Improving Early Cancer Diagnosis Following Clinical Presentation of Symptomatic Patients

A Scoping Review

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Third-Party Materials

General Disclaimer

Summary of Findings

- This review included 88 published articles and 16 unpublished articles (grey literature).
- Most of the publications are from the United Kingdom; about half of all identified published literature and 83% of the identified unpublished literature.
- Of the studied interventions, rapid referral pathways and technology for streamlining the diagnosis process were the most reported.
- There was scant reporting on interventions for underserved populations and none focused specifically on interventions for indigenous populations.
- Most of the interventions was evaluated in lung cancer patient populations.
- Methodological approaches varied significantly across publications, with diverse study designs (mostly observational) and approaches to outcome assessment.
- Varied interventions were identified including local, regional and national centralized/coordinated diagnostic services, interventions in diagnostic services, multidisciplinary team development, patient navigation approaches, rapid referral pathways, standardized care pathways, support for primary care providers, targets or benchmarks for wait times, technologies to support the diagnosis process, and insights regarding variations between remote/rural and urban populations.
- Performance metrics to measure improvements in the suspicion to diagnosis phase are mainly intervention-dependent; however, time from presentation to diagnosis and from referral to specialist consultation appear to be the most consistent metrics across many interventions.
- Performance metrics to measure patients' experience mainly centered on patient-reported satisfaction and quality of life.
- None of the performance metrics measured if an intervention achieved health equity.
- A common theme among the effective interventions (especially arising from Canada) involved multidisciplinary cooperation and a nurse navigator.
- Effectiveness, or ineffectiveness, of an intervention was based solely on the reported outcome by study authors.
- Interventions were mostly complex and organization specific. As such it is not possible to specify one approach alone that was effective within an intervention.
- 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 despite this information being provided.
- There is little evidence to suggest that patients were involved in the design, development, and implementation of interventions.

Introduction

Cancer is the second leading cause of death globally, with about 1 in 6 deaths attributable to the disease.[1] In 2020, it is estimated 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 it can occur at any age, the risk of cancer 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. Significant improvements can be made in the lives of cancer patients with timely symptomatic presentation and diagnosis. Moreover, many cancers have a high chance of effective treatment 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 timely symptomatic presentation, cancer diagnosis often occurs at more advanced stages of the disease; when treatment may be less effective. Early cancer diagnosis of symptomatic patients entails carefully planned, well integrated, culturally sensitive and accessible clinical evaluation and diagnostic services,[4] designed to reduce delays in and barriers to, diagnosis and treatment, allowing patients to be diagnosed earlier on as the disease develops and to access 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 varied levels of successes. Knowledge of these available interventions, and how well they have worked, is necessary to inform the development, implementation, and evaluation of evidence-based programs to improve early cancer diagnosis of symptomatic patients in Canada.

Objectives

To summarize contemporary interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals.

Methods

We undertook a scoping review following the Joanna Briggs Institute's methodological framework 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. Further, we report our findings in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping reviews (PRISMA-ScR) guidelines.[6]

Review Questions

Key Question 1: Are there practice guidelines, care pathways or other initiatives such as benchmarks or targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and patient navigation strategies to streamline and enhance accurate and timely cancer diagnosis in symptomatic individuals?

- Were patients involved in the design, development and/or implementation of these initiatives?
- Were primary care providers (physicians and nurses) involved in the design, development and/or implementation of these initiatives?

Key Question 2: What are the leading innovative interventions (for example, technological) or approaches to seamless (minimally disruptive) care of symptomatic individuals in the pre-cancer diagnosis phase?

- 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?
- Were patients involved in the design, development and/or implementation of these interventions?

Key Question 3: What are the identified performance metrics that can be used to measure improvements in the suspicion to diagnosis phase of cancer?

- Are there specific metrics used to measure the patient experience?
- Is there evidence on sustainability of the model?

Key Question 4: What are the key points of care as patients navigate the health system, from initial symptomatic suspicion to diagnosis of cancer?

Key Question 5: Have specific considerations been applied to underserved populations, including Indigenous and rural or remote populations?

Literature 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 CINAHL (EbscoHOST) and Psycinfo (Ovid) bibliographic databases. The search strategy for each of the databases is presented in the appendices (Appendix 1 - 3). In addition to searching bibliographic databases, we searched websites of relevant organizations and professional bodies (Appendix 4).

Study selection
We included published (peer reviewed) and unpublished (grey literature) articles in the English language from January 2017 to January 2021 that answered any of the review questions, with the focus being on articles for comparative studies. All retrieved citations from the literature search were imported and manage in EndNote software, 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 (Figure 1).

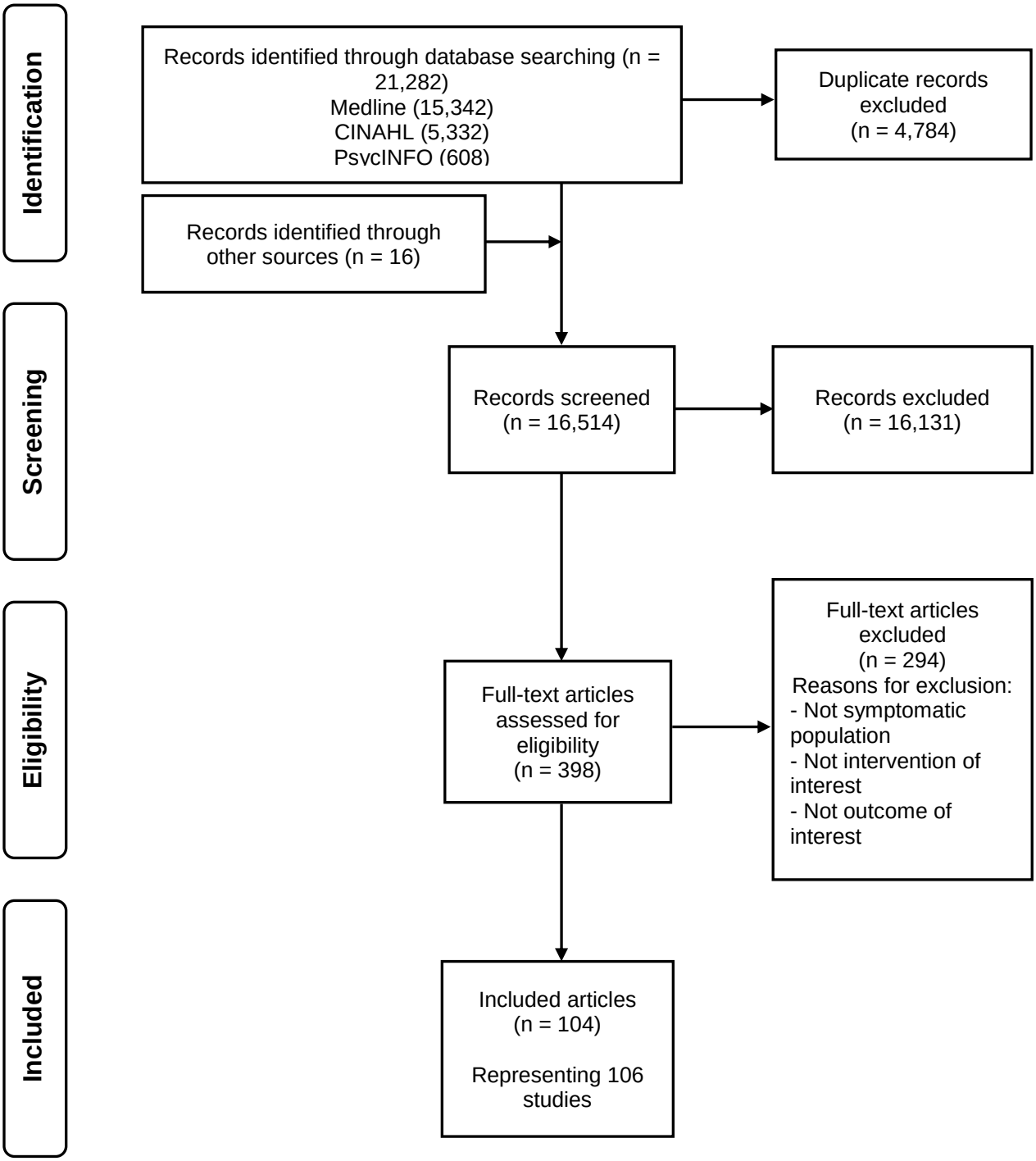
Data extraction
One reviewer extracted relevant data from the included articles in an Excel workbook and another reviewer independently checked the extracted data for errors. Disagreements between the reviewers were resolved through discussion or involvement of a third reviewer.

