from this analysis confirm that suicidality is increased in MNSDs in LMICs, given that the lower confidence intervals in the pooled effect sizes for many of the associations of suicidal behaviour with MNSDs were greater than one. Our approach for relative risks of suicide is similar to two other reviews [25,26] which predominantly focused on articles from HIC, or a mixture of both HIC and LMIC. The metanalytic pooled OR of 1•98 for any MNSD in our study was statistically significant supporting findings from another review of studies from HIC conducted in 2019 by Too et al. [25], that the risk for suicide is elevated in those with MNSDs. The associations in our analysis differed by region, economic class, study settings and source of sample. This stratification of estimates is useful in understanding variability, since formal analysis in a multivariable meta-regression analysis did not clearly identify independent associations. Additionally, we found that few of the eligible studies (38%) computed associations for odds ratios and relative risks of suicidality in MNSDs, this however, is more informative and robust than the frequency distribution in MNSDs, without comparison groups.

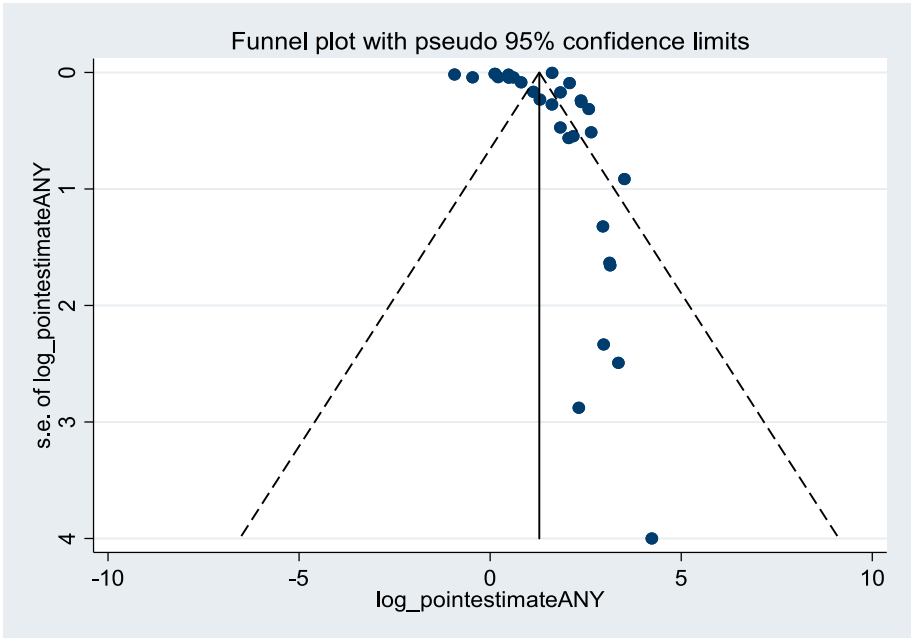
The risk for suicidality in LMIC was highest for depressive disorders in the median analysis (OR = 23•14 (1•12–208•20)). Other studies have similarly identified depression as the strongest contributor to suicidality among the psychiatry morbidities [27]. Some have attributed this strong link to shared genetic link between the two conditions [28]. Depression leads to an individual's impairment in cognitive, social, physical, and emotional functioning resulting in a worsening quality of life, factors that are known to increase the risk of suicide [29–31]. The review by Too et al. [25], found lower OR for depressive disorders (OR = 12•3) than in our study (OR = 23•14), perhaps related to poor capacity to manage these disorders in LMIC, due to their misperception as less severe MNSDs.

