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Timeliness of diagnosis of breast and cervical cancers and associated factors in low- and middle-income countries: A scoping review

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Abstract

Objectives: Addressing the barriers to early breast and cervical cancer diagnosis in low- and middle-income countries (LMICs) requires a sound understanding and accurate assessment of diagnostic timeliness. This review aimed to map the current evidence on the time to breast and cervical cancer diagnosis and associated factors in LMICs.

Design: Scoping review

Sources: MEDLINE (via PubMed), Cochrane Library, Scopus and CINAHL.

Eligibility criteria: Studies describing the time to diagnosis and associated factors in the context of breast and cervical cancer in LMICs published from 1 January 2010 to 20 May 2021.

Study selection and data synthesis: Two reviewers independently screened all abstracts and full-texts using predefined inclusion criteria. The review was reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). Evidence was narratively synthesised using predefined themes.

Results: Twenty-six studies conducted across 24 LMICs were included in the review, most (24/26) of which focused on breast cancer. Studies varied considerably in their conceptualisation and assessment of diagnostic time, events, intervals and delays, with a minority of the studies reporting the use of validated methods and tools. Patient-related intervals and delays were more frequently evaluated and reported than provider- and health system-related intervals and delays. Across studies, there were variations in the estimated lengths of the appraisal, help-seeking, patient and diagnostic intervals for both cancers and the factors associated with them.

Conclusions: Despite the significant burden of breast and cervical cancer in LMICs, there is limited information on the timeliness of diagnosis of these cancers. Major limitations included variations in conceptualization and assessment of diagnostic events and intervals. These underscore the need for the use of validated and standardised tools, to improve accuracy and translation of findings to better inform interventions for addressing diagnostic delays in LMICs.

Keywords: Cancer, breast, cervical, diagnosis, time, delay, LMICs.

Strengths and limitations of this study

- This scoping review was conducted in accordance with an enhanced evidence synthesis methodology and reported using standard reporting guidelines.
- This review updates the evidence base relating to the nature of the time to diagnosis of breast and cervical cancer and associated factors in LMICs.
- Literature searches were comprehensive, covering both peer-reviewed and relevant grey literature.
- Due to the broad nature of the topic, it is possible that not all relevant evidence sources were identified by the search strategy, however comprehensive.

Introduction

Breast and cervical cancer constitute a growing public health burden globally.[1,2] The incidence, morbidity and mortality burdens of both cancers are disproportionately high among women in low- and middle-income countries (LMICs).[2,3] Breast cancer is most commonly occurring cancer and the leading cause of cancer deaths among women worldwide, with an age-standardised incidence rate (ASIR) of 31 per 100,000 women in LMICs.[4,5] Cervical cancer is the fourth most common cancer among women, with an ASIR of 16 per 100,000 women.[2] Cancer survival rates are low in LMICs, the major attributable factors of which include late-stage diagnosis and suboptimal access to quality healthcare.[1,6]

Timely diagnosis is critical for optimising patients' navigation of the pathway from cancer symptom awareness to treatment, and improving survival.[7-9] However, the majority of breast and cervical cancers are diagnosed at a late stage when treatment is often less effective and more expensive.[10-12] In LMICs, barriers to timely cancer diagnosis include individual and disease-related factors, as well as health system constraints.[13-15] Individual-level factors may include demographic, behavioural and psychosocial factors, in addition to those associated with underlying sociocultural barriers to timely diagnosis, such as lay beliefs that cancers are contagious and that they are inevitably fatal.[16,17] Disease-related factors include those related to the site, size, clinical manifestation and growth of tumours.[15] Health system factors in LMICs include health policy, access, quality and service delivery barriers, such as inadequate diagnostic capacity, weak referral systems, sup-optimal access to treatment and insufficient human resources.[6,18,19] While there is substantial evidence on the association between these factors and cancer diagnostic delays, not much is known about the extent to which they influence time to diagnosis and diagnostic intervals, particularly in LMICs.

Various approaches and tools have been used for assessing time to diagnosis and diagnostic intervals, while their use in LMICs has grown over the years.[17,19,20] However, the tools commonly used often ignore existing models of patient behaviour, and are poorly or inadequately validated.[15,21,22] To bolster better conceptual understanding of patient's navigation, Walter, Scott and colleagues proposed a Model of Pathways to Treatment that describes the distinct phases of cancer patients' pathways from symptom awareness to diagnosis and treatment.[15,22] To aid the development of valid tools for measuring time to

cancer diagnosis, the Aarhus checklist has been proposed for guiding the design and reporting of early cancer diagnosis studies.[23]

A good understanding of the timeliness of breast or cervical cancer diagnosis, the diagnostic intervals and associated factors is important to guide interventions for addressing the growing public health problem of diagnostic delays in LMICs.[24-26] In 2017, the World Health Organization (WHO) published the *WHO Guide to Cancer Early Diagnosis* to provide a global standard for addressing barriers that may impede timely cancer diagnosis and treatment.[27,28] Addressing these barriers requires an accurate assessment and understanding of the time to diagnosis, related intervals and the multidimensional factors associated with the timeliness of diagnosis.[28]

This review aims to provide an updated and comprehensive synthesis of the evidence on the time to diagnosis and its associated factors, in the context of symptomatic breast and cervical cancer diagnosis in LMICs. It contributes a systematically organised evidence summary for health policy makers, cancer programme managers, oncologists and other cancer care providers for guiding policy and practice decision making. In addition, the findings will be useful for informing the design of interventions and strategies for addressing existing breast and cervical cancer diagnostic delays in resource-limited settings, while identifying gaps for future research efforts at measuring and appraising diagnostic timeliness.

Methods and analysis

Conceptual framework

This scoping review used the Model of Pathways to Treatment framework proposed by Walter, Scott and colleagues[15,22] to map the identified evidence on the timeliness, time intervals and associated factors of breast and cervical cancer diagnosis. The framework specifies the essential events, processes, and time intervals that may occur in the period prior to diagnosis and the start of medical treatment and identifies the factors that may influence each interval.

Study design

The design of this study was guided by Arksey and O'Malley's scoping review methodology[29], as enhanced by Levac and colleagues.[30] The enhanced framework involves six stages for

undertaking a scoping review: (1) identifying the research question; (2) identifying the relevant studies (defining the inclusion and exclusion criteria); (3) searching and selecting the evidence; (4) charting the evidence; (5) collating, summarising and reporting the evidence and (6) consultation with relevant stakeholders. Findings of the review are reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).[31] The full details of the study design have been published elsewhere.[32]

Data sources

The literature search was guided by the review objectives and the population, concept and content (PCC) criteria. The search strategy was developed with guidance from a health sciences subject librarian and applied in accordance with the Peer Review of Electronic Search Strategies (PRESS) guidelines.[33] The search strategy was pre-tested prior to the actual search. Search terms and free-text words were combined using the Boolean operators 'AND' and 'OR', such as (breast OR cervical OR cervix, cancer OR neoplasm OR malignancy OR tumours) AND (diagnosis OR diagnostic OR detection OR discovery) AND (early OR timely OR time OR late OR delay). Search terms included the use of controlled descriptors (such as MeSH terms, CINAHL and headings) and their synonyms. In order to restrict search to LMICs, a location-filter containing all countries currently classified as part of LMICs and synonymous geographical, regional and economic categorisations were incorporated. The search strategy, as applied to the various literature databases, is outlined in the appendix. More details of the search strategy are described in the review protocol published elsewhere.[32]

Between 17 October 2020 and 20 May 2021, a comprehensive literature search was conducted on the following electronic databases: MEDLINE (via PubMed), Cochrane Library (including the Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effects (DARE)), Scopus, CINAHL and the International Clinical Trials Registry Platform (ICTRP). Additionally, relevant grey literature sources were searched for potentially eligible articles, including the publication database of the WHO's International Agency for Research on Cancer (IARC), the Cancer Atlas of the Union for International Cancer Control (UICC) and the Global Cancer Project Map. A hand-search of reference lists of included studies was conducted. For recency, only articles published from 1 January 2010 to the last

date of search (20 May 2021) were considered eligible. No language restrictions were applied, and any potentially eligible article in a language other than English would have been translated using a Web-based translation tool.[34]

Eligibility criteria

The inclusion criteria were defined using the using the PCC (Population, Concept and Contexts) framework, proposed by Peters and colleagues.[35] Eligible population Included women with breast or cervical cancer and healthcare providers living in LMIC contexts. The concepts of interest were time to diagnosis and diagnostic intervals of breast and/or cervical cancers. To be considered eligible for inclusion, studies need to have measured time to diagnosis in the context of breast and/or cervical cancer diagnosis in LMICs, using specific methods, tools or strategies; and/or assessed diagnostic intervals of breast and/or cervical cancers in LMIC settings; whether or not they evaluated the factors associated with diagnostic time or time intervals. The definition of LMICs was based on the World Bank's current classification using per capita gross national income.[36] Multinational literature involving LMIC and non-LMIC countries and meeting inclusion criteria were eligible for inclusion, except where country-specific information could not be abstracted. Similarly, articles involving multiple cancer types were eligible for inclusion, except in case where the relevant cancer type-specific information could not be abstracted.

Articles focused solely or mainly on theoretical and conceptual understanding of timeliness of breast or cervical cancer diagnosis without assessing the timeliness of diagnosis in specific LMIC contexts were excluded, as were those assessing cancer patient pathways that are not related to diagnostic time and intervals. Studies focused primarily on screening of asymptomatic individuals were also excluded. Study design eligibility included randomised trials, non-randomised trials, and observational studies, with or without controls. However, inclusion was limited to primary studies; while systematic, scoping reviews and other forms of aggregated evidence were excluded.

Study selection

The review process consisted of two levels of screening: a title and abstract screening to identify potentially eligible publications and review of full-texts to select those to be included in the review based on pre-defined inclusion/exclusion criteria. For the first level of screening,

two reviewers (CAN and PK) independently screened the titles and abstracts of all retrieved records from the search output. Articles considered relevant by either or both of the reviewers were included in the full-text assessment. Following the removal of duplicates, full texts of remaining studies were retrieved. In the second step, the two reviewers (CAN and EE) independently assessed the full-texts to determine if they met the inclusion/exclusion criteria. Disagreements in eligibility assessment were resolved through consensus between.

Data extraction

Two reviewers (CAN and EE) independently abstracted and recorded all relevant data using a standardised data abstraction tool, adapted from the framework proposed by Carlos and colleagues.[37] The tool includes four domains: (1) study identification details (article title; journal title; authors; country of the study; language; publication year; host institution of the study); (2) methodological characteristics (study design; study objective or research question or hypothesis; sample characteristics (e.g. sample size; sex; age, ethnicity; groups and controls; follow-up duration; validation of measures; statistical analyses); (3) main findings, and (4) conclusions. Study eligibility were re-verified at the start of/during data extraction. Any discrepancies in the abstracted data between the two reviewers were resolved by discussion. CAN combined the two spreadsheets of abstracted data for analysis. JM and FMW reviewed analysed data for accuracy and consistency with protocol.

Data analysis

The evidence identified was synthesised and reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guidelines.[31] Findings were narratively summarised and reported based on themes that emerged from the charted evidence. Where applicable, quantitative evidence was aggregated using summary statistics. Time to diagnosis and diagnostic intervals were described based on the Model of Pathways to Treatment proposed.[15,22] The Model also allowed for the assessment of patient-; health care provider and health system-; and disease-related factors that could influence diagnostic timeliness.

Results

Search results

A total of 10591 records were identified from literature database searches. After the removal of duplicates, there were 9347 unique records. These were screened by their titles and abstracts, following which 9174 clearly ineligible publications were excluded. The full texts of the remaining 173 potentially eligible studies were reviewed against predefined inclusion and exclusion criteria; 26 of which were included in the review, while 147 were excluded for various reasons. Figure 1 presents the PRISMA flow chart of the study selection process and reasons for exclusion.

Characteristics of included studies

Table 1 describes the characteristics of included studies. Most (24/26) of the studies were focused on breast cancer, with only two focusing on cervical cancer. The studies were published between 2011 and 2020, conducted across 24 LMICs across the regions of Africa, Europe, Latin America, Middle-East Asia and South-East Asia. The following countries (number of studies) were represented: Bulgaria (1), Colombia (1), Ethiopia (3), Haiti (1), India (2), Iran (1), Libya (1), Malaysia (2), Mali (1), Mexico (1), Namibia (1), Nepal (1), Nigeria (3), Peru (1), Pakistan (3), Russia (1), Rwanda (1), Serbia (1), South Africa (2), Sudan (1), Thailand (1), Turkey (1), Uganda (1) and Zambia (1). Figure 2 illustrates the geographical distribution of included studies.

Nearly all (24/26) of the studies included were quantitative in design, including cross-sectional (21), cohort-type longitudinal (2) and case control (1) studies. One study had a mixed-methods cross-sectional design, while another was a qualitative study. Most (24/26) of studies primarily focused on breast cancer, whereas the remaining two focused on cervical cancer. Participants were mostly adult women with newly diagnosed breast or cervical cancer. All of the studies were conducted within healthcare settings, of which 18 were urban, 3 were rural and 5 were both rural and urban.

Methods of diagnosis

In the majority (20/26) of the studies, diagnosis was defined based on pathological or histological confirmation.[7,18,19,38-54] The rest of the studies relied on clinical assessment as a diagnostic modality.[55-60]

Methods/tools used for assessing diagnostic timeliness and intervals

Table 1 describes the various methods and tools used for assessing diagnostic timeliness and intervals across studies. In most (23/26) of the studies, diagnostic events, timeliness and intervals were assessed using questionnaires or interviews that relied on participants' recall[7,18,19,38-56,59], seven of which combined patients' reports obtained from questionnaires or interviews with diagnostic information derived from facility-based medical records.[40,43,50,52-54,59] Three studies assessed diagnostic events and intervals using medical records alone, without questionnaires or interviews.[38,57,60]

To define diagnostic timeliness and intervals, 14 studies relied on authors' definition[18,38-41,44,45,49,52-54,57,59] while four studies adopted definitions as used in previous studies.[47,50,51,56] Four studies adopted the Model of Pathways to Treatment[7,19,43,55], three studies adopted the Aarhus Statemen[42,46,55], while two studies adopted the Anderson Model.[48,58]

The studies varied considerably in the use of common terminologies relating to diagnostic events and intervals. Only two studies defined the appraisal interval (time between discovery of symptoms and perceiving reasons to seek help) and help-seeking interval (time between symptom recognition and first HCP consultation) as separate intervals as defined by the Model of Pathways to Treatment.[7,55] Most other studies combined both appraisal and help-seeking intervals as a single interval (time between symptom recognition and first HCP visit/consultation). Varying terminologies were used across studies to refer to this single interval, including help-seeking interval[43,55], patient [-related] interval (also patient delay or patient time)[7,18,42,44-47,49-54,58,59] , time to action[56], pre-contact time[41], consultation time[40,48] and presentation interval.[60]

Diagnostic interval was defined in various ways across studies as: the time commencing from the point of symptom detection to diagnosis[40,48,57], time from first clinical consultation to

diagnosis[7,18,19,41,42,44,47,49,50,52,54] and time from first presentation at a diagnostic centre to diagnosis.[46] Notably, the diagnostic interval was also referred to as primary care interval (time between first HCP visit and first specialist visit).[44,46,55] Less than half (10/26) of the studies defined total diagnostic interval (time from symptom detection to diagnosis).[19,38-41,44,47,48,50,55]

Similarly, the thresholds for defining intervals as delayed also varied across studies. Notably, a patient interval was considered as delayed if longer than two months in one study[44], whereas two other studies considered it as delayed if longer than three months.[49,53] Likewise, a diagnostic interval was considered as delayed if longer than seven days[44] but considered as delayed if longer than one month[53] and longer than two months[49] in other studies.

