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Improving early cancer diagnosis following clinical presentation of symptomatic patients: A scoping review

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Transparency declaration: The corresponding author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Abstract

Objectives: To summarize the current evidence regarding interventions for accurate and timely cancer diagnosis among symptomatic individuals.

Design: A scoping review following the Joanna Briggs Institute's (JBI's) methodological framework for the conduct of scoping reviews and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping reviews (PRISMA-ScR) checklist.

Data sources: MEDLINE (Ovid), CINAHL (EBSCOhost) and PsycINFO (Ovid) bibliographic databases, and websites of relevant organizations.

Methods: Published (peer reviewed) and unpublished literature in the English language were searched for from January 2017 to January 2021. Study participants were individuals of any age presenting at clinics with symptoms indicative of cancer. Interventions included practice guidelines, care pathways or other initiatives focused on achieving pre-defined benchmarks or targets for wait times, streamlined or rapid cancer diagnostic services, multidisciplinary teams, and patient navigation strategies. Outcomes included accuracy and timeliness of cancer diagnosis. We summarized findings graphically and descriptively.

Results: From 21,298 retrieved citations, 88 unique published (peer-reviewed) articles and 16 unique unpublished documents (grey literature on 18 study reports), met the eligibility for inclusion. About half of the published literature and 83% of the unpublished literature were from the United Kingdom. Most of the studies were on interventions in lung cancer patients. Rapid referral pathways and technology for supporting and streamlining the cancer diagnosis process were the most studied interventions. Interventions were mostly complex and organization-

specific. Common themes among the effective interventions were multidisciplinary collaboration and the use of a nurse navigator.

Conclusions: Multidisciplinary cooperation and involvement of a nurse navigator may be unique features to consider when designing, delivering, and evaluating interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals. Future research should examine the effectiveness of the complex and organization-specific nature of the interventions identified through this review.

Review protocol registration details: Protocol submitted as an appendix.

Keywords: Early cancer diagnosis; Symptomatic patients; Interventions; Scoping review

Strengths and limitations of this study

- A knowledge synthesis librarian developed the search strategy for this review and this was peer reviewed by an independent knowledge synthesis librarian using the PRESS checklist.
- The literature search was limited to evidence from the last 4 years and only evidence from English-language publications and organizational websites.
- This review did not summarize effectiveness of interventions across cancer patient types and regions.
- We adhered to known guidelines and standards in the conduct and reporting of the review.
- In line with the JBI's guidance for the conduct of scoping reviews, we did not attempt to evaluate the quality of the included studies or provide an assessment of the quality of the evidence.

Introduction

Cancer is the second leading cause of death globally, with about 1 in 6 deaths attributable to the disease.[1] It was estimated in 2020 that over 19 million new cases and about 10 million deaths were attributable to cancer globally.[2] This rate is estimated to be over 28 million new cases by 2040.[2] High human development index (HDI) countries such as Canada will likely experience the greatest increase in incidence in absolute cancer burden, with an estimated over 4 million new cases more in 2040 compared with 2020.[2] This is mostly due to the growth and aging of the population and increasing prevalence of cancer risk factors.[2] Estimates from Canada alone suggest that every day 617 people in Canada will be diagnosed with cancer, with about 228 also dying from the disease.[3]

Although cancer can occur at any age, the risk of the disease increases with age. Globally, cancer incidence rates vary, mostly because of differences in risk factors and early detection practices. Likewise, cancer death rates vary, partly because of differences in availability and effectiveness of cancer control strategies, such as early diagnosis and access to timely and effective treatment. With timely diagnosis and treatment initiation, significant improvements can be made in the lives of cancer patients. Moreover, many cancers have higher curative and survival rates if diagnosed early. This means that cancer burden could be reduced substantially through early detection and management of patients who present with symptoms.[4]

When not diagnosed following early symptomatic presentation, cancer diagnosis often occurs at more advanced stages of the disease, when treatment may be less effective and cancer prognosis will be poor. Early cancer diagnosis of symptomatic patients entails carefully planned, well-integrated, culturally safe and equitable clinical evaluation and diagnostic services.[4] These

services should be designed to reduce delays in and barriers to diagnosis to allow detection at earlier stages of the disease and commence treatment in a timely manner.

There are various service-focused interventions to improve early cancer diagnosis of symptomatic patients. Interventions such as centralized or coordinated diagnostic services, multidisciplinary team development and support, patient navigational strategies and referral pathways, service targets or benchmarks for wait times, and technology to support diagnosis have been implemented with varying levels of success. Knowledge of the available interventions and how they have been implemented is necessary to inform the development, implementation, and evaluation of effective early cancer diagnosis initiatives.

Methods

This report is a summary of the study commissioned by the Canadian Partnership Against Cancer (the Partnership). The Partnership contributed to specifying the study objectives and questions, and in summarizing the evidence.

We undertook a scoping review following the Joanna Briggs Institute's (JBI's) guidance for the conduct of scoping reviews.[5] This framework includes defining and aligning the objective(s) and question(s) for the review, developing and aligning the inclusion criteria with the review objective(s) and question(s), and describing the planned approach to evidence searching. It also includes selecting, extracting, and charting of evidence; summarizing the evidence in relation to the objectives and questions; and consultation of information scientists, librarians, and/or experts throughout the process. **Appendix 1** is the work plan approved by the Partnership for the scoping review.

We summarized the current evidence regarding interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals, including practice guidelines, care pathways or targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and patient navigation strategies. We also summarized innovative interventions (for example, those with a technological component) and approaches to seamless (minimally disruptive) care of symptomatic individuals and identified performance metrics that can be used to measure improvements in the pre-diagnosis phase. Additionally, we summarized the key points of the patient trajectory from initial symptom presentation to cancer diagnosis.

We report our findings in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Reviews (PRISMA-ScR) checklist.[6]

Search strategy

A knowledge synthesis librarian designed a search strategy for MEDLINE (Ovid). This search strategy was peer-reviewed independently by another knowledge synthesis librarian using the Peer Review of Electronic Search Strategies (PRESS) checklist.[7] The revised search strategy was then adapted for Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCOhost) and PsycINFO (Ovid) bibliographic databases. The search strategy for each of the databases is presented in the appendices (**Appendix 2 - 4**). In addition to searching bibliographic databases, we searched websites of relevant organizations and professional bodies (**Appendix 5**) and hand-searched reference lists of potentially relevant publications.

Study selection criteria and data extraction

The review questions were: (1) are there practice guidelines, care pathways or other initiatives (example, benchmarks/ targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, patient navigators and/or navigation) that have been found to enhance accurate and timely cancer diagnosis in symptomatic individuals?; (2) what are the leading interventions (e.g., technology-based) to seamless care (i.e., minimally disruptive care that is found to be more convenient/coordinated/timely/less stressful to the patients) in the cancer pre-diagnosis phase within Canada and abroad?; (3) what are the identified performance metrics that can be used to measure the suspicion to diagnosis phase; and where and how are these metrics used?; and (4) have specific considerations been applied to underserviced populations including Indigenous, rural, and remote populations within the context of each of the questions above?

Published (peer-reviewed) and unpublished (grey literature) articles in the English language from January 2017 to January 2021 were included. The decision to include articles

from 2017 was because the Partnership had previously summarized prior evidence (https://bit.ly/3xlACsR) and the present focus was on current interventions. Study participants were individuals of any age presenting at clinics with symptoms. Interventions included practice guidelines, care pathways or other initiatives focused on achieving pre-defined benchmarks or targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and patient navigation strategies. Outcomes included accuracy and timeliness of cancer diagnosis.

All retrieved citations from the literature search were imported and managed in EndNote (Version X9). One reviewer screened each citation for eligibility. Two reviewers independently screened the full texts of relevant citations and reviewed the reference list of the included full-text articles for potentially relevant citations. Disagreements between the reviewers were resolved through discussion or involvement of a third reviewer. The number of screened citations and both the number and reason for exclusion of full-text articles were documented. Extraction and charting of relevant data from the included articles was performed by one reviewer and another reviewer independently checked the data for errors. Disagreements between the reviewers were resolved through discussion or involvement of a third reviewer.

Data synthesis and analysis

Characteristics of the included published articles are presented in a tabular form and descriptive analysis is reported graphically and descriptively. Characteristics of the included unpublished articles are reported descriptively only. Relevant findings from the review of both published and unpublished articles are summarized separately and descriptively, by review question, focusing on the interventions related to each question. Interventions are grouped as centralized or coordinated diagnostic service; interventions to enhance diagnostic services; multidisciplinary

team; patient navigation; rapid referral pathway; remote or rural populations-focused; standardized care pathway; support for primary care providers; target or benchmark; and technology to support the diagnostic process. These interventions are defined in **Appendix 6**. Effectiveness of an intervention was determined based on relevant study results.

Patient and public involvement

Involvement of patients or the public in this study was based on the Strategy for Patient Oriented-Research (SPOR) initiative.

Results

Out of a total of 21,298 retrieved citations, 88 unique published articles[8-95] and 16 unique unpublished (grey literature representing 18 different reports)[96-111] met the inclusion criteria. The article selection process is detailed below (**Figure 1**). Fifty-seven of the published articles were from Europe, 14 articles from North America, 9 articles from Oceania, 3 articles each from Africa and Asia, and one article each from the Middle East and South America. Almost half of these articles (n = 40) were from the United Kingdom (UK) alone. A geographic map of published articles is shown in **Figure 2**.

Of the 18 unpublished reports (16 articles), 83% were from the UK, 11% from Canada and 6% from the United States of America (USA). Forty percent (n = 35) of the published articles were for case-control studies, 29% (n = 26) for cross-sectional studies, 22% (n = 19) for before-and-after studies, 7% (n = 6) for randomized controlled studies, and 1% (n = 1) each for guideline development and mixed methods studies. In terms of the unpublished articles, 89% (n = 16) were before-and-after studies and the rest (n = 2) were cross-sectional studies. **Figure 3** shows the distribution of the cancer types reported by the published articles; approximately 30% (n = 26) reported on multiple cancer types, while the rest reported on specific cancer types, of which lung cancer was the most frequent (about 23% of the publications (n = 20)). Of the unpublished articles, half reported on lung cancer, 28% on multiple cancer types, 11% on breast cancer, and 5.5% each on brain and gastrointestinal cancers.

Figure 4 shows the distribution of intervention types across the published articles. Nearly 20% of the published articles were on rapid referral pathway interventions while less than 1% each were on multidisciplinary team, patient navigation, and remote/rural-focused interventions. Of the unpublished articles, half reported on rapid referral pathway interventions, 11% each

reported on standardized care pathway, target/ benchmark for wait times, and technology to support the diagnosis process, and 5.5% each reported on centralized or coordinated diagnostic service and interventions to enhance diagnostic services. Most of the published articles (94%; n = 83) reported a performance metric used to measure an improvement in the suspicion to diagnosis phase of cancer.

Eighty-three percent (n = 73) of the articles reported either a practice guideline, care pathway or an initiative such as benchmark/target for wait times, streamlined or rapid diagnostic service, multidisciplinary team development, and a patient navigation strategy to enhance accurate and timely cancer diagnosis. Thirty-one percent (n = 27) of the articles reported (not explicitly) on a key point of care as patients navigate the health system, from initial suspicion to diagnosis of cancer. Twenty-nine percent (n = 25) of the articles reported on a leading innovative intervention or approach to seamless care in the pre-cancer diagnosis phase, while 4.5% (n = 4) of the articles reported on some form of consideration for underserved populations. Some of the articles reported on two or more of the above. Details of relevant characteristics of the published articles are presented in **Table 1** (those reporting effective interventions) and **Appendix 7** (those reporting ineffective interventions) **and Appendix 8** (those focused on remote/and rural populations).

Initiatives to enhance accurate and timely cancer diagnosis

This review identified various initiatives to enhance accurate and timely cancer diagnosis. These were often designed, developed, and implemented often with the involvement of primary care providers (physicians and nurses), but not patients. These initiatives are grouped into related interventions and the evidence regarding each intervention is discussed below.

Centralized or coordinated diagnostic services

Nine published articles on centralized or coordinated diagnostic services for adult lung cancer (n = 5) and breast cancer (n = 4) patients were identified.[18,21,30,31,42,52-54,91] Five were from Canada,[21,31,42,52,53] and there was one each from Denmark,[18] New Zealand,[91] South Africa,[54] and the UK[30]. The focus and metrics for assessment of the effectiveness of these diagnostic services varied, but all were found to be effective. These include the rapid access to pulmonary investigation and diagnosis (RAPID) program in Wythenshawe Hospital, Manchester, UK with expedited (next working day) computed tomography (CT) and reporting in suspected lung cancer cases,[30] and the Thoracic Triage Panel in a tertiary care centre in St. John's, Newfoundland, Canada, a multidisciplinary centralized referral program, whose key components include a nurse navigator who coordinates patient care and act as the contact person for patients and clinicians involved in the program, weekly multidisciplinary (thoracic specialists) meetings, and regular communications with the primary care provider.[21] The diagnostic services also include the rapid investigation clinic in a tertiary health centre in Montreal, Canada established to coordinate and accelerate the workup of patients with suspected lung cancer,[31] the improved respiratory fast track clinic (RFTC) in Northland district of New Zealand that comprises reserved slots for CT for those referred with a suspicion of lung cancer, bronchoscopy slots and CT-guided biopsy,[91] and the Danish lung cancer package at the Center for Lung Cancer, Odense University Hospital, Odense, Denmark, a fast-track diagnostic pathway in the hospital setting.[18] Further, there was the rapid access breast clinic in British Columbia, Canada that provides close collaboration between clinicians and radiologists, facilitated by clinical pathways and nurse navigation,[52,53] the diagnostic assessment units in Ontario, Canada, focusing on diagnosis at a dedicated breast assessment unit,[42] and the breast clinic at a tertiary hospital in Western Cape Province of South

Africa, an open-access one-stop diagnostic breast clinic where women may present with a letter from a primary level provider (nurse practitioner or doctor) and receive the same day clinical and cytological evaluation with referral to the combined breast clinic if the breast cytology is positive for malignancy.[54]

In addition to the above, one unpublished article was identified.[111] This was for the Breast ACCESS Project in Ohio, USA, which scheduled patients for a surgical consult within 2 days and a biopsy within 5 days after the surgical consult, with the aim of reducing wait times between abnormal diagnostic mammogram findings to biopsy from 26 to 7 days (7-day ACCESS goal).

Interventions to enhance diagnostic services

Twelve published articles on interventions to enhance diagnostic services were identified.[8,15,22,50,51,62,73,75,76,78,81,92] These articles were focused on varied cancer types; four on multiple cancers, two on lung cancer, two on skin cancer, and one each on breast, gastrointestinal, haematological and prostate cancers. Four articles were from the UK,[15,50,51,76] two articles each from Canada[22,62] and Sweden,[8,78] and one article each from Botswana,[92] Columbia,[73] Indonesia,[75] and the USA.[81] The focus and metrics for assessment of the effectiveness of the interventions varied across the publications, and while most were effective, one intervention for lung cancer and one intervention for skin cancer in the UK[51] and Sweden[8], respectively, were ineffective. The effective interventions were reducing diagnosis through emergency presentation by improving general practice referral in England, UK,[50] the guided personal quality of life (QoL) feedback intervention during the Cancer Research UK's North West regional summer roadshow in Manchester, UK, aimed at offering guided feedback about personal QoL to adults with potential cancer symptoms, living in deprived communities to

promote help seeking in primary care among the communities,[76] the mandatory primary care access to faecal immunochemical testing (FIT) in Nottingham, UK, integrated with the 2-week wait pathway, aimed at improving gastrointestinal cancer diagnosis rather than relying on age and symptoms alone,[15] the Stronach Regional Cancer Centre lung diagnostic assessment program (DAP) at Southlake Regional Health Centre, Ontario, Canada, aimed at using learnings from a Lean improvement event to provide coordinated, expedited care for all patients undergoing a possible lung cancer diagnosis and to achieve/improve upon the provincial wait time target from consultation to diagnosis for lung cancer patients,[22] the nurse practitioner-led lymphoma rapid diagnosis clinic in a tertiary care cancer center (Princess Margaret Cancer Centre, part of University Health Network) in Ontario, Canada, aimed at reducing wait times for a definitive diagnosis of lymphoma,[62] the expedited one-stop prostate cancer diagnosis using advanced imaging and biopsy techniques in a health institution (name not reported) in the USA, aimed at expediting prostate cancer diagnosis.[81] There were also the Swedish Diagnostic Center at the Central Hospital of Kristianstad, Sweden, introduced as a separate outpatient unit within the Department of Internal Medicine to expedite diagnostics,[78] the Partners for Cancer Care and Prevention action plan in Cali, Columbia, aimed at improving access to a coordinated program of screening and early diagnosis of breast and cervical cancers in three health care centers that serve subsidized populations,[73] the dermatology-led quality improvement initiatives in Gaborone, Botswana, aimed at improving multispecialty care coordination,[92] and the culturally sensitive, narrative self-help intervention named PERANTARA (PEngantar peRAwataN kesehaTAn payudaRA [translated as introduction to breast health treatment]) across four hospitals in Bandung, West Java, Indonesia, aimed at reducing time to diagnosis in women with breast cancer symptoms.[75] In addition to the above, one unpublished article on the Accelerate,

Coordinate, Evaluate (ACE) program in the UK was identified.[98] This program was an early cancer diagnosis initiative and focused on testing innovations that either identify individuals at high risk of cancer earlier or streamline diagnostic pathways.

The ineffective interventions were the standardized care diagnostic pathway at the Department of Clinical Pathology, Akademiska University Hospital in Uppsala, Sweden (introduced by the Swedish health authorities to eliminate unwanted delay in the diagnostics of melanoma)[8] and the 4-week national lung cancer symptom awareness campaign in Wales, UK, aimed at increasing urgent suspected cancer referrals and clinical outcomes.[51]

Multidisciplinary team

Three multidisciplinary team lung cancer approaches were identified from published articles: from the USA[66,83] and Australia.[48] The focus and metrics for assessment of the effectiveness of the approaches varied across the publications. One approach from the USA was found to be effective,[66] whereas the others were found to be ineffective. The effective approach was the lung cancer strategist program, a thoracic surgeon-guided, multidisciplinary (disciplines not reported) care program in hospitals in Massachusetts, USA, aimed at improving timeliness of lung cancer diagnosis and treatment.[66] The ineffective approaches were the pre-diagnosis multidisciplinary tumour board (physicians from radiology, medical and radiation oncology, and pulmonary medicine) discussions in a clinic in Cleveland, USA aimed at improving the timeliness of diagnostic evaluation in lung cancer,[83] and the Victorian lung cancer service redesign project in Victoria, Australia, which involved multidisciplinary (patients, governance, administration, clinicians and health information services) evaluation aimed at quality improvement collaborative on timeliness and management in lung cancer.[48] In addition, nine unpublished articles from the UK were identified.[97,99-101,104,106,107,110] These included four articles

regarding a "straight to CT access" pathway, on community pharmacy direct referral to lung cancer pathway, rapid colorectal diagnostic pathway, and optometrist direct referral to neuroscience pathway. All but the chest x-ray pathway[107] were found to be effective.

Standardized care pathways

Eleven published articles on standardized care pathways were identified.[9,10,24,33,37,39,47,57,61,68,69] These articles were focused on varied cancer types (4 each for multiple cancers, and 1 each for ear-nose-throat, urinary tract, and gastrointestinal cancers). Three articles were from Denmark,[24,37,39] two from the UK,[33,68] and one each from Canada,[57] Norway,[47] Sweden,[61] Spain,[10] and Saudi Arabia.[9] The publications were on adult patient populations with one also involving paediatric patients. The focus and metrics for assessment of the effectiveness of the pathways varied across the publications. The main effective pathways were the national diagnostic cancer pathway in Norway, with recommended maximum limits for time spent in the diagnostic process as well as mandatory reporting of the actual time intervals for all patients with suspected lung cancer,[47] and the standardized triage process in the Southeastern Ontario, Canada, which entailed a twice-weekly nurse–physician triage, preordered staging tests and scheduling according to urgency, redirection and recommendations for inappropriate referrals, and new small nodule clinic.[57] Other main effective pathways were the standardized diagnostic pathway for suspected urothelial cancer initiated by primary healthcare providers and specialists in Skane County, Sweden, and comprises CT urography, urinary cytology and cystoscopy,[61] the early colonoscopy track (within 30 days from referral) in a tertiary referral hospital in Tenerife, Spain,[10] and the fast-track cancer care pathway in Denmark (national), with maximum acceptable time thresholds from referral to diagnosis and treatment.[37] In addition, two unpublished articles

from Canada[109] and the UK[96] focusing on breast and lung cancers, respectively, were identified. These were the Alberta Health Services Diagnostic Assessment Pathway and the Somerset Integrated Lung Cancer Pathway. While the Canadian pathway was found to be effective, the pathway from the United Kingdom was not effective.

Support for primary care providers

There were four publications on support for primary care providers (PCP), all from the UK.[25,29,46,95] Two were focused on multiple cancer types, and one each focused on gastrointestinal and brain cancers. The publications were on adult patient populations with one being also involving paediatric patients. The focus and metrics for assessment of the effectiveness of the support packages (all educational and informational) varied across the publications. None of the support packages was found to be effective, with the identified common theme being a lack of awareness of referral guidelines and associated knowledge by GPs. These ineffective support packages were the use of the Kernick and NICE guidelines as evidence-based support to assist primary care physicians in identifying patients most at risk of having a brain tumour, but also on the fastest route to achieve diagnosis (example, direct access imaging versus urgent secondary care referral) in Scotland, the UK,[95] the use of the national cancer waiting times monitoring dataset for system performance assessment by primary care physicians in England, the UK,[25] and the use of safety netting by primary care physicians in Oxfordshire, UK to ensure that patients are monitored until their symptoms or signs are explained, and to guard against delays in diagnosis.[29]

Target or benchmark for wait times

There were eight published articles related to targets or benchmarks for wait times.[13,40,41,67,71,79,86,94] Three of these articles were from the UK,[67,71,79] two articles from Australia,[40,86] and one article each from China,[41] Sweden,[94] and New Zealand[13]. These publications were focused on varied cancer types (2 each for multiple, lung and gastrointestinal cancers, and 1 each for prostate and skin cancers), and were on adult patient populations, with one publication involving paediatric patients. The focus and metrics for assessment of the effectiveness of the target or benchmarks varied across the publications, and all but two targets/benchmarks[13,86] were found to be effective. The effective targets or benchmarks were the 28-day faster diagnosis standard in the National Health Service England, UK, defined as the time within which the patient is informed whether they do or do not have cancer,[71] the fast-track diagnostic workup for men with suspected prostate cancer at the Urology Department at Orebro University Hospital in Sweden, which entailed targeting the shortest possible waiting-time for a diagnostic workup process,[94] and the optimal timeframes for referral and diagnosis of lung lesion at Latrobe Regional Hospital in Victoria, Australia established by the National Cancer Expert Reference Group as part of the optimal care pathway for people with lung cancer.[40] The ineffective targets or benchmarks was the New Zealand Ministry of Health's "faster cancer treatment" standards of service provision for melanoma patients, with a target of histopathological diagnosis of melanoma reported within five working days in 80% of cases, and all cases reported in 10 working days.[13] In addition, two unpublished articles from Canada[103] and the UK[105] focusing on multiple cancers were identified, and these were the "2-week wait" benchmark in the UK (already discussed under rapid referral pathways) and the Canadian Breast Cancer Screening Network targets for diagnostic intervals: ≥ 90% of abnormal screens to be

resolved within 5 weeks if no biopsy is required and ≥ 90% within 7 weeks if a tissue biopsy is required.

Innovative interventions to enhanced care in cancer pre-diagnosis phase

This review identified 17 published articles related to technological interventions for enhanced care in the pre-diagnosis phase of cancer.[14,19,20,27,35,36,49,55,56,60,63,64,77,80,85,87,89] Ten of these articles were from the UK,[20,27,35,36,49,55,60,63,64,89] two articles were from New Zealand,[77,80] and one article each was from Denmark,[87] Netherlands,[19] Italy,[14] India,[85] and Spain.[56] These publications focused on varied cancer types in adult patient populations, with two also involving paediatric patients. The interventions had little patient input in their design, development, or implementation. The focus and metrics for assessment of the effectiveness of the interventions varied across the publications. The main identified interventions were the use of teledermatology in skin cancer diagnosis. This involved the taking of images, including dermoscopy by GPs and sending them for evaluation to specialized dermatologists.[36,60,77,87] The process is embedded in an e-referral system developed in Auckland, New Zealand for suspected skin malignancy,[80] and included teledermatology images triaged as confirmed, likely or suspected melanoma, the use of a web-based referral tool for head and neck cancers at two different hospitals in Birmingham, West Midlands, and Wexham, Berkshire, UK.[49] There was also the use of the Digitally Assembled Referral Toolkit (DART) for 2-week referral, accessible via a cloud-based template, which contained new referral forms native to GP clinical systems in the UK.[27] Additionally, there was the use of an electronic straight-to-test pathway at a large tertiary referral hospital in England, UK to remove hospital-based triage from suspected colorectal cancer pathways; this allows GPs to book tests supported by a decision aid based on the NICE guidance, thus,

eliminating the need for a standard referral form or triage process.[63] Further, there was the use of electronic clinical decision support for melanoma in four general practices in the Southeast of England, UK, which involved the use of an electronic-based 7-point checklist to assess pigmented lesions,[64] the use of machine learning algorithms in Newcastle, UK to classify patients referred on the 2-week wait pathway for suspected head and neck cancer into different diagnostic groups, albeit very broad ones: cancer and non-cancer,[55] the use of nurse-led assessments to evaluate certain groups of patients suspected to have bowel cancer in England, the UK,[20] and the use of varied smartphone-based skin and oral self-monitoring and screening applications, in England, UK[89] and in the India,[85] respectively. In addition, two unpublished articles from the UK were identified.[104,108] These were for a cancer decision support tool (computer-based programs integrated into a GP's usual patient management system) in Gateshead, London, and a clinical web portal (CWP) electronic system in Manchester, England, with the fundamental part of the CWP being that local clinicians had to take personal responsibility for data input.

Performance metrics to measure improvements in suspicion to diagnosis phase

Varied performance metrics were identified by this review. The main metrics are summarized according to intervention type (**Appendix 9**). While performance metrics appear to be mainly intervention-dependent, time from presentation in primary care to diagnosis and from referral from primary care to specialist consultation, appear to be the most consistent metrics used for evaluation. Performance metrics to measure patients' experience mainly centered on patients' satisfaction and quality of life.

Specific considerations for underserved populations

Four published articles focused on issues related specifically to underserved populations, with all focused on remote/rural populations.[16,28,58,86] These publications were from the UK,[58] Australia,[28,86] and Mexico.[16] A fifth publication only used the patients' area of residence as part of their model.[93] All of the publications were on multiple cancer types and adult populations, although one included a paediatric population. The specific considerations for underserved populations and the evidence regarding them included a publication from Scotland, the UK, a national audit of cancer diagnosis in Scottish and English general practices, exploring and comparing patient characteristics, diagnostic intervals, and routes to diagnosis,[58] the publication from New South Wales, Australia on a study that examined geographic variations in time intervals leading up to treatment for head and neck cancer, with assessment of differences based on remoteness of residence (regional/remote or metropolitan) at two tertiary referral centres,[86] a publication from Mexico City, Mexico on evaluation of a patient navigation program to reduce referral time to cancer centers for underserved patients with a suspicion or diagnosis of cancer at a public general hospital,[16] and a publication from Western Australia, a cluster-randomized controlled trial of a complex intervention to reduce time to diagnosis in rural cancer patients with the aim of measuring the effect of community-based symptom awareness and general practice-based educational interventions on the time to diagnosis in rural patients presenting with breast, prostate, colorectal or lung cancer.[28]

Discussion

This scoping review of 88 published and 16 unpublished documents from January 2017 to January 2021 summarizes the evidence on current interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals. The identified articles were from varied study designs including case-control (most common), cross-sectional, before-and-after, and mixed methods studies, and randomized controlled trials. There was little evidence to suggest that patients were involved in the design, development, or implementation of interventions to enhanced care in cancer pre-diagnosis phase.

The evidence suggests that interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals are active topics of research. The UK appears to be championing this area of research, contributing about half of all identified published literature and 83% of the identified unpublished literature. Of the specific cancer patient types, lung cancer patients appear to be the most researched, ranking highest among the patient populations of published and unpublished literature. Of the studied interventions, rapid referral pathways and technology for supporting and streamlining the diagnosis process were the two most reported interventions. Overall, varied national and regional centralized or coordinated diagnostic services, interventions to enhance diagnostic services, multidisciplinary team approaches, patient navigation approaches, rapid referral pathways, standardized care pathways, support for primary care providers, target or benchmarks, technologies to support diagnosis process, and insights regarding variations between remote/rural and urban populations have been reported although there were no articles that focused specifically on Indigenous populations. Many of these intervention types could be adapted to suit different health systems and jurisdictions around the world.

The interventions mostly comprised multiple interventions/ changes to the healthcare pathway. As such, the interventions examined varied widely across the studies. This was true even when applied to the same cancer patient populations and in the same jurisdictions/ countries, including those where an intervention was part of the standard care pathway. As such, it is difficult, perhaps impossible, to identify one main approach alone that drives an intervention. Methodological approaches also varied significantly with regard to outcome assessment. A common theme among the effective centralized or coordinated diagnostic services, interventions to enhance diagnostic services, patient navigation approaches, and standardized care pathways is multidisciplinary collaboration and the involvement of a nurse navigator.

The implications of the findings from this scoping review are that it is difficult to determine a specific intervention, or stand-alone approach to an intervention. It is also difficult to assess the true effectiveness of many of the interventions, especially considering the differing composite nature of the interventions, the fact that the evidence is mostly from observational studies, and the range of outcome measures used to measure effectiveness. While many of the interventions could be adapted to suit different health systems and jurisdictions, emphasis should be on the context and the strengths and limitations of the individual health system, and a clear evidence-based performance metric for appropriate evaluation of effectiveness of an intervention ought to be determined a priority. Diagnosing cancer faster and more accurately at an earlier stage is a key priority of the 2019-2029 Canadian Strategy for Cancer Control (www.partnershipagainstcancer.ca/cancer-strategy/). Over the next 5 years, the Canadian Partnership Against Cancer will leverage findings from this scoping review, as one of several

inputs, and partner with Canadian jurisdictions to continue to test innovative models of care that expedite cancer diagnosis, especially for Indigenous and underserved populations.

Limitations and merits

There are some limitations to this study. The literature search was developed by a knowledge synthesis librarian and peer reviewed by an independent knowledge synthesis librarian using the PRESS checklist, searching of appropriate databases and websites for literature, and adherence to known guidelines and standards in the conduct and reporting of the review. Even so, the literature search was limited to evidence from the last 4 years and only evidence from English-language publications and organizational websites. As such, potentially eligible articles could have been missed.

The eligibility criteria for inclusion were not limited to only comparative studies. This meant that the focus of some of the included studies was not specifically on the assessment of effectiveness of an intervention, which was based solely on the reported outcome in the articles. As such, an intervention that appeared effective in a study may be ineffective in another study depending on the assessed outcome with no clear reason for this discrepancy. Furthermore, this review did not assess effectiveness of interventions across cancer patient types and jurisdictions/regions. This would have allowed assessment of any differences in intervention effectiveness by patient type and study jurisdiction. Lastly, and in line with the JBI's guidance for the conduct of scoping reviews, we did not attempt to evaluate the quality of the included studies or provide an assessment of the quality of the evidence.

Conclusions

The evidence suggests that interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals are active topics of research, particularly in lung cancer patient populations, and that the UK is championing this area of research. While the themes of the studied interventions are similar, the interventions differ in many ways within the same intervention group. Multidisciplinary cooperation and involvement of a nurse navigator appeared to be unique features of many of the effective interventions. Canadian and other jurisdictions can leverage these lessons learned to develop and implement strategies adapted to local health system needs to improve the cancer pre-diagnosis phase. Future research should examine the effectiveness of the complex and organization-specific nature of the interventions identified through this review.

Data sharing statement: All the data for this study are reported in the text and appendices. No additional data available.

Ethics approval: Not applicable.

Details of the role of the study sponsors: The Canadian Partnership Against Cancer (the study commissioner) contributed to specifying the study objectives and questions, and in summarizing the evidence.

Patient and public involvement: Involvement of patients or the public in this study was based on the Strategy for Patient Oriented-Research (SPOR) initiative.

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Table 1: Summary of the characteristics of the included published articles that reported data on effective interventions

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
Centralized or coordinated diagnostic service	Christensen 2020[18]	Denmark (Odense)	Cross-sectional (2016-2017)	Lung (Adult) [20]	Patients' perspective, experiences, and expectations	Although patients experienced anxiety with the fast-track diagnostic pathway, they still wanted to move through with diagnosis as quickly as possible (Effective)
	Common 2018[21]	Canada (Newfoundland)	Case-Control (2015-2016)	Lung (Adult) [133]	Time from first abnormal image to biopsy	There was a statistically significant decline in wait times for patients from 61.5 to 36.0 days ($p<0.0001$) (Effective)
	Evison 2020[30]	UK (Manchester)	Before-and-After (2016-2019)	Lung (Adult) [1035]	Mean time from referral to CT	The median time from referral to CT was 3 days. Overall 56% and 90% of patients had completed a CT and consultation within 3 and 7 days of referral, respectively (0% and 24% prior to implementation) (Effective)
	Ezer 2017[31]	Canada (Montreal)	Case-Control (2010-2011)	Lung (Adult) [327 (195 RIC; 132 non-RIC)]	Time from first contact with physician to diagnosis	Time from first contact to pathological diagnosis was shorter (median (M) 26 days; IQR 14–42 days) vs. control patients (M 40 days; IQR 16–68 days) (Effective)
	Jiang 2018[42]	Canada (Ontario)	Case-Control (2011)	Breast (Adult) [4381]	Time to diagnosis	The Canadian timeliness targets (time from patients' first referral or test to the cancer diagnosis) were achieved more often than for usual care (71.7% vs. 58.1%, respectively), with associated 10-day (95% CI: 7.8–11.9) reduction in the median diagnostic interval (Effective)
	McKevitt 2017[52]	Canada (British Columbia)	Case-Control (2009)	Breast (NR) [373]	Diagnostic wait time	Patients had a decreased time to surgical consultation (33 vs 86 days, $p<0.0001$) for both malignant (36 vs 59 days, $p=0.0007$) and benign diagnoses (31 vs 95 days, $p<0.0001$) (Effective)

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
	McKevitt 2018[53]	Canada (Vancouver)	Case-Control (2012)	Breast (NR) [176 (40 RABC; 136 TS)]	Time from presentation to surgical consultation	Time from presentation to surgeon evaluation was shorter in the RABC group for patients with breast symptoms (81 vs 35 days, p < .0001) (Effective)
	Moodley 2018[54]	South Africa (Western Cape province)	Cross-sectional (2015-2016)	Breast (Adult) [201]	Time between first health care provider visit and date of diagnosis	The median time between the first health care visit and a breast cancer diagnosis was 28 days (IQR 13–58 days). Women whose initial reaction was denial of the breast symptom had a significantly shorter diagnostic interval (11 days vs. 29 days, p = 0.010) (Effective)
	Williams 2018[91]	New Zealand (Northland district)	Before-and-After (2015-2016)	Lung (Adult) [212 (70 in phase 1, 46 in phase 2 and 71 in phase 3)]	Time from GP referral to first specialist appointment	Time from GP referral to first specialist appointment improved significantly (p=0.005) (Effective)
Intervention	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Results**
Interventions to enhance diagnostic services	Chapman 2020[15]	UK (Nottingham)	Cross-sectional (2017-2018)	Gastrointestinal (Adult) [1934]	Colorectal cancer (CRC) detection rate after a FIT	The symptomatic pathway incorporating FIT was feasible and appeared more clinically effective than pathways based on age and symptoms alone, with FIT results identifying patients with a significantly higher risk of CRC (Effective)
	Cotton 2020[22]	Canada (Ontario)	Before-and-After (2017-2018)	Lung (NR) [NR]	Referral to diagnosis	Monthly patient volumes increased by 65%, and wait time improved by 60% (Effective)
	Laudicella 2018[50]	UK (England)	Case-Control (2006-2009)	Multiple (Adult) [372353]	Survival of patients	Rerouting patients from emergency presentation to new referral resulted in better patient survival in all cancer cohorts (Effective)

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
	Nixon 2020[62]	Canada (Ontario)	Case-Control (2015-2017)	Haematological (Adult) [126]	Time from initial consultation to diagnosis of lymphoma	Median time to lymphoma diagnosis was 16 days for patients assessed in the nurse practitioner–led lymphoma rapid diagnosis clinic and 28 days for historical controls (P<0.001) (Effective)
	Sardi 2019[73]	Colombia (Cali)	Before-and-After (2012-2016)	Multiple (NR) [114]	Time from initial consultation to biopsy	The average time from initial consult to biopsy decreased from 65 to 20 days and from biopsy to diagnosis from 33 to 4 days (Effective)
	Setyowibowo 2020[75]	Indonesia (Bandung West Java)	RCT (2017)	Breast (Adult) [107]	Time between first visit to the hospital and a definitive diagnosis	The intervention reduced the time to definitive diagnosis: mean difference = −13.26, 95% CI = −24.51 to −2.00, P=0.02) (Effective)
	Skevington 2020[76]	UK (Manchester)	RCT (2015-2016)	Multiple (Adult) [107]	Quality of life	Psychological quality of life increased (Effective)
	Stenman 2019[78]	Sweden (Kristianstad)	Cross-sectional (2015)	Multiple (Adult) [290]	Total diagnostic interval	Shorter diagnostic interval (time from referral decision in primary care to diagnosis). The median primary care interval was 21 days, and the median diagnostic interval was 11 days (Effective)
	Tafuri 2020[81]	USA (NR)	Case-Control (2016-2018)	Prostate (Adult) [370]	Time from multiparametric Magnetic Resonance Imaging (mpMRI) to biopsy	One-Stop patients experienced shorter time from mpMRI to biopsy (0 vs 7 days; p< 0.01) (Effective)
	Williams 2019[92]	Botswana (Gaborone)	Before-and-After (2015-2017)	Skin (Adult) [218]	Diagnostic histology turnaround times	Median turnaround in the post dermatology quality improvement interval was 11 days (IQR, 12-23 days) compared with 32 days in the pre-dermatology quality improvement interval (IQR, 24-56 days; P<0.001) (Effective)

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
Multidisciplinary team	Phillips 2019[66]	USA (NR)	Case-Control (2014-2016)	Lung (NR) [218]	Time to diagnosis	Compared to controls, patients with lung cancer in the Lung Cancer Strategist Program cohort had an expedited time from suspicious finding to diagnosis (34 vs 44 days, p=0.027) (Effective)
Patient navigation	Chavarri-Guerra 2019[16]	Mexico (Mexico City)	Before-and-After (2016-2017)	Multiple (Adult) [70]	Feasibility	91% of patients successfully obtained appointments at cancer centers in <3 months (Effective)
	Drudge-Coates 2019[26]	UK (London)	Before-and-After (2012-2015)	Prostate (Adult) [60]	Waiting times from the GP referral to initial clinic assessment	Compared with the previous physician-led service, waiting times for patient appointment fell by 52% over a 3-year study period (Effective)
	Whitley 2017[90]	USA (Boston, Denver, San Antonio, and Tampa)	Case-Control (2007-2011)	Multiple (Adult) [6349]	Delays in diagnostic resolution based on Charlson Comorbidity Index score	Patient navigation reduced delays in diagnostic resolution, with the greatest benefits seen for those with a Charlson Comorbidity Index score ≥2 (Effective)
Intervention	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Results**
Rapid referral pathway	Antel 2020[11]	South Africa (Cape Town)	Before-and-After (2017-2019)	Haematological (Adult) [130]	Diagnostic interval	Compared with a historical cohort, the diagnostic interval (time from first health visit to diagnostic biopsy) for patients with lymphoma was significantly shorter, 13.5 vs 48 days (p=0.002) (Effective)
	Arhi 2020[12]	UK (National)	Case-Control (2000-2013)	Gastrointestinal (Adult) [7130]	Hazard ratios of death	Patients referred between 2 weeks to 3 months, and after 3 months with red-flag symptoms demonstrated a significantly worse prognosis than patients who were referred within 2 weeks (Effective)
	Chng 2020[17]	UK (Newcastle-upon-Tyne)	Case-Control (2015-2019)	Brain (Adult) [101]	Tumour detection rate	With guideline adherence, the brain tumour detection rate was 3-fold higher (36.0% vs 11.5%, p¼0.02) (Effective)

