REVIEW

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A systematic review of factors prolonging or reducing the duration of untreated psychosis for people with psychosis in low- and middle-income countries

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Abstract

Aim: This review aims to identify factors that may prolong or reduce the duration of untreated psychosis for people with psychosis in low- and middle-income countries.

Methods: Electronic searches of six databases were conducted, to find studies from low- and middle-income countries on people with psychotic disorders provided they statistically measured an association between factors that may prolong or reduce the duration of untreated psychosis. Studies were critically appraised and a narrative synthesis exploring differences between and within studies is presented. A socio-ecological model is used to convey the main findings.

Results: Thirty studies of 16 473 participants in total were included in this review. Taken together participants were 51.5% male and 48.5% female. Various factors potentially associated with longer duration of untreated psychosis for people with psychosis in low- and middle-income countries were found. Examples of these factors are an insidious mode of onset, greater family stigma and low social class. Other factors, such as marital status, educational level, diagnostic type, predominant symptoms and employment status, yielded inconsistent results.

Conclusions: The methodological quality of the included studies limits the conclusions of this review. The results indicate an urgent need for further high-quality research in these countries. The socio-ecological model is a helpful framework for clinicians, scholars, and decision-makers to conceptualize factors that may affect the duration of untreated psychosis, highlight gaps in the literature as well as reflect on potential prevention strategies that may ultimately support early intervention services for people with psychosis in developing countries.

KEYWORDS
developing countries, early intervention, psychotic disorders, systematic review, treatment delay

1 | INTRODUCTION

Psychotic disorders are characterized by alterations in an individual's perception, thought, mood, and behaviour (WHO, 2016). Symptoms are frequently regrouped into positive symptoms, namely hallucinations and delusions, and negative symptoms, including anhedonia and poverty of speech (Laprevote et al., 2016). Psychotic disorders, typically arising in early adulthood (Patel, 2012), are one of the main

causes of disability globally and may lead to premature death (Correll et al., 2018). These have a relatively high prevalence and a lifetime risk of 3%–3.5% (Malla & McGorry, 2019). The onset of psychotic symptoms may create marked distress in affected individuals and families (NICE, 2014). The personal, social, and financial repercussions of psychotic disorders make them a major public health issue (Malla & McGorry, 2019).

In recent decades, in response to often suboptimal clinical outcomes of people with first-episode psychosis (FEP), early intervention services (EIS) have been developed (Bird et al., 2010). EIS have spread across high-income countries (HICs) (Bird et al., 2010) and recently gained attention in low- and middle-income countries (LMICs) (Singh & Javed, 2020). There is mounting evidence that this form of secondary prevention may positively impact employment outcomes, global functioning, and quality of life as well as reduce psychotic symptoms, long-term disability, and comorbidities (Mwesiga et al., 2021). High-quality evidence has demonstrated that their effectiveness far exceeds usual care (Malla & McGorry, 2019). EIS include recommended treatments, for example, initiation of low-dose antipsychotic medication combined with psychoeducation (WHO, 2016). Reducing the duration of untreated psychosis (DUP) is also a fundamental objective of EIS (NICE, 2014), with the critical period hypothesis suggesting that a patient's prognosis is determined during the early stages of psychosis—meaning that the longer the DUP, the worse the patient's clinical outcomes (Fabri Cabral & Chaves, 2009).

DUP has similarly received increasing attention in research and clinical settings since the 1980s (Devi Thakoor et al., 2016). Although there are disagreements as to the exact definition of DUP, the current literature broadly defines it as the period between the appearance of psychotic symptoms to the start of initiating antipsychotic medication (Kaminga, Dai, et al., 2019). Delayed help-seeking is a common occurrence for people experiencing psychotic symptoms and this has led to DUP being reported in terms of months and even years (Sharifi et al., 2009). There is considerable variation in reported lengths of DUP depending on the population studied (Sadeghieh Ahari et al., 2013).

There is an association between longer DUP and a lower rate of remission (Sadeghieh Ahari et al., 2013), slower recovery (Davis et al., 2016), increased rate of relapse (Sadeghieh Ahari et al., 2013), greater symptom severity (Fresan et al., 2020), and poorer response to antipsychotic drugs (Fresan et al., 2020). Additionally, studies have reported a link between longer DUP and impaired cognition (Qiu et al., 2017), lower employment rates (Sadeghieh Ahari et al., 2013) and poor quality of life (Fresan et al., 2020). Chen et al. (2019) also reported an association between higher mortality rate and longer DUP in LMICs.

Research has yet to identify the distinct mechanisms underlying an association between DUP and clinical outcomes (Fresan et al., 2020). A range of factors have been postulated to affect the DUP (e.g., sociocultural factors, Qiu et al., 2017), as a potentially modifiable prognostic factor. Possible factors influencing the DUP have been identified (Fresan et al., 2020), although results from different studies are often conflicting (Okasha et al., 2016). Given that treatment delay appears to have negative implications for people with

psychosis (Chen et al., 2019), understanding the potential contributing factors to DUP could facilitate the identification, planning and implementation of targeted efforts in hopes of reducing DUP, improving outcomes of people with psychosis and alleviating suffering (Kaminga, Dai, et al., 2019).

This is a particularly pressing matter in LMICs where approximately 80% of all FEP occur (Singh & Javed, 2020). Early intervention for people with psychosis in developing countries is high on the agenda of the World Psychiatric Association (Vaitheswaran et al., 2021). Despite unique challenges, such as limited funding and scarcity of specialized mental health workers (Singh & Javed, 2020), EIS have been implemented across LMICs (Corrêa-Oliveira et al., 2021). However, benefits of EIS may not be fully exploited if little attention is given to reducing DUP (Dama et al., 2019). It therefore seems beneficial to work on both EIS and DUP simultaneously (Dama et al., 2019), especially since research has highlighted a substantially longer average DUP in LMICs (Maric et al., 2016) and DUP has been associated with an unfavourable prognosis for people with psychosis in LMICs too (Burns & Kirkbride, 2012).

The purpose of this review is to systematically assess studies to answer the research question: What are the factors prolonging or reducing the duration of untreated psychosis for people with psychosis in LMICs?

A Socio-Ecological Model (SEM) was chosen to help conceptualize and illustrate the diverse factors potentially affecting DUP, and their overlapping influence on people with psychosis in LMICs (McCloskey et al., 2011, pp. 20–23). SEM was originally proposed in the 1980s as a theory-based framework for understanding the many interactive forces affecting health (Kilanowski, 2017). Since then, it has been used across disciplines as a framework for prevention (Centers for Disease Control and Prevention, 2022).

2 | METHODS

2.1 | Search strategy

Electronic searches were conducted on 2 August, 2022, across: CINAHL (EBSCOhost), PsycINFO (EBSCOhost), PubMed, EMBASE (Ovid), Medline (Ovid) and Web of Science Core Collection. The search strategy encompassed: (1) psychosis, (2) DUP and (3) LMICs (e.g. Supporting Information, Appendix A). No methodological search filters were applied to ensure adequate retrieval of studies (Boland et al., 2017, pp. 68–70).

2.2 | Screening and selection process

All retrieved search results were imported into EndNote. Titles and abstracts were independently screened for relevance. All potentially eligible papers were fully reviewed and assessed against the predetermined eligibility criteria developed using the PICOSS method (Boland et al., 2017, p.51) and outlined in Table 1. Only studies written in English were accepted and grey literature data were excluded.

TABLE 1 Key eligibility criteria, in terms of the PICOS framework.

Population	• Inclusion: Study participants with psychotic disorders, first-episode psychosis and mixed samples of study participants with non-affective and affective psychoses regardless of age and gender • Exclusion: Study participants with affective psychosis only, mixed samples including study participants with other mental health disorders than previously defined as well as studies with study participants where organic conditions have led to a diagnosis of psychosis
Intervention(s)/ exposure(s)	• Inclusion: All types of factors that may prolong or reduce the duration of untreated psychosis (DUP) • Exclusion: Data on anything other than factors that may prolong or reduce the DUP, such as, the association between the DUP and clinical outcomes
Comparator(s)/ control	• None
Outcome	• Inclusion: A statistical measure of the association of the DUP with factors which may prolong or reduce it
Study design	• Inclusion: Original research reports of observational studies published in peer-reviewed journals • Exclusion: Interventional studies
Setting	• Inclusion: Research occurring in any healthcare setting was approved if they were in low- and middle-income countries (LMICs) and conducted by clinicians. Studies reporting data from both high-income countries (HICs) and LMICs were accepted if the data from LMICs was easily isolated and retrieved • Exclusion: Studies conducted in HICs only

Backward and forward citation searching were performed on included studies using Google Scholar (Boland et al., 2017, pp. 71–72). Studies that did not meet the inclusion criteria were excluded. Borderline cases were discussed and resolved through consensus with LB.

2.3 | Data extraction

Data summary tables were created to summarize descriptive and analytic data from the studies. The study design was determined for several studies using the Centre for Evidence-Based Medicine Study Designs resource (www.cebm.ox.ac.uk, n.d.). Age is reported verbatim. Country income level was defined using World Bank Data (2022).

2.4 | Quality assessment

Both the AXIS tool for cross-sectional studies and the SIGN methodology checklist for case–control studies were used as they share

comparable scales assessing quality of reporting, study design quality and risk of bias (Downes et al., 2016; SIGN, 2021). The AXIS tool is a concise tool of 20 questions developed by medical experts (Downes et al., 2016). The SIGN methodology checklist for case–control studies is a 14-question checklist developed by the SIGN executive in collaboration with healthcare professionals, individuals, and patient organisations (SIGN, 2021).