Table 1: Characteristics of included studies

Study ID	Cancer site	Study design	Country	Study setting	Participant number and characteristics	Methods/tools used for assessing diagnostic timeliness and intervals
Agodirin 2020	Breast	Cross-sectional	Nigeria	Health facility; urban	420 women with newly diagnosed breast cancer Age range: 24-95 years	**Data collection tool:** structured questionnaire **Definition of diagnostic events and intervals:** adapted from the Aarhus statement and the Model of Pathways to Treatment **Diagnosis:** based on specialist evaluation **Appraisal interval:** time (days) from the detection of first breast symptom to first disclosure (e.g. to partners, family and friends) **Help-seeking interval:** time (days) between symptom detection and first HCP visit **Primary care interval:** time (days) between first HCP visit and first specialist visit **Specialist care interval:** time (days) between symptom detection and first specialist visit
Begoihn 2019	Cervix	Retrospective cohort	Ethiopia	Health facility; rural and urban	1575 women with primary diagnosis of invasive cervical cancer Mean age: 49 ±11.6 years HIV+: 135/8.6%	**Data collection tool:** patients' medical records **Definition of diagnostic events and intervals:** authors **Diagnosis:** based on histology **Patient interval:** time (weeks) between patient reported onset of symptoms and pathological diagnosis
Dianatinasab 2016	Breast	Cross-sectional	Iran	Health facility; rural and urban	505 women with newly diagnosed breast cancer Mean age: 47.8 ±10.65 years	**Data collection tool:** Questionnaire (pre-tested and revised with a pilot study) **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology **Delay time:** interval (days) between the date that patient noticed the first breast cancer symptom until the date that pathology report was issued
Dye 2012	Breast	Mixed methods observational	Ethiopia	Health facility; urban	55 women diagnosed with breast cancer	**Data collection tool:** Structured questionnaire and qualitative interviews

					Age: <50 years	**Diagnostic events and intervals definition:** adapted from previous study **Diagnosis:** based on clinical assessment **Time to action:** time (years) between symptom detection and first HCP visit
Ermiah 2012	Breast	Cross-sectional	Libya	Health facility; urban	200 women with breast cancer Median age: 45.4 (22–75) years	**Data collection tool:** Questionnaire and patients' medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology **Consultation time:** time (months) from first symptom to first HCP visit. **Diagnostic time:** time (months) from the date of the first symptoms to the date of final breast cancer diagnosis
Foerster 2020	Breast	Cohort study	Multi-country: Nigeria Namibia Uganda Zambia	Health facility; rural and urban	1429 women diagnosed with breast cancer Mean age: 50.1 years	**Data collection tool:** ABC-DO study questionnaire **Diagnostic events and intervals definition:** authors **Diagnosis:** based on ENCR guidelines (prioritising histology. If histological confirmation was not available, diagnosis was based on clinical history or imaging). **Pre-contact interval:** time (months) between date of symptom discovery to first HCP visit **Post-contact interval:** time (months) between first HCP visit to definitive diagnosis) **Total diagnostic interval:** pre-contact interval + post-contact interval
Gebremariam 2019	Breast	Cross-sectional	Ethiopia	Health facilities; urban	441 women with newly diagnosed breast cancer Mean age: 44.4 ±12.2 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the Aarhus statement **Diagnosis:** based on histology **Patient interval:** time (days) from recognition of first symptom to date of first clinical presentation/consultation

						Diagnostic interval: time (days) from first clinical consultation to the date of diagnosis
Grosse Frie 2019	Breast	Cross-sectional	Mali	Health facility; urban	124 women with breast-related symptoms Age ranger: 16-80 years	**Data collection tool:** Questionnaire and health/pathological records **Diagnostic events and intervals definition:** adapted from the Model of Pathways to Treatment) **Diagnosis:** based on histology **Help-seeking interval:** time (days) from date of first symptom recognition to date of first HCP visit. **Diagnostic interval:** time (days) from first HCP visit to date of receiving pathology results
Gyenwali 2014	Cervix	Cross-sectional	Nepal	Health facility; urban	110 women diagnosed with cervical cancer Mean age: 52.72 ±10.6 years	**Data collection tool:** Questionnaire (pre-tested) **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology **Patient delay:** time (days) between symptom awareness and first HCP visit (≥60 days was defined as long) **HCP delay:** time (days) between first HCP visit and final referral by HCP to the cancer diagnostic centre (>7days was defined as long) **Referral delay**: time (days) between the date of final referral to diagnostic centre and first appointment at the cervical cancer diagnostic centre (>7day was referred as long). **Diagnostic waiting time**: time (days) for all relevant investigations of symptoms in the diagnostic centre (>7 days was defined long waiting time). **Total diagnostic delay:** patient delay + HCP delay + referral delay + diagnostic waiting time (>90 days was referred as long)
Jassem 2014	Breast	Cross-secttional	Multi-country: Bulgaria, India, Russia, Serbia and Turkey	Health facility; rural and urban	6588 women with breast cancer Age: majority were aged 40–69 years	**Data collection tool:** Questionnaires administered during nation-wide surveys **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology

						Patient-related delay time: time (weeks) between the onset of first symptoms and the first medical visit. **System-related delay time:** time (weeks) between the first medical visit and the start of therapy. **Total delay time:** sum of the patient-related delay and system-related delay time
Khaliq 2019	Breast	Cross-sectional	Pakistan	Health facility; urban	200 women diagnosed with breast cancer Mean age: 45 ±14.25 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the Aarhus Statement **Diagnosis:** based on histology **Patient interval:** time (days) between experiencing signs and symptoms and seeking first care. **Referral interval:** time (days) between presentation and referral to a diagnostic centre; **Diagnostic interval:** time (days) from presentation at a diagnostic centre to receipt of a diagnosis of breast cancer
Khokher 2016	Breast	Cross-sectional	Pakistan	Health facility; urban	261 2omen with breast cancer Mean age: 46.8±13 years	**Data collection tool:** medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on clinical assessment **Diagnostic delay:** time (years) between symptom detection and first HCP visit
Martínez-Pérez 2020	Breast	Cross-sectional study	Colombia	Health facility; urban	242 women diagnosed with breast cancer Age: >18 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from a previously validated tool) **Diagnosis:** based on histology **Patient interval:** time (days) between detection of the first sign/symptom and the first medical consultation. **Provider interval:** time (days) between the first medical consultation and diagnosis by histopathological diagnosis. **Total interval:** time (days) from detection of the first sign/symptom till histopathological diagnosis

Moodley 2016	Breast	Qualitative (In depth interviews)	South Africa	Health facility; urban	20 newly diagnosed breast cancer patients	**Data collection tool:** Interview questions **Diagnostic events and intervals definition:** adapted from the Model of Pathways to Treatment) **Diagnosis:** based on histology **Appraisal interval:** time (days) between discovery of breast symptoms and perceiving reasons to seek help **Help-seeking interval:** time (days) between perceiving reasons to seek help and presentation to the first healthcare provider **Diagnostic interval:** time (days) between assessment by the first health provider and diagnosis at the tertiary hospital.
Moodley 2018	Breast	Cross-sectional	South Africa	Health facility; urban	201 newly diagnosed breast cancer patients Median age: 54 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the Model of Pathways to Treatment) **Diagnosis:** based on histology **Patient interval:** time (days) between date of first breast change to date of first health care provider consultation **Diagnostic interval:** time (days) between the first health care provider visit and the date of diagnosis **Pre-treatment interval:** time (days) between date of diagnosis and the date of scheduled treatment **Total time:** time (days) between a woman noticing the first breast change and the date of scheduled treatment
Mujar 2017	Breast	Cross-sectional	Malaysia	Health facility; urban	340 newly diagnosed women with breast Median age: 53 (23 to 74) years	**Data collection tool:** Questionnaires and medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** method not specified **Patient interval:** time (months) from symptom discovery to first presentation at a primary care facility **Diagnosis interval:** time (months) taken from first presentation to diagnosis

Norsa'adah 2011	Breast	Cross-sectional	Malaysia	Health facility; urban	328 women with histological diagnosis of BC Mean age: 47.9 ±9.4 years.	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the Andersen Model) **Diagnosis:** based on histology **Consultation time:** time (months) from symptom recognition to first general practitioner visit **The time to diagnosis:** time (months) from the date of the recognition of symptoms to the date of final diagnosis **Diagnostic delay:** more than 6 months from the recognition of symptoms to the histological diagnosis
Olarewaju 2019	Breast	Cross-sectional	Nigeria	Health facility; urban	275 women with breast cancer Mean age: 49± 11.9 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology **Patient interval:** time (months) between symptom detection and HCP visit; delay was considered to be a time lag of greater than 3 months **Time to diagnosis:** time (months) from first HCP visit to a definitive diagnosis; delay was defined as an interval exceeding 2 months
Pace 2015	Breast	Cross-sectional	Rwanda	Health facility; rural	144 women with BC complaints Median age: 49 years	**Data collection tool:** Questionnaires and medical records **Diagnostic events and intervals definition:** adapted from a previous study **Diagnosis:** based on histology **Patient delay:** time (months) between symptom detection and first HCP visit. **System delay:** time (months) between the first HCP visit and definitive diagnosis
Poum 2014	Breast	Cross-sectional	Thailand	Health facility; urban	180 women with newly diagnosed invasive breast cancer Mean age: 50±11 years	**Data collection tool:** Questionnaire and medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology

						Patient delay: time (days) from first reported symptoms to first consultation with a health provider **Doctor delay:** time (days) from first consultation with a health provider to diagnosis of breast cancer
Romanoff 2017	Breast	Cross-sectional	Peru	Health facility; urban	113 women with breast cancer Mean age: 54± 10.8 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from a previously validated tool) and medical records **Patient-attributable delay:** time (days) from symptom onset to first medical visit **Diagnosis:** based on histology **Health system delay:** time (days) from initial medical consultation at any facility to initiation of treatment
Salih 2016	Breast	Cross sectional	Sudan	Health facility; urban	63 women with breast cancer Mean age: 46.89 ±14.99 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the Andersen model **Diagnosis:** based on clinical assessment **Patient delay:** time (months) between symptom recognition and first HCP visit/consultation.
Shamsi 2020	Breast	Cross-sectional	Pakistan	Health facility; rural and urban	499 women diagnosed with breast cancer Mean age: 48.0±12.3 years	**Data collection tool:** Questionnaire (pre-tested) and patients' medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on clinical assessment and imaging **Patient delay:** time (months) between the appearances of first symptoms of breast cancer and the date of initial consultation for diagnostic mammography, ultrasonography, or medical advice.
Sharma 2012	Breast	Case-control	Haiti	Health facility; rural	90 women with breast cancer symptoms Median age: 45 (39–53) years	**Data collection tool:** Patients' medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on clinical assessment

						Presentation interval: time (weeks) from discovery of first breast cancer sign or symptom to initial presentation to a healthcare provider; delay defined as an interval of 12 weeks or greater
Shreyamsa 2020	Breast	Cross-sectional	India	Health facility; rural	435 mostly persons (mostly women but including 3 men) diagnosed with breast cancer Age: majority >40 years	**Data collection tool:** Questionnaire and patients' records **Diagnostic events and intervals definition:** authors **Patient interval:** time (months) between noticing symptoms and first consult with a medical doctor; patient delay is an interval of >3 months **Provider interval:** time (month) between first consultation and starting definitive treatment; provider delay is an interval >1 month
Unger-Saldaña 2018	Breast	Cross-sectional	Mexico	Health facility; urban	886 newly referred women with probable breast cancer Mean age: 50.9 ±13.17 years	**Data collection tool:** Questionnaire and patients' records **Diagnostic events and intervals definition:** adapted from the Aarhus statement **Diagnosis:** based on histology **Patient interval:** time (months) between the identification of the condition and the first medical consultation **Diagnosis interval:** time (months) from the first medical consultation to definitive diagnosis

Aarhus statement (AS); HCP (Health care provider); Model of pathways to treatment (MPT); NR (Not reported), IQR (Interquartile range); European Network of Cancer Registries guidelines (ENCR);

Breast cancer intervals

Appraisal and help-seeking intervals as separate intervals

Only one study assessed appraisal interval (between the detection of breast symptoms to first disclosure, e.g. to partners, family and friends) and help-seeking interval (between symptom detection and first visit to a healthcare provider [HCP]) as separate intervals.[55] The study found a median appraisal interval of 6 days (approximately one week) and a median help-seeking interval of 6 weeks among women (N= 420) with breast cancer in Nigeria.

Patient interval (combination of appraisal and help-seeking intervals)

In most (22/24) of the studies focusing on breast cancer, appraisal and help-seeking intervals were assessed together as a single 'patient interval' or 'time to action' (between the detection of breast symptoms and first HCP visit). The interval ranged from 10 days among breast cancer patients in Mexico (N=886)[52] to 2 weeks in Thailand (N=180)[18]; 3 weeks in Colombia (N=242)[47] and South Africa (N=201)[7]; 4 weeks in Ethiopia (N=441)[42]; 8 weeks in Malaysia (N=328)[48]; 10 weeks in Malaysia (N=340)[54]; 16 weeks in India (N=435)[53]; and Libya (N=200)[40]; 19 weeks in Mali (N=124)[43]; 20 weeks in Rwanda (N=144)[50]; 23 weeks in South Africa (N=20)[19]; 28 weeks in Peru (N=113)[51]; 48 weeks in Sudan (N=63)[58]; 63 weeks in Pakistan (N=449)[59]; and 81 weeks in Ethiopia (N=55).[56] One multi-country study (N=1429) assessed patient intervals for Namibia (1 week in non-black women and 5 weeks in Black women), Nigeria (15 weeks), Uganda (14 weeks) and Zambia (4 weeks).[41] Another multi-country study (N=6588) reported patient intervals for Bulgaria (19 weeks), India (24 weeks), Russia (19 weeks), Serbia (18 weeks) and Turkey (19 weeks).[45]

Diagnostic interval

The majority (16/24) of the studies focusing on breast cancer measured diagnostic intervals (between the first HCP visit and diagnosis of breast cancer). The interval ranged from 3 weeks in Mali (N=124)[43] and Thailand (N=180)[18]; to 4 weeks in South Africa (N=201)[7] and Malaysia (N=340)[54]; 8 weeks in Colombia (N=242)[47]; 10 weeks in Ethiopia (N=441)[42]; 13 weeks in another South African study (N=20)[19]; 15 weeks in Nigeria (N= 420)[55]; 18 weeks in Mexico (N=886)[52]; 20 weeks in Rwanda (N=144)[50]; and 22 weeks in Malaysia (N=328).[48] One multi-country study (N=1429) assessed diagnostic intervals for Namibia (3 weeks in non-black women and 8 weeks in Black women), Nigeria (1 week), Uganda (19 weeks) and Zambia (10 weeks).[41]

Diagnostic endpoints varied across studies, with pathology (histology) being the most commonly used method, while a minority defined diagnosis based on clinical and/or radiological assessment.

Total diagnostic interval (combination of appraisal, help-seeking and diagnostic intervals)

A minority (7/24) breast cancer studies assessed total diagnostic interval (between the awareness of symptoms and diagnosis). This interval ranged from 15 weeks in Colombia (N=242)[47]; to 21 weeks in Iran (N=505)[39]; 30 weeks in Libya (N=200)[40]; 34 weeks in Nigeria (N=420)[55]; 36 weeks in South Africa (N=20)[19]; 60 weeks in Rwanda (N=144).[50] One multi-country study (N=1429) reported total diagnostic intervals for Namibia (10 weeks in non-black women and 26 weeks in Black women), Nigeria (22 weeks), Uganda (45 weeks) and Zambia (33 weeks).[41] Table 2 summarises the intervals.

Cervical cancer intervals

Appraisal and help-seeking intervals as separate intervals

Neither of the two cervical studies assessed appraisal interval (between the detection of cervical symptoms to first disclosure, e.g. to partners, family and friends) and help-seeking interval (between symptom detection and first HCP visit) as separate intervals.

Patient interval (combination of appraisal and help-seeking intervals)

One of the two cervical cancer studies assessed appraisal and help-seeking intervals together as a single 'patient interval' (between the detection of cervical symptoms and first HCP visit). It found a patient interval of 10 weeks among women (N=110) with cervical cancer in Nepal.[44]

Diagnostic interval

One cervical cancer study evaluated diagnostic intervals (between the first HCP visit and diagnosis). It found a patient interval of 8 weeks among women with cervical cancer in Nepal (N=110).[44]

Total diagnostic interval (combination of appraisal, help-seeking and diagnostic intervals)

Both cervical cancer studies assessed total diagnostic interval (between the awareness of symptoms and diagnosis). The interval was 22 weeks among women with cervical cancer in Nepal (N=110)[44] and 30 weeks among women in Ethiopia (N=1575).[38]

Table 2: Diagnostic intervals and factors associated with diagnostic timeliness

Study ID	Cancer site	Country	Appraisal interval (length in weeks)	Help-seeking interval (length in weeks)	Diagnostic interval (length in weeks)	Total diagnostic interval (length in weeks)	Factors associated with diagnostic timeliness
Agodirin 2020	Breast	Nigeria	6 (1–28) days (1 week)	42 (7–150) days (6 weeks)	106 (13–337) days (15 weeks)	240 (90–372) days (34 weeks)	Receiving correct advice and having a large tumour were associated with shorter health seeking interval
Begoihn 2019	Cervix	Ethiopia	30 (0–526) weeks			30 (0–526) weeks	Patients residing in rural are more likely to have longer patient intervals than those in urban areas.
Dianatinasab 2016	Breast	Iran	146 (±188) days 21 weeks			146 (±188) days 21 weeks	Shorter diagnostic delay was associated with higher education, urban residence, screening behaviour (ability to conduct self-breast exam), ductal carcinoma and detection of lump by patient
Dye 2012	Breast	Ethiopia	1.5 years 81 weeks		NR	NR	The most common reason for initiating action was worsening of, or development of new symptoms
Ermiah 2012	Breast	Libya	4 (1-24) months 16 weeks		NR	7.5 (1-25) months 30 weeks	Delay tended to be higher among women who did not report monthly breast self-examination, older women and those at lower educational levels.
Foerster 2020	Breast	Multi-country: Namibia Nigeria Uganda Zambia	Namibia (Blacks): 1.3 (0.2-6.2) months (5 weeks) Namibia (non-Black): 0.3 (0.0-2.1) months (1 week) Nigeria: 3.7 (1.0 – 8.1) months (15 weeks) Uganda: 3.5 (1.0-9.9) months 14 weeks Zambia: 1.1 (0.2-9.1) months (4 weeks)		Namibia (Blacks): 2.0 (0.5-7.0) months (8 weeks) Namibia (non-Black): 0.7 (0.2-2.0) months (3 weeks) Nigeria: 0.2 (0.0-3.0) months (1 week) Uganda: 4.7 (1.3-11.8) months (19 weeks) Zambia: 2.6 (1.1-9.9) months	Namibia (Blacks): 6.5 (2.3-13.1) months (26 weeks) Namibia (non-Black): 2.4 (0.6-5.5) months (10 weeks) Nigeria: 5.6 (2.3-13.1) months (22 weeks) Uganda: 11.3 (5.7-21.2) months (45 weeks) Zambia: 8.2 (3.4-16.4) months	Prolonged diagnostic journey is associated with wrong attribution of symptoms, lower educational status, lower socioeconomic status, being single, lay beliefs, detection of lump and access to informal HCP