On the contrary suicide risk for psychotic disorders were lower in our study (OR = 4•09) than in estimates from HIC (OR = 13•2), possibly because the background risk for suicide in the population forming the comparison groups is significantly lower in HIC than in LMIC, and that

**Table 6**  
Pooled estimates for association for suicidality and mental and neurological disorder.

	All studies			High quality studies		
	No. of studies	Pooled Estimates (95% CI)	I <sup>2</sup>	No. of studies	Pooled Estimate (95% CI)	I <sup>2</sup>
Depressive Disorders	14	3•26 (2•88–3•63)	99•8%	13	3•19 (2•79–3•59)	99•8%
Schizophrenia Spectrum and Other Psychotic Disorders	5	1•84 (0•89–2•79)	22•6%	5	1•84 (0•89–2•79)	22•6%
Bipolar and Related Disorders	5	1•92 (0•80–3•04)	68•6%	5	1•92 (0•80–3•04)	68•6%
Anxiety Disorders	5	1•42 (0•47–2•37)	47•3%	4	1•69 (0•54–2•84)	66•9%
Substance-Related and Addictive Disorders	9	4•03 (–0•60–8•66)	91•8%	9	4•03 (–0•60–8•66)	91•8%
Any MNSDs	28	1•98 (1•80–2•16)	98•7%	26	2•01 (1•82–2•20)	98•8%

MNSDs with less than five studies were excluded from this meta-analysis.



**Fig. 1.** Funnel plot assessing publication bias.

most psychotic disorders ending in suicides may go undiagnosed in LMIC stemming from reduced access to care and stigma [32]. The elevated risk of suicide in persons with psychotic disorders has been attributed to symptomatology of the disorder specifically the presence of depression and hallucinations [33]. Insight into the impact of the psychotic illness diagnosis on the individual’s quality of life especially among highly functioning patients is a significant contributor to suicide risk [34]. Some studies have additionally shown a link between the side effects of antipsychotic medications such as tardive dyskinesia and akathisia with increased suicide risk [35].

The most studied antecedent for suicide was mood disorders followed by psychotic disorders, both of which are frequently observed in fatal and non-fatal suicidal behaviour. While suicidality is very specific to mood disorders, there is an urgent need to conduct studies of suicidal behaviour in other MNSDs, e.g., in post-traumatic stress disorder (PTSD). Suicidality occurs in up to 54% of persons with PTSD in Europe, where violence and conflicts that may cause PTSD are potentially less frequent than in Africa or South America [36].

Borderline personality disorders were surprisingly associated with very high odds ratios for suicide, which was reported in another review of both HIC and LMIC studies [25]. An increased suicide risk in this population has been linked to impulsivity and anger dysregulation personality traits [37] as well as high comorbidity of substance use and depressive disorders [38]. Personality disorders are estimated to be presented in 40% of suicide attempters [38]. Despite this they are likely to be easily overlooked as a category of MNSDs in LMIC because of the lack of extensive diagnostic evaluation available. Our results suggest

that it should be prioritised for interventions to reduce suicides in this group of patients in LMIC.

Even if some MNSDs such as substance abuse had low odds for suicide of 2–3, these risks are comparable to those of other lifestyle diseases that are moderators of suicide rather than causes per se e.g. smoking, alcohol use, and internet addiction, for which there is enormous investments in prevention of suicide [39]. Risk for suicide was often relatively small for anxiety disorders and substance related and addictive disorders, perhaps because these conditions are also relatively common in the populations that formed the comparison group.

<sup>3640</sup>Common neurological disorders were included in the search criteria, but these were surprisingly under-represented in this review, with only one study for epilepsy. Epilepsy is the most studied neurological disorders in LMIC, according to a recent systematic review [40], and has increased risk for suicidality (OR 3.89) especially in frontal-temporal epilepsy syndromes [41]. Manifestations of neurological disorders e.g. paralysis from stroke, tremors for Parkinson’s disease, infirmity from cerebral palsy can lead to social isolation and exclusions [42], which are risk factors for depression and suicidality [43]. Sustained funding to understand the relative contribution of specific MNSDS including neurological disorders are justified to inform targeted interventions.