An overall category assessment for each was defined as excellent, good, fair, or poor. 'Excellent' was assigned when all studies fulfilled all criteria for a category, 'good' when all studies met >50% of criteria for a category, 'fair' when the majority of studies fulfilled >50% of the criteria for a category and 'poor' when no study met 50% of the criteria for a category.

2.5 | Synthesis and analysis methods

All studies underwent data synthesis, and no data were suitable for a meta-analysis given the heterogeneity of the studies (Boland et al., 2017, p.142–145). A narrative synthesis summarising and exploring key findings between and within studies is presented. This review adheres to the PRISMA checklist guideline (Page et al., 2021) and was informed by the Synthesis Without Meta-Analysis guideline (Campbell et al., 2020). Main findings are presented using SEM levels (Centers for Disease Control and Prevention, 2022; Figure 1).

3 | RESULTS

3.1 | Study selection

The initial search taken together yielded 432 articles. After removing duplicates, the title and abstract of 287 articles were reviewed. Of the 23 reports subsequently sought for retrieval, two reports were not accessed due to the inability to contact the authors. A remaining 14 articles were ultimately included. Backward and forward citation searching of these articles yielded 17 additional articles that were assessed for eligibility, bringing the total number of included articles included to 30. For details, please see Figure 2.

3.2 | Study characteristics

Twenty-nine cross-sectional studies and one case–control study were included. Each study investigated one or more factors potentially influencing DUP. At least 60% of the studies ($n = 19$) took place in psychiatric hospitals or psychiatric units of general hospitals. Nearly half of the studies ($n = 14$) came from the Asian continent followed closely by the African continent. One study was conducted across two countries, China and Mauritius (Devi Thakoor et al., 2016). Please see Figure 3 (MapChart, 2022).

Almost all studies ($n = 27$) were from middle-income countries. Sample size ranged from 37 (Ananthi et al., 2017) to 7252 participants

Reference: Centers for Disease Control and Prevention (2022). *The Social-Ecological Model: A Framework for Prevention*. [online] Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/violenceprevention/about/social-ecologicalmodel.html.

FIGURE 1 Socio-Ecological Model adapted by the Centers for Disease Control and Prevention. *Source*: Centers for Disease Control and Prevention, 2022. *The Social-Ecological Model: A Framework for Prevention*. Centres for Disease Control and Prevention. http://www.cdc.gov/violenceprevention/about/social-ecologicalmodel.html

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources
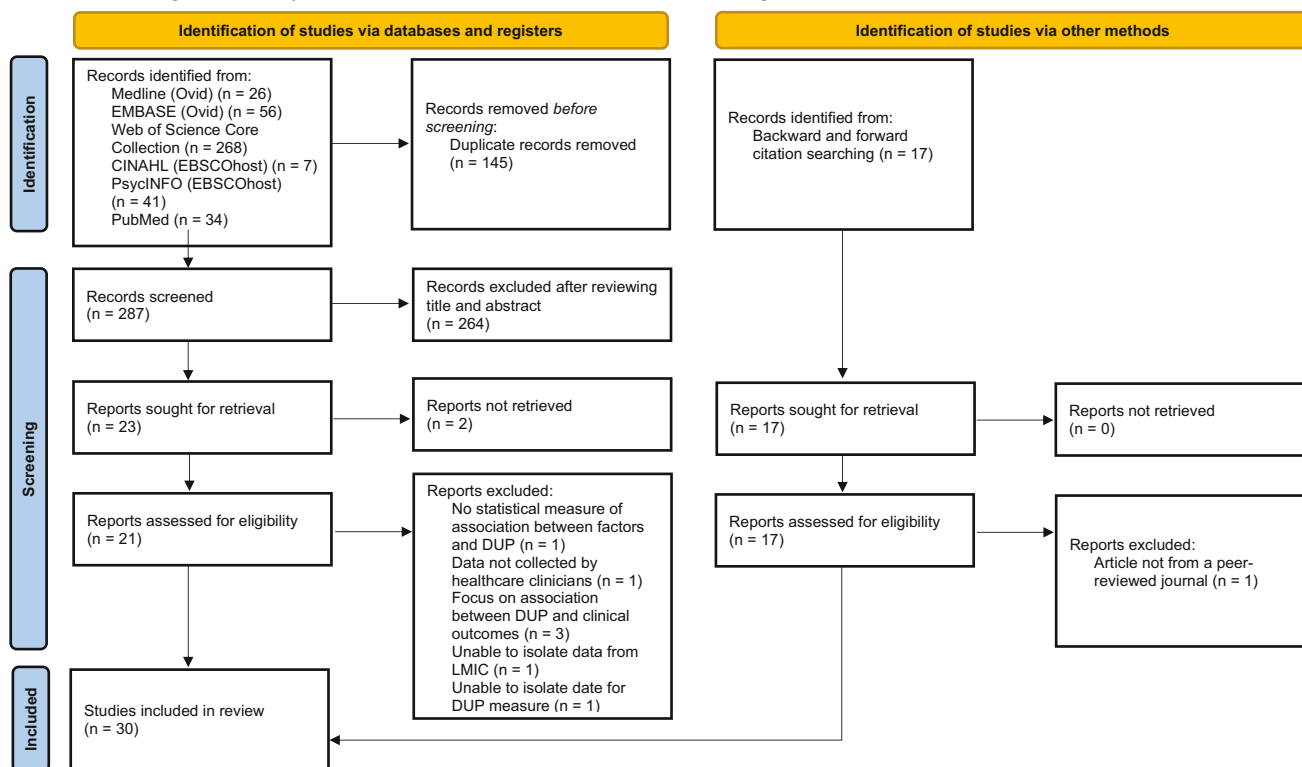
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

FIGURE 2 PRISMA Flow Diagram.

(Chen et al., 2019), with a median sample size of 107.5. Of the 16 473 participants, 51.5% were male and 48.5% were female. Please see Table 2 for more details and characteristics. Most researchers opted for either the Diagnostic and Statistical Manual of Mental Disorders ($n = 17$) published in 1994, or the 10th revision of the International Statistical Classification of Diseases and Related Health Problems ($n = 11$) published in 2015.

3.3 | Factors and instruments

DUP was inconsistently defined, although all studies defined the onset of psychosis as the start of DUP more than half of the studies ($n = 18$) did not provide details on this. The rest incorporated further information in their definition, on the type of psychotic symptoms, duration of symptoms, or who observed or reported these symptoms.
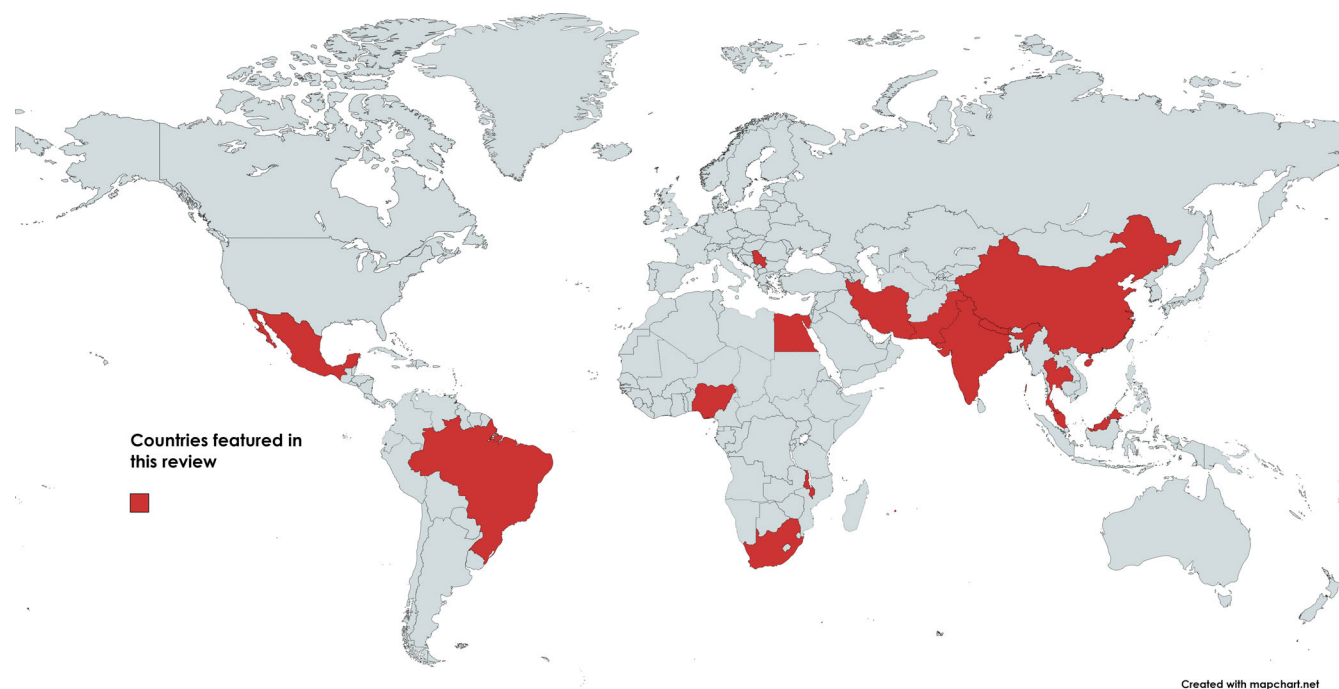
FIGURE 3 Countries featured in this review. *Source*: MapChart (2022). *World Map: Simple*. MapChart. Available at: https://www.mapchart.net/world.html

The end of DUP was defined by phrases of varying specificity. The most common definitions were 'until the first contact with mental health services' ($n = 7$) and 'until the start of antipsychotic medication' ($n = 6$). Another frequent definition was 'until the initiation of adequate treatment' ($n = 4$). The factors studied also varied with 55 distinct factors investigated. Several studies investigated sociodemographic factors ($n = 29$), clinical factors ($n = 22$) and pathway to care ($n = 14$). Other investigated factors include stigma ($n = 3$) and socioeconomic factors ($n = 3$). Examples of validated instruments used to assess these factors were the Positive and Negative Syndrome Scale ($n = 14$), Premorbid Adjustment Scale ($n = 4$), Calgary Depression Scale ($n = 2$) and the Global Assessment of Functioning ($n = 2$). Examples of instruments chosen to determine DUP were the Pathway Encounter Form ($n = 5$), Nottingham Onset Schedule ($n = 2$), Symptom Onset of Schizophrenia ($n = 2$) and Beiser Scale ($n = 2$).