Data analysis: Characteristics of the included published articles are presented in a tabular form and descriptive analysis is reported graphically and narratively. Characteristics of the included unpublished articles are reported narratively only (not available in the table of characteristics). Relevant findings from the review of both the published and unpublished articles are summarized separately, narratively, by review question, focusing on the interventions related to each question. Interventions are grouped under the following groups:

- 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 share 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.

Results

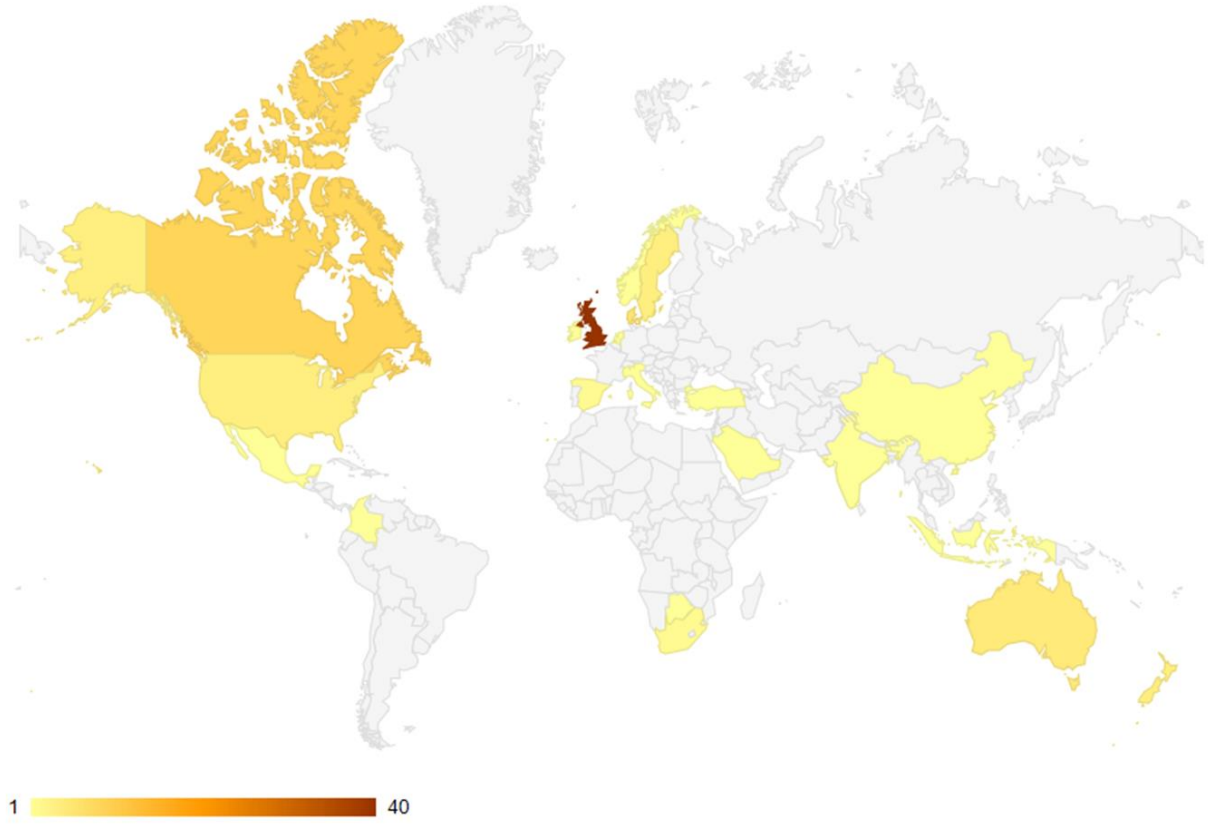
Out of a total of 21,298 retrieved citations, 88 published articles[8-95] and 16 unpublished (grey literature) articles (representing 18 different reports)[96-111] met the inclusion criteria. The articles selection process is detailed below (**Figure 1**).



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. The published articles are mapped geographically below (**Figure 2**). Of the 18 unpublished articles, about 83% were from the UK, 11% from Canada and 6% from the United States of America (USA).

Figure 1: *Geographical mapping of the included articles*



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. On the other hand, 89% (n = 16) of the unpublished articles were for before-and-after studies and the rest (n = 2) were for cross-sectional studies.

Figure 3 is the distribution of the cancer types reported by published articles. About 30% (n = 26) of the published articles reported on multiple cancer types while the rest reported on specific cancer types, of which lung cancer was the most reported (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 2: *Cancer types reported by the articles*

