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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-055488
Article Type:	Original research
Date Submitted by the Author:	13-Jul-2021
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Keywords:	ONCOLOGY, PREVENTIVE MEDICINE, PRIMARY CARE, PUBLIC HEALTH

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3 **1 Improving early cancer diagnosis following clinical presentation of symptomatic patients:**

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5 **2 A scoping review**

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27 36 **Funding:** This study was funded in part by the Canadian Partnership Against Cancer (the

28
29 37 Partnership) and the Canadian Institutes of Health Research (CIHR) under the Strategy for

30
31 38 Patient Oriented-Research (SPOR) initiative, through the SPOR Evidence Alliance. Andrea

32
33 39 Tricco is funded by a Tier 2 Canada Research Chair in Knowledge Synthesis.

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35 40

36
37 41 **Competing interests declaration:** All authors declare that they have no conflicts of interest: no

38
39 42 financial relationships with any organisations that might have an interest in the submitted work,

40
41 43 and no relationships or activities that could appear to have influenced the submitted work.

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45 45 **Patient consent:** Not applicable

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3 47 **Contributor and guarantor information:** Conceptualization (A Prashad, J Stiff, W Zarin, A
4 Tricco); Methodology (GN Okoli, A Prashad, J Stiff, W Zarin, A Tricco & AM Abou-Setta);
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10 50 Formal analysis (GN Okoli); Draft manuscript (GN Okoli & AM Abou-Setta); Final manuscript
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15
16 53 corresponding author (the manuscript's guarantor) attests that all listed authors meet authorship
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18 54 criteria and that no others meeting the criteria have been omitted.
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49 67 accurate, and transparent account of the study being reported; that no important aspects of the
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51 68 study have been omitted; and that any discrepancies from the study as planned have been
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53 69 explained.
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1
2
3 70 **Abstract**

4
5 71 **Objectives:** To summarize the current evidence regarding interventions for accurate and timely
6
7 72 cancer diagnosis among symptomatic individuals.

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9
10 73 **Design:** A scoping review following the Joanna Briggs Institute's (JBI's) methodological
11
12 74 framework for the conduct of scoping reviews and reported in accordance with the Preferred
13
14 75 Reporting Items for Systematic Reviews and Meta-analyses extension for scoping reviews
15
16 76 (PRISMA-ScR) checklist.

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19
20 77 **Data sources:** MEDLINE (Ovid), CINAHL (EBSCOhost) and PsycINFO (Ovid) bibliographic
21
22 78 databases, and websites of relevant organizations.

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24
25 79 **Methods:** Published (peer reviewed) and unpublished literature in the English language were
26
27 80 searched for from January 2017 to January 2021. Study participants were individuals of any age
28
29 81 presenting at clinics with symptoms indicative of cancer. Interventions included practice
30
31 82 guidelines, care pathways or other initiatives focused on achieving pre-defined benchmarks or
32
33 83 targets for wait times, streamlined or rapid cancer diagnostic services, multidisciplinary teams,
34
35 84 and patient navigation strategies. Outcomes included accuracy and timeliness of cancer
36
37 85 diagnosis. We summarized findings graphically and descriptively.

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42 86 **Results:** From 21,298 retrieved citations, 88 unique published (peer-reviewed) articles and 16
43
44 87 unique unpublished documents (grey literature on 18 study reports), met the eligibility for
45
46 88 inclusion. About half of the published literature and 83% of the unpublished literature were from
47
48 89 the United Kingdom. Most of the studies were on interventions in lung cancer patients. Rapid
49
50 90 referral pathways and technology for supporting and streamlining the cancer diagnosis process
51
52
53 91 were the most studied interventions. Interventions were mostly complex and organization-

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3 92 specific. Common themes among the effective interventions were multidisciplinary collaboration
4
5 93 and the use of a nurse navigator.
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7

8 94 **Conclusions:** Multidisciplinary cooperation and involvement of a nurse navigator may be unique
9
10 95 features to consider when designing, delivering, and evaluating interventions focused on
11
12 96 improving accurate and timely cancer diagnosis among symptomatic individuals. Future research
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14 97 should examine the effectiveness of the complex and organization-specific nature of the
15
16 98 interventions identified through this review.
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20 99
21
22 100 **Review protocol registration details:** Protocol submitted as an appendix.
23
24

25 101
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27 102 **Keywords:** Early cancer diagnosis; Symptomatic patients; Interventions; Scoping review
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3 103 **Strengths and limitations of this study**
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- 5 104 • A knowledge synthesis librarian developed the search strategy for this review and this
6
7 was peer reviewed by an independent knowledge synthesis librarian using the PRESS
8 105
9 checklist.
10 106
11
12 107 • The literature search was limited to evidence from the last 4 years and only evidence
13
14 from English-language publications and organizational websites.
15 108
16
17 109 • This review did not summarize effectiveness of interventions across cancer patient types
18
19 and regions.
20 110
21
22 111 • We adhered to known guidelines and standards in the conduct and reporting of the
23
24 review.
25 112
26
27 113 • In line with the JBI's guidance for the conduct of scoping reviews, we did not attempt to
28
29 evaluate the quality of the included studies or provide an assessment of the quality of the
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31 evidence.
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126 **Introduction**

127 Cancer is the second leading cause of death globally, with about 1 in 6 deaths attributable to the
128 disease.¹ It was estimated in 2020 that over 19 million new cases and about 10 million deaths
129 were attributable to cancer globally.² This rate is estimated to be over 28 million new cases by
130 2040.² High human development index (HDI) countries such as Canada will likely experience
131 the greatest increase in incidence in absolute cancer burden, with an estimated over 4 million
132 new cases more in 2040 compared with 2020.² This is mostly due to the growth and aging of the
133 population and increasing prevalence of cancer risk factors.² Estimates from Canada alone
134 suggest that every day 617 people in Canada will be diagnosed with cancer, with about 228 also
135 dying from the disease.³

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

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

1
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3 148 services should be designed to reduce delays in and barriers to diagnosis to allow detection at
4
5 149 earlier stages of the disease and commence treatment in a timely manner.
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7
8 150 There are various service-focused interventions to improve early cancer diagnosis of
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10 151 symptomatic patients. Interventions such as centralized or coordinated diagnostic services,
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12 152 multidisciplinary team development and support, patient navigational strategies and referral
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14 153 pathways, service targets or benchmarks for wait times, and technology to support diagnosis
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16 154 have been implemented with varying levels of success. Knowledge of the available interventions
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18 155 and how they have been implemented is necessary to inform the development, implementation,
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20 156 and evaluation of effective early cancer diagnosis initiatives.
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24 157

158 **Methods**

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

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

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

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

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181 *Search strategy*

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

191 *Study selection criteria and data extraction*

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

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

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3 204 from 2017 was because the Partnership had previously summarized prior evidence
4
5 205 (<https://bit.ly/3xlACsR>) and the present focus was on current interventions. Study participants
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8 206 were individuals of any age presenting at clinics with symptoms. Interventions included practice
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10 207 guidelines, care pathways or other initiatives focused on achieving pre-defined benchmarks or
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12 208 targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, and
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15 209 patient navigation strategies. Outcomes included accuracy and timeliness of cancer diagnosis.