3.4 | Main findings

Findings are presented using four SEM levels: individual, relationship, community and societal. Please refer to Table 3 for more details.

3.4.1 | Individual level

Many investigated factors generated conflicting results. Two studies (Kini et al., 2015; Okasha et al., 2016) found that a lower age was associated with shorter DUP while others ($n = 8$) did not find an

association between the two. Two studies reported an association between male gender and longer DUP (Chen et al., 2019; Fresan et al., 2020) while one study showed the opposite (Chee et al., 2010) and it was a non-significant result in nearly half of the studies ($n = 13$). Two studies from a lower-middle income country found a link between living in a rural area and longer DUP (Nallapanemi et al., 2015; Okasha et al., 2016) while other studies (with the same income level) did not (Ananthi et al., 2017; Kini et al., 2015; Sharifi et al., 2009).

Ethnicity was statistically associated with DUP in two different studies. A shorter DUP was associated with indigenous ethnicity compared with Malay, Chinese and Indian ethnicities (Chee et al., 2010) and black ethnicity compared with non-black ethnicity (Burns & Kirkbride, 2012).

Two interconnected factors were measured heterogeneously across studies with inconsistent results. Patients with a lower educational level had longer DUP (Chee et al., 2010; Chen et al., 2019; Kaminga, Dai, et al., 2019; Kini et al., 2015; Okasha et al., 2016) although this was non-significant in 10 studies. A relationship was found between employment and shorter DUP (Fresan et al., 2020; Okasha et al., 2016; Qiu et al., 2017), while seven found no association and another study showed the inverse relationship (Myaba et al., 2021).

Several studies did not find an association with a family history of mental illness and DUP (Chee et al., 2010; Kini et al., 2015; Nallapanemi et al., 2015; Paruk et al., 2015), however two studies identified an association with shorter DUP (Okasha et al., 2016; Takizawa et al., 2020).

Four studies examined substance use in relation to DUP using semi-structured questionnaires (Nallapanemi et al., 2015; Takizawa

TABLE 2 Study, patient, and illness characteristics.

Reference	Study design	Study aim	Study setting	Country	Income level	Sample size	Reported age	Male, %	Psychiatric diagnoses included	Diagnostic approach
Adeosun et al., 2013	Cross-sectional†	"[To assess] the pathways to mental health care in patients with schizophrenia, at their first contact with a mental health service in Lagos, southwestern Nigeria."	Federal Neuro-Psychiatric Hospital in Yaba, Lagos	Nigeria	LMI	138	Mean age (SD): 36.29 (11.12)	39.90%	Schizophrenia	ICD-10
Ananthi et al., 2017	Cross-sectional†	"[To assess] the factors affecting the Duration of untreated psychosis among patients with first episode psychosis in General hospital setup."	Chettinad Hospital and Research Institute	India	LMI	37	Mean average age: 30.75 years old	58%	Schizophrenia Schizotypal disorder Delusional disorder Brief psychotic disorder Shared psychotic disorder Schizoaffective disorder Other psychotic disorder or unspecified psychosis not due to a substance or known physiological condition	ICD-10
Ayres et al., 2007	Case–control	"[To investigate] whether cognitive deficits would be detectable in psychosis subjects relative to controls, and whether the DUP would be significantly associated with the severity of cognitive deficits."	Mental health services in Sao Paulo	Brazil	UMI	179 with psychosis, 383 controls	Mean age (SD) of participants with psychosis: 32.2 years old (11.4)	48%	Schizophrenia Schizophreniform disorder Bipolar disorder Major depressive disorder Schizoaffective disorder Brief psychosis Psychotic disorder NOS	DSM-IV
Burns et al., 2010	Cross-sectional	"[To evaluate] the relationship between causal attributions and pathways to care and features of FEP that have prognostic value."	Town Hill Hospital in KwaZulu-Natal	South Africa	UMI	54	Mean age (SD): 25.8 years old (8.1)	70%	Schizophrenia Schizophreniform disorder Schizoaffective disorder	DSM-IV-TR
Burns & Kirkbride, 2012	Cross-sectional	"[To investigate] the relationship between DUP and individual and neighbourhood-level socio-environmental factors, including household income and independent measures	Town Hill Hospital in KwaZulu-Natal	South Africa	UMI	54	Male's median age at onset (IQR): 21.5 years old (19–26) Female's median age at onset (IQR): 26.5 years old (20.5–38.5)	70%	Schizophrenia Schizoaffective disorder Schizophreniform disorder	DSM-IV-TR

TABLE 2 (Continued)

Reference	Study design	Study aim	Study setting	Country	Income level	Sample size	Reported age	Male, %	Psychiatric diagnoses included	Diagnostic approach
		of neighbourhood social capital, in a South African context."								
Chee et al., 2010	Cross-sectional	"[To study] study the relationships between DUP and sociodemographic and clinical parameters among the different ethnic groups."	74 study settings from the National Mental Health Registry (e.g. primary care health centres, departments of psychiatry and university hospitals)	Malaysia	UMI	5745	Mean age (SD): 31.3 years old (11.7)	62%	Schizophrenia	DSM-IV
Chen et al., 2019	Cross-sectional†	"[To explore] the duration of untreated schizophrenia and associated factors in Northwest China."	Mental health care institutes across the city of Yulin	China	UMI	7252	Mean age (SD) of male participants: 28 years old (14) Mean age (SD) of female participants: 31 years old (14)	40.70%	Schizophrenia	ICD-10
Davis et al., 2016	Cross-sectional	"[To examine] substance use as a potential factor predicting the DUP."	A psychiatric hospital in Pietermaritzburg	South Africa	UMI	87	40.2% were aged between 21 and 29 years old	56.30%	Schizophrenia Schizoaffective disorder Bipolar disorder Psychotic disorder NOS	DSM-IV-TR
Devi Thakoor et al., 2016	Cross-sectional	"[To explore] whether the DUP was different in Chinese and Mauritians and to clarify potential influencing factors to a long DUP (>3 months)."	Mental Health Institute of Second Xiangya Hospital in Changsha, China Brown Sequard Mental Health Care Centre in Beau Bassin, Mauritius	China Mauritius	UMI	300, including 200 from China and 100 from Mauritius	Mean age (SD) of participants from China: 24.8 years old (8.1) Mean age (SD) of participants from Mauritius: 40 years old (12.8)	China: 42%; Mauritius: 58%	Schizophrenia Major depression Bipolar disorder	DSM-IV-TR
Effiong & Albert, 2016	Cross-sectional	"[To delineate] the pathways patients navigate on their way to psychiatric services and to explore the socio-demographic and clinical factors on the delay of referral for treatment."	University of Uyo Teaching Hospital	Nigeria	LMI	108	Mean age (SD): 36.02 years old (11)	66.70%	Schizophrenia	ICD-10
Fresan et al., 2020	Cross-sectional†	"[To answer] three research questions: 1) Are DUP estimates similar in two very different settings and samples? 2) Are	Instituto Nacional de Psiquiatria Ramon de la Fuente Muniz in Mexico City	Mexico	UMI	145	Median age (IQR): 27 years old (12.0)	58.60%	Non-affective psychotic disorder	DSM-IV

TABLE 2 (Continued)