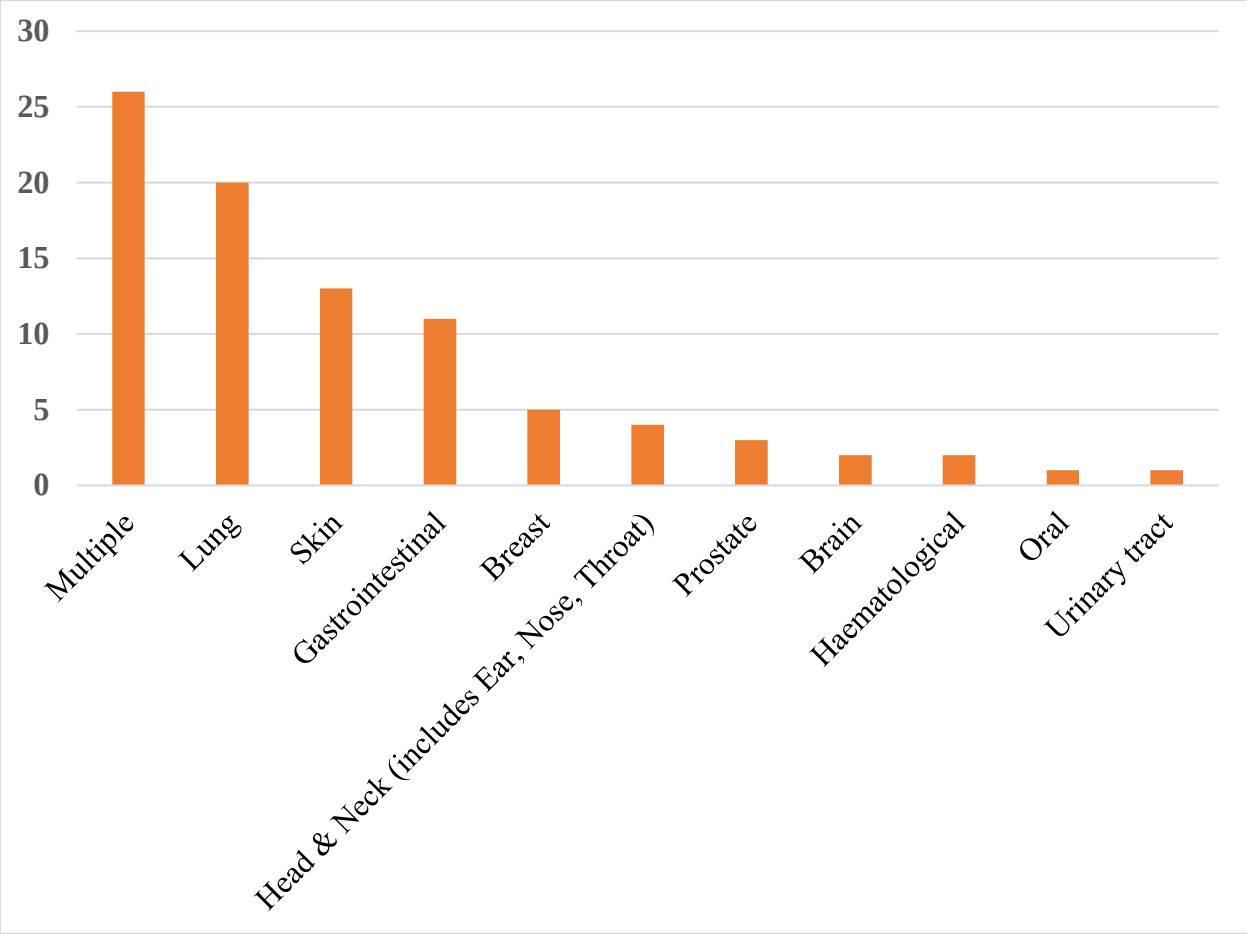
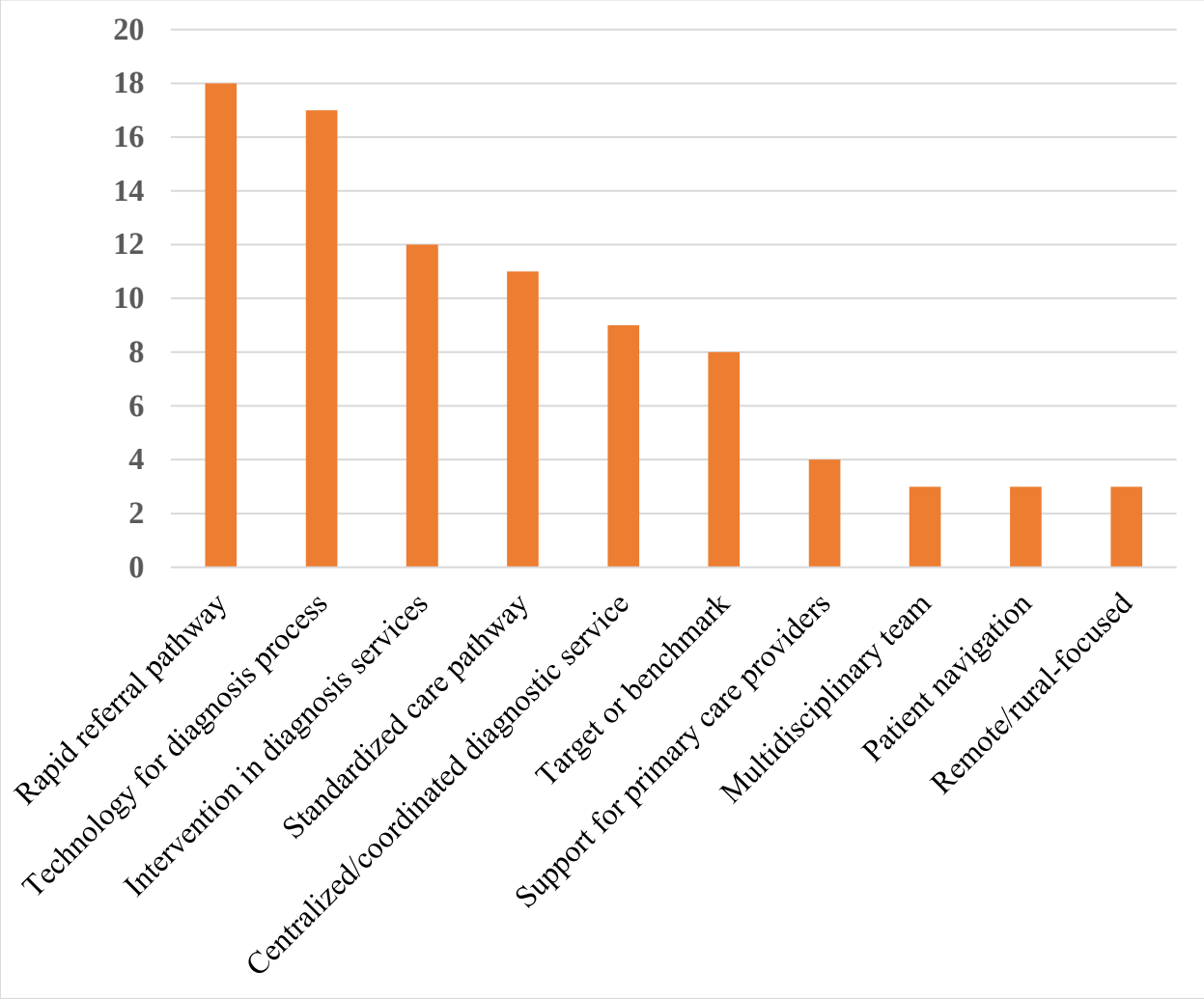


Figure 4 is the distribution of intervention types across the published articles. Nearly 20% of the published articles were on rapid referral pathway interventions while <1% each were on multidisciplinary team, patient navigation, and remote/rural-focused interventions. Of the unpublished articles, half 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 in diagnostic services.