16
17 210 All retrieved citations from the literature search were imported and managed in EndNote
18
19 211 (Version X9). One reviewer screened each citation for eligibility. Two reviewers independently
20
21 212 screened the full texts of relevant citations and reviewed the reference list of the included full-
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23 213 text articles for potentially relevant citations. Disagreements between the reviewers were
24
25
26 214 resolved through discussion or involvement of a third reviewer. The number of screened citations
27
28 215 and both the number and reason for exclusion of full-text articles were documented. Extraction
29
30 216 and charting of relevant data from the included articles was performed by one reviewer and
31
32
33 217 another reviewer independently checked the data for errors. Disagreements between the
34
35 218 reviewers were resolved through discussion or involvement of a third reviewer.

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40 220 ***Data synthesis and analysis***

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42 221 Characteristics of the included published articles are presented in a tabular form and descriptive
43
44 222 analysis is reported graphically and descriptively. Characteristics of the included unpublished
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46 223 articles are reported descriptively only. Relevant findings from the review of both published and
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49 224 unpublished articles are summarized separately and descriptively, by review question, focusing
50
51 225 on the interventions related to each question. Interventions are grouped as centralized or
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54 226 coordinated diagnostic service; interventions to enhance diagnostic services; multidisciplinary

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3 227 team; patient navigation; rapid referral pathway; remote or rural populations-focused;
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5 228 standardized care pathway; support for primary care providers; target or benchmark; and
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8 229 technology to support the diagnostic process. These interventions are defined in **Appendix 6**.

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10 230 Effectiveness of an intervention was determined based on relevant study results.
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14 232 ***Patient and public involvement***

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17 233 Involvement of patients or the public in this study was based on the Strategy for Patient
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19 234 Oriented-Research (SPOR) initiative.
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235 **Results**

236 Out of a total of 21,298 retrieved citations, 88 unique published articles⁸⁻⁹⁵ and 16 unique
237 unpublished (grey literature representing 18 different reports)⁹⁶⁻¹¹¹ met the inclusion criteria. The
238 article selection process is detailed below (**Figure 1**). Fifty-seven of the published articles were
239 from Europe, 14 articles from North America, 9 articles from Oceania, 3 articles each from
240 Africa and Asia, and one article each from the Middle East and South America. Almost half of
241 these articles (n = 40) were from the United Kingdom (UK) alone. A geographic map of
242 published articles is shown in **Figure 2**.

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

254 **Figure 4** shows the distribution of intervention types across the published articles. Nearly
255 20% of the published articles were on rapid referral pathway interventions while less than 1%
256 each were on multidisciplinary team, patient navigation, and remote/rural-focused interventions.
257 Of the unpublished articles, half reported on rapid referral pathway interventions, 11% each

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3 258 reported on standardized care pathway, target/ benchmark for wait times, and technology to
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5 259 support the diagnosis process, and 5.5% each reported on centralized or coordinated diagnostic
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7 260 service and interventions to enhance diagnostic services. Most of the published articles (94%; n
8
9 = 83) reported a performance metric used to measure an improvement in the suspicion to
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11 261 diagnosis phase of cancer.
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15 263 Eighty-three percent (n = 73) of the articles reported either a practice guideline, care
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17 264 pathway or an initiative such as benchmark/target for wait times, streamlined or rapid diagnostic
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19 265 service, multidisciplinary team development, and a patient navigation strategy to enhance
20
21 266 accurate and timely cancer diagnosis. Thirty-one percent (n = 27) of the articles reported (not
22
23 267 explicitly) on a key point of care as patients navigate the health system, from initial suspicion to
24
25 268 diagnosis of cancer. Twenty-nine percent (n = 25) of the articles reported on a leading innovative
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27 269 intervention or approach to seamless care in the pre-cancer diagnosis phase, while 4.5% (n = 4)
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29 270 of the articles reported on some form of consideration for underserved populations. Some of the
30
31 271 articles reported on two or more of the above. Details of relevant characteristics of the published
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33 272 articles are presented in **Table 1** (those reporting effective interventions) and **Appendix 7** (those
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35 273 reporting ineffective interventions) and **Appendix 8** (those focused on remote/and rural
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37 274 populations).
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44 276 **Initiatives to enhance accurate and timely cancer diagnosis**

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46 277 This review identified various initiatives to enhance accurate and timely cancer diagnosis. These
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48 278 were often designed, developed, and implemented often with the involvement of primary care
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50 279 providers (physicians and nurses), but not patients. These initiatives are grouped into related
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52 280 interventions and the evidence regarding each intervention is discussed below.
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282 *Centralized or coordinated diagnostic services*

283 Nine published articles on centralized or coordinated diagnostic services for adult lung cancer (n
284 = 5) and breast cancer (n = 4) patients were identified.^{18,21,30,31,42,52-54,91} Five were from
285 Canada,^{21,31,42,52,53} and there was one each from Denmark,¹⁸ New Zealand,⁹¹ South Africa,⁵⁴ and
286 the UK³⁰. The focus and metrics for assessment of the effectiveness of these diagnostic services
287 varied, but all were found to be effective. These include the rapid access to pulmonary
288 investigation and diagnosis (RAPID) program in Wythenshawe Hospital, Manchester, UK with
289 expedited (next working day) computed tomography (CT) and reporting in suspected lung cancer
290 cases,³⁰ and the Thoracic Triage Panel in a tertiary care centre in St. John's, Newfoundland,
291 Canada, a multidisciplinary centralized referral program, whose key components include a nurse
292 navigator who coordinates patient care and act as the contact person for patients and clinicians
293 involved in the program, weekly multidisciplinary (thoracic specialists) meetings, and regular
294 communications with the primary care provider.²¹ The diagnostic services also include the rapid
295 investigation clinic in a tertiary health centre in Montreal, Canada established to coordinate and
296 accelerate the workup of patients with suspected lung cancer,³¹ the improved respiratory fast
297 track clinic (RFTC) in Northland district of New Zealand that comprises reserved slots for CT
298 for those referred with a suspicion of lung cancer, bronchoscopy slots and CT-guided biopsy,⁹¹
299 and the Danish lung cancer package at the Center for Lung Cancer, Odense University Hospital,
300 Odense, Denmark, a fast-track diagnostic pathway in the hospital setting.¹⁸ Further, there was the
301 rapid access breast clinic in British Columbia, Canada that provides close collaboration between
302 clinicians and radiologists, facilitated by clinical pathways and nurse navigation,^{52,53} the
303 diagnostic assessment units in Ontario, Canada, focusing on diagnosis at a dedicated breast
304 assessment unit,⁴² and the breast clinic at a tertiary hospital in Western Cape Province of South