Reference	Study design	Study aim	Study setting	Country	Income level	Sample size	Reported age	Male, %	Psychiatric diagnoses included	Diagnostic approach
		demographic variables, premorbid adjustment, and symptom severity similarly related to DUP in two different settings? 3) Does the same set of variables account for a similar proportion of variance in DUP in the two settings?"								
Gupta et al., 2021	Cross-sectional	"[To assess] the pathways to care, supernatural beliefs, and impact on the duration of untreated psychosis in patients with schizophrenia."	National Medical College Teaching Hospital in Birgunj	Nepal	LMI	133	Mean age (SD): 29 years old (10.06)	70.70%	Paranoid schizophrenia Unspecified psychosis not due to a substance or known physiological condition	ICD-10
Kaminga et al., 2019	Cross-sectional	"[To investigate] the effects of socio-demographic characteristics, premorbid functioning, and insight on DUP in patients with first-episode schizophrenia or schizophreniform disorder."	Saint John of God community services	Malawi	LI	110	Mean age (SD): 37.09 years old (11.89)	63.64%	Schizophrenia Schizophreniform disorder	DSM-IV-TR
Kaminga et al., 2019	Cross-sectional†	"[To examine] the association between referral source and duration of untreated psychosis (DUP) and explore determinants of referral source; when adjusting for pathways to care, positive and negative symptoms, diagnosis and socio-demographic characteristics."	Saint John of God community services	Malawi	LI	140	Median age (min-max), Q1, Q3: 33.0 (18.0–65.0), 25.0, 42.8	60%	Schizophrenia Schizoaffective disorder Bipolar 1 disorder Schizophreniform disorder Delusional disorder Brief psychotic disorder Psychotic disorder NOS Major depressive disorder	DSM-IV-TR
Kini et al., 2015	Cross-sectional†	"[To assess] the association of DUP with sociodemographic and clinical variables in	Government Medical College in Kozhikode	India	LMI	45	N/A	55.55%	Schizophrenia Persistent Delusional Disorder Acute and Transient	ICD-10

TABLE 2 (Continued)

Reference	Study design	Study aim	Study setting	Country	Income level	Sample size	Reported age	Male, %	Psychiatric diagnoses included	Diagnostic approach
		patients experiencing FEP."							Psychotic Disorder Unspecified Nonorganic Psychosis Mania with Psychotic Symptoms Severe Depressive Episode with Psychotic Symptoms	
Maric et al., 2016	Cross-sectional†	"[To determine] duration of untreated psychosis (DUP) in patients with schizophrenia-spectrum disorders from Serbia and to analyse factors that potentially contribute to the treatment delay, with focus on personality traits."	A psychiatric clinic and regional hospital in and around Belgrade	Serbia	UMI	57	Mean age (SD): 29.9 years old (6.0)	54.40%	Schizophrenia-spectrum disorders	ICD-10
Mishra et al., 2021	Cross-sectional	"[To identify] variables associated with longer DUP in patients from lower socioeconomic strata who were diagnosed with first-episode psychosis and who were seeking medical care for the illness for the first time."	Grant Medical College and Sir JJ Group of Hospitals in Mumbai	India	LMI	60	Mean age (SD): 30.5 years old (10.5)	50%	Schizophrenia Schizophreniform disorder Brief psychotic disorder	DSM-IV-TR
Mo'tamedi et al., 2014	Cross-sectional†	"[To investigate], within the framework of the resiliency model of family stress, adjustment, and adaptation, the association between family coping strategies, resource management factors and duration of untreated psychosis (DUP) in Iranian families with one adult child with FEP."	Three hospitals in Tehran	Iran	LMI	107	Mean age (SD): 27.47 years old (4.61)	54.20%	Schizophrenia Schizophreniform disorder Schizoaffective disorder Brief psychosis Delusional disorder Psychosis NOS Bipolar disorder severe with psychotic features	DSM-IV

TABLE 2 (Continued)

Reference	Study design	Study aim	Study setting	Country	Income level	Sample size	Reported age	Male, %	Psychiatric diagnoses included	Diagnostic approach
Myaba et al., 2021	Cross-sectional	"[To determine] the psychosocial and clinical predictors of DUP in first episode psychosis in Malawi."	Saint John of God Mental Hospital	Malawi	LI	140	Median age (range): 33 years old (47)	60%	Schizophrenia Schizoaffective disorder	DSM-IV
Nallapaneni, Lanka and Paritala, 2015	Cross-sectional	"[To study] the factors influencing DUP in a tertiary psychiatric care centre in a metropolitan city."	Tertiary care psychiatric hospital	India	LMI	38	40% aged between 16 and 25 years old	52%	Schizophrenia and other psychosis Mood disorders Substance-induced psychosis	ICD-10
Naqvi et al., 2009	Cross-sectional†	N/A	AKUH hospital in Karachi	Pakistan	LMI	93	Mean age (SD) of male participants: 35 years old (10.4) Mean age (SD) of female participants: 32 years old (10.0)	59%	Schizophrenia	ICD-10
Odinka et al., 2014	Cross-sectional	"[To assess] the association between the positive and negative symptoms of schizophrenia, help-seeking and DUP."	Federal Neuropsychiatric Hospital in Enugu	Nigeria	LMI	360	Mean age (SD): 34.81 years old (12.05)	51.10%	Schizophrenia	ICD-10
Okasha et al., 2016	Cross-sectional	"[To study] DUP in Egyptian patients with psychotic disorders and to investigate how certain illnesses, patient, socio-cultural risk factors and help-seeking behaviour are correlated with prolonged DUP."	Psychiatry Centre at Ain Shams University in Eastern Cairo	Egypt	LMI	100	Mean age (SD): 30.8 years old (11.43)	68%	Schizophrenia Schizophreniform disorder Acute psychotic disorder Delusional disorder	DSM-IV-TR
Oliveira et al., 2010	Cross-sectional†	"[To investigate] the DUP in a sample of first contact psychosis, using data from the "Schizophrenia and other Psychoses at unveiling and long-term outcome" study (Sao Paulo), a large population-based epidemiological investigation of first episode psychosis in Sao Paulo, Brazil."	Mental health services in Sao Paulo	Brazil	UMI	200	Mean age (SD): 32.3 years old (11.3)	47.50%	Affective psychoses Non-affective psychoses	DSM-IV

TABLE 2 (Continued)

Reference	Study design	Study aim	Study setting	Country	Income level	Sample size	Reported age	Male, %	Psychiatric diagnoses included	Diagnostic approach
Paruk et al., 2015	Cross-sectional	"[To examine] the socio-demographic profile and clinical correlates of and substance use patterns in early onset psychosis in an adolescent population in urban KwaZulu-Natal, South Africa."	4 psychiatric units in the province of KwaZulu-Natal	South Africa	UMI	45	Mean age (SD): 15.9 years old (1.8)	69%	Affective psychoses Non-affective psychoses	DSM-IV-TR
Qiu et al., 2017	Cross-sectional†	"[To explore] social and clinical factors for DUP in South China and to learn the influence that family plays on DUP through their awareness of psychosis."	Third Affiliated Hospital of Sun Yatsen University	China	UMI	216	Mean age (SD): 25.11 years old (10.37)	53.20%	Schizophrenia Schizophreniform disorder Brief psychotic disorder Delusional disorder Schizoaffective psychosis	DSM-V
Sadeghieh Ahari et al., 2013	Cross-sectional	"[To investigate] DUP and the affecting factors in the psychiatric clinics of Razi Hospital (Tabriz) and Fatemi hospital (Ardabil) in two north-west provinces of Iran."	Psychiatric clinics of Razi Hospital, Tabriz Psychiatric clinics of Fatemi Hospital, Ardabil	Iran	LMI	80, 40 in each hospital	Mean age (SD) of participants from Razi Hospital: 32.75 years old (9.31) Mean age (SD) of participants from Fatemi Hospital: 30.13 years old (7.85)	Razi Hospital: 70% Fatemi Hospital: 45%	Schizophreniform disorder Schizophrenia Schizoaffective disorder	DSM-IV
Sharifi et al., 2009	Cross-sectional†	"[To examine] the duration of untreated psychosis and its correlates."	A psychiatric hospital in Tehran	Iran	LMI	91	Mean age at illness onset (SD): 27.4 years old (9.8)	58.20%	Schizophrenia Other non-affective psychotic disorders Bipolar disorder Major depressive disorder	DSM-IV
Takizawa et al., 2020	Cross-sectional†	"[To compare] the characteristics of patients in Thailand with first-episode schizophrenia (FES) who delayed seeking treatment with those of the patients with FES who sought timely treatment."	Psychiatric, general, and community-based hospitals, six general hospitals across Thailand	Thailand	UMI	302	Mean age (SD): 33 years old (10)	66%	Schizophrenia	ICD-10

(Continues)

et al., 2020) or the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) (Davis et al., 2016; Paruk et al., 2015). None found an association with drugs such as alcohol, cannabis or nicotine and DUP. However, one found a relationship between lifetime use of amphetamines or Mandrax and longer DUP (Davis et al., 2016).

Numerous investigations examined the potential influence of clinical factors on DUP. For instance, middle eastern and Asian studies demonstrated an association between an insidious mode of onset of psychosis and longer DUP (Kini et al., 2015; Mishra et al., 2021; Okasha et al., 2016; Qiu et al., 2017; Sharifi et al., 2009). Higher age at illness onset was associated with shorter DUP in numerous studies (Burns & Kirkbride, 2012; Chen et al., 2019; Kaminga, Myaba, et al., 2019; Nallapanemi et al., 2015; Paruk et al., 2015) while another study indicated the opposite (Okasha et al., 2016). Additionally, a study with a national sample size of 5745 found an association with medical comorbidities and longer DUP (Chee et al., 2010) whereas another study with a small sample size of 60 reported the reverse conclusion (Mishra et al., 2021).