Figure 3: *Intervention types reported by the articles*



Most of the published articles (about 94%; n = 83) reported a performance metric used to measure an improvement in the suspicion to diagnosis phase of cancer. About 83% (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 streamline and enhance accurate and timely cancer diagnosis. About 31% (n = 27) of the articles reported (not explicitly) on a key point of care as patients navigate the health system, from initial symptomatic suspicion to diagnosis of cancer. About 29% (n = 25) of the articles reported on a leading innovative intervention or approach to seamless care in the pre-cancer diagnosis phase while about 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 only the published articles are presented in **Table 1**.

Initiatives to streamline/enhance accurate and timely diagnosis

This review identified various initiatives to streamline/enhance accurate and timely cancer diagnosis. These were 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.

Table 1: Characteristics of the published articles

A) Effective interventions.

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Centralized or coordinated diagnostic service					
Christensen 2020[18]	Denmark (Odense)	Cross-sectional (2016-2017)	Lung (Adult) [20]	Patients' perspective, experiences, 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)
McKevitt 2018[53]	Canada (Vancouver)	Case-Control (2012)	Breast (NR) [176 (40 RABC; 136 TS - traditional system)]	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	The median time between the first health care visit and a breast cancer diagnosis was 28 days (IQR 13–58 days). Surprisingly, women whose initial reaction was denial of the breast symptom

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
				and date of diagnosis	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)
Interventions in 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 to better patient survival in all cancer cohorts (Effective)
Nixon 2020[62]	Canada (Ontario)	Case-Control (2015-2017)	Haemato-logical (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<.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 diagnostic	The intervention reduced the time to definitive diagnosis: mean difference = −13.26, 95% CI = −24.51 to −2.00, P=.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

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
					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 MRI (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<0.00) (Effective)
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)
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)

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
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]	Tumor detection rate	With guideline adherence, the brain tumour detection rate was 3-fold higher (36.0% vs 11.5%, p¼0.02) (Effective)
Creak 2020[23]	UK (Brighton; Sussex)	Cross-sectional (2015-2018)	Multiple (Adult) [258]	Time to diagnosis	Direct GP referrals are 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 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 of emergency diagnosis of cancer	A lower proportion of emergency diagnosis of cancer was found with higher 2 weeks wait referral and 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 positive experience (PR = 1.21 [95% CI: 1.11–1.30]) (Effective)

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
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)
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)
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=.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)
Target or benchmark for wait times					

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
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 of 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)
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 are 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	Time from referral to first appointment	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)

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
			referrals paired with 75 standard “Face to Face” controls)]	and diagnostic rates	
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 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 ranging 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)

B) Ineffective interventions.

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Cancer waiting time targets: support for primary care providers					
Di Girolamo 2018[25]	UK (England)	Cross-sectional (2009-2013)	Multiple (Mixed age) [360643 (CRC 164890, lung 171208, ovarian 24545)]	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)
Interventions in diagnostic services					
Agnarsdottir 2019[8]	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[51]	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[48]	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[83]	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) are 65 days in controls (SD=42.67) and 75 days (SD=58.27) in tumor board cases (p=0.39) (Ineffective)
Rapid referral pathway					
Fallon 2019[32]	UK (Luton)	Case-Control (2015-2017)	Gastrointestinal (Adult) [509 (148 UGI; 361 LGI)]	Stage of malignancy at time of presentation	2 weeks wait referral did not achieve an earlier diagnosis compared with non-2 week wait routes of referral in upper gastrointestinal ($\chi2(3)=2.6$, p=0.458) and lower gastrointestinal ($\chi2(3)=0.884$, p=0.829) malignancies (Ineffective)
Jefferson 2019[38]	UK (A Northern English city)	Cross-sectional (2016-2018)	Multiple (Adult) [24]	Factors affecting patients' non-attendance	Identified were system flaws; GP difficulties with booking appointments; patient difficulties with navigating the appointment system, patients leading 'difficult lives'; and patients' expectations of the referral, informed by their beliefs,

				following referral	circumstances, priorities, and the perceived prognosis (Ineffective)
Kassirian 2020[45]	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[59]	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[74]	UK (Countrywide)	Case-Control (2009-2011)	Multiple (Mixed age) [10314]	Cancer occurrence 5 years after among negative diagnosis	4.0% for those referred via pathway and 2.1% for those routinely referred (Ineffective)
Talwar 2020[82]	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)
Standardized care pathway					
Almuammar 2019[9]	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[33]	UK (Edinburgh)	Case-Control (2016-2018)	Ear, Nose and Throat (Mixed age) [62]	Time from referral to diagnosis	Patients referred by GP on the 'urgent suspicion of cancer' pathway were seen more quickly than those referred routinely were. However, these differences were not significant (Ineffective)
Iachina 2017[37]	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[39]	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 among the pathway referred (excess hazard ratios = 0.86 (95% CI: 0.73;1.01) (Ineffective)

Price 2020[68]	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 over all cancers (Ineffective)
Support for primary care providers					
Evans 2018[29]	UK (Oxfordshire)	Cross-sectional (2016-2017)	Multiple (Adult) [NR]	GP perspectives on safety netting	GPs revealed uncertainty about which aspects of clinical practice are considered safety netting (Ineffective)
Kidney 2017[46]	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[95]	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)
Target or benchmark for wait times					
Brian 2017[13]	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[86]	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)
Technology to support diagnosis process					
Chung 2020[19]	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[49]	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[64]	UK (NR)	Cross-sectional (2016-2017)	Skin (Adult) [14]	Patient perspectives on the implementation and usefulness	No patients were aware that the electronic clinical decision support had been used during their consultation (Ineffective)
Walter 2020[89]	UK (Eastern England)	RCT (2016-2017)	Skin (Adult) [238]	Time between first noticing a	There were no statistically significant differences between trial groups on any of the secondary outcome measures (Ineffective)

				change and consultation	

C) Effectiveness not applicable.

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Target or benchmark for wait times					
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, and it was difficult for patients to understand how the new standard could affect upon time progressing 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)

D) Remote or rural populations

Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
Chavarri-Guerra 2019[16]	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[28]	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[58]	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[86]	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[93]	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.

CRC = colorectal cancer; CT = computed tomography; FIT = faecal immunochemical testing; GP = general practitioner; HB = haemoglobin; LGI = upper gastrointestinal; NA = not applicable; NICE = National Institute for Health and Care Excellence; 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; UGI = upper gastrointestinal; UK = United Kingdom; USA = United States of America

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 were 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.