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
	Creak 2020[23]	UK (Brighton; Sussex)	Cross-sectional (2015-2018)	Multiple (Adult) [258]	Time to diagnosis	Direct GP referrals were feasible and manageable within a tertiary clinic and resulted in high rates of cancer diagnoses and early contact with an oncologist and nurse specialist, cutting short the 'limbo' time of high anxiety before diagnosis (Effective)
	Hennessy 2020[34]	Ireland (Dublin)	Case-Control (2012-2018)	Lung (NR) [864]	Time to diagnosis	Time to diagnosis was longer in those who had attended a post Rapid Access Lung Cancer Clinic CT (34.5 versus 21 days) (Effective)
	Jones 2018[43]	UK (East Midlands)	Case-Control (2013-2015)	Gastrointestinal (NR) [1401 (340 STTP, 495 traditional pathway, 566 control trusts)]	Time from referral to diagnosis	The pathway saved a mean of 7 days from referral to treatment (with a 95% CI of 3 to 11 days, p<0.008) and a mean of 16 days from referral to diagnosis, when compared with a traditional pathway (Effective)
	Joyce 2020[44]	UK (National)	Cross-sectional (2017-2018)	Multiple (Mixed age) [NR]	Proportion with emergency diagnosis of cancer	A lower proportion of emergency diagnosis of cancer was found with higher 2 weeks wait referral conversion rate (Effective)
	Pearson 2020[65]	UK (National)	Case-Control (2014)	Multiple (Mixed age) [12873]	Primary care interval	Compared with patients with a specific alarm symptom, patients with non-specific but concerning symptoms had higher odds of having longer primary care intervals (adjusted OR: 1.24 (1.11 to 1.36)) (Effective)
	Round 2020[70]	UK (National)	Case-Control (2011-2017)	Multiple (Mixed age) [1469103]	Risk of death	Cancer patients from the highest referring practices had a lower hazard of death (hazard ratio [HR] = 0.96; 95% confidence interval [CI] = 0.95 to 0.97) (Effective)
	Sandager 2019[72]	Denmark (National)	Cross-sectional (2010)	Multiple (Adult) [2256]	Patient experience	Overall, pathway referred patients were 21% more likely than non-pathway referred patients to report a

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
						positive experience (PR = 1.21 [95% CI: 1.11–1.30]) (Effective)
	Thanapal 2020[84]	UK (London)	Before-and-After (2012-2018)	Gastrointestinal (Adult) [1648]	Time to diagnosis	Patients on the pathway took 25 days to obtain results as compared to 40 days in the standard pathway (Effective)
	Vijayakumar 2020[88]	UK (Buckinghamshire)	Cross-sectional (2018)	Lung (NR) [111]	Patient satisfaction	High satisfaction with the service, with scores above 93% in all parameters (Effective)
Intervention	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Results**
Standardized care pathway	Alonso-Abreu 2017[10]	Spain (Tenerife)	Case-Control (2008-2010)	Gastrointestinal (Adult) [257]	Survival rates	Survival rates at 12 and 60 months after treatment were significantly higher in the early colonoscopy group compared with the standard schedule colonoscopy group ($p < 0.001$) (Effective)
	Dahl 2017[24]	Denmark (Countrywide)	Before-and-After (2004-2010)	Multiple (Adult) [3292]	Patient satisfaction for waiting time from referral to consultation at a hospital	Implementation of pathway was associated with a reduced level of patient-reported dissatisfaction with long waiting time from the time of referral to the first consultation at the hospital (Effective)
	Laerum 2020[47]	Norway (Kristiansand)	Before-and-After (2007-2016)	Lung (Adult) [780]	Referral interval	The median referral interval among all patients was reduced by two days from baseline to the next time period when the local diagnostic algorithm was streamlined (Effective)
	Mullin 2020[57]	Canada (Ontario)	Before-and-After (2018-2019)	Lung (NR) [833]	Time from referral to diagnosis	Time from referral to positron emission tomography decreased (from 38.5 to 15.7 days), time from referral to brain imaging decreased (from 33.4 to 13.1 days), and time from referral to diagnosis decreased (from 38.0 to 22.7 days), all demonstrating special-cause variation (Effective)

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
	Nilbert 2018[61]	Sweden (Skane County)	Case-Control (2015-2016)	Urinary tract (Adult) [1871]	Time from sign/symptom to diagnosis	The standardized care pathway shortened the diagnostic delay to a median of 25 days compared to 35 days for regular referral (p=0.01) (Effective)
	Rankin 2017[69]	Australia (New South Wales)	Cross-sectional (2014)	Lung (Adult) [19]	Patient concerns urgency, advocacy, and referral	Patients and general practitioners expressed similar themes across the diagnostic and pretreatment intervals (Effective)
Intervention	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Results**
Target or benchmark for wait times	Jeyakumar 2020[40]	Australia (Victoria)	Case-Control (2018)	Lung (Adult) [46]	Mean time from initial CT to tissue diagnosis	The Standard Care group met the target for treatment commencement in 33.3% of cases whereas the Rapid Access Clinic group achieved this in 77% (Effective)
	Jiang 2017[41]	China (Shanghai)	Case-Control (2011-2015)	Lung (NR) [4000]	Time from initial respiratory consultation to treatment decision	Takes a median 4 workdays (range 3 to 6) for a new patient from initial respiratory consultation to treatment decision, whereas in many countries, 14 workdays are considered a reasonable timeline (Effective)
	Sagar 2020[71]	UK (Milton, Somerset)	Before-and-After (2019-2020)	Gastrointestinal (Mixed age) [1255]	28-day target attainment	Attainment of the 28-day diagnosis target for all suspected colorectal cancer referrals improved following the establishment of a new pathway (88% vs. 82%, P < 0.0001) (Effective)
	Stevenson-Hornby 2018[79]	UK (Wigan)	Before-and-After (2017)	Gastrointestinal (NR) [NR]	Percentage diagnosed	55% of all referrals were found to have hepatobiliary-pancreatic cancer after pathway trial compared with 19% before (Effective)
	Zhu 2020[94]	Sweden (Orebro)	RCT (2015-2018)	Prostate (Adult) [204]	Self-reported symptoms of stress	Significant changes in depression symptoms and self-rated sleep quality suggested a benefit of the fast-track workup intervention (Effective)

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
	*Piano 2019[67]	UK (Guildford, Bradford)	Cross-sectional (NR)	Multiple (Adult) [29]	Patient attitudes within the context of their recent referral experiences	Most patients had experienced swift referral. It was difficult for patients to understand how the new standard could affect upon the time that it takes to progress through the system. Responsibility for meeting the standard was also a concern as patients did not see their own behaviours as a form of Involvement (NA)
Intervention	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Results**
Technology to support diagnosis process	Cazzaniga 2019[14]	Italy (Bergamo)	Case-Control (2017)	Skin (Adult) [232]	Diagnostic accuracy	The diagnostic accuracy of the online assessment compared with direct clinical examination was significant (Effective)
	Cock 2017[20]	UK (NR)	Guideline development (2014-2016)	Gastrointestinal (Adult) [NR]	Patient satisfaction	Audits were being conducted to assess and compare patient satisfaction with face-to-face versus telephone assessments, although intervention was well-received (Effective)
	Eastham 2017[27]	UK (Leeds)	Before-and-After (2015-2016)	Multiple (Adult) [NR]	Form completion rates and time spent processing forms	Form completion rates improved from a mean of 44% of forms at baseline (n = 210) to 99% post-intervention n = 236). Time spent processing forms also decreased from a mean of 96 seconds to 35 seconds post-introduction of the new system (Effective)
	Hirst 2018[35]	UK (London)	Cross-sectional (2016)	Multiple (Adult) [NR]	GP perspectives on txt-netting	Text messages were perceived to be an acceptable potential strategy for safety netting patients with low-risk cancer symptoms (Effective)
	Hunt 2020[36]	UK (England)	Case-Control (2018)	Skin (Adult) [150 (75 consecutive TD referrals	Time from referral to first appointment and diagnostic rates	There was a 23% absolute and 37% relative increase in diagnostic completion rates in the mobile van

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
				paired with 75 standard "Face to Face" controls)]		compared with the central hospital facility (p=0.0001) (Effective)
	Moor 2019[55]	UK (Newcastle-upon-Tyne; Birmingham)	Case-Control (2007-2010)	Head and Neck (Mixed age) [4715]	Diagnostic accuracy	Machine learning algorithms accurately and effectively classify patients referred with suspected head and neck cancer symptoms (Effective)
	Moreno-Ramirez 2017[56]	Spain (Southern region)	Case-Control (2004-2015)	Skin (NR) [2009]	Waiting times for referral	Waiting times for referral for teledermatology network versus conventional letter referral system 12.31 (8.22–16.40) vs 88.62 (38.42–138.82) (Effective)
	Nicholson 2020[60]	UK (London)	Cross-sectional (2018-2019)	Skin (NR) [60]	Patient satisfaction	Over 80% (49) would recommend the service, and the majority felt confident with the teledermatology model. Overall, patients would be happy to complete electronic questionnaires and receive results electronically, with younger patients being more amenable to this (Effective)
	Orchard 2020[63]	UK (Bristol)	Before-and-After (2014-2017)	Gastrointestinal (Mixed age) [11357]	Time from referral to diagnosis	Time from referral to diagnosis reduced from 39 to 21 days and led to a dramatic improvement in patients starting treatment within 62 days (Effective)
	Snoswell 2018[77]	New Zealand (Countrywide)	Not clear (2012)	Skin (Adult) [300]	Time to clinical resolution	Mean time to clinical resolution was 9 days (range, 1-50 days) with teledermoscopy referral compared with 35 days (range, 0-138 days) with usual care alone (difference, 26 days; 95%credible interval 13-38 days) (Effective)
	Sunderland 2020[80]	New Zealand (Auckland)	Case-Control (2016)	Skin (NR) [809]	Efficacy of diagnostic tool	A positive predictive value (PPV) of 38.1% and number needed to excise (NNE) of 2.6, with less than 10% of referrals triaged for teledermatoscopy

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
						confirmed as melanoma (24/264) (Effective)
	Uthoff 2018[85]	India (Bangalore, Dimapur)	Case-Control (NR)	Oral (Adult) [99]	Diagnostic accuracy	Sensitivities, specificities, positive predictive values, and negative predictive values ranged from 81.25% to 94.94% (Effective)
	Vestergaard 2020[87]	Denmark (Southern Denmark)	Case-Control (2018)	Skin (Adult) [519]	Percentage of lesions not requiring further in-person assessment	On evaluation by teledermoscopy, 31.5% of lesions did not need further in-person assessment (Effective)

CRC = colorectal cancer; CT = computed tomography; FIT = faecal immunochemical testing; GP = general practitioner; NR = not reported; RABC = rapid access breast clinic; RCT = randomized controlled trial; RIC = rapid investigation clinic; STTP = straight to test pathway; TD = teledermatology; TS = traditional system; UK = United Kingdom; USA = United States of America; * = effective but not applicable; IQR = interquartile range

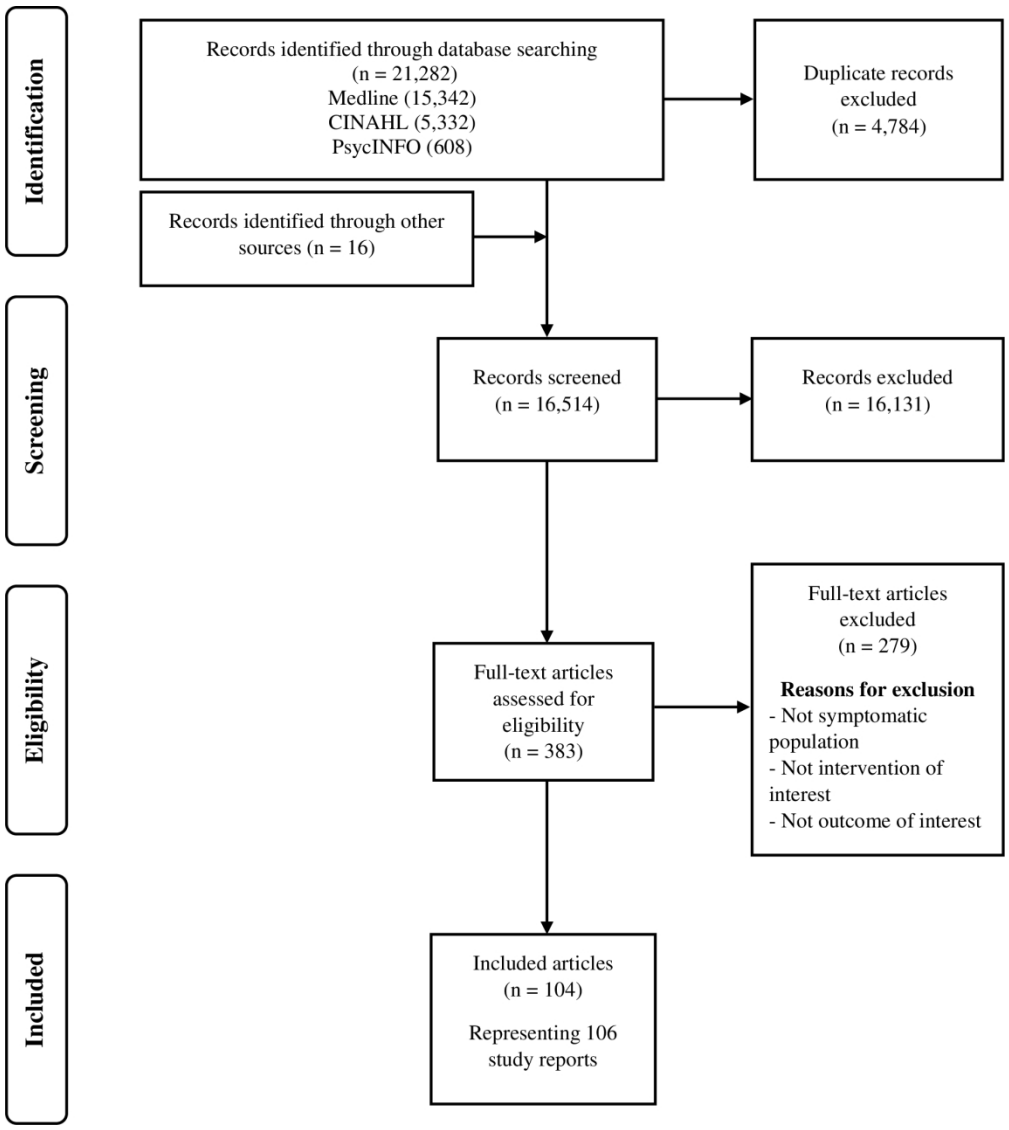
Figures

Figure 1: Modified PRISMA flow chart

Figure 2: Geographical mapping of the included published articles

Figure 3: Summary of cancer types reported by the included published articles

Figure 4: Summary of intervention types reported by the included published articles



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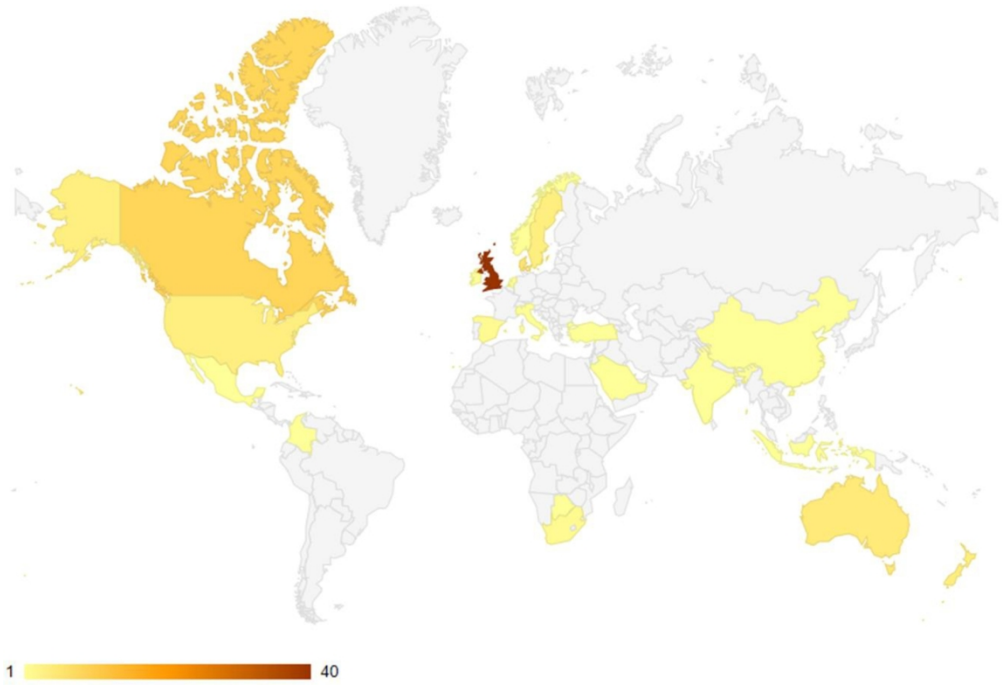

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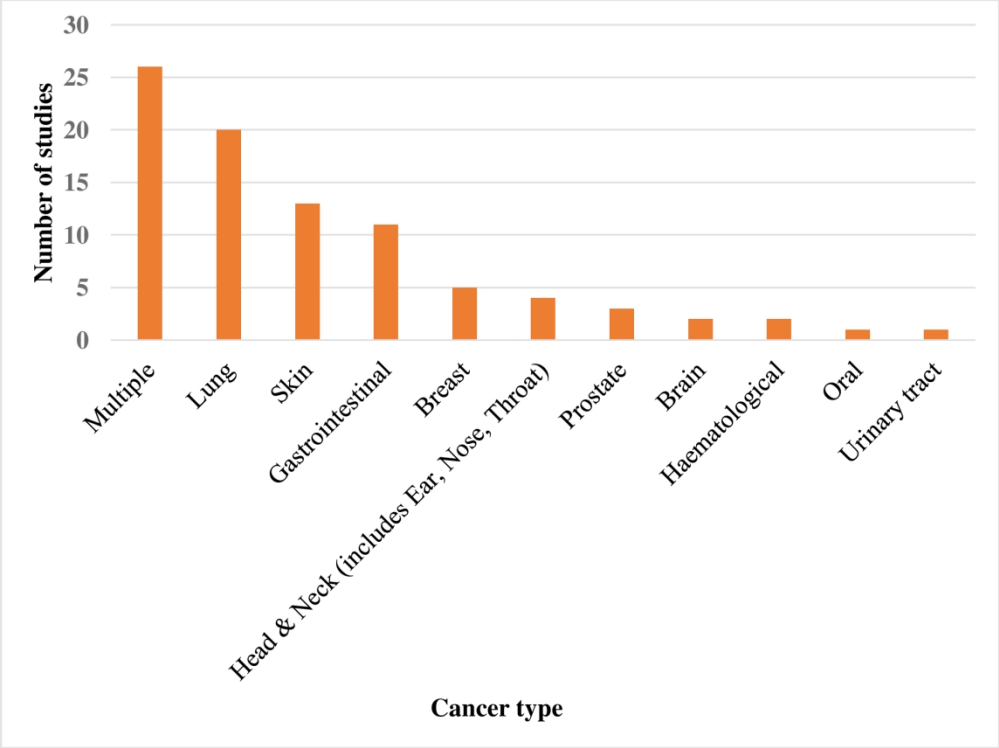

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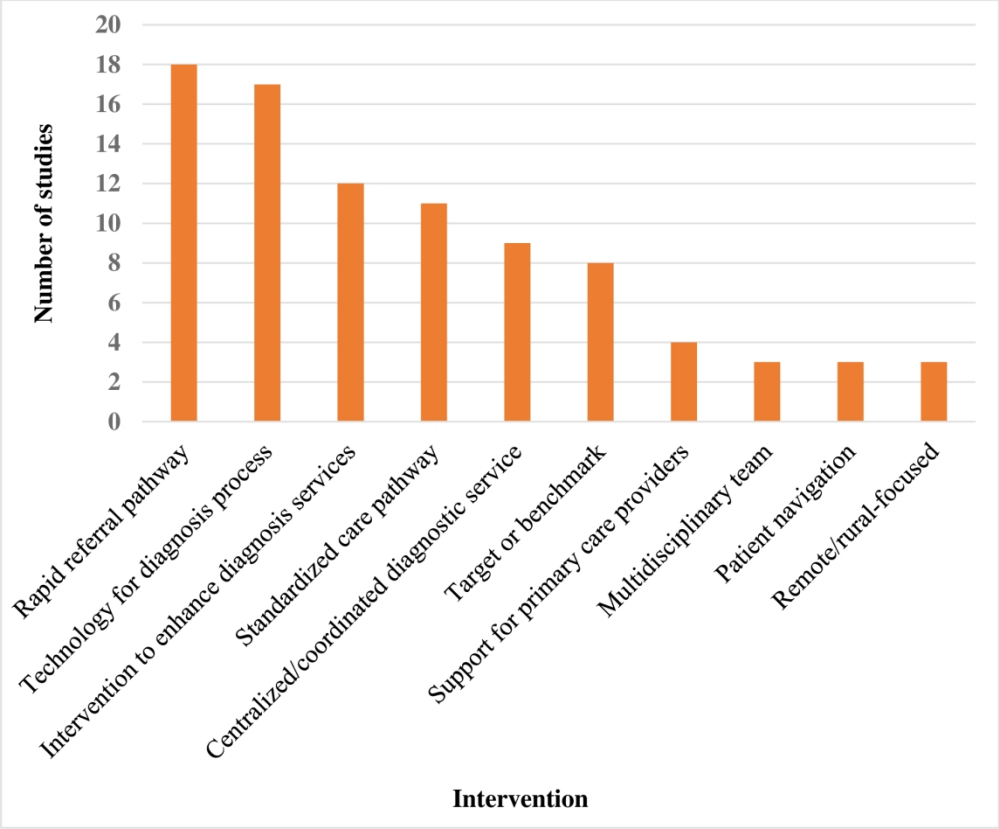

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Appendices

Appendix 1: Project work plan

About the Project Team

At the Knowledge Synthesis Team, George and Fay Yee Centre for Healthcare Innovation, we have an experienced team of methodologists, systematic reviewers, a medical librarian and biostatistician. Over the past 8 years we have supported numerous research teams and guideline developers by providing training, support and conducting evidence syntheses on their behalf. In addition, several of our team members hold academic positions with the University of Manitoba where they teach, supervise students, and advance the science and practice of knowledge synthesis.

Proposed Method

Methods

Using a team of experienced systematic reviews and methodologists, with expertise in research methodology, knowledge synthesis and implementation science, we will update the 2018 peer-reviewed and grey literature scan by conducting a rapid scoping review to include contemporary, national and international leading interventions for improving accurate and timely cancer diagnosis focusing on the symptomatic population and summarize efficacy, impact and sustainability of identified interventions. We will identify evidence to answer the following key questions:

KQ 1. Are there practice guidelines, care pathways or other initiatives (e.g., benchmarks/ targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, patient navigators and/or navigation, etc.) that have been found to streamline and enhance accurate and timely diagnosis in symptomatic individuals?

- How were patients involved in the design, development and/ or implementation of these initiatives?
- How were providers (e.g., primary care providers) involved in the design, development and/or implementation of these initiatives?

KQ 2. What are the leading interventions for innovative and/or virtual approaches (e.g., technology-based) to seamless care (i.e., minimally disruptive care that is found to be more convenient/coordinated/timely/less stressful to the patients) in the pre-diagnosis phase within Canada and abroad?

- How have these interventions been applied, including identification of successes and lessons learned where possible?
- Were these interventions evaluated and if so, what were the findings?
- How were patients involved in the design, development and/ or implementation of these interventions?

KQ 3. What are the identified performance metrics that can be used to measure the suspicion to diagnosis phase; and where and how are these metrics used?

- Are there specific metrics used to measure the patient experience?
- What data is captured by decision-support systems and how does the data and clinical systems work together?
- Is there evidence on sustainability of the model?

KQ 4. What are the key points of care in a patient's experience (e.g., diagnostic tests, physician consultations, etc.) as they navigate the system from initial symptoms/ suspicion of cancer to diagnosis?

KQ 5. Have specific considerations been applied to underserviced populations including Indigenous, rural, and remote populations within the context of each of the questions above?

Study eligibility criteria
This review will focus on published and unpublished studies that answer the key questions since 2017. Our focus is on comparative studies that applied a protocol/guideline or a specific intervention or intervention plan. Having said that, we anticipate the need to review lower quality study designs (e.g., retrospective, and uncontrolled studies). As such, there will be no restriction on the study design, but will be limited to English language publications for feasibility.

Search strategy and study selection
A knowledge synthesis librarian has designed and executed a literature search strategy in MEDLINE (Ovid). The search strategy was peer-reviewed by a second librarian and adapted for other bibliographic databases: Cinahl (Ebsco) and Psycinfo (Ovid). Search strategies are presented in Appendix 1. All retrieved records were imported into EndNote for citation management.
One reviewer will screen each identified citation for eligibility. Full texts of all relevant citations will be reviewed by two reviewers. All conflicts will be resolved by discussion and/ or a third reviewer, as needed. We will record the number of ineligible citations at the title/ abstract screening stage, and both the number and reason for ineligibility at the full-text articles.

Data extraction
We will develop data extraction forms and pilot them on a small selection of studies. Extracted data will be stored and managed in MS Excel. One reviewer will independently extract data from included studies and another reviewer will independently check the extracted data for errors. Disagreements will be resolved by discussion between reviewers and/ or by involving a third reviewer, as needed.

Data analysis
We will present specific characteristics of all included studies in a tabular form. The analysis of the extracted data will be descriptive. We will use appropriate risk of bias/ quality assessment tools based on the study designs identified in the search.

Study dissemination
We will submit reports from this study as a technical report to CPAC.

Knowledge User Engagement Plan

We will be providing a bi-weekly update to CPAC on the progression of the review. Specifically, we will engage during specific time points to review progress and next steps:

- Protocol
- Level I Screening (Title/ Abstract screening phase)
- Level II Screening (Full-text screening phase)
- Data Extraction
- Data Analysis
- Report

Declaration of Conflict of Interest

None

Appendix 2: MEDLINE (Ovid) search strategy

1.	"early detection of cancer"/	26241
2.	(cancer* or tumo?r* or neoplasm* or malignan* or metasta* or oncogen* or oncolog*).ti	1795604
3.	(carcinoma* or adenoma* or adenocarcinoma* or adeno-carcinoma* or blastoma* or carcinosarcoma* or carcino-sarcoma* or leukemia* or leukaemia* or lymphoma* or melanoma* or mesenchymoma* or mesothelioma* or sarcoma* or thymoma*).ti	844480
4.	or/2-3	2477759
5.	1 or 4	2483642
6.	early diagnosis/ or delayed diagnosis/	33272
7.	(prediagnos* or pre-diagnos* or care path? or cancer path? or care pathway* or cancer pathway* or diagnos* phase* or diagnos* path? or referral path? or diagnos* pathway* or referral pathway* or diagnos* interval* or referral interval* or consult* interval* or "time-to-treat" or "time-to-treatment").ti,ab,kf.	26471
8.	((early or earlier or prompt* or late or later or rapid or wait* or delay* or timel* or longtime or interval* or route*) adj3 (diagnos* or refer or referred or referral* or referring or consult*)).ti,ab,kf.	214615
9.	((diagnos* or confirm* or refer* or consult* or investigat*) adj4 (timelapse* or time lapse* or time elapse* or fasttrack* or fast-track* or timeline* or time line*)).ti,ab	1510
10.	delay*.ti	74391
11.	wait* time*.ti,ab.	13384
12.	or/6-11	338665
13.	4 and 12	58490
14.	diagnos*.ti,ab,kf	2562935
15.	13 and (1 or 14)	48832
16.	(interprofessional* or inter-professional* or multidisciplin* or multi-disciplin* or navigator* or coordinator* or co-ordinator* or ((patient* or cancer* or care) adj2 (navigat* or coordinat* or co-ordinat* or journey* or continuum*)) or mobile or phone* or smartphone* or reminder* or tele* or information technolog* or communicat*).ti	177088
17.	16 and 5	10725
18.	15 or 17	59240
19.	limit 18 to english language	49045
20.	(exp animal experiment/ or exp animal model/ or exp transgenic animal/ or animal/ or chordata/ or vertebrate/ or tetrapod/ or amniote/ or exp amphibia/ or mammal/ or exp reptile/ or therian/ or placental mammals/ or exp marsupial/ or euarchontoglires/ or exp xenarthra/ or primate/ or exp scandentia/ or haplorhini/ or exp prosimian/ or simian/ or exp tarsiiform/ or catarrhini/ or exp platyrrhini/ or ape/ or exp cercopithecidae/ or hominid/ or exp hylobatidae/ or exp chimpanzee/ or exp gorilla/ or (animal or animals or pisces or fish or fishes or catfish or catfishes or sheatfish or silurus or arius or heteropneustes or clarias or gariepinus or fathead minnow or fathead minnows or pimephales or promelas or cichlidae or trout or trouts or char	4778446

	or chars or salvelinus or salmo or oncorhynchus or guppy or guppies or millionfish or poecilia or goldfish or goldfishes or carassius or auratus or mullet or mullets or mugil or curema or shark or sharks or cod or cods or gadus or morhua or carp or carps or cyprinus or carpio or killifish or eel or eels or anguilla or zander or sander or lucioperca or stizostedion or turbot or turbots or psetta or flatfish or flatfishes or plaice or pleuronectes or platessa or tilapia or tilapias or oreochromis or sarotherodon or common sole or dover sole or solea or zebrafish or zebrafishes or danio or rerio or seabass or dicentrarchus or labrax or morone or lamprey or lampreys or petromyzon or pumpkinseed or pumpkinseeds or lepomis or gibbosus or herring or clupea or harengus or amphibia or amphibian or amphibians or anura or salientia or frog or frogs or rana or toad or toads or bufo or xenopus or laevis or bombina or epidalea or calamita or salamander or salamanders or newt or newts or triturus or reptilia or reptile or reptiles or bearded dragon or pogona or vitticeps or iguana or iguanas or lizard or lizards or anguis fragilis or turtle or turtles or snakes or snake or aves or bird or birds or quail or quails or coturnix or bobwhite or colinus or virginianus or poultry or poultries or fowl or fowls or chicken or chickens or gallus or zebra finch or taeniopygia or guttata or canary or canaries or serinus or canaria or parakeet or parakeets or grasskeet or parrot or parrots or psittacine or psittacines or shelduck or tadorna or goose or geese or branta or leucopsis or woodlark or lullula or flycatcher or ficedula or hypoleuca or dove or doves or geopelia or cuneata or duck or ducks or greylag or graylag or anser or harrier or circus pygargus or red knot or great knot or calidris or canutus or godwit or limosa or lapponica or meleagris or gallopavo or jackdaw or corvus or monedula or ruff or philomachus or pugnax or lapwing or peewit or plover or vanellus or swan or cygnus or columbianus or bewickii or gull or chroicocephalus or ridibundus or albifrons or great tit or parus or aythya or fuligula or streptopelia or risoria or spoonbill or platalea or leucorodia or blackbird or turdus or merula or blue tit or cyanistes or pigeon or pigeons or columba or pintail or anas or starling or sturnus or owl or athene noctua or pochard or ferina or cockatiel or nymphicus or hollandicus or skylark or alauda or tern or sterna or teal or crecca or oystercatcher or haematopus or ostralegus or shrew or shrews or sorex or araneus or crocidura or russula or european mole or talpa or chiroptera or bat or bats or eptesicus or serotinus or myotis or dasycneme or daubentonii or pipistrelle or pipistrellus or cat or cats or felis or catus or feline or dog or dogs or canis or canine or canines or otter or otters or lutra or badger or badgers or meles or fitchew or fitch or foumart or foulmart or ferrets or ferret or polecat or polecats or mustela or putorius or weasel or weasels or fox or foxes or vulpes or common seal or phoca or vitulina or grey seal or halichoerus or horse or horses or equus or equine or equidae or donkey or donkeys or mule or mules or pig or pigs or swine or swines or hog or hogs or boar or boars or porcine or piglet or piglets or sus or scrofa or llama or llamas or lama or glama or deer or deers or cervus or elaphus or cow or cows or bos taurus or bos indicus or bovine or bull or bulls or cattle or bison or bisons or sheep or sheeps or ovis aries or ovine or lamb or lambs or mouflon or mouflons or goat or goats or capra or caprine or chamois or rupicapra or leporidae or lagomorpha or lagomorph or rabbit or rabbits or oryctolagus or cuniculus or laprine or hares or lepus or rodentia or rodent or rodents or murinae or mouse or mice or mus or musculus or murine or woodmouse or apodemus or rat or rats or rattus or norvegicus or guinea pig or guinea pigs or cavia or porcellus or hamster or hamsters or mesocricetus or cricetulus or cricetus or gerbil or gerbils or jird or jirds or meriones or unguiculatus or jerboa or jerboas or jaculus or chinchilla or chinchillas or beaver or beavers or castor fiber or castor canadensis or sciuridae or squirrel or squirrels or sciurus or chipmunk or chipmunks or marmot or marmots or marmota or suslik or susliks or spermophilus or cynomys or cottonrat or cottonrats or sigmodon or vole or voles or microtus or myodes or glareolus or primate or primates or prosimian or prosimians or lemur or lemurs or lemuridae or loris or bush baby or bush babies or bushbaby or bushbabies or galago or galagos or anthropoidea or anthropoids or simian or simians or monkey or monkeys or	

	marmoset or marmosets or callithrix or cebuella or tamarin or tamarins or saguinus or leontopithecus or squirrel monkey or squirrel monkeys or saimiri or night monkey or night monkeys or owl monkey or owl monkeys or douroucoulis or aotus or spider monkey or spider monkeys or ateles or baboon or baboons or papio or rhesus monkey or macaque or macaca or mulatta or cynomolgus or fascicularis or green monkey or green monkeys or chlorocebus or vervet or vervets or pygerythrus or hominoidea or ape or apes or hylobatidae or gibbon or gibbons or siamang or siamangs or nomascus or symphalangus or hominidae or orangutan or orangutans or pongo or chimpanzee or chimpanzees or pan troglodytes or bonobo or bonobos or pan paniscus or gorilla or gorillas or troglodytes).ti,ab,kf.) not (human/ or (human$ or man or men or woman or women or child or children or patient$).ti,ab,kf.)	
21.	19 not 20	48488
22.	limit 21 to yr="2017 -Current"	15342

Appendix 3: CINAHL (EbscoHOST) search strategy

1.	(MH "early detection of cancer")	9365
2.	TI (cancer* OR tumo#r* OR neoplasm* OR malignan* OR metasta* OR oncogen* OR oncolog*)	382286
3.	TI (carcinoma* OR adenoma* OR adenocarcinoma* OR blastoma* OR carcinosarcoma* OR leukemia* OR leukaemia* OR lymphoma* OR melanoma* OR mesenchymoma* OR mesothelioma* OR sarcoma* OR thymoma*)	110746
4.	S2 OR S3	469442
5.	S1 OR S4	471736
6.	(MH "early diagnosis") OR (MH "diagnosis, delayed")	14703
7.	(TI (prediagnos* OR "pre-diagnosis" OR (care N1 path#) OR (cancer N1 path#) OR (care N1 pathway*) OR (cancer N1 pathway*) OR (diagnos* N1 phase*) OR (diagnos* N1 path#) OR (referral N1 path#) OR (diagnos* N1 pathway*) OR (referral N1 pathway*) OR (diagnos* N1 interval*) OR (referral N1 interval*) OR (consult* N1 interval*) OR "time-to-treat" OR "time-to-treatment")) OR (AB (prediagnos* OR "pre-diagnosis" OR (care N1 path#) OR (cancer N1 path#) OR (care N1 pathway*) OR (cancer N1 pathway*) OR (diagnos* N1 phase*) OR (diagnos* N1 path#) OR (referral N1 path#) OR (diagnos* N1 pathway*) OR (referral N1 pathway*) OR (diagnos* N1 interval*) OR (referral N1 interval*) OR (consult* N1 interval*) OR "time-to-treat" OR "time-to-treatment"))	11308
8.	(TI ((early OR earlier OR prompt* OR late OR later OR rapid OR wait* OR delay* OR timel* OR longtime OR interval* OR route*) N3 (diagnos* OR refer OR referred OR referral* OR referring OR consult*))) OR (AB ((early OR earlier OR prompt* OR late OR later OR rapid OR wait* OR delay* OR timel* OR longtime OR interval* OR route*) N3 (diagnos* OR refer OR referred OR referral* OR referring OR consult*)))	47662
9.	(TI ((diagnos* OR confirm* OR refer* OR consult* OR investigat*) N4 (timelapse* OR (time N1 lapse*) OR (time N1 elapse*) OR fasttrack* OR (fast N1 track*) OR timeline* OR (time N1 line*)))) OR (AB ((diagnos* OR confirm* OR refer* OR consult* OR investigat*) N4 (timelapse* OR (time N1 lapse*) OR (time N1 elapse*) OR fasttrack* OR (fast N1 track*) OR timeline* OR (time N1 line*))))	582
10.	TI delay*	17790
11.	(TI (wait* N1 time*)) OR (AB (wait* N1 time*))	6047
12.	S6 OR S7 OR S8 OR S9 OR S10 OR S11	88476
13.	S4 AND S12	13005
14.	(TI diagnos*) OR (AB diagnos*)	526863
15.	S13 AND (S1 OR S14)	9687
16.	TI (interprofessional* OR (inter N1 professional*) OR multidisciplin* OR (multi N1 disciplin*) OR navigator* OR coordinator* OR ordinator* OR ((patient* OR cancer* OR care) N2 (navigat* OR coordinat* OR ordinat* OR journey* OR continuum*)) OR mobile OR phone* OR smartphone* OR reminder* OR tele* OR (information N1 technolog*) OR communicat*)	94165
17.	S16 AND S5	5442
18.	S15 OR S17	14982
19.	S18 Limiters - English Language	14767
20.	((MH "animals+") OR (MH invertebrates+) OR (MH birds+) OR (MH fish) OR (MH "frogs and toads") OR (MH "animals, genetically modified") OR (MH reptiles+) OR (MH mammals) OR (MH bats) OR (MH camels) OR (MH cats) OR (MH cattle) OR (MH dogs) OR (MH dolphins) OR (MH goats) OR (MH horses) OR (MH rabbits) OR (MH rodents+) OR (MH	216053

	sheep) OR (MH swine) OR (MH primates) OR (animal OR animals OR pisces OR fish OR fishes OR catfish OR catfishes OR sheatfish OR silurus OR arius OR heteropneustes OR clarias OR gariepinus OR "fathead minnow" OR "fathead minnows" OR pimephales OR promelas OR cichlidae OR trout OR trouts OR char OR chars OR salvelinus OR salmo OR oncorhynchus OR guppy OR guppies OR millionfish OR poecilia OR goldfish OR goldfishes OR carassius OR auratus OR mullet OR mullets OR mugil OR curema OR shark OR sharks OR cod OR cods OR gadus OR morhua OR carp OR carps OR cyprinus OR carpio OR killifish OR eel OR eels OR anguilla OR zander OR sander OR lucioperca OR stizostedion OR turbot OR turbots OR psetta OR flatfish OR flatfishes OR plaice OR pleuronectes OR platessa OR tilapia OR tilapias OR oreochromis OR sarotherodon OR "common sole" OR "dover sole" OR solea OR zebrafish OR zebrafishes OR danio OR rerio OR seabass OR dicentrarchus OR labrax OR morone OR lamprey OR lampreys OR petromyzon OR pumpkinseed OR pumpkinseeds OR lepomis OR gibbosus OR herring OR clupea OR harengus OR amphibia OR amphibian OR amphibians OR anura OR salientia OR frog OR frogs OR rana OR toad OR toads OR bufo OR xenopus OR laevis OR bombina OR epidalea OR calamita OR salamander OR salamanders OR newt OR newts OR triturus OR reptilia OR reptile OR reptiles OR "bearded dragon" OR pogona OR vitticeps OR iguana OR iguanas OR lizard OR lizards OR "anguis fragilis" OR turtle OR turtles OR snakes OR snake OR aves OR bird OR birds OR quail OR quails OR coturnix OR bobwhite OR colinus OR virginianus OR poultry OR poultries OR fowl OR fowls OR chicken OR chickens OR gallus OR "zebra finch" OR taeniopygia OR guttata OR canary OR canaries OR serinus OR canaria OR parakeet OR parakeets OR grasskeet OR parrot OR parrots OR psittacine OR psittacines OR shelduck OR tadorna OR goose OR geese OR branta OR leucopsis OR woodlark OR lullula OR flycatcher OR ficedula OR hypoleuca OR dove OR doves OR geopelia OR cuneata OR duck OR ducks OR greylag OR graylag OR anser OR harrier OR circus pygargus OR red knot OR "great knot" OR calidris OR canutus OR godwit OR limosa OR lapponica OR meleagris OR gallopavo OR jackdaw OR corvus OR monedula OR ruff OR philomachus OR pugnax OR lapwing OR peewit OR plover OR vanellus OR swan OR cygnus OR columbianus OR bewickii OR gull OR chroicocephalus OR ridibundus OR albifrons OR "great tit" OR parus OR aythya OR fuligula OR streptopelia OR risoria OR spoonbill OR platalea OR leucorodia OR blackbird OR turdus OR merula OR blue tit OR cyanistes OR pigeon OR pigeons OR columba OR pintail OR anas OR starling OR sturnus OR owl OR "athene noctua" OR pochard OR ferina OR cockatiel OR nymphicus OR hollandicus OR skylark OR alauda OR tern OR sterna OR teal OR crecca OR oystercatcher OR haematopus OR ostralegus OR shrew OR shrews OR sorex OR araneus OR crocidura OR russula OR "european mole" OR talpa OR chiroptera OR bat OR bats OR eptesicus OR serotinus OR myotis OR dasycneme OR daubentonii OR pipistrelle OR pipistrellus OR cat OR cats OR felis OR catus OR feline OR dog OR dogs OR canis OR canine OR canines OR otter OR otters OR lutra OR badger OR badgers OR meles OR fitchew OR fitch OR foumart OR foulmart OR ferrets OR ferret OR polecat OR polecats OR mustela OR putorius OR weasel OR weasels OR fox OR foxes OR vulpes OR "common seal" OR phoca OR vitulina OR grey seal OR halichoerus OR horse OR horses OR equus OR equine OR equidae OR donkey OR donkeys OR mule OR mules OR pig OR pigs OR swine OR swines OR hog OR hogs OR boar OR boars OR porcine OR piglet OR piglets OR sus OR scrofa OR llama OR llamas OR lama OR glama OR deer OR deers OR cervus OR elaphus OR cow OR cows OR "bos taurus" OR "bos indicus" OR bovine OR bull OR bulls OR cattle OR bison OR bisons OR sheep OR sheeps OR "ovis aries" OR ovine OR lamb OR lambs OR mouflon OR mouflons OR goat OR goats OR capra OR caprine OR chamois OR rupicapra OR leporidae OR lagomorpha OR lagomorph OR rabbit OR rabbits OR oryctolagus OR cuniculus OR laprine OR hares OR lepus OR rodentia OR rodent OR rodents OR murinae OR mouse OR mice OR mus OR musculus OR murine OR woodmouse	