				(10 weeks)	(33 weeks)	
Gebremariam 2019	Breast	Ethiopia	30 (6–132) days (4 weeks)	69 (22–213) days (10 weeks)	NR	Longer diagnostic and patient delays were associated with age (>60 years), lower education status, ≥5 children, lack of symptom awareness and use of traditional medicine
Grosse Frie 2019	Breast	Mali	91 (IQR NR) days 13 weeks	21 (IQR NR) days 3 weeks	NR	Patients who initially visited private clinics had the shortest health seeking interval, but the longest diagnostic interval. Patients visiting community healthcare centres and referral hospitals had the longest help-seeking interval, but shorter diagnostic interval. Patients who initially visited a tertiary hospital had shortest help-seeking and diagnostic intervals, but did not follow the recommended referral pathway
Gyenwali 2014	Cervix	Nepal	68 (8-404) days (10 weeks)	54 (0-582) days (8 weeks)	157 (22-718) days (22 weeks)	Longer total diagnostic delay was observed among patients aged 50 years or more, women with lower literacy and those residing farther from the health facility. Long patient delay and total diagnostic delay were found in patients with early symptoms like foul smelling vaginal discharge. HCP delay and total diagnostic delay were longer among women whose cervix was not examined in initial consultation.
Jassem 2014	Breast	Multi-country: Bulgaria India Russia Serbia Turkey	Bulgaria 4.83 (±0.22) months (19 weeks) India 6.10 ((±0.33) months (24 weeks) Russia 4.81 0.17) months (19 weeks) Serbia 4.47 (±0.19) months (18 weeks) Turkey 4.84 (±0.18) months (19 weeks)	NR	NR	Longer patient-related delay times were associated with distrust and disregard, and shorter patient-related delay times were associated with fear of breast cancer, practicing self-examination, higher education level, being employed, having support from friends and family and living in big cities
Khaliq 2019	Breast	Pakistan	31 to 128 days (4 – 18 weeks)	Referral interval: 7 - 194 days (1-27 weeks)	NR	Older age, seeking care from several health practitioners and traditional health practitioners were significantly associated with longer

				Diagnostic interval: 15 -30 days (2-4 weeks)		diagnostic delay. Employment status showed a negative relationship with diagnostic delay
Khokher 2016	Breast	Pakistan	<1 year for 70% of patients (<52 weeks)	NR	NR	NR
Martínez-Pérez 2020	Breast	Colombia	20 (IQR NR) days (3 weeks)	53 (IQR NR) days (8 weeks)	104.5 (IQR NR) days (15 weeks)	Significant association between delayed diagnosis and seeking care at government subsidised health facilities and age over 40 years.
Moodley 2016	Breast	South Africa	164 days (average) (23 weeks)	92 days (average) (13 weeks)	256 days (average) (36 weeks)	Deficits in breast self-awareness, knowledge of breast cancer symptoms and disease-related factors such as the absence of pain contributed to delays in seeking care.
Moodley 2018	Breast	South Africa	23 (6–64) days (3 weeks)	28 (13–58) days (4 weeks)	NR	Factors associated with the longer patient interval included older age, initial symptom denial, waiting for a lump to increase in size before seeking care. Factors associated with diagnostic interval were presence of co-morbidities and denial breast symptoms.
Mujar 2017	Breast	Malaysia	2.4 (0-120) months (10 weeks)	1 (0-9.3) months (4 weeks)	NR	Use of complementary medicine was associated with longer delays
Norsa'adah 2011	Breast	Malaysia	2 (0-132) months (8 weeks)	NR	5.5 (0-192) months (22 weeks)	Factors associated with diagnosis delay included the use of alternative therapy, breast ulcer, palpable axillary lymph node, false-negative diagnostic test, non-cancer interpretation and negative attitude toward treatment.
Olarewaju 2019	Breast	Nigeria	≤3 months for 65% of patients (≤12 weeks)	≤2 months for 70% of patients (≤8 weeks)	NR	Delays were related to factors such as age (older), ethnicity, and marital status (married)
Pace 2015	Breast	Rwanda	5 (1–13) months (20 weeks)	5 (2–14) months (20 weeks)	15 (8–32) months (60 weeks)	Longer patient delay was associated with low level of education and consulting a traditional healer Longer system delay was associated with visiting ≥5 health facilities before the diagnosis

Poum 2014	Breast	Thailand	12 (IQR NR) days (2 weeks)	21 (IQR NR) days (3 weeks)	NR	Longer patient delay was associated with higher family income, self-treatment and seeking medical advice from family or friends. Longer diagnostic delay was associated with older age, employed status, longer distance from home to hospital, increased travel time from home to hospital and higher number of consultations with a surgeon before diagnosis.
Romanoff 2017	Breast	Peru	198 (±449) days (28 weeks)	NR	NR	Women who underwent a previous clinical breast examination were more likely to have shorter patient delays compared with women who had never undergone a previous clinical breast examination
Salih 2016	Breast	Sudan	11.9 (±11.2) months (48 weeks)	NR	NR	Financial incapacity, ignorance about breast cancer, and misinterpreting symptoms were the top three factors associated with delay
Shamsi 2020	Breast	Pakistan	15.7 months (±25.9) 63 weeks	NR	NR	Longer patient delay was associated with lower socioeconomic status, lower educational status, use of traditional medicine Shorter patient delay was associated with presence of a family history of breast cancer
Sharma 2012	Breast	Haiti	1 (1-4) week in 58% of the patients 26 (17-77) weeks in 42% of the patients	NR	NR	Lower education status, failure to initially recognise mass as important, and fear of treatment cost were shown to independently predict delayed patient presentation.
Shreyamsa 2020	Breast	India	4 (0-24) months (16 weeks)	NR	NR	Misdiagnosis at first consult was the most common factor perceived by patients as a barrier, followed by delay in referral, distance from hospitals, lack of information and financial constraints.
Unger-Saldaña 2018	Breast	Mexico	10 (IQR NR) days (1 week)	128 (IQR NR) days (18 weeks)	NR	Patient interval was longer for patients who were single, younger, had interpreted their symptoms as not worrisome, had concealed symptoms, had lower socioeconomic status, and lived outside of the city. Diagnostic interval was

						longer among those who used several different health services prior to diagnosis.

NR (Not reported)

Factors associated with diagnostic timeliness

Appraisal and health-seeking intervals

Women who reported the presence of a family history of breast cancer[59], women who reported the fear of breast cancer[45], and those that initially visited private clinics/tertiary hospitals[43] tended to have shorter help-seeking intervals. Also, being employed[45], receiving supports from family/friends[45], living in big cities[45], receiving correct advice[55], presence of a large tumor[55], and worsening of, or development of new, symptoms[56] were associated with shorter health-seeking interval. Longer help-seeking intervals were associated with not practising self-breast examination[40,51], older age[40,42,50], not receiving a cervical examination at first consultation[44], living in rural areas or farther away from cities[38,52], having ≥5 children[42], low health literacy level[7,40,42,58-60], use of traditional/complementary medicine[42,50,54,59], lower socioeconomic status[42,52,58,59] and living in denial or waiting for symptoms to increase.[7,52] Higher family income[18], fear of high treatment cost[60], self-medication[18)], nondisclosure[52], seeking medical advice from family or friends[18] and the use of community healthcare centres and referral hospitals were also associated with longer help-seeking intervals.[43]

Diagnostic interval

Shorter diagnostic delay was associated with higher educational level[39], urban residence[39], screening behaviour (ability to conduct self-breast exam)[39], and self-detection of lump.[39] On the other hand, longer diagnostic interval was associated with none/wrong attribution of symptoms[41,48], low heath literacy[19,41,44,53], symptom denial[7], presence of co-mobidities[7], unemployment status[18,46], lower socioeconomic status[41,52,53], old age[18,44,46,47,49], marital status (i.e. being single)[41,49], ethnicity[49], lay beliefs[41], residing far from a health facility[41,44,53] and longer travel time.[18] Other factors associated with longer diagnostic interval were lack of cervical examination at first consultation[44], seeking care from multiple health practitioners and complementary/alternative care before diagnosis[18,46,48,50,54], health-seeking in government subsidised facilities[47], referral delays[53], false negative diagnosis[48,53], and poor treatment behaviour.[48] Notably, patients who initially visited private clinics/tertiary hospitals tended to have shorter help-seeking intervals but longer diagnostic delays.[43] Table 2 highlights the factors associated with diagnostic timeliness.

Discussion

Addressing the barriers to early diagnosis of breast and cervical cancer requires a sound understanding of diagnostic timeliness, intervals and delays, and the factors associated with them. This review offers up-to-date evidence with which to bolster that understanding. Overall, it demonstrates that patient-related and health-system-related delays are common in LMICs. However, it is difficult to infer and compare findings across studies owing to variations in how diagnostic time, events, intervals and delays were conceptualised and assessed. While the amount of evidence identified points to the substantial and growing attention paid to early breast and cervical cancer in LMICs over the past decade, this review has also identified gaps both in terms of quantity and methodological diversity of the available literature.

The current evidence shows a dearth of studies evaluating the timeliness of cervical cancer diagnosis, with only two of such studies identified in this review (constituting less than 10% of studies found). This is despite the substantial burden of cervical cancer and late-stage diagnosis in LMICs.[1-5] Consistent with finding from previous reviews of cancer diagnostic delays[10,61], a major methodological issue identified by this review is the marked variability in the conceptualisation and operationalisation of the time to diagnosis and corresponding intervals. In spite of the availability of validated tools and methods for evaluating cancer diagnostic timeliness, only a minority of the studies reported the use of such tools in the context of breast and cervical cancer – including the Anderson model[48,58], the Model of Pathways to Treatment[7,19,43,55] and the Aarhus Statement.[42,46]

The studies varied considerably in the use of common terminologies relating to diagnostic events and intervals. There were also variations in the thresholds used for defining delays. For instance, a patient interval was considered as delayed if longer than two months in one study[44], whereas two other studies considered it as delayed if longer than three months.[49,53] Similarly, different time-points were used to define intervals. For instance, the endpoint for diagnosis was operationalised as the date of diagnosis based on clinical or imaging evaluation in some studies, while it was the date of pathological diagnosis in others. It is therefore important to standardise methods of assessing and reporting of diagnostic endpoints, one approach of which are the European Network of Cancer Registries (ENCR) guidelines.[62] The wide discrepancy between the estimated patient-related intervals of 4 weeks and 81 weeks among women with breast cancer in Ethiopia, as reported by two different studies[42,56], starkly

reflects such within-country variations. These further complicate the interpretation and comparison of findings across studies.

Patient-related intervals and delays were more frequently evaluated and reported than provider- and health system-related ones. This is consistent with the findings of a previous review on cancer diagnostic delays in LMICs.[10] The trend may be a reflection of the patient-sided way in which diagnostic delays are currently perceived in LMICs and underscores the need for more balanced and system-wide approaches to assessing and understanding the barriers to early diagnosis of breast and cervical cancer diagnostic. It also has important implications for policy and practice. For instance, focusing on patient-centred strategies such as improving awareness, without addressing provider- and health system-related factors may yield limited results.

It is noteworthy that most of the studies that assessed and reported patient-related intervals did not evaluate the appraisal interval as a distinct form of patient-related interval, but rather assessed the appraisal and help-seeking intervals as a single interval. Only two studies made such distinction.[7,55] This highlights the need for more attention to be paid to this internal among women with breast and cervical cancer symptoms as a distinct and important aspect of their journey from symptom awareness to treatment. To develop evidence-based policies and holistic interventions for addressing diagnostic delays and barriers to early cancer diagnosis in LMICs, it is vital to understand the time and events that characterise patients' journey from the perception of bodily changes to discerning the need and urgency to seek help, as these will ultimately influence time to diagnosis and treatment.

Our review also identified a multiplicity of patient and health system-related factors associated with diagnostic timeliness and delay across specific diagnostic intervals. While the factors influencing one interval (such as the help-seeking interval) might be distinct (at least empirically) from those affecting other intervals (such as the diagnostic or provider interval), this may not be so in practice as the length of each interval is likely to be the result of a complex interplay between patient and health system drivers. For instance, women may delay help-seeking not only because of patient-related factors (such as having a low level of cancer awareness) but also due to health-system factors such as the non-availability of a health facility or health care providers in their areas of residence.

Likewise, women with symptoms of cancer presenting at health facilities may delay definitive diagnosis following referral, due to fear of the consequences of being diagnosed with cancer (such as mastectomy, stigma and death). Hence, it is essential that these interrelationships are taken into consideration when conceptualising, evaluating and interpreting diagnostic intervals and the factors associated with them. We again emphasise the importance of standardising the assessment and reporting of cancer diagnostic intervals and barriers, to improve the translation of research findings and to better inform interventions for addressing the growing public health challenge of delayed diagnosis of breast and cervical cancer in LMICs.

Limitations

While our review adds significantly to the existing body of literature on cancer diagnostic timeliness in LMIC contexts, it is not without limitations. First, as has been acknowledged earlier, the heterogeneous nature of the studies and the use of non-standardised methods limit the interpretation and comparability of findings. Besides, the small sample size and non-representativeness of participants of some of the studies limited both internal and external validity of the studies, making it difficult to interpret findings in the context of their reference geographic populations.

The cross-sectional retrospective nature of many of the studies and the reliance on patients' recall to estimate events such as the time they first discovered their symptoms come with the risk of recall bias. These also come with the potential of social desirability bias that can lead to under-estimation of patient and diagnostic delays. Another important limitation of this review is that, as in most scoping reviews; a formal quality appraisal of included literature was not conducted. As such, the strength of the evidence cannot be ascertained. Lastly, while our literature search was comprehensive, covering both peer-reviewed and relevant grey literature; it is possible that the review did not include all relevant literature available, as some may not have been accessible at the time search.

Conclusions

Despite the significant burden of breast and cervical cancer in LMICs, there is limited evidence on the timeliness of diagnosis of both cancers. Available evidence demonstrates between- and within-country variations in how diagnostic timeliness and intervals of breast and cervical

cancer are conceptualised and measured in LMICs. Such variations underscore the need for the increased use of validated and standardised tools for assessing diagnostic timeliness in more reproducible and comparable ways to more accurately inform interventions for addressing the growing public health problem of diagnostic delays in LMICs.

Patient and public involvement

As this is a scoping review of already existing literature, and no participant recruitment took place, patients were not directly involved in the design and conduct of this study.

Ethics approval

This is a scoping review of publicly available literature, with no primary data collection. Hence, it did not require ethics approval.

Authors' contributions: JM conceived the study and provided conceptual guidance for the design of the protocol. CAN wrote the first draft of the manuscript. PK, FMW and JM supported the development of the study protocol. EE supported full text review, data extraction and analysis. JM and FMW provided critical insights and guided the coherence of the manuscript. All authors have contributed to, and approved, the final version of the manuscript.