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3 305 Africa, an open-access one-stop diagnostic breast clinic where women may present with a letter
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5 306 from a primary level provider (nurse practitioner or doctor) and receive the same day clinical and
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7 307 cytological evaluation with referral to the combined breast clinic if the breast cytology is positive
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10 308 for malignancy.⁵⁴

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12 309 In addition to the above, one unpublished article was identified.¹¹¹ This was for the Breast
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14 310 ACCESS Project in Ohio, USA, which scheduled patients for a surgical consult within 2 days
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16 311 and a biopsy within 5 days after the surgical consult, with the aim of reducing wait times
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18 312 between abnormal diagnostic mammogram findings to biopsy from 26 to 7 days (7-day ACCESS
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20 313 goal).

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22 314

23 24 315 *Interventions to enhance diagnostic services*

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26 316 Twelve published articles on interventions to enhance diagnostic services were
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28 317 identified.^{8,15,22,50,51,62,73,75,76,78,81,92} These articles were focused on varied cancer types; four on
29
30 318 multiple cancers, two on lung cancer, two on skin cancer, and one each on breast,
31
32 319 gastrointestinal, haematological and prostate cancers. Four articles were from the UK,^{15,50,51,76}
33
34 320 two articles each from Canada^{22,62} and Sweden,^{8,78} and one article each from Botswana,⁹²
35
36 321 Columbia,⁷³ Indonesia,⁷⁵ and the USA.⁸¹ The focus and metrics for assessment of the
37
38 322 effectiveness of the interventions varied across the publications, and while most were effective,
39
40 323 one intervention for lung cancer and one intervention for skin cancer in the UK⁵¹ and Sweden⁸,
41
42 324 respectively, were ineffective. The effective interventions were reducing diagnosis through
43
44 325 emergency presentation by improving general practice referral in England, UK,⁵⁰ the guided
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46 326 personal quality of life (QoL) feedback intervention during the Cancer Research UK's North
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48 327 West regional summer roadshow in Manchester, UK, aimed at offering guided feedback about
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50 328 personal QoL to adults with potential cancer symptoms, living in deprived communities to

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3 329 promote help seeking in primary care among the communities,⁷⁶ the mandatory primary care
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5 330 access to faecal immunochemical testing (FIT) in Nottingham, UK, integrated with the 2-week
6
7 331 wait pathway, aimed at improving gastrointestinal cancer diagnosis rather than relying on age
8
9 332 and symptoms alone,¹⁵ the Stronach Regional Cancer Centre lung diagnostic assessment program
10
11 333 (DAP) at Southlake Regional Health Centre, Ontario, Canada, aimed at using learnings from a
12
13 334 Lean improvement event to provide coordinated, expedited care for all patients undergoing a
14
15 335 possible lung cancer diagnosis and to achieve/improve upon the provincial wait time target from
16
17 336 consultation to diagnosis for lung cancer patients,²² the nurse practitioner-led lymphoma rapid
18
19 337 diagnosis clinic in a tertiary care cancer center (Princess Margaret Cancer Centre, part of
20
21 338 University Health Network) in Ontario, Canada, aimed at reducing wait times for a definitive
22
23 339 diagnosis of lymphoma,⁶² the expedited one-stop prostate cancer diagnosis using advanced
24
25 340 imaging and biopsy techniques in a health institution (name not reported) in the USA, aimed at
26
27 341 expediting prostate cancer diagnosis.⁸¹ There were also the Swedish Diagnostic Center at the
28
29 342 Central Hospital of Kristianstad, Sweden, introduced as a separate outpatient unit within the
30
31 343 Department of Internal Medicine to expedite diagnostics,⁷⁸ the Partners for Cancer Care and
32
33 344 Prevention action plan in Cali, Columbia, aimed at improving access to a coordinated program of
34
35 345 screening and early diagnosis of breast and cervical cancers in three health care centers that serve
36
37 346 subsidized populations,⁷³ the dermatology-led quality improvement initiatives in Gaborone,
38
39 347 Botswana, aimed at improving multispecialty care coordination,⁹² and the culturally sensitive,
40
41 348 narrative self-help intervention named PERANTARA (PEngantar peRAwataN kesehaTAn
42
43 349 payudaRA [translated as introduction to breast health treatment]) across four hospitals in
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45 350 Bandung, West Java, Indonesia, aimed at reducing time to diagnosis in women with breast
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47 351 cancer symptoms.⁷⁵ In addition to the above, one unpublished article on the Accelerate,
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3 352 Coordinate, Evaluate (ACE) program in the UK was identified.⁹⁸ This program was an early
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5 353 cancer diagnosis initiative and focused on testing innovations that either identify individuals at
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8 354 high risk of cancer earlier or streamline diagnostic pathways.
9

10 355 The ineffective interventions were the standardized care diagnostic pathway at the
11
12 356 Department of Clinical Pathology, Akademiska University Hospital in Uppsala, Sweden
13
14 357 (introduced by the Swedish health authorities to eliminate unwanted delay in the diagnostics of
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16
17 358 melanoma)⁸ and the 4-week national lung cancer symptom awareness campaign in Wales, UK,
18
19 359 aimed at increasing urgent suspected cancer referrals and clinical outcomes.⁵¹
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23 24 361 *Multidisciplinary team*