	OR apodemus OR rat OR rats OR rattus OR norvegicus OR "guinea pig" OR "guinea pigs" OR cavia OR porcellus OR hamster OR hamsters OR mesocricetus OR cricetulus OR cricetus OR gerbil OR gerbils OR jird OR jirds OR meriones OR unguiculatus OR jerboa OR jerboas OR jaculus OR chinchilla OR chinchillas OR beaver OR beavers OR "castor fiber" OR "castor canadensis" OR sciuridae OR squirrel OR squirrels OR sciurus OR chipmunk OR chipmunks OR marmot OR marmots OR marmota OR suslik OR susliks OR spermophilus OR cynomys OR cottonrat OR cottonrats OR sigmodon OR vole OR voles OR microtus OR myodes OR glareolus OR primate OR primates OR prosimian OR prosimians OR lemur OR lemurs OR lemuridae OR loris OR "bush baby" OR "bush babies" OR bushbaby OR bushbabies OR galago OR galagos OR anthropoidea OR anthropoids OR simian OR simians OR monkey OR monkeys OR marmoset OR marmosets OR callithrix OR cebuella OR tamarin OR tamarins OR saguinus OR leontopithecus OR squirrel monkey OR squirrel monkeys OR saimiri OR "night monkey" OR "night monkeys" OR "owl monkey" OR "owl monkeys" OR douroucoulis OR aotus OR "spider monkey" OR "spider monkeys" OR ateles OR baboon OR baboons OR papio OR "rhesus monkey" OR macaque OR macaca OR mulatta OR cynomolgus OR fascicularis OR "green monkey" OR "green monkeys" OR chlorocebus OR vervet OR vervets OR pygerythrus OR hominoidea OR ape OR apes OR hylobatidae OR gibbon OR gibbons OR siamang OR siamangs OR nomascus OR symphalangus OR hominidae OR orangutan OR orangutans OR pongo OR chimpanzee OR chimpanzees OR "pan troglodytes" OR bonobo OR bonobos OR "pan paniscus" OR gorilla OR gorillas OR troglodytes)) NOT ((MH human) OR (human# OR man OR men OR woman OR women OR child OR children OR patient#))	
21.	S19 NOT S20	14678
22.	S21 Limiters - Published Date: 20170101-20201231	5333

Appendix 4: Psycinfo (Ovid) search strategy

1.	cancer screening/	4776
2.	(cancer* or tumo?r* or neoplasm* or malignan* or metasta* or oncogen* or oncolog*).ti	44464
3.	(carcinoma* or adenoma* or adenocarcinoma* or adeno-carcinoma* or blastoma* or carcinosarcoma* or carcino-sarcoma* or leukemia* or leukaemia* or lymphoma* or melanoma* or mesenchymoma* or mesothelioma* or sarcoma* or thymoma*).ti	2705
4.	or/2-3	46737
5.	1 or 4	47903
6.	(prediagnos* or pre-diagnos* or care path? or cancer path? or care pathway* or cancer pathway* or diagnos* phase* or diagnos* path? or referral path? or diagnos* pathway* or referral pathway* or diagnos* interval* or referral interval* or consult* interval* or "time-to-treat" or "time-to-treatment").ti,ab,id.	3896
7.	((early or earlier or prompt* or late or later or rapid or wait* or delay* or timel* or longtime or interval* or route*) adj3 (diagnos* or refer or referred or referral* or referring or consult*)).ti,ab,id.	13853
8.	((diagnos* or confirm* or refer* or consult* or investigat*) adj4 (timelapse* or time lapse* or time elapse* or fasttrack* or fast-track* or timeline* or time line*)).ti,ab	168
9.	delay*.ti	14212
10.	wait* time*.ti,ab.	1957
11.	or/6-10	33241
12.	4 and 11	1613
13.	diagnos*.ti,ab,id	324967
14.	12 and (1 or 13)	1345
15.	(interprofessional* or inter-professional* or multidisciplin* or multi-disciplin* or navigator* or coordinator* or co-ordinator* or ((patient* or cancer* or care) adj2 (navigat* or coordinat* or co-ordinat* or journey* or continuum*)) or mobile or phone* or smartphone* or reminder* or tele* or information technolog* or communicat*).ti	81166
16.	15 and 5	1650
17.	14 or 16	2949
18.	limit 17 to english language	2756
19.	(exp animal research/ or animal models/ or exp animals/ or ("20").po or (animal or animals or pisces or fish or fishes or catfish or catfishes or sheatfish or silurus or arius or heteropneustes or clarias or gariepinus or fathead minnow or fathead minnows or pimephales or promelas or cichlidae or trout or trouts or char or chars or salvelinus or salmo or oncorhynchus or guppy or guppies or millionfish or poecilia or goldfish or goldfishes or carassius or auratus or mullet or mullets or mugil or curema or shark or sharks or cod or cods or gadus or morhua or carp or carps or cyprinus or carpio or killifish or eel or eels or anguilla or zander or sander or lucioperca or stizostedion or turbot or turbots or psetta or flatfish or flatfishes or plaice or pleuronectes or platessa or tilapia or tilapias or oreochromis or sarotherodon or common sole or dover sole or solea or zebrafish or zebrafishes or danio or rerio or seabass or dicentrarchus or labrax or morone or lamprey or lampreys or petromyzon or pumpkinseed or pumpkinseeds or lepomis or gibbosus or herring or clupea or harengus or amphibia or amphibian or amphibians or anura or salientia or frog or frogs or rana or toad or toads or bufo or xenopus or laevis or bombina or epidalea or calamita or salamander or salamanders or newt or newts or triturus or reptilia or reptile or reptiles or bearded dragon or pogona or vitticeps or iguana or iguanas or lizard or lizards or anguis fragilis or turtle or turtles or snakes or snake or aves or bird or birds or quail or quails or coturnix or bobwhite or colinus or virginianus or poultry or poultries or	339315

	fowl or fowls or chicken or chickens or gallus or zebra finch or taeniopygia or guttata or canary or canaries or serinus or canaria or parakeet or parakeets or grasskeet or parrot or parrots or psittacine or psittacines or shelduck or tadorna or goose or geese or branta or leucopsis or woodlark or lullula or flycatcher or ficedula or hypoleuca or dove or doves or geopelia or cuneata or duck or ducks or greylag or graylag or anser or harrier or circus pygargus or red knot or great knot or calidris or canutus or godwit or limosa or lapponica or meleagris or gallopavo or jackdaw or corvus or monedula or ruff or philomachus or pugnax or lapwing or peewit or plover or vanellus or swan or cygnus or columbianus or bewickii or gull or chroicocephalus or ridibundus or albifrons or great tit or parus or aythya or fuligula or streptopelia or risoria or spoonbill or platalea or leucorodia or blackbird or turdus or merula or blue tit or cyanistes or pigeon or pigeons or columba or pintail or anas or starling or sturnus or owl or athene noctua or pochard or ferina or cockatiel or nymphicus or hollandicus or skylark or alauda or tern or sterna or teal or crecca or oystercatcher or haematopus or ostralegus or shrew or shrews or sorex or araneus or crocidura or russula or european mole or talpa or chiroptera or bat or bats or eptesicus or serotinus or myotis or dasycneme or daubentonii or pipistrelle or pipistrellus or cat or cats or felis or catus or feline or dog or dogs or canis or canine or canines or otter or otters or lutra or badger or badgers or meles or fitchew or fitch or foumart or foulmart or ferrets or ferret or polecat or polecats or mustela or putorius or weasel or weasels or fox or foxes or vulpes or common seal or phoca or vitulina or grey seal or halichoerus or horse or horses or equus or equine or equidae or donkey or donkeys or mule or mules or pig or pigs or swine or swines or hog or hogs or boar or boars or porcine or piglet or piglets or sus or scrofa or llama or llamas or lama or glama or deer or deers or cervus or elaphus or cow or cows or bos taurus or bos indicus or bovine or bull or bulls or cattle or bison or bisons or sheep or sheeps or ovis aries or ovine or lamb or lambs or mouflon or mouflons or goat or goats or capra or caprine or chamois or rupicapra or leporidae or lagomorpha or lagomorph or rabbit or rabbits or oryctolagus or cuniculus or laprine or hares or lepus or rodentia or rodent or rodents or murinae or mouse or mice or mus or musculus or murine or woodmouse or apodemus or rat or rats or rattus or norvegicus or guinea pig or guinea pigs or cavia or porcellus or hamster or hamsters or mesocricetus or cricetulus or cricetus or gerbil or gerbils or jird or jirds or meriones or unguiculatus or jerboa or jerboas or jaculus or chinchilla or chinchillas or beaver or beavers or castor fiber or castor canadensis or sciuridae or squirrel or squirrels or sciurus or chipmunk or chipmunks or marmot or marmots or marmota or suslik or susliks or spermophilus or cynomys or cottonrat or cottonrats or sigmodon or vole or voles or microtus or myodes or glareolus or primate or primates or prosimian or prosimians or lemur or lemurs or lemuridae or loris or bush baby or bush babies or bushbaby or bushbabies or galago or galagos or anthropoidea or anthropoids or simian or simians or monkey or monkeys or marmoset or marmosets or callithrix or cebuella or tamarin or tamarins or saguinus or leontopithecus or squirrel monkey or squirrel monkeys or saimiri or night monkey or night monkeys or owl monkey or owl monkeys or douroucoulis or aotus or spider monkey or spider monkeys or ateles or baboon or baboons or papio or rhesus monkey or macaque or macaca or mulatta or cynomolgus or fascicularis or green monkey or green monkeys or chlorocebus or vervet or vervets or pygerythrus or hominoidea or ape or apes or hylobatidae or gibbon or gibbons or siamang or siamangs or nomascus or symphalangus or hominidae or orangutan or orangutans or pongo or chimpanzee or chimpanzees or pan troglodytes or bonobo or bonobos or pan paniscus or gorilla or gorillas or troglodytes).ti,ab,id.) not (("10").po or (human$ or man or men or woman or women or child or children or patient$).ti,ab,id.)	
20.	18 not 19	2754
21.	limit 20 to yr="2017 -Current"	608

Appendix 5: Websites of relevant organizations and professional bodies searched for literature

Canada

- Alberta Cancer Foundation
- BC Cancer Foundation
- BC Cancer Agency
- Cancer Care Manitoba
- Cancer Care Nova Scotia
- Cancer Care Ontario
- CancerControl Alberta
- Canada Health Infoway
- Canadian Association of Nurses in Oncology
- Canadian Association of Psychosocial Oncology
- Canadian Cancer Society
- Canadian Foundation for Healthcare Improvement
- Canadian Foundation for Innovation
- Canadian Institutes of Health Research
- Cancer and Primary Care Research
- Cancer Quality Council of Ontario
- Cancerview.ca
- CanIMPACT
- College of Family Physicians of Canada
- International Network
- New Brunswick Cancer Network
- Ontario Institute for Cancer Research
- Quebec Health and Social Services (Direction québécoise de cancérologie, Ministère de la Santé et des Services sociaux)
- Royal College of Physicians and Surgeons of Canada
- Saskatchewan Cancer Agency
- Trillium Health Partners

International

- Association of Community Cancer Centres – USA
- Centers for Disease Control and Prevention – USA
- Commission on Cancer of the American College of Surgeons – USA
- Institute of Medicine – USA
- National Cancer Institute – USA
- National Comprehensive Cancer Network – USA
- Cancer Research UK (including the Accelerate, Coordinate, Evaluate Programme) – UK
- Kings Fund – UK
- National Health Service (NHS) – UK
- National Institute for Health and Care Excellence (NICE) – UK
- Northern Cancer Network – New Zealand
- Cancer Australia – Australia
- Sax Institute – Australia
- Denmark (Ministry of Health)
- Sweden (Ministry of Health)
- European Organization for Research and Treatment of Cancer – Europe
- European Society for Medical Oncology – Europe
- European Partnership Action Against Cancer – Europe
- World Health Organization – International

Appendix 6: Definition for interventions related to the review questions

- *Centralized or coordinated diagnostic service*: Brings together various tests/procedures and care providers needed to determine a definitive diagnosis at one location.
- *Interventions in diagnostic services*: An initiative that aims to improve diagnostic services within a jurisdiction.
- *Multidisciplinary team*: Working with multiple departments, such as diagnostic imaging, pathology, medical oncology, and research.
- *Patient navigation*: A dedicated role to help facilitate the navigation for patients across the cancer journey – helps the patient through testing, appointments, health literacy, etc.
- *Rapid referral pathway*: Provides urgent access to specialists and/or diagnostic services for patients.
- *Remote or rural populations*: This refers to populations that may live in non-urban areas. They often do not have access to the same services as those who reside in more urban areas.
- *Standardized care pathway*: Sets expectations for cancer care based on evidence and shares information about how to provide and what care to provide at each point of diagnosis, treatment, and survivorship. Initiative is often integrated into the current health system.
- *Support for primary care providers*: Initiative focusing on educating and supporting primary care providers on care pathways and how to care for individuals presenting with potential or confirmed cancer symptoms.
- *Target or benchmark*: A figure used as a goal by jurisdictions to measure progress towards the desired outcome of an initiative.
- *Technology to support diagnosis process*: Technological innovations to enhance efficiency of initiatives.

Appendix 7: Summary of the characteristics of the included published articles that reported data on ineffective interventions

Interventions	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Interventions to enhance diagnostic services	Agnarsdottir 2019	Sweden (Uppsala)	Cross-sectional (2016-2018)	Skin (Adult) [286]	Reporting time	The reporting time increased from 18 to 31 days for the non-priority cases and from 15 to 25 days for all cases with invasive melanomas (Ineffective)
	McCutchan 2020	UK (Wales)	Before-and-After (2016)	Lung (Mixed age) [1011 (pre-campaign); 1013 (post-campaign)]	Urgent suspected referrals to specialist	There was no statistically significant change in urgent suspected cancer referrals (p = 0.82) in routes to diagnosis (Ineffective)
Multidisciplinary team	Largey 2020	Australia (Victoria)	Before-and-After (2016-2017)	Lung (Adult) [429]	Time interval from referral to first specialist appointment	Referral to first specialist appointment interval was reduced in the post intervention period from median (IQR) 6 (0-15) to 4 (1-10) days, with no significant trend (p=0.962) (Ineffective)
	Thalanayar Muthukrishnan 2020	USA (Cleveland)	Case-Control (2015-2017)	Lung (NR) [161]	Time interval from suspicion to diagnosis	The mean time intervals for imaging to staging (with standard deviations) were 65 days in controls (SD=42.67) and 75 days (SD=58.27) in tumor board cases (p=0.39) (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Rapid referral pathway	Fallon 2019	UK (Luton)	Case-Control (2015-2017)	Gastrointestinal (Adult) [509 (148 UGI; 361 LGI)]	Stage of malignancy at time of presentation	Two weeks wait referral did not achieve an earlier diagnosis compared with non-2 week wait routes of referral in upper gastrointestinal ($\chi 2(3)=2.6$, p=0.458) and lower gastrointestinal ($\chi 2(3)=0.884$, p=0.829) malignancies (Ineffective)
	Jefferson 2019	UK	Cross-sectional (2016-2018)	Multiple (Adult) [24]	Factors affecting patients' non-	The following were identified: system flaws; GP difficulties with booking

		(A Northern English city)			attendance following referral	appointments; patient difficulties with navigating the appointment system, patients leading 'difficult lives'; and patients' expectations of the referral, informed by their beliefs, circumstances, priorities, and the perceived prognosis (Ineffective)
	Kassirian 2020	Canada (London, Ontario)	Cross-sectional (2017-2018)	Ear, Nose and Throat (Adult) [102]	Time from presentation to appointment at the multi-disciplinary clinic	The average time for patients to have their first appointment was 15.1 months, consisting of 3.9 months for patients to see a health care provider for the first time since symptom onset and 10.7 months from first appointment to being seen at the clinic – representing significant delays (Ineffective)
	Neal 2017	UK (Wales; Yorkshire)	RCT (2012-2015)	Lung (Adult) [255]	Anxiety and depression scores	There was no evidence of a difference in post-randomisation anxiety scores between trial arms (median (IQR): 6 (3–8) in control vs 5 (3–9) in intervention, z=0.32; P=0.75) (Ineffective)
	Scott 2020	UK (Countrywide)	Case-Control (2009-2011)	Multiple (Mixed age) [10314]	Cancer occurrence 5 years after negative diagnosis	4.0% for those referred via pathway and 2.1% for those routinely referred (Ineffective)
	Talwar 2020	UK (Merseyside)	Cross-sectional (2017-2019)	Head and Neck (NR) [113]	Time from referral to being seen in hospital	The time taken from referral to being seen in hospital was a median (IQR) of 10 (6–13) days (range 1–28 days) with 11/110 (10%) exceeding 14 days (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Standardized care pathway	Almuammar 2019	Saudi Arabia (Countrywide)	Cross-sectional (2010-2012)	Multiple (Adult) [20]	Patient satisfaction with GP in the pathway	Patients felt that GPs did not listen to them, and were likely to undermine the role of GPs as active practitioners in healthcare provision (Ineffective)
	Gardner 2020	UK (Edinburgh)	Case-Control (2016-2018)	Ear, Nose and Throat	Time from referral to diagnosis	Patients referred by GP on the 'urgent suspicion of cancer' pathway were seen more quickly than those referred

				(Mixed age) [62]		routinely were. However, these differences were not significant (Ineffective)
	Iachina 2017	Denmark (Countrywide)	Case-Control (2008-2012)	Lung (Adult) [11273]	Time from referral to end of primary investigation	Time from referral to the end of primary investigation did not significantly change (1.00 (0.93;1.08)) (Ineffective)
	Jensen 2017	Denmark (Countrywide)	Case-Control (2004-2010)	Multiple (Adult) [7725]	Mortality	When comparing pathway-referred patients against non-pathway-referred patients, non-significant lower excess mortality was observed among the pathway referred (excess hazard ratios = 0.86 (95% CI: 0.73;1.01) (Ineffective)
	Price 2020	UK (National)	Cross-sectional (2006-2017)	Multiple (Adult) [83935]	Diagnostic interval	Median New-NICE values were consistently longer (99, 40–212 in 2006 vs 103, 42–236 days in 2017) than Old-NICE values across all cancers (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Support for primary care providers	Evans 2018	UK (Oxfordshire)	Cross-sectional (2016-2017)	Multiple (Adult) [NR]	GP perspectives on safety netting	GPs revealed uncertainty about which aspects of clinical practice were considered safety netting (Ineffective)
	Kidney 2017	UK (Urban West Midlands)	Cross-sectional (2014)	Gastrointestinal (Adult) [NR]	Barriers for referral	A desire to avoid over-referral, lack of knowledge of guidelines, and the use of individually derived decision rules for further investigation or referral of symptoms (Ineffective)
	Zienius 2019	UK (Scotland)	Cross-sectional (2010-2015)	Brain (Adult) [2938]	Predictive value of referral guidelines for imaging where a tumour is suspected	With symptom-based referral guidelines, primary care doctors can identify patients with a 3% positive predictive value (Ineffective)
	Di Girolamo 2018	UK (England)	Cross-sectional (2009-2013)	Multiple (Mixed age) [360643 (CRC 164890, lung	1-year survival of patients	For 31-day and 62-day targets survival was worse for those for whom the targets were and were not met (Ineffective)

				171208, ovarian 24545)]		
Target or benchmark for wait times	Brian 2017	New Zealand (Hamilton)	Before-and-After (2016)	Skin (Adult) [143]	Time to diagnosis	Compliance with recommended time intervals was poor for patients referred with skin lesions suspicious for melanoma; from referral to diagnostic skin biopsy, compliance was 17.6% (Ineffective)
	Venchairutti 2016	Australia (New South Wales)	Case-Control (2008-2013)	Multiple (Adult) [224]	Time from symptom onset to diagnosis	Regional/remote patients had a longer interval from symptom onset to diagnosis (median 5.4 months [IQR 9.2 months]) compared with metropolitan patients (median 2.1 months [IQR 4.3 months]) (P = 0.002) (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Technology to support diagnosis process	Chung 2020	Netherlands (Amsterdam; Rotterdam)	Cross-sectional (2017)	Skin (Adult) [125]	Risk assessment performance	The inter-observer agreement between the ratings of the automated risk assessment and the dermatologist was poor (Ineffective)
	Lau 2018	UK (West Midlands and Berkshire)	Case-Control (2009-2013)	Multiple (Adult) [1005]	False-negative rate	A sensitivity of 31% and specificity of 92% (Ineffective)
	Pannebakker 2019	UK (NR)	Cross-sectional (2016-2017)	Skin (Adult) [14]	Patient perspectives on implementation and usefulness	No patients were aware that the electronic clinical decision support had been used during their consultation (Ineffective)
	Walter 2020	UK (Eastern England)	RCT (2016-2017)	Skin (Adult) [238]	Time between first noticing a change and consultation	There were no statistically significant differences between trial groups on any of the secondary outcome measures (Ineffective)

CRC = colorectal cancer; GP = general practitioner; LGI = upper gastrointestinal; NICE = National Institute for Health and Care Excellence; NR = not reported; RCT = randomized controlled trial; UGI = upper gastrointestinal; UK = United Kingdom; USA = United States of America; IQR = interquartile range

Appendix 8: Summary of the characteristics of the included published articles that reported data on remote or rural populations

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Chavarri-Guerra 2019	Mexico (Mexico City)	Before-and-After (2016-2017)	Multiple (Adult) [70]	Feasibility of patient navigation	All patients were from an under-served population. 91% of patients successfully obtained appointments at cancer centers in <3 months.
Emery 2017	Australia (Western Australia)	RCT (2011-2013)	Multiple (Adult) [1358]	Time to diagnosis	All patients were from a rural population. There were no significant differences on the time to diagnosis with and without intervention.
Murchie 2020	UK (Scotland; England)	Cross-sectional (2017)	Multiple (Mixed age) [1314]	Time from presentation in primary care to diagnosis	The median primary care interval was 5 days (IQR 0-23 days) and median diagnostic interval was 30 days (IQR 13-68). Diagnostic intervals were longer in the most remote patients.
Venchairutti 2016	Australia (New South Wales)	Case-Control (2008-2013)	Multiple (Adult) [224]	Time from symptom onset to diagnosis	Regional/remote patients had a longer interval from symptom onset to diagnosis (median 5.4 months [IQR 9.2 months]) compared with metropolitan patients (median 2.1 months [IQR 4.3 months]) (P = 0.002).
Yeşiler 2020	Turkey (Ankara)	Cross-sectional (2010-2011)	Lung (Adult) [122]	Delay in diagnosis times	No significant difference in the mean duration from symptom onset to pathological diagnosis. No significant differences were identified based on patient residence.

UK = United Kingdom; IQR = interquartile range

Appendix 9: Summary of performance metrics to measure improvements in suspicion to diagnosis phase

Intervention Type	Performance Metric
Centralized or coordinated diagnostic service	• Time from presentation in primary care to diagnosis • Time from referral from primary care to specialist consultation • Time from first abnormal image to biopsy
Interventions to enhance diagnostic services	• Time from referral from primary care to specialist consultation • Time from initial specialist consultation to diagnosis • Time from initial specialist consultation to biopsy • Time from first abnormal image to biopsy • Time from presentation in primary care to biopsy • Total diagnostic interval • Turnaround time for diagnosis following histology • Number of urgent referrals to specialist • Cancer detection rate • Patient survival
Multidisciplinary team	• Time from referral from primary care to specialist consultation • Time from first abnormal image to diagnosis
Patient navigation	• Waiting times from the point of referral from primary care to initial specialist assessment • Feasibility of program/process • Delays in diagnostic resolutions

Summary of findings

- This scoping review explores contemporary interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals.
- It included 88 unique published (peer-reviewed) articles and 16 unique unpublished articles (grey literature; representing 18 different reports).
- The United Kingdom appears to be championing this area of research, contributing about half of all identified published literature and 83% of the identified unpublished literature.
- Rapid referral pathways and technology for supporting and streamlining the diagnosis process were the most commonly studied interventions.
- Most of the interventions were in lung cancer patients.
- There was scant reporting on interventions for underserved/Indigenous populations.
- Performance metrics utilized in studies were mainly intervention-dependent; however, time from presentation to diagnosis and from referral to specialist consultation were most consistent metrics across the majority of interventions, with performance metrics to measure patients' experience mainly centered on patient-reported satisfaction and quality of life.
- A common theme among the effective interventions (based on author-reported outcomes) involved multidisciplinary cooperation and a nurse navigator, with interventions generally complex and organization-specific.
- None of the support packages for primary care providers (all educational and informational) was found to be effective; the identified common theme across the publications was a lack of awareness of referral guidelines and associated knowledge by general practitioners notwithstanding this information being provided.

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.	4-5
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.	7-8
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.	8-9
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.	9
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.	10-11
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.	10
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix 2 - 4
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	10-11
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.	11-12
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Appendix 6
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).	Not applicable

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	11-12
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.	Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Table 1
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not applicable
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.	14-24
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	13-24
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.	25-27
Limitations	20	Discuss the limitations of the scoping review process.	27
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.	28
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.	2

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).

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.

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Interventions to improve early cancer diagnosis of symptomatic patients: A scoping review

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Transparency declaration: The corresponding author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Abstract

Objectives: To summarize the current evidence regarding interventions for accurate and timely cancer diagnosis among symptomatic individuals.

Design: A scoping review following the Joanna Briggs Institute's methodological framework for the conduct of scoping reviews and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping reviews (PRISMA-ScR) checklist.

Data sources: MEDLINE (Ovid), CINAHL (EBSCOhost) and PsycINFO (Ovid) bibliographic databases, and websites of relevant organizations. Published and unpublished literature (grey literature) of any study type in the English language were searched for from January 2017 to January 2021.

Eligibility and criteria: Study participants were individuals of any age presenting at clinics with symptoms indicative of cancer. Interventions included practice guidelines, care pathways or other initiatives focused on achieving pre-defined benchmarks or targets for wait times, streamlined or rapid cancer diagnostic services, multidisciplinary teams, and patient navigation strategies. Outcomes included accuracy and timeliness of cancer diagnosis.

Data extraction and synthesis: We summarized findings graphically and descriptively.

Results: From 21,298 retrieved citations, 88 unique published articles and 16 unique unpublished documents (on 18 study reports), met the eligibility for inclusion. About half of the published literature and 83% of the unpublished literature were from the United Kingdom. Most of the studies were on interventions in lung cancer patients. Rapid referral pathways and technology for supporting and streamlining the cancer diagnosis process were the most studied interventions.

Interventions were mostly complex and organization-specific. Common themes among the studies that concluded intervention was effective were multidisciplinary collaboration and the use of a nurse navigator.

Conclusions: Multidisciplinary cooperation and involvement of a nurse navigator may be unique features to consider when designing, delivering, and evaluating interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals. Future research should examine the effectiveness of the interventions identified through this review.

Keywords: Early cancer diagnosis; Symptomatic patients; Interventions; Scoping review

Strengths and limitations of this study

- A knowledge synthesis librarian developed the search strategy for this review and this was peer reviewed by an independent knowledge synthesis librarian using the PRESS checklist.
- The literature search was limited to evidence from the last 4 years and only evidence from English-language publications and organizational websites.
- This review did not summarize effectiveness of interventions across cancer patient types and regions.
- We adhered to known guidelines and standards in the conduct and reporting of the review.
- In line with the JBI's guidance for the conduct of scoping reviews, we did not attempt to evaluate the quality of the included studies or provide an assessment of the quality of the evidence.

Introduction

Cancer is the second leading cause of death globally, with about 1 in 6 deaths attributable to the disease.[1] It was estimated in 2020 that over 19 million new cases and about 10 million deaths were attributable to cancer globally.[2] This rate is estimated to be over 28 million new cases by 2040.[2] High Human Development Index (HDI) countries such as Canada will likely experience the greatest increase in incidence in absolute cancer burden, with an estimated over 4 million new cases more in 2040 compared with 2020.[2] This is mostly due to the growth and aging of the population and increasing prevalence of cancer risk factors.[2] Estimates from Canada alone suggest that every day 617 people in Canada will be diagnosed with cancer, with about 228 also dying from the disease.[3]

Although cancer can occur at any age, the risk of the disease increases with age.[4] Globally, cancer incidence rates vary, mostly because of differences in risk factors and early detection practices. Likewise, cancer death rates vary, partly because of differences in availability and effectiveness of cancer control strategies, such as early diagnosis and access to timely and effective treatment.[2] With timely diagnosis and treatment initiation, significant improvements can be made in the lives of cancer patients. Moreover, many cancers have higher curative and survival rates if diagnosed early. This means that cancer burden could be reduced substantially through early detection and management of patients who present with symptoms.[5]

When not diagnosed following early symptomatic presentation, cancer diagnosis often occurs at more advanced stages of the disease, when treatment may be less effective and cancer prognosis will be poor. Early cancer diagnosis of symptomatic patients entails carefully planned, well-integrated, culturally safe and equitable clinical evaluation and diagnostic services.[5] These

services should be designed to reduce delays in and barriers to diagnosis to allow detection at earlier stages of the disease and commence treatment in a timely manner.

Various service-focused interventions to improve early cancer diagnosis of symptomatic patients have been implemented in various jurisdictions with varying levels of success. Knowledge of the available interventions, strategies used to implement them, and how successful they might have been is necessary to inform the development, implementation, and evaluation of effective early cancer diagnosis initiatives.

Methods

This report is a summary of the study commissioned by the Canadian Partnership Against Cancer (the Partnership). The Partnership contributed to specifying the study objectives and questions, and in summarizing the evidence.

We undertook a scoping review following the Joanna Briggs Institute's (JBI's) guidance for the conduct of scoping reviews.[6] This framework includes defining and aligning the objective(s) and question(s) for the review, developing and aligning the inclusion criteria with the review objective(s) and question(s), and describing the planned approach to evidence searching. It also includes selecting, extracting, and charting of evidence; summarizing the evidence in relation to the objectives and questions; and consultation of information scientists, librarians, and/or experts throughout the process. **Appendix 1** is the work plan approved by the Partnership for the scoping review.

We summarized the current evidence regarding interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals, including practice guidelines, care pathways or targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and patient navigation strategies. We also summarized innovative interventions (for example, those with a technological component) and approaches to seamless (minimally disruptive) care of symptomatic individuals and identified performance metrics that can be used to measure improvements in the pre-diagnosis phase. Additionally, we summarized the key points of the patient trajectory from initial symptom presentation to cancer diagnosis.

We report our findings in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Reviews (PRISMA-ScR) checklist.[7]

Search strategy

A knowledge synthesis librarian (NA) designed a search strategy for MEDLINE (Ovid). This search strategy was peer-reviewed independently by another knowledge synthesis librarian using the Peer Review of Electronic Search Strategies (PRESS) checklist.[8] The revised search strategy was then adapted for Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCOhost) and PsycINFO (Ovid) bibliographic databases. The search strategy for each of the databases is presented in the appendices (**Appendix 2 - 4**). In addition to searching bibliographic databases, we searched websites of relevant organizations and professional bodies (**Appendix 5**) and hand-searched reference lists of potentially relevant publications.

Study selection criteria and data extraction

We sought to summarize practice guidelines, care pathways and initiatives such as benchmarks/targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and patient navigation strategies that have been found to enhance accurate and timely cancer diagnosis in symptomatic individuals. We also sought to summarize the leading interventions to seamless care in the cancer pre-diagnosis phase, performance metrics that can be used to measure the suspicion to diagnosis phase and how these metrics have been used. Further, we sought for specific considerations for underserviced populations in studies, including considerations for Indigenous, rural, and remote populations.

Published (peer-reviewed) and unpublished (grey literature) articles in the English language from January 2017 to January 2021 were included. The decision to include articles from 2017 was because the Partnership had previously summarized prior evidence, not included in this current report.[9] Study participants were individuals of any age presenting in any clinical

settings with symptoms. Interventions included practice guidelines, care pathways or other initiatives focused on achieving pre-defined benchmarks or targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and patient navigation strategies. Outcomes included accuracy and timeliness of cancer diagnosis.

All retrieved citations from the literature search were imported and managed in EndNote (Version X9). One reviewer (GNO or OLTL or VKR or LC) screened each citation for eligibility. Two reviewers (GNO, OLTL, VKR, and LC in pairs) independently screened the full texts of relevant citations and reviewed the reference list of the included full-text articles for potentially relevant citations. Disagreements between the reviewers were resolved through discussion or involvement of a third reviewer (AMAS). The number of screened citations and both the number and reason for exclusion of full-text articles were documented. One reviewer (GNO or OLTL or VKR or LC) performed data extraction and charting, and another reviewer (GNO or OLTL or VKR or LC) independently checked the extracted and charted data for errors. Disagreements between the reviewers were resolved through discussion or involvement of a third reviewer (AMAS).

Data synthesis and analysis

Characteristics of the included published articles are presented in a tabular form and descriptive analysis is reported graphically and descriptively. Characteristics of the included unpublished articles are reported descriptively only. Relevant findings from the review of both published and unpublished articles are summarized separately and descriptively, by review question, focusing on the interventions related to each question. Interventions are grouped as centralized or coordinated diagnostic service; interventions to enhance diagnostic services; multidisciplinary

team; patient navigation; rapid referral pathway; remote or rural populations-focused; standardized care pathway; support for primary care providers; target or benchmark; and technology to support the diagnostic process. These interventions are defined in **Appendix 6**. Effectiveness of an intervention was author-defined.

Patient and public involvement

There was no active engagement of patients and/or members of the public.

Results

Out of a total of 21,298 retrieved citations, 88 unique published articles[10-97] and 16 unique unpublished (grey literature representing 18 different reports)[98-113] met the inclusion criteria. The article selection process is detailed below (**Figure 1**). Fifty-seven of the published articles were from Europe, 14 articles from North America, 9 articles from Oceania, 3 articles each from Africa and Asia, and one article each from the Middle East and South America. Almost half of these articles (n = 40) were from the United Kingdom (UK) alone. A geographic map of published articles is shown in **Figure 2**.

Of the 18 unpublished reports (16 articles), 83% were from the UK, 11% from Canada and 6% from the United States of America (USA). Forty percent (n = 35) of the published articles were for case-control studies, 29% (n = 26) for cross-sectional studies, 22% (n = 19) for before-and-after studies, 7% (n = 6) for randomized controlled studies, and 1% (n = 1) each for guideline development and mixed methods studies. In terms of the unpublished articles, 89% (n = 16) were before-and-after studies and the rest (n = 2) were cross-sectional studies. **Figure 3** shows the distribution of the cancer types reported by the published articles; approximately 30% (n = 26) reported on multiple cancer types, while the rest reported on specific cancer types, of which lung cancer was the most frequent (about 23% of the publications (n = 20)). Of the unpublished articles, half reported on lung cancer, 28% on multiple cancer types, 11% on breast cancer, and 5.5% each on brain and gastrointestinal cancers.

Figure 4 shows the distribution of intervention types across the published articles. Nearly 20% of the published articles were on rapid referral pathway interventions while less than 1% each were on multidisciplinary team, patient navigation, and remote/rural-focused interventions. Of the unpublished articles, half reported on rapid referral pathway interventions, 11% each

reported on standardized care pathway, target/ benchmark for wait times, and technology to support the diagnosis process, and 5.5% each reported on centralized or coordinated diagnostic service and interventions to enhance diagnostic services. Most of the published articles (94%; n = 83) reported a performance metric used to measure an improvement in the suspicion to diagnosis phase of cancer.

Eighty-three percent (n = 73) of the articles reported either a practice guideline, care pathway or an initiative such as benchmark/target for wait times, streamlined or rapid diagnostic service, multidisciplinary team development, and a patient navigation strategy to enhance accurate and timely cancer diagnosis. Thirty-one percent (n = 27) of the articles reported (not explicitly) on a key point of care as patients navigate the health system, from initial suspicion to diagnosis of cancer. Twenty-nine percent (n = 25) of the articles reported on a leading innovative intervention or approach to seamless care in the pre-cancer diagnosis phase, while 4.5% (n = 4) of the articles reported on some form of consideration for underserved populations. Some of the articles reported on two or more of the above. Details of relevant characteristics of the published articles are presented in **Table 1** (those reporting effective interventions) and **Appendix 7** (those reporting ineffective interventions) **and Appendix 8** (those focused on remote/and rural populations).

Initiatives to enhance accurate and timely cancer diagnosis

This review identified various initiatives to enhance accurate and timely cancer diagnosis. These were often designed, developed, and implemented often with the involvement of primary care providers (physicians and nurses), but not patients. These initiatives are grouped into related interventions and the evidence regarding each intervention is discussed below.