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Supplementary files

Figure 1: PRISMA flow chart of the study selection process

Figure 2: Geographical distribution of included studies

Appendix: Search strategy

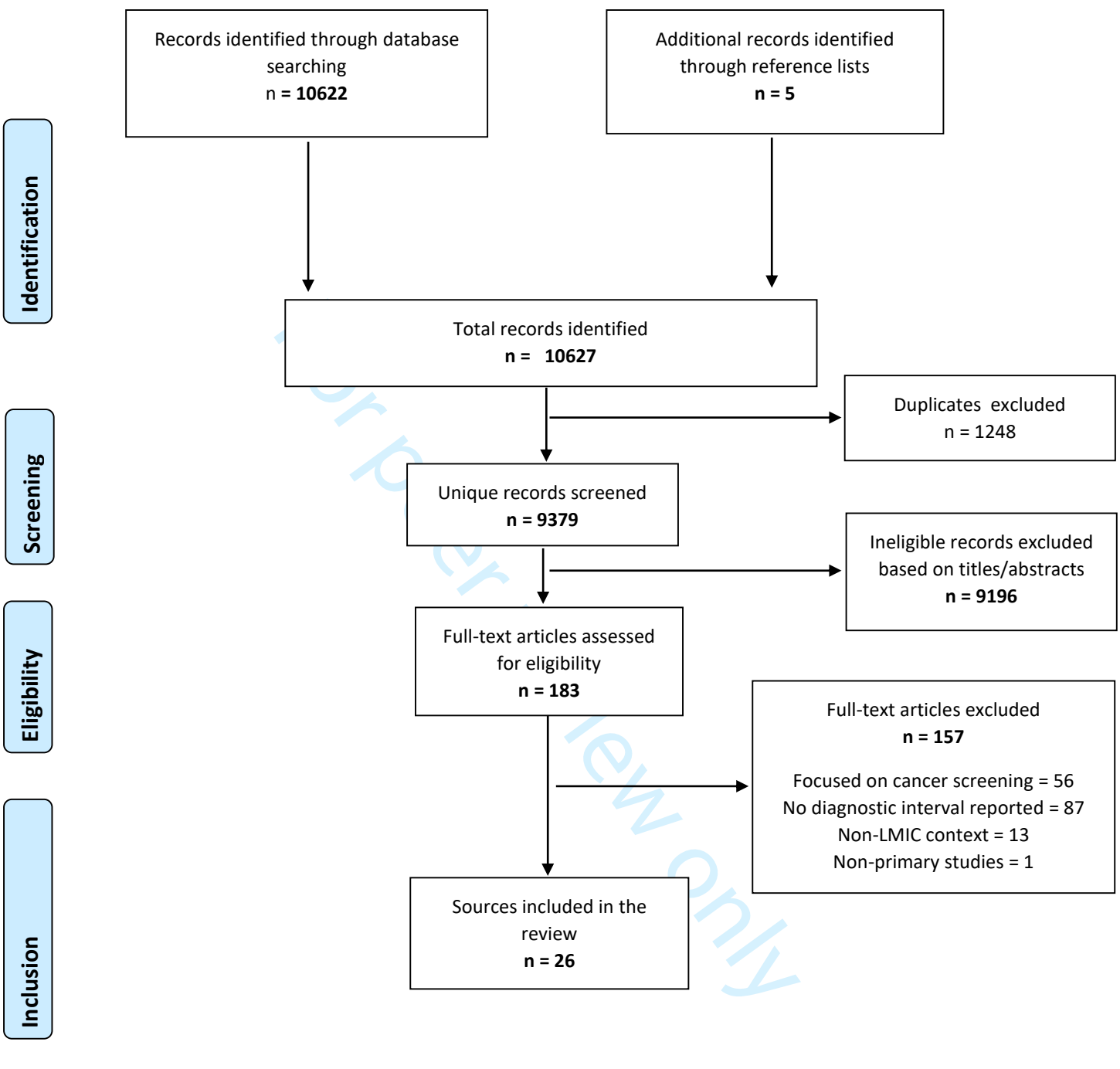

Figure 1: PRISMA flow diagram showing study selection process

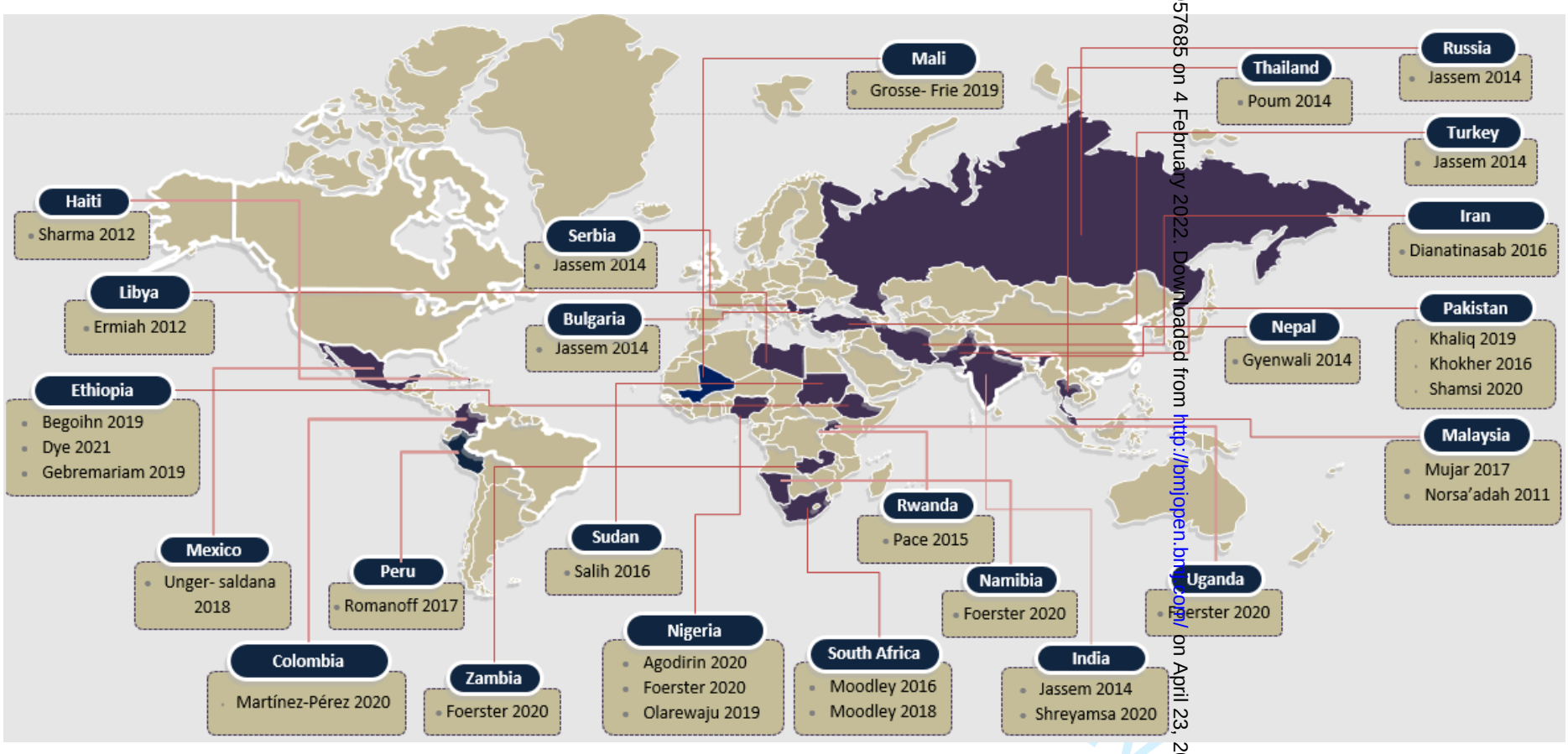

Figure 2: Geographical distribution of included studies (map created by authors using an open-source template sourced from https://yourfreetemplates.com/)

Appendix: Search strategy

Search strategy for MEDLINE (via PubMed); last searched 20 May 2021

#1	Breast Neoplasms [Mesh] OR Breast cancer[Title/Abstract] OR breast[Title/Abstract] OR cervical cancer[Title/Abstract] OR cervix[Title/Abstract] OR cancer[Title/Abstract] OR malignant[Title/Abstract] OR neoplasm[Title/Abstract] OR neoplasia[Title/Abstract] OR malignancy[Title/Abstract] OR tumour[Title/Abstract]
#2	Diagnosis [Mesh] OR diagnostic[Title/Abstract] OR diagnosis[Title/Abstract] OR diagnosis[Title/Abstract] OR detection[Title/Abstract] OR discovery[Title/Abstract] OR Patient navigation[Title/Abstract] OR Patient pathway[Title/Abstract] OR care continuum[Title/Abstract]
#3	early[Title/Abstract] OR timely[Title/Abstract] OR time[Title/Abstract] OR late[Title/Abstract] OR delay[Title/Abstract]
#4	#2 AND #3
#5	Developing Countries OR Developing Country OR Developing Economies OR Developing Economy OR Developing Nation OR Developing Nations OR Developing Population OR Developing Populations OR Developing World OR LAMI Countries OR LAMI Country OR Less Developed Countries OR Less Developed Country OR Less Developed Economies OR Less Developed Nation OR Less Developed Nations OR Less Developed World OR Lesser Developed Countries OR Lesser Developed Nations OR LMIC OR LMICS OR Low GDP OR Low GNP OR Low Gross Domestic OR Low Gross National OR Low Income OR Lower GDP OR lower gross domestic OR Lower Income OR Middle Income OR Poor Countries OR Poor Country OR Poor Economies OR Poor Economy OR Poor Nation OR Poor Nations OR Poor Population OR Poor Populations OR poor world OR Poorer Countries OR Poorer Economies OR Poorer Economy OR Poorer Nations OR Poorer Population OR Poorer Populations OR Third World OR Transitional Countries OR Transitional Country OR Transitional Economies OR Transitional Economy OR Under Developed Countries OR Under Developed Country OR under developed nations OR Under Developed World OR Under Served Population OR Under Served Populations OR Underdeveloped Countries OR Underdeveloped Country OR underdeveloped economies OR underdeveloped nations OR underdeveloped population OR Underdeveloped World OR Underserved Countries OR Underserved Nations OR Underserved Population OR Underserved Populations OR Afghanistan OR Albania OR Algeria OR American Samoa OR Angola OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Byelarus OR Belorussia OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia OR Botswana OR Brazil OR Bulgaria OR Burma OR Burkina Faso OR Burundi OR Cabo Verde OR Cape Verde OR Cambodia OR Cameroon OR Central African Republic OR Chad OR China OR Colombia OR Comoros OR Comores OR Comoro OR Congo OR Costa Rica OR Côte d'Ivoire OR Cuba OR Djibouti OR Dominica OR Dominican Republic OR Ecuador OR Egypt OR El Salvador OR Equatorial Guinea OR Eritrea OR Ethiopia OR Fiji OR Gabon OR Gambia OR Gaza OR Georgia OR Georgia Republic OR Ghana OR Grenada OR Grenadines OR Guatemala OR Guinea OR Guinea- Bissau OR Guyana OR Haiti OR Herzegovina OR Hercegovina OR Honduras OR India OR Indonesia OR Iran OR Iraq OR Ivory Coast OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Democratic People's Republic of Korea OR Kosovo OR Kyrgyz OR Kirghizia OR Kirghiz OR Kyrgyzstan OR Lao PDR OR Laos OR Lebanon OR Lesotho OR Liberia OR Libya OR Macedonia OR Madagascar OR Malawi OR Malay OR Malaya OR

	Malaysia OR Maldives OR Mali OR Marshall Islands OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Palau OR Papua New Guinea OR Paraguay OR Peru OR Philippines OR Principe OR Romania OR Ruanda OR Rwanda OR Samoa OR Sao Tome OR Senegal OR Serbia OR Sierra Leone OR Solomon Islands OR Somalia OR South Africa OR South Sudan OR Sri Lanka OR St Lucia OR St Vincent OR Sudan OR Surinam OR Suriname OR Swaziland OR Syria OR Syrian Arab Republic OR Tajikistan OR Tadzhikistan OR Tajikistan OR Tadzhik OR Tanzania OR Thailand OR Timor OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmen OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uzbek OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR West Bank OR Yemen OR Zambia OR Zimbabwe
#6	#1 AND #4 AND #5

Search strategy for Scopus; last searched 20 May 2021

Search #	Search Texts and Syntaxes
#1	(Breast cancer) OR breast OR (cervical cancer) OR cervix OR cancer OR malignant OR neoplasm OR neoplasia OR malignancy OR tumour
#2	Diagnosis OR diagnostic OR diagnosis OR diagnosis OR detection OR discovery OR (Patient navigation) OR (Patient pathway) OR (care continuum)
#3	Early OR timely OR time OR late OR delay OR interval
#4	#2 AND #3
#5	TITLE-ABS-KEY "Deprived Countries" OR "Deprived Population" OR "Deprived Populations" OR "Developing Countries" OR "Developing Country" OR "Developing Economies" OR "Developing Economy" OR "Developing Nation" OR "Developing Nations" OR "Developing Population" OR "Developing Populations" OR "Developing World" OR "LAMI Countries" OR "LAMI Country" OR "Less Developed Countries" OR "Less Developed Country" OR "Less Developed Economies" OR "Less Developed Nation" OR "Less Developed Nations" OR "Less Developed World" OR "Lesser Developed Countries" OR "Lesser Developed Nations" OR LMIC OR LMICS OR "Low GDP" OR "Low GNP" OR "Low Gross Domestic" OR "Low Gross National" OR "Low Income" OR "Lower income" OR "Lower GDP" OR "Lower Gross Domestic" OR "Middle Income" OR "Poor Countries" OR "Poor Country" OR "Poor Economies" OR "Poor Economy" OR "Poor Nation" OR "Poor Nations" OR "Poor Population" OR "Poor Populations" OR "poor world" OR "Poorer Countries" OR "Poorer Economies" OR "Poorer Economy" OR "Poorer Nations" OR "Poorer Population" OR "Poorer Populations" OR "Third World" OR "Transitional Countries" OR "Transitional Country" OR "Transitional Economies" OR "Transitional Economy" OR "Under Developed" OR "Under Served" OR "Underdeveloped Countries" OR "Underdeveloped Country" OR "underdeveloped economies" OR "underdeveloped nations" OR "underdeveloped population" OR "Underdeveloped World" OR "Underserved Countries" OR "Underserved Nations" OR "Underserved Population" OR "Underserved Populations" OR Afghanistan OR Albania OR Algeria OR "American Samoa" OR Angola OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Byelarus OR Belorussia OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia OR Botswana OR Brazil OR Bulgaria OR Burma OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR "Cape Verde" OR Cambodia OR Cameroon OR "Central African Republic" OR Chad OR China OR Colombia OR Comoros OR Comores OR Comoro OR Congo OR "Costa Rica" OR "Côte d'Ivoire" OR Cuba OR "Democratic People's Republic of Korea" OR Djibouti OR Dominica OR "Dominican Republic" OR Ecuador OR Egypt OR "El Salvador" OR Eritrea OR Ethiopia OR "Equatorial Guinea" OR Fiji OR Gabon OR Gambia OR Gaza OR "Georgia Republic" OR Georgia OR Ghana OR Grenada OR Grenadines OR Guatemala OR Guinea OR "Guinea Bissau" OR Guyana OR Haiti OR Herzegovina OR Hercegovina OR Honduras OR India OR Indonesia OR Iran OR Iraq OR "Ivory Coast" OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyz OR Kirghizia OR Kirghiz OR Kyrgyzstan

	OR “Lao PDR” OR Laos OR Lebanon OR Lesotho OR Liberia OR Libya OR Macedonia OR Madagascar OR Malawi OR Malay OR Malaya OR Malaysia OR Maldives OR Mali OR “Marshall Islands” OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Palau OR Papua New Guinea OR Paraguay OR Peru OR Philippines OR Principe OR Romania OR Rwanda OR Ruanda OR Samoa OR “Sao Tome” OR Senegal OR Serbia OR “Sierra Leone” OR “Solomon Islands” OR Somalia OR “South Africa” OR “South Sudan” OR “Sri Lanka” OR “St Lucia” OR “St Vincent” OR Sudan OR Surinam OR Suriname OR Swaziland OR Syria OR “Syrian Arab Republic” OR Tajikistan OR Tadzhikistan OR Tajikistan OR Tadzhik OR Tanzania OR Thailand OR Timor OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmen OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uzbek OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR “West Bank” OR Yemen OR Zambia OR Zimbabwe
#6	#1 AND #4 AND #5

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	4-5
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	5
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	6
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	7
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	6
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	7-8
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	8
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	n/a
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	8

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	9
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	9
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	n/a
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	9-27
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	9-27
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	28
Limitations	20	Discuss the limitations of the scoping review process.	30
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	30
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	31

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

Adapted from: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

BMJ Open

Timeliness of diagnosis of breast and cervical cancers and associated factors in low- and middle-income countries: A scoping review

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Timeliness of diagnosis of breast and cervical cancers and associated factors in low- and middle-income countries: A scoping review

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Abstract

Objectives: Addressing the barriers to early breast and cervical cancer diagnosis in low- and middle-income countries (LMICs) requires a sound understanding and accurate assessment of diagnostic timeliness. This review aimed to map the current evidence on the time to breast and cervical cancer diagnosis and associated factors in LMICs.

Design: Scoping review

Sources: MEDLINE (via PubMed), Cochrane Library, Scopus and CINAHL.

Eligibility criteria: Studies describing the time to diagnosis and associated factors in the context of breast and cervical cancer in LMICs published from 1 January 2010 to 20 May 2021.

Study selection and data synthesis: Two reviewers independently screened all abstracts and full-texts using predefined inclusion criteria. The review was reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR). Evidence was narratively synthesised using predefined themes.

Results: Twenty-six studies conducted across 24 LMICs were included in the review, most (24/26) of which focused on breast cancer. Studies varied considerably in their conceptualisation and assessment of diagnostic time, events, intervals and delays, with a minority of the studies reporting the use of validated methods and tools. Patient-related intervals and delays were more frequently evaluated and reported than provider- and health system-related intervals and delays. Across studies, there were variations in the estimated lengths of the appraisal, help-seeking, patient and diagnostic intervals for both cancers and the factors associated with them.

Conclusions: Despite the significant burden of breast and cervical cancer in LMICs, there is limited information on the timeliness of diagnosis of these cancers. Major limitations included variations in conceptualization and assessment of diagnostic events and intervals. These underscore the need for the use of validated and standardised tools, to improve accuracy and translation of findings to better inform interventions for addressing diagnostic delays in LMICs.

Keywords: Cancer, breast, cervical, diagnosis, time, delay, LMICs.

Strengths and limitations of this study

- This scoping review was conducted in accordance with an enhanced evidence synthesis methodology and reported using standard reporting guidelines.
- This review updates the evidence base relating to the nature of the time to diagnosis of breast and cervical cancer and associated factors in LMICs.
- Literature searches were comprehensive, covering both peer-reviewed and relevant grey literature.
- Due to the broad nature of the topic, it is possible that not all relevant evidence sources were identified by the search strategy, however comprehensive.

Introduction

Breast and cervical cancer constitute a growing public health burden globally.[1,2] The incidence, morbidity and mortality burdens of both cancers are disproportionately high among women in low- and middle-income countries (LMICs).[2,3] Breast cancer is the most commonly occurring cancer and the leading cause of cancer deaths among women worldwide, with an age-standardised incidence rate (ASIR) of 31 per 100,000 women in LMICs.[4,5] Cervical cancer is the fourth most common cancer among women, with an ASIR of 16 per 100,000 women.[2] Cancer survival rates are low in LMICs, the major attributable factors of which include late-stage diagnosis and suboptimal access to quality healthcare.[1,6]

Timely diagnosis is critical for optimising patients' navigation of the pathway from cancer symptom awareness to treatment, and improving survival.[7-9] However, the majority of breast and cervical cancers are diagnosed at a late stage when treatment is often less effective and more expensive.[10-12] In LMICs, barriers to timely cancer diagnosis include individual and disease-related factors, as well as health system constraints.[13-15] Individual-level factors may include demographic, behavioural and psychosocial factors, in addition to those associated with underlying sociocultural barriers to timely diagnosis, such as lay beliefs that cancers are contagious and that they are inevitably fatal.[16,17] Disease-related factors include those related to the site, size, clinical manifestation and growth of tumours.[15] Health system factors in LMICs include health policy, access, quality and service delivery barriers, such as inadequate diagnostic capacity, weak referral systems, sup-optimal access to treatment and insufficient human resources.[6,18,19] While there is substantial evidence on the association between these factors and cancer diagnostic delays, not much is known about the extent to which they influence time to diagnosis and diagnostic intervals, particularly in LMICs.