Effective approaches

- The rapid access to pulmonary investigation and diagnosis (RAPID) programme, a lung cancer pathway in Wythenshawe Hospital, Manchester, UK which offers next working day computed tomography (CT) following suspected lung cancer referral along with immediate 'hot' reporting of the CT by a specialist thoracic radiologist.[30] Prior to implementation of the pathway, the department conducted an investigation into the existing processes. An investigation into the referral pathway for general practitioner (GP) suspected lung cancer referrals revealed several inefficiencies. To achieve the objectives of the programme, a number of interventions were undertaken, including recruiting a pathway navigator to oversee the referral process and serve as the link between radiology, respiratory, booking centre and patient. The booking centre would contact the patient by phone on receipt of a referral and invite the patient to the CT department at 8am the following working day before the referral and patient details are handed over to the pathway navigator who then adds the patient to the appointments system for both CT and outpatient clinic.
- The Thoracic Triage Panel in a tertiary care centre in St. John's, Newfoundland, Canada,[21] a multidisciplinary centralized referral program, whose key components include nurse navigation whose role is to coordinate 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. Referral to the program begins when a plain film or CT study reported as concerning for lung cancer is identified and sent by the reporting radiologist and faxed to the program team for review.
- 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 clinic is staffed by a rotating pulmonary physician and nurse-clinician and operates twice a week. The nurse-clinician is responsible for monitoring the investigation progress, assisting with coordination of care, and providing patients with the necessary psychosocial support. At the first encounter, preference is on the invasive diagnostic procedure felt to have the best yield/risk ratio based on CT findings, with procedures that allow simultaneous diagnosis and staging favored.
- The improved respiratory fast track clinic (RFTC) in Northland district of New Zealand that comprises three clinic slots per week for those referred with a suspicion of lung cancer and aimed at providing allocated CT scans, two bronchoscopy slots and one for CT-guided biopsy.[91] This was modelled on observed distribution of biopsy methods in the standard clinic model. Patients were identified through the lung cancer multi-disciplinary meeting and clinic lists. The RFTC introduction was bi-phasic with staggered introduction of CT and then biopsy, to the first service appointment.
- 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] To gain knowledge

of patients' and relatives' perspectives on, experiences with, and expectations and quality assessment of the fast-track diagnostic pathway, and to further develop clinical management strategies of the diagnostic pathway based on user knowledge, a qualitative study was conducted, comprising participant observation and semi-structured interviews. A co-researcher group confirmed the main themes that resulted from the principal investigator's preliminary analysis of the data from the semi-structured interviews with patients and their relatives.

- The rapid access breast clinic in British Columbia, Canada that provided triple evaluation of patients with close collaboration between clinicians and radiologists, facilitated by clinical pathways and nurse navigation.[52,53] The clinic was established to offer a single site for coordinated clinical and radiological assessment of breast problems, and followed the guidelines for breast centers as recommended by the European Society of Mastology (EUSOMA). Patients were referred to the clinic with either an abnormal screening mammogram through the screening mammography program at the hospital or just by their family physician for assessment of a breast symptom. The development of the clinic in conjunction with the radiology department created a unique situation in which the breast surgeons saw patients managed by two separate diagnostic pathways.
- The diagnostic assessment units in Ontario, Canada, focusing on diagnosis at a dedicated breast assessment unit.[42] These units are made up of breast assessment affiliates, designed partly to improve the chance of a timely diagnosis, and structured to provide diagnostic services by a multidisciplinary team that includes a nurse navigator, and breast assessment centres designed to expedite the diagnostic process.
- 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 a 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, established to improve access to coordinated, high-quality, team-based care for women with a breast concern, with the aim of reducing wait time between abnormal diagnostic mammogram finding to biopsy from 26 to 7 days (7-day ACCESS goal). The plan to achieve this goal is to schedule patients for a surgical consult within 2 days and a biopsy within 5 days after the surgical consult. A program team was established to meet monthly and coordinate plans for meeting the project goals, to improve accuracy and early detection, and to reduce callback and error rates for exams.

Ineffective approaches

None of the identified services were found to be ineffective.

Interventions in diagnostic services

Twelve published articles on interventions in 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.

Effective approaches

The identified interventions were as follows:

- The rerouting of diagnoses from emergency presentation to general practice referral in England, UK, aimed at reducing the number of emergency diagnoses and associated mortality risk and producing benefits to patients against modest additional costs to the National Health System.[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] This service taps into an individual's perception of their life in the context of their culture, value systems, and life goals, expectations, standards and concerns. Weekly advertising publicised a roadshow mobile location for the intervention in high streets and shopping centres, and specialist nurses offered simple health measurements, private conversations and health messages, to increase cancer awareness and signpost individuals to a GP, where appropriate.
- The mandatory primary care access to faecal immunochemical testing (FIT) in Nottingham, UK, integrated with the two week wait pathway, aimed at improving gastrointestinal cancer diagnosis rather than relying on age and symptoms alone.[15] In this intervention, GPs are able to access the FIT via a computerized requesting system commonly used for diagnostic tests GPs, but are advised to avoid FIT in patients with overt rectal bleeding or a palpable rectal mass. GPs can request FIT independently and follow up on the result, as they would do with any other test. The GP receive notification on each FIT result with clear guidance on the interpretation of results and guidance on subsequent actions. GPs are also able to submit a rapid pathway referral form to secondary care at the same time as requesting a FIT (secondary pathway).
- 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 key touchpoints were referral review and nurse navigator calls to patients for intake assessments (utilizing a tracking system), appointments for image-guided biopsy time, and clinics availability. The diagnostic imaging process was streamlined to meet and align with patient needs to enable multiple same-day procedures/testing to both reduce wait time and improve patient experience.
- 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 clinic arrangement

included a 0.20 full-time equivalent nurse practitioner commitment, surgical and interventional radiology engagement, and provision of 2 hours of dedicated operating room time weekly for excisional lymph node biopsies. Criteria for referral to the clinic are lymphadenopathy based upon clinical assessment or imaging, biopsy results suspicious for lymphoma, or peripheral blood abnormalities. Referral to surgical services for consideration of excisional lymph node biopsy or radiology for image-guided core biopsy requested based on location and size of lymphadenopathy.

- The expedited one-stop prostate cancer diagnosis using multi-parametric magnetic resonance imaging (mpMRI) and same-day trans-rectal ultrasound fusion-guided prostate biopsy (TRUS-PBx) in a health institution (name not reported) in the USA, aimed at expediting prostate cancer diagnosis.[81] A protocol for the one-stop diagnosis included as follows: (1) the radiology team informed of patients ahead of time; (2) mpMRI acquisition followed by stat-expedited reading of the mpMRI; (3) MRI/TRUS-PBx performed within 3 hours after mpMRI, to allow for adequate imaging processing and interpretation of mpMRI.
- The Swedish Diagnostic Center at the Central Hospital of Kristianstad, Sweden, introduced as a separate outpatient unit within the Department of Internal Medicine, and implemented to expedite diagnostics.[78] The Centre was staffed with a half-time physician specialized in internal medicine and family medicine, a full-time nurse, and a full-time medical secretary. Patients in primary care that met one or more of the referral criteria, without focal symptoms, were offered an appointment with a family physician within two to three working days after their first contact with the center. If focal symptoms or signs of specific disease were found during the diagnostic workup in primary care, the patients were referred to a respective medical specialist or standardized care pathway.
- The Partners for Cancer Care and Prevention action plan in Cali, Columbia, aimed at improving access to coordinated program of screening and early diagnosis of breast and cervical cancers in three health care centers that serve subsidized populations by supporting these centers with the implementation of a comprehensive cancer program.[73] The program included a patient navigation program that acts as a bridge between the patient and health care system, with patient navigators being professionals trained in health care or health-associated fields such as nursing, provision of technology for early diagnosis, improved medical education, and community education.
- The dermatology-led quality improvement initiatives in Gaborone, Botswana, aimed at improving multispecialty care coordination.[92] The initiatives were developed in collaboration with dermatology, oncology, and pathology departments at Princess Marina Hospital, University of Botswana, and University of Pennsylvania and the National Health Laboratory Gaborone, and involved organization and implementation of a workflow for dermatology clinic and dermatopathology. A newly employed dermatologist (the only available in the hospital) was responsible for the organization, implementation, and evaluation of the workflow.
- 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] PERANTARA consists of health education and psychoeducation and uses a narrative strategy, which involves the use of testimonials and storytelling, a strategy known to be acceptable for patients with low health literacy for communication of breast cancer-related information. A combination of printed and audio-visual health education and psychoeducation materials are used.