Other researchers explored associations between diagnosis type or symptoms and DUP. Seven studies that investigated predominant symptoms in relation to DUP used the Positive and Negative Syndrome Scale, finding mixed results. Four showed that a predominance of negative symptoms was associated with longer DUP (Effiong & Albert, 2016; Fresan et al., 2020; Odinka et al., 2014; Okasha et al., 2016) while another study found the opposite (Kini et al., 2015) and two did not find an association (Paruk et al., 2015; Sharifi et al., 2009). Another study reported that patients having auditory hallucinations compared to other positive symptoms had longer DUP (Sadeghieh Ahari et al., 2013). Additionally, a longer DUP was associated with a diagnosis of schizophrenia in two Malawian studies (Kaminga, Dai, et al., 2019; Myaba et al., 2021) and the diagnosis of delusional disorder in an Egyptian study (Okasha et al., 2016). Studies conducted in India and China found no relationship between DUP and diagnosis types (Devi Thakoor et al., 2016; Nallapanemi et al., 2015).

Several studies supported an association between psychological factors and DUP. A study from Serbia demonstrated that shorter DUP was associated with a greater openness to experience, or the presence of a stressor at illness onset (Maric et al., 2016). Chinese patients with the perception that an intimate relationship might be broken due to mental illness had longer DUP (Devi Thakoor et al., 2016). Other factors predictive of a longer DUP were having public self-consciousness (Myaba et al., 2021) and poorer social adjustment (Fresan et al., 2020). Researchers from Malawi found a link between poor insight level and longer DUP (Kaminga, Myaba, et al., 2019) while this was inconclusive in another study from the same country (Myaba et al., 2021).

Help-seeking behaviour had mixed results. Findings from four studies demonstrated an association between seeking a first contact with non-medical professionals with longer DUP (Adeosun et al., 2013; Effiong & Albert, 2016; Gupta et al., 2021; Tomita et al., 2015) whereas other studies found no association between types of first contact and DUP (Kini et al., 2015; Nallapanemi et al., 2015; Sharifi et al., 2009). Spiritual, and traditional causal

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TABLE 2 (Continued)

Reference	Study design	Study aim	Study setting	Country	Income level	Sample size	Reported age	Male, %	Psychiatric diagnoses included	Diagnostic approach
Tomita et al., 2015	Cross-sectional	"[To examine] the role of THPs in treatment pathways for individuals with severe mental illness (SMI) attending mental health services in South Africa."	Psychiatric government hospital in KwaZulu-Natal	South Africa	UMI	57	Age: 42.1% were aged between 21 and 29 years old	64.90%	Schizophrenia Schizoaffective disorder Bipolar disorder Psychosis NOS	N/A

Abbreviations: DUP, duration of untreated psychosis; FEP, first-episode psychosis; LMI, lower middle-income; UMI, upper middle-income; SD, standard deviation; IQR, interquartile range; NOS, not otherwise specified; ICD-10, International Classification of Diseases, 10th edition; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, 4th edition; DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision.

TABLE 3 Main findings.

Reference	Findings	Statistical test	Metric	Reported value[a]
Adeosun et al., 2013	Association between seeking a first contact with a non-physician in the pathway to mental health services and longer DUP	Chi-square test	Chi-square value	$\chi^2 = 32.47$, p value <0.001
Ananthi et al., 2017	No association between age, gender, marital status, education, socio-economic status and place of residence and DUP	Chi-square test	Chi-square value	NS
Ayres et al., 2007	No association between a greater severity of cognitive deficits in FEP subjects and longer DUP	Multiple regression analyses	Regression coefficient	NS
Burns et al., 2010	Association between spiritual/traditional attribution of illness causation and longer DUP Association between previous consultation with a traditional healer with longer DUP	Kruskal-Wallis test Mann–Whitney U	p Value	$p = 0.001$ $p = 0.005$
Burns & Kirkbride, 2012	Association between an increased age at onset and shorter DUP Association between police involvement in the pathway to care and shorter DUP Association between non-black ethnicity compared with black ethnicity and longer DUP Association between a greater level of either one of the two subdomains of social capital, community participation and neighbourhood connectedness, and longer DUP No association between these factors and DUP: • Gender • Income	Cox regression analyses	Hazard ratio	HR = 2.47, 95% CI (1.17–4.85), p value = 0.02 HR = 5.66, 95% CI (1.20–26.80), p value = 0.03 HR = 0.19, 95% CI (0.04–0.81), p value = 0.03 Community participation: HR = 0.46, 95% CI (0.22–0.93, p value = 0.03 Neighbourhood connectedness: HR = 0.19, 95% CI (0.04–0.78), p value = 0.02 HR = 0.27, 95% CI (0.05–1.42), p value = 0.13 HR = 1.41, 95% CI (0.08–17.90), p value = 0.80
Chee et al., 2010	Association between indigenous ethnicity with shorter DUP compared with Malay, Chinese and Indian ethnicities Association between female gender and longer DUP Association between lower educational level and longer DUP Association between comorbidity with medical illness and longer DUP No association between circumstances leading to contact, employment status, care setting during first contact, family history of mental illness, subtype of schizophrenia	ANOVA test	Mean difference of months of DUP	Mean difference between DUP of indigenous ethnicity with Malay ethnicity = −10.21, 95% CI (−17.61 to −2.81), p value = 0.002 Mean difference between DUP of indigenous ethnicity with Chinese ethnicity = −14.28, 95% CI (−22.57 to −5.98), p value <0.001 Mean difference between DUP of indigenous ethnicity with Indian ethnicity = −14.26, 95% CI (−24.86 to −3.66), p value = 0.002 *Similar comparisons were made between each group; Indigenous groups were the only ones that had significantly different DUPs from the other ethnic groups p value <0.001 Mean difference between DUP of people with no formal education with people with a primary

TABLE 3 (Continued)

Reference	Findings	Statistical test	Metric	Reported value[a]
				level = 31.68, 95% CI (20.99–42.36), p value <0.001 Mean difference between DUP of people with no formal education with people with a secondary level = 39.76, 95% CI (29.73–49.79), p value <0.001 Mean difference between DUP of people with no formal education with people with a tertiary level = 42.75, 95% CI (30.16–55.34), p value <0.001 *Similar comparisons were made between each group; the lower education level groups were the only ones that had significantly different DUPs from the other education level groups Mean difference between DUP of people with medical comorbidities and people without medical
Chen et al., 2019	Association between older age and shorter DUP Association between male gender and shorter DUP Association between unmarried status and shorter DUP Association between widowed status and longer DUP Association between a high level of education and shorter DUP No association between these factors and DUP: • Occupation (farmer, others) • Family history of psychosis • Economic family situation	Multivariate survival analysis	Hazard ratio	HR = 1.6, 95% CI (1.4–1.7), p value <0.001 HR = 1.1, 95% CI (1.0–1.2), p value = 0.007 HR = 1.1, 95% CI (1.0–1.2), p value = 0.037 HR = 0.6, 95% CI (0.5–0.8), p value <0.001 HR = 1.8, 95% CI (1.6–2.1), p value <0.001 HR = 1.0, 95% CI (0.9–1.1), p value = 0.551 HR = 1.0, 95% CI (0.9–1.2), p value = 0.665 HR = 1.0, 95% CI (0.9–1.1), p value = 0.465
Davis et al., 2016	Association between amphetamine use and longer DUP Association between Mandrax use and longer DUP No association between these factors and DUP: • Tobacco products • Alcohol beverages • Cannabis • Cocaine • Inhalants • Sedatives or sleeping pills • Hallucinogens • Opioids • Nyaope/sugars • Whoonga	Adjusted Poisson's regression analyses	β Coefficient	β = 0.26, SE = 0.10, z = 2.61, p value = 0.01 β = 0.27, SE = 0.10, z = 2.84, p value <0.01 β = 0.21, SE = 0.12, z = 1.79, p value = 0.07 β = 0.15, SE = 0.13, z = 1.17, p value = 0.24 β = 0.04, SE = 0.09, z = 0.40, p value = 0.69 β = 0.08, SE = 0.11, z = 0.76, p value = 0.45 β = 0.04, SE = 0.11, z = 0.40, p value = 0.69 β = 0.05, SE = 0.09, z = 0.52, p value = 0.60 β = 0.09, SE = 0.12, z = 0.76, p value = 0.44 β = −0.44, SE = 0.58, z = −0.77, p value = 0.44 β = −0.19, SE = 0.29, z = −0.66, p value = 0.51 β = 0.10, SE = 0.11, z = 0.92, p value = 0.36

TABLE 3 (Continued)