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26 362 Three multidisciplinary team lung cancer approaches were identified from published articles:
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28 363 from the USA^{66,83} and Australia.⁴⁸ The focus and metrics for assessment of the effectiveness of
29
30 364 the approaches varied across the publications. One approach from the USA was found to be
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32
33 365 effective,⁶⁶ whereas the others were found to be ineffective. The effective approach was the lung
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35 366 cancer strategist program, a thoracic surgeon-guided, multidisciplinary (disciplines not reported)
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37 367 care program in hospitals in Massachusetts, USA, aimed at improving timeliness of lung cancer
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39
40 368 diagnosis and treatment.⁶⁶ The ineffective approaches were the pre-diagnosis multidisciplinary
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42 369 tumour board (physicians from radiology, medical and radiation oncology, and
43
44 370 pulmonary medicine) discussions in a clinic in Cleveland, USA aimed at improving the
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47 371 timeliness of diagnostic evaluation in lung cancer,⁸³ and the Victorian lung cancer service
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49 372 redesign project in Victoria, Australia, which involved multidisciplinary (patients, governance,
50
51 373 administration, clinicians and health information services) evaluation aimed at quality
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54 374 improvement collaborative on timeliness and management in lung cancer.⁴⁸ In addition, nine
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56 375 unpublished articles from the UK were identified.^{97,99-101,104,106,107,110} These included four articles
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3 376 regarding a “straight to CT access” pathway, on community pharmacy direct referral to lung
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5 377 cancer pathway, rapid colorectal diagnostic pathway, and optometrist direct referral to
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7 378 neuroscience pathway. All but the chest x-ray pathway¹⁰⁷ were found to be effective.
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10 379

11 380 *Standardized care pathways*

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14 381 Eleven published articles on standardized care pathways were identified.^{9,10,24,33,37,39,47,57,61,68,69}
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16 382 These articles were focused on varied cancer types (4 each for multiple cancers, and 1 each for
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18 383 ear-nose-throat, urinary tract, and gastrointestinal cancers). Three articles were from
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20 384 Denmark,^{24,37,39} two from the UK,^{33,68} and one each from Canada,⁵⁷ Norway,⁴⁷ Sweden,⁶¹
21
22 385 Spain,¹⁰ and Saudi Arabia.⁹ The publications were on adult patient populations with one also
23
24 386 involving paediatric patients. The focus and metrics for assessment of the effectiveness of the
25
26 387 pathways varied across the publications. The main effective pathways were the national
27
28 388 diagnostic cancer pathway in Norway, with recommended maximum limits for time spent in the
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30 389 diagnostic process as well as mandatory reporting of the actual time intervals for all patients with
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32 390 suspected lung cancer,⁴⁷ and the standardized triage process in the Southeastern Ontario, Canada,
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34 391 which entailed a twice-weekly nurse–physician triage, preordered staging tests and scheduling
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36 392 according to urgency, redirection and recommendations for inappropriate referrals, and new
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38 393 small nodule clinic.⁵⁷ Other main effective pathways were the standardized diagnostic pathway
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40 394 for suspected urothelial cancer initiated by primary healthcare providers and specialists in Skane
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42 395 County, Sweden, and comprises CT urography, urinary cytology and cystoscopy,⁶¹ the early
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44 396 colonoscopy track (within 30 days from referral) in a tertiary referral hospital in Tenerife,
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46 397 Spain,¹⁰ and the fast-track cancer care pathway in Denmark (national), with maximum acceptable
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48 398 time thresholds from referral to diagnosis and treatment.³⁷ In addition, two unpublished articles
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3 399 from Canada¹⁰⁹ and the UK⁹⁶ focusing on breast and lung cancers, respectively, were identified.
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5 400 These were the Alberta Health Services Diagnostic Assessment Pathway and the Somerset
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7 401 Integrated Lung Cancer Pathway. While the Canadian pathway was found to be effective, the
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10 402 pathway from the United Kingdom was not effective.
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14 404 ***Support for primary care providers***

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17 405 There were four publications on support for primary care providers (PCP), all from the
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19 406 UK.^{25,29,46,95} Two were focused on multiple cancer types, and one each focused on
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21 407 gastrointestinal and brain cancers. The publications were on adult patient populations with one
22
23 408 being also involving paediatric patients. The focus and metrics for assessment of the
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25 409 effectiveness of the support packages (all educational and informational) varied across the
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27
28 410 publications. None of the support packages was found to be effective, with the identified
29
30 411 common theme being a lack of awareness of referral guidelines and associated knowledge by
31
32 412 GPs. These ineffective support packages were the use of the Kernick and NICE guidelines as
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34 413 evidence-based support to assist primary care physicians in identifying patients most at risk of
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36 414 having a brain tumour, but also on the fastest route to achieve diagnosis (example, direct access
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38 415 imaging versus urgent secondary care referral) in Scotland, the UK,⁹⁵ the use of the national
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40 416 cancer waiting times monitoring dataset for system performance assessment by primary care
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42 417 physicians in England, the UK,²⁵ and the use of safety netting by primary care physicians in
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44 418 Oxfordshire, UK to ensure that patients are monitored until their symptoms or signs are
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46 419 explained, and to guard against delays in diagnosis.²⁹
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53 421 ***Target or benchmark for wait times***

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3 422 There were eight published articles related to targets or benchmarks for wait
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5 423 times.^{13,40,41,67,71,79,86,94} Three of these articles were from the UK,^{67,71,79} two articles from
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7 424 Australia,^{40,86} and one article each from China,⁴¹ Sweden,⁹⁴ and New Zealand¹³. These
8
9 425 publications were focused on varied cancer types (2 each for multiple, lung and gastrointestinal
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11 426 cancers, and 1 each for prostate and skin cancers), and were on adult patient populations, with
12
13 427 one publication involving paediatric patients. The focus and metrics for assessment of the
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15 428 effectiveness of the target or benchmarks varied across the publications, and all but two
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17 429 targets/benchmarks^{13,86} were found to be effective. The effective targets or benchmarks were the
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19 430 28-day faster diagnosis standard in the National Health Service England, UK, defined as the time
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21 431 within which the patient is informed whether they do or do not have cancer,⁷¹ the fast-track
22
23 432 diagnostic workup for men with suspected prostate cancer at the Urology Department at Orebro
24
25 433 University Hospital in Sweden, which entailed targeting the shortest possible waiting-time for a
26
27 434 diagnostic workup process,⁹⁴ and the optimal timeframes for referral and diagnosis of lung lesion
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29 435 at Latrobe Regional Hospital in Victoria, Australia established by the National Cancer Expert
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31 436 Reference Group as part of the optimal care pathway for people with lung cancer.⁴⁰ The
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33 437 ineffective targets or benchmarks was the New Zealand Ministry of Health's "faster cancer
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35 438 treatment" standards of service provision for melanoma patients, with a target of
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37 439 histopathological diagnosis of melanoma reported within five working days in 80% of cases, and
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39 440 all cases reported in 10 working days.¹³ In addition, two unpublished articles from Canada¹⁰³ and
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41 441 the UK¹⁰⁵ focusing on multiple cancers were identified, and these were the "2-week wait"
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43 442 benchmark in the UK (already discussed under rapid referral pathways) and the Canadian Breast
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45 443 Cancer Screening Network targets for diagnostic intervals: $\geq 90\%$ of abnormal screens to be
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3 444 resolved within 5 weeks if no biopsy is required and $\geq 90\%$ within 7 weeks if a tissue biopsy is
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5 445 required.