Centralized or coordinated diagnostic services

Nine published articles on centralized or coordinated diagnostic services for adult lung cancer (n = 5) and breast cancer (n = 4) patients were identified.[20,23,32,33,44,54-56,93] Five were from Canada,[23,33,44,54,55] and there was one each from Denmark,[20] New Zealand,[93] South Africa,[56] and the UK[32]. The focus and metrics for assessment of the effectiveness of these diagnostic services varied, but all were found to be effective. These include the rapid access to pulmonary investigation and diagnosis (RAPID) program in Wythenshawe Hospital, Manchester, UK with expedited (next working day) computed tomography (CT) and reporting in suspected lung cancer cases,[32] and the Thoracic Triage Panel in a tertiary care centre in St. John's, Newfoundland, Canada, a multidisciplinary centralized referral program, whose key components include a nurse navigator who coordinates patient care and act as the contact person for patients and clinicians involved in the program, weekly multidisciplinary (thoracic specialists) meetings, and regular communications with the primary care provider.[23] The diagnostic services also include the rapid investigation clinic in a tertiary health centre in Montreal, Canada established to coordinate and accelerate the workup of patients with suspected lung cancer,[33] the improved respiratory fast track clinic (RFTC) in Northland district of New Zealand that comprises reserved slots for CT for those referred with a suspicion of lung cancer, bronchoscopy slots and CT-guided biopsy,[93] and the Danish lung cancer package at the Center for Lung Cancer, Odense University Hospital, Odense, Denmark, a fast-track diagnostic pathway in the hospital setting.[20] Further, there was the rapid access breast clinic in British Columbia, Canada that provides close collaboration between clinicians and radiologists, facilitated by clinical pathways and nurse navigation,[54,55] the diagnostic assessment units in Ontario, Canada, focusing on diagnosis at a dedicated breast assessment unit,[44] and the breast clinic at a tertiary hospital in Western Cape Province of South

Africa, an open-access one-stop diagnostic breast clinic where women may present with a letter from a primary level provider (nurse practitioner or doctor) and receive the same day clinical and cytological evaluation with referral to the combined breast clinic if the breast cytology is positive for malignancy.[56]

In addition to the above, one unpublished article was identified.[113] This was for the Breast ACCESS Project in Ohio, USA, which scheduled patients for a surgical consult within 2 days and a biopsy within 5 days after the surgical consult, with the aim of reducing wait times between abnormal diagnostic mammogram findings to biopsy from 26 to 7 days (7-day ACCESS goal).

Interventions to enhance diagnostic services

Twelve published articles on interventions to enhance diagnostic services were identified.[10,17,24,52,53,64,75,77,78,80,83,94] These articles were focused on varied cancer types; four on multiple cancers, two on lung cancer, two on skin cancer, and one each on breast, gastrointestinal, haematological and prostate cancers. Four articles were from the UK,[17,52,53,78] two articles each from Canada[24,64] and Sweden,[10,80] and one article each from Botswana,[94] Columbia,[75] Indonesia,[77] and the USA.[83] The focus and metrics for assessment of the effectiveness of the interventions varied across the publications, and while most were effective, one intervention for lung cancer and one intervention for skin cancer in the UK[53] and Sweden[10], respectively, were ineffective. The effective interventions were reducing diagnosis through emergency presentation by improving general practice referral in England, UK,[52] the guided personal quality of life (QoL) feedback intervention during the Cancer Research UK's North West regional summer roadshow in Manchester, UK, aimed at offering guided feedback about personal QoL to adults with potential cancer symptoms, living in deprived communities to

promote help seeking in primary care among the communities,[78] the mandatory primary care access to faecal immunochemical testing (FIT) in Nottingham, UK, integrated with the 2-week wait pathway, aimed at improving gastrointestinal cancer diagnosis rather than relying on age and symptoms alone,[17] the Stronach Regional Cancer Centre lung diagnostic assessment program (DAP) at Southlake Regional Health Centre, Ontario, Canada, aimed at using learnings from a Lean improvement event to provide coordinated, expedited care for all patients undergoing a possible lung cancer diagnosis and to achieve/improve upon the provincial wait time target from consultation to diagnosis for lung cancer patients,[24] the nurse practitioner-led lymphoma rapid diagnosis clinic in a tertiary care cancer center (Princess Margaret Cancer Centre, part of University Health Network) in Ontario, Canada, aimed at reducing wait times for a definitive diagnosis of lymphoma,[64] the expedited one-stop prostate cancer diagnosis using advanced imaging and biopsy techniques in a health institution (name not reported) in the USA, aimed at expediting prostate cancer diagnosis.[83] There were also the Swedish Diagnostic Center at the Central Hospital of Kristianstad, Sweden, introduced as a separate outpatient unit within the Department of Internal Medicine to expedite diagnostics,[80] the Partners for Cancer Care and Prevention action plan in Cali, Columbia, aimed at improving access to a coordinated program of screening and early diagnosis of breast and cervical cancers in three health care centers that serve subsidized populations,[75] the dermatology-led quality improvement initiatives in Gaborone, Botswana, aimed at improving multispecialty care coordination,[94] and the culturally sensitive, narrative self-help intervention named PERANTARA (PEngantar peRAwataN kesehaTAn payudaRA [translated as introduction to breast health treatment]) across four hospitals in Bandung, West Java, Indonesia, aimed at reducing time to diagnosis in women with breast cancer symptoms.[77] In addition to the above, one unpublished article on the Accelerate,

Coordinate, Evaluate (ACE) program in the UK was identified.[100] This program was an early cancer diagnosis initiative and focused on testing innovations that either identify individuals at high risk of cancer earlier or streamline diagnostic pathways.

The ineffective interventions were the standardized care diagnostic pathway at the Department of Clinical Pathology, Akademiska University Hospital in Uppsala, Sweden (introduced by the Swedish health authorities to eliminate unwanted delay in the diagnostics of melanoma)[10] and the 4-week national lung cancer symptom awareness campaign in Wales, UK, aimed at increasing urgent suspected cancer referrals and clinical outcomes.[53]

Multidisciplinary team

Three multidisciplinary team lung cancer approaches were identified from published articles: from the USA[68,85] and Australia.[50] The focus and metrics for assessment of the effectiveness of the approaches varied across the publications. One approach from the USA was found to be effective,[68] whereas the others were found to be ineffective. The effective approach was the lung cancer strategist program, a thoracic surgeon-guided, multidisciplinary (disciplines not reported) care program in hospitals in Massachusetts, USA, aimed at improving timeliness of lung cancer diagnosis and treatment.[68] The ineffective approaches were the pre-diagnosis multidisciplinary tumour board (physicians from radiology, medical and radiation oncology, and pulmonary medicine) discussions in a clinic in Cleveland, USA aimed at improving the timeliness of diagnostic evaluation in lung cancer,[85] and the Victorian lung cancer service redesign project in Victoria, Australia, which involved multidisciplinary (patients, governance, administration, clinicians and health information services) evaluation aimed at quality improvement collaborative on timeliness and management in lung cancer.[50] In addition, nine unpublished articles from the UK were identified.[99,101-103,106,108,109,112] These included four

articles regarding a "straight to CT access" pathway, on community pharmacy direct referral to lung cancer pathway, rapid colorectal diagnostic pathway, and optometrist direct referral to neuroscience pathway. All but the chest x-ray pathway[109] were found to be effective.

Standardized care pathways

Eleven published articles on standardized care pathways were identified.[11,12,26,35,39,41,49,59,63,70,71] These articles were focused on varied cancer types (4 each for multiple cancers, and 1 each for ear-nose-throat, urinary tract, and gastrointestinal cancers). Three articles were from Denmark,[26,39,41] two from the UK,[35,70] and one each from Canada,[59] Norway,[49] Sweden,[63] Spain,[12] and Saudi Arabia.[11] The publications were on adult patient populations with one also involving paediatric patients. The focus and metrics for assessment of the effectiveness of the pathways varied across the publications. The main effective pathways were the national diagnostic cancer pathway in Norway, with recommended maximum limits for time spent in the diagnostic process as well as mandatory reporting of the actual time intervals for all patients with suspected lung cancer,[49] and the standardized triage process in the Southeastern Ontario, Canada, which entailed a twice-weekly nurse–physician triage, preordered staging tests and scheduling according to urgency, redirection and recommendations for inappropriate referrals, and new small nodule clinic.[59] Other main effective pathways were the standardized diagnostic pathway for suspected urothelial cancer initiated by primary healthcare providers and specialists in Skane County, Sweden, and comprises CT urography, urinary cytology and cystoscopy,[63] the early colonoscopy track (within 30 days from referral) in a tertiary referral hospital in Tenerife, Spain,[12] and the fast-track cancer care pathway in Denmark (national), with maximum acceptable time thresholds from referral to diagnosis and treatment.[39] In addition, two unpublished articles

from Canada[111] and the UK[98] focusing on breast and lung cancers, respectively, were identified. These were the Alberta Health Services Diagnostic Assessment Pathway and the Somerset Integrated Lung Cancer Pathway. While the Canadian pathway was found to be effective, the pathway from the United Kingdom was not effective.

Support for primary care providers

There were four publications on support for primary care providers (PCP), all from the UK.[27,31,48,97] Two were focused on multiple cancer types, and one each focused on gastrointestinal and brain cancers. The publications were on adult patient populations with one being also involving paediatric patients. The focus and metrics for assessment of the effectiveness of the support packages (all educational and informational) varied across the publications. None of the support packages was found to be effective, with the identified common theme being a lack of awareness of referral guidelines and associated knowledge by GPs. These ineffective support packages were the use of the Kernick and NICE guidelines as evidence-based support to assist primary care physicians in identifying patients most at risk of having a brain tumour, but also on the fastest route to achieve diagnosis (example, direct access imaging versus urgent secondary care referral) in Scotland, the UK,[97] the use of the national cancer waiting times monitoring dataset for system performance assessment by primary care physicians in England, the UK,[27] and the use of safety netting by primary care physicians in Oxfordshire, UK to ensure that patients are monitored until their symptoms or signs are explained, and to guard against delays in diagnosis.[31]

Target or benchmark for wait times

There were eight published articles related to targets or benchmarks for wait times.[15,42,43,69,73,81,88,96] Three of these articles were from the UK,[69,73,81] two articles from Australia,[42,88] and one article each from China,[43] Sweden,[96] and New Zealand[15]. These publications were focused on varied cancer types (2 each for multiple, lung and gastrointestinal cancers, and 1 each for prostate and skin cancers), and were on adult patient populations, with one publication involving paediatric patients. The focus and metrics for assessment of the effectiveness of the target or benchmarks varied across the publications, and all but two targets/benchmarks[15,88] were found to be effective. The effective targets or benchmarks were the 28-day faster diagnosis standard in the National Health Service England, UK, defined as the time within which the patient is informed whether they do or do not have cancer,[73] the fast-track diagnostic workup for men with suspected prostate cancer at the Urology Department at Orebro University Hospital in Sweden, which entailed targeting the shortest possible waiting-time for a diagnostic workup process,[96] and the optimal timeframes for referral and diagnosis of lung lesion at Latrobe Regional Hospital in Victoria, Australia established by the National Cancer Expert Reference Group as part of the optimal care pathway for people with lung cancer.[42] The ineffective targets or benchmarks was the New Zealand Ministry of Health's "faster cancer treatment" standards of service provision for melanoma patients, with a target of histopathological diagnosis of melanoma reported within five working days in 80% of cases, and all cases reported in 10 working days.[15] In addition, two unpublished articles from Canada[105] and the UK[107] focusing on multiple cancers were identified, and these were the "2-week wait" benchmark in the UK (already discussed under rapid referral pathways) and the Canadian Breast Cancer Screening Network targets for diagnostic intervals: ≥ 90% of abnormal screens to be

resolved within 5 weeks if no biopsy is required and ≥ 90% within 7 weeks if a tissue biopsy is required.

Innovative interventions to enhanced care in cancer pre-diagnosis phase

This review identified 17 published articles related to technological interventions for enhanced care in the pre-diagnosis phase of cancer.[16,21,22,29,37,38,51,57,58,62,65,66,79,82,87,89,91] Ten of these articles were from the UK,[22,29,37,38,51,57,62,65,66,91] two articles were from New Zealand,[79,82] and one article each was from Denmark,[89] Netherlands,[21] Italy,[16] India,[87] and Spain.[58] These publications focused on varied cancer types in adult patient populations, with two also involving paediatric patients. The interventions had little patient input in their design, development, or implementation. The focus and metrics for assessment of the effectiveness of the interventions varied across the publications. The main identified interventions were the use of teledermatology in skin cancer diagnosis. This involved the taking of images, including dermoscopy by GPs and sending them for evaluation to specialized dermatologists.[38,62,79,89] The process is embedded in an e-referral system developed in Auckland, New Zealand for suspected skin malignancy,[82] and included teledermatology images triaged as confirmed, likely or suspected melanoma, the use of a web-based referral tool for head and neck cancers at two different hospitals in Birmingham, West Midlands, and Wexham, Berkshire, UK.[51] There was also the use of the Digitally Assembled Referral Toolkit (DART) for 2-week referral, accessible via a cloud-based template, which contained new referral forms native to GP clinical systems in the UK.[29] Additionally, there was the use of an electronic straight-to-test pathway at a large tertiary referral hospital in England, UK to remove hospital-based triage from suspected colorectal cancer pathways; this allows GPs to book tests supported by a decision aid based on the NICE guidance, thus,

eliminating the need for a standard referral form or triage process.[65] Further, there was the use of electronic clinical decision support for melanoma in four general practices in the Southeast of England, UK, which involved the use of an electronic-based 7-point checklist to assess pigmented lesions,[66] the use of machine learning algorithms in Newcastle, UK to classify patients referred on the 2-week wait pathway for suspected head and neck cancer into different diagnostic groups, albeit very broad ones: cancer and non-cancer,[57] the use of nurse-led assessments to evaluate certain groups of patients suspected to have bowel cancer in England, the UK,[22] and the use of varied smartphone-based skin and oral self-monitoring and screening applications, in England, UK[91] and in the India,[87] respectively. In addition, two unpublished articles from the UK were identified.[106,110] These were for a cancer decision support tool (computer-based programs integrated into a GP's usual patient management system) in Gateshead, London, and a clinical web portal (CWP) electronic system in Manchester, England, with the fundamental part of the CWP being that local clinicians had to take personal responsibility for data input.

Performance metrics to measure improvements in suspicion to diagnosis phase

Varied performance metrics were identified by this review. The main metrics are summarized according to intervention type (**Appendix 9**). While performance metrics appear to be mainly intervention-dependent, time from presentation in primary care to diagnosis and from referral from primary care to specialist consultation, appear to be the most consistent metrics used for evaluation. Performance metrics to measure patients' experience mainly centered on patients' satisfaction and quality of life.

Specific considerations for underserved populations

Four published articles focused on issues related specifically to underserved populations, with all focused on remote/rural populations.[18,30,60,88] These publications were from the UK,[60] Australia,[30,88] and Mexico.[18] A fifth publication only used the patients' area of residence as part of their model.[95] All of the publications were on multiple cancer types and adult populations, although one included a paediatric population. The specific considerations for underserved populations and the evidence regarding them included a publication from Scotland, the UK, a national audit of cancer diagnosis in Scottish and English general practices, exploring and comparing patient characteristics, diagnostic intervals, and routes to diagnosis,[60] the publication from New South Wales, Australia on a study that examined geographic variations in time intervals leading up to treatment for head and neck cancer, with assessment of differences based on remoteness of residence (regional/remote or metropolitan) at two tertiary referral centres,[88] a publication from Mexico City, Mexico on evaluation of a patient navigation program to reduce referral time to cancer centers for underserved patients with a suspicion or diagnosis of cancer at a public general hospital,[18] and a publication from Western Australia, a cluster-randomized controlled trial of a complex intervention to reduce time to diagnosis in rural cancer patients with the aim of measuring the effect of community-based symptom awareness and general practice-based educational interventions on the time to diagnosis in rural patients presenting with breast, prostate, colorectal or lung cancer.[30]

Discussion

This scoping review of 88 published and 16 unpublished documents from January 2017 to January 2021 summarizes the evidence on current interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals. The identified articles were from varied study designs including case-control (most common), cross-sectional, before-and-after, and mixed methods studies, and randomized controlled trials. There was little evidence to suggest that patients were involved in the design, development, or implementation of interventions to enhanced care in cancer pre-diagnosis phase.

The evidence suggests that interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals are active topics of research. The UK appears to be championing this area of research, contributing about half of all identified published literature and 83% of the identified unpublished literature. Of the specific cancer patient types, lung cancer patients appear to be the most researched, ranking highest among the patient populations of published and unpublished literature. Of the studied interventions, rapid referral pathways and technology for supporting and streamlining the diagnosis process were the two most reported interventions. Overall, varied national and regional centralized or coordinated diagnostic services, interventions to enhance diagnostic services, multidisciplinary team approaches, patient navigation approaches, rapid referral pathways, standardized care pathways, support for primary care providers, target or benchmarks, technologies to support diagnosis process, and insights regarding variations between remote/rural and urban populations have been reported although there were no articles that focused specifically on Indigenous populations. Many of these intervention types could be adapted to suit different health systems and jurisdictions around the world.

The interventions mostly comprised multiple interventions/ changes to the healthcare pathway. As such, the interventions examined varied widely across the studies. This was true even when applied to the same cancer patient populations and in the same jurisdictions/ countries, including those where an intervention was part of the standard care pathway. As such, it is difficult, perhaps impossible, to identify one main approach alone that drives an intervention. Methodological approaches also varied significantly with regard to outcome assessment. A common theme among the effective centralized or coordinated diagnostic services, interventions to enhance diagnostic services, patient navigation approaches, and standardized care pathways is multidisciplinary collaboration and the involvement of a nurse navigator.

The implications of the findings from this scoping review are that it is difficult to determine a specific intervention, or stand-alone approach to an intervention. It is also difficult to assess the true effectiveness of many of the interventions, especially considering the differing composite nature of the interventions, the fact that the evidence is mostly from observational studies, and the range of outcome measures used to measure effectiveness. While many of the interventions could be adapted to suit different health systems and jurisdictions, emphasis should be on the context and the strengths and limitations of the individual health system, and a clear evidence-based performance metric for appropriate evaluation of effectiveness of an intervention ought to be determined a priority. Diagnosing cancer faster and more accurately at an earlier stage is a key priority of the 2019-2029 Canadian Strategy for Cancer Control.[114] Over the next 5 years, the Canadian Partnership Against Cancer will leverage findings from this scoping review, as one of several inputs, and partner with Canadian jurisdictions to continue to test innovative

models of care that expedite cancer diagnosis, especially for Indigenous and underserved populations.

Limitations and merits

There are some limitations to this study. The literature search was developed by a knowledge synthesis librarian and peer reviewed by an independent knowledge synthesis librarian using the PRESS checklist. We searched appropriate databases and websites for literature, and adhered to known guidelines and standards in the conduct and reporting of the review. Even so, the literature search was limited to evidence from the last 4 years and only evidence from English-language publications and organizational websites. As such, potentially eligible articles could have been missed.

The eligibility criteria for inclusion were not limited to only comparative studies. This meant that the focus of some of the included studies was not specifically on the assessment of effectiveness of an intervention, which was based solely on the reported outcome in the articles. As such, an intervention that appeared effective in a study may be ineffective in another study depending on the assessed outcome with no clear reason for this discrepancy. Furthermore, this review did not assess effectiveness of interventions across cancer patient types and jurisdictions/regions. This would have allowed assessment of any differences in intervention effectiveness by patient type and study jurisdiction. Lastly, and in line with the JBI's guidance for the conduct of scoping reviews, we did not attempt to evaluate the quality of the included studies or provide an assessment of the quality of the evidence.

Conclusions

The evidence suggests that interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals are active topics of research, particularly in lung cancer patient populations, and that the UK is championing this area of research. While the themes of the studied interventions are similar, the interventions differ in many ways within the same intervention group. Multidisciplinary cooperation and involvement of a nurse navigator appeared to be unique features of many of the effective interventions. Canadian and other jurisdictions can leverage these lessons learned to develop and implement strategies adapted to local health system needs to improve the cancer pre-diagnosis phase. Future research should examine the effectiveness of the interventions identified through this review.

Data availability statement: No additional data are available.

Ethics approval: Not applicable.

Details of the role of the study sponsors: The Canadian Partnership Against Cancer (the study commissioner) contributed to specifying the study objectives and questions, and in summarizing the evidence.

Patient and public involvement: There was no active engagement of patients and/or members of the public.

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Table 1: Summary of the characteristics of the included published articles that reported data on effective interventions

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
Centralized or coordinated diagnostic service	Christensen 2020[20]	Denmark (Odense)	Cross-sectional (2016-2017)	Lung (Adult) [20]	Patients' perspective, experiences, and expectations	Although patients experienced anxiety with the fast-track diagnostic pathway, they still wanted to move through with diagnosis as quickly as possible (Effective)
	Common 2018[23]	Canada (Newfoundland)	Case-Control (2015-2016)	Lung (Adult) [133]	Time from first abnormal image to biopsy	There was a statistically significant decline in wait times for patients from 61.5 to 36.0 days (p<0.0001) (Effective)
	Evison 2020[32]	UK (Manchester)	Before-and-After (2016-2019)	Lung (Adult) [1035]	Mean time from referral to CT	The median time from referral to CT was 3 days. Overall 56% and 90% of patients had completed a CT and consultation within 3 and 7 days of referral, respectively (0% and 24% prior to implementation) (Effective)
	Ezer 2017[33]	Canada (Montreal)	Case-Control (2010-2011)	Lung (Adult) [327 (195 RIC; 132 non-RIC)]	Time from first contact with physician to diagnosis	Time from first contact to pathological diagnosis was shorter (median (M) 26 days; IQR 14–42 days) vs. control patients (M 40 days; IQR 16–68 days) (Effective)
	Jiang 2018[44]	Canada (Ontario)	Case-Control (2011)	Breast (Adult) [4381]	Time to diagnosis	The Canadian timeliness targets (time from patients' first referral or test to the cancer diagnosis) were achieved more often than for usual care (71.7% vs. 58.1%, respectively), with associated 10-day (95% CI: 7.8–11.9) reduction in the median diagnostic interval (Effective)
	McKevitt 2017[54]	Canada (British Columbia)	Case-Control (2009)	Breast (NR) [373]	Diagnostic wait time	Patients had a decreased time to surgical consultation (33 vs 86 days, p<0.0001) for both malignant (36 vs 59 days, p=0.0007) and benign diagnoses (31 vs 95 days, p<0.0001) (Effective)
	McKevitt 2018[55]	Canada (Vancouver)	Case-Control (2012)	Breast (NR) [176 (40 RABC; 136 TS)]	Time from presentation to surgeon evaluation	Time from presentation to surgeon evaluation was shorter in the RABC group for patients with breast symptoms (81 vs 35 days, p < .0001) (Effective)
	Moodley 2018[56]	South Africa (Western Cape province)	Cross-sectional (2015-2016)	Breast (Adult) [201]	Time between first health care provider visit and date of diagnosis	The median time between the first health care visit and a breast cancer diagnosis was 28 days (IQR 13–58 days). Women whose initial reaction was denial of the breast symptom had a significantly shorter diagnostic interval (11 days vs. 29 days, p = 0.010) (Effective)
	Williams 2018[93]	New Zealand (Northland district)	Before-and-After (2015-2016)	Lung (Adult) [212 (70 in phase 1, 46 in phase 2 and 71 in phase 3)]	Time from GP referral to first specialist appointment	Time from GP referral to first specialist appointment improved significantly (p=0.005) (Effective)
Interventions to enhance diagnostic services	Chapman 2020[17]	UK (Nottingham)	Cross-sectional (2017-2018)	Gastrointestinal (Adult) [1934]	Colorectal cancer (CRC) detection rate	The symptomatic pathway incorporating FIT was feasible and appeared more clinically effective than pathways based on age and symptoms alone, with FIT results identifying patients with a significantly higher risk

					after a FIT	of CRC (Effective)
	Cotton 2020[24]	Canada (Ontario)	Before-and-After (2017-2018)	Lung (NR) [NR]	Referral to diagnosis	Monthly patient volumes increased by 65%, and wait time improved by 60% (Effective)
	Laudicella 2018[52]	UK (England)	Case-Control (2006-2009)	Multiple (Adult) [372353]	Survival of patients	Rerouting patients from emergency presentation to new referral resulted in better patient survival in all cancer cohorts (Effective)
	Nixon 2020[64]	Canada (Ontario)	Case-Control (2015-2017)	Haematological (Adult) [126]	Time from initial consultation to diagnosis of lymphoma	Median time to lymphoma diagnosis was 16 days for patients assessed in the nurse practitioner–led lymphoma rapid diagnosis clinic and 28 days for historical controls (P<0.001) (Effective)
	Sardi 2019[75]	Colombia (Cali)	Before-and-After (2012-2016)	Multiple (NR) [114]	Time from initial consultation to biopsy	The average time from initial consult to biopsy decreased from 65 to 20 days and from biopsy to diagnosis from 33 to 4 days (Effective)
	Setyowibowo 2020[77]	Indonesia (Bandung West Java)	RCT (2017)	Breast (Adult) [107]	Time between first visit to the hospital and a definitive diagnosis	The intervention reduced the time to definitive diagnosis: mean difference = −13.26, 95% CI = −24.51 to −2.00, P=0.02) (Effective)
	Skevington 2020[78]	UK (Manchester)	RCT (2015-2016)	Multiple (Adult) [107]	Quality of life	Psychological quality of life increased (Effective)
	Stenman 2019[80]	Sweden (Kristianstad)	Cross-sectional (2015)	Multiple (Adult) [290]	Total diagnostic interval	Shorter diagnostic interval (time from referral decision in primary care to diagnosis). The median primary care interval was 21 days, and the median diagnostic interval was 11 days (Effective)
	Tafuri 2020[83]	USA (NR)	Case-Control (2016-2018)	Prostate (Adult) [370]	Time from multiparametric Magnetic Resonance Imaging (mpMRI) to biopsy	One-Stop patients experienced shorter time from mpMRI to biopsy (0 vs 7 days; p< 0.01) (Effective)
	Williams 2019[94]	Botswana (Gaborone)	Before-and-After (2015-2017)	Skin (Adult) [218]	Diagnostic histology turnaround times	Median turnaround in the post dermatology quality improvement interval was 11 days (IQR, 12-23 days) compared with 32 days in the pre-dermatology quality improvement interval (IQR, 24-56 days; P<0.001) (Effective)
Multidisciplinary team	Phillips 2019[68]	USA (NR)	Case-Control (2014-2016)	Lung (NR) [218]	Time to diagnosis	Compared to controls, patients with lung cancer in the Lung Cancer Strategist Program cohort had an expedited time from suspicious finding to diagnosis (34 vs 44 days, p=0.027) (Effective)
Patient navigation	Chavarri-Guerra 2019[18]	Mexico (Mexico City)	Before-and-After (2016-2017)	Multiple (Adult) [70]	Feasibility	91% of patients successfully obtained appointments at cancer centers in <3 months (Effective)
	Drudge-Coates 2019[28]	UK (London)	Before-and-After (2012-2015)	Prostate (Adult) [60]	Waiting times from the GP	Compared with the previous physician-led service, waiting times for patient appointment fell by 52% over a 3-year study period (Effective)

					referral to initial clinic assessment	
	Whitley 2017[92]	USA (Boston, Denver, San Antonio, and Tampa)	Case-Control (2007-2011)	Multiple (Adult) [6349]	Delays in diagnostic resolution based on Charlson Comorbidity Index score	Patient navigation reduced delays in diagnostic resolution, with the greatest benefits seen for those with a Charlson Comorbidity Index score ≥2 (Effective)
Rapid referral pathway	Antel 2020[13]	South Africa (Cape Town)	Before-and-After (2017-2019)	Haematological (Adult) [130]	Diagnostic interval	Compared with a historical cohort, the diagnostic interval (time from first health visit to diagnostic biopsy) for patients with lymphoma was significantly shorter, 13.5 vs 48 days (p=0.002) (Effective)
	Arhi 2020[14]	UK (National)	Case-Control (2000-2013)	Gastrointestinal (Adult) [7130]	Hazard ratios of death	Patients referred between 2 weeks to 3 months, and after 3 months with red-flag symptoms demonstrated a significantly worse prognosis than patients who were referred within 2 weeks (Effective)
	Chng 2020[19]	UK (Newcastle-upon-Tyne)	Case-Control (2015-2019)	Brain (Adult) [101]	Tumour detection rate	With guideline adherence, the brain tumour detection rate was 3-fold higher (36.0% vs 11.5%, p¼0.02) (Effective)
	Creak 2020[25]	UK (Brighton; Sussex)	Cross-sectional (2015-2018)	Multiple (Adult) [258]	Time to diagnosis	Direct GP referrals were feasible and manageable within a tertiary clinic and resulted in high rates of cancer diagnoses and early contact with an oncologist and nurse specialist, cutting short the 'limbo' time of high anxiety before diagnosis (Effective)
	Hennessy 2020[36]	Ireland (Dublin)	Case-Control (2012-2018)	Lung (NR) [864]	Time to diagnosis	Time to diagnosis was longer in those who had attended a post Rapid Access Lung Cancer Clinic CT (34.5 versus 21 days) (Effective)
	Jones 2018[45]	UK (East Midlands)	Case-Control (2013-2015)	Gastrointestinal (NR) [1401 (340 STTP, 495 traditional pathway, 566 control trusts)]	Time from referral to diagnosis	The pathway saved a mean of 7 days from referral to treatment (with a 95% CI of 3 to 11 days, p<0.008) and a mean of 16 days from referral to diagnosis, when compared with a traditional pathway (Effective)
	Joyce 2020[46]	UK (National)	Cross-sectional (2017-2018)	Multiple (Mixed age) [NR]	Proportion with emergency diagnosis of cancer	A lower proportion of emergency diagnosis of cancer was found with higher 2 weeks wait referral conversion rate (Effective)
	Pearson 2020[67]	UK (National)	Case-Control (2014)	Multiple (Mixed age) [12873]	Primary care interval	Compared with patients with a specific alarm symptom, patients with non-specific but concerning symptoms had higher odds of having longer primary care intervals (adjusted OR: 1.24 (1.11 to 1.36)) (Effective)
	Round 2020[72]	UK (National)	Case-Control (2011-2017)	Multiple (Mixed age) [1469103]	Risk of death	Cancer patients from the highest referring practices had a lower hazard of death (hazard ratio [HR] = 0.96; 95% confidence interval [CI] = 0.95 to 0.97) (Effective)
	Sandager 2019[74]	Denmark (National)	Cross-sectional (2010)	Multiple (Adult) [2256]	Patient experience	Overall, pathway referred patients were 21% more likely than non-pathway referred patients to report a positive experience (PR = 1.21 [95% CI: 1.11–1.30]) (Effective)

	Thanapal 2020[86]	UK (London)	Before-and-After (2012-2018)	Gastrointestinal (Adult) [1648]	Time to diagnosis	Patients on the pathway took 25 days to obtain results as compared to 40 days in the standard pathway (Effective)
	Vijayakumar 2020[90]	UK (Buckinghamshire)	Cross-sectional (2018)	Lung (NR) [111]	Patient satisfaction	High satisfaction with the service, with scores above 93% in all parameters (Effective)
Standardized care pathway	Alonso-Abreu 2017[12]	Spain (Tenerife)	Case-Control (2008-2010)	Gastrointestinal (Adult) [257]	Survival rates	Survival rates at 12 and 60 months after treatment were significantly higher in the early colonoscopy group compared with the standard schedule colonoscopy group ($p < 0.001$) (Effective)
	Dahl 2017[26]	Denmark (Countrywide)	Before-and-After (2004-2010)	Multiple (Adult) [3292]	Patient satisfaction for waiting time from referral to consultation at a hospital	Implementation of pathway was associated with a reduced level of patient-reported dissatisfaction with long waiting time from the time of referral to the first consultation at the hospital (Effective)
	Laerum 2020[49]	Norway (Kristiansand)	Before-and-After (2007-2016)	Lung (Adult) [780]	Referral interval	The median referral interval among all patients was reduced by two days from baseline to the next time period when the local diagnostic algorithm was streamlined (Effective)
	Mullin 2020[59]	Canada (Ontario)	Before-and-After (2018-2019)	Lung (NR) [833]	Time from referral to diagnosis	Time from referral to positron emission tomography decreased (from 38.5 to 15.7 days), time from referral to brain imaging decreased (from 33.4 to 13.1 days), and time from referral to diagnosis decreased (from 38.0 to 22.7 days), all demonstrating special-cause variation (Effective)
	Nilbert 2018[63]	Sweden (Skane County)	Case-Control (2015-2016)	Urinary tract (Adult) [1871]	Time from sign/symptom to diagnosis	The standardized care pathway shortened the diagnostic delay to a median of 25 days compared to 35 days for regular referral ($p=0.01$) (Effective)
	Rankin 2017[71]	Australia (New South Wales)	Cross-sectional (2014)	Lung (Adult) [19]	Patient concerns urgency, advocacy, and referral	Patients and general practitioners expressed similar themes across the diagnostic and pretreatment intervals (Effective)
Target or benchmark for wait times	Jeyakumar 2020[42]	Australia (Victoria)	Case-Control (2018)	Lung (Adult) [46]	Mean time from initial CT to tissue diagnosis	The Standard Care group met the target for treatment commencement in 33.3% of cases whereas the Rapid Access Clinic group achieved this in 77% (Effective)
	Jiang 2017[43]	China (Shanghai)	Case-Control (2011-2015)	Lung (NR) [4000]	Time from initial respiratory consultation to treatment decision	Takes a median 4 workdays (range 3 to 6) for a new patient from initial respiratory consultation to treatment decision, whereas in many countries, 14 workdays are considered a reasonable timeline (Effective)
	Sagar 2020[73]	UK (Milton, Somerset)	Before-and-After (2019-2020)	Gastrointestinal (Mixed age) [1255]	28-day target attainment	Attainment of the 28-day diagnosis target for all suspected colorectal cancer referrals improved following the establishment of a new pathway (88% vs. 82%, $P < 0.0001$) (Effective)
	Stevenson-Hornby 2018[81]	UK (Wigan)	Before-and-After (2017)	Gastrointestinal (NR) [NR]	Percentage diagnosed	55% of all referrals were found to have hepatobiliary-pancreatic cancer after pathway trial compared with 19% before (Effective)
	Zhu 2020[96]	Sweden (Orebro)	RCT (2015-2018)	Prostate (Adult) [204]	Self-reported symptoms of	Significant changes in depression symptoms and self-rated sleep quality suggested a benefit of the fast-track

					stress	workup intervention (Effective)
	*Piano 2019[69]	UK (Guildford, Bradford)	Cross-sectional (NR)	Multiple (Adult) [29]	Patient attitudes within the context of their recent referral experiences	Most patients had experienced swift referral. It was difficult for patients to understand how the new standard could affect upon the time that it takes to progress through the system. Responsibility for meeting the standard was also a concern as patients did not see their own behaviours as a form of Involvement (NA)
Technology to support diagnosis process	Cazzaniga 2019[16]	Italy (Bergamo)	Case-Control (2017)	Skin (Adult) [232]	Diagnostic accuracy	The diagnostic accuracy of the online assessment compared with direct clinical examination was significant (Effective)
	Cock 2017[22]	UK (NR)	Guideline development (2014-2016)	Gastrointestinal (Adult) [NR]	Patient satisfaction	Audits were being conducted to assess and compare patient satisfaction with face-to-face versus telephone assessments, although intervention was well-received (Effective)
	Eastham 2017[29]	UK (Leeds)	Before-and-After (2015-2016)	Multiple (Adult) [NR]	Form completion rates and time spent processing forms	Form completion rates improved from a mean of 44% of forms at baseline (n = 210) to 99% post-intervention n = 236). Time spent processing forms also decreased from a mean of 96 seconds to 35 seconds post-introduction of the new system (Effective)
	Hirst 2018[37]	UK (London)	Cross-sectional (2016)	Multiple (Adult) [NR]	GP perspectives on txt-netting	Text messages were perceived to be an acceptable potential strategy for safety netting patients with low-risk cancer symptoms (Effective)
	Hunt 2020[38]	UK (England)	Case-Control (2018)	Skin (Adult) [150 (75 consecutive TD referrals paired with 75 standard "Face to Face" controls)]	Time from referral to first appointment and diagnostic rates	There was a 23% absolute and 37% relative increase in diagnostic completion rates in the mobile van compared with the central hospital facility (p=0.0001) (Effective)
	Moor 2019[57]	UK (Newcastle-upon-Tyne; Birmingham)	Case-Control (2007-2010)	Head and Neck (Mixed age) [4715]	Diagnostic accuracy	Machine learning algorithms accurately and effectively classify patients referred with suspected head and neck cancer symptoms (Effective)
	Moreno-Ramirez 2017[58]	Spain (Southern region)	Case-Control (2004-2015)	Skin (NR) [2009]	Waiting times for referral	Waiting times for referral for teledermatology network versus conventional letter referral system 12.31 (8.22–16.40) vs 88.62 (38.42–138.82) (Effective)
	Nicholson 2020[62]	UK (London)	Cross-sectional (2018-2019)	Skin (NR) [60]	Patient satisfaction	Over 80% (49) would recommend the service, and the majority felt confident with the teledermatology model. Overall, patients would be happy to complete electronic questionnaires and receive results electronically, with younger patients being more amenable to this (Effective)
	Orchard 2020[65]	UK (Bristol)	Before-and-After (2014-2017)	Gastrointestinal (Mixed age) [11357]	Time from referral to diagnosis	Time from referral to diagnosis reduced from 39 to 21 days and led to a dramatic improvement in patients starting treatment within 62 days (Effective)
	Snoswell 2018[79]	New Zealand (Countrywide)	Not clear (2012)	Skin (Adult) [300]	Time to clinical resolution	Mean time to clinical resolution was 9 days (range, 1-50 days) with teledermoscopy referral compared with 35 days (range, 0-138 days) with usual care alone (difference, 26 days; 95%credible interval 13-38 days) (Effective)

	Sunderland 2020[82]	New Zealand (Auckland)	Case-Control (2016)	Skin (NR) [809]	Efficacy of diagnostic tool	A positive predictive value (PPV) of 38.1% and number needed to excise (NNE) of 2.6, with less than 10% of referrals triaged for teledermatoscopy confirmed as melanoma (24/264) (Effective)
	Uthoff 2018[87]	India (Bangalore, Dimapur)	Case-Control (NR)	Oral (Adult) [99]	Diagnostic accuracy	Sensitivities, specificities, positive predictive values, and negative predictive values ranged from 81.25% to 94.94% (Effective)
	Vestergaard 2020[89]	Denmark (Southern Denmark)	Case-Control (2018)	Skin (Adult) [519]	Percentage of lesions not requiring further in-person assessment	On evaluation by teledermoscopy, 31.5% of lesions did not need further in-person assessment (Effective)

CRC = colorectal cancer; CT = computed tomography; FIT = faecal immunochemical testing; GP = general practitioner; NR = not reported; RABC = rapid access breast clinic; RCT = randomized controlled trial; RIC = rapid investigation clinic; STTP = straight to test pathway; TD = teledermatology; TS = traditional system; UK = United Kingdom; USA = United States of America; * = effective but not applicable; IQR = interquartile range

Figures

Figure 1: Modified PRISMA flow chart

Figure 2: Geographical mapping of the included published articles

Figure 3: Summary of cancer types reported by the included published articles

Figure 4: Summary of intervention types reported by the included published articles