In addition to the above, one unpublished article on the Accelerate, Coordinate, Evaluate (ACE) programme 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. Initiated in June 2014 as a 3-year National Health Services (NHS) England initiative, supported by Cancer Research UK and Macmillan Cancer Support, with an organized team of staff. The aim of the ACE is to address the NHS outcome of preventing premature deaths, as well as improving overall patient experience along the diagnostic pathway. Among innovative ideas from the ACE is a new electronic referral system from GPs to radiologists, enabling triage advice on the most suitable imaging for a patient with suspected cancer. Other ideas include whether community pharmacies could help diagnose cancer earlier, given their accessibility, opening hours and familiarity with the local population, as well as establishing the skills and knowledge pharmacy staff need to perform such activities, and how to organise training for them. Another of the ACE's ideas was a one-stop diagnostic pathway for patients with non-specific but concerning symptoms, an approach incorporating a multidisciplinary diagnostic centre. The ACE programme was shown to be effective.

Ineffective approaches

The identified interventions were as follows:

- 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] According to the standardized care diagnostic clinical melanoma guidelines, physicians are expected to clearly write on the pathology requisition form that the clinical diagnosis is melanoma, or highly suspected melanoma, and the diagnostic pathway should not be used for ruling out melanoma of diagnosing other skin malignancies. The idea is to treat as priority resulting in shorter reporting time, but without any additional cost for the healthcare provider. Following implementation however, prolonged reporting times for invasive melanoma was observed, thought to be because of crowd-out effect of diagnostic samples, limited personnel resources, and inaccuracy of the clinical diagnosis.
- The four-week national lung cancer symptom awareness campaign in Wales, UK, aimed at increasing urgent suspected cancer referrals and clinical outcomes.[51] To inform the campaign, six focus groups were undertaken. After minor adaptations from the English campaign, the awareness campaign was launched with the strapline "*If you've had a cough for three weeks or more, tell your doctor*". A mass-media campaign on awareness, presentation behaviour and lung cancer outcomes rolled out, and while symptom awareness, presentation and GP-ordered chest X-rays increased during the campaign, this did not translate into increased urgent suspected cancer referrals or clinical outcomes changes.

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.

Effective approaches

The identified approach was as follows:

- The lung cancer strategist program, a thoracic surgeon-guided, multidisciplinary care program in hospitals in Massachusetts, USA, aimed at improving timeliness of lung cancer diagnosis and treatment.[66] While it was reported to expedite the time from suspicious finding to diagnosis, the report did not clearly detail the steps involved in their approach.

Ineffective approaches

The identified approaches were as follows:

- The pre-diagnosis multidisciplinary tumor board (MTB) discussions in a clinic in Cleveland, USA aimed at improving the timeliness of diagnostic evaluation in lung cancer.[83] This involved an MTB meeting every other week to discuss lung nodules and masses, and the participants included radiologists, medical and radiation oncologists, and pulmonary medicine physicians, with experience in endobronchial ultrasound. The group plus pathology and cardiothoracic surgery representatives conducted a separate tumor board to discuss previously diagnosed lung cancer for planning further steps on alternate weeks.
- The Victorian lung cancer service redesign project in Victoria, Australia, which involved multidisciplinary evaluation and solution committee meetings including patients, governance, administration, clinicians and health information services, and aimed at quality improvement collaborative on timeliness and management in lung cancer.[48] Local service gaps, drivers of variation and barriers to timeliness of care were identified using high-level process maps. Root cause analysis of factors affecting timeliness was conducted and targets prioritised for improvement. A series of education forums were conducted for all participants, with focus on collaborative learning, shared problem identification and solution sharing.

The article reported on the lengths and causes of delay until presentation to a high-volume head-and-neck cancer multi-disciplinary clinic at the London Regional Cancer Program in Southwestern Ontario, Canada, focusing on time from presentation to appointment at the clinic.

In addition to the above, nine unpublished articles from the UK were identified.[97,99-101,104,106,107,110] These included four articles regarding “straight to CT access” pathway, and articles on community pharmacy direct referral pathways for lung cancer and for chest x-ray, rapid colorectal diagnostic ‘straight to test’ pathway, and optometrist direct referral to neuroscience pathway. All but the chest x-ray pathway[107] were found to be effective.

Standardized care pathway

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 and 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 being also involving pediatric patients. The focus and metrics for assessment of the effectiveness of the pathways varied across the publications.

Effective approaches

The main identified pathways in the publications (all found to be effective) were as follows:

- The national diagnostic cancer pathway in Norway, which included new 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] Local adaptions were introduced to comply with the new recommendations. As established by the national pathway, the date of receiving referral letter at primary care to the first hospital consultation should not be more than 7 days and the date of first hospital consultation in pulmonary department to diagnosis and treatment decision should not be more than 21 days. Overall, time from referral from primary care to diagnosis should not be more than 28 days. In addition, delays must be reported.
- The standardized triage process in the Southeastern Ontario region, Canada was part of improvement initiatives aimed at reducing the time from referral to diagnosis, and included twice-weekly nurse–physician triage, triage to pathways with preordered staging tests and scheduling according to urgency, redirection and recommendations for inappropriate referrals, and new small nodule clinic.[57]
- The standardized diagnostic pathway for suspected urothelial cancer in Skane County, Sweden, a pathway initiated by primary healthcare providers and specialists, and comprises CT urography, urinary cytology and cystoscopy.[61] The pathway involves defined lead times and improved administration by a coordinator of all necessary measures and logistics, including prioritized or pre-booked appointments for cystoscopy and pre-booked CT–urography examinations. The coordinator had access to operating capacity assigned to patients diagnosed within the pathways.
- The early colonoscopy track (within 30 days from referral) in a tertiary referral hospital in Tenerife, Spain.[10] Implementation of the pathway involved instruction period consisting of organized talks in all the primary healthcare centers of the reference area, involving GPs, gastroenterologists, and surgeons working in primary care.
- The fast-track cancer care pathway in Denmark (national), with maximum acceptable time thresholds from referral to diagnosis and treatment and implemented to unify and accelerate the diagnosis and treatment of cancer.[37] The time from referral to end of primary investigation (time of diagnosis), must not be more than 28 days.