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10 447 ***Innovative interventions to enhanced care in cancer pre-diagnosis phase***

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12 448 This review identified 17 published articles related to technological interventions for enhanced
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14 449 care in the pre-diagnosis phase of cancer.^{14,19,20,27,35,36,49,55,56,60,63,64,77,80,85,87,89} Ten of these articles
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16 450 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
17
18 451 each was from Denmark,⁸⁷ Netherlands,¹⁹ Italy,¹⁴ India,⁸⁵ and Spain.⁵⁶ These publications
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20 452 focused on varied cancer types in adult patient populations, with two also involving paediatric
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22 453 patients. The interventions had little patient input in their design, development, or
23
24 454 implementation. The focus and metrics for assessment of the effectiveness of the interventions
25
26 455 varied across the publications. The main identified interventions were the use of teledermatology
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28 456 in skin cancer diagnosis. This involved the taking of images, including dermoscopy by GPs and
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30 457 sending them for evaluation to specialized dermatologists.^{36,60,77,87} The process is embedded in
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32 458 an e-referral system developed in Auckland, New Zealand for suspected skin malignancy,⁸⁰ and
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34 459 included teledermatology images triaged as confirmed, likely or suspected melanoma, the use of
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36 460 a web-based referral tool for head and neck cancers at two different hospitals in Birmingham,
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38 461 West Midlands, and Wexham, Berkshire, UK.⁴⁹ There was also the use of the Digitally
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40 462 Assembled Referral Toolkit (DART) for 2-week referral, accessible via a cloud-based template,
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42 463 which contained new referral forms native to GP clinical systems in the UK.²⁷ Additionally,
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44 464 there was the use of an electronic straight-to-test pathway at a large tertiary referral hospital in
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46 465 England, UK to remove hospital-based triage from suspected colorectal cancer pathways; this
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54 466 allows GPs to book tests supported by a decision aid based on the NICE guidance, thus,

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3 467 eliminating the need for a standard referral form or triage process.⁶³ Further, there was the use of
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5 468 electronic clinical decision support for melanoma in four general practices in the Southeast of
6
7 469 England, UK, which involved the use of an electronic-based 7-point checklist to assess
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10 470 pigmented lesions,⁶⁴ the use of machine learning algorithms in Newcastle, UK to classify
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12 471 patients referred on the 2-week wait pathway for suspected head and neck cancer into different
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14 472 diagnostic groups, albeit very broad ones: cancer and non-cancer,⁵⁵ the use of nurse-led
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16 473 assessments to evaluate certain groups of patients suspected to have bowel cancer in England,
17
18 474 the UK,²⁰ and the use of varied smartphone-based skin and oral self-monitoring and screening
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20 475 applications, in England, UK⁸⁹ and in the India,⁸⁵ respectively. In addition, two unpublished
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22 476 articles from the UK were identified.^{104,108} These were for a cancer decision support tool
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24 477 (computer-based programs integrated into a GP's usual patient management system) in
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26 478 Gateshead, London, and a clinical web portal (CWP) electronic system in Manchester, England,
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28 479 with the fundamental part of the CWP being that local clinicians had to take personal
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31 480 responsibility for data input.
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38 482 *Performance metrics to measure improvements in suspicion to diagnosis phase*

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40 483 Varied performance metrics were identified by this review. The main metrics are summarized
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42 484 according to intervention type (**Appendix 9**). While performance metrics appear to be mainly
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44 485 intervention-dependent, time from presentation in primary care to diagnosis and from referral
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46 486 from primary care to specialist consultation, appear to be the most consistent metrics used for
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48 487 evaluation. Performance metrics to measure patients' experience mainly centered on patients'
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50 488 satisfaction and quality of life.
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3 490 *Specific considerations for underserved populations*

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5 491 Four published articles focused on issues related specifically to underserved populations, with all
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7 492 focused on remote/rural populations.^{16,28,58,86} These publications were from the UK,⁵⁸
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9 493 Australia,^{28,86} and Mexico.¹⁶ A fifth publication only used the patients' area of residence as part
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11 494 of their model.⁹³ All of the publications were on multiple cancer types and adult populations,
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13 495 although one included a paediatric population. The specific considerations for underserved
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15 496 populations and the evidence regarding them included a publication from Scotland, the UK, a
16
17 497 national audit of cancer diagnosis in Scottish and English general practices, exploring and
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19 498 comparing patient characteristics, diagnostic intervals, and routes to diagnosis,⁵⁸ the publication
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21 499 from New South Wales, Australia on a study that examined geographic variations in time
22
23 500 intervals leading up to treatment for head and neck cancer, with assessment of differences based
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25 501 on remoteness of residence (regional/remote or metropolitan) at two tertiary referral centres,⁸⁶ a
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27 502 publication from Mexico City, Mexico on evaluation of a patient navigation program to reduce
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29 503 referral time to cancer centers for underserved patients with a suspicion or diagnosis of cancer at
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31 504 a public general hospital,¹⁶ and a publication from Western Australia, a cluster-randomized
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33 505 controlled trial of a complex intervention to reduce time to diagnosis in rural cancer patients with
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35 506 the aim of measuring the effect of community-based symptom awareness and general practice-
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37 507 based educational interventions on the time to diagnosis in rural patients presenting with breast,
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39 508 prostate, colorectal or lung cancer.²⁸

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510 **Discussion**

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

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

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3 533 The interventions mostly comprised multiple interventions/ changes to the healthcare
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5 534 pathway. As such, the interventions examined varied widely across the studies. This was true
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8 535 even when applied to the same cancer patient populations and in the same jurisdictions/
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10 536 countries, including those where an intervention was part of the standard care pathway. As such,
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12 537 it is difficult, perhaps impossible, to identify one main approach alone that drives an
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14 538 intervention. Methodological approaches also varied significantly with regard to outcome
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16 539 assessment. A common theme among the effective centralized or coordinated diagnostic
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18 540 services, interventions to enhance diagnostic services, patient navigation approaches, and
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20 541 standardized care pathways is multidisciplinary collaboration and the involvement of a nurse
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22 542 navigator.