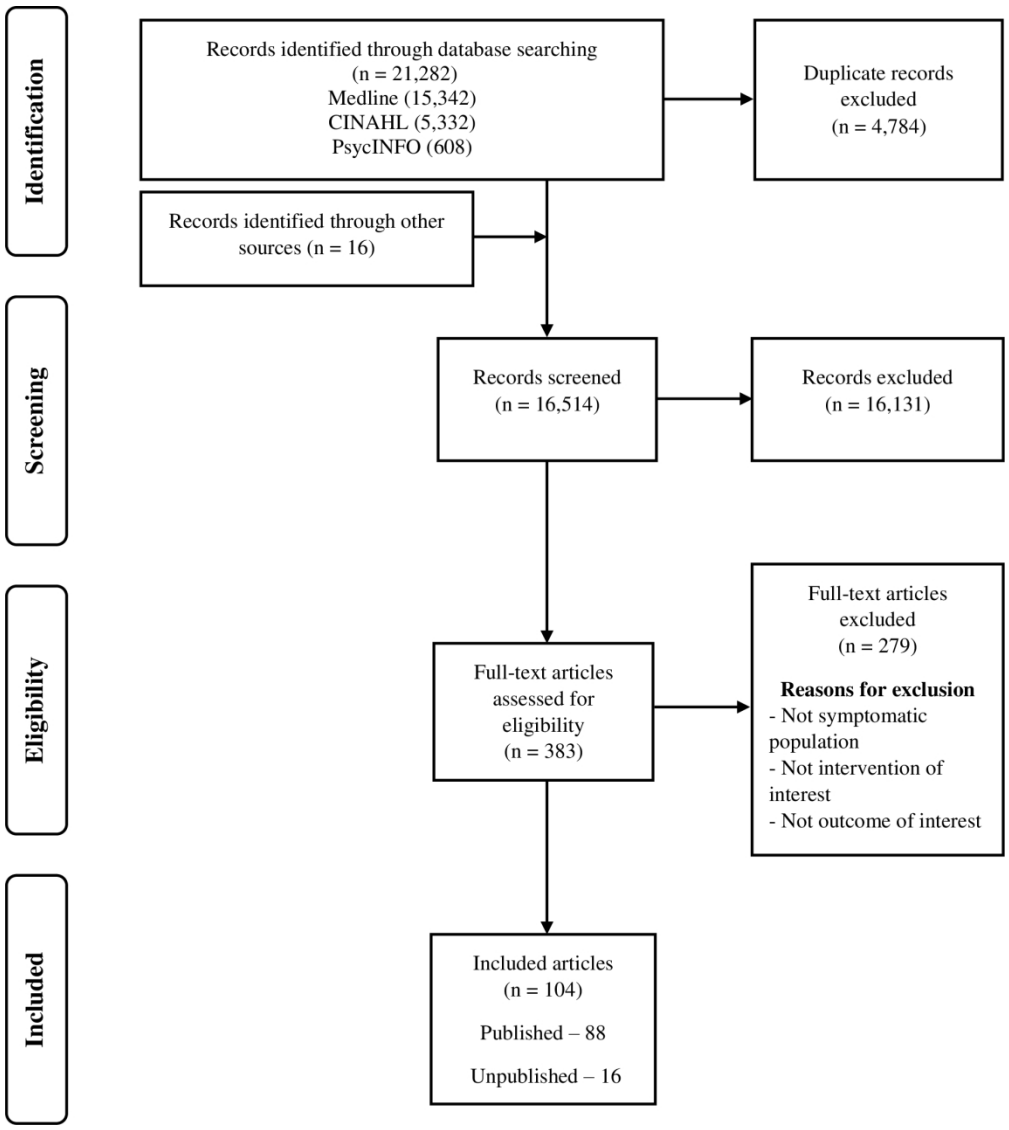

Figure 1: Modified PRISMA flow chart

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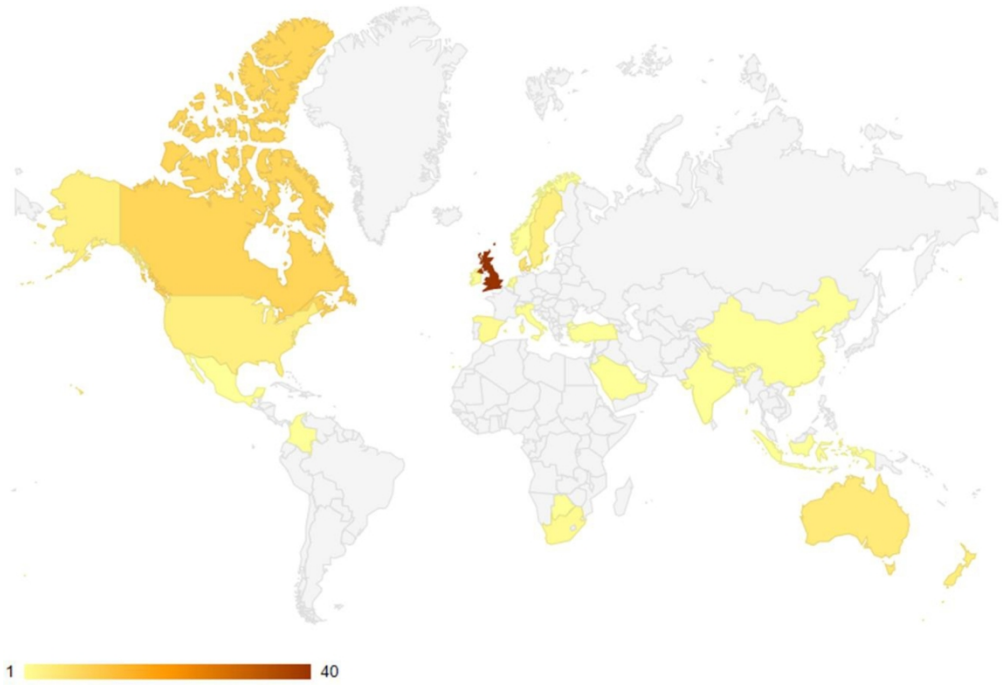

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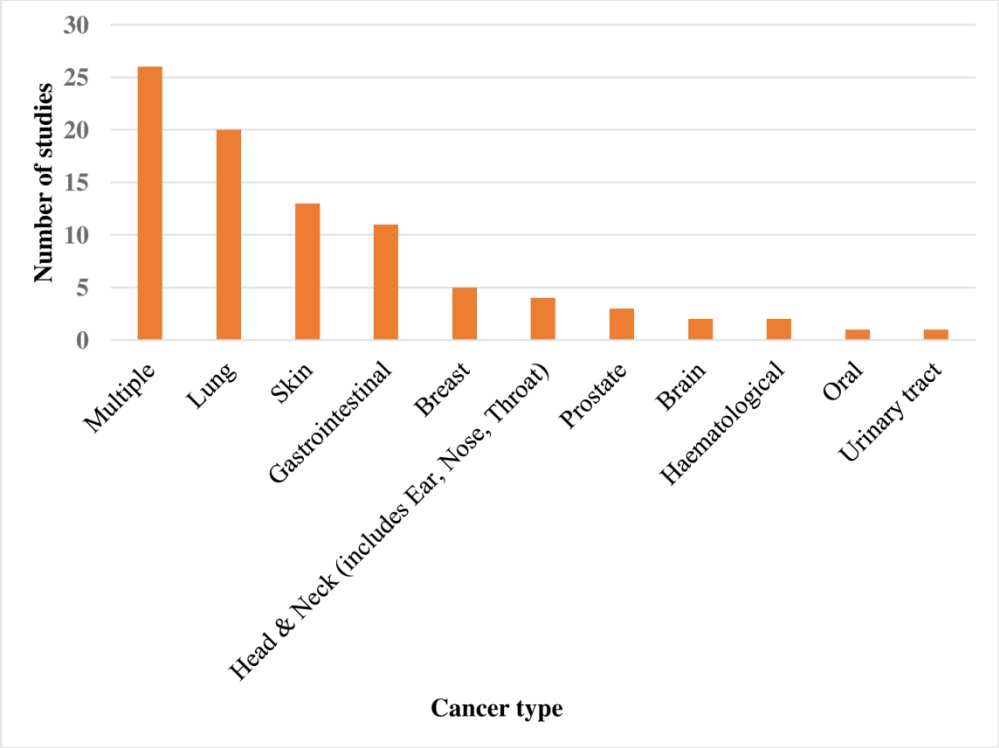

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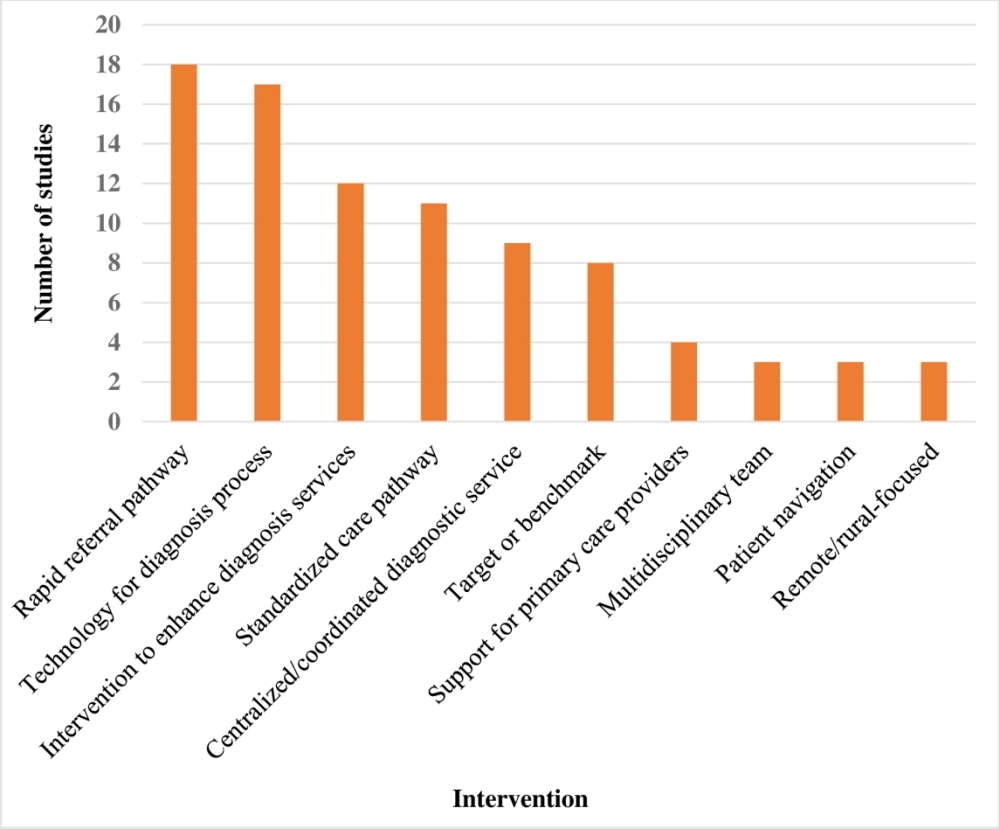

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Appendices

Appendix 1: Project work plan

About the Project Team

At the Knowledge Synthesis Team, George and Fay Yee Centre for Healthcare Innovation, we have an experienced team of methodologists, systematic reviewers, a medical librarian and biostatistician. Over the past 8 years we have supported numerous research teams and guideline developers by providing training, support and conducting evidence syntheses on their behalf. In addition, several of our team members hold academic positions with the University of Manitoba where they teach, supervise students, and advance the science and practice of knowledge synthesis.

Proposed Method

Methods

Using a team of experienced systematic reviews and methodologists, with expertise in research methodology, knowledge synthesis and implementation science, we will update the 2018 peer-reviewed and grey literature scan by conducting a rapid scoping review to include contemporary, national and international leading interventions for improving accurate and timely cancer diagnosis focusing on the symptomatic population and summarize efficacy, impact and sustainability of identified interventions. We will identify evidence to answer the following key questions:

KQ 1. Are there practice guidelines, care pathways or other initiatives (e.g., benchmarks/ targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, patient navigators and/or navigation, etc.) that have been found to streamline and enhance accurate and timely diagnosis in symptomatic individuals?

- How were patients involved in the design, development and/ or implementation of these initiatives?
- How were providers (e.g., primary care providers) involved in the design, development and/or implementation of these initiatives?

KQ 2. What are the leading interventions for innovative and/or virtual approaches (e.g., technology-based) to seamless care (i.e., minimally disruptive care that is found to be more convenient/coordinated/timely/less stressful to the patients) in the pre-diagnosis phase within Canada and abroad?

- How have these interventions been applied, including identification of successes and lessons learned where possible?
- Were these interventions evaluated and if so, what were the findings?
- How were patients involved in the design, development and/ or implementation of these interventions?

KQ 3. What are the identified performance metrics that can be used to measure the suspicion to diagnosis phase; and where and how are these metrics used?

- Are there specific metrics used to measure the patient experience?
- What data is captured by decision-support systems and how does the data and clinical systems work together?
- Is there evidence on sustainability of the model?

KQ 4. What are the key points of care in a patient's experience (e.g., diagnostic tests, physician consultations, etc.) as they navigate the system from initial symptoms/ suspicion of cancer to diagnosis?

KQ 5. Have specific considerations been applied to underserviced populations including Indigenous, rural, and remote populations within the context of each of the questions above?

Study eligibility criteria
This review will focus on published and unpublished studies that answer the key questions since 2017. Our focus is on comparative studies that applied a protocol/guideline or a specific intervention or intervention plan. Having said that, we anticipate the need to review lower quality study designs (e.g., retrospective, and uncontrolled studies). As such, there will be no restriction on the study design, but will be limited to English language publications for feasibility.

Search strategy and study selection
A knowledge synthesis librarian has designed and executed a literature search strategy in MEDLINE (Ovid). The search strategy was peer-reviewed by a second librarian and adapted for other bibliographic databases: Cinahl (Ebsco) and Psycinfo (Ovid). Search strategies are presented in Appendix 1. All retrieved records were imported into EndNote for citation management.
One reviewer will screen each identified citation for eligibility. Full texts of all relevant citations will be reviewed by two reviewers. All conflicts will be resolved by discussion and/ or a third reviewer, as needed. We will record the number of ineligible citations at the title/ abstract screening stage, and both the number and reason for ineligibility at the full-text articles.

Data extraction
We will develop data extraction forms and pilot them on a small selection of studies. Extracted data will be stored and managed in MS Excel. One reviewer will independently extract data from included studies and another reviewer will independently check the extracted data for errors. Disagreements will be resolved by discussion between reviewers and/ or by involving a third reviewer, as needed.

Data analysis
We will present specific characteristics of all included studies in a tabular form. The analysis of the extracted data will be descriptive.

Study dissemination
We will submit reports from this study as a technical report to CPAC.

Knowledge User Engagement Plan

We will be providing a bi-weekly update to CPAC on the progression of the review. Specifically, we will engage during specific time points to review progress and next steps:

- Protocol
- Level I Screening (Title/ Abstract screening phase)
- Level II Screening (Full-text screening phase)
- Data Extraction
- Data Analysis
- Report

Declaration of Conflict of Interest

None

Appendix 2: MEDLINE (Ovid) search strategy

1.	"early detection of cancer"/	26241
2.	(cancer* or tumo?r* or neoplasm* or malignan* or metasta* or oncogen* or oncolog*).ti	1795604
3.	(carcinoma* or adenoma* or adenocarcinoma* or adeno-carcinoma* or blastoma* or carcinosarcoma* or carcino-sarcoma* or leukemia* or leukaemia* or lymphoma* or melanoma* or mesenchymoma* or mesothelioma* or sarcoma* or thymoma*).ti	844480
4.	or/2-3	2477759
5.	1 or 4	2483642
6.	early diagnosis/ or delayed diagnosis/	33272
7.	(prediagnos* or pre-diagnos* or care path? or cancer path? or care pathway* or cancer pathway* or diagnos* phase* or diagnos* path? or referral path? or diagnos* pathway* or referral pathway* or diagnos* interval* or referral interval* or consult* interval* or "time-to-treat" or "time-to-treatment").ti,ab,kf.	26471
8.	((early or earlier or prompt* or late or later or rapid or wait* or delay* or timel* or longtime or interval* or route*) adj3 (diagnos* or refer or referred or referral* or referring or consult*)).ti,ab,kf.	214615
9.	((diagnos* or confirm* or refer* or consult* or investigat*) adj4 (timelapse* or time lapse* or time elapse* or fasttrack* or fast-track* or timeline* or time line*)).ti,ab	1510
10.	delay*.ti	74391
11.	wait* time*.ti,ab.	13384
12.	or/6-11	338665
13.	4 and 12	58490
14.	diagnos*.ti,ab,kf	2562935
15.	13 and (1 or 14)	48832
16.	(interprofessional* or inter-professional* or multidisciplin* or multi-disciplin* or navigator* or coordinator* or co-ordinator* or ((patient* or cancer* or care) adj2 (navigat* or coordinat* or co-ordinat* or journey* or continuum*)) or mobile or phone* or smartphone* or reminder* or tele* or information technolog* or communicat*).ti	177088
17.	16 and 5	10725
18.	15 or 17	59240
19.	limit 18 to english language	49045
20.	(exp animal experiment/ or exp animal model/ or exp transgenic animal/ or animal/ or chordata/ or vertebrate/ or tetrapod/ or amniote/ or exp amphibia/ or mammal/ or exp reptile/ or therian/ or placental mammals/ or exp marsupial/ or euarchontoglires/ or exp xenarthra/ or primate/ or exp scandentia/ or haplorhini/ or exp prosimian/ or simian/ or exp tarsiiform/ or catarrhini/ or exp platyrrhini/ or ape/ or exp cercopithecidae/ or hominid/ or exp hylobatidae/ or exp chimpanzee/ or exp gorilla/ or (animal or animals or pisces or fish or fishes or catfish or catfishes or sheatfish or silurus or arius or heteropneustes or clarias or gariepinus or fathead minnow or fathead minnows or pimephales or promelas or cichlidae or trout or trouts or char	4778446

	or chars or salvelinus or salmo or oncorhynchus or guppy or guppies or millionfish or poecilia or goldfish or goldfishes or carassius or auratus or mullet or mullets or mugil or curema or shark or sharks or cod or cods or gadus or morhua or carp or carps or cyprinus or carpio or killifish or eel or eels or anguilla or zander or sander or lucioperca or stizostedion or turbot or turbots or psetta or flatfish or flatfishes or plaice or pleuronectes or platessa or tilapia or tilapias or oreochromis or sarotherodon or common sole or dover sole or solea or zebrafish or zebrafishes or danio or rerio or seabass or dicentrarchus or labrax or morone or lamprey or lampreys or petromyzon or pumpkinseed or pumpkinseeds or lepomis or gibbosus or herring or clupea or harengus or amphibia or amphibian or amphibians or anura or salientia or frog or frogs or rana or toad or toads or bufo or xenopus or laevis or bombina or epidalea or calamita or salamander or salamanders or newt or newts or triturus or reptilia or reptile or reptiles or bearded dragon or pogona or vitticeps or iguana or iguanas or lizard or lizards or anguis fragilis or turtle or turtles or snakes or snake or aves or bird or birds or quail or quails or coturnix or bobwhite or colinus or virginianus or poultry or poultries or fowl or fowls or chicken or chickens or gallus or zebra finch or taeniopygia or guttata or canary or canaries or serinus or canaria or parakeet or parakeets or grasskeet or parrot or parrots or psittacine or psittacines or shelduck or tadorna or goose or geese or branta or leucopsis or woodlark or lullula or flycatcher or ficedula or hypoleuca or dove or doves or geopelia or cuneata or duck or ducks or greylag or graylag or anser or harrier or circus pygargus or red knot or great knot or calidris or canutus or godwit or limosa or lapponica or meleagris or gallopavo or jackdaw or corvus or monedula or ruff or philomachus or pugnax or lapwing or peewit or plover or vanellus or swan or cygnus or columbianus or bewickii or gull or chroicocephalus or ridibundus or albifrons or great tit or parus or aythya or fuligula or streptopelia or risoria or spoonbill or platalea or leucorodia or blackbird or turdus or merula or blue tit or cyanistes or pigeon or pigeons or columba or pintail or anas or starling or sturnus or owl or athene noctua or pochard or ferina or cockatiel or nymphicus or hollandicus or skylark or alauda or tern or sterna or teal or crecca or oystercatcher or haematopus or ostralegus or shrew or shrews or sorex or araneus or crocidura or russula or european mole or talpa or chiroptera or bat or bats or eptesicus or serotinus or myotis or dasycneme or daubentonii or pipistrelle or pipistrellus or cat or cats or felis or catus or feline or dog or dogs or canis or canine or canines or otter or otters or lutra or badger or badgers or meles or fitchew or fitch or foumart or foulmart or ferrets or ferret or polecat or polecats or mustela or putorius or weasel or weasels or fox or foxes or vulpes or common seal or phoca or vitulina or grey seal or halichoerus or horse or horses or equus or equine or equidae or donkey or donkeys or mule or mules or pig or pigs or swine or swines or hog or hogs or boar or boars or porcine or piglet or piglets or sus or scrofa or llama or llamas or lama or glama or deer or deers or cervus or elaphus or cow or cows or bos taurus or bos indicus or bovine or bull or bulls or cattle or bison or bisons or sheep or sheeps or ovis aries or ovine or lamb or lambs or mouflon or mouflons or goat or goats or capra or caprine or chamois or rupicapra or leporidae or lagomorpha or lagomorph or rabbit or rabbits or oryctolagus or cuniculus or laprine or hares or lepus or rodentia or rodent or rodents or murinae or mouse or mice or mus or musculus or murine or woodmouse or apodemus or rat or rats or rattus or norvegicus or guinea pig or guinea pigs or cavia or porcellus or hamster or hamsters or mesocricetus or cricetulus or cricetus or gerbil or gerbils or jird or jirds or meriones or unguiculatus or jerboa or jerboas or jaculus or chinchilla or chinchillas or beaver or beavers or castor fiber or castor canadensis or sciuridae or squirrel or squirrels or sciurus or chipmunk or chipmunks or marmot or marmots or marmota or suslik or susliks or spermophilus or cynomys or cottonrat or cottonrats or sigmodon or vole or voles or microtus or myodes or glareolus or primate or primates or prosimian or prosimians or lemur or lemurs or lemuridae or loris or bush baby or bush babies or bushbaby or bushbabies or galago or galagos or anthropoidea or anthropoids or simian or simians or monkey or monkeys or	

	marmoset or marmosets or callithrix or cebuella or tamarin or tamarins or saguinus or leontopithecus or squirrel monkey or squirrel monkeys or saimiri or night monkey or night monkeys or owl monkey or owl monkeys or douroucoulis or aotus or spider monkey or spider monkeys or ateles or baboon or baboons or papio or rhesus monkey or macaque or macaca or mulatta or cynomolgus or fascicularis or green monkey or green monkeys or chlorocebus or vervet or vervets or pygerythrus or hominoidea or ape or apes or hylobatidae or gibbon or gibbons or siamang or siamangs or nomascus or symphalangus or hominidae or orangutan or orangutans or pongo or chimpanzee or chimpanzees or pan troglodytes or bonobo or bonobos or pan paniscus or gorilla or gorillas or troglodytes).ti,ab,kf.) not (human/ or (human$ or man or men or woman or women or child or children or patient$).ti,ab,kf.)	
21.	19 not 20	48488
22.	limit 21 to yr="2017 -Current"	15342

Appendix 3: CINAHL (EbscoHOST) search strategy

1.	(MH "early detection of cancer")	9365
2.	TI (cancer* OR tumo#r* OR neoplasm* OR malignan* OR metasta* OR oncogen* OR oncolog*)	382286
3.	TI (carcinoma* OR adenoma* OR adenocarcinoma* OR blastoma* OR carcinosarcoma* OR leukemia* OR leukaemia* OR lymphoma* OR melanoma* OR mesenchymoma* OR mesothelioma* OR sarcoma* OR thymoma*)	110746
4.	S2 OR S3	469442
5.	S1 OR S4	471736
6.	(MH "early diagnosis") OR (MH "diagnosis, delayed")	14703
7.	(TI (prediagnos* OR "pre-diagnosis" OR (care N1 path#) OR (cancer N1 path#) OR (care N1 pathway*) OR (cancer N1 pathway*) OR (diagnos* N1 phase*) OR (diagnos* N1 path#) OR (referral N1 path#) OR (diagnos* N1 pathway*) OR (referral N1 pathway*) OR (diagnos* N1 interval*) OR (referral N1 interval*) OR (consult* N1 interval*) OR "time-to-treat" OR "time-to-treatment")) OR (AB (prediagnos* OR "pre-diagnosis" OR (care N1 path#) OR (cancer N1 path#) OR (care N1 pathway*) OR (cancer N1 pathway*) OR (diagnos* N1 phase*) OR (diagnos* N1 path#) OR (referral N1 path#) OR (diagnos* N1 pathway*) OR (referral N1 pathway*) OR (diagnos* N1 interval*) OR (referral N1 interval*) OR (consult* N1 interval*) OR "time-to-treat" OR "time-to-treatment"))	11308
8.	(TI ((early OR earlier OR prompt* OR late OR later OR rapid OR wait* OR delay* OR timel* OR longtime OR interval* OR route*) N3 (diagnos* OR refer OR referred OR referral* OR referring OR consult*))) OR (AB ((early OR earlier OR prompt* OR late OR later OR rapid OR wait* OR delay* OR timel* OR longtime OR interval* OR route*) N3 (diagnos* OR refer OR referred OR referral* OR referring OR consult*)))	47662
9.	(TI ((diagnos* OR confirm* OR refer* OR consult* OR investigat*) N4 (timelapse* OR (time N1 lapse*) OR (time N1 elapse*) OR fasttrack* OR (fast N1 track*) OR timeline* OR (time N1 line*)))) OR (AB ((diagnos* OR confirm* OR refer* OR consult* OR investigat*) N4 (timelapse* OR (time N1 lapse*) OR (time N1 elapse*) OR fasttrack* OR (fast N1 track*) OR timeline* OR (time N1 line*))))	582
10.	TI delay*	17790
11.	(TI (wait* N1 time*)) OR (AB (wait* N1 time*))	6047
12.	S6 OR S7 OR S8 OR S9 OR S10 OR S11	88476
13.	S4 AND S12	13005
14.	(TI diagnos*) OR (AB diagnos*)	526863
15.	S13 AND (S1 OR S14)	9687
16.	TI (interprofessional* OR (inter N1 professional*) OR multidisciplin* OR (multi N1 disciplin*) OR navigator* OR coordinator* OR ordinator* OR ((patient* OR cancer* OR care) N2 (navigat* OR coordinat* OR ordinat* OR journey* OR continuum*)) OR mobile OR phone* OR smartphone* OR reminder* OR tele* OR (information N1 technolog*) OR communicat*)	94165
17.	S16 AND S5	5442
18.	S15 OR S17	14982
19.	S18 Limiters - English Language	14767
20.	((MH "animals+") OR (MH invertebrates+) OR (MH birds+) OR (MH fish) OR (MH "frogs and toads") OR (MH "animals, genetically modified") OR (MH reptiles+) OR (MH mammals) OR (MH bats) OR (MH camels) OR (MH cats) OR (MH cattle) OR (MH dogs) OR (MH dolphins) OR (MH goats) OR (MH horses) OR (MH rabbits) OR (MH rodents+) OR (MH	216053

	sheep) OR (MH swine) OR (MH primates) OR (animal OR animals OR pisces OR fish OR fishes OR catfish OR catfishes OR sheatfish OR silurus OR arius OR heteropneustes OR clarias OR gariepinus OR "fathead minnow" OR "fathead minnows" OR pimephales OR promelas OR cichlidae OR trout OR trouts OR char OR chars OR salvelinus OR salmo OR oncorhynchus OR guppy OR guppies OR millionfish OR poecilia OR goldfish OR goldfishes OR carassius OR auratus OR mullet OR mullets OR mugil OR curema OR shark OR sharks OR cod OR cods OR gadus OR morhua OR carp OR carps OR cyprinus OR carpio OR killifish OR eel OR eels OR anguilla OR zander OR sander OR lucioperca OR stizostedion OR turbot OR turbots OR psetta OR flatfish OR flatfishes OR plaice OR pleuronectes OR platessa OR tilapia OR tilapias OR oreochromis OR sarotherodon OR "common sole" OR "dover sole" OR solea OR zebrafish OR zebrafishes OR danio OR rerio OR seabass OR dicentrarchus OR labrax OR morone OR lamprey OR lampreys OR petromyzon OR pumpkinseed OR pumpkinseeds OR lepomis OR gibbosus OR herring OR clupea OR harengus OR amphibia OR amphibian OR amphibians OR anura OR salientia OR frog OR frogs OR rana OR toad OR toads OR bufo OR xenopus OR laevis OR bombina OR epidalea OR calamita OR salamander OR salamanders OR newt OR newts OR triturus OR reptilia OR reptile OR reptiles OR "bearded dragon" OR pogona OR vitticeps OR iguana OR iguanas OR lizard OR lizards OR "anguis fragilis" OR turtle OR turtles OR snakes OR snake OR aves OR bird OR birds OR quail OR quails OR coturnix OR bobwhite OR colinus OR virginianus OR poultry OR poultries OR fowl OR fowls OR chicken OR chickens OR gallus OR "zebra finch" OR taeniopygia OR guttata OR canary OR canaries OR serinus OR canaria OR parakeet OR parakeets OR grasskeet OR parrot OR parrots OR psittacine OR psittacines OR shelduck OR tadorna OR goose OR geese OR branta OR leucopsis OR woodlark OR lullula OR flycatcher OR ficedula OR hypoleuca OR dove OR doves OR geopelia OR cuneata OR duck OR ducks OR greylag OR graylag OR anser OR harrier OR circus pygargus OR red knot OR "great knot" OR calidris OR canutus OR godwit OR limosa OR lapponica OR meleagris OR gallopavo OR jackdaw OR corvus OR monedula OR ruff OR philomachus OR pugnax OR lapwing OR peewit OR plover OR vanellus OR swan OR cygnus OR columbianus OR bewickii OR gull OR chroicocephalus OR ridibundus OR albifrons OR "great tit" OR parus OR aythya OR fuligula OR streptopelia OR risoria OR spoonbill OR platalea OR leucorodia OR blackbird OR turdus OR merula OR blue tit OR cyanistes OR pigeon OR pigeons OR columba OR pintail OR anas OR starling OR sturnus OR owl OR "athene noctua" OR pochard OR ferina OR cockatiel OR nymphicus OR hollandicus OR skylark OR alauda OR tern OR sterna OR teal OR crecca OR oystercatcher OR haematopus OR ostralegus OR shrew OR shrews OR sorex OR araneus OR crocidura OR russula OR "european mole" OR talpa OR chiroptera OR bat OR bats OR eptesicus OR serotinus OR myotis OR dasycneme OR daubentonii OR pipistrelle OR pipistrellus OR cat OR cats OR felis OR catus OR feline OR dog OR dogs OR canis OR canine OR canines OR otter OR otters OR lutra OR badger OR badgers OR meles OR fitchew OR fitch OR foumart OR foulmart OR ferrets OR ferret OR polecat OR polecats OR mustela OR putorius OR weasel OR weasels OR fox OR foxes OR vulpes OR "common seal" OR phoca OR vitulina OR grey seal OR halichoerus OR horse OR horses OR equus OR equine OR equidae OR donkey OR donkeys OR mule OR mules OR pig OR pigs OR swine OR swines OR hog OR hogs OR boar OR boars OR porcine OR piglet OR piglets OR sus OR scrofa OR llama OR llamas OR lama OR glama OR deer OR deers OR cervus OR elaphus OR cow OR cows OR "bos taurus" OR "bos indicus" OR bovine OR bull OR bulls OR cattle OR bison OR bisons OR sheep OR sheeps OR "ovis aries" OR ovine OR lamb OR lambs OR mouflon OR mouflons OR goat OR goats OR capra OR caprine OR chamois OR rupicapra OR leporidae OR lagomorpha OR lagomorph OR rabbit OR rabbits OR oryctolagus OR cuniculus OR laprine OR hares OR lepus OR rodentia OR rodent OR rodents OR murinae OR mouse OR mice OR mus OR musculus OR murine OR woodmouse	

	OR apodemus OR rat OR rats OR rattus OR norvegicus OR "guinea pig" OR "guinea pigs" OR cavia OR porcellus OR hamster OR hamsters OR mesocricetus OR cricetulus OR cricetus OR gerbil OR gerbils OR jird OR jirds OR meriones OR unguiculatus OR jerboa OR jerboas OR jaculus OR chinchilla OR chinchillas OR beaver OR beavers OR "castor fiber" OR "castor canadensis" OR sciuridae OR squirrel OR squirrels OR sciurus OR chipmunk OR chipmunks OR marmot OR marmots OR marmota OR suslik OR susliks OR spermophilus OR cynomys OR cottonrat OR cottonrats OR sigmodon OR vole OR voles OR microtus OR myodes OR glareolus OR primate OR primates OR prosimian OR prosimians OR lemur OR lemurs OR lemuridae OR loris OR "bush baby" OR "bush babies" OR bushbaby OR bushbabies OR galago OR galagos OR anthropoidea OR anthropoids OR simian OR simians OR monkey OR monkeys OR marmoset OR marmosets OR callithrix OR cebuella OR tamarin OR tamarins OR saguinus OR leontopithecus OR squirrel monkey OR squirrel monkeys OR saimiri OR "night monkey" OR "night monkeys" OR "owl monkey" OR "owl monkeys" OR douroucoulis OR aotus OR "spider monkey" OR "spider monkeys" OR ateles OR baboon OR baboons OR papio OR "rhesus monkey" OR macaque OR macaca OR mulatta OR cynomolgus OR fascicularis OR "green monkey" OR "green monkeys" OR chlorocebus OR vervet OR vervets OR pygerythrus OR hominoidea OR ape OR apes OR hylobatidae OR gibbon OR gibbons OR siamang OR siamangs OR nomascus OR symphalangus OR hominidae OR orangutan OR orangutans OR pongo OR chimpanzee OR chimpanzees OR "pan troglodytes" OR bonobo OR bonobos OR "pan paniscus" OR gorilla OR gorillas OR troglodytes)) NOT ((MH human) OR (human# OR man OR men OR woman OR women OR child OR children OR patient#))	
21.	S19 NOT S20	14678
22.	S21 Limiters - Published Date: 20170101-20201231	5333

Appendix 4: Psycinfo (Ovid) search strategy

1.	cancer screening/	4776
2.	(cancer* or tumo?r* or neoplasm* or malignan* or metasta* or oncogen* or oncolog*).ti	44464
3.	(carcinoma* or adenoma* or adenocarcinoma* or adeno-carcinoma* or blastoma* or carcinosarcoma* or carcino-sarcoma* or leukemia* or leukaemia* or lymphoma* or melanoma* or mesenchymoma* or mesothelioma* or sarcoma* or thymoma*).ti	2705
4.	or/2-3	46737
5.	1 or 4	47903
6.	(prediagnos* or pre-diagnos* or care path? or cancer path? or care pathway* or cancer pathway* or diagnos* phase* or diagnos* path? or referral path? or diagnos* pathway* or referral pathway* or diagnos* interval* or referral interval* or consult* interval* or "time-to-treat" or "time-to-treatment").ti,ab,id.	3896
7.	((early or earlier or prompt* or late or later or rapid or wait* or delay* or timel* or longtime or interval* or route*) adj3 (diagnos* or refer or referred or referral* or referring or consult*)).ti,ab,id.	13853
8.	((diagnos* or confirm* or refer* or consult* or investigat*) adj4 (timelapse* or time lapse* or time elapse* or fasttrack* or fast-track* or timeline* or time line*)).ti,ab	168
9.	delay*.ti	14212
10.	wait* time*.ti,ab.	1957
11.	or/6-10	33241
12.	4 and 11	1613
13.	diagnos*.ti,ab,id	324967
14.	12 and (1 or 13)	1345
15.	(interprofessional* or inter-professional* or multidisciplin* or multi-disciplin* or navigator* or coordinator* or co-ordinator* or ((patient* or cancer* or care) adj2 (navigat* or coordinat* or co-ordinat* or journey* or continuum*)) or mobile or phone* or smartphone* or reminder* or tele* or information technolog* or communicat*).ti	81166
16.	15 and 5	1650
17.	14 or 16	2949
18.	limit 17 to english language	2756
19.	(exp animal research/ or animal models/ or exp animals/ or ("20").po or (animal or animals or pisces or fish or fishes or catfish or catfishes or sheatfish or silurus or arius or heteropneustes or clarias or gariepinus or fathead minnow or fathead minnows or pimephales or promelas or cichlidae or trout or trouts or char or chars or salvelinus or salmo or oncorhynchus or guppy or guppies or millionfish or poecilia or goldfish or goldfishes or carassius or auratus or mullet or mullets or mugil or curema or shark or sharks or cod or cods or gadus or morhua or carp or carps or cyprinus or carpio or killifish or eel or eels or anguilla or zander or sander or lucioperca or stizostedion or turbot or turbots or psetta or flatfish or flatfishes or plaice or pleuronectes or platessa or tilapia or tilapias or oreochromis or sarotherodon or common sole or dover sole or solea or zebrafish or zebrafishes or danio or rerio or seabass or dicentrarchus or labrax or morone or lamprey or lampreys or petromyzon or pumpkinseed or pumpkinseeds or lepomis or gibbosus or herring or clupea or harengus or amphibia or amphibian or amphibians or anura or salientia or frog or frogs or rana or toad or toads or bufo or xenopus or laevis or bombina or epidalea or calamita or salamander or salamanders or newt or newts or triturus or reptilia or reptile or reptiles or bearded dragon or pogona or vitticeps or iguana or iguanas or lizard or lizards or anguis fragilis or turtle or turtles or snakes or snake or aves or bird or birds or quail or quails or coturnix or bobwhite or colinus or virginianus or poultry or poultries or	339315

	fowl or fowls or chicken or chickens or gallus or zebra finch or taeniopygia or guttata or canary or canaries or serinus or canaria or parakeet or parakeets or grasskeet or parrot or parrots or psittacine or psittacines or shelduck or tadorna or goose or geese or branta or leucopsis or woodlark or lullula or flycatcher or ficedula or hypoleuca or dove or doves or geopelia or cuneata or duck or ducks or greylag or graylag or anser or harrier or circus pygargus or red knot or great knot or calidris or canutus or godwit or limosa or lapponica or meleagris or gallopavo or jackdaw or corvus or monedula or ruff or philomachus or pugnax or lapwing or peewit or plover or vanellus or swan or cygnus or columbianus or bewickii or gull or chroicocephalus or ridibundus or albifrons or great tit or parus or aythya or fuligula or streptopelia or risoria or spoonbill or platalea or leucorodia or blackbird or turdus or merula or blue tit or cyanistes or pigeon or pigeons or columba or pintail or anas or starling or sturnus or owl or athene noctua or pochard or ferina or cockatiel or nymphicus or hollandicus or skylark or alauda or tern or sterna or teal or crecca or oystercatcher or haematopus or ostralegus or shrew or shrews or sorex or araneus or crocidura or russula or european mole or talpa or chiroptera or bat or bats or eptesicus or serotinus or myotis or dasycneme or daubentonii or pipistrelle or pipistrellus or cat or cats or felis or catus or feline or dog or dogs or canis or canine or canines or otter or otters or lutra or badger or badgers or meles or fitchew or fitch or foumart or foulmart or ferrets or ferret or polecat or polecats or mustela or putorius or weasel or weasels or fox or foxes or vulpes or common seal or phoca or vitulina or grey seal or halichoerus or horse or horses or equus or equine or equidae or donkey or donkeys or mule or mules or pig or pigs or swine or swines or hog or hogs or boar or boars or porcine or piglet or piglets or sus or scrofa or llama or llamas or lama or glama or deer or deers or cervus or elaphus or cow or cows or bos taurus or bos indicus or bovine or bull or bulls or cattle or bison or bisons or sheep or sheeps or ovis aries or ovine or lamb or lambs or mouflon or mouflons or goat or goats or capra or caprine or chamois or rupicapra or leporidae or lagomorpha or lagomorph or rabbit or rabbits or oryctolagus or cuniculus or laprine or hares or lepus or rodentia or rodent or rodents or murinae or mouse or mice or mus or musculus or murine or woodmouse or apodemus or rat or rats or rattus or norvegicus or guinea pig or guinea pigs or cavia or porcellus or hamster or hamsters or mesocricetus or cricetulus or cricetus or gerbil or gerbils or jird or jirds or meriones or unguiculatus or jerboa or jerboas or jaculus or chinchilla or chinchillas or beaver or beavers or castor fiber or castor canadensis or sciuridae or squirrel or squirrels or sciurus or chipmunk or chipmunks or marmot or marmots or marmota or suslik or susliks or spermophilus or cynomys or cottonrat or cottonrats or sigmodon or vole or voles or microtus or myodes or glareolus or primate or primates or prosimian or prosimians or lemur or lemurs or lemuridae or loris or bush baby or bush babies or bushbaby or bushbabies or galago or galagos or anthropoidea or anthropoids or simian or simians or monkey or monkeys or marmoset or marmosets or callithrix or cebuella or tamarin or tamarins or saguinus or leontopithecus or squirrel monkey or squirrel monkeys or saimiri or night monkey or night monkeys or owl monkey or owl monkeys or douroucoulis or aotus or spider monkey or spider monkeys or ateles or baboon or baboons or papio or rhesus monkey or macaque or macaca or mulatta or cynomolgus or fascicularis or green monkey or green monkeys or chlorocebus or vervet or vervets or pygerythrus or hominoidea or ape or apes or hylobatidae or gibbon or gibbons or siamang or siamangs or nomascus or symphalangus or hominidae or orangutan or orangutans or pongo or chimpanzee or chimpanzees or pan troglodytes or bonobo or bonobos or pan paniscus or gorilla or gorillas or troglodytes).ti,ab,id.) not (("10").po or (human$ or man or men or woman or women or child or children or patient$).ti,ab,id.)	
20.	18 not 19	2754
21.	limit 20 to yr="2017 -Current"	608

Appendix 5: Websites of relevant organizations and professional bodies searched for literature

Canada

- Alberta Cancer Foundation
- BC Cancer Foundation
- BC Cancer Agency
- Cancer Care Manitoba
- Cancer Care Nova Scotia
- Cancer Care Ontario
- CancerControl Alberta
- Canada Health Infoway
- Canadian Association of Nurses in Oncology
- Canadian Association of Psychosocial Oncology
- Canadian Cancer Society
- Canadian Foundation for Healthcare Improvement
- Canadian Foundation for Innovation
- Canadian Institutes of Health Research
- Cancer and Primary Care Research
- Cancer Quality Council of Ontario
- Cancerview.ca
- CanIMPACT
- College of Family Physicians of Canada
- International Network
- New Brunswick Cancer Network
- Ontario Institute for Cancer Research
- Quebec Health and Social Services (Direction québécoise de cancérologie, Ministère de la Santé et des Services sociaux)
- Royal College of Physicians and Surgeons of Canada
- Saskatchewan Cancer Agency
- Trillium Health Partners

International

- Association of Community Cancer Centres – USA
- Centers for Disease Control and Prevention – USA
- Commission on Cancer of the American College of Surgeons – USA
- Institute of Medicine – USA
- National Cancer Institute – USA
- National Comprehensive Cancer Network – USA
- Cancer Research UK (including the Accelerate, Coordinate, Evaluate Programme) – UK
- Kings Fund – UK
- National Health Service (NHS) – UK
- National Institute for Health and Care Excellence (NICE) – UK
- Northern Cancer Network – New Zealand
- Cancer Australia – Australia
- Sax Institute – Australia
- Denmark (Ministry of Health)
- Sweden (Ministry of Health)
- European Organization for Research and Treatment of Cancer – Europe
- European Society for Medical Oncology – Europe
- European Partnership Action Against Cancer – Europe
- World Health Organization – International

Appendix 6: Definition for interventions related to the review questions

- *Centralized or coordinated diagnostic service*: Brings together various tests/procedures and care providers needed to determine a definitive diagnosis at one location.
- *Interventions in diagnostic services*: An initiative that aims to improve diagnostic services within a jurisdiction.
- *Multidisciplinary team*: Working with multiple departments, such as diagnostic imaging, pathology, medical oncology, and research.
- *Patient navigation*: A dedicated role to help facilitate the navigation for patients across the cancer journey – helps the patient through testing, appointments, health literacy, etc.
- *Rapid referral pathway*: Provides urgent access to specialists and/or diagnostic services for patients.
- *Remote or rural populations*: This refers to populations that may live in non-urban areas. They often do not have access to the same services as those who reside in more urban areas.
- *Standardized care pathway*: Sets expectations for cancer care based on evidence and shares information about how to provide and what care to provide at each point of diagnosis, treatment, and survivorship. Initiative is often integrated into the current health system.
- *Support for primary care providers*: Initiative focusing on educating and supporting primary care providers on care pathways and how to care for individuals presenting with potential or confirmed cancer symptoms.
- *Target or benchmark*: A figure used as a goal by jurisdictions to measure progress towards the desired outcome of an initiative.
- *Technology to support diagnosis process*: Technological innovations to enhance efficiency of initiatives.