Various approaches and tools have been used for assessing time to diagnosis and diagnostic intervals, while their use in LMICs has grown over the years.[17,19,20] However, the tools commonly used often ignore existing models of patient behaviour, and are poorly or inadequately validated.[15,21,22] To bolster better conceptual understanding of patient's navigation, Walter, Scott and colleagues proposed a Model of Pathways to Treatment that describes the distinct phases of cancer patients' pathways from symptom awareness to diagnosis and treatment.[15,22] To aid the development of valid tools for measuring time to

cancer diagnosis, the Aarhus checklist has been proposed for guiding the design and reporting of early cancer diagnosis studies.[23]

A good understanding of the timeliness of breast or cervical cancer diagnosis, the diagnostic intervals and associated factors is important to guide interventions for addressing the growing public health problem of diagnostic delays in LMICs.[24-26] In 2017, the World Health Organization (WHO) published the *WHO Guide to Cancer Early Diagnosis* to provide a global standard for addressing barriers that may impede timely cancer diagnosis and treatment.[27,28] Addressing these barriers requires an accurate assessment and understanding of the time to diagnosis, related intervals and the multidimensional factors associated with the timeliness of diagnosis.[28]

This review aims to provide an updated and comprehensive synthesis of the evidence on the time to diagnosis and its associated factors, in the context of symptomatic breast and cervical cancer diagnosis in LMICs. It contributes a systematically organised evidence summary for health policy makers, cancer programme managers, oncologists and other cancer care providers for guiding policy and practice decision making. In addition, the findings will be useful for informing the design of interventions and strategies for addressing existing breast and cervical cancer diagnostic delays in resource-limited settings, while identifying gaps for future research efforts at measuring and appraising diagnostic timeliness.

Methods and analysis

Conceptual framework

This scoping review used the Model of Pathways to Treatment to map the identified evidence on the timeliness, time intervals and associated factors of breast and cervical cancer diagnosis.[15,22] The framework specifies the essential events, processes, and time intervals that may occur in the period prior to diagnosis and the start of medical treatment and identifies the factors that may influence each interval.

Study design

The design of this study was guided by Arksey and O'Malley's scoping review methodology[29], as enhanced by Levac and colleagues.[30] The enhanced framework involves six stages for undertaking a scoping review: (1) identifying the research question; (2) identifying the relevant studies (defining the inclusion and exclusion criteria); (3) searching and selecting the

evidence; (4) charting the evidence; (5) collating, summarising and reporting the evidence and (6) consultation with relevant stakeholders. The review was reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).[31] Full details of the study design have been published elsewhere.[32]

Data sources

The literature search was guided by the review objectives and the population, concept and content (PCC) criteria. The search strategy was developed with guidance from a health sciences subject librarian and applied in accordance with the Peer Review of Electronic Search Strategies (PRESS) guidelines.[33] The search strategy was pre-tested prior to the actual search. Search terms and free-text words were combined using the Boolean operators 'AND' and 'OR'. Search terms included the use of controlled descriptors (such as MeSH terms, CINAHL and headings) and their synonyms. In order to restrict search to LMICs, a location-filter containing all countries currently classified as part of LMICs and synonymous geographical, regional and economic categorisations were incorporated. The search strategy, as applied to the various literature databases, is outlined in the appendix. More details of the search strategy are described in the review protocol published elsewhere.[32]

A comprehensive literature search was conducted on the following electronic databases: MEDLINE (via PubMed), Cochrane Library (including the Cochrane Central Register of Controlled Trials (CENTRAL) and the Database of Abstracts of Reviews of Effects (DARE)), Scopus, CINAHL and the International Clinical Trials Registry Platform (ICTRP). Additionally, relevant grey literature sources were searched for potentially eligible articles, including the publication database of the WHO's International Agency for Research on Cancer (IARC), the Cancer Atlas of the Union for International Cancer Control (UICC) and the Global Cancer Project Map. A hand-search of reference lists of included studies was conducted. For recency, only articles published from 1 January 2010 to the last date of search (20 May 2021) were considered eligible. No language restrictions were applied. Non-English potentially eligible articles would have been translated using a Web-based translation tool.[34]

Eligibility criteria

Inclusion criteria were defined using the using the PCC (Population, Concept and Contexts) framework, proposed by Peters and colleagues.[35] Eligible population included women with

breast or cervical cancer and health care providers (HCP) in LMIC contexts. The definition of LMICs was based on the World Bank's current classification using per capita gross national income.[36] The concepts of interest were time to diagnosis and diagnostic intervals of breast and/or cervical cancers. To be considered eligible for inclusion, studies need to have measured time to diagnosis in the context of breast and/or cervical cancer diagnosis in LMICs, using specific methods, tools or strategies; and/or assessed diagnostic intervals of breast and/or cervical cancers; whether or not they evaluated the factors associated with diagnostic time or time intervals. Multinational literature involving LMIC and non-LMIC countries and meeting inclusion criteria were eligible for inclusion, except where country-specific information could not be abstracted. Similarly, articles involving multiple cancer types were eligible for inclusion, except relevant cancer type-specific information could not be abstracted.

Articles focused solely or mainly on theoretical and conceptual understanding of timeliness of breast or cervical cancer diagnosis were excluded, as were those assessing cancer patient pathways that are not related to diagnostic time and intervals. Studies focused primarily on screening of asymptomatic individuals were also excluded. Study design eligibility included randomised trials, non-randomised trials, and observational studies, with or without controls. Only primary studies were included; while systematic, scoping reviews and other forms of aggregated evidence were excluded.

Study selection

The review process consisted of two levels of screening. For the first level of screening, two reviewers (CAN and PK) independently screened the titles and abstracts of all retrieved records from the search output. Articles considered relevant by either or both of the reviewers were included in the full-text assessment. Following the removal of duplicates, full texts of remaining studies were retrieved. In the second step, the two reviewers (CAN and EE) independently assessed the full-texts to determine if they met the inclusion/exclusion criteria. Disagreements in eligibility assessment were resolved through consensus between.

Data extraction

Two reviewers (CAN and EE) independently abstracted data from all included studies using a standardised data abstraction tool, adapted from the framework proposed by Carlos and colleagues.[37] The tool includes four domains: (1) study identification details (article title;

journal title; authors; country of the study; language; publication year; host institution of the study); (2) methodological characteristics (study design; study objective or research question or hypothesis; sample characteristics (e.g. sample size; sex; age, ethnicity; groups and controls; follow-up duration; validation of measures; statistical analyses); (3) main findings, and (4) conclusions. Study eligibility were re-verified at the start of/during data extraction. Any discrepancies in the abstracted data between the two reviewers were resolved by discussion. CAN combined the two spreadsheets of abstracted data for analysis. JM and FMW reviewed analysed data for accuracy and consistency with protocol.

Data analysis

Findings were narratively summarised and reported based on themes that emerged from the charted evidence. Where applicable, quantitative evidence was aggregated using summary statistics. Time to diagnosis and diagnostic intervals were described based on the Model of Pathways to Treatment.[15,22] The Model also allowed for the assessment of patient-; health care provider and health system-; and disease-related factors that could influence diagnostic timeliness.

Patient and public involvement

Patients or the public were not involved in this research.

Results

Search results

A total of 10591 records were identified from literature database searches. After the removal of duplicates, there were 9347 unique records. These were screened by their titles and abstracts, following which 9174 clearly ineligible publications were excluded. The full texts of the remaining 173 potentially eligible studies were reviewed against predefined inclusion and exclusion criteria; 26 of which were included in the review, while 147 were excluded for various reasons. Figure 1 presents the PRISMA flow chart of the study selection process and reasons for exclusion.

Characteristics of included studies

Supplementary Table 1 describes the characteristics of included studies. Most (24/26) of the studies were focused on breast cancer, with only two focusing on cervical cancer. The studies were published between 2011 and 2020, conducted across 24 LMICs across the regions of Africa, Europe, Latin America, Middle-East Asia and South-East Asia. The following countries (number of studies) were represented: Bulgaria (1), Colombia (1), Ethiopia (3), Haiti (1), India (2), Iran (1), Libya (1), Malaysia (2), Mali (1), Mexico (1), Namibia (1), Nepal (1), Nigeria (3), Peru (1), Pakistan (3), Russia (1), Rwanda (1), Serbia (1), South Africa (2), Sudan (1), Thailand (1), Turkey (1), Uganda (1) and Zambia (1). Figure 2 illustrates the geographical distribution of included studies.

Nearly all (24/26) of the studies included were quantitative in design, including cross-sectional (21), cohort-type longitudinal (2) and case control (1) studies. One study had a mixed-methods cross-sectional design, while another was a qualitative study. Most (24/26) of studies primarily focused on breast cancer, whereas the remaining two focused on cervical cancer. Participants were mostly adult women with newly diagnosed breast or cervical cancer. All of the studies were conducted within healthcare settings, of which 18 were urban, 3 were rural and 5 were both rural and urban.

Methods of diagnosis

In the majority (20/26) of the studies, diagnosis was defined based on pathological or histological confirmation.[7,18,19,38-54] The rest of the studies relied on clinical assessment as a diagnostic modality.[55-60]

Methods/tools used for assessing diagnostic timeliness and intervals

Supplementary Table 1 describes the various methods and tools used for assessing diagnostic timeliness and intervals across studies. In most (23/26) of the studies, diagnostic events, timeliness and intervals were assessed using questionnaires or interviews that relied on participants' recall[7,18,19,38-56,59], seven of which combined patients' reports obtained from questionnaires or interviews with diagnostic information derived from facility-based medical records.[40,43,50,52-54,59] Three studies assessed diagnostic events and intervals using medical records.[38,57,60]

To define diagnostic time and intervals, 14 studies relied on authors' definition[18,38-41,44,45,49,52-54,57,59] while four adopted definitions from previous studies.[47,50,51,56] Four studies adopted the Model of Pathways to Treatment[7,19,43,55], three studies adopted the Aarhus Statement[42,46,55], while two studies adopted the Anderson Model.[48,58]

The studies varied considerably in the use of common terminologies relating to diagnostic events and intervals. Only two studies defined the appraisal interval (time between discovery of symptoms and perceiving reasons to seek help) and help-seeking interval (time between symptom recognition and first HCP consultation) as separate intervals as defined by the Model of Pathways to Treatment.[7,55] Most other studies combined both appraisal and help-seeking intervals as a single interval (time between symptom recognition and first HCP visit/consultation). Varying terminologies were used across studies to refer to this single interval, including help-seeking interval[43,55], patient [-related] interval (also patient delay or patient time)[7,18,42,44-47,49-54,58,59] , time to action[56], pre-contact time[41], consultation time[40,48] and presentation interval.[60] Table 1 describes how diagnostic timeliness and intervals were defined across studies.

Diagnostic interval was defined in various ways across studies: the time commencing from the point of symptom detection to diagnosis[40,48,57], time from first clinical consultation to diagnosis[7,18,19,41,42,44,47,49,50,52,54] and time from first presentation at a diagnostic centre to diagnosis.[46] Notably, the diagnostic interval was also referred to as primary care interval (time between first HCP visit and first specialist visit).[44,46,55] Less than half (10/26) of the studies defined total diagnostic interval (time from symptom detection to diagnosis).[19,38-41,44,47,48,50,55]

Similarly, the thresholds for defining intervals as delayed also varied across studies. Notably, a patient interval was considered as delayed if longer than two months in one study[44], whereas two other studies considered it as delayed if longer than three months.[49,53] Likewise, a diagnostic interval was considered as delayed if longer than seven days[44] but considered as delayed if longer than one month[53] and longer than two months[49] in other studies.

Table 1: Diagnostic timeliness and intervals as assessed by included studies

Study ID	Cancer site	Study design	Country	Diagnostic timeliness and intervals assessed
Agodirin 2020	Breast	Cross-sectional	Nigeria	**Appraisal interval:** time (days) from the detection of first breast symptom to first disclosure (e.g. to partners, family and friends) **Help-seeking interval:** time (days) between symptom detection and first HCP visit **Primary care interval:** time (days) between first HCP visit and first specialist visit **Specialist care interval:** time (days) between symptom detection and first specialist visit
Begoihn 2019	Cervix	Retrospective cohort	Ethiopia	**Patient interval:** time (weeks) between patient reported onset of symptoms and pathological diagnosis
Dianatinasab 2016	Breast	Cross-sectional	Iran	**Delay time:** interval (days) between the date that patient noticed the first breast cancer symptom until the date that pathology report was issued
Dye 2012	Breast	Mixed methods observational	Ethiopia	**Time to action:** time (years) between symptom detection and first HCP visit
Ermiah 2012	Breast	Cross-sectional	Libya	**Consultation time:** time (months) from first symptom to first HCP visit. **Diagnostic time:** time (months) from the date of the first symptoms to the date of final breast cancer diagnosis
Foerster 2020	Breast	Cohort study	Multi-country: Nigeria, Namibia, Uganda and Zambia	**Pre-contact interval:** time (months) between date of symptom discovery to first HCP visit **Post-contact interval:** time (months) between first HCP visit to definitive diagnosis) **Total diagnostic interval:** pre-contact interval + post-contact interval
Gebremariam 2019	Breast	Cross-sectional	Ethiopia	**Patient interval:** time (days) from recognition of first symptom to date of first clinical consultation **Diagnostic interval:** time (days) from first clinical consultation to the date of diagnosis
Grosse Frie 2019	Breast	Cross-sectional	Mali	**Help-seeking interval:** time (days) from date of first symptom recognition to date of first HCP visit. **Diagnostic interval:** time (days) from first HCP visit to date of receiving pathology results
Gyenwali 2014	Cervix	Cross-sectional	Nepal	**Patient delay:** time (days) between symptom awareness and first HCP visit (≥60 days was defined as long) **HCP delay:** time (days) between first HCP visit and final referral by HCP to the cancer diagnostic centre (>7days was defined as long) **Referral delay**: time (days) between the date of final referral to diagnostic centre and first appointment at the cervical cancer diagnostic centre (>7day was referred as long). **Diagnostic waiting time**: time (days) for all relevant investigations of symptoms in the diagnostic centre (>7 days was defined long waiting time). **Total diagnostic delay:** patient delay + HCP delay + referral delay + diagnostic waiting time (>90 days was referred as long)

Jassem 2014	Breast	Cross-secttional	Multi-country: Bulgaria, India, Russia, Serbia and Turkey	**Patient-related delay time:** time (weeks) between the onset of first symptoms and the first medical visit. **System-related delay time:** time (weeks) between the first medical visit and the start of therapy. **Total delay time:** sum of the patient-related delay and system-related delay time
Khaliq 2019	Breast	Cross-sectional	Pakistan	**Patient interval:** time (days) between experiencing signs and symptoms and seeking first care. **Referral interval:** time (days) between presentation and referral to a diagnostic centre; **Diagnostic interval:** time (days) from presentation at a diagnostic centre to receipt of a diagnosis of breast cancer
Khokher 2016	Breast	Cross-sectional	Pakistan	**Diagnostic delay:** time (years) between symptom detection and first HCP visit
Martínez-Pérez 2020	Breast	Cross-sectional study	Colombia	**Patient interval:** time (days) between detection of the first sign/symptom and the first medical consultation. **Provider interval:** time (days) between the first medical consultation and diagnosis by histopathological diagnosis. **Total interval:** time (days) from detection of the first sign/symptom till histopathological diagnosis
Moodley 2016	Breast	Qualitative (In depth interviews)	South Africa	**Appraisal interval:** time (days) between discovery of breast symptoms and perceiving reasons to seek help **Help-seeking interval:** time (days) between perceiving reasons to seek help and presentation to the first HCP **Diagnostic interval:** time (days) between assessment by the first HCP and diagnosis at the tertiary hospital.
Moodley 2018	Breast	Cross-sectional	South Africa	**Patient interval:** time (days) between date of first breast change to date of first HCP consultation **Diagnostic interval:** time (days) between the first HCP visit and the date of diagnosis **Pre-treatment interval:** time (days) between date of diagnosis and the date of scheduled treatment **Total time:** time (days) between a woman noticing the first breast change and the date of scheduled treatment
Mujar 2017	Breast	Cross-sectional	Malaysia	**Patient interval:** time (months) from symptom discovery to first presentation at a primary care facility **Diagnosis interval:** time (months) taken from first presentation to diagnosis
Norsa'adah 2011	Breast	Cross-sectional	Malaysia	**Consultation time:** time (months) from symptom recognition to first general practitioner visit **The time to diagnosis:** time (months) from the date of the recognition of symptoms to the date of final diagnosis **Diagnostic delay:** more than 6 months from the recognition of symptoms to the histological diagnosis
Olarewaju 2019	Breast	Cross-sectional	Nigeria	**Patient interval:** time (months) between symptom detection and HCP visit; delay was considered to be a time lag of greater than 3 months **Time to diagnosis:** time (months) from first HCP visit to a definitive diagnosis; delay was defined as an interval exceeding 2 months
Pace 2015	Breast	Cross-sectional	Rwanda	**Patient delay:** time (months) between symptom detection and first HCP visit. **System delay:** time (months) between the first HCP visit and definitive diagnosis

Poum 2014	Breast	Cross-sectional	Thailand	**Patient delay:** time (days) from first reported symptoms to first HCP consultation **Doctor delay:** time (days) from first HCP consultation to diagnosis of breast cancer
Romanoff 2017	Breast	Cross-sectional	Peru	**Patient-attributable delay:** time (days) from symptom onset to first medical visit **Diagnosis:** based on histology **Health system delay:** time (days) from initial medical consultation at any facility to initiation of treatment
Salih 2016	Breast	Cross sectional	Sudan	**Patient delay:** time (months) between symptom recognition and first HCP visit/consultation.
Shamsi 2020	Breast	Cross-sectional	Pakistan	**Patient delay:** time (months) between the appearance of first symptoms of breast cancer and the date of initial consultation for diagnostic mammography, ultrasonography, or medical advice.
Sharma 2012	Breast	Case-control	Haiti	**Presentation interval:** time (weeks) from discovery of first breast cancer sign or symptom to initial presentation to a HCP; delay defined as an interval of 12 weeks or greater
Shreyamsa 2020	Breast	Cross-sectional	India	**Patient interval:** time (months) between noticing symptoms and first consult with a medical doctor; patient delay is an interval of >3 months **Provider interval:** time (month) between first consultation and starting definitive treatment; provider delay is an interval >1 month
Unger-Saldaña 2018	Breast	Cross-sectional	Mexico	**Patient interval:** time (months) between the identification of the condition and the first medical consultation **Diagnosis interval:** time (months) from the first medical consultation to definitive diagnosis

Breast cancer intervals

Appraisal and help-seeking intervals as separate intervals

Only one study assessed appraisal interval (between the detection of breast symptoms to first disclosure, e.g. to partners, family and friends) and help-seeking interval (between symptom detection and first HCP visit) as separate intervals.[55] The study found a median appraisal interval of 6 days (approximately one week) and a median help-seeking interval of 6 weeks among women (N= 420) with breast cancer in Nigeria.