Reference	Findings	Statistical test	Metric	Reported value[a]
Devi Thakoor et al., 2016	Mauritius Association between low monthly income and longer DUP Association between decreased awareness of mental illness and related issues from patient and longer DUP Association between decreased awareness of mental illness and related issues from family members and longer DUP China Association between patient' perception that intimate relationships could be broken up due to mental illness and longer DUP Association between family's stigma and longer DUP Both No association between type of diagnosis and DUP	Binary logistic regression analysis	Odds ratio NR	Mauritius OR = 0.14, 95% CI (0.04–0.51), p value <0.01 OR = 0.31, 95% CI (0.1–0.92, p value <0.05 OR = 0.14, 95% CI (0.05–0.43), p value <0.01 China OR = 2.22, 95% CI (1.04–4.72), p value = 0.04 OR = 6.47, 95% CI (1.46–18.08), p value = 0.01 NS
Effiong & Albert, 2016	Association between seeking a first contact with unorthodox healers in the pathway to mental health services and longer DUP Association between negative symptoms of schizophrenia and longer DUP No association between these factors and DUP: • Gender • Educational level • Employment status	Chi-square test	Chi-square value	$\chi^2 = 5.54$, p value = 0.01 $\chi^2 = 4.78$, p value = 0.02 $\chi^2 = 1.89$, p value = 0.17 $\chi^2 = 1.81$, p value = 0.18 $\chi^2 = 1.59$, p value = 0.21
Fresan et al., 2020	Association between female gender and shorter DUP Association between being employed and shorter DUP Association between poorer social adjustment and longer DUP Association between a lesser severity of positive symptom sand longer DUP No association between age and DUP	Multiple linear regressions	Spearman correlation coefficient	$\rho = 0.05$, p value <0.001 $\rho = 0.08$, p value <0.001 $\rho = 0.25$, p value <0.001 $\rho = -0.23$, p value <0.05 $\rho = 0.09$, p value = 0.27
Gupta et al., 2021	Association between seeking first help from non-medical professionals and longer DUP	Mann–Whitney U test	Mann–Whitney U value	Mann–Whitney U value = 1278, p value <0.001
Kaminga, Dai, et al., 2019	Association between a lower level of education and longer DUP Association between poor insight and longer DUP Association between a younger age and longer DUP Association between having at least one parent deceased and longer DUP No association between marital status and DUP	Multivariate logistic regression	adjusted Odds Ratio	aOR =3.94, 95% CI (1.22–12.72), p value = 0.022 aOR =3.57, 95% CI (1.05–12.13), p value = 0.041 aOR = 0.92, 95% CI (0.87–0.97), p value = 0.004 aOR = 5.71, 95% CI (1.77–18.40), p value = 0.004 aOR =0.99, 95% CI (0.97–1.01), p value = 0.349

TABLE 3 (Continued)

Reference	Findings	Statistical test	Metric	Reported value[a]
Kaminga, Myaba, et al., 2019	Association between having a referral from a community-based volunteers or traditional healers and longer DUP Association between a greater severity of negative symptoms and longer DUP Association between a diagnosis of schizophrenia and longer DUP	Multivariable logistic regression analyses	adjusted Odds Ratio	aOR = 4.23, 95% CI (1.57–11.36), p value = 0.004 aOR = 1.15, 95% CI (1.02–1.30), p value = 0.024 aOR = 7.11, 95% CI (2.70–18.71), p value <0.001
Kini et al., 2015	• Association between lower age and shorter DUP • Association between predominant negative symptom or higher PANSS general psychopathology scores and shorter DUP • Association between being married and shorter DUP • Association between higher educational level and shorter DUP • Association between an acute mode of onset with and shorter DUP • No association between these factors and DUP: • Sex • Place of residence • Occupation • Socioeconomic status • Family history of mental illness • Type of first contact	t-Test Fisher's exact test Chi-square test	t-Value Fisher's exact value Chi-square value	$t = -2.731$, df = 43, p value = 0.009 Higher PANSS negative symptom score: $t = 2.473$, df = 43, p value = 0.01 Higher PANSS general psychopathology score: $t = 3.053$, df = 43, p value = 0.004 Fisher's exact value = −6.073, p value = 0.03 $\chi^2 = 5.867$, p value = 0.01 $\chi^2 = 36.450$, p value <0.001 $\chi^2 = 0.180$, p value = 0.75 $\chi^2 = 0.064$, p value = 1 $\chi^2 = 4.397$, p value = 0.20 $\chi^2 = 1.029$, p value = 0.45 $\chi^2 = 1.125$, p value = 0.35 $\chi^2\chi^2 = 2.612$, p value = 0.50
Maric et al., 2016	Association between openness to experience and shorter DUP No association between these factors and DUP: • Neuroticism • Extraversion • Agreeableness • Conscientiousness	Cox regression analysis	β coefficient	$\beta = 0.804$, 95% CI (1.110–4.496), p value = 0.024 $\beta = -0.275$, 95% CI (0.407–1.418), p value = 0.388 $\beta = 0.200$, 95% CI (0.646–2.309), p value = 0.538 $\beta = 0.059$, 95% CI (0.572–1.964), p value = 0.852 $\beta = 0.133$, 95% CI (0.616–2.115), p value = 0.674
Mishra et al., 2021	Association between lower level of family stigma and shorter DUP Association between the presence of a stressor at the time of onset and shorter DUP Association between an acute mode of onset and shorter DUP Association between the presence of medical comorbidities and shorter DUP Association between a greater level of social attainment and shorter DUP No association between age, gender, religion, living situation, educational level, marital status, employment status and monthly family income and DUP	Spearman's Rho test Mann–Whitney test Spearman's Rho test	Spearman's rank correlation coefficient Comparison between median and p value Spearman's rank correlation coefficient NR	rho = 0.27, p value = 0.037 Presence vs absence of a clinically significant antecedent stressor: median 30 vs 184 days, p value = 0.014 Acute vs insidious onset of psychosis: 30 vs 520 days, p value <0.001 Presence vs absence of medical comorbidities: median, 30 vs 150 days, p value = 0.023 rho = −0.38, p value = 0.003 NS

TABLE 3 (Continued)

Reference	Findings	Statistical test	Metric	Reported value[a]
Mo'tamedi et al., 2014	Association between higher family resiliency, especially acquiring social support, and shorter DUP	t-Test	t-value	t = −4.923, p value <0.001
Myaba et al., 2021	Association between being employed and longer DUP Association between having a diagnosis of schizophrenia and longer DUP Association between having negative symptoms and longer DUP Association between having public self-consciousness and longer DUP Association between having greater social quality of life and longer DUP No association between these factors and DUP: • Sex • Age • Marital status • Educational level • Insight level • Attitude towards drugs • Depressive symptoms • Level of functioning • Locus of control	Logistic regression model	adjusted Odds Ratio Unadjusted Odds Ratio (uOR)	aOR = 5.35, 95% CI (1.49–19.20), statistically significant aOR = 10.93, 95% CI (3.08–38.89), statistically significant aOR = 1.31, 95% CI (1.06–1.62), statistically significant aOR = 0.07, 95% CI (0.01–0.55), statistically significant aOR = 1.21, 95% CI (1.01–1.44), statistically significant uOR = 0.97, 95% CI (0.45–2.09) uOR = 1.03, 95% CI (1.00–1.07) uOR = 1.56, 95% CI (0.73–3.33) uOR = 0.67, 95% CI (0.30–1.50) uOR = 0.78, 95% CI (0.27–2.30) uOR = 0.76, 95% CI (0.25–2.30) uOR = 1.2, 95% CI (0.40–3.64) uOR = 1.02, 95% CI (0.98–1.06) uOR = 0.46, 95% CI (0.16–1.30)
Nallapanemi et al., 2015	Association between greater age of onset and shorter DUP Association between patients living in urban areas and shorter DUP No association between these factors and DUP: • Gender • Age • Educational level • Occupation • Religion • Economic status • Living arrangement • Marital status • Family history of mental illness • Diagnosis • Type of first contact • Type of symptoms • History of substance abuse • Type of person who brought patient to consultation	Chi-square test	Chi-square p value	Chi-square p value (df) = 0.02 (6) Chi-square p value (df) = 0.037 (2) p value (df) = 0.143 (2) p value (df) = 0.19 (6) p value (df) = 0.84 (6) p value (df) = 0.086 (8) p value (df) = 0.585 (4) p value (df) = 0.447 (2) p value (df) = 0.232 (2) p value (df) = 0.367 (4) p value (df) = 0.544 (2) p value (df) = 0.773 (4) p value (df) = 0.246 (2) p value (df) = 0.785 (8) p value (df) = 0.244 (2) p value = 0.68
Naqvi et al., 2009	Association between positive symptoms of schizophrenia and shorter DUP No association between these factors and DUP: • Gender • Marital status • Educational level • Premorbid functioning	Chi-square test	Chi-square value	χ^2 = 7.928, df = 1, Sig. 0.005 χ^2 = 0.003, df = 1 χ^2 = 1.157, df = 2 χ^2 = 0.05, df = 2 χ^2 = 0.329, df = 2

(Continues)

TABLE 3 (Continued)

Reference	Findings	Statistical test	Metric	Reported value[a]
Odinka et al., 2014	Association between predominant negative symptoms of schizophrenia and longer DUP	Chi-square test	Chi-square value	$\chi^2 = -0.156$, p value = 0.003
Okasha et al., 2016	Association between being in the age group of 18 to 30 years old and shorter DUP Association between a lower level of education and longer DUP Association between a rural place of residence and longer DUP Association between an insidious mode of onset and longer DUP Association between having an available caregiver and shorter DUP Association between a negative family history of psychiatric disorder and longer DUP Association between an age at onset below 18 years old and shorter DUP Association between being in a low social class and longer DUP Association between being employed and shorter DUP Association between having a diagnosis of delusional disorder and longer DUP An association between predominant negative symptoms with a longer DUP No association between gender and DUP	t-test Chi-square test Mann–Whitney U test	t-value Chi-square value Mann–Whitney U value NR	$t = 7.887$, p value <0.001 $t = 6.337$, p value <0.001 $t = 2.772$, p value = 0.007 $t = 13.729$, p value <0.001 $t = -2.907$, p value = 0.005 $t = 11.146$, p value <0.001 $\chi^2 = 10.064$, $df = 4$, p value = 0.039 $\chi^2 = 6.2$, $df = 2$, p value = 0.03 $\chi^2 = 27$, $df = 2$, p value = 0.001 $\chi^2 = 68.73$, $df = 3$, p value = 0.001 $U = 136.00$, p value = 0.003 NS
Oliveira et al., 2010	Association between individuals living with a relative and shorter DUP No association between these factors and DUP: • Age • Gender • Marital status • Educational level • Economic status • Religion	Multivariable logistic regression analyses	Odds ratio	OR = 2.63, 95% CI (0.98–7.04), p value = 0.05 OR = 0.99, 95% CI (0.97–1.01), p value = 0.39 OR = 1, 95% CI (0.76–2.32), p value = 0.31 NS OR = 1, p value = 0.09 OR = 1, 95% CI (0.74–2.29), p value = 0.35 OR = 1, p value = 0.39