Ineffective approaches

None of the identified pathways were found to be ineffective.

In addition to the above, 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 (not detailed in article) and the Somerset Integrated Lung Cancer Pathway (not detailed in article), both focusing on expedited care. While the Canadian pathway was found to be effective, the pathway from the United Kingdom was not found to be 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 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.

Effective approaches

None of the identified supports for PCPs were found to be effective.

Ineffective approaches

The main identified support packages in the publications were as follows:

- 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]
- 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 pediatric patients. The focus and metrics for assessment of the effectiveness of the target or benchmarks varied across the publications, and all but two target/benchmarks[13,86] were found to be effective.

Effective approaches

The main identified targets or benchmarks in the publications were as follows:

- The 28-day faster diagnosis standard in the National Health Service England, UK, defined as the time at within which the patient is informed whether they do or do not have cancer.[71] This diagnostic standard facilitates a patient-centred and rapid approach to cancer diagnosis, and it is different from the urgent referrals (patients seen by a specialist within 2 weeks) because it extends further along the cancer care pathway to include the time it takes to confirm or rule out a diagnosis, rather than just the time to the first specialist appointment.
- 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]
- 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 established target is for the initial review of suspicious investigations to take place by GPs within 1 week of the test, with a referral to an appropriate specialist occurring at the same time. As established, specialists should conduct their initial consultation within 2 weeks of this referral.

Ineffective approaches

The main identified targets or benchmarks in the publications were as follows:

- 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] Even so, compliance to the intervention was poor (17.6%).

In addition to the above, two unpublished articles from Canada[103] and the UK[105] focusing on multiple cancers were identified. These were the "two 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 five weeks if no biopsy is required and ≥ 90% within seven weeks if a tissue biopsy is required.

Innovative interventions/approaches to seamless/enhanced care in the pre-diagnosis phase

This review identified seventeen published articles related to innovative technological interventions/approaches to seamless/enhanced care in 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 (10 on skin cancer, 3 on multiple cancer types, 2 on gastrointestinal cancers, and 1 each for oral, and head and neck cancers), and were on adult patient populations with two also involving pediatric patients. The innovations had little patient input in their design, development, and implementation. The focus and metrics for assessment of the effectiveness of these innovations varied across the publications.

The main identified innovations are as follows:

- The use of teledermatology in skin cancer diagnosis was reported by several publications and mostly involved taking of images, including dermoscopy by GPs and sending them for evaluation to specialized dermatologists.[36,60,77,87] This 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. Rather than writing referrals, the GP captures and sends a teledermoscopy image with clinical notes to any participating dermatologist and, once reviewed by a dermatologist, the teledermoscopy information could be used either to advise the GP of management options or to schedule the patient for an in-person dermatologist consultation.
- 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] This tool was based on a scoring system that determines the risk of head and neck cancer in a patient, and then calculate the percentage of risk of cancer in the patient and advice the GP whether or not to refer patient via the 2-week referral system. There was also the use of the Digitally Assembled Referral Toolkit (DART) for 2-week referral, accessible via a cloud-based template, and contains new referral forms native to GP clinical systems in the UK.[27] The forms contain mandatory fields for core clinical information, and this reduces the risk of incomplete forms and, consequent delay in assessment.
- 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, allowing 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] Prior to commencement of this electronic pathway, GPs were given guidance on recommendation of tests to book for each presenting symptom complex based on the NICE guidance. The online booking system, which GPs already used to order non-urgent tests, was used as the platform for referrals and test requests, and GPs could access radiology and endoscopic tests from the electronic system and had link to clinic appointments and further advice and guidance if required. The challenge was that after the launch of the electronic pathway, the NICE guidance for symptoms of colorectal cancer requiring urgent referral changed although the pathway was subsequently adapted appropriately.
- The use of electronic clinical decision support for melanoma in four general practices in the Southeast England, UK, which involved the use of an electronic-based 7-point checklist to

assess pigmented lesions.[64] This checklist consists of three major features (each scored 2 points): change in size, irregular shape, and irregular colour, and four minor features (each scored 1 point): diameter greater than 7mm, inflammation, oozing, and change in sensation. The paper version of the checklist has been validated tool as a diagnostic aid for pigmented skin lesions in general practice.

- The use of machine learning algorithms to classify patients referred on the 2-week wait pathway for suspected head and neck cancer in Newcastle, the UK into different diagnostic groups, albeit very broad ones: cancer and non-cancer.[55] This involved the assessment of varied machine learning techniques, with the performance of each presented using confusion matrix scores, a standard machine learning approach that provides all combinations of results classified into actual and predicted categories, thus, aiding determination of the most clinically useful technique.
- The use of nurse-led assessments to evaluate certain groups of patients suspected to have bowel cancer in England, the UK.[20] This was about making the 2-week wait pathway flexible. During the consultation, a thorough history is taken, and signs and symptoms are identified in addition to symptom onset, past medical and surgical history, medications, social and family background. The patient's abdomen and rectum are examination for rectal lesions. If a low rectal cancer or an anal squamous cell carcinoma is suspected, a consultant is called to the clinic to verify the diagnosis, and immediately request additional tests at the earliest opportunity.
- 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 to the above, 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 performance metrics depended largely on the type of intervention and the focus of publication. The main metrics are summarized in a tabular form below according to intervention type.

Table 2: *Performance metrics according to intervention assessed*

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 • 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
Interventions in diagnostic services	• 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 • Time from presentation in primary care to specialist appointment
Rapid referral pathway	• Time from referral from primary care to specialist appointment • Time from referral in primary care to diagnosis • Cancer detection rate • Stage of malignancy at time of presentation
Standardized care pathway	• Time from presentation in primary care to diagnosis • Time from referral from primary care to diagnosis • Survival rates
Support for primary care providers	• Barriers to referral • Physicians' perspective on safety netting
Target or benchmark	• Time from presentation in primary care to diagnosis
Innovative interventions/approaches to seamless/enhanced care	• Diagnostic test accuracy • Risk assessment performance • Proportion of lesions not requiring further in-person assessment • Time from referral from primary care to diagnosis

Performance metrics to measure patients' experience

- Quality of life
- Patients' perspectives, expectations, and attitudes
- Patients' satisfaction with process/technology/waiting times/physicians
- Hospital anxiety and depression scores

Key points of care during navigation of the health system, from symptom to diagnosis