Patient interval (combination of appraisal and help-seeking intervals)

In most (22/24) of the studies focusing on breast cancer, appraisal and help-seeking intervals were assessed together as a single 'patient interval' or 'time to action' (between the detection of breast symptoms and first HCP visit). The interval ranged from 10 days among breast cancer patients in Mexico (N=886)[52] to 2 weeks in Thailand (N=180)[18]; 3 weeks in Colombia (N=242)[47] and South Africa (N=201)[7]; 4 weeks in Ethiopia (N=441)[42]; 8 weeks in Malaysia (N=328)[48]; 10 weeks in Malaysia (N=340)[54]; 16 weeks in India (N=435)[53]; and Libya (N=200)[40]; 19 weeks in Mali (N=124)[43]; 20 weeks in Rwanda (N=144)[50]; 23 weeks in South Africa (N=20)[19]; 28 weeks in Peru (N=113)[51]; 48 weeks in Sudan (N=63)[58]; 63 weeks in Pakistan (N=449)[59]; and 81 weeks in Ethiopia (N=55).[56] One multi-country study (N=1429) assessed patient intervals for Namibia (1 week in non-black women and 5 weeks in Black women), Nigeria (15 weeks), Uganda (14 weeks) and Zambia (4 weeks).[41] Another multi-country study (N=6588) reported patient intervals for Bulgaria (19 weeks), India (24 weeks), Russia (19 weeks), Serbia (18 weeks) and Turkey (19 weeks).[45]

Diagnostic interval

The majority (16/24) of the studies focusing on breast cancer measured diagnostic intervals (between the first HCP visit and diagnosis of breast cancer). The interval ranged from 3 weeks in Mali (N=124)[43] and Thailand (N=180)[18]; to 4 weeks in South Africa (N=201)[7] and Malaysia (N=340)[54]; 8 weeks in Colombia (N=242)[47]; 10 weeks in Ethiopia (N=441)[42]; 13 weeks in another South African study (N=20)[19]; 15 weeks in Nigeria (N= 420)[55]; 18 weeks in Mexico (N=886)[52]; 20 weeks in Rwanda (N=144)[50]; and 22 weeks in Malaysia (N=328).[48] One multi-country study (N=1429) assessed diagnostic intervals for Namibia (3 weeks in non-black women and 8 weeks in Black women), Nigeria (1 week), Uganda (19 weeks) and Zambia (10 weeks).[41]

Diagnostic endpoints varied across studies, with pathology (histology) being the most commonly used method, while a minority defined diagnosis based on clinical and/or radiological assessment.

Total diagnostic interval (combination of appraisal, help-seeking and diagnostic intervals)

A minority (7/24) breast cancer studies assessed total diagnostic interval (between the awareness of symptoms and diagnosis). This interval ranged from 15 weeks in Colombia (N=242)[47]; to 21 weeks in Iran (N=505)[39]; 30 weeks in Libya (N=200)[40]; 34 weeks in Nigeria (N=420)[55]; 36 weeks in South Africa (N=20)[19]; 60 weeks in Rwanda (N=144).[50] One multi-country study (N=1429) reported total diagnostic intervals for Namibia (10 weeks in non-black women and 26 weeks in Black women), Nigeria (22 weeks), Uganda (45 weeks) and Zambia (33 weeks).[41] Table 2 summarises the intervals.

Cervical cancer intervals

Appraisal and help-seeking intervals as separate intervals

Neither of the two cervical studies assessed appraisal interval (between the detection of cervical symptoms to first disclosure, e.g. to partners, family and friends) and help-seeking interval (between symptom detection and first HCP visit) as separate intervals.

Patient interval (combination of appraisal and help-seeking intervals)

One of the two cervical cancer studies assessed appraisal and help-seeking intervals together as a single 'patient interval' (between the detection of cervical symptoms and first HCP visit). It found a patient interval of 10 weeks among women (N=110) with cervical cancer in Nepal.[44]

Diagnostic interval

One cervical cancer study evaluated diagnostic intervals (between the first HCP visit and diagnosis). It found an interval of 8 weeks among women with cervical cancer in Nepal (N=110).[44]

Total diagnostic interval (combination of appraisal, help-seeking and diagnostic intervals)

Both cervical cancer studies assessed total diagnostic interval (between the awareness of symptoms and diagnosis). The interval was 22 weeks in a cohort of women in Nepal (N=110)[44] and 30 weeks in Ethiopia (N=1575).[38]

Table 2: Diagnostic intervals and factors associated with diagnostic timeliness

Study ID	Cancer site	Country	Appraisal interval (length in weeks)	Help-seeking interval (length in weeks)	Diagnostic interval (length in weeks)	Total diagnostic interval (length in weeks)
Agodirin 2020	Breast	Nigeria	6 (1–28) days (1 week)	42 (7–150) days (6 weeks)	106 (13–337) days (15 weeks)	240 (90–372) days (34 weeks)
Begoihn 2019	Cervix	Ethiopia	30 (0–526) weeks			30 (0–526) weeks
Dianatinasab 2016	Breast	Iran	146 (±188) days 21 weeks			146 (±188) days 21 weeks
Dye 2012	Breast	Ethiopia	1.5 years 81 weeks		NR	NR
Ermiah 2012	Breast	Libya	4 (1-24) months 16 weeks		NR	7.5 (1-25) months 30 weeks
Foerster 2020	Breast	Multi-country: Namibia Nigeria Uganda Zambia	Namibia (Blacks): 1.3 (0.2-6.2) months (5 weeks) Namibia (non-Black): 0.3 (0.0-2.1) months (1 week) Nigeria: 3.7 (1.0 – 8.1) months (15 weeks) Uganda: 3.5 (1.0-9.9) months 14 weeks Zambia: 1.1 (0.2-9.1) months (4 weeks)		Namibia (Blacks): 2.0 (0.5-7.0) months (8 weeks) Namibia (non-Black): 0.7 (0.2-2.9) months (3 weeks) Nigeria: 0.2 (0.0-3.0) months (1 week) Uganda: 4.7 (1.3-11.8) months (19 weeks) Zambia: 2.6 (1.1-9.9) months (10 weeks)	Namibia (Blacks): 6.5 (2.3-13.1) months (26 weeks) Namibia (non-Black): 2.4 (0.6-5.5) months (10 weeks) Nigeria: 5.6 (2.3-13.1) months (22 weeks) Uganda: 11.3 (5.7-21.2) months (45 weeks) Zambia: 8.2 (3.4-16.4) months (33 weeks)
Gebremariam 2019	Breast	Ethiopia	30 (6–132) days (4 weeks)		69 (22–213) days (10 weeks)	NR
Grosse Frie 2019	Breast	Mali	91 (IQR NR) days 13 weeks		21 (IQR NR) days 3 weeks	NR
Gyenwali 2014	Cervix	Nepal	68 (8-404) days (10 weeks)		54 (0-582) days (8 weeks)	157 (22-718) days (22 weeks)
Jassem 2014	Breast	Multi-country: Bulgaria India	Bulgaria 4.83 (±0.22) months (19 weeks) India 6.10 ((±0.33) months (24 weeks)		NR	NR

		Russia Serbia Turkey	Russia 4.81 0.17) months (19 weeks) Serbia 4.47 (±0.19) months (18 weeks) Turkey 4.84 (±0.18) months (19 weeks)		
Khaliq 2019	Breast	Pakistan	31 to 128 days (4 – 18 weeks)	Referral interval: 7 -194 days (1-27 weeks) Diagnostic interval: 15 -30 days (2-4 weeks)	NR
Khokher 2016	Breast	Pakistan	<1 year for 70% of patients (<52 weeks)	NR	NR
Martínez-Pérez 2020	Breast	Colombia	20 (IQR NR) days (3 weeks)	53 (IQR NR) days (8 weeks)	104.5 (IQR NR) days (15 weeks)
Moodley 2016	Breast	South Africa	164 days (average) (23 weeks)	92 days (average) (13 weeks)	256 days (average) (36 weeks)
Moodley 2018	Breast	South Africa	23 (6–64) days (3 weeks)	28 (13–58) days (4 weeks)	NR
Mujar 2017	Breast	Malaysia	2.4 (0-120) months (10 weeks)	1 (0-9.3) months (4 weeks)	NR
Norsa'adah 2011	Breast	Malaysia	2 (0-132) months (8 weeks)	NR	5.5 (0-192) months (22 weeks)
Olarewaju 2019	Breast	Nigeria	≤3 months for 65% of patients (≤12 weeks)	≤2 months for 70% of patients (≤8 weeks)	NR
Pace 2015	Breast	Rwanda	5 (1–13) months (20 weeks)	5 (2–14) months (20 weeks)	15 (8–32) months (60 weeks)
Poum 2014	Breast	Thailand	12 (IQR NR) days (2 weeks)	21 (IQR NR) days (3 weeks)	NR
Romanoff 2017	Breast	Peru	198 (±449) days (28 weeks)	NR	NR
Salih 2016	Breast	Sudan	11.9 (±11.2) months (48 weeks)	NR	NR
Shamsi 2020	Breast	Pakistan	15.7 months (±25.9) 63 weeks	NR	NR
Sharma 2012	Breast	Haiti	1 (1-4) week in 58% of the patients 26 (17-77) weeks in 42% of the patients	NR	NR

Shreyamsa 2020	Breast	India	4 (0-24) months (16 weeks)	NR	NR
Unger-Saldaña 2018	Breast	Mexico	10 (IQR NR) days (1 week)	128 (IQR NR) days (18 weeks)	NR

NR; not reported

Factors associated with diagnostic timeliness

Appraisal and health-seeking intervals

Supplementary Table 2 summarises the factors associated with diagnostic timeliness and interval lengths across studies. Women who reported the presence of a family history of breast cancer[59], women who reported the fear of breast cancer[45], and those that initially visited private clinics/tertiary hospitals[43] tended to have shorter help-seeking intervals. Also, being employed[45], receiving supports from family/friends[45], living in big cities[45], receiving correct advice[55], presence of a large tumor[55], and worsening of, or development of new, symptoms[56] were associated with shorter health-seeking interval. Longer help-seeking intervals were associated with not practising self-breast examination[40,51], older age[40,42,50], not receiving a cervical examination at first consultation[44], living in rural areas or farther away from cities[38,52], having ≥5 children[42], low health literacy level[7,40,42,58-60], use of traditional/complementary medicine[42,50,54,59], lower socioeconomic status[42,52,58,59] and living in denial.[7,52] Higher family income[18], fear of high treatment cost[60], self-medication[18)], nondisclosure[52], and seeking medical advice from family or friends[18] were also associated with longer help-seeking intervals.

Diagnostic interval

Shorter diagnostic delay was associated with higher educational level[39], urban residence[39], ability to conduct self-breast exam)[39], and self-detection of lump.[39] On the other hand, longer diagnostic interval was associated with wrong attribution of symptoms[41,48], low heath literacy[19,41,44,53], symptom denial[7], presence of co-mobidities[7], unemployment[18,46], lower socioeconomic status[41,52,53], older age[18,44,46,47,49], being unmarried[41,49], lay beliefs[41], residing far from a health facility[41,44,53] and longer travel time.[18] Other factors associated with longer diagnostic interval were lack of cervical examination at first consultation[44], seeking care from multiple health practitioners and complementary/alternative care before diagnosis[18,46,48,50,54], health-seeking in government subsidised facilities[47], referral delays[53], false negative diagnosis[48,53], and poor treatment behaviour.[48] Notably, patients who initially visited private clinics/tertiary hospitals tended to have shorter help-seeking intervals but longer diagnostic delays.[43]

Discussion

Addressing the barriers to early diagnosis of breast and cervical cancer requires a sound understanding of diagnostic timeliness, intervals and delays, and the factors associated with them. This review offers up-to-date evidence with which to bolster that understanding. Overall, it demonstrates that patient-related and health-system-related delays are common in LMICs. However, it is difficult to infer and compare findings across studies owing to variations in how diagnostic time, events, intervals and delays were conceptualised and assessed. While the amount of evidence identified points to the substantial and growing attention paid to early breast and cervical cancer in LMICs over the past decade, this review has also identified gaps both in terms of quantity and methodological diversity of the available literature.

The current evidence shows a dearth of studies evaluating the timeliness of cervical cancer diagnosis, with only two of such studies identified in this review (constituting <10% of studies found). This is despite the substantial burden of cervical cancer and late-stage diagnosis in LMICs.[1-5] Consistent with finding from previous reviews of cancer diagnostic delays[10,61], a major methodological issue identified by this review is the marked variability in the conceptualisation and operationalisation of the time to diagnosis and corresponding intervals. In spite of the availability of validated tools and methods for evaluating cancer diagnostic timeliness, a minority of the studies reported the use of such tools in the context of breast and cervical cancer – including the Anderson model[48,58], the Model of Pathways to Treatment[7,19,43,55] and the Aarhus Statement.[42,46]

The studies varied considerably in the use of common terminologies relating to diagnostic events and intervals. There were also variations in the thresholds used for defining delays. For instance, a patient interval was considered as delayed if longer than two months in one study[44], whereas two other studies considered it as delayed if longer than three months.[49,53] Similarly, different time-points were used to define intervals. For instance, the endpoint for diagnosis was operationalised as the date of diagnosis based on clinical or imaging evaluation in some studies, while it was the date of pathological diagnosis in others. It is therefore important to standardise methods of assessing and reporting of diagnostic endpoints, one approach of which are the European Network of Cancer Registries (ENCR) guidelines.[62] The wide discrepancy between the estimated patient-related intervals of 4 weeks and 81 weeks among women with breast cancer in Ethiopia, as reported by two different studies[42,56], starkly

reflects such within-country variations. These further complicate the interpretation and comparison of findings across studies.

Patient-related intervals and delays were more frequently evaluated and reported than provider- and health system-related ones. This is consistent with the findings of a previous review on cancer diagnostic delays in LMICs.[10] The trend may be a reflection of the patient-sided way in which diagnostic delays are currently perceived in LMICs and underscores the need for more balanced and system-wide approaches to assessing and understanding the barriers to early diagnosis of breast and cervical cancer diagnostic. It also has important implications for policy and practice. For instance, focusing on patient-centred strategies such as improving awareness, without addressing provider- and health system-related factors may yield limited results.

It is noteworthy that most of the studies that assessed and reported patient-related intervals did not evaluate the appraisal interval as a distinct form of patient-related interval, but rather assessed the appraisal and help-seeking intervals as a single interval. Only two studies made such distinction.[7,55] This highlights the need for more attention to be paid to this interval among women with breast and cervical cancer symptoms as a distinct and important aspect of their journey from symptom awareness to treatment. To develop evidence-based policies and holistic interventions for addressing diagnostic delays and barriers to early cancer diagnosis in LMICs, it is imperative to understand the time and events that characterise patients' journey from the perception of bodily changes to discerning the need and urgency to seek help, as these will ultimately influence time to diagnosis and treatment.

Our review also identified a multiplicity of patient and health system-related factors associated with diagnostic timeliness and delay across specific diagnostic intervals. While the factors influencing one interval (such as the help-seeking interval) might be distinct (at least empirically) from those affecting other intervals (such as the diagnostic or provider interval), this may not be so in practice as the length of each interval is likely to be the result of a complex interplay between patient and health system drivers. For instance, women may delay help-seeking not only due to patient-related factors (such as having a low level of cancer awareness) but also due to health-system factors such as the non-availability of a health facility or HCPs.

Likewise, women with symptoms of cancer presenting at health facilities may delay definitive diagnosis following referral, due to fear of the consequences of being diagnosed with cancer (such as mastectomy, stigma and death). Hence, it is essential that these interrelationships are taken into consideration when conceptualising, evaluating and interpreting diagnostic intervals and the factors associated with them. We again emphasise the importance of standardising the assessment and reporting of cancer diagnostic intervals, to improve the translation of research findings and to better inform interventions for addressing the growing public health challenge of delayed breast and cervical cancer in resource-limited settings.

Limitations

While our review adds significantly to the existing body of literature on cancer diagnostic timeliness in LMIC contexts, it is not without limitations. First, as has been acknowledged earlier, the heterogeneous nature of the studies and the use of non-standardised methods limit the interpretation and comparability of findings. Besides, the small sample size and non-representativeness of participants of some of the studies limited both internal and external validity of the studies, making it difficult to interpret findings in the context of their reference geographic populations.