Appendix 7: Summary of the characteristics of the included published articles that reported data on ineffective interventions

Interventions	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Interventions to enhance diagnostic services	Agnarsdottir 2019	Sweden (Uppsala)	Cross-sectional (2016-2018)	Skin (Adult) [286]	Reporting time	The reporting time increased from 18 to 31 days for the non-priority cases and from 15 to 25 days for all cases with invasive melanomas (Ineffective)
	McCutchan 2020	UK (Wales)	Before-and-After (2016)	Lung (Mixed age) [1011 (pre-campaign); 1013 (post-campaign)]	Urgent suspected referrals to specialist	There was no statistically significant change in urgent suspected cancer referrals (p = 0.82) in routes to diagnosis (Ineffective)
Multidisciplinary team	Largey 2020	Australia (Victoria)	Before-and-After (2016-2017)	Lung (Adult) [429]	Time interval from referral to first specialist appointment	Referral to first specialist appointment interval was reduced in the post intervention period from median (IQR) 6 (0-15) to 4 (1-10) days, with no significant trend (p=0.962) (Ineffective)
	Thalanayar Muthukrishnan 2020	USA (Cleveland)	Case-Control (2015-2017)	Lung (NR) [161]	Time interval from suspicion to diagnosis	The mean time intervals for imaging to staging (with standard deviations) were 65 days in controls (SD=42.67) and 75 days (SD=58.27) in tumor board cases (p=0.39) (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Rapid referral pathway	Fallon 2019	UK (Luton)	Case-Control (2015-2017)	Gastrointestinal (Adult) [509 (148 UGI; 361 LGI)]	Stage of malignancy at time of presentation	Two weeks wait referral did not achieve an earlier diagnosis compared with non-2 week wait routes of referral in upper gastrointestinal ($\chi 2(3)=2.6$, p=0.458) and lower gastrointestinal ($\chi 2(3)=0.884$, p=0.829) malignancies (Ineffective)
	Jefferson 2019	UK	Cross-sectional (2016-2018)	Multiple (Adult) [24]	Factors affecting patients' non-	The following were identified: system flaws; GP difficulties with booking

		(A Northern English city)			attendance following referral	appointments; patient difficulties with navigating the appointment system, patients leading 'difficult lives'; and patients' expectations of the referral, informed by their beliefs, circumstances, priorities, and the perceived prognosis (Ineffective)
	Kassirian 2020	Canada (London, Ontario)	Cross-sectional (2017-2018)	Ear, Nose and Throat (Adult) [102]	Time from presentation to appointment at the multi-disciplinary clinic	The average time for patients to have their first appointment was 15.1 months, consisting of 3.9 months for patients to see a health care provider for the first time since symptom onset and 10.7 months from first appointment to being seen at the clinic – representing significant delays (Ineffective)
	Neal 2017	UK (Wales; Yorkshire)	RCT (2012-2015)	Lung (Adult) [255]	Anxiety and depression scores	There was no evidence of a difference in post-randomisation anxiety scores between trial arms (median (IQR): 6 (3–8) in control vs 5 (3–9) in intervention, z=0.32; P=0.75) (Ineffective)
	Scott 2020	UK (Countrywide)	Case-Control (2009-2011)	Multiple (Mixed age) [10314]	Cancer occurrence 5 years after negative diagnosis	4.0% for those referred via pathway and 2.1% for those routinely referred (Ineffective)
	Talwar 2020	UK (Merseyside)	Cross-sectional (2017-2019)	Head and Neck (NR) [113]	Time from referral to being seen in hospital	The time taken from referral to being seen in hospital was a median (IQR) of 10 (6–13) days (range 1–28 days) with 11/110 (10%) exceeding 14 days (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Standardized care pathway	Almuammar 2019	Saudi Arabia (Countrywide)	Cross-sectional (2010-2012)	Multiple (Adult) [20]	Patient satisfaction with GP in the pathway	Patients felt that GPs did not listen to them, and were likely to undermine the role of GPs as active practitioners in healthcare provision (Ineffective)
	Gardner 2020	UK (Edinburgh)	Case-Control (2016-2018)	Ear, Nose and Throat	Time from referral to diagnosis	Patients referred by GP on the 'urgent suspicion of cancer' pathway were seen more quickly than those referred

				(Mixed age) [62]		routinely were. However, these differences were not significant (Ineffective)
	Iachina 2017	Denmark (Countrywide)	Case-Control (2008-2012)	Lung (Adult) [11273]	Time from referral to end of primary investigation	Time from referral to the end of primary investigation did not significantly change (1.00 (0.93;1.08)) (Ineffective)
	Jensen 2017	Denmark (Countrywide)	Case-Control (2004-2010)	Multiple (Adult) [7725]	Mortality	When comparing pathway-referred patients against non-pathway-referred patients, non-significant lower excess mortality was observed among the pathway referred (excess hazard ratios = 0.86 (95% CI: 0.73;1.01) (Ineffective)
	Price 2020	UK (National)	Cross-sectional (2006-2017)	Multiple (Adult) [83935]	Diagnostic interval	Median New-NICE values were consistently longer (99, 40–212 in 2006 vs 103, 42–236 days in 2017) than Old-NICE values across all cancers (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Support for primary care providers	Evans 2018	UK (Oxfordshire)	Cross-sectional (2016-2017)	Multiple (Adult) [NR]	GP perspectives on safety netting	GPs revealed uncertainty about which aspects of clinical practice were considered safety netting (Ineffective)
	Kidney 2017	UK (Urban West Midlands)	Cross-sectional (2014)	Gastrointestinal (Adult) [NR]	Barriers for referral	A desire to avoid over-referral, lack of knowledge of guidelines, and the use of individually derived decision rules for further investigation or referral of symptoms (Ineffective)
	Zienius 2019	UK (Scotland)	Cross-sectional (2010-2015)	Brain (Adult) [2938]	Predictive value of referral guidelines for imaging where a tumour is suspected	With symptom-based referral guidelines, primary care doctors can identify patients with a 3% positive predictive value (Ineffective)
	Di Girolamo 2018	UK (England)	Cross-sectional (2009-2013)	Multiple (Mixed age) [360643 (CRC 164890, lung	1-year survival of patients	For 31-day and 62-day targets survival was worse for those for whom the targets were and were not met (Ineffective)

				171208, ovarian 24545)]		
Target or benchmark for wait times	Brian 2017	New Zealand (Hamilton)	Before-and-After (2016)	Skin (Adult) [143]	Time to diagnosis	Compliance with recommended time intervals was poor for patients referred with skin lesions suspicious for melanoma; from referral to diagnostic skin biopsy, compliance was 17.6% (Ineffective)
	Venchairutti 2016	Australia (New South Wales)	Case-Control (2008-2013)	Multiple (Adult) [224]	Time from symptom onset to diagnosis	Regional/remote patients had a longer interval from symptom onset to diagnosis (median 5.4 months [IQR 9.2 months]) compared with metropolitan patients (median 2.1 months [IQR 4.3 months]) (P = 0.002) (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Technology to support diagnosis process	Chung 2020	Netherlands (Amsterdam; Rotterdam)	Cross-sectional (2017)	Skin (Adult) [125]	Risk assessment performance	The inter-observer agreement between the ratings of the automated risk assessment and the dermatologist was poor (Ineffective)
	Lau 2018	UK (West Midlands and Berkshire)	Case-Control (2009-2013)	Multiple (Adult) [1005]	False-negative rate	A sensitivity of 31% and specificity of 92% (Ineffective)
	Pannebakker 2019	UK (NR)	Cross-sectional (2016-2017)	Skin (Adult) [14]	Patient perspectives on implementation and usefulness	No patients were aware that the electronic clinical decision support had been used during their consultation (Ineffective)
	Walter 2020	UK (Eastern England)	RCT (2016-2017)	Skin (Adult) [238]	Time between first noticing a change and consultation	There were no statistically significant differences between trial groups on any of the secondary outcome measures (Ineffective)

CRC = colorectal cancer; GP = general practitioner; LGI = upper gastrointestinal; NICE = National Institute for Health and Care Excellence; NR = not reported; RCT = randomized controlled trial; UGI = upper gastrointestinal; UK = United Kingdom; USA = United States of America; IQR = interquartile range

Appendix 8: Summary of the characteristics of the included published articles that reported data on remote or rural populations

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Chavarri-Guerra 2019	Mexico (Mexico City)	Before-and-After (2016-2017)	Multiple (Adult) [70]	Feasibility of patient navigation	All patients were from an under-served population. 91% of patients successfully obtained appointments at cancer centers in <3 months.
Emery 2017	Australia (Western Australia)	RCT (2011-2013)	Multiple (Adult) [1358]	Time to diagnosis	All patients were from a rural population. There were no significant differences on the time to diagnosis with and without intervention.
Murchie 2020	UK (Scotland; England)	Cross-sectional (2017)	Multiple (Mixed age) [1314]	Time from presentation in primary care to diagnosis	The median primary care interval was 5 days (IQR 0-23 days) and median diagnostic interval was 30 days (IQR 13-68). Diagnostic intervals were longer in the most remote patients.
Venchairutti 2016	Australia (New South Wales)	Case-Control (2008-2013)	Multiple (Adult) [224]	Time from symptom onset to diagnosis	Regional/remote patients had a longer interval from symptom onset to diagnosis (median 5.4 months [IQR 9.2 months]) compared with metropolitan patients (median 2.1 months [IQR 4.3 months]) (P = 0.002).
Yeşiler 2020	Turkey (Ankara)	Cross-sectional (2010-2011)	Lung (Adult) [122]	Delay in diagnosis times	No significant difference in the mean duration from symptom onset to pathological diagnosis. No significant differences were identified based on patient residence.

UK = United Kingdom; IQR = interquartile range

Appendix 9: Summary of performance metrics to measure improvements in suspicion to diagnosis phase

Intervention Type	Performance Metric
Centralized or coordinated diagnostic service	• Time from presentation in primary care to diagnosis • Time from referral from primary care to specialist consultation • Time from first abnormal image to biopsy
Interventions to enhance diagnostic services	• Time from referral from primary care to specialist consultation • Time from initial specialist consultation to diagnosis • Time from initial specialist consultation to biopsy • Time from first abnormal image to biopsy • Time from presentation in primary care to biopsy • Total diagnostic interval • Turnaround time for diagnosis following histology • Number of urgent referrals to specialist • Cancer detection rate • Patient survival
Multidisciplinary team	• Time from referral from primary care to specialist consultation • Time from first abnormal image to diagnosis
Patient navigation	• Waiting times from the point of referral from primary care to initial specialist assessment • Feasibility of program/process • Delays in diagnostic resolutions

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.	4-5
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.	7-8
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.	8-9
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.	9
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.	10-11
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.	10
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix 2 - 4
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	10-11
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.	11-12
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Appendix 6
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).	Not applicable

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	11-12
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.	Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Table 1
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not applicable
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.	14-24
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	13-24
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.	25-27
Limitations	20	Discuss the limitations of the scoping review process.	27
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.	28
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.	2

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).

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.

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Interventions to improve early cancer diagnosis of symptomatic individuals: A scoping review

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Interventions to improve early cancer diagnosis of symptomatic individuals: A scoping review

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Transparency declaration: The corresponding author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Abstract

Objectives: To summarize the current evidence regarding interventions for accurate and timely cancer diagnosis among symptomatic individuals.

Design: A scoping review following the Joanna Briggs Institute's methodological framework for the conduct of scoping reviews and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping reviews (PRISMA-ScR) checklist.

Data sources: MEDLINE (Ovid), CINAHL (EBSCOhost) and PsycINFO (Ovid) bibliographic databases, and websites of relevant organizations. Published and unpublished literature (grey literature) of any study type in the English language were searched for from January 2017 to January 2021.

Eligibility and criteria: Study participants were individuals of any age presenting at clinics with symptoms indicative of cancer. Interventions included practice guidelines, care pathways or other initiatives focused on achieving pre-defined benchmarks or targets for wait times, streamlined or rapid cancer diagnostic services, multidisciplinary teams, and patient navigation strategies. Outcomes included accuracy and timeliness of cancer diagnosis.

Data extraction and synthesis: We summarized findings graphically and descriptively.

Results: From 21,298 retrieved citations, 88 unique published articles and 16 unique unpublished documents (on 18 study reports), met the eligibility for inclusion. About half of the published literature and 83% of the unpublished literature were from the United Kingdom. Most of the studies were on interventions in lung cancer patients. Rapid referral pathways and technology for supporting and streamlining the cancer diagnosis process were the most studied interventions.

Interventions were mostly complex and organization-specific. Common themes among the studies that concluded intervention was effective were multidisciplinary collaboration and the use of a nurse navigator.

Conclusions: Multidisciplinary cooperation and involvement of a nurse navigator may be unique features to consider when designing, delivering, and evaluating interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals. Future research should examine the effectiveness of the interventions identified through this review.

Keywords: Early cancer diagnosis; Symptomatic individuals; Interventions; Scoping review

Strengths and limitations of this study

- A knowledge synthesis librarian developed the search strategy for this review and this was peer reviewed by an independent knowledge synthesis librarian using the PRESS checklist.
- The literature search was limited to evidence from the last 4 years and only evidence from English-language publications and organizational websites.
- This review did not summarize effectiveness of interventions across cancer patient types and regions.
- We adhered to known guidelines and standards in the conduct and reporting of the review.
- In line with the JBI's guidance for the conduct of scoping reviews, we did not attempt to evaluate the quality of the included studies or provide an assessment of the quality of the evidence.

Introduction

Cancer is the second leading cause of death globally, with about 1 in 6 deaths attributable to the disease.[1] It was estimated in 2020 that over 19 million new cases and about 10 million deaths were attributable to cancer globally.[2] This rate is estimated to be over 28 million new cases by 2040.[2] High Human Development Index (HDI) countries such as Canada will likely experience the greatest increase in incidence in absolute cancer burden, with an estimated over 4 million new cases more in 2040 compared with 2020.[2] This is mostly due to the growth and aging of the population and increasing prevalence of cancer risk factors.[2] Estimates from Canada alone suggest that every day 617 people in Canada will be diagnosed with cancer, with about 228 also dying from the disease.[3]

Although cancer can occur at any age, the risk of the disease increases with age.[4] Globally, cancer incidence rates vary, mostly because of differences in risk factors and early detection practices. Likewise, cancer death rates vary, partly because of differences in availability and effectiveness of cancer control strategies, such as early diagnosis and access to timely and effective treatment.[2] With timely diagnosis and treatment initiation, significant improvements can be made in the lives of cancer patients. Moreover, many cancers have higher curative and survival rates if diagnosed early. This means that cancer burden could be reduced substantially through early detection and management of patients who present with symptoms.[5]

When not diagnosed following early symptomatic presentation, cancer diagnosis often occurs at more advanced stages of the disease, when treatment may be less effective and cancer prognosis will be poor. Early cancer diagnosis of symptomatic individuals entails carefully planned, well-integrated, culturally safe and equitable clinical evaluation and diagnostic

services.[5] These services should be designed to reduce delays in and barriers to diagnosis to allow detection at earlier stages of the disease and commence treatment in a timely manner.

Various service-focused interventions to improve early cancer diagnosis of symptomatic individuals have been implemented in various jurisdictions with varying levels of success. Knowledge of the available interventions, strategies used to implement them, and how successful they might have been is necessary to inform the development, implementation, and evaluation of effective early cancer diagnosis initiatives.

Methods

This report is a summary of the study commissioned by the Canadian Partnership Against Cancer (the Partnership). The Partnership contributed to specifying the study objectives and questions, and in summarizing the evidence.

We undertook a scoping review following the Joanna Briggs Institute's (JBI's) guidance for the conduct of scoping reviews.[6] This framework includes defining and aligning the objective(s) and question(s) for the review, developing and aligning the inclusion criteria with the review objective(s) and question(s), and describing the planned approach to evidence searching. It also includes selecting, extracting, and charting of evidence; summarizing the evidence in relation to the objectives and questions; and consultation of information scientists, librarians, and/or experts throughout the process. **Appendix 1** is the work plan approved by the Partnership for the scoping review.

We summarized the current evidence regarding interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals, including practice guidelines, care pathways or targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and patient navigation strategies. We also summarized innovative interventions (for example, those with a technological component) and approaches to seamless (minimally disruptive) care of symptomatic individuals and identified performance metrics that can be used to measure improvements in the pre-diagnosis phase. Additionally, we summarized the key points of the patient trajectory from initial symptom presentation to cancer diagnosis.

We report our findings in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for Scoping Reviews (PRISMA-ScR) checklist.[7]

Search strategy

A knowledge synthesis librarian (NA) designed a search strategy for MEDLINE (Ovid). This search strategy was peer-reviewed independently by another knowledge synthesis librarian using the Peer Review of Electronic Search Strategies (PRESS) checklist.[8] The revised search strategy was then adapted for Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCOhost) and PsycINFO (Ovid) bibliographic databases. The search strategy for each of the databases is presented in the appendices (**Appendix 2 - 4**). In addition to searching bibliographic databases, we searched websites of relevant organizations and professional bodies (**Appendix 5**) and hand-searched reference lists of potentially relevant publications.

Study selection criteria and data extraction

We sought to summarize practice guidelines, care pathways and initiatives such as benchmarks/targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and patient navigation strategies that have been found to enhance accurate and timely cancer diagnosis in symptomatic individuals. We also sought to summarize the leading interventions to seamless care in the cancer pre-diagnosis phase, performance metrics that can be used to measure the suspicion to diagnosis phase and how these metrics have been used. Further, we sought for specific considerations for underserviced populations in studies, including considerations for Indigenous, rural, and remote populations.

Published (peer-reviewed) and unpublished (grey literature) articles in the English language from January 2017 to January 2021 were included. The decision to include articles from 2017 was because the Partnership had previously summarized prior evidence, not included in this current report.[9] Study participants were individuals of any age presenting in any clinical

settings with symptoms. Interventions included practice guidelines, care pathways or other initiatives focused on achieving pre-defined benchmarks or targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and patient navigation strategies. Outcomes included accuracy and timeliness of cancer diagnosis.

All retrieved citations from the literature search were imported and managed in EndNote (Version X9). One reviewer (GNO or OLTL or VKR or LC) screened each citation for eligibility. Two reviewers (GNO, OLTL, VKR, and LC in pairs) independently screened the full texts of relevant citations and reviewed the reference list of the included full-text articles for potentially relevant citations. Disagreements between the reviewers were resolved through discussion or involvement of a third reviewer (AMAS). The number of screened citations and both the number and reason for exclusion of full-text articles were documented. One reviewer (GNO or OLTL or VKR or LC) performed data extraction and charting, and another reviewer (GNO or OLTL or VKR or LC) independently checked the extracted and charted data for errors. Disagreements between the reviewers were resolved through discussion or involvement of a third reviewer (AMAS).

Data synthesis and analysis

Characteristics of the included published articles are presented in a tabular form and descriptive analysis is reported graphically and descriptively. Characteristics of the included unpublished articles are reported descriptively only. Relevant findings from the review of both published and unpublished articles are summarized separately and descriptively, by review question, focusing on the interventions related to each question. Interventions are grouped as centralized or coordinated diagnostic service; interventions to enhance diagnostic services; multidisciplinary

team; patient navigation; rapid referral pathway; remote or rural populations-focused; standardized care pathway; support for primary care providers; target or benchmark; and technology to support the diagnostic process. These interventions are defined in **Appendix 6**. We determined the effectiveness of an intervention based on study findings and conclusions reported by the primary study's authors with respect to intervention effect. As such, effective interventions were those interventions that were found to have had a statistically significant positive effect on an author-determined outcome for effectiveness evaluation. It is important to note that the authors of this scoping review did not assess risk of bias nor rate the quality of evidence and thus definitive conclusions on effectiveness cannot be drawn.

Patient and public involvement

There was no active engagement of patients and/or members of the public.

Results

Out of a total of 21,298 retrieved citations, 88 unique published articles[10-97] and 16 unique unpublished (grey literature representing 18 different reports)[98-113] met the inclusion criteria. The article selection process is detailed below (**Figure 1**). Fifty-seven of the published articles were from Europe, 14 articles from North America, 9 articles from Oceania, 3 articles each from Africa and Asia, and one article each from the Middle East and South America. Almost half of these articles (n = 40) were from the United Kingdom (UK) alone. A geographic map of published articles is shown in **Figure 2**.

Of the 18 unpublished reports (16 articles), 83% were from the UK, 11% from Canada and 6% from the United States of America (USA). Forty percent (n = 35) of the published articles were for case-control studies, 29% (n = 26) for cross-sectional studies, 22% (n = 19) for before-and-after studies, 7% (n = 6) for randomized controlled studies, and 1% (n = 1) each for guideline development and mixed methods studies. In terms of the unpublished articles, 89% (n = 16) were before-and-after studies and the rest (n = 2) were cross-sectional studies. **Figure 3** shows the distribution of the cancer types reported by the published articles; approximately 30% (n = 26) reported on multiple cancer types, while the rest reported on specific cancer types, of which lung cancer was the most frequent (about 23% of the publications (n = 20)). Of the unpublished articles, half reported on lung cancer, 28% on multiple cancer types, 11% on breast cancer, and 5.5% each on brain and gastrointestinal cancers.

Figure 4 shows the distribution of intervention types across the published articles. Nearly 20% of the published articles were on rapid referral pathway interventions while less than 1% each were on multidisciplinary team, patient navigation, and remote/rural-focused interventions. Of the unpublished articles, half reported on rapid referral pathway interventions, 11% each

reported on standardized care pathway, target/ benchmark for wait times, and technology to support the diagnosis process, and 5.5% each reported on centralized or coordinated diagnostic service and interventions to enhance diagnostic services. Most of the published articles (94%; n = 83) reported a performance metric used to measure an improvement in the suspicion to diagnosis phase of cancer.

Eighty-three percent (n = 73) of the articles reported either a practice guideline, care pathway or an initiative such as benchmark/target for wait times, streamlined or rapid diagnostic service, multidisciplinary team development, and a patient navigation strategy to enhance accurate and timely cancer diagnosis. Thirty-one percent (n = 27) of the articles reported (not explicitly) on a key point of care as patients navigate the health system, from initial suspicion to diagnosis of cancer. Twenty-nine percent (n = 25) of the articles reported on a leading innovative intervention or approach to seamless care in the pre-cancer diagnosis phase, while 4.5% (n = 4) of the articles reported on some form of consideration for underserved populations. Some of the articles reported on two or more of the above. Details of relevant characteristics of the published articles are presented in **Table 1** (those reporting effective interventions) and **Appendix 7** (those reporting ineffective interventions) **and Appendix 8** (those focused on remote/and rural populations).

Initiatives to enhance accurate and timely cancer diagnosis

This review identified various initiatives to enhance accurate and timely cancer diagnosis. These were often designed, developed, and implemented often with the involvement of primary care providers (physicians and nurses), but not patients. These initiatives are grouped into related interventions and the evidence regarding each intervention is discussed below.

Centralized or coordinated diagnostic services

Nine published articles on centralized or coordinated diagnostic services for adult lung cancer (n = 5) and breast cancer (n = 4) patients were identified.[20,23,32,33,44,54-56,93] Five were from Canada,[23,33,44,54,55] and there was one each from Denmark,[20] New Zealand,[93] South Africa,[56] and the UK[32]. The focus and metrics for assessment of the effectiveness of these diagnostic services varied, but all were found to be effective. These include the rapid access to pulmonary investigation and diagnosis (RAPID) program in Wythenshawe Hospital, Manchester, UK with expedited (next working day) computed tomography (CT) and reporting in suspected lung cancer cases,[32] and the Thoracic Triage Panel in a tertiary care centre in St. John's, Newfoundland, Canada, a multidisciplinary centralized referral program, whose key components include a nurse navigator who coordinates patient care and act as the contact person for patients and clinicians involved in the program, weekly multidisciplinary (thoracic specialists) meetings, and regular communications with the primary care provider.[23] The diagnostic services also include the rapid investigation clinic in a tertiary health centre in Montreal, Canada established to coordinate and accelerate the workup of patients with suspected lung cancer,[33] the improved respiratory fast track clinic (RFTC) in Northland district of New Zealand that comprises reserved slots for CT for those referred with a suspicion of lung cancer, bronchoscopy slots and CT-guided biopsy,[93] and the Danish lung cancer package at the Center for Lung Cancer, Odense University Hospital, Odense, Denmark, a fast-track diagnostic pathway in the hospital setting.[20] Further, there was the rapid access breast clinic in British Columbia, Canada that provides close collaboration between clinicians and radiologists, facilitated by clinical pathways and nurse navigation,[54,55] the diagnostic assessment units in Ontario, Canada, focusing on diagnosis at a dedicated breast assessment unit,[44] and the breast clinic at a tertiary hospital in Western Cape Province of South

Africa, an open-access one-stop diagnostic breast clinic where women may present with a letter from a primary level provider (nurse practitioner or doctor) and receive the same day clinical and cytological evaluation with referral to the combined breast clinic if the breast cytology is positive for malignancy.[56]

In addition to the above, one unpublished article was identified.[113] This was for the Breast ACCESS Project in Ohio, USA, which scheduled patients for a surgical consult within 2 days and a biopsy within 5 days after the surgical consult, with the aim of reducing wait times between abnormal diagnostic mammogram findings to biopsy from 26 to 7 days (7-day ACCESS goal).

Interventions to enhance diagnostic services

Twelve published articles on interventions to enhance diagnostic services were identified.[10,17,24,52,53,64,75,77,78,80,83,94] These articles were focused on varied cancer types; four on multiple cancers, two on lung cancer, two on skin cancer, and one each on breast, gastrointestinal, haematological and prostate cancers. Four articles were from the UK,[17,52,53,78] two articles each from Canada[24,64] and Sweden,[10,80] and one article each from Botswana,[94] Columbia,[75] Indonesia,[77] and the USA.[83] The focus and metrics for assessment of the effectiveness of the interventions varied across the publications, and while most were effective, one intervention for lung cancer and one intervention for skin cancer in the UK[53] and Sweden[10], respectively, were ineffective. The effective interventions were reducing diagnosis through emergency presentation by improving general practice referral in England, UK,[52] the guided personal quality of life (QoL) feedback intervention during the Cancer Research UK's North West regional summer roadshow in Manchester, UK, aimed at offering guided feedback about personal QoL to adults with potential cancer symptoms, living in deprived communities to

promote help seeking in primary care among the communities,[78] the mandatory primary care access to faecal immunochemical testing (FIT) in Nottingham, UK, integrated with the 2-week wait pathway, aimed at improving gastrointestinal cancer diagnosis rather than relying on age and symptoms alone,[17] the Stronach Regional Cancer Centre lung diagnostic assessment program (DAP) at Southlake Regional Health Centre, Ontario, Canada, aimed at using learnings from a Lean improvement event to provide coordinated, expedited care for all patients undergoing a possible lung cancer diagnosis and to achieve/improve upon the provincial wait time target from consultation to diagnosis for lung cancer patients,[24] the nurse practitioner-led lymphoma rapid diagnosis clinic in a tertiary care cancer center (Princess Margaret Cancer Centre, part of University Health Network) in Ontario, Canada, aimed at reducing wait times for a definitive diagnosis of lymphoma,[64] the expedited one-stop prostate cancer diagnosis using advanced imaging and biopsy techniques in a health institution (name not reported) in the USA, aimed at expediting prostate cancer diagnosis.[83] There were also the Swedish Diagnostic Center at the Central Hospital of Kristianstad, Sweden, introduced as a separate outpatient unit within the Department of Internal Medicine to expedite diagnostics,[80] the Partners for Cancer Care and Prevention action plan in Cali, Columbia, aimed at improving access to a coordinated program of screening and early diagnosis of breast and cervical cancers in three health care centers that serve subsidized populations,[75] the dermatology-led quality improvement initiatives in Gaborone, Botswana, aimed at improving multispecialty care coordination,[94] and the culturally sensitive, narrative self-help intervention named PERANTARA (PEngantar peRAwataN kesehaTAn payudaRA [translated as introduction to breast health treatment]) across four hospitals in Bandung, West Java, Indonesia, aimed at reducing time to diagnosis in women with breast cancer symptoms.[77] In addition to the above, one unpublished article on the Accelerate,

Coordinate, Evaluate (ACE) program in the UK was identified.[100] This program was an early cancer diagnosis initiative and focused on testing innovations that either identify individuals at high risk of cancer earlier or streamline diagnostic pathways.

The ineffective interventions were the standardized care diagnostic pathway at the Department of Clinical Pathology, Akademiska University Hospital in Uppsala, Sweden (introduced by the Swedish health authorities to eliminate unwanted delay in the diagnostics of melanoma)[10] and the 4-week national lung cancer symptom awareness campaign in Wales, UK, aimed at increasing urgent suspected cancer referrals and clinical outcomes.[53]

Multidisciplinary team

Three multidisciplinary team lung cancer approaches were identified from published articles: from the USA[68,85] and Australia.[50] The focus and metrics for assessment of the effectiveness of the approaches varied across the publications. One approach from the USA was found to be effective,[68] whereas the others were found to be ineffective. The effective approach was the lung cancer strategist program, a thoracic surgeon-guided, multidisciplinary (disciplines not reported) care program in hospitals in Massachusetts, USA, aimed at improving timeliness of lung cancer diagnosis and treatment.[68] The ineffective approaches were the pre-diagnosis multidisciplinary tumour board (physicians from radiology, medical and radiation oncology, and pulmonary medicine) discussions in a clinic in Cleveland, USA aimed at improving the timeliness of diagnostic evaluation in lung cancer,[85] and the Victorian lung cancer service redesign project in Victoria, Australia, which involved multidisciplinary (patients, governance, administration, clinicians and health information services) evaluation aimed at quality improvement collaborative on timeliness and management in lung cancer.[50] In addition, nine unpublished articles from the UK were identified.[99,101-103,106,108,109,112] These included four

articles regarding a "straight to CT access" pathway, on community pharmacy direct referral to lung cancer pathway, rapid colorectal diagnostic pathway, and optometrist direct referral to neuroscience pathway. All but the chest x-ray pathway[109] were found to be effective.

Standardized care pathways

Eleven published articles on standardized care pathways were identified.[11,12,26,35,39,41,49,59,63,70,71] These articles were focused on varied cancer types (4 each for multiple cancers, and 1 each for ear-nose-throat, urinary tract, and gastrointestinal cancers). Three articles were from Denmark,[26,39,41] two from the UK,[35,70] and one each from Canada,[59] Norway,[49] Sweden,[63] Spain,[12] and Saudi Arabia.[11] The publications were on adult patient populations with one also involving paediatric patients. The focus and metrics for assessment of the effectiveness of the pathways varied across the publications. The main effective pathways were the national diagnostic cancer pathway in Norway, with recommended maximum limits for time spent in the diagnostic process as well as mandatory reporting of the actual time intervals for all patients with suspected lung cancer,[49] and the standardized triage process in the Southeastern Ontario, Canada, which entailed a twice-weekly nurse–physician triage, preordered staging tests and scheduling according to urgency, redirection and recommendations for inappropriate referrals, and new small nodule clinic.[59] Other main effective pathways were the standardized diagnostic pathway for suspected urothelial cancer initiated by primary healthcare providers and specialists in Skane County, Sweden, and comprises CT urography, urinary cytology and cystoscopy,[63] the early colonoscopy track (within 30 days from referral) in a tertiary referral hospital in Tenerife, Spain,[12] and the fast-track cancer care pathway in Denmark (national), with maximum acceptable time thresholds from referral to diagnosis and treatment.[39] In addition, two unpublished articles

from Canada[111] and the UK[98] focusing on breast and lung cancers, respectively, were identified. These were the Alberta Health Services Diagnostic Assessment Pathway and the Somerset Integrated Lung Cancer Pathway. While the Canadian pathway was found to be effective, the pathway from the United Kingdom was not effective.

Support for primary care providers

There were four publications on support for primary care providers (PCP), all from the UK.[27,31,48,97] Two were focused on multiple cancer types, and one each focused on gastrointestinal and brain cancers. The publications were on adult patient populations with one being also involving paediatric patients. The focus and metrics for assessment of the effectiveness of the support packages (all educational and informational) varied across the publications. None of the support packages was found to be effective, with the identified common theme being a lack of awareness of referral guidelines and associated knowledge by GPs. These ineffective support packages were the use of the Kernick and NICE guidelines as evidence-based support to assist primary care physicians in identifying patients most at risk of having a brain tumour, but also on the fastest route to achieve diagnosis (example, direct access imaging versus urgent secondary care referral) in Scotland, the UK,[97] the use of the national cancer waiting times monitoring dataset for system performance assessment by primary care physicians in England, the UK,[27] and the use of safety netting by primary care physicians in Oxfordshire, UK to ensure that patients are monitored until their symptoms or signs are explained, and to guard against delays in diagnosis.[31]

Target or benchmark for wait times

There were eight published articles related to targets or benchmarks for wait times.[15,42,43,69,73,81,88,96] Three of these articles were from the UK,[69,73,81] two articles from Australia,[42,88] and one article each from China,[43] Sweden,[96] and New Zealand[15]. These publications were focused on varied cancer types (2 each for multiple, lung and gastrointestinal cancers, and 1 each for prostate and skin cancers), and were on adult patient populations, with one publication involving paediatric patients. The focus and metrics for assessment of the effectiveness of the target or benchmarks varied across the publications, and all but two targets/benchmarks[15,88] were found to be effective. The effective targets or benchmarks were the 28-day faster diagnosis standard in the National Health Service England, UK, defined as the time within which the patient is informed whether they do or do not have cancer,[73] the fast-track diagnostic workup for men with suspected prostate cancer at the Urology Department at Orebro University Hospital in Sweden, which entailed targeting the shortest possible waiting-time for a diagnostic workup process,[96] and the optimal timeframes for referral and diagnosis of lung lesion at Latrobe Regional Hospital in Victoria, Australia established by the National Cancer Expert Reference Group as part of the optimal care pathway for people with lung cancer.[42] The ineffective targets or benchmarks was the New Zealand Ministry of Health's "faster cancer treatment" standards of service provision for melanoma patients, with a target of histopathological diagnosis of melanoma reported within five working days in 80% of cases, and all cases reported in 10 working days.[15] In addition, two unpublished articles from Canada[105] and the UK[107] focusing on multiple cancers were identified, and these were the "2-week wait" benchmark in the UK (already discussed under rapid referral pathways) and the Canadian Breast Cancer Screening Network targets for diagnostic intervals: ≥ 90% of abnormal screens to be

resolved within 5 weeks if no biopsy is required and ≥ 90% within 7 weeks if a tissue biopsy is required.