Patient navigation focuses on identifying and reducing barriers to care that patients may experience as they navigate the health care system and may reduce delays and loss to follow-up after a suspicious test result. None of the literature reported explicitly on the key points of care during patients' navigation of the health system. However, based on a few reported frameworks and flow-charts for standardized care pathways, key points of care during navigation of the health system appears to vary from health system to health system and significant differences may exist between developing and developed health systems, and between health systems with publicly funded health care and those with non-publicly funded health care. In most of the developed health systems with publicly-funded health care such as the UK, Canada, Australia, New Zealand and several European countries, a patient's journey usually starts with presentation to a primary care physician (a general practitioner or a family physician) who may request for some medical tests based on suspicions of diseases, and from which a patient may be referred to a tertiary care physician (a specialist) for further assessment/work-up. Findings at this point determine the next point of care, which may be, referral back to the primary care provider (if further course of action is not needed) or referral to any needed specialist diagnostic unit for further work-up. Following this stage and, if a patient is assessed to need treatment, the next course of action is determined by the specialist physician or by a multidisciplinary team, and the primary care physician from whom referral was made to the specialist physician is usually notified of the diagnosis and the next course of action. The services of patient navigators may be utilized in some of these processes to help address patient needs, facilitate and coordinate their access to services, and to make the cancer journey a safe experience. Overall, slight differences in the entire process may exist between jurisdictions. There is no clear charting of patients' journey in most of the developing health systems, especially those without publicly funded health care. As such, key points of care during patients' navigation of these health systems are not clearly delineated.

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 patient residence as part of their model.[93] All of the publications were on multiple cancer types and adult populations although one included pediatric population. The specific considerations for underserved populations and the evidence regarding them are as follows:

- The publication from Scotland, the UK was 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 analysis focused on two key intervals in the diagnostic pathway: primary care interval (PCI) and diagnostic interval and comparison was made between remote and urban populations, with the key diagnostic intervals found to be longer for the most remote patients. Primary care physician-judged avoidable delays were found to be more frequent in remote patients. However, no solutions were offered as to how to bridge the gap in primary care and diagnostic intervals between remote and urban populations.
- The publication from New South Wales, Australia was 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] Regional/remote patients were found to experience longer times to

diagnosis. However, no solutions were offered as to how to bridge the gap between remote and metropolitan populations.

- The publication from Mexico City, Mexico was 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] A patient navigator assisted patients with scheduling, completing paperwork, obtaining results in a timely manner, transportation, and addressing other barriers to care. The primary outcome was the proportion of patients who obtained a specialized consultation within the first 3 months after enrollment, and 90% of the patients successfully obtained appointments in <3 months, suggesting immense success of the patient navigation program.
- The publication from Western Australia reported on improving rural cancer outcomes trial, a cluster-randomized controlled trial of a complex intervention to reduce time to diagnosis in rural cancer patients.[28] The aim was to measure 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. The community intervention included cancer symptom awareness campaign tailored for rural Australians, while the primary care physician intervention included resource card with symptom risk assessment charts and local cancer referral pathways implemented through multiple academic detailing visits. However, no effects were observed for both interventions.

Discussion

This scoping review of 88 published and 16 unpublished articles from January 2017 to January 2021 summarizes the evidence on contemporary 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, and implementation of innovative interventions/approaches to seamless/enhanced care in the 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 in 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 could be adapted to suit different health systems and jurisdictions around the world.

The interventions were mostly compositing of multiple interventions/ changes to the healthcare pathway. As such, no two interventions of the same kind were a mirror image of each other. This was true even when applied to the same cancer patient populations and in the same jurisdictions/ countries, including in 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 regards to outcome assessment. 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. A common theme among the effective centralized or coordinated diagnostic services, interventions in diagnostic services, patient navigation approaches, and standardized care pathways is multidisciplinary cooperation and the involvement of a nurse navigator. This was observed mostly in Canada. None of the support packages for primary care providers (all educational and informational) was found to be effective; the identified common theme being a lack of awareness of referral guidelines and associated lack of knowledge of the primary care physicians despite the information being provided.

The implications of the findings from this scoping review is that it is difficult to determine a specific intervention, or stand-alone approach to an intervention that makes an intervention effective. 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.

Limitations and merits

The review findings answer important public health and health systems questions to inform evidence-based decision-making regarding improving accurate and timely cancer diagnosis among symptomatic individuals. 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 five years and only evidence from English-language bibliographic databases and organizational websites. As such, potentially eligible articles could have been missed.

The eligibility criteria for inclusion was 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 effectiveness of interventions as reported in this review 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.

Conclusion

The evidence suggests that interventions focused on improving accurate and timely cancer diagnosis among symptomatic individuals are active topics of research particularly among lung cancer patients, and that the UK is championing this area of research. While the themes of the studied interventions are similar, they 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. While many of the interventions could be adapted to suit different health systems and jurisdictions, emphasis should be on the context, and a clear evidence-based performance metric ought to be determined a priori for appropriate evaluation of effectiveness of an intervention. It is advised that the notion of a “one size fits all” be discouraged when designing, delivering and evaluating interventions.

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Appendices

Appendix 1: *MEDLINE (Ovid) search strategy*

1.	"early detection of cancer"/
2.	(cancer* or tumo?r* or neoplasm* or malignan* or metasta* or oncogen* or oncolog*).ti
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
4.	or/2-3
5.	1 or 4
6.	early diagnosis/ or delayed diagnosis/
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.
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.
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
10.	delay*.ti
11.	wait* time*.ti,ab.
12.	or/6-11
13.	4 and 12
14.	diagnos*.ti,ab,kf
15.	13 and (1 or 14)
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
17.	16 and 5
18.	15 or 17
19.	limit 18 to english language
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 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
22.	limit 21 to yr="2017 -Current"

Appendix 2: *CINAHL (EbscoHOST) search strategy*

1.	(MH "early detection of cancer")
2.	TI (cancer* OR tumo#r* OR neoplasm* OR malignan* OR metasta* OR oncogen* OR oncolog*)
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*)
4.	S2 OR S3
5.	S1 OR S4
6.	(MH "early diagnosis") OR (MH "diagnosis, delayed")
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"))
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*)))
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*))))
10.	TI delay*

11.	(TI (wait* N1 time*)) OR (AB (wait* N1 time*))
12.	S6 OR S7 OR S8 OR S9 OR S10 OR S11
13.	S4 AND S12
14.	(TI diagnos*) OR (AB diagnos*)
15.	S13 AND (S1 OR S14)
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*)
17.	S16 AND S5
18.	S15 OR S17
19.	S18 Limiters - English Language
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 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
22.	S21 Limiters - Published Date: 20170101-20201231

Appendix 3: *Psycinfo (Ovid) search strategy*

1.	cancer screening/
2.	(cancer* or tumo?r* or neoplasm* or malignan* or metasta* or oncogen* or oncolog*).ti
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
4.	or/2-3
5.	1 or 4
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.
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.
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
9.	delay*.ti
10.	wait* time*.ti,ab.
11.	or/6-10
12.	4 and 11
13.	diagnos*.ti,ab,id
14.	12 and (1 or 13)
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
16.	15 and 5
17.	14 or 16
18.	limit 17 to english language
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 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
21.	limit 20 to yr="2017 -Current"

Appendix 4: *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