Suicidal behaviour is thought to be very common in adolescents, yet this important group was under-represented (3%) in the studies reviewed. A report commissioned by WHO concluded that determinants of suicidal behaviours among the youths e.g., violence, bullying, lacking friends, and alcohol use are universal, and can be addressed with

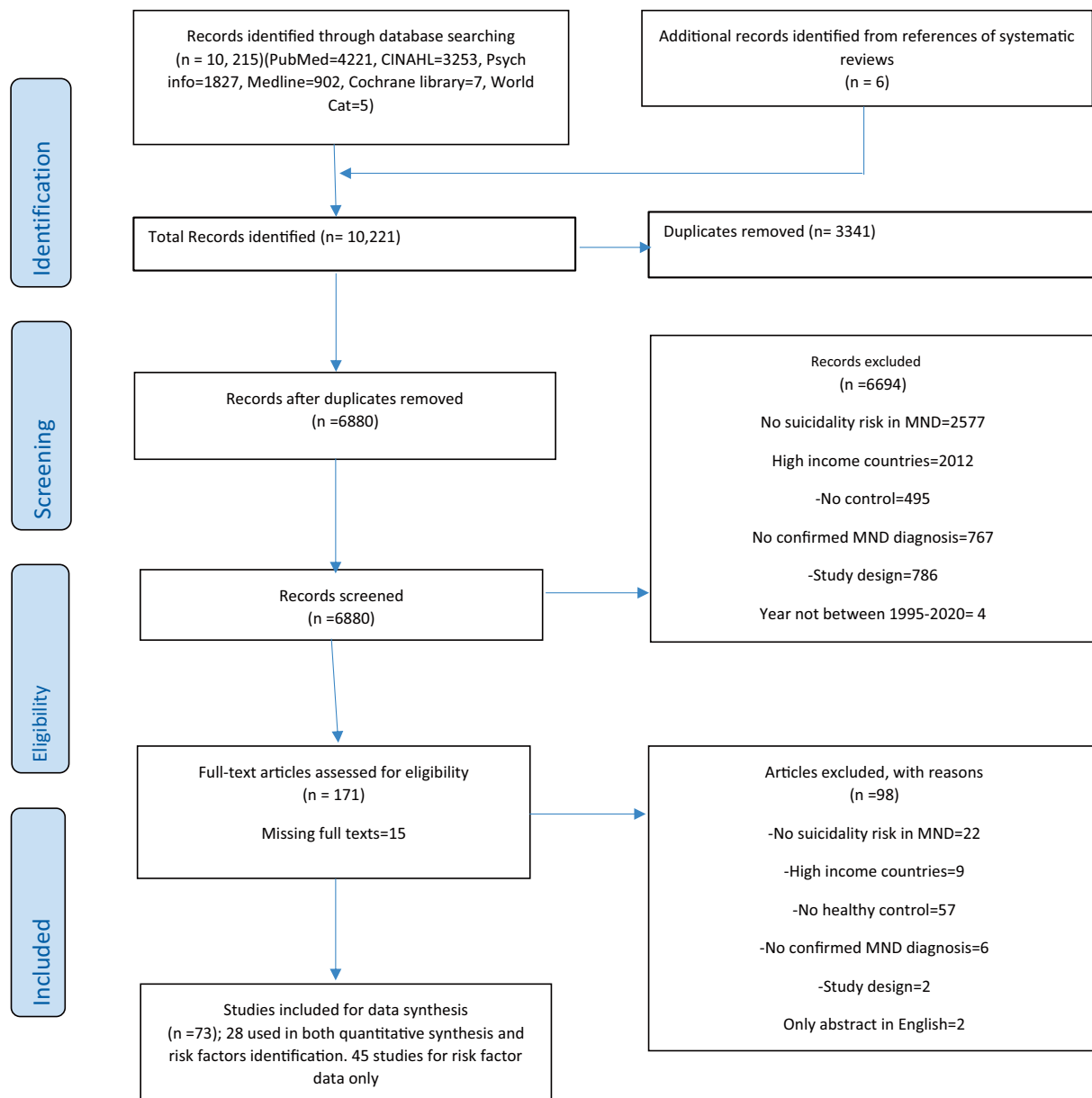


Fig. 2. Flowchart of studies included in the review.

interventions targeted at schools [44].

There were conspicuously few studies from Africa, on suicidality, perhaps because of logistical difficulties of identification of MNSDs in these settings where both the psychiatrist-patient ratio is very low and research infrastructure to conduct these studies is lacking. Diagnostic, treatment and research gaps should be closed since available reports indicate that suicidal behaviour is common in Western Kenya and on the Kenyan coast [45,14]. Recognised risk factors for MNSDs in Africa e.g., infections, conflicts, and socioeconomic disadvantages may moderate or modify suicidality following MNSDs and need to be clarified in community-based studies. The mental health needs in LMIC can be addressed by investment in research on mental health issues, infrastructure, and training mental health specialists. A feasible solution would be training the existing cadre of health care providers e.g., lay counsellors and community health volunteers to offer psychosocial support, while nurses and clinical officers can task share in the identification and management of MNSDs.