Innovative interventions to enhanced care in cancer pre-diagnosis phase

This review identified 17 published articles related to technological interventions for enhanced care in the pre-diagnosis phase of cancer.[16,21,22,29,37,38,51,57,58,62,65,66,79,82,87,89,91] Ten of these articles were from the UK,[22,29,37,38,51,57,62,65,66,91] two articles were from New Zealand,[79,82] and one article each was from Denmark,[89] Netherlands,[21] Italy,[16] India,[87] and Spain.[58] These publications focused on varied cancer types in adult patient populations, with two also involving paediatric patients. The interventions had little patient input in their design, development, or implementation. The focus and metrics for assessment of the effectiveness of the interventions varied across the publications. The main identified interventions were the use of teledermatology in skin cancer diagnosis. This involved the taking of images, including dermoscopy by GPs and sending them for evaluation to specialized dermatologists.[38,62,79,89] The process is embedded in an e-referral system developed in Auckland, New Zealand for suspected skin malignancy,[82] and included teledermatology images triaged as confirmed, likely or suspected melanoma, the use of a web-based referral tool for head and neck cancers at two different hospitals in Birmingham, West Midlands, and Wexham, Berkshire, UK.[51] There was also the use of the Digitally Assembled Referral Toolkit (DART) for 2-week referral, accessible via a cloud-based template, which contained new referral forms native to GP clinical systems in the UK.[29] Additionally, there was the use of an electronic straight-to-test pathway at a large tertiary referral hospital in England, UK to remove hospital-based triage from suspected colorectal cancer pathways; this allows GPs to book tests supported by a decision aid based on the NICE guidance, thus,

eliminating the need for a standard referral form or triage process.[65] Further, there was the use of electronic clinical decision support for melanoma in four general practices in the Southeast of England, UK, which involved the use of an electronic-based 7-point checklist to assess pigmented lesions,[66] the use of machine learning algorithms in Newcastle, UK to classify patients referred on the 2-week wait pathway for suspected head and neck cancer into different diagnostic groups, albeit very broad ones: cancer and non-cancer,[57] the use of nurse-led assessments to evaluate certain groups of patients suspected to have bowel cancer in England, the UK,[22] and the use of varied smartphone-based skin and oral self-monitoring and screening applications, in England, UK[91] and in the India,[87] respectively. In addition, two unpublished articles from the UK were identified.[106,110] These were for a cancer decision support tool (computer-based programs integrated into a GP's usual patient management system) in Gateshead, London, and a clinical web portal (CWP) electronic system in Manchester, England, with the fundamental part of the CWP being that local clinicians had to take personal responsibility for data input.

Performance metrics to measure improvements in suspicion to diagnosis phase

Varied performance metrics were identified by this review. The main metrics are summarized according to intervention type (**Appendix 9**). While performance metrics appear to be mainly intervention-dependent, time from presentation in primary care to diagnosis and from referral from primary care to specialist consultation, appear to be the most consistent metrics used for evaluation. Performance metrics to measure patients' experience mainly centered on patients' satisfaction and quality of life.

Specific considerations for underserved populations

Four published articles focused on issues related specifically to underserved populations, with all focused on remote/rural populations.[18,30,60,88] These publications were from the UK,[60] Australia,[30,88] and Mexico.[18] A fifth publication only used the patients' area of residence as part of their model.[95] All of the publications were on multiple cancer types and adult populations, although one included a paediatric population. The specific considerations for underserved populations and the evidence regarding them included a publication from Scotland, the UK, a national audit of cancer diagnosis in Scottish and English general practices, exploring and comparing patient characteristics, diagnostic intervals, and routes to diagnosis,[60] the publication from New South Wales, Australia on a study that examined geographic variations in time intervals leading up to treatment for head and neck cancer, with assessment of differences based on remoteness of residence (regional/remote or metropolitan) at two tertiary referral centres,[88] a publication from Mexico City, Mexico on evaluation of a patient navigation program to reduce referral time to cancer centers for underserved patients with a suspicion or diagnosis of cancer at a public general hospital,[18] and a publication from Western Australia, a cluster-randomized controlled trial of a complex intervention to reduce time to diagnosis in rural cancer patients with the aim of measuring the effect of community-based symptom awareness and general practice-based educational interventions on the time to diagnosis in rural patients presenting with breast, prostate, colorectal or lung cancer.[30]

Discussion

This scoping review of 88 published and 16 unpublished documents from January 2017 to January 2021 summarizes the evidence on current interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals. The identified articles were from varied study designs including case-control (most common), cross-sectional, before-and-after, and mixed methods studies, and randomized controlled trials. There was little evidence to suggest that patients were involved in the design, development, or implementation of interventions to enhanced care in cancer pre-diagnosis phase.

The evidence suggests that interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals are active topics of research. The UK appears to be championing this area of research, contributing about half of all identified published literature and 83% of the identified unpublished literature. Of the specific cancer patient types, lung cancer patients appear to be the most researched, ranking highest among the patient populations of published and unpublished literature. Of the studied interventions, rapid referral pathways and technology for supporting and streamlining the diagnosis process were the two most reported interventions. Overall, varied national and regional centralized or coordinated diagnostic services, interventions to enhance diagnostic services, multidisciplinary team approaches, patient navigation approaches, rapid referral pathways, standardized care pathways, support for primary care providers, target or benchmarks, technologies to support diagnosis process, and insights regarding variations between remote/rural and urban populations have been reported although there were no articles that focused specifically on Indigenous populations. Many of these intervention types could be adapted to suit different health systems and jurisdictions around the world.

The interventions mostly comprised multiple interventions/ changes to the healthcare pathway. As such, the interventions examined varied widely across the studies. This was true even when applied to the same cancer patient populations and in the same jurisdictions/ countries, including those where an intervention was part of the standard care pathway. As such, it is difficult, perhaps impossible, to identify one main approach alone that drives an intervention. Methodological approaches also varied significantly with regard to outcome assessment. A common theme among the effective centralized or coordinated diagnostic services, interventions to enhance diagnostic services, patient navigation approaches, and standardized care pathways is multidisciplinary collaboration and the involvement of a nurse navigator.

The findings from this scoping review compare considerably with those of the previously summarized evidence (prior to the ongoing coronavirus disease 2019 (COVID-19) pandemic) not included in this review.[9] However, while the previous evidence summary identified similar leading interventions to enhance seamless and coordinated cancer care in symptomatic individuals, intervention effectiveness was not summarized to enable comparison with the findings from this current review. As a result, assessment of the potential impact of the COVID-19 pandemic on intervention effectiveness was not possible; despite reports of decline and delays in cancer diagnosis of symptomatic individuals even in jurisdictions that utilize interventions that have been found to be effective from this review.[114,115] A survey by the Canadian Cancer Survivor Network (CCSN) showed that 54% of those surveyed (with about 75% of pre-diagnosis and recently diagnosed patients among them) have had their cancer care appointments cancelled, postponed, or rescheduled because of COVID-19.[116] Further, a modelling study in England, by Maringe and colleagues concluded that substantial increases should be expected in the number of

avoidable cancer deaths as a result of diagnostic delays due to the COVID-19 pandemic.[117] The conclusions of the available evidence reviews suggest that cancer screening programs and diagnoses in symptomatic individuals, have been clearly interrupted since the onset of the COVID-19 pandemic, with delayed diagnosis and marked increases in the numbers of avoidable cancer deaths.[118,119]

It was difficult to determine a specific intervention or a stand-alone approach to an intervention from this scoping review. It was also difficult to assess the true effectiveness of many of the interventions, especially considering the differing composite nature of the interventions, the fact that the evidence is mostly from observational studies, and the range of outcome measures used to measure effectiveness. While many of the interventions could be adapted to suit different health systems and jurisdictions, emphasis should be on the context and the strengths and limitations of the individual health system, and a clear evidence-based performance metric for appropriate evaluation of effectiveness of an intervention ought to be determined a priori. Diagnosing cancer faster and more accurately at an earlier stage is a key priority of the 2019-2029 Canadian Strategy for Cancer Control.[120] Over the next 5 years, the Canadian Partnership Against Cancer will leverage findings from this scoping review, as one of several inputs, and partner with Canadian jurisdictions to continue to test innovative models of care that expedite cancer diagnosis, especially for Indigenous and underserved populations.

Limitations and merits

There are some limitations to this study. The literature search was developed by a knowledge synthesis librarian and peer reviewed by an independent knowledge synthesis librarian using the PRESS checklist. We searched appropriate databases and websites for literature, and adhered to

known guidelines and standards in the conduct and reporting of the review. Even so, the literature search was limited to evidence from the last 4 years and only evidence from English-language publications and organizational websites. As such, potentially eligible articles could have been missed.

The eligibility criteria for inclusion were not limited to only comparative studies. This meant that the focus of some of the included studies was not specifically on the assessment of effectiveness of an intervention and therefore, effectiveness may have been underreported for some interventions. Moreover, an intervention's effectiveness assessment was based solely on author-determined outcome, which may or may not have been an appropriate outcome for assessing effectiveness of certain interventions. As such, an intervention that appeared effective in a study may be ineffective in another study depending on the assessed outcome, with no clear reason for such a discrepancy. Furthermore, this review did not assess effectiveness of interventions across cancer patient types and jurisdictions/regions. This would have allowed assessment of any differences in intervention effectiveness by patient type and study jurisdiction. Lastly, and in line with the JBI's guidance for the conduct of scoping reviews, we did not attempt to provide an assessment of the quality of the evidence and, as such, the risk of bias in randomized controlled trials and quality assessment of observational studies, including assessment for important potential biases such as selection, case ascertainment and measurement biases, and potential confounders in studies were not considered in this review; hence, the findings on effectiveness are not conclusive of the performance of the interventions.

Conclusions

The evidence suggests that interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals are active topics of research, particularly in lung cancer patient populations, and that the UK is championing this area of research. While the themes of the studied interventions are similar, the interventions differ in many ways within the same intervention group. Multidisciplinary cooperation and involvement of a nurse navigator appeared to be unique features of many of the effective interventions. Canadian and other jurisdictions can leverage these lessons learned to develop and implement strategies adapted to local health system needs to improve the cancer pre-diagnosis phase. Future research should examine the effectiveness of the interventions identified through this review.

Data availability statement: No additional data are available.

Ethics approval: Not applicable.

Details of the role of the study sponsors: The Canadian Partnership Against Cancer (the study commissioner) contributed to specifying the study objectives and questions, and in summarizing the evidence.

Patient and public involvement: There was no active engagement of patients and/or members of the public.

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Table 1: Summary of the characteristics of the included published articles that reported data on effective interventions

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
Centralized or coordinated diagnostic service	Christensen 2020[20]	Denmark (Odense)	Cross-sectional (2016-2017)	Lung (Adult) [20]	Patients' perspective, experiences, and expectations	Although patients experienced anxiety with the fast-track diagnostic pathway, they still wanted to move through with diagnosis as quickly as possible (Effective)
	Common 2018[23]	Canada (Newfoundland)	Case-Control (2015-2016)	Lung (Adult) [133]	Time from first abnormal image to biopsy	There was a statistically significant decline in wait times for patients from 61.5 to 36.0 days (p<0.0001) (Effective)
	Evison 2020[32]	UK (Manchester)	Before-and-After (2016-2019)	Lung (Adult) [1035]	Mean time from referral to CT	The median time from referral to CT was 3 days. Overall 56% and 90% of patients had completed a CT and consultation within 3 and 7 days of referral, respectively (0% and 24% prior to implementation) (Effective)
	Ezer 2017[33]	Canada (Montreal)	Case-Control (2010-2011)	Lung (Adult) [327 (195 RIC; 132 non-RIC)]	Time from first contact with physician to diagnosis	Time from first contact to pathological diagnosis was shorter (median (M) 26 days; IQR 14–42 days) vs. control patients (M 40 days; IQR 16–68 days) (Effective)
	Jiang 2018[44]	Canada (Ontario)	Case-Control (2011)	Breast (Adult) [4381]	Time to diagnosis	The Canadian timeliness targets (time from patients' first referral or test to the cancer diagnosis) were achieved more often than for usual care (71.7% vs. 58.1%, respectively), with associated 10-day (95% CI: 7.8–11.9) reduction in the median diagnostic interval (Effective)
	McKevitt 2017[54]	Canada (British Columbia)	Case-Control (2009)	Breast (NR) [373]	Diagnostic wait time	Patients had a decreased time to surgical consultation (33 vs 86 days, p<0.0001) for both malignant (36 vs 59 days, p=0.0007) and benign diagnoses (31 vs 95 days, p<0.0001) (Effective)
	McKevitt 2018[55]	Canada (Vancouver)	Case-Control (2012)	Breast (NR) [176 (40 RABC; 136 TS)]	Time from presentation to surgeon evaluation	Time from presentation to surgeon evaluation was shorter in the RABC group for patients with breast symptoms (81 vs 35 days, p < .0001) (Effective)
	Moodley 2018[56]	South Africa (Western Cape province)	Cross-sectional (2015-2016)	Breast (Adult) [201]	Time between first health care provider visit and date of diagnosis	The median time between the first health care visit and a breast cancer diagnosis was 28 days (IQR 13–58 days). Women whose initial reaction was denial of the breast symptom had a significantly shorter diagnostic interval (11 days vs. 29 days, p = 0.010) (Effective)
	Williams 2018[93]	New Zealand (Northland district)	Before-and-After (2015-2016)	Lung (Adult) [212 (70 in phase 1, 46 in phase 2 and 71 in phase 3)]	Time from GP referral to first specialist appointment	Time from GP referral to first specialist appointment improved significantly (p=0.005) (Effective)
Interventions to enhance diagnostic services	Chapman 2020[17]	UK (Nottingham)	Cross-sectional (2017-2018)	Gastrointestinal (Adult) [1934]	Colorectal cancer (CRC) detection rate	The symptomatic pathway incorporating FIT was feasible and appeared more clinically effective than pathways based on age and symptoms alone, with FIT results identifying patients with a significantly higher risk

					after a FIT	of CRC (Effective)
	Cotton 2020[24]	Canada (Ontario)	Before-and-After (2017-2018)	Lung (NR) [NR]	Referral to diagnosis	Monthly patient volumes increased by 65%, and wait time improved by 60% (Effective)
	Laudicella 2018[52]	UK (England)	Case-Control (2006-2009)	Multiple (Adult) [372353]	Survival of patients	Rerouting patients from emergency presentation to new referral resulted in better patient survival in all cancer cohorts (Effective)
	Nixon 2020[64]	Canada (Ontario)	Case-Control (2015-2017)	Haematological (Adult) [126]	Time from initial consultation to diagnosis of lymphoma	Median time to lymphoma diagnosis was 16 days for patients assessed in the nurse practitioner–led lymphoma rapid diagnosis clinic and 28 days for historical controls (P<0.001) (Effective)
	Sardi 2019[75]	Colombia (Cali)	Before-and-After (2012-2016)	Multiple (NR) [114]	Time from initial consultation to biopsy	The average time from initial consult to biopsy decreased from 65 to 20 days and from biopsy to diagnosis from 33 to 4 days (Effective)
	Setyowibowo 2020[77]	Indonesia (Bandung West Java)	RCT (2017)	Breast (Adult) [107]	Time between first visit to the hospital and a definitive diagnosis	The intervention reduced the time to definitive diagnosis: mean difference = −13.26, 95% CI = −24.51 to −2.00, P=0.02) (Effective)
	Skevington 2020[78]	UK (Manchester)	RCT (2015-2016)	Multiple (Adult) [107]	Quality of life	Psychological quality of life increased (Effective)
	Stenman 2019[80]	Sweden (Kristianstad)	Cross-sectional (2015)	Multiple (Adult) [290]	Total diagnostic interval	Shorter diagnostic interval (time from referral decision in primary care to diagnosis). The median primary care interval was 21 days, and the median diagnostic interval was 11 days (Effective)
	Tafuri 2020[83]	USA (NR)	Case-Control (2016-2018)	Prostate (Adult) [370]	Time from multiparametric Magnetic Resonance Imaging (mpMRI) to biopsy	One-Stop patients experienced shorter time from mpMRI to biopsy (0 vs 7 days; p< 0.01) (Effective)
	Williams 2019[94]	Botswana (Gaborone)	Before-and-After (2015-2017)	Skin (Adult) [218]	Diagnostic histology turnaround times	Median turnaround in the post dermatology quality improvement interval was 11 days (IQR, 12-23 days) compared with 32 days in the pre-dermatology quality improvement interval (IQR, 24-56 days; P<0.001) (Effective)
Multidisciplinary team	Phillips 2019[68]	USA (NR)	Case-Control (2014-2016)	Lung (NR) [218]	Time to diagnosis	Compared to controls, patients with lung cancer in the Lung Cancer Strategist Program cohort had an expedited time from suspicious finding to diagnosis (34 vs 44 days, p=0.027) (Effective)
Patient navigation	Chavarri-Guerra 2019[18]	Mexico (Mexico City)	Before-and-After (2016-2017)	Multiple (Adult) [70]	Feasibility	91% of patients successfully obtained appointments at cancer centers in <3 months (Effective)
	Drudge-Coates 2019[28]	UK (London)	Before-and-After (2012-2015)	Prostate (Adult) [60]	Waiting times from the GP	Compared with the previous physician-led service, waiting times for patient appointment fell by 52% over a 3-year study period (Effective)

					referral to initial clinic assessment	
	Whitley 2017[92]	USA (Boston, Denver, San Antonio, and Tampa)	Case-Control (2007-2011)	Multiple (Adult) [6349]	Delays in diagnostic resolution based on Charlson Comorbidity Index score	Patient navigation reduced delays in diagnostic resolution, with the greatest benefits seen for those with a Charlson Comorbidity Index score ≥2 (Effective)
Rapid referral pathway	Antel 2020[13]	South Africa (Cape Town)	Before-and-After (2017-2019)	Haematological (Adult) [130]	Diagnostic interval	Compared with a historical cohort, the diagnostic interval (time from first health visit to diagnostic biopsy) for patients with lymphoma was significantly shorter, 13.5 vs 48 days (p=0.002) (Effective)
	Arhi 2020[14]	UK (National)	Case-Control (2000-2013)	Gastrointestinal (Adult) [7130]	Hazard ratios of death	Patients referred between 2 weeks to 3 months, and after 3 months with red-flag symptoms demonstrated a significantly worse prognosis than patients who were referred within 2 weeks (Effective)
	Chng 2020[19]	UK (Newcastle-upon-Tyne)	Case-Control (2015-2019)	Brain (Adult) [101]	Tumour detection rate	With guideline adherence, the brain tumour detection rate was 3-fold higher (36.0% vs 11.5%, p¼0.02) (Effective)
	Creak 2020[25]	UK (Brighton; Sussex)	Cross-sectional (2015-2018)	Multiple (Adult) [258]	Time to diagnosis	Direct GP referrals were feasible and manageable within a tertiary clinic and resulted in high rates of cancer diagnoses and early contact with an oncologist and nurse specialist, cutting short the 'limbo' time of high anxiety before diagnosis (Effective)
	Hennessy 2020[36]	Ireland (Dublin)	Case-Control (2012-2018)	Lung (NR) [864]	Time to diagnosis	Time to diagnosis was longer in those who had attended a post Rapid Access Lung Cancer Clinic CT (34.5 versus 21 days) (Effective)
	Jones 2018[45]	UK (East Midlands)	Case-Control (2013-2015)	Gastrointestinal (NR) [1401 (340 STTP, 495 traditional pathway, 566 control trusts)]	Time from referral to diagnosis	The pathway saved a mean of 7 days from referral to treatment (with a 95% CI of 3 to 11 days, p<0.008) and a mean of 16 days from referral to diagnosis, when compared with a traditional pathway (Effective)
	Joyce 2020[46]	UK (National)	Cross-sectional (2017-2018)	Multiple (Mixed age) [NR]	Proportion with emergency diagnosis of cancer	A lower proportion of emergency diagnosis of cancer was found with higher 2 weeks wait referral conversion rate (Effective)
	Pearson 2020[67]	UK (National)	Case-Control (2014)	Multiple (Mixed age) [12873]	Primary care interval	Compared with patients with a specific alarm symptom, patients with non-specific but concerning symptoms had higher odds of having longer primary care intervals (adjusted OR: 1.24 (1.11 to 1.36)) (Effective)
	Round 2020[72]	UK (National)	Case-Control (2011-2017)	Multiple (Mixed age) [1469103]	Risk of death	Cancer patients from the highest referring practices had a lower hazard of death (hazard ratio [HR] = 0.96; 95% confidence interval [CI] = 0.95 to 0.97) (Effective)
	Sandager 2019[74]	Denmark (National)	Cross-sectional (2010)	Multiple (Adult) [2256]	Patient experience	Overall, pathway referred patients were 21% more likely than non-pathway referred patients to report a positive experience (PR = 1.21 [95% CI: 1.11–1.30]) (Effective)

	Thanapal 2020[86]	UK (London)	Before-and-After (2012-2018)	Gastrointestinal (Adult) [1648]	Time to diagnosis	Patients on the pathway took 25 days to obtain results as compared to 40 days in the standard pathway (Effective)
	Vijayakumar 2020[90]	UK (Buckinghamshire)	Cross-sectional (2018)	Lung (NR) [111]	Patient satisfaction	High satisfaction with the service, with scores above 93% in all parameters (Effective)
Standardized care pathway	Alonso-Abreu 2017[12]	Spain (Tenerife)	Case-Control (2008-2010)	Gastrointestinal (Adult) [257]	Survival rates	Survival rates at 12 and 60 months after treatment were significantly higher in the early colonoscopy group compared with the standard schedule colonoscopy group ($p < 0.001$) (Effective)
	Dahl 2017[26]	Denmark (Countrywide)	Before-and-After (2004-2010)	Multiple (Adult) [3292]	Patient satisfaction for waiting time from referral to consultation at a hospital	Implementation of pathway was associated with a reduced level of patient-reported dissatisfaction with long waiting time from the time of referral to the first consultation at the hospital (Effective)
	Laerum 2020[49]	Norway (Kristiansand)	Before-and-After (2007-2016)	Lung (Adult) [780]	Referral interval	The median referral interval among all patients was reduced by two days from baseline to the next time period when the local diagnostic algorithm was streamlined (Effective)
	Mullin 2020[59]	Canada (Ontario)	Before-and-After (2018-2019)	Lung (NR) [833]	Time from referral to diagnosis	Time from referral to positron emission tomography decreased (from 38.5 to 15.7 days), time from referral to brain imaging decreased (from 33.4 to 13.1 days), and time from referral to diagnosis decreased (from 38.0 to 22.7 days), all demonstrating special-cause variation (Effective)
	Nilbert 2018[63]	Sweden (Skane County)	Case-Control (2015-2016)	Urinary tract (Adult) [1871]	Time from sign/symptom to diagnosis	The standardized care pathway shortened the diagnostic delay to a median of 25 days compared to 35 days for regular referral ($p=0.01$) (Effective)
	Rankin 2017[71]	Australia (New South Wales)	Cross-sectional (2014)	Lung (Adult) [19]	Patient concerns urgency, advocacy, and referral	Patients and general practitioners expressed similar themes across the diagnostic and pretreatment intervals (Effective)
Target or benchmark for wait times	Jeyakumar 2020[42]	Australia (Victoria)	Case-Control (2018)	Lung (Adult) [46]	Mean time from initial CT to tissue diagnosis	The Standard Care group met the target for treatment commencement in 33.3% of cases whereas the Rapid Access Clinic group achieved this in 77% (Effective)
	Jiang 2017[43]	China (Shanghai)	Case-Control (2011-2015)	Lung (NR) [4000]	Time from initial respiratory consultation to treatment decision	Takes a median 4 workdays (range 3 to 6) for a new patient from initial respiratory consultation to treatment decision, whereas in many countries, 14 workdays are considered a reasonable timeline (Effective)
	Sagar 2020[73]	UK (Milton, Somerset)	Before-and-After (2019-2020)	Gastrointestinal (Mixed age) [1255]	28-day target attainment	Attainment of the 28-day diagnosis target for all suspected colorectal cancer referrals improved following the establishment of a new pathway (88% vs. 82%, $P < 0.0001$) (Effective)
	Stevenson-Hornby 2018[81]	UK (Wigan)	Before-and-After (2017)	Gastrointestinal (NR) [NR]	Percentage diagnosed	55% of all referrals were found to have hepatobiliary-pancreatic cancer after pathway trial compared with 19% before (Effective)
	Zhu 2020[96]	Sweden (Orebro)	RCT (2015-2018)	Prostate (Adult) [204]	Self-reported symptoms of	Significant changes in depression symptoms and self-rated sleep quality suggested a benefit of the fast-track

					stress	workup intervention (Effective)
	*Piano 2019[69]	UK (Guildford, Bradford)	Cross-sectional (NR)	Multiple (Adult) [29]	Patient attitudes within the context of their recent referral experiences	Most patients had experienced swift referral. It was difficult for patients to understand how the new standard could affect upon the time that it takes to progress through the system. Responsibility for meeting the standard was also a concern as patients did not see their own behaviours as a form of Involvement (NA)
Technology to support diagnosis process	Cazzaniga 2019[16]	Italy (Bergamo)	Case-Control (2017)	Skin (Adult) [232]	Diagnostic accuracy	The diagnostic accuracy of the online assessment compared with direct clinical examination was significant (Effective)
	Cock 2017[22]	UK (NR)	Guideline development (2014-2016)	Gastrointestinal (Adult) [NR]	Patient satisfaction	Audits were being conducted to assess and compare patient satisfaction with face-to-face versus telephone assessments, although intervention was well-received (Effective)
	Eastham 2017[29]	UK (Leeds)	Before-and-After (2015-2016)	Multiple (Adult) [NR]	Form completion rates and time spent processing forms	Form completion rates improved from a mean of 44% of forms at baseline (n = 210) to 99% post-intervention n = 236). Time spent processing forms also decreased from a mean of 96 seconds to 35 seconds post-introduction of the new system (Effective)
	Hirst 2018[37]	UK (London)	Cross-sectional (2016)	Multiple (Adult) [NR]	GP perspectives on txt-netting	Text messages were perceived to be an acceptable potential strategy for safety netting patients with low-risk cancer symptoms (Effective)
	Hunt 2020[38]	UK (England)	Case-Control (2018)	Skin (Adult) [150 (75 consecutive TD referrals paired with 75 standard "Face to Face" controls)]	Time from referral to first appointment and diagnostic rates	There was a 23% absolute and 37% relative increase in diagnostic completion rates in the mobile van compared with the central hospital facility (p=0.0001) (Effective)
	Moor 2019[57]	UK (Newcastle-upon-Tyne; Birmingham)	Case-Control (2007-2010)	Head and Neck (Mixed age) [4715]	Diagnostic accuracy	Machine learning algorithms accurately and effectively classify patients referred with suspected head and neck cancer symptoms (Effective)
	Moreno-Ramirez 2017[58]	Spain (Southern region)	Case-Control (2004-2015)	Skin (NR) [2009]	Waiting times for referral	Waiting times for referral for teledermatology network versus conventional letter referral system 12.31 (8.22–16.40) vs 88.62 (38.42–138.82) (Effective)
	Nicholson 2020[62]	UK (London)	Cross-sectional (2018-2019)	Skin (NR) [60]	Patient satisfaction	Over 80% (49) would recommend the service, and the majority felt confident with the teledermatology model. Overall, patients would be happy to complete electronic questionnaires and receive results electronically, with younger patients being more amenable to this (Effective)
	Orchard 2020[65]	UK (Bristol)	Before-and-After (2014-2017)	Gastrointestinal (Mixed age) [11357]	Time from referral to diagnosis	Time from referral to diagnosis reduced from 39 to 21 days and led to a dramatic improvement in patients starting treatment within 62 days (Effective)
	Snoswell 2018[79]	New Zealand (Countrywide)	Not clear (2012)	Skin (Adult) [300]	Time to clinical resolution	Mean time to clinical resolution was 9 days (range, 1-50 days) with teledermoscopy referral compared with 35 days (range, 0-138 days) with usual care alone (difference, 26 days; 95%credible interval 13-38 days) (Effective)

	Sunderland 2020[82]	New Zealand (Auckland)	Case-Control (2016)	Skin (NR) [809]	Efficacy of diagnostic tool	A positive predictive value (PPV) of 38.1% and number needed to excise (NNE) of 2.6, with less than 10% of referrals triaged for teledermatoscopy confirmed as melanoma (24/264) (Effective)
	Uthoff 2018[87]	India (Bangalore, Dimapur)	Case-Control (NR)	Oral (Adult) [99]	Diagnostic accuracy	Sensitivities, specificities, positive predictive values, and negative predictive values ranged from 81.25% to 94.94% (Effective)
	Vestergaard 2020[89]	Denmark (Southern Denmark)	Case-Control (2018)	Skin (Adult) [519]	Percentage of lesions not requiring further in-person assessment	On evaluation by teledermoscopy, 31.5% of lesions did not need further in-person assessment (Effective)

CRC = colorectal cancer; CT = computed tomography; FIT = faecal immunochemical testing; GP = general practitioner; NR = not reported; RABC = rapid access breast clinic; RCT = randomized controlled trial; RIC = rapid investigation clinic; STTP = straight to test pathway; TD = teledermatology; TS = traditional system; UK = United Kingdom; USA = United States of America; * = effective but not applicable; IQR = interquartile range

Figures

Figure 1: Modified PRISMA flow chart

Figure 2: Geographical mapping of the included published articles

Figure 3: Summary of cancer types reported by the included published articles

Figure 4: Summary of intervention types reported by the included published articles

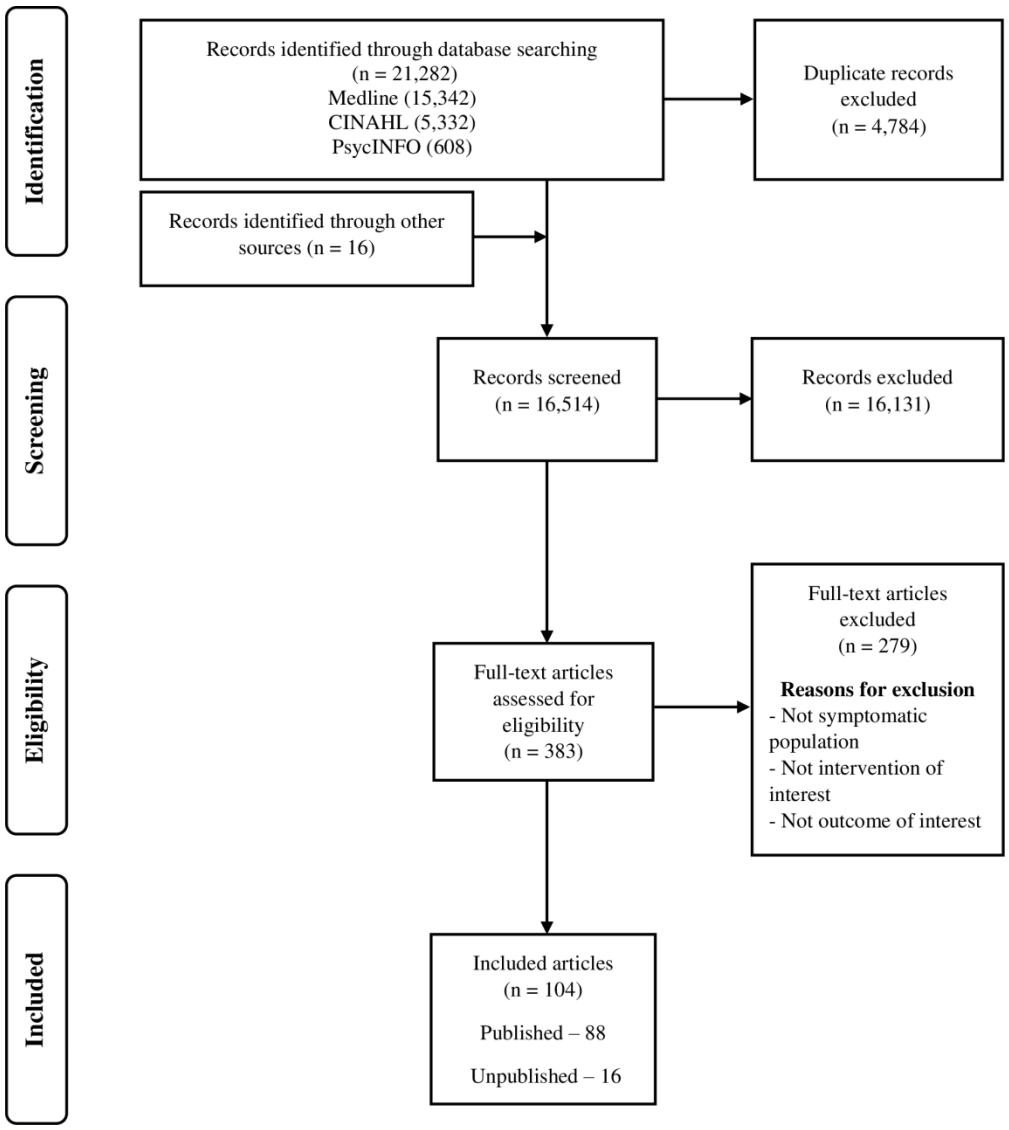

Figure 1: Modified PRISMA flow chart

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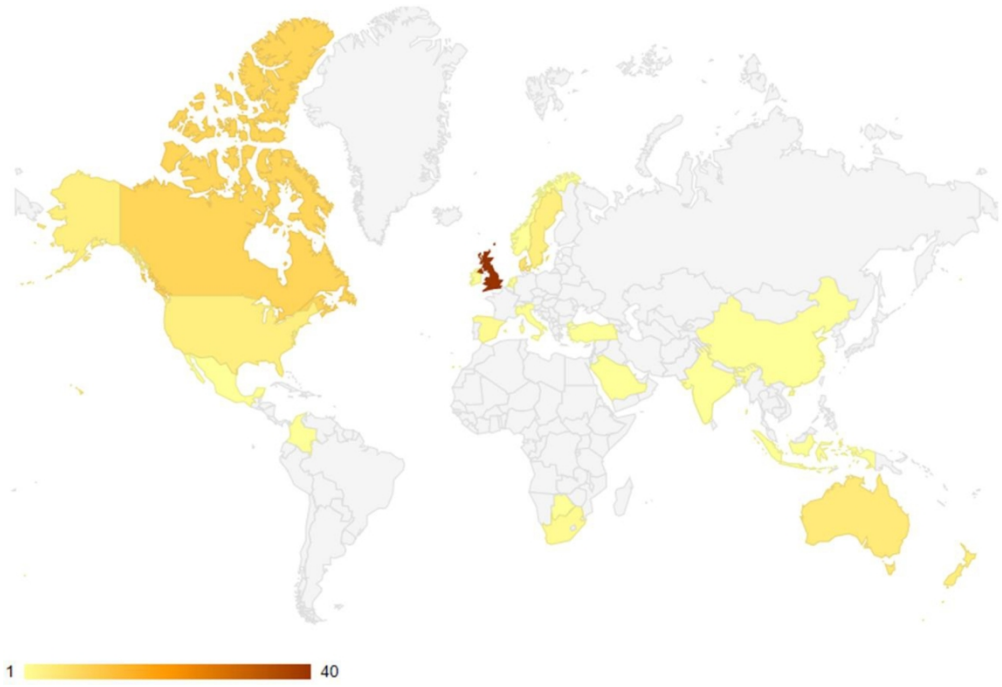

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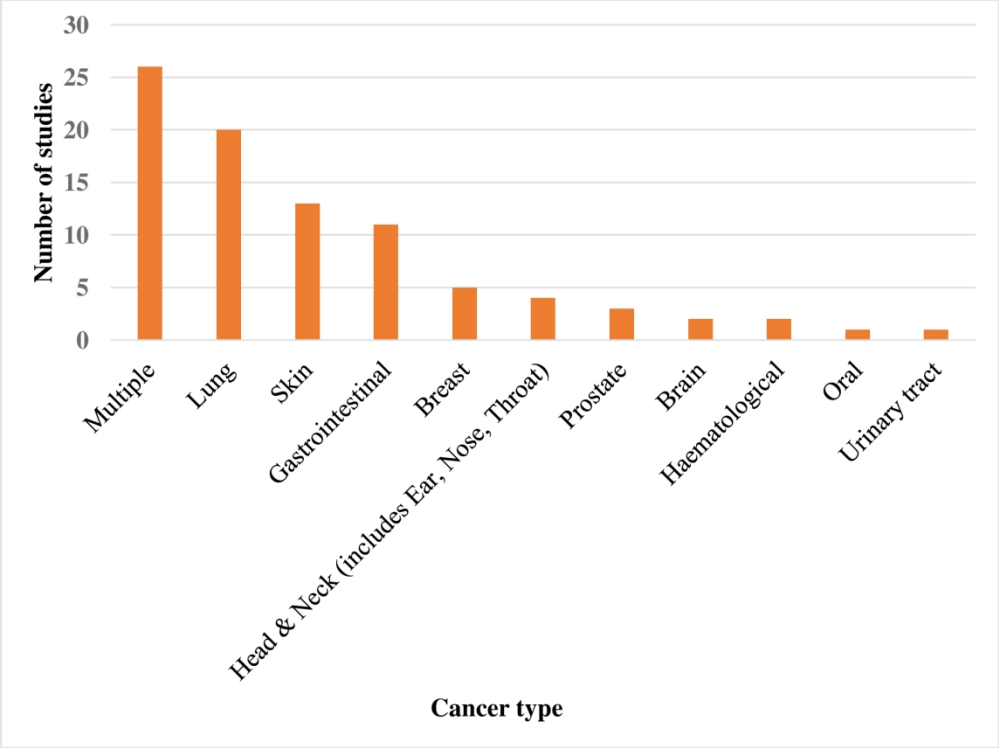

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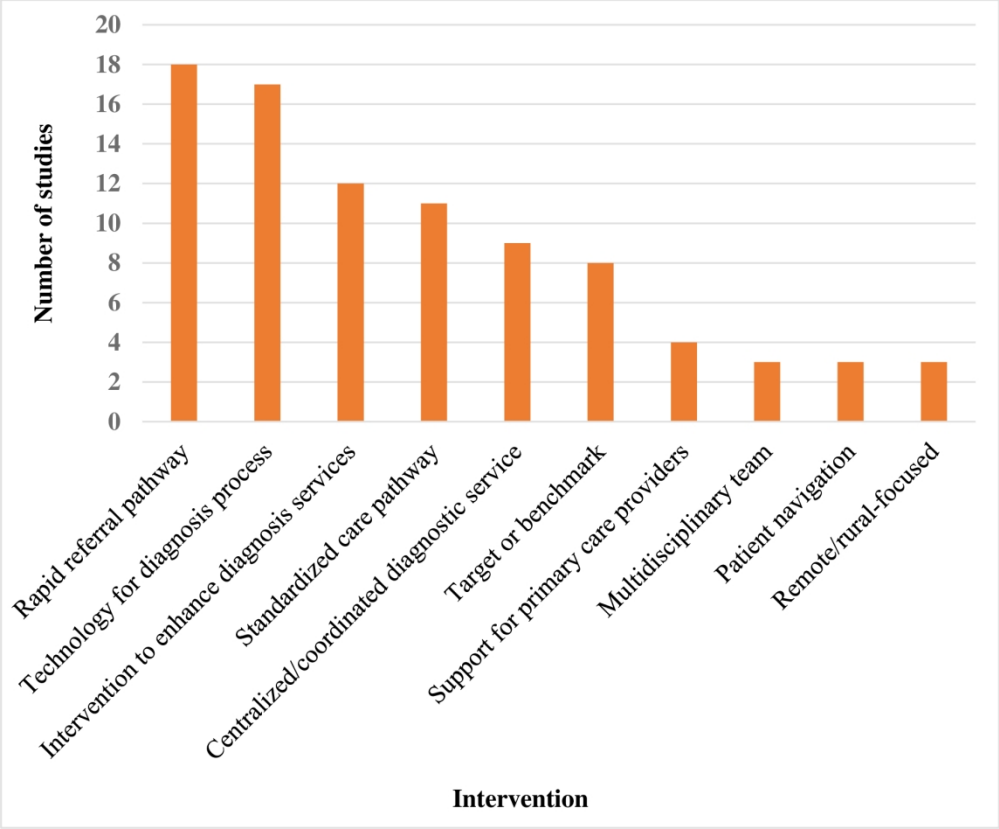

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Appendices

Appendix 1: Project work plan

About the Project Team

At the Knowledge Synthesis Team, George and Fay Yee Centre for Healthcare Innovation, we have an experienced team of methodologists, systematic reviewers, a medical librarian and biostatistician. Over the past 8 years we have supported numerous research teams and guideline developers by providing training, support and conducting evidence syntheses on their behalf. In addition, several of our team members hold academic positions with the University of Manitoba where they teach, supervise students, and advance the science and practice of knowledge synthesis.

Proposed Method

Methods

Using a team of experienced systematic reviews and methodologists, with expertise in research methodology, knowledge synthesis and implementation science, we will update the 2018 peer-reviewed and grey literature scan by conducting a rapid scoping review to include contemporary, national and international leading interventions for improving accurate and timely cancer diagnosis focusing on the symptomatic population and summarize efficacy, impact and sustainability of identified interventions. We will identify evidence to answer the following key questions:

KQ 1. Are there practice guidelines, care pathways or other initiatives (e.g., benchmarks/ targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, patient navigators and/or navigation, etc.) that have been found to streamline and enhance accurate and timely diagnosis in symptomatic individuals?