The cross-sectional retrospective nature of many of the studies and the reliance on patients' recall to estimate events such as the time they first discovered their symptoms come with the risk of recall bias. These also come with the potential of social desirability bias that can lead to under-estimation of patient and diagnostic delays. Another important limitation of this review is that, as in most scoping reviews; a formal quality appraisal of included literature was not conducted. As such, the strength of the evidence cannot be ascertained. Lastly, while our literature search was comprehensive, it is possible that the review did not include all relevant literature available, as some may not have been accessible at the time search.

Conclusions

Despite the significant burden of breast and cervical cancer in LMICs, there is limited evidence on the timeliness of diagnosis of both cancers. Available evidence demonstrates between- and within-country variations in how diagnostic timeliness and intervals of breast and cervical cancer are conceptualised and measured in LMICs. Such variations underscore the need for the increased use of validated and standardised tools for assessing diagnostic timeliness in

more reproducible and comparable ways to more accurately inform interventions for addressing the growing public health problem of diagnostic delays in LMICs.

Ethics approval

This is a scoping review of publicly available literature, with no primary data collection. Hence, it did not require ethics approval.

Authors' contributions: JM conceived the study and provided conceptual guidance for the design of the protocol. CAN wrote the first draft of the manuscript. PK, FMW and JM supported the refinement of the study protocol. CAN and PK performed literature search and study selection. CAN and EE conducted full text review, data extraction and analysis. JM and FMW provided critical insights and guided the coherence of the manuscript. All authors have contributed to, and approved, the final version of the manuscript.

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Patient consent for publication: Not required.

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Supplementary files

Figure 1: PRISMA flow chart of the study selection process

Figure 2: Geographical distribution of included studies

Appendix: Search strategies

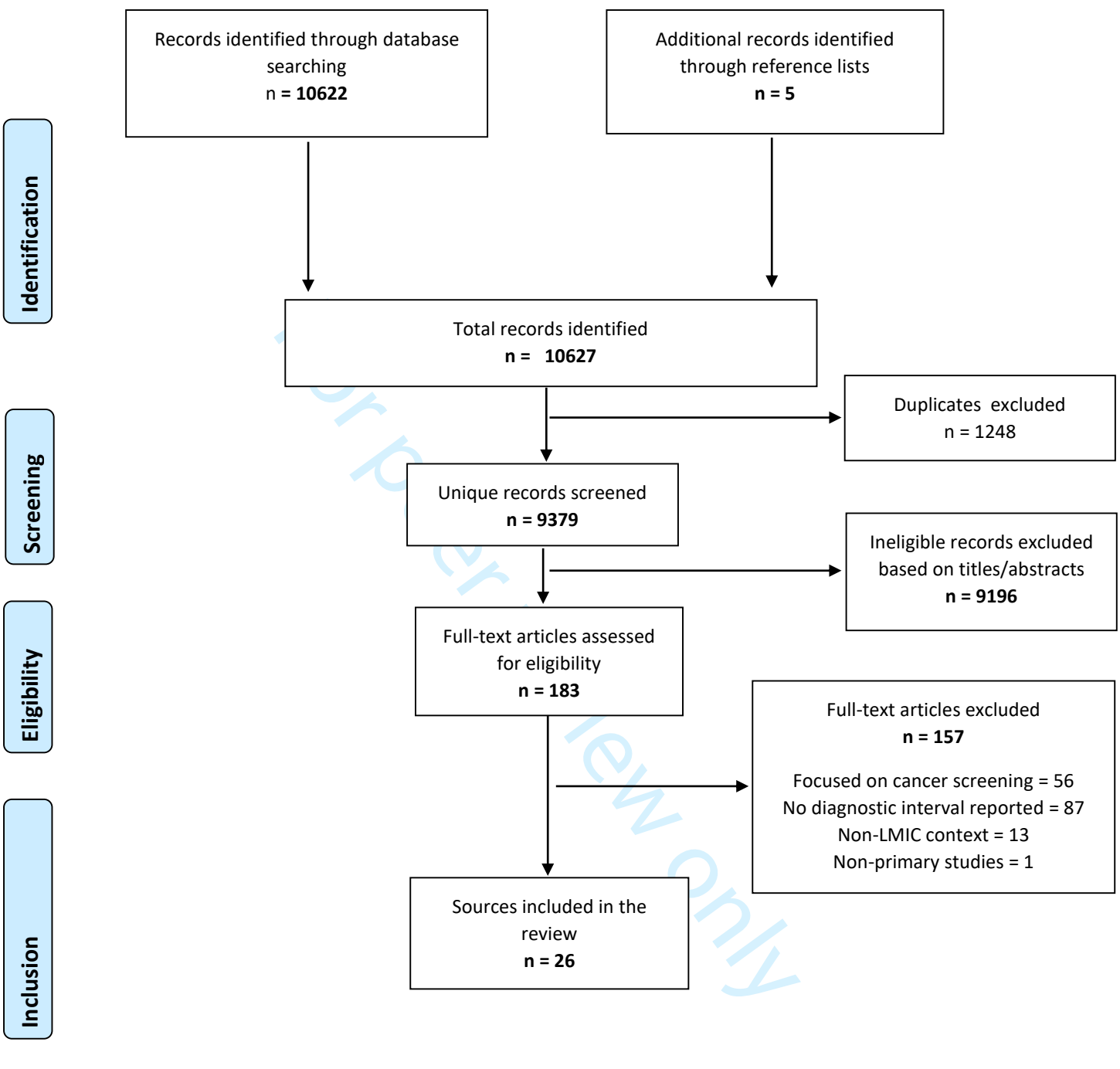

Figure 1: PRISMA flow diagram showing study selection process

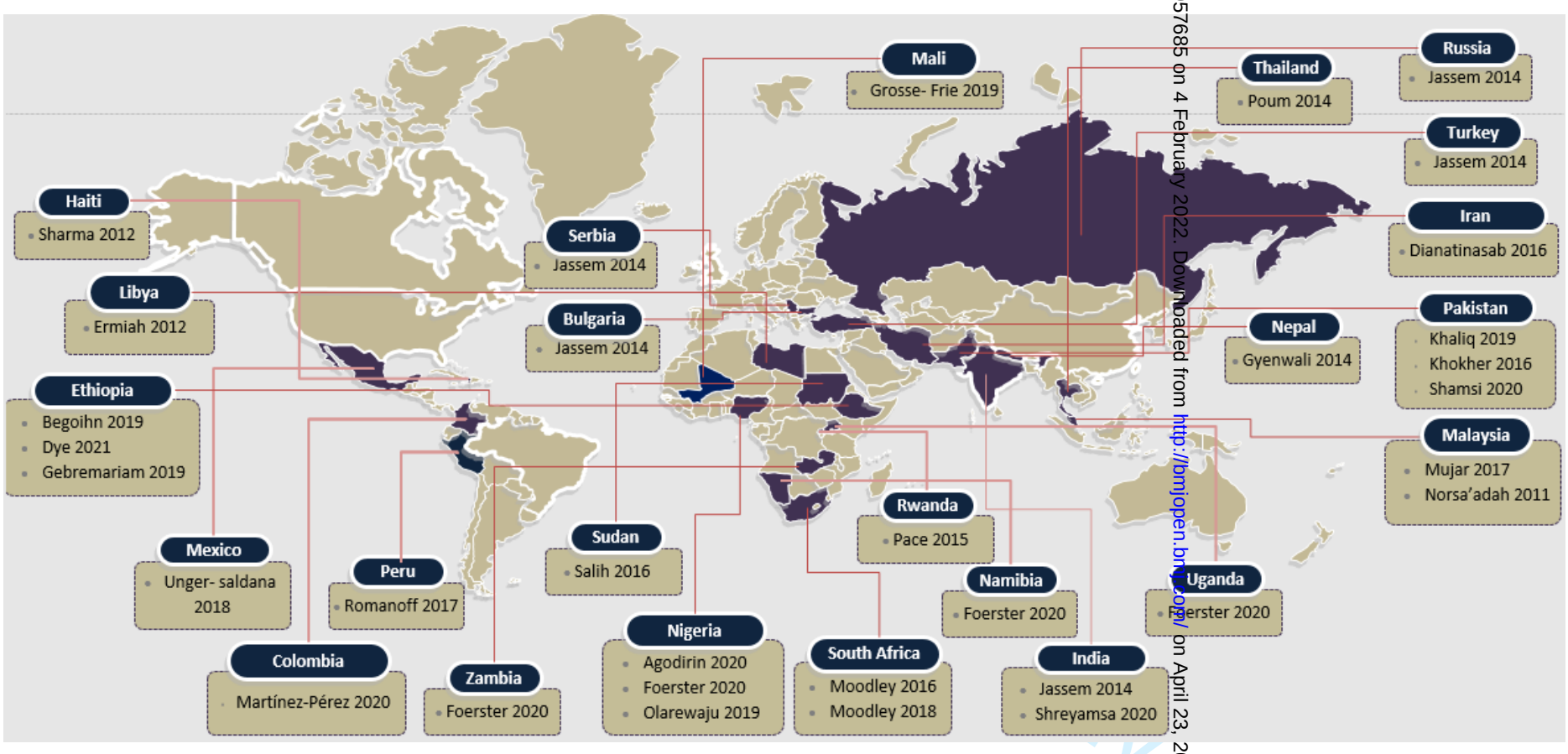

Figure 2: Geographical distribution of included studies (map created by authors using an open-source template sourced from https://yourfreetemplates.com/)

Appendix: Search strategies

Search strategy for MEDLINE (via PubMed); last searched 20 May 2021

Search #	Search Texts and Syntaxes
#1	Breast Neoplasms [Mesh] OR Breast cancer[Title/Abstract] OR breast[Title/Abstract] OR cervical cancer[Title/Abstract] OR cervix[Title/Abstract] OR cancer[Title/Abstract] OR malignant[Title/Abstract] OR neoplasm[Title/Abstract] OR neoplasia[Title/Abstract] OR malignancy[Title/Abstract] OR tumour[Title/Abstract]
#2	Diagnosis [Mesh] OR diagnostic[Title/Abstract] OR diagnosis[Title/Abstract] OR diagnosis[Title/Abstract] OR detection[Title/Abstract] OR discovery[Title/Abstract] OR Patient navigation[Title/Abstract] OR Patient pathway[Title/Abstract] OR care continuum[Title/Abstract]
#3	early[Title/Abstract] OR timely[Title/Abstract] OR time[Title/Abstract] OR late[Title/Abstract] OR delay[Title/Abstract]
#4	#2 AND #3
#5	Developing Countries OR Developing Country OR Developing Economies OR Developing Economy OR Developing Nation OR Developing Nations OR Developing Population OR Developing Populations OR Developing World OR LAMI Countries OR LAMI Country OR Less Developed Countries OR Less Developed Country OR Less Developed Economies OR Less Developed Nation OR Less Developed Nations OR Less Developed World OR Lesser Developed Countries OR Lesser Developed Nations OR LMIC OR LMICS OR Low GDP OR Low GNP OR Low Gross Domestic OR Low Gross National OR Low Income OR Lower GDP OR lower gross domestic OR Lower Income OR Middle Income OR Poor Countries OR Poor Country OR Poor Economies OR Poor Economy OR Poor Nation OR Poor Nations OR Poor Population OR Poor Populations OR poor world OR Poorer Countries OR Poorer Economies OR Poorer Economy OR Poorer Nations OR Poorer Population OR Poorer Populations OR Third World OR Transitional Countries OR Transitional Country OR Transitional Economies OR Transitional Economy OR Under Developed Countries OR Under Developed Country OR under developed nations OR Under Developed World OR Under Served Population OR Under Served Populations OR Underdeveloped Countries OR Underdeveloped Country OR underdeveloped economies OR underdeveloped nations OR underdeveloped population OR Underdeveloped World OR Underserved Countries OR Underserved Nations OR Underserved Population OR Underserved Populations OR Afghanistan OR Albania OR Algeria OR American Samoa OR Angola OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Byelarus OR Belorussia OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia OR Botswana OR Brazil OR Bulgaria OR Burma OR Burkina Faso OR

	Burundi OR Cabo Verde OR Cape Verde OR Cambodia OR Cameroon OR Central African Republic OR Chad OR China OR Colombia OR Comoros OR Comores OR Comoro OR Congo OR Costa Rica OR Côte d'Ivoire OR Cuba OR Djibouti OR Dominica OR Dominican Republic OR Ecuador OR Egypt OR El Salvador OR Equatorial Guinea OR Eritrea OR Ethiopia OR Fiji OR Gabon OR Gambia OR Gaza OR Georgia OR Georgia Republic OR Ghana OR Grenada OR Grenadines OR Guatemala OR Guinea OR Guinea- Bissau OR Guyana OR Haiti OR Herzegovina OR Hercegovina OR Honduras OR India OR Indonesia OR Iran OR Iraq OR Ivory Coast OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Democratic People's Republic of Korea OR Kosovo OR Kyrgyz OR Kirghizia OR Kirghiz OR Kyrgyzstan OR Lao PDR OR Laos OR Lebanon OR Lesotho OR Liberia OR Libya OR Macedonia OR Madagascar OR Malawi OR Malay OR Malaya OR Malaysia OR Maldives OR Mali OR Marshall Islands OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Palau OR Papua New Guinea OR Paraguay OR Peru OR Philippines OR Principe OR Romania OR Ruanda OR Rwanda OR Samoa OR Sao Tome OR Senegal OR Serbia OR Sierra Leone OR Solomon Islands OR Somalia OR South Africa OR South Sudan OR Sri Lanka OR St Lucia OR St Vincent OR Sudan OR Surinam OR Suriname OR Swaziland OR Syria OR Syrian Arab Republic OR Tajikistan OR Tadzhikistan OR Tajikistan OR Tadzhik OR Tanzania OR Thailand OR Timor OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmen OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uzbek OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR West Bank OR Yemen OR Zambia OR Zimbabwe
#6	#1 AND #4 AND #5

Search strategy for Scopus; last searched 20 May 2021

Search #	Search Texts and Syntaxes
#1	(Breast cancer) OR breast OR (cervical cancer) OR cervix OR cancer OR malignant OR neoplasm OR neoplasia OR malignancy OR tumour
#2	Diagnosis OR diagnostic OR diagnosis OR diagnosis OR detection OR discovery OR (Patient navigation) OR (Patient pathway) OR (care continuum)
#3	Early OR timely OR time OR late OR delay OR interval
#4	#2 AND #3

#5	TITLE-ABS-KEY “Deprived Countries” OR “Deprived Population” OR “Deprived Populations” OR “Developing Countries” OR “Developing Country” OR “Developing Economies” OR “Developing Economy” OR “Developing Nation” OR “Developing Nations” OR “Developing Population” OR “Developing Populations” OR “Developing World” OR “LAMI Countries” OR “LAMI Country” OR “Less Developed Countries” OR “Less Developed Country” OR “Less Developed Economies” OR “Less Developed Nation” OR “Less Developed Nations” OR “Less Developed World” OR “Lesser Developed Countries” OR “Lesser Developed Nations” OR LMIC OR LMICS OR “Low GDP” OR “Low GNP” OR “Low Gross Domestic” OR “Low Gross National” OR “Low Income” OR “Lower income” OR “Lower GDP” OR “Lower Gross Domestic” OR “Middle Income” OR “Poor Countries” OR “Poor Country” OR “Poor Economies” OR “Poor Economy” OR “Poor Nation” OR “Poor Nations” OR “Poor Population” OR “Poor Populations” OR “poor world” OR “Poorer Countries” OR “Poorer Economies” OR “Poorer Economy” OR “Poorer Nations” OR “Poorer Population” OR “Poorer Populations” OR “Third World” OR “Transitional Countries” OR “Transitional Country” OR “Transitional Economies” OR “Transitional Economy” OR “Under Developed” OR “Under Served” OR “Underdeveloped Countries” OR “Underdeveloped Country” OR “underdeveloped economies” OR “underdeveloped nations” OR “underdeveloped population” OR “Underdeveloped World” OR “Underserved Countries” OR “Underserved Nations” OR “Underserved Population” OR “Underserved Populations” OR Afghanistan OR Albania OR Algeria OR “American Samoa” OR Angola OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Byelarus OR Belorussia OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia OR Botswana OR Brazil OR Bulgaria OR Burma OR “Burkina Faso” OR Burundi OR “Cabo Verde” OR “Cape Verde” OR Cambodia OR Cameroon OR “Central African Republic” OR Chad OR China OR Colombia OR Comoros OR Comores OR Comoro OR Congo OR “Costa Rica” OR “Côte d'Ivoire” OR Cuba OR “Democratic People’s Republic of Korea” OR Djibouti OR Dominica OR “Dominican Republic” OR Ecuador OR Egypt OR “El Salvador” OR Eritrea OR Ethiopia OR “Equatorial Guinea” OR Fiji OR Gabon OR Gambia OR Gaza OR “Georgia Republic” OR Georgia OR Ghana OR Grenada OR Grenadines OR Guatemala OR Guinea OR “Guinea Bissau” OR Guyana OR Haiti OR Herzegovina OR Hercegovina OR Honduras OR India OR Indonesia OR Iran OR Iraq OR “Ivory Coast” OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyz OR Kirghizia OR Kirghiz OR Kyrgyzstan OR “Lao PDR” OR Laos OR Lebanon OR Lesotho OR Liberia

	OR Libya OR Macedonia OR Madagascar OR Malawi OR Malay OR Malaya OR Malaysia OR Maldives OR Mali OR "Marshall Islands" OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Palau OR Papua New Guinea OR Paraguay OR Peru OR Philippines OR Principe OR Romania OR Rwanda OR Ruanda OR Samoa OR "Sao Tome" OR Senegal OR Serbia OR "Sierra Leone" OR "Solomon Islands" OR Somalia OR "South Africa" OR "South Sudan" OR "Sri Lanka" OR "St Lucia" OR "St Vincent" OR Sudan OR Surinam OR Suriname OR Swaziland OR Syria OR "Syrian Arab Republic" OR Tajikistan OR Tadzhikistan OR Tajikistan OR Tadzhik OR Tanzania OR Thailand OR Timor OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmen OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uzbek OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR "West Bank" OR Yemen OR Zambia OR Zimbabwe
#6	#1 AND #4 AND #5