Paruk et al., 2015	Association between a younger age of onset and longer DUP
	No association between these factors and DUP:
	• Types of symptoms
	  Positive
	  Negative
	• General
	• Family history of mental illness
	• Lifetime cannabis use
	• Symptom severity
	• Previous consultation with traditional healer
		Chi-square test
		t-Test
			Pearson correlation coefficient
			t-Test p value
				$r = -0.61$, p value <0.001
				$r = 0.19$
				$r = 0.25$
				$r = 0.02$
				NS
				NS
				NS
				p value = 0.101

TABLE 3 (Continued)

Reference	Findings	Statistical test	Metric	Reported value[a]
Qiu et al., 2017	Association between an insidious mode of onset and longer DUP Association between unemployment and longer DUP No association between these factors and DUP: • Age • Gender • Living arrangement • Partner status • Method of payment to hospital • Educational level • Family member's education • Monthly household income • Family member's job	Multivariate cox regression Spearman rank test	Adjusted hazard ratio Spearman correlation coefficient	aHR = 6.782, 95% CI (4.623–9.949), p value <0.001 aHR = 2.149, 95% CI (1.411–3.274), p value <0.001 $r = -0.074$, p value = 0.278 $r = 0.041$, p value = 0.546 $r = 0.004$, p value = 0.959 $r = 0.179$, p value = 0.019 $r = -0.075$, p value = 0.271 $r = 0.047$, p value = 0.495 $r = 0.006$, p value = 0.930 $r = 0$, p value = 0.998 $r = -0.012$, p value = 0.857
Sadeghieh Ahari et al., 2013	Association between having auditory hallucinations compared with other positive symptoms and longer DUP No association between these factors and DUP: • Visual hallucinations • Persecutory delusion • Harm to self and others	NR	Mean difference of DUP	Mean difference of DUP between people with auditory hallucination, visual hallucination, persecutory delusion and harm to self and others: p value = 0.03 $p = 0.60$ $p = 0.23$ $p = 0.22$ Mean difference of DUP between people with auditory hallucination, visual hallucination, persecutory delusion and harm to self and others: p value = 0.03 $p = 0.60$ $p = 0.23$ $p = 0.22$
Sharifi et al., 2009	Association between an acute mode of onset and shorter DUP Association between a rural place of residence and shorter DUP No association between these factors and DUP: • Gender • Marital status • Educational level • Type of initial symptoms • Type of first contact	Multiple linear regressions	β coefficient Z score Chi-square value NR	$\beta = 1.407$, 95% CI (1.083–1.732), Sig. <0.001 $\beta = 0.646$, 95% CI (0.016–1.275), Sig. 0.045 $Z = -1.87$, p value = 0.065 $Z = -0.82$, NS $\chi^2 = 2.2$, NS $\chi^2 = 7.95$, p value = 0.093 NS
Takizawa et al., 2020	Association between a distance greater than 5 km from the hospital and longer DUP Association between a family history of mental illness and shorter DUP No association between age, sex, marital, status, educational level, employment status, living arrangements, substance use history and hospital types and DUP	Logistic regression analyses	adjusted Odds Ratio	aOR = 2.15, 95% CI (1.02–4.48) aOR = 0.34 NS
Tomita et al., 2015	An association between seeking a first contact with THPs and longer DUP	Adjusted Poisson's regressions analyses	β Coefficient	$\beta = 1.57$, SE = 0.37, $z = 4.22$, p value <0.01

Values were entered in tables as reported by original authors unless specified.

Abbreviations: aHR, adjusted hazard ratio; aOR, adjusted odds ratio; CI, confidence interval; df, degrees of freedom; DUP, duration of untreated psychosis; FEP, first episode psychosis; HR, hazard ratio; NR, not reported; NS, non-significant; OR, odds ratio, PANSS, Positive And Negative Syndrome Scale.

attribution of mental illness was associated with longer DUP in Burns et al. (2010). Lower patient awareness of mental illness was another predictor of longer DUP (Devi Thakoor et al., 2016).

Several additional factors were not found to be linked with DUP at the individual level, including the method of payment for treatment (Qiu et al., 2017), family history of psychosis (Chen et al., 2019), presence of depressive symptoms (Myaba et al., 2021), symptom severity (Paruk et al., 2015) religion (Nallapaneni, Lanka and Paritala, 2015; Mishra et al., 2021; Oliveira et al., 2010), subtypes of schizophrenia (Chee et al., 2010), premorbid functioning (Naqvi et al., 2009) and level of functioning (Myaba et al., 2021). No relationships between neuropsychological factors like locus of control (Myaba et al., 2021), attitude towards drugs (Myaba et al., 2021) and cognitive deficits (Ayres et al., 2007) and DUP were demonstrated.

3.4.2 | Relationship level

Multiple studies revealed a relationship between family-related factors and DUP. For instance, higher family stigma (Devi Thakoor et al., 2016; Mishra et al., 2021), lower family resiliency (Mo'tamedi et al., 2014) and lower family awareness of mental illness (Devi Thakoor et al., 2016) were associated with longer DUP. Nonetheless, a family member's education or occupation did not yield significant results (Qiu et al., 2017). A study from South America reported an association between living with a relative and shorter DUP (Oliveira et al., 2010) while four studies from Asia did not establish that association (Nallapaneni, Lanka and Paritala, 2015; Qiu et al., 2017; Takizawa et al., 2020; Mishra et al., 2021). Furthermore, having no available caregiver (Okasha et al., 2016) and having at least one parent deceased (Kaminga, Myaba, et al., 2019) were statistically associated with longer DUP.

There were mixed results in two Asian studies with markedly different numbers of participants (45 vs. 7252) with regard to marital status. Kini et al. (2015), found a link between married status and shorter DUP, while Chen et al. (2019) showed evidence to the contrary. In contrast, nine studies reported no association (Ananthi et al., 2017; Kaminga, Dai, et al., 2019; Mishra et al., 2021; Myaba et al., 2021; Nallapanemi et al., 2015; Naqvi et al., 2009; Oliveira et al., 2010; Sharifi et al., 2009; Takizawa et al., 2020). Furthermore, one study found no association between having a stable partner and DUP (Qiu et al., 2017) while another study demonstrated that widowed status was associated with a longer DUP (Chen et al., 2019).

3.4.3 | Community level

A study from South Africa with participants with a mean age of 25.8 years old established an association between an earlier meeting with a traditional healer and longer DUP (Burns et al., 2010) although another study from the same country with participants with a mean age of 15.9 years old did not (Paruk et al., 2015). Multiple studies investigated the type of person leading to contact in relation to DUP.

Kaminga, Myaba, et al. (2019) reported a link between a longer DUP and getting a referral from a community-based volunteer or a traditional healer. Alternatively, police involvement in the pathway to care yielded divergent results. One study reported that when police officers played a role in the pathway to care, patients had shorter DUP (Burns & Kirkbride, 2012) although this was not statistically significant in other studies (Chee et al., 2010; Nallapanemi et al., 2015). The type of care setting at first contact was not significant in two studies (Chee et al., 2010; Takizawa et al., 2020). Alternatively, Burns and Kirkbride (2012) demonstrated an association between a greater level of community participation and neighbourhood connectedness, and a longer DUP. Another potential predictor of a longer DUP is higher level of social quality of life (Myaba et al., 2021).

3.4.4 | Societal level

Two related factors were positively associated with a longer DUP, namely lower social attainment (Mishra et al., 2021) and low social class (Okasha et al., 2016). Low family income, which was inconsistently measured across studies, was linked to a longer DUP in Devi Thakoor et al. (2016) although no association was found in 25% of the studies ($n = 8$). Lastly, a greater distance from a house to the hospital was more likely to prolong DUP in Takizawa et al. (2020).

4 | RESULTS OF QUALITY ASSESSMENT

The overall quality of reporting of the cross-sectional studies was good. Each met more than 50% of the AXIS tool criteria for the quality of reporting, namely five of the seven criteria or more, except one study (Okasha et al., 2016) which met three criteria. Overall, studies adequately described their methods, results, and limitations. Nevertheless, 40% of studies ($n = 12$) did not define the target population, only the study population, and 20% of studies ($n = 6$) did not clearly indicate their study objective. The case–control study (Ayres et al., 2007) met three of the five questions of the SIGN methodology because it did not report the participation rate as well as the confidence intervals.