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26 543 The implications of the findings from this scoping review are that it is difficult to
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28 544 determine a specific intervention, or stand-alone approach to an intervention. It is also difficult to
29
30 545 assess the true effectiveness of many of the interventions, especially considering the differing
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32 546 composite nature of the interventions, the fact that the evidence is mostly from observational
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34 547 studies, and the range of outcome measures used to measure effectiveness. While many of the
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36 548 interventions could be adapted to suit different health systems and jurisdictions, emphasis should
37
38 549 be on the context and the strengths and limitations of the individual health system, and a clear
39
40 550 evidence-based performance metric for appropriate evaluation of effectiveness of an intervention
41
42 551 ought to be determined a priority. Diagnosing cancer faster and more accurately at an earlier
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44 552 stage is a key priority of the 2019-2029 Canadian Strategy for Cancer Control
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46 553 (www.partnershipagainstcancer.ca/cancer-strategy/). Over the next 5 years, the Canadian
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51 554 Partnership Against Cancer will leverage findings from this scoping review, as one of several
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3 555 inputs, and partner with Canadian jurisdictions to continue to test innovative models of care that
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5 556 expedite cancer diagnosis, especially for Indigenous and underserved populations.
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10 558 **Limitations and merits**

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12 559 There are some limitations to this study. The literature search was developed by a knowledge
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14 560 synthesis librarian and peer reviewed by an independent knowledge synthesis librarian using the
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16 561 PRESS checklist, searching of appropriate databases and websites for literature, and adherence to
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18 562 known guidelines and standards in the conduct and reporting of the review. Even so, the
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20 563 literature search was limited to evidence from the last 4 years and only evidence from English-
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22 564 language publications and organizational websites. As such, potentially eligible articles could
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24 565 have been missed.
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28 566 The eligibility criteria for inclusion were not limited to only comparative studies. This
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30 567 meant that the focus of some of the included studies was not specifically on the assessment of
31
32 568 effectiveness of an intervention, which was based solely on the reported outcome in the articles.
33
34 569 As such, an intervention that appeared effective in a study may be ineffective in another study
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36 570 depending on the assessed outcome with no clear reason for this discrepancy. Furthermore, this
37
38 571 review did not assess effectiveness of interventions across cancer patient types and
39
40 572 jurisdictions/regions. This would have allowed assessment of any differences in intervention
41
42 573 effectiveness by patient type and study jurisdiction. Lastly, and in line with the JBI's guidance
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44 574 for the conduct of scoping reviews, we did not attempt to evaluate the quality of the included
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46 575 studies or provide an assessment of the quality of the evidence.
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54 577 **Conclusions**

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3 578 The evidence suggests that interventions focused on improving accurate and timely cancer
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5 579 diagnosis among symptomatic individuals are active topics of research, particularly in lung
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7 580 cancer patient populations, and that the UK is championing this area of research. While the
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9 581 themes of the studied interventions are similar, the interventions differ in many ways within the
10
11 582 same intervention group. Multidisciplinary cooperation and involvement of a nurse navigator
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13 583 appeared to be unique features of many of the effective interventions. Canadian and other
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15 584 jurisdictions can leverage these lessons learned to develop and implement strategies adapted to
16
17 585 local health system needs to improve the cancer pre-diagnosis phase. Future research should
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19 586 examine the effectiveness of the complex and organization-specific nature of the interventions
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21 587 identified through this review.
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28 589 **Data sharing statement:** All the data for this study are reported in the text and appendices. No
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30 additional data available.
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35 592 **Ethics approval:** Not applicable.
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40 594 **Details of the role of the study sponsors:** The Canadian Partnership Against Cancer (the study
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42 595 commissioner) contributed to specifying the study objectives and questions, and in summarizing
43
44 596 the evidence.
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49 598 **Patient and public involvement:** Involvement of patients or the public in this study was based
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51 599 on the Strategy for Patient Oriented-Research (SPOR) initiative.
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Table 1: Summary of the characteristics of the included published articles that reported data on effective interventions

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

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

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

Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results	
Multidisciplinary team	Phillips 2019 ⁶⁶	USA (NR)	Case-Control (2014-2016)	Lung (NR) [218]	Time to diagnosis	Compared to controls, patients with lung cancer in the Lung Cancer Strategist Program cohort had an expedited time from suspicious finding to diagnosis (34 vs 44 days, p=0.027) (Effective)	
	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)	
Patient navigation	Whitley 2017 ⁹⁰	USA (Boston, Denver, San Antonio, and Tampa)	Case-Control (2007-2011)	Multiple (Adult) [6349]	Delays in diagnostic resolution based on Charlson Comorbidity Index score	Patient navigation reduced delays in diagnostic resolution, with the greatest benefits seen for those with a Charlson Comorbidity Index score ≥2 (Effective)	
	Intervention	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Results
	Rapid referral pathway	Antel 2020 ¹¹	South Africa (Cape Town)	Before-and-After (2017-2019)	Haematological (Adult) [130]	Diagnostic interval	Compared with a historical cohort, the diagnostic interval (time from first health visit to diagnostic biopsy) for patients with lymphoma was significantly shorter, 13.5 vs 48 days (p=0.002) (Effective)
Arhi 2020 ¹²		UK (National)	Case-Control (2000-2013)	Gastrointestinal (Adult) [7130]	Hazard ratios of death	Patients referred between 2 weeks to 3 months, and after 3 months with red-flag symptoms demonstrated a significantly worse prognosis than patients who were referred within 2 weeks (Effective)	
Chng 2020 ¹⁷		UK (Newcastle-upon-Tyne)	Case-Control (2015-2019)	Brain (Adult) [101]	Tumour detection rate	With guideline adherence, the brain tumour detection rate was 3-fold higher (36.0% vs 11.5%, p=0.02) (Effective)	