CINAHL search strategy; last searched 20 May 2021

1. MH: "Breast Neoplasms" OR "Breast cancer" OR breast OR "cervical cancer" OR cervix OR cancer OR malignant OR neoplasm OR neoplasia OR malignancy OR tumour
2. Diagnosis OR diagnostic OR diagnosis OR diagnosis OR detection OR discovery OR "Patient navigation" OR "Patient pathway" OR "care continuum"
3. early OR timely OR time OR late OR delay
4. #2 AND #3
5. "Deprived Countries" OR "Deprived Population" OR "Deprived Populations" OR "Developing Countries" OR "Developing Country" OR "Developing Economies" OR "Developing Economy" OR "Developing Nation" OR "Developing Nations" OR "Developing Population" OR "Developing Populations" OR "Developing World" OR "LAMI Countries" OR "LAMI Country" OR "Less Developed Countries" OR "Less Developed Country" OR "Less Developed Economies" OR "Less Developed Nation" OR "Less Developed Nations" OR "Less Developed World" OR "Lesser Developed Countries" OR "Lesser Developed Nations" OR LMIC OR LMICS OR "Low GDP" OR "Low GNP" OR "Low Gross Domestic" OR "Low Gross National" OR "Low Income" OR "Lower income" OR "Lower GDP" OR "Lower Gross Domestic" OR "Middle Income" OR "Poor Countries" OR "Poor Country" OR "Poor Economies" OR "Poor Economy" OR "Poor Nation" OR "Poor Nations" OR "Poor Population" OR "Poor Populations" OR "poor

world" OR "Poorer Countries" OR "Poorer Economies" OR "Poorer Economy" OR "Poorer Nations" OR "Poorer Population" OR "Poorer Populations" OR "Third World" OR "Transitional Countries" OR "Transitional Country" OR "Transitional Economies" OR "Transitional Economy" OR "Under Developed" OR "Under Served" OR "Underdeveloped Countries" OR "Underdeveloped Country" OR "underdeveloped economies" OR "underdeveloped nations" OR "underdeveloped population" OR "Underdeveloped World" OR "Underserved Countries" OR "Underserved Nations" OR "Underserved Population" OR "Underserved Populations" OR Afghanistan OR Albania OR Algeria OR "American Samoa" OR Angola OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Byelarus OR Belorussia OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia OR Botswana OR Brazil OR Bulgaria OR Burma OR "Burkina Faso" OR Burundi OR "Cabo Verde" OR "Cape Verde" OR Cambodia OR Cameroon OR "Central African Republic" OR Chad OR China OR Colombia OR Comoros OR Comores OR Comoro OR Congo OR "Costa Rica" OR "Côte d'Ivoire" OR Cuba OR "Democratic People's Republic of Korea" OR Djibouti OR Dominica OR "Dominican Republic" OR Ecuador OR Egypt OR "El Salvador" OR Eritrea OR Ethiopia OR "Equatorial Guinea" OR Fiji OR Gabon OR Gambia OR Gaza OR "Georgia Republic" OR Georgia OR Ghana OR Grenada OR Grenadines OR Guatemala OR Guinea OR "Guinea Bissau" OR Guyana OR Haiti OR Herzegovina OR Hercegovina OR Honduras OR India OR Indonesia OR Iran OR Iraq OR "Ivory Coast" OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyz OR Kirghizia OR Kirghiz OR Kyrgyzstan OR "Lao PDR" OR Laos OR Lebanon OR Lesotho OR Liberia OR Libya OR Macedonia OR Madagascar OR Malawi OR Malay OR Malaya OR Malaysia OR Maldives OR Mali OR "Marshall Islands" OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Palau OR Papua New Guinea OR Paraguay OR Peru OR Philippines OR Principe OR Romania OR Rwanda OR Ruanda OR Samoa OR "Sao Tome" OR Senegal OR Serbia OR "Sierra Leone" OR "Solomon Islands" OR Somalia OR "South Africa" OR "South Sudan" OR "Sri Lanka" OR "St Lucia" OR "St Vincent" OR Sudan OR Surinam OR Suriname OR Swaziland OR Syria OR "Syrian Arab Republic" OR Tajikistan OR Tadzhikistan OR Tajikistan OR Tadzhik OR Tanzania OR Thailand OR Timor OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmen OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uzbek OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR "West Bank" OR Yemen OR Zambia OR Zimbabwe

6. #1 AND #4 AND #5

Cochrane CENTRAL search strategy; last searched 20 May 2021

1. Breast Neoplasms OR Breast cancer OR breast OR cervical cancer OR cervix OR cancer OR malignant OR neoplasm OR neoplasia OR malignancy OR tumour

2. Diagnosis OR diagnostic OR diagnosis OR diagnosis OR detection OR discovery OR Patient navigation OR Patient pathway OR care continuum
3. early OR timely OR time OR late OR delay
4. #2 AND #3
5. #1 AND #4

WHO ICTRP search strategy; last searched 20 May 2021

breast cancer (OR cervical cancer] AND early (OR timely OR timeliness OR delay) AND diagnosis

Supplementary Table 1: Characteristics of included studies

Study ID	Cancer site	Study design	Country	Study setting	Participant characteristics	Methods/tools used for assessing diagnostic timeliness and intervals
Agodirin 2020	Breast	Cross-sectional	Nigeria	Health facility; urban	420 women with newly diagnosed breast cancer Age range: 24-95 years	**Data collection tool:** structured questionnaire **Definition of diagnostic events and intervals:** adapted from the MPT and AS **Diagnosis:** based on specialist evaluation
Begoihn 2019	Cervix	Retrospective cohort	Ethiopia	Health facility; rural and urban	1575 women with primary diagnosis of invasive cervical cancer Mean age: 49 ±11.6 years HIV+: 135/8.6%	**Data collection tool:** patients' medical records **Definition of diagnostic events and intervals:** authors **Diagnosis:** based on histology
Dianatinasab 2016	Breast	Cross-sectional	Iran	Health facility; rural and urban	505 women with newly diagnosed breast cancer Mean age: 47.8 ±10.65 years	**Data collection tool:** Questionnaire (pre-tested and revised with a pilot study) **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology
Dye 2012	Breast	Mixed methods observational	Ethiopia	Health facility; urban	55 women diagnosed with breast cancer Age: <50 years	**Data collection tool:** Structured questionnaire and qualitative interviews
Ermiah 2012	Breast	Cross-sectional	Libya	Health facility; urban	200 women with breast cancer Median age: 45.4 (22–75) years	**Data collection tool:** Questionnaire and patients' medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology
Foerster 2020	Breast	Cohort study	Multi-country: Nigeria Namibia Uganda Zambia	Health facility; rural and urban	1429 women diagnosed with breast cancer Mean age: 50.1 years	**Data collection tool:** ABC-DO study questionnaire **Diagnostic events and intervals definition:** authors **Diagnosis:** based on ENCR guidelines (prioritising histology. If histological confirmation was not available, diagnosis was based on clinical history or imaging).
Gebremariam 2019	Breast	Cross-sectional	Ethiopia	Health facilities; urban	441 women with newly diagnosed breast cancer Mean age: 44.4 ±12.2 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the AS **Diagnosis:** based on histology

Grosse Frie 2019	Breast	Cross-sectional	Mali	Health facility; urban	124 women with breast-related symptoms Age range: 16-80 years	**Data collection tool:** Questionnaire and health/pathological records **Diagnostic events and intervals definition:** adapted from the MPT **Diagnosis:** based on histology
Gyenwali 2014	Cervix	Cross-sectional	Nepal	Health facility; urban	110 women diagnosed with cervical cancer Mean age: 52.72 ±10.6 years	**Data collection tool:** Questionnaire (pre-tested) **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology
Jassem 2014	Breast	Cross-secttional	Multi-country: Bulgaria, India, Russia, Serbia and Turkey	Health facility; rural and urban	6588 women with breast cancer Age: majority were aged 40–69 years	**Data collection tool:** Questionnaires administered during nation-wide surveys **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology
Khaliq 2019	Breast	Cross-sectional	Pakistan	Health facility; urban	200 women diagnosed with breast cancer Mean age: 45 ±14.25 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the AS **Diagnosis:** based on histology
Khokher 2016	Breast	Cross-sectional	Pakistan	Health facility; urban	261 2omen with breast cancer Mean age: 46.8±13 years	**Data collection tool:** medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on clinical assessment
Martínez-Pérez 2020	Breast	Cross-sectional study	Colombia	Health facility; urban	242 women diagnosed with breast cancer Age: >18 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from a previously validated tool **Diagnosis:** based on histology
Moodley 2016	Breast	Qualitative (In depth interviews)	South Africa	Health facility; urban	20 newly diagnosed breast cancer patients Mean age: 52 years (range 30–74 years)	**Data collection tool:** Interview questions **Diagnostic events and intervals definition:** adapted from the MPT **Diagnosis:** based on histology
Moodley 2018	Breast	Cross-sectional	South Africa	Health facility; urban	201 newly diagnosed breast cancer patients Median age: 54 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the MPT

						Diagnosis: based on histology
Mujar 2017	Breast	Cross-sectional	Malaysia	Health facility; urban	340 newly diagnosed women with breast Median age: 53 (23 to 74) years	**Data collection tool:** Questionnaires and medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** method not specified
Norsa'adah 2011	Breast	Cross-sectional	Malaysia	Health facility; urban	328 women with histological diagnosis of BC Mean age: 47.9 ±9.4 years.	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the Andersen Model **Diagnosis:** based on histology
Olarewaju 2019	Breast	Cross-sectional	Nigeria	Health facility; urban	275 women with breast cancer Mean age: 49± 11.9 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology
Pace 2015	Breast	Cross-sectional	Rwanda	Health facility; rural	144 women with BC complaints Median age: 49 years	**Data collection tool:** Questionnaires and medical records **Diagnostic events and intervals definition:** adapted from a previous study **Diagnosis:** based on histology
Poum 2014	Breast	Cross-sectional	Thailand	Health facility; urban	180 women with newly diagnosed invasive breast cancer Mean age: 50±11 years	**Data collection tool:** Questionnaire and medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on histology
Romanoff 2017	Breast	Cross-sectional	Peru	Health facility; urban	113 women with breast cancer Mean age: 54± 10.8 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from a previously validated tool) and medical records **Patient-attributable delay:** time (days) from symptom onset to first medical visit **Diagnosis:** based on histology
Salih 2016	Breast	Cross sectional	Sudan	Health facility; urban	63 women with breast cancer Mean age: 46.89 ±14.99 years	**Data collection tool:** Questionnaire **Diagnostic events and intervals definition:** adapted from the Andersen model **Diagnosis:** based on clinical assessment.
Shamsi 2020	Breast	Cross-sectional	Pakistan	Health facility; rural and urban	499 women diagnosed with breast cancer Mean age: 48.0±12.3 years	**Data collection tool:** Questionnaire (pre-tested) and patients' medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on clinical assessment and imaging

Sharma 2012	Breast	Case-control	Haiti	Health facility; rural	90 women with breast cancer symptoms Median age: 45 (39–53) years	**Data collection tool:** Patients' medical records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on clinical assessment
Shreyamsa 2020	Breast	Cross-sectional	India	Health facility; rural	435 mostly persons (mostly women but including 3 men) diagnosed with breast cancer Age: majority >40 years	**Data collection tool:** Questionnaire and patients' records **Diagnostic events and intervals definition:** authors **Diagnosis:** based on clinical assessment
Unger-Saldaña 2018	Breast	Cross-sectional	Mexico	Health facility; urban	886 newly referred women with probable breast cancer Mean age: 50.9 ±13.17 years	**Data collection tool:** Questionnaire and patients' records **Diagnostic events and intervals definition:** adapted from the AS **Diagnosis:** based on histology

Aarhus statement (AS); HCP (Health care provider); Model of pathways to treatment (MPT); NR (Not reported), IQR (Interquartile range); European Network of Cancer Registries guidelines (ENCR)

Supplementary Table 2: Factors associated with diagnostic timeliness and interval lengths

Study ID	Cancer site	Country setting	Factors associated with diagnostic timeliness
Agodirin 2020	Breast	Nigeria	Receiving correct advice and having a large tumour were associated with shorter health seeking interval
Begoihn 2019	Cervix	Ethiopia	Patients residing in rural are more likely to have longer patient intervals than those in urban areas.
Dianatinasab 2016	Breast	Iran	Shorter diagnostic delay was associated with higher education, urban residence, screening behaviour (ability to conduct self-breast exam), ductal carcinoma and detection of lump by patient
Dye 2012	Breast	Ethiopia	The most common reason for initiating action was worsening of or development of new symptoms
Ermiah 2012	Breast	Libya	Delay tended to be higher among women who did not report monthly breast self-examination, older women and those at lower educational levels.
Foerster 2020	Breast	Multi-country: Nigeria, Namibia, Uganda and Zambia	Prolonged diagnostic journey is associated with wrong attribution of symptoms, lower educational status, lower socioeconomic status, being single, lay beliefs, detection of lump and access to informal HCP
Gebremariam 2019	Breast	Ethiopia	Longer diagnostic and patient delays were associated with age (>60 years), lower education status, ≥5 children, lack of symptom awareness and use of traditional medicine
Grosse Frie 2019	Breast	Mali	Patients who initially visited private clinics had the shortest health seeking interval, but the longest diagnostic interval. Patients visiting community healthcare centres and referral hospitals had the longest help-seeking interval, but shorter diagnostic interval. Patients who initially visited a tertiary hospital had shortest help-seeking and diagnostic intervals, but did not follow the recommended referral pathway
Gyenwali 2014	Cervix	Nepal	Longer total diagnostic delay was observed among patients aged 50 years or more, women with lower literacy and those residing farther from the health facility. Long patient delay and total diagnostic delay were found in patients with early symptoms like foul smelling vaginal discharge. HCP delay and total diagnostic delay were longer among women whose cervix was not examined in initial consultation.
Jassem 2014	Breast	Multi-country: Bulgaria, India, Russia, Serbia and Turkey	Longer patient-related delay times were associated with distrust and disregard, and shorter patient-related delay times were associated with fear of breast cancer, practicing self-examination, higher education level, being employed, having support from friends and family and living in big cities
Khaliq 2019	Breast	Pakistan	Older age, seeking care from several health practitioners and traditional health practitioners were significantly associated with longer diagnostic delay. Employment status showed a negative relationship with diagnostic delay
Khokher 2016	Breast	Pakistan	NR
Martínez-Pérez 2020	Breast	Colombia	Significant association between delayed diagnosis and seeking care at government subsidised health facilities and age over 40 years.
Moodley 2016	Breast	South Africa	Deficits in breast self-awareness, knowledge of breast cancer symptoms and disease-related factors such as the absence of pain contributed to delays in seeking care.

Moodley 2018	Breast	South Africa	Factors associated with the longer patient interval included older age, initial symptom denial, waiting for a lump to increase in size before seeking care. Factors associated with diagnostic interval were presence of co-morbidities and denial breast symptoms.
Mujar 2017	Breast	Malaysia	Use of complementary medicine was associated with longer delays
Norsa'adah 2011	Breast	Malaysia	Factors associated with diagnosis delay included the use of alternative therapy, breast ulcer, palpable axillary lymph node, false-negative diagnostic test, non-cancer interpretation and negative attitude toward treatment.
Olarewaju 2019	Breast	Nigeria	Delays were related to factors such as age (older), ethnicity, and marital status (married)
Pace 2015	Breast	Rwanda	Longer patient delay was associated with low level of education and consulting a traditional healer Longer system delay was associated with visiting ≥5 health facilities before the diagnosis
Poum 2014	Breast	Thailand	Longer patient delay was associated with higher family income, self-treatment and seeking medical advice from family or friends. Longer diagnostic delay was associated with older age, employed status, longer distance from home to hospital, increased travel time from home to hospital and higher number of consultations with a surgeon before diagnosis.
Romanoff 2017	Breast	Peru	Women who underwent a previous clinical breast examination were more likely to have shorter patient delays compared with women who had never undergone a previous clinical breast examination
Salih 2016	Breast	Sudan	Financial incapacity, ignorance about breast cancer, and misinterpreting symptoms were the top three factors associated with delay
Shamsi 2020	Breast	Pakistan	Longer patient delay was associated with lower socioeconomic status, lower educational status, use of traditional medicine Shorter patient delay was associated with presence of a family history of breast cancer
Sharma 2012	Breast	Haiti	Lower education status, failure to initially recognise mass as important, and fear of treatment cost were shown to independently predict delayed patient presentation.
Shreyamsa 2020	Breast	India	Misdiagnosis at first consult was the most common factor perceived by patients as a barrier, followed by delay in referral, distance from hospitals, lack of information and financial constraints.
Unger-Saldaña 2018	Breast	Mexico	Patient interval was longer for patients who were single, younger, had interpreted their symptoms as not worrisome, had concealed symptoms, had lower socioeconomic status, and lived outside of the city. Diagnostic interval was longer among those who used several different health services prior to diagnosis.

NR; not reported

Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	4-5
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	5
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	6
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	7
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	6
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	7-8
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	8
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	8
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	n/a
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	8

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	9
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	9
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	n/a
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	9-27
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	9-27
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	28
Limitations	20	Discuss the limitations of the scoping review process.	30
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	30
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	31

JBI = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

Adapted from: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.