Although formal statistical approaches did not identify differences across settings, economic classes and regions, a few notable observations

were apparent in the stratified analysis. Estimates of suicide for any MNSD were higher in rural areas than urban areas, and it could be because of risk factors such as poverty and poor care in the former. However, the estimates were highest in UMIC than LMIC, which may be related to infrastructural capacity to identify and report these problems in fairly economically developed settings. The continents with largest OR e.g., South America and Asia, also had many studies on MNSDs such as depressive disorders, which had large odds ratios. The relationship between suicidal behaviour and MNSDs was revealed more strongly in hospital settings compared to community settings. MNSDs in hospital settings may be more severe and thus increased risk for suicidal behaviour. This underscores the need for integrating suicide risk screening and assessment in the hospital settings [46]. These variations in risks of suicide in MNSDs should be interpreted carefully because of the methodological differences in studies including sample size, and source of sample e.g., hospital vs community, although these were not significant in the metaregression analysis. More country specific estimates of suicidality in MNSDs, especially where there were no studies, are warranted to inform context specific interventions.

**Table 7**  
Risk factors for suicidality in MNSDs and the corresponding median odds ratios with ranges.

Risk factor	No of studies	Depressive disorders	Schizophrenia spectrum and related disorders	Bipolar and related disorders	Anxiety disorders	Obsessive compulsive and related disorders	Personality disorders	Substance related and addictive disorders	Trauma and stressor related disorders	All MNSDs
<b>Demographic Factors</b>										
Sex (male sex)	6 (8•22%)	–	–	–	–	–	–	–	–	1•00 (0•60–1•80)*
Marital status (unmarried, separated)	7 (9•59%)	3•12 (2•90–4•19)	3•12 (2•90–4•19)	3•61 (3•03–4•19)	3•61 (3•03–4•19)	–	–	3•12 (2•90–4•19)	3•03 (2•90–4•19)	–
Education Level (no formal education)	6 (8•33%)	4•05 (3•40–4•70)	4•05 (3•40–4•70)	4•70 (2•35–9•79)*	4•70 (2•35–9•79)*	–	–	4•05 (3•40–4•70)	4•70 (2•35–9•79)*	–
Economic Status (unemployment, poverty)	10 (14•08%)	4•60 (2•40–8•65)	4•60 (2•40–8•65)	6•15 (4•43–8•65)	5•29 (2•40–8•65)	6•15 (328–11•55)*	4•84 (3•52–6•15)	4•60 (2•40–8•65)	4•43 (2•40–8•65)	–
<b>Biological Factors</b>	32 (43•84%)	–	–	–	–	–	–	–	–	1•40 (0•87–2•26)*
Family history of suicide	3 (4•1%)	–	–	–	–	–	–	–	–	12•75 (4•69–48•59)*
<b>Psychosocial Factors</b>	15 (20•55%)	4•22 (0•91–27•98)	5•45 (0•1–27•98)	17•64 (7•3–28•0)	7•29 (4•8–27•98)	27•98 (15•02–52•74)	27•98 (15•02–52•74)*	5•45 (0•91–27•98)	7•29 (3•60–27•98)	27•98 (15•02–52•74)*
<b>Physical Illness</b>	7 (9•59%)	4•17 (2•2–17•5)	7•8 (2•20–17•50)	4•17 (1•67–12•42)*	4•17 (1•67–12•42)*	–	–	6•00 (2•20–17•50)	10•84 (4•17–17•50)	–