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

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

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

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

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

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

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

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3 **Figures**
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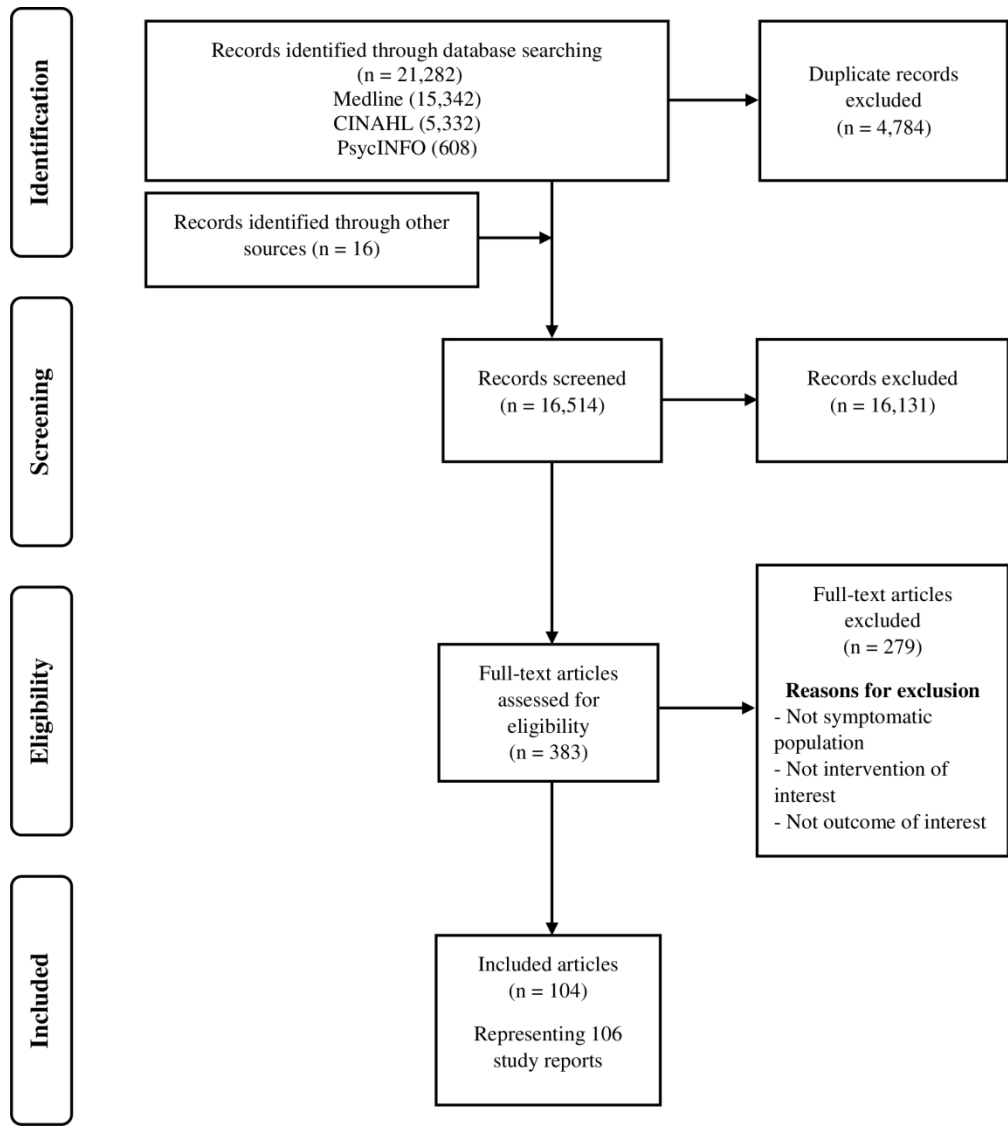
7 **Figure 1:** Modified PRISMA flow chart
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10 **Figure 2:** Geographical mapping of the included published articles
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14 **Figure 3:** Summary of cancer types reported by the included published articles
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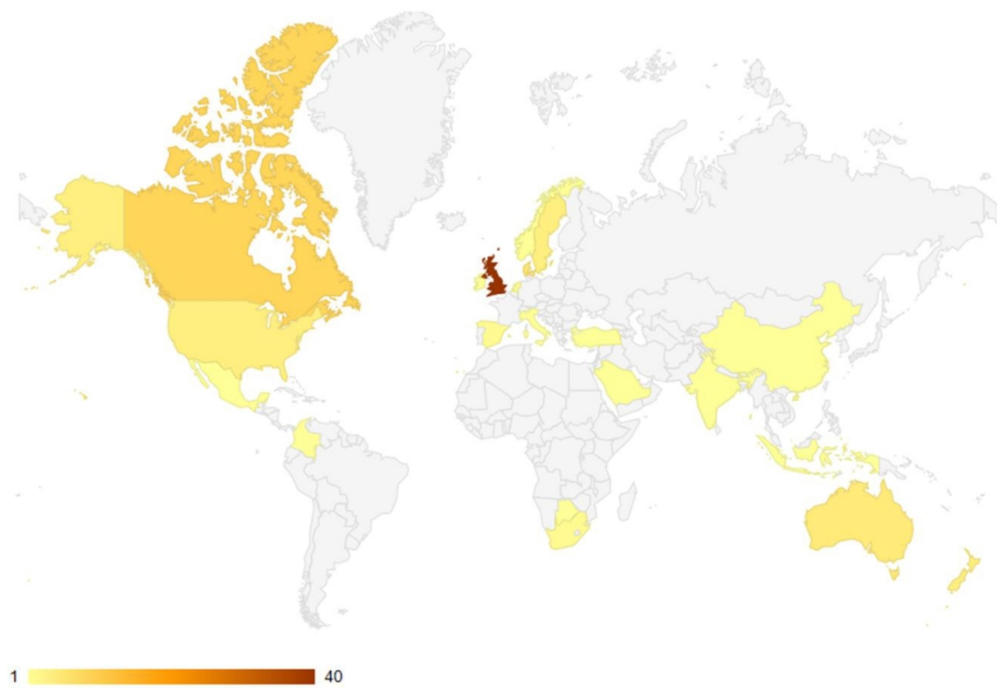
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18 **Figure 4:** Summary of intervention types reported by the included published articles
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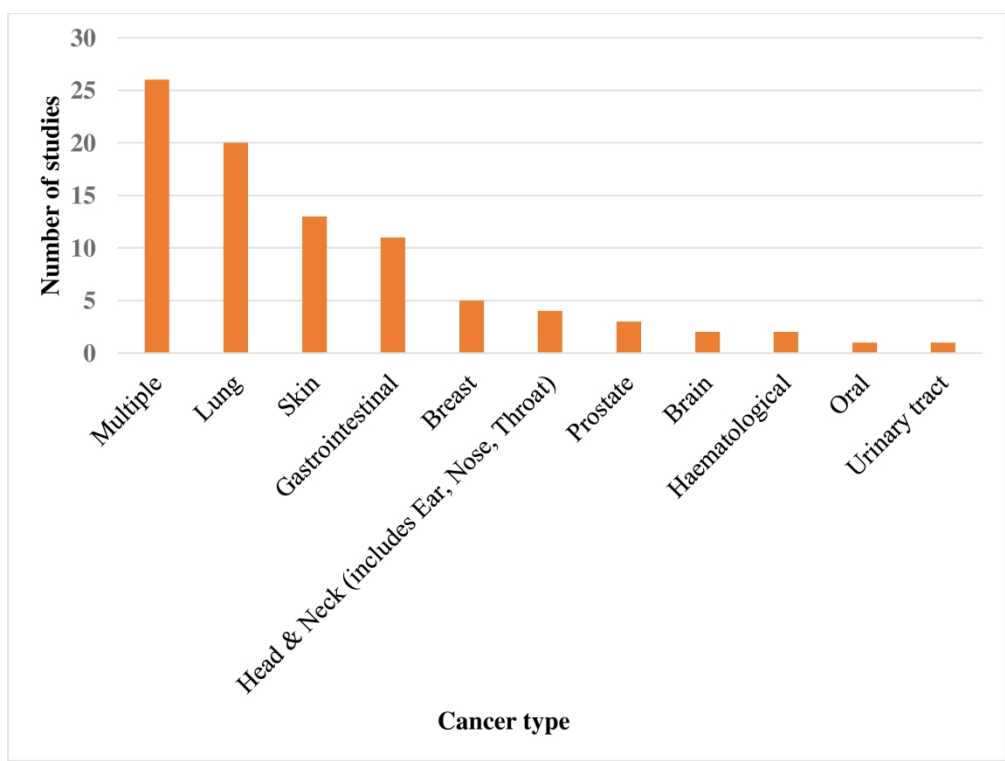
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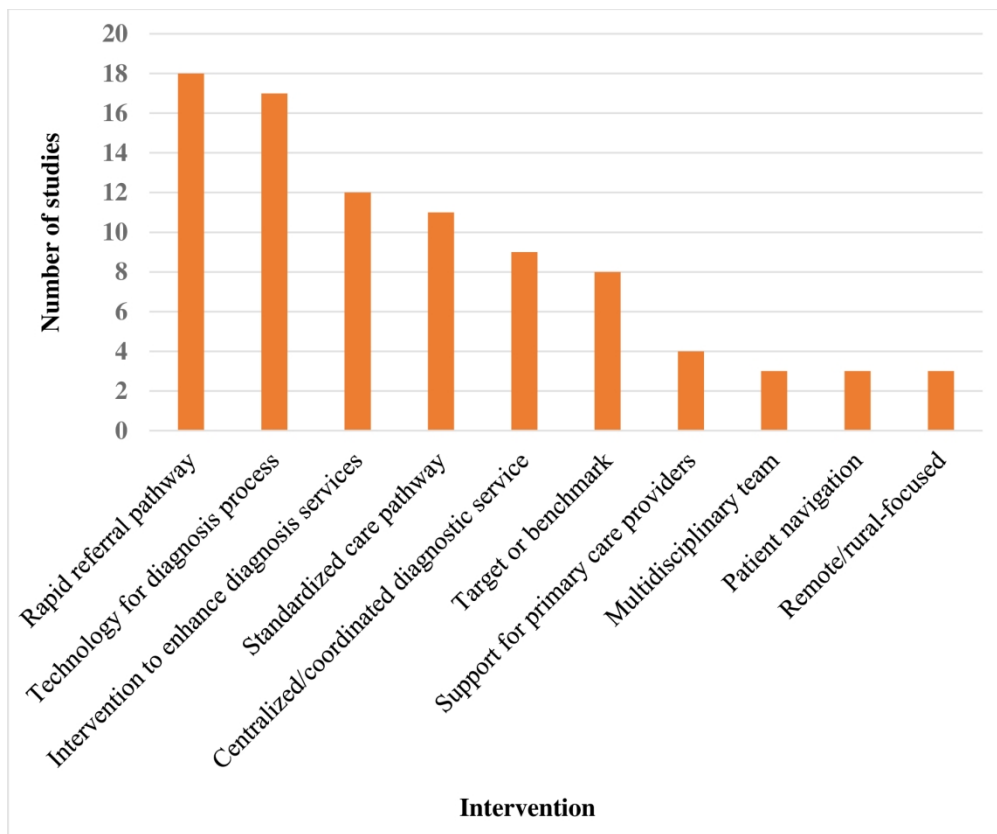
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Appendices