- How were patients involved in the design, development and/ or implementation of these initiatives?
- How were providers (e.g., primary care providers) involved in the design, development and/or implementation of these initiatives?

KQ 2. What are the leading interventions for innovative and/or virtual approaches (e.g., technology-based) to seamless care (i.e., minimally disruptive care that is found to be more convenient/coordinated/timely/less stressful to the patients) in the pre-diagnosis phase within Canada and abroad?

- How have these interventions been applied, including identification of successes and lessons learned where possible?
- Were these interventions evaluated and if so, what were the findings?
- How were patients involved in the design, development and/ or implementation of these interventions?

KQ 3. What are the identified performance metrics that can be used to measure the suspicion to diagnosis phase; and where and how are these metrics used?

- Are there specific metrics used to measure the patient experience?
- What data is captured by decision-support systems and how does the data and clinical systems work together?
- Is there evidence on sustainability of the model?

KQ 4. What are the key points of care in a patient's experience (e.g., diagnostic tests, physician consultations, etc.) as they navigate the system from initial symptoms/ suspicion of cancer to diagnosis?

KQ 5. Have specific considerations been applied to underserviced populations including Indigenous, rural, and remote populations within the context of each of the questions above?

Study eligibility criteria
This review will focus on published and unpublished studies that answer the key questions since 2017. Our focus is on comparative studies that applied a protocol/guideline or a specific intervention or intervention plan. Having said that, we anticipate the need to review lower quality study designs (e.g., retrospective, and uncontrolled studies). As such, there will be no restriction on the study design, but will be limited to English language publications for feasibility.

Search strategy and study selection
A knowledge synthesis librarian has designed and executed a literature search strategy in MEDLINE (Ovid). The search strategy was peer-reviewed by a second librarian and adapted for other bibliographic databases: Cinahl (Ebsco) and Psycinfo (Ovid). Search strategies are presented in Appendix 1. All retrieved records were imported into EndNote for citation management.
One reviewer will screen each identified citation for eligibility. Full texts of all relevant citations will be reviewed by two reviewers. All conflicts will be resolved by discussion and/ or a third reviewer, as needed. We will record the number of ineligible citations at the title/ abstract screening stage, and both the number and reason for ineligibility at the full-text articles.

Data extraction
We will develop data extraction forms and pilot them on a small selection of studies. Extracted data will be stored and managed in MS Excel. One reviewer will independently extract data from included studies and another reviewer will independently check the extracted data for errors. Disagreements will be resolved by discussion between reviewers and/ or by involving a third reviewer, as needed.

Data analysis
We will present specific characteristics of all included studies in a tabular form. The analysis of the extracted data will be descriptive.

Study dissemination
We will submit reports from this study as a technical report to CPAC.

Knowledge User Engagement Plan

We will be providing a bi-weekly update to CPAC on the progression of the review. Specifically, we will engage during specific time points to review progress and next steps:

- Protocol
- Level I Screening (Title/ Abstract screening phase)
- Level II Screening (Full-text screening phase)
- Data Extraction
- Data Analysis
- Report

Declaration of Conflict of Interest

None

Appendix 2: MEDLINE (Ovid) search strategy

1.	"early detection of cancer"/	26241
2.	(cancer* or tumo?r* or neoplasm* or malignan* or metasta* or oncogen* or oncolog*).ti	1795604
3.	(carcinoma* or adenoma* or adenocarcinoma* or adeno-carcinoma* or blastoma* or carcinosarcoma* or carcino-sarcoma* or leukemia* or leukaemia* or lymphoma* or melanoma* or mesenchymoma* or mesothelioma* or sarcoma* or thymoma*).ti	844480
4.	or/2-3	2477759
5.	1 or 4	2483642
6.	early diagnosis/ or delayed diagnosis/	33272
7.	(prediagnos* or pre-diagnos* or care path? or cancer path? or care pathway* or cancer pathway* or diagnos* phase* or diagnos* path? or referral path? or diagnos* pathway* or referral pathway* or diagnos* interval* or referral interval* or consult* interval* or "time-to-treat" or "time-to-treatment").ti,ab,kf.	26471
8.	((early or earlier or prompt* or late or later or rapid or wait* or delay* or timel* or longtime or interval* or route*) adj3 (diagnos* or refer or referred or referral* or referring or consult*)).ti,ab,kf.	214615
9.	((diagnos* or confirm* or refer* or consult* or investigat*) adj4 (timelapse* or time lapse* or time elapse* or fasttrack* or fast-track* or timeline* or time line*)).ti,ab	1510
10.	delay*.ti	74391
11.	wait* time*.ti,ab.	13384
12.	or/6-11	338665
13.	4 and 12	58490
14.	diagnos*.ti,ab,kf	2562935
15.	13 and (1 or 14)	48832
16.	(interprofessional* or inter-professional* or multidisciplin* or multi-disciplin* or navigator* or coordinator* or co-ordinator* or ((patient* or cancer* or care) adj2 (navigat* or coordinat* or co-ordinat* or journey* or continuum*)) or mobile or phone* or smartphone* or reminder* or tele* or information technolog* or communicat*).ti	177088
17.	16 and 5	10725
18.	15 or 17	59240
19.	limit 18 to english language	49045
20.	(exp animal experiment/ or exp animal model/ or exp transgenic animal/ or animal/ or chordata/ or vertebrate/ or tetrapod/ or amniote/ or exp amphibia/ or mammal/ or exp reptile/ or therian/ or placental mammals/ or exp marsupial/ or euarchontoglires/ or exp xenarthra/ or primate/ or exp scandentia/ or haplorhini/ or exp prosimian/ or simian/ or exp tarsiiform/ or catarrhini/ or exp platyrrhini/ or ape/ or exp cercopithecidae/ or hominid/ or exp hylobatidae/ or exp chimpanzee/ or exp gorilla/ or (animal or animals or pisces or fish or fishes or catfish or catfishes or sheatfish or silurus or arius or heteropneustes or clarias or gariepinus or fathead minnow or fathead minnows or pimephales or promelas or cichlidae or trout or trouts or char	4778446

	or chars or salvelinus or salmo or oncorhynchus or guppy or guppies or millionfish or poecilia or goldfish or goldfishes or carassius or auratus or mullet or mullets or mugil or curema or shark or sharks or cod or cods or gadus or morhua or carp or carps or cyprinus or carpio or killifish or eel or eels or anguilla or zander or sander or lucioperca or stizostedion or turbot or turbots or psetta or flatfish or flatfishes or plaice or pleuronectes or platessa or tilapia or tilapias or oreochromis or sarotherodon or common sole or dover sole or solea or zebrafish or zebrafishes or danio or rerio or seabass or dicentrarchus or labrax or morone or lamprey or lampreys or petromyzon or pumpkinseed or pumpkinseeds or lepomis or gibbosus or herring or clupea or harengus or amphibia or amphibian or amphibians or anura or salientia or frog or frogs or rana or toad or toads or bufo or xenopus or laevis or bombina or epidalea or calamita or salamander or salamanders or newt or newts or triturus or reptilia or reptile or reptiles or bearded dragon or pogona or vitticeps or iguana or iguanas or lizard or lizards or anguis fragilis or turtle or turtles or snakes or snake or aves or bird or birds or quail or quails or coturnix or bobwhite or colinus or virginianus or poultry or poultries or fowl or fowls or chicken or chickens or gallus or zebra finch or taeniopygia or guttata or canary or canaries or serinus or canaria or parakeet or parakeets or grasskeet or parrot or parrots or psittacine or psittacines or shelduck or tadorna or goose or geese or branta or leucopsis or woodlark or lullula or flycatcher or ficedula or hypoleuca or dove or doves or geopelia or cuneata or duck or ducks or greylag or graylag or anser or harrier or circus pygargus or red knot or great knot or calidris or canutus or godwit or limosa or lapponica or meleagris or gallopavo or jackdaw or corvus or monedula or ruff or philomachus or pugnax or lapwing or peewit or plover or vanellus or swan or cygnus or columbianus or bewickii or gull or chroicocephalus or ridibundus or albifrons or great tit or parus or aythya or fuligula or streptopelia or risoria or spoonbill or platalea or leucorodia or blackbird or turdus or merula or blue tit or cyanistes or pigeon or pigeons or columba or pintail or anas or starling or sturnus or owl or athene noctua or pochard or ferina or cockatiel or nymphicus or hollandicus or skylark or alauda or tern or sterna or teal or crecca or oystercatcher or haematopus or ostralegus or shrew or shrews or sorex or araneus or crocidura or russula or european mole or talpa or chiroptera or bat or bats or eptesicus or serotinus or myotis or dasycneme or daubentonii or pipistrelle or pipistrellus or cat or cats or felis or catus or feline or dog or dogs or canis or canine or canines or otter or otters or lutra or badger or badgers or meles or fitchew or fitch or foumart or foulmart or ferrets or ferret or polecat or polecats or mustela or putorius or weasel or weasels or fox or foxes or vulpes or common seal or phoca or vitulina or grey seal or halichoerus or horse or horses or equus or equine or equidae or donkey or donkeys or mule or mules or pig or pigs or swine or swines or hog or hogs or boar or boars or porcine or piglet or piglets or sus or scrofa or llama or llamas or lama or glama or deer or deers or cervus or elaphus or cow or cows or bos taurus or bos indicus or bovine or bull or bulls or cattle or bison or bisons or sheep or sheeps or ovis aries or ovine or lamb or lambs or mouflon or mouflons or goat or goats or capra or caprine or chamois or rupicapra or leporidae or lagomorpha or lagomorph or rabbit or rabbits or oryctolagus or cuniculus or laprine or hares or lepus or rodentia or rodent or rodents or murinae or mouse or mice or mus or musculus or murine or woodmouse or apodemus or rat or rats or rattus or norvegicus or guinea pig or guinea pigs or cavia or porcellus or hamster or hamsters or mesocricetus or cricetulus or cricetus or gerbil or gerbils or jird or jirds or meriones or unguiculatus or jerboa or jerboas or jaculus or chinchilla or chinchillas or beaver or beavers or castor fiber or castor canadensis or sciuridae or squirrel or squirrels or sciurus or chipmunk or chipmunks or marmot or marmots or marmota or suslik or susliks or spermophilus or cynomys or cottonrat or cottonrats or sigmodon or vole or voles or microtus or myodes or glareolus or primate or primates or prosimian or prosimians or lemur or lemurs or lemuridae or loris or bush baby or bush babies or bushbaby or bushbabies or galago or galagos or anthropoidea or anthropoids or simian or simians or monkey or monkeys or	

	marmoset or marmosets or callithrix or cebuella or tamarin or tamarins or saguinus or leontopithecus or squirrel monkey or squirrel monkeys or saimiri or night monkey or night monkeys or owl monkey or owl monkeys or douroucoulis or aotus or spider monkey or spider monkeys or ateles or baboon or baboons or papio or rhesus monkey or macaque or macaca or mulatta or cynomolgus or fascicularis or green monkey or green monkeys or chlorocebus or vervet or vervets or pygerythrus or hominoidea or ape or apes or hylobatidae or gibbon or gibbons or siamang or siamangs or nomascus or symphalangus or hominidae or orangutan or orangutans or pongo or chimpanzee or chimpanzees or pan troglodytes or bonobo or bonobos or pan paniscus or gorilla or gorillas or troglodytes).ti,ab,kf.) not (human/ or (human$ or man or men or woman or women or child or children or patient$).ti,ab,kf.)	
21.	19 not 20	48488
22.	limit 21 to yr="2017 -Current"	15342

Appendix 3: CINAHL (EbscoHOST) search strategy

1.	(MH "early detection of cancer")	9365
2.	TI (cancer* OR tumo#r* OR neoplasm* OR malignan* OR metasta* OR oncogen* OR oncolog*)	382286
3.	TI (carcinoma* OR adenoma* OR adenocarcinoma* OR blastoma* OR carcinosarcoma* OR leukemia* OR leukaemia* OR lymphoma* OR melanoma* OR mesenchymoma* OR mesothelioma* OR sarcoma* OR thymoma*)	110746
4.	S2 OR S3	469442
5.	S1 OR S4	471736
6.	(MH "early diagnosis") OR (MH "diagnosis, delayed")	14703
7.	(TI (prediagnos* OR "pre-diagnosis" OR (care N1 path#) OR (cancer N1 path#) OR (care N1 pathway*) OR (cancer N1 pathway*) OR (diagnos* N1 phase*) OR (diagnos* N1 path#) OR (referral N1 path#) OR (diagnos* N1 pathway*) OR (referral N1 pathway*) OR (diagnos* N1 interval*) OR (referral N1 interval*) OR (consult* N1 interval*) OR "time-to-treat" OR "time-to-treatment")) OR (AB (prediagnos* OR "pre-diagnosis" OR (care N1 path#) OR (cancer N1 path#) OR (care N1 pathway*) OR (cancer N1 pathway*) OR (diagnos* N1 phase*) OR (diagnos* N1 path#) OR (referral N1 path#) OR (diagnos* N1 pathway*) OR (referral N1 pathway*) OR (diagnos* N1 interval*) OR (referral N1 interval*) OR (consult* N1 interval*) OR "time-to-treat" OR "time-to-treatment"))	11308
8.	(TI ((early OR earlier OR prompt* OR late OR later OR rapid OR wait* OR delay* OR timel* OR longtime OR interval* OR route*) N3 (diagnos* OR refer OR referred OR referral* OR referring OR consult*))) OR (AB ((early OR earlier OR prompt* OR late OR later OR rapid OR wait* OR delay* OR timel* OR longtime OR interval* OR route*) N3 (diagnos* OR refer OR referred OR referral* OR referring OR consult*)))	47662
9.	(TI ((diagnos* OR confirm* OR refer* OR consult* OR investigat*) N4 (timelapse* OR (time N1 lapse*) OR (time N1 elapse*) OR fasttrack* OR (fast N1 track*) OR timeline* OR (time N1 line*)))) OR (AB ((diagnos* OR confirm* OR refer* OR consult* OR investigat*) N4 (timelapse* OR (time N1 lapse*) OR (time N1 elapse*) OR fasttrack* OR (fast N1 track*) OR timeline* OR (time N1 line*))))	582
10.	TI delay*	17790
11.	(TI (wait* N1 time*)) OR (AB (wait* N1 time*))	6047
12.	S6 OR S7 OR S8 OR S9 OR S10 OR S11	88476
13.	S4 AND S12	13005
14.	(TI diagnos*) OR (AB diagnos*)	526863
15.	S13 AND (S1 OR S14)	9687
16.	TI (interprofessional* OR (inter N1 professional*) OR multidisciplin* OR (multi N1 disciplin*) OR navigator* OR coordinator* OR ordinator* OR ((patient* OR cancer* OR care) N2 (navigat* OR coordinat* OR ordinat* OR journey* OR continuum*)) OR mobile OR phone* OR smartphone* OR reminder* OR tele* OR (information N1 technolog*) OR communicat*)	94165
17.	S16 AND S5	5442
18.	S15 OR S17	14982
19.	S18 Limiters - English Language	14767
20.	((MH "animals+") OR (MH invertebrates+) OR (MH birds+) OR (MH fish) OR (MH "frogs and toads") OR (MH "animals, genetically modified") OR (MH reptiles+) OR (MH mammals) OR (MH bats) OR (MH camels) OR (MH cats) OR (MH cattle) OR (MH dogs) OR (MH dolphins) OR (MH goats) OR (MH horses) OR (MH rabbits) OR (MH rodents+) OR (MH	216053

	sheep) OR (MH swine) OR (MH primates) OR (animal OR animals OR pisces OR fish OR fishes OR catfish OR catfishes OR sheatfish OR silurus OR arius OR heteropneustes OR clarias OR gariepinus OR "fathead minnow" OR "fathead minnows" OR pimephales OR promelas OR cichlidae OR trout OR trouts OR char OR chars OR salvelinus OR salmo OR oncorhynchus OR guppy OR guppies OR millionfish OR poecilia OR goldfish OR goldfishes OR carassius OR auratus OR mullet OR mullets OR mugil OR curema OR shark OR sharks OR cod OR cods OR gadus OR morhua OR carp OR carps OR cyprinus OR carpio OR killifish OR eel OR eels OR anguilla OR zander OR sander OR lucioperca OR stizostedion OR turbot OR turbots OR psetta OR flatfish OR flatfishes OR plaice OR pleuronectes OR platessa OR tilapia OR tilapias OR oreochromis OR sarotherodon OR "common sole" OR "dover sole" OR solea OR zebrafish OR zebrafishes OR danio OR rerio OR seabass OR dicentrarchus OR labrax OR morone OR lamprey OR lampreys OR petromyzon OR pumpkinseed OR pumpkinseeds OR lepomis OR gibbosus OR herring OR clupea OR harengus OR amphibia OR amphibian OR amphibians OR anura OR salientia OR frog OR frogs OR rana OR toad OR toads OR bufo OR xenopus OR laevis OR bombina OR epidalea OR calamita OR salamander OR salamanders OR newt OR newts OR triturus OR reptilia OR reptile OR reptiles OR "bearded dragon" OR pogona OR vitticeps OR iguana OR iguanas OR lizard OR lizards OR "anguis fragilis" OR turtle OR turtles OR snakes OR snake OR aves OR bird OR birds OR quail OR quails OR coturnix OR bobwhite OR colinus OR virginianus OR poultry OR poultries OR fowl OR fowls OR chicken OR chickens OR gallus OR "zebra finch" OR taeniopygia OR guttata OR canary OR canaries OR serinus OR canaria OR parakeet OR parakeets OR grasskeet OR parrot OR parrots OR psittacine OR psittacines OR shelduck OR tadorna OR goose OR geese OR branta OR leucopsis OR woodlark OR lullula OR flycatcher OR ficedula OR hypoleuca OR dove OR doves OR geopelia OR cuneata OR duck OR ducks OR greylag OR graylag OR anser OR harrier OR circus pygargus OR red knot OR "great knot" OR calidris OR canutus OR godwit OR limosa OR lapponica OR meleagris OR gallopavo OR jackdaw OR corvus OR monedula OR ruff OR philomachus OR pugnax OR lapwing OR peewit OR plover OR vanellus OR swan OR cygnus OR columbianus OR bewickii OR gull OR chroicocephalus OR ridibundus OR albifrons OR "great tit" OR parus OR aythya OR fuligula OR streptopelia OR risoria OR spoonbill OR platalea OR leucorodia OR blackbird OR turdus OR merula OR blue tit OR cyanistes OR pigeon OR pigeons OR columba OR pintail OR anas OR starling OR sturnus OR owl OR "athene noctua" OR pochard OR ferina OR cockatiel OR nymphicus OR hollandicus OR skylark OR alauda OR tern OR sterna OR teal OR crecca OR oystercatcher OR haematopus OR ostralegus OR shrew OR shrews OR sorex OR araneus OR crocidura OR russula OR "european mole" OR talpa OR chiroptera OR bat OR bats OR eptesicus OR serotinus OR myotis OR dasycneme OR daubentonii OR pipistrelle OR pipistrellus OR cat OR cats OR felis OR catus OR feline OR dog OR dogs OR canis OR canine OR canines OR otter OR otters OR lutra OR badger OR badgers OR meles OR fitchew OR fitch OR foumart OR foulmart OR ferrets OR ferret OR polecat OR polecats OR mustela OR putorius OR weasel OR weasels OR fox OR foxes OR vulpes OR "common seal" OR phoca OR vitulina OR grey seal OR halichoerus OR horse OR horses OR equus OR equine OR equidae OR donkey OR donkeys OR mule OR mules OR pig OR pigs OR swine OR swines OR hog OR hogs OR boar OR boars OR porcine OR piglet OR piglets OR sus OR scrofa OR llama OR llamas OR lama OR glama OR deer OR deers OR cervus OR elaphus OR cow OR cows OR "bos taurus" OR "bos indicus" OR bovine OR bull OR bulls OR cattle OR bison OR bisons OR sheep OR sheeps OR "ovis aries" OR ovine OR lamb OR lambs OR mouflon OR mouflons OR goat OR goats OR capra OR caprine OR chamois OR rupicapra OR leporidae OR lagomorpha OR lagomorph OR rabbit OR rabbits OR oryctolagus OR cuniculus OR laprine OR hares OR lepus OR rodentia OR rodent OR rodents OR murinae OR mouse OR mice OR mus OR musculus OR murine OR woodmouse	

	OR apodemus OR rat OR rats OR rattus OR norvegicus OR "guinea pig" OR "guinea pigs" OR cavia OR porcellus OR hamster OR hamsters OR mesocricetus OR cricetulus OR cricetus OR gerbil OR gerbils OR jird OR jirds OR meriones OR unguiculatus OR jerboa OR jerboas OR jaculus OR chinchilla OR chinchillas OR beaver OR beavers OR "castor fiber" OR "castor canadensis" OR sciuridae OR squirrel OR squirrels OR sciurus OR chipmunk OR chipmunks OR marmot OR marmots OR marmota OR suslik OR susliks OR spermophilus OR cynomys OR cottonrat OR cottonrats OR sigmodon OR vole OR voles OR microtus OR myodes OR glareolus OR primate OR primates OR prosimian OR prosimians OR lemur OR lemurs OR lemuridae OR loris OR "bush baby" OR "bush babies" OR bushbaby OR bushbabies OR galago OR galagos OR anthropoidea OR anthropoids OR simian OR simians OR monkey OR monkeys OR marmoset OR marmosets OR callithrix OR cebuella OR tamarin OR tamarins OR saguinus OR leontopithecus OR squirrel monkey OR squirrel monkeys OR saimiri OR "night monkey" OR "night monkeys" OR "owl monkey" OR "owl monkeys" OR douroucoulis OR aotus OR "spider monkey" OR "spider monkeys" OR ateles OR baboon OR baboons OR papio OR "rhesus monkey" OR macaque OR macaca OR mulatta OR cynomolgus OR fascicularis OR "green monkey" OR "green monkeys" OR chlorocebus OR vervet OR vervets OR pygerythrus OR hominoidea OR ape OR apes OR hylobatidae OR gibbon OR gibbons OR siamang OR siamangs OR nomascus OR symphalangus OR hominidae OR orangutan OR orangutans OR pongo OR chimpanzee OR chimpanzees OR "pan troglodytes" OR bonobo OR bonobos OR "pan paniscus" OR gorilla OR gorillas OR troglodytes)) NOT ((MH human) OR (human# OR man OR men OR woman OR women OR child OR children OR patient#))	
21.	S19 NOT S20	14678
22.	S21 Limiters - Published Date: 20170101-20201231	5333

Appendix 4: Psycinfo (Ovid) search strategy

1.	cancer screening/	4776
2.	(cancer* or tumo?r* or neoplasm* or malignan* or metasta* or oncogen* or oncolog*).ti	44464
3.	(carcinoma* or adenoma* or adenocarcinoma* or adeno-carcinoma* or blastoma* or carcinosarcoma* or carcino-sarcoma* or leukemia* or leukaemia* or lymphoma* or melanoma* or mesenchymoma* or mesothelioma* or sarcoma* or thymoma*).ti	2705
4.	or/2-3	46737
5.	1 or 4	47903
6.	(prediagnos* or pre-diagnos* or care path? or cancer path? or care pathway* or cancer pathway* or diagnos* phase* or diagnos* path? or referral path? or diagnos* pathway* or referral pathway* or diagnos* interval* or referral interval* or consult* interval* or "time-to-treat" or "time-to-treatment").ti,ab,id.	3896
7.	((early or earlier or prompt* or late or later or rapid or wait* or delay* or timel* or longtime or interval* or route*) adj3 (diagnos* or refer or referred or referral* or referring or consult*)).ti,ab,id.	13853
8.	((diagnos* or confirm* or refer* or consult* or investigat*) adj4 (timelapse* or time lapse* or time elapse* or fasttrack* or fast-track* or timeline* or time line*)).ti,ab	168
9.	delay*.ti	14212
10.	wait* time*.ti,ab.	1957
11.	or/6-10	33241
12.	4 and 11	1613
13.	diagnos*.ti,ab,id	324967
14.	12 and (1 or 13)	1345
15.	(interprofessional* or inter-professional* or multidisciplin* or multi-disciplin* or navigator* or coordinator* or co-ordinator* or ((patient* or cancer* or care) adj2 (navigat* or coordinat* or co-ordinat* or journey* or continuum*)) or mobile or phone* or smartphone* or reminder* or tele* or information technolog* or communicat*).ti	81166
16.	15 and 5	1650
17.	14 or 16	2949
18.	limit 17 to english language	2756
19.	(exp animal research/ or animal models/ or exp animals/ or ("20").po or (animal or animals or pisces or fish or fishes or catfish or catfishes or sheatfish or silurus or arius or heteropneustes or clarias or gariepinus or fathead minnow or fathead minnows or pimephales or promelas or cichlidae or trout or trouts or char or chars or salvelinus or salmo or oncorhynchus or guppy or guppies or millionfish or poecilia or goldfish or goldfishes or carassius or auratus or mullet or mullets or mugil or curema or shark or sharks or cod or cods or gadus or morhua or carp or carps or cyprinus or carpio or killifish or eel or eels or anguilla or zander or sander or lucioperca or stizostedion or turbot or turbots or psetta or flatfish or flatfishes or plaice or pleuronectes or platessa or tilapia or tilapias or oreochromis or sarotherodon or common sole or dover sole or solea or zebrafish or zebrafishes or danio or rerio or seabass or dicentrarchus or labrax or morone or lamprey or lampreys or petromyzon or pumpkinseed or pumpkinseeds or lepomis or gibbosus or herring or clupea or harengus or amphibia or amphibian or amphibians or anura or salientia or frog or frogs or rana or toad or toads or bufo or xenopus or laevis or bombina or epidalea or calamita or salamander or salamanders or newt or newts or triturus or reptilia or reptile or reptiles or bearded dragon or pogona or vitticeps or iguana or iguanas or lizard or lizards or anguis fragilis or turtle or turtles or snakes or snake or aves or bird or birds or quail or quails or coturnix or bobwhite or colinus or virginianus or poultry or poultries or	339315

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Appendix 5: Websites of relevant organizations and professional bodies searched for literature

Canada

- Alberta Cancer Foundation
- BC Cancer Foundation
- BC Cancer Agency
- Cancer Care Manitoba
- Cancer Care Nova Scotia
- Cancer Care Ontario
- CancerControl Alberta
- Canada Health Infoway
- Canadian Association of Nurses in Oncology
- Canadian Association of Psychosocial Oncology
- Canadian Cancer Society
- Canadian Foundation for Healthcare Improvement
- Canadian Foundation for Innovation
- Canadian Institutes of Health Research
- Cancer and Primary Care Research
- Cancer Quality Council of Ontario
- Cancerview.ca
- CanIMPACT
- College of Family Physicians of Canada
- International Network
- New Brunswick Cancer Network
- Ontario Institute for Cancer Research
- Quebec Health and Social Services (Direction québécoise de cancérologie, Ministère de la Santé et des Services sociaux)
- Royal College of Physicians and Surgeons of Canada
- Saskatchewan Cancer Agency
- Trillium Health Partners

International

- Association of Community Cancer Centres – USA
- Centers for Disease Control and Prevention – USA
- Commission on Cancer of the American College of Surgeons – USA
- Institute of Medicine – USA
- National Cancer Institute – USA
- National Comprehensive Cancer Network – USA
- Cancer Research UK (including the Accelerate, Coordinate, Evaluate Programme) – UK
- Kings Fund – UK
- National Health Service (NHS) – UK
- National Institute for Health and Care Excellence (NICE) – UK
- Northern Cancer Network – New Zealand
- Cancer Australia – Australia
- Sax Institute – Australia
- Denmark (Ministry of Health)
- Sweden (Ministry of Health)
- European Organization for Research and Treatment of Cancer – Europe
- European Society for Medical Oncology – Europe
- European Partnership Action Against Cancer – Europe
- World Health Organization – International

Appendix 6: Definition for interventions related to the review questions

- *Centralized or coordinated diagnostic service*: Brings together various tests/procedures and care providers needed to determine a definitive diagnosis at one location.
- *Interventions in diagnostic services*: An initiative that aims to improve diagnostic services within a jurisdiction.
- *Multidisciplinary team*: Working with multiple departments, such as diagnostic imaging, pathology, medical oncology, and research.
- *Patient navigation*: A dedicated role to help facilitate the navigation for patients across the cancer journey – helps the patient through testing, appointments, health literacy, etc.
- *Rapid referral pathway*: Provides urgent access to specialists and/or diagnostic services for patients.
- *Remote or rural populations*: This refers to populations that may live in non-urban areas. They often do not have access to the same services as those who reside in more urban areas.
- *Standardized care pathway*: Sets expectations for cancer care based on evidence and shares information about how to provide and what care to provide at each point of diagnosis, treatment, and survivorship. Initiative is often integrated into the current health system.
- *Support for primary care providers*: Initiative focusing on educating and supporting primary care providers on care pathways and how to care for individuals presenting with potential or confirmed cancer symptoms.
- *Target or benchmark*: A figure used as a goal by jurisdictions to measure progress towards the desired outcome of an initiative.
- *Technology to support diagnosis process*: Technological innovations to enhance efficiency of initiatives.

Appendix 7: Summary of the characteristics of the included published articles that reported data on ineffective interventions

Interventions	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Interventions to enhance diagnostic services	Agnarsdottir 2019	Sweden (Uppsala)	Cross-sectional (2016-2018)	Skin (Adult) [286]	Reporting time	The reporting time increased from 18 to 31 days for the non-priority cases and from 15 to 25 days for all cases with invasive melanomas (Ineffective)
	McCutchan 2020	UK (Wales)	Before-and-After (2016)	Lung (Mixed age) [1011 (pre-campaign); 1013 (post-campaign)]	Urgent suspected referrals to specialist	There was no statistically significant change in urgent suspected cancer referrals (p = 0.82) in routes to diagnosis (Ineffective)
Multidisciplinary team	Largey 2020	Australia (Victoria)	Before-and-After (2016-2017)	Lung (Adult) [429]	Time interval from referral to first specialist appointment	Referral to first specialist appointment interval was reduced in the post intervention period from median (IQR) 6 (0-15) to 4 (1-10) days, with no significant trend (p=0.962) (Ineffective)
	Thalanayar Muthukrishnan 2020	USA (Cleveland)	Case-Control (2015-2017)	Lung (NR) [161]	Time interval from suspicion to diagnosis	The mean time intervals for imaging to staging (with standard deviations) were 65 days in controls (SD=42.67) and 75 days (SD=58.27) in tumor board cases (p=0.39) (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Rapid referral pathway	Fallon 2019	UK (Luton)	Case-Control (2015-2017)	Gastrointestinal (Adult) [509 (148 UGI; 361 LGI)]	Stage of malignancy at time of presentation	Two weeks wait referral did not achieve an earlier diagnosis compared with non-2 week wait routes of referral in upper gastrointestinal ($\chi 2(3)=2.6$, p=0.458) and lower gastrointestinal ($\chi 2(3)=0.884$, p=0.829) malignancies (Ineffective)
	Jefferson 2019	UK	Cross-sectional (2016-2018)	Multiple (Adult) [24]	Factors affecting patients' non-	The following were identified: system flaws; GP difficulties with booking

		(A Northern English city)			attendance following referral	appointments; patient difficulties with navigating the appointment system, patients leading 'difficult lives'; and patients' expectations of the referral, informed by their beliefs, circumstances, priorities, and the perceived prognosis (Ineffective)
	Kassirian 2020	Canada (London, Ontario)	Cross-sectional (2017-2018)	Ear, Nose and Throat (Adult) [102]	Time from presentation to appointment at the multi-disciplinary clinic	The average time for patients to have their first appointment was 15.1 months, consisting of 3.9 months for patients to see a health care provider for the first time since symptom onset and 10.7 months from first appointment to being seen at the clinic – representing significant delays (Ineffective)
	Neal 2017	UK (Wales; Yorkshire)	RCT (2012-2015)	Lung (Adult) [255]	Anxiety and depression scores	There was no evidence of a difference in post-randomisation anxiety scores between trial arms (median (IQR): 6 (3–8) in control vs 5 (3–9) in intervention, z=0.32; P=0.75) (Ineffective)
	Scott 2020	UK (Countrywide)	Case-Control (2009-2011)	Multiple (Mixed age) [10314]	Cancer occurrence 5 years after negative diagnosis	4.0% for those referred via pathway and 2.1% for those routinely referred (Ineffective)
	Talwar 2020	UK (Merseyside)	Cross-sectional (2017-2019)	Head and Neck (NR) [113]	Time from referral to being seen in hospital	The time taken from referral to being seen in hospital was a median (IQR) of 10 (6–13) days (range 1–28 days) with 11/110 (10%) exceeding 14 days (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Standardized care pathway	Almuammar 2019	Saudi Arabia (Countrywide)	Cross-sectional (2010-2012)	Multiple (Adult) [20]	Patient satisfaction with GP in the pathway	Patients felt that GPs did not listen to them, and were likely to undermine the role of GPs as active practitioners in healthcare provision (Ineffective)
	Gardner 2020	UK (Edinburgh)	Case-Control (2016-2018)	Ear, Nose and Throat	Time from referral to diagnosis	Patients referred by GP on the 'urgent suspicion of cancer' pathway were seen more quickly than those referred

				(Mixed age) [62]		routinely were. However, these differences were not significant (Ineffective)
	Iachina 2017	Denmark (Countrywide)	Case-Control (2008-2012)	Lung (Adult) [11273]	Time from referral to end of primary investigation	Time from referral to the end of primary investigation did not significantly change (1.00 (0.93;1.08)) (Ineffective)
	Jensen 2017	Denmark (Countrywide)	Case-Control (2004-2010)	Multiple (Adult) [7725]	Mortality	When comparing pathway-referred patients against non-pathway-referred patients, non-significant lower excess mortality was observed among the pathway referred (excess hazard ratios = 0.86 (95% CI: 0.73;1.01) (Ineffective)
	Price 2020	UK (National)	Cross-sectional (2006-2017)	Multiple (Adult) [83935]	Diagnostic interval	Median New-NICE values were consistently longer (99, 40–212 in 2006 vs 103, 42–236 days in 2017) than Old-NICE values across all cancers (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Support for primary care providers	Evans 2018	UK (Oxfordshire)	Cross-sectional (2016-2017)	Multiple (Adult) [NR]	GP perspectives on safety netting	GPs revealed uncertainty about which aspects of clinical practice were considered safety netting (Ineffective)
	Kidney 2017	UK (Urban West Midlands)	Cross-sectional (2014)	Gastrointestinal (Adult) [NR]	Barriers for referral	A desire to avoid over-referral, lack of knowledge of guidelines, and the use of individually derived decision rules for further investigation or referral of symptoms (Ineffective)
	Zienius 2019	UK (Scotland)	Cross-sectional (2010-2015)	Brain (Adult) [2938]	Predictive value of referral guidelines for imaging where a tumour is suspected	With symptom-based referral guidelines, primary care doctors can identify patients with a 3% positive predictive value (Ineffective)
	Di Girolamo 2018	UK (England)	Cross-sectional (2009-2013)	Multiple (Mixed age) [360643 (CRC 164890, lung	1-year survival of patients	For 31-day and 62-day targets survival was worse for those for whom the targets were and were not met (Ineffective)

				171208, ovarian 24545)]		
Target or benchmark for wait times	Brian 2017	New Zealand (Hamilton)	Before-and-After (2016)	Skin (Adult) [143]	Time to diagnosis	Compliance with recommended time intervals was poor for patients referred with skin lesions suspicious for melanoma; from referral to diagnostic skin biopsy, compliance was 17.6% (Ineffective)
	Venchairutti 2016	Australia (New South Wales)	Case-Control (2008-2013)	Multiple (Adult) [224]	Time from symptom onset to diagnosis	Regional/remote patients had a longer interval from symptom onset to diagnosis (median 5.4 months [IQR 9.2 months]) compared with metropolitan patients (median 2.1 months [IQR 4.3 months]) (P = 0.002) (Ineffective)
Interventions	**Article**	**Study country (Region)**	**Study type (Study years)**	**Cancer type (Population) [Sample size]**	**Assessment metric**	**Result**
Technology to support diagnosis process	Chung 2020	Netherlands (Amsterdam; Rotterdam)	Cross-sectional (2017)	Skin (Adult) [125]	Risk assessment performance	The inter-observer agreement between the ratings of the automated risk assessment and the dermatologist was poor (Ineffective)
	Lau 2018	UK (West Midlands and Berkshire)	Case-Control (2009-2013)	Multiple (Adult) [1005]	False-negative rate	A sensitivity of 31% and specificity of 92% (Ineffective)
	Pannebakker 2019	UK (NR)	Cross-sectional (2016-2017)	Skin (Adult) [14]	Patient perspectives on implementation and usefulness	No patients were aware that the electronic clinical decision support had been used during their consultation (Ineffective)
	Walter 2020	UK (Eastern England)	RCT (2016-2017)	Skin (Adult) [238]	Time between first noticing a change and consultation	There were no statistically significant differences between trial groups on any of the secondary outcome measures (Ineffective)

CRC = colorectal cancer; GP = general practitioner; LGI = upper gastrointestinal; NICE = National Institute for Health and Care Excellence; NR = not reported; RCT = randomized controlled trial; UGI = upper gastrointestinal; UK = United Kingdom; USA = United States of America; IQR = interquartile range

Appendix 8: Summary of the characteristics of the included published articles that reported data on remote or rural populations

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Chavarri-Guerra 2019	Mexico (Mexico City)	Before-and-After (2016-2017)	Multiple (Adult) [70]	Feasibility of patient navigation	All patients were from an under-served population. 91% of patients successfully obtained appointments at cancer centers in <3 months.
Emery 2017	Australia (Western Australia)	RCT (2011-2013)	Multiple (Adult) [1358]	Time to diagnosis	All patients were from a rural population. There were no significant differences on the time to diagnosis with and without intervention.
Murchie 2020	UK (Scotland; England)	Cross-sectional (2017)	Multiple (Mixed age) [1314]	Time from presentation in primary care to diagnosis	The median primary care interval was 5 days (IQR 0-23 days) and median diagnostic interval was 30 days (IQR 13-68). Diagnostic intervals were longer in the most remote patients.
Venchairutti 2016	Australia (New South Wales)	Case-Control (2008-2013)	Multiple (Adult) [224]	Time from symptom onset to diagnosis	Regional/remote patients had a longer interval from symptom onset to diagnosis (median 5.4 months [IQR 9.2 months]) compared with metropolitan patients (median 2.1 months [IQR 4.3 months]) (P = 0.002).
Yeşiler 2020	Turkey (Ankara)	Cross-sectional (2010-2011)	Lung (Adult) [122]	Delay in diagnosis times	No significant difference in the mean duration from symptom onset to pathological diagnosis. No significant differences were identified based on patient residence.

UK = United Kingdom; IQR = interquartile range

Appendix 9: Summary of performance metrics to measure improvements in suspicion to diagnosis phase

Intervention Type	Performance Metric
Centralized or coordinated diagnostic service	• Time from presentation in primary care to diagnosis • Time from referral from primary care to specialist consultation • Time from first abnormal image to biopsy
Interventions to enhance diagnostic services	• Time from referral from primary care to specialist consultation • Time from initial specialist consultation to diagnosis • Time from initial specialist consultation to biopsy • Time from first abnormal image to biopsy • Time from presentation in primary care to biopsy • Total diagnostic interval • Turnaround time for diagnosis following histology • Number of urgent referrals to specialist • Cancer detection rate • Patient survival
Multidisciplinary team	• Time from referral from primary care to specialist consultation • Time from first abnormal image to diagnosis
Patient navigation	• Waiting times from the point of referral from primary care to initial specialist assessment • Feasibility of program/process • Delays in diagnostic resolutions

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.	4-5
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.	7-8
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.	8-9
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.	9
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.	10-11
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.	10
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix 2 - 4
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	10-11
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.	11-12
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Appendix 6
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).	Not applicable

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	11-12
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.	Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Table 1
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not applicable
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.	14-24
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	13-24
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.	25-27
Limitations	20	Discuss the limitations of the scoping review process.	27
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.	28
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.	2

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).

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.