The studies reported risk factors that increase the risk of suicidality in MNSD, some of which are modifiable and can be targeted for preventative interventions. Psychosocial factors were a key contributor to the risk of suicidality in MNSDs. These risk factors comprise a large category of factors that include psychosocial stress, stress-vulnerable personality type, low social integration or support, and low socio-economic status and hence may impact on suicidality through various mechanisms [47]. For example, low socio-economic status has been linked with higher levels of adversity thereby increasing an individual's vulnerability to mental illness. This coupled with psychological distress symptoms like hopelessness and anxiety increase the risk of suicide [48]. Further, psychosocial risk factors foster unhealthy behaviours such as harmful alcohol and substance use, which in themselves are known risk factors for suicidality [49]. Risk for suicide was increased in males and unmarried persons with MNSD, and these groups should be prioritised for assessment and care for suicidality when they present at psychiatric facilities. Based on the added impact of these psychosocial factors, it is important that suicide risk in patients with MNSDs such as depression is assessed not only as a symptom of a psychiatry disorder but also in a contextualized and phenomenological manner [50]. Poor economic factors can cause both MNSDs and suicide through the vicious cycle of social causation and selection, and measures to decrease poverty, and to empower communities. Study findings on the relationship between cholesterol levels and suicidal behaviour have been conflicting [51–53]. Some studies have reported higher risk of suicidal behaviour in persons with low cholesterol [52]. This has been linked to the low level of exposure of serotonin receptors on brain cell membrane surface found in low cholesterol [54]. However, in our review, we found an elevated cholesterol level was a common mediator of suicide and MNSDs. The reasons for this relationship are not clear though it has been suggested that patients with high total cholesterol levels would likely have maladaptive nutritional habits which in turn may be associated with suicidal behaviour [55]. A change in lipid profile, that is, both higher and lower total cholesterol has been thought to have an impact on serotonergic function [56]. Thus, more future longitudinal studies would be useful to clarify this relationship. Identification of biological factors was particularly interesting as this may help development of biomarkers for identifying those at risk. Accumulating genetic data from the literature and from ongoing studies can be collated to construct predictive scores or profiles for those at risk.

The strength of this study is reporting of associations as measured by OR or RR which is more informative than simple reporting of prevalence distributions, which may be misleading without comparison groups. We included both fatal and non-fatal suicidal behaviour which provides a clearer picture of progression of suicide in MNSDs. Inclusion of all MNSDs allowed identification for the need for more research for neurological disorders such as epilepsy, which is common in many LMICs. However, this study is limited by the heterogeneity associated with identification, reporting of suicides, and MNSDs, confirmed through stratified analysis, but not through formal metaregression analysis. We used medians and interquartile ranges for sub-group analysis for which there were few studies to conduct a meta-analysis. While the median estimates are useful in summarizing the risks across the studies, they do not assess how the individual studies estimates differ from each other. The composition of the comparison groups and the sample size was variable across studies, which can affect the size of reported OR. Further, there may be underrepresentation of non-English articles in the major databases used in the search strategy for the study [57].

In conclusion, this study confirms a strong association between suicide and MNSDs in LMICs beyond the high prevalence distribution reported in previous studies. Suicidal behaviour is not only associated with mood disorders but also with other MNSDs such as psychotic disorders and personality disorders, although there is little data for neurological conditions such as epilepsy, which are common in many LMIC. The association between MNSDs and suicide can be modified by risk factors

such as economic status and psychosocial factors, and biological factors, some of which can be addressed through psychosocial support, economic empowerment and lifestyle changes. However, the evidence is far from robust. There was limited data from low-income countries on the relationship between suicide and MNSDs. Well-powered empirical studies are required in many of these LMIC settings, especially Africa, to have a better picture of the association between suicidal behaviour and MNSDs. Improving access for care for those with MNSD and institution of targeted interventions for risk factors may prevent dying by suicide.

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## Contributors

LO, SK and CN designed the study. LO, SK, BP, CN planned the statistical analysis. MN, CT and LO and extracted and analysed data with assistance from SK and LO. MN, CT and LO assessed study eligibility and quality. LO and SK monitored the review process. LO, SK, MN and CT wrote the first draft of the manuscript. All authors contributed to the interpretation and subsequent edits of the manuscript.

## Declaration of Competing Interest

The authors declare no competing interests.

## Data availability

Extracted data are available on reasonable request to the corresponding author.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.comppsy.2023.152382>.

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