The overall study design quality of the studies was fair. Most of the cross-sectional studies met more than 50% of the criteria in the AXIS tool for the study design quality. Nearly all studies ($n = 23$) met four of the seven criteria, but the remaining studies did not (Ananthi et al., 2017; Devi Thakoor et al., 2016; Naqvi et al., 2009; Paruk et al., 2015; Sadeghieh Ahari et al., 2013). The study design quality was undermined by several factors. More than 85% of studies ($n = 25$) did not provide a sample size justification and did not select a sample frame similar to the target population. Additionally, almost half of the studies ($n = 12$) did not meet the criterion of justified conclusions and discussion because they did not discuss relevant information such as confounders and non-significant results. The case–control study (Ayres et al., 2007) did not meet two of the six criteria due to an inability to confidently assess whether an association

between the exposure and the outcome was real and whether the study results were directly applicable to the targeted patient group.

The risk of bias results of the cross-sectional studies was poor. All of these met less than 50% of the AXIS tool risk of bias criteria. Almost 80% of the studies ($n = 23$) did not mention information about response rate and non-responders and thus did not pass three of the seven criteria from the outset. Furthermore, more than 25% of the studies ($n = 8$) did not demonstrate a selection process ensuring representativeness of the reference population. More than half of the studies ($n = 18$) used a combination of validated and non-validated instruments to measure their risk factors, which was not sufficient. Similarly, most studies ($n = 23$) did not use a validated measure for DUP, while $n = 5$ did. The risk of bias management for the case–control study (Ayres et al., 2007) was excellent as it met all three criteria for that category in the SIGN methodology checklist. Results of the study quality assessment are provided in Supporting Information, Appendix B.

5 | DISCUSSION

5.1 | Interpretation of the results

The main finding is that various factors may be associated with DUP for people with psychosis in LMICs. Twenty-three factors were associated with a longer DUP, 17 had inconsistent results, and 15 were non-significant. Certain results are consistent with earlier studies. For instance, numerous studies from HICs also support that an insidious mode of onset is related to longer DUP (Broussard et al., 2013; Chen et al., 2019; Compton et al., 2008; Hui et al., 2013; Kalla et al., 2002). Moreover, results from the case–control study by Ayres et al. (2007) are aligned with a recent systematic review that reported no overall association between DUP and cognition (Allott et al., 2017). Although this review found mixed results regarding gender, 80% of the studies that investigated that factor ($n = 13$) did not find an association with DUP, consistent with Cascio et al. (2012). Boonstra et al. (2012) found a link between negative symptoms and a longer DUP which is aligned with the results of 60% of the studies that investigated it in this review ($n = 7$). A systematic review on ethnicity and DUP highlighted that three studies found an association between black ethnicity and shorter DUP (Anderson et al., 2013) which echoes the finding of an included study (Burns & Kirkbride, 2012).

On another note, we found different directions of association and potential determinants of DUP across continents and LMICs. These conflicting results likely reflect the limitations of evidence, but may also reflect the influence of culture on potential factors related to DUP. This hypothesis was highlighted in Devi Thakoor et al. (2016) who compared two LMICs using the same methods and obtained divergent factors for each country. Another study that compared DUP correlates of two HICs also reported this (Kalla et al., 2002) although research on this is scarce. Thus, more investigations comparing potential factors influencing DUP between cultures is needed. These studies could take the form of comparison between LMICS, between HICS

and LMICs or between ethnic subgroups. This may help to better understand the reasons for the variations between studies.

Another key finding is that the methodological quality of the studies substantially limits the conclusions and recommendations of this review. Almost all 23 factors ($n = 20$) associated with DUP were supported by a single study, suggesting that they were insufficiently studied across LMICs. There were exceptions however, namely mode of onset, family stigma and ethnicity were supported by five or fewer studies. In comparison, factors with contradictory results were supported by a significantly higher number of studies. Examples of these factors are educational level ($n = 15$) and first contact with non-medical providers ($n = 7$). Almost half of the studies ($n = 13$) had small sample sizes, which may have led to type 2 errors (Downes et al., 2016). Many studies did not control for confounding factors which most likely skewed the result of their associations (Downes et al., 2016). Furthermore, our sample was almost entirely comprised of cross-sectional studies, which makes it impossible to determine causal relationships (Setia, 2016).

There was a low level of representativeness and therefore generalizability due to the use of convenience sampling, heterogenous illness characteristics, and concerns of non-response bias (Downes et al., 2016). To add to this, these studies were conducted within the formal healthcare systems of the varying nations, meaning that harder-to-reach patients or those using informal health services may not have been included, likely representing a significant number of people in LMICs (Kumah, 2022). Moreover, the use of non-validated instruments to measure factors and DUP compromised the validity, reliability, and comparability of the results (Downes et al., 2016). The reliance on retrospective data collection and self-reports of DUP introduced a risk of recall and desirability biases (Devi Thakoor et al., 2016). These limitations should inform future actions. Funding, development, and replication of higher-quality studies across LMICs is strongly recommended to provide relevant conclusions, policy recommendations and to help understand inconsistencies between studies. To achieve this, the use of reliable and validated instruments to measure factors and the determination of a consensus for the definition of DUP is imperative.

A secondary finding of this review is that a SEM is a relevant framework for healthcare professionals, researchers, and decision-makers to conceptualise factors, map findings, and highlight gaps in the literature. As an illustration, studies were represented at all levels of the SEM, although nearly all studies ($n = 29$) investigated individual-level factors and fewer studies explored other levels. It is worth mentioning that the factors at the societal levels could be debated, but including these four factors here appeared reasonable as they were all closely related to social constructs or healthcare infrastructure. Further research to uncover more potential determinants of DUP at these levels is essential. For instance, future research comparing how macro-level factors may influence DUP could enable the subsequent development and implementation of interventions to target societal factors that are known to perpetuate disparities in access to care for people living in poorer resource settings (Burns & Kirkbride, 2012).

Three selected results encompassing different levels of the SEM will be highlighted as they embody important aspects of LMICs and could be potential targets to DUP reduction if more results are compiled over time. The first example is taken from Davis et al. (2016) who demonstrated an association between a longer DUP and the use of amphetamines or Mandrax. Substance use disorders are prevalent public health problems in LMICs (Sarkar et al., 2021) and are projected to increase in coming years (Nadkarni et al., 2022). Given that substance use and psychosis are common co-occurring disorders (Davis et al., 2016), brief psychosocial interventions to target substance use in LMICs (WHO, 2016) may be useful potential strategies for DUP reduction. The second example comes from two studies that found a link between family stigma and longer DUP (Devi Thakoor et al., 2016; Mishra et al., 2021). This is consistent with previous evidence that stigma towards people with mental illnesses may delay mental health treatment (Wainberg et al., 2017). Stigma is an important issue in the global mental health community as it is a significant contributing factor to lack of access to mental health services (Wainberg et al., 2017). The development of promising methods such as contact-based interventions and educational campaigns (Patel et al., 2014) may be interesting future avenues to reduce DUP for people with psychosis in LMICs. The last example comes from Kaminga et al. (2019) who reported a relationship between referral from community-based volunteers or traditional healers and longer DUP. This reflects an important reality and challenge of LMICs which is the presence of medical pluralism (Orr & Bindi, 2017). Many people in LMICs will seek out traditional healers for their mental health needs (Orr & Bindi, 2017). A collaborative model with traditional healers may be an interesting solution to improve access (Gureje et al., 2020) for people with psychosis in LMICs.

At present, too little robust data on these and other potential factors influencing DUP are available, as this review indicates. As the understanding of the factors and their relationship to each other becomes clearer, it may be possible to develop and implement targeted interventions. It is unlikely that a single intervention would be effective in reducing DUP in LMICs (Malla, 2022). The SEM would allow for a synergistic and multisectoral approach to this endeavour. Future concerted and sustained efforts to reduce DUP at all levels of SEM may in turn improve EIS, clinical outcomes, and overall well-being of people with psychosis in LMICs.

5.2 | Strengths and limitations of the review

This systematic review has several limitations. The sample overrepresents certain regions of the world while underrepresenting low-income countries. The investigation of more specific world regions or income levels might have changed the findings. In the same vein, conclusions about potential determinants of DUP might have been more accurate had this review investigated a more specific study population (e.g. non-affective psychoses only) (Large et al., 2008). Moreover, this review included studies of lower methodological quality which may

have reduced its own quality (Boland et al., 2017, p. 122). Due to resource and time constraints, only studies available in English and published in peer-reviewed journals were included, which exposed this review to language and publication bias (Boland et al., 2017, p. 53). Additionally, we may have unintentionally omitted relevant studies that could have altered the results. The reliability of the research process might have been affected by this review being conducted by a single individual although guidance was received at every step (Boland et al., 2017, p. 18). This review also has its share of strengths. An explicit methodology was followed, and a rigorous quality appraisal was performed (Owens, 2021). Additionally, the search of six different databases established an appropriate degree of comprehensiveness which is indicative of current evidence on this subject (Boland et al., 2017).

6 | CONCLUSION

In conclusion, this review found many potential determinants of DUP for people with psychosis in LMICs. These factors range from mode of onset and substance use to family stigma and causal attribution of mental illness. However, factors such as gender, marital status, educational level, medical comorbidities, or family history of mental illness led to conflicting results. The findings should be viewed with caution given the methods employed by the studies. This review draws attention to the urgent need for higher quality research on this subject in LMICs. The results of this review are a starting point, and the SEM is a useful framework to consider for healthcare professionals, researchers, and policymakers. It is the ethical duty of the global mental health community to identify factors that may influence DUP to subsequently implement targeted efforts to reduce it, which in turn could facilitate access to EIS and improve the prognosis of those affected by psychosis in LMICs.

CONFLICT OF INTEREST STATEMENT
The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT
Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.