Appendix 1: Project work plan

About the Project Team

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

Proposed Method

Methods

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

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

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

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

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

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

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

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

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4 KQ 5. Have specific considerations been applied to underserved populations including Indigenous,
5 rural, and remote populations within the context of each of the questions above?
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8 **Study eligibility criteria**

9 This review will focus on published and unpublished studies that answer the key questions since 2017.
10 Our focus is on comparative studies that applied a protocol/guideline or a specific intervention or
11 intervention plan. Having said that, we anticipate the need to review lower quality study designs (e.g.,
12 retrospective, and uncontrolled studies). As such, there will be no restriction on the study design, but will
13 be limited to English language publications for feasibility.
14

15 **Search strategy and study selection**

16 A knowledge synthesis librarian has designed and executed a literature search strategy in MEDLINE
17 (Ovid). The search strategy was peer-reviewed by a second librarian and adapted for other bibliographic
18 databases: Cinahl (Ebsco) and Psycinfo (Ovid). Search strategies are presented in Appendix 1. All
19 retrieved records were imported into EndNote for citation management.
20 One reviewer will screen each identified citation for eligibility. Full texts of all relevant citations will be
21 reviewed by two reviewers. All conflicts will be resolved by discussion and/ or a third reviewer, as
22 needed. We will record the number of ineligible citations at the title/ abstract screening stage, and both
23 the number and reason for ineligibility at the full-text articles.
24

25 **Data extraction**

26 We will develop data extraction forms and pilot them on a small selection of studies. Extracted data will
27 be stored and managed in MS Excel. One reviewer will independently extract data from included studies
28 and another reviewer will independently check the extracted data for errors. Disagreements will be
29 resolved by discussion between reviewers and/ or by involving a third reviewer, as needed.
30

31 **Data analysis**

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

38 We will submit reports from this study as a technical report to CPAC.
39
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41 **Knowledge User Engagement Plan**

42 We will be providing a bi-weekly update to CPAC on the progression of the review. Specifically, we will
43 engage during specific time points to review progress and next steps:
44

- 45 - Protocol
- 46 - Level I Screening (Title/ Abstract screening phase)
- 47 - Level II Screening (Full-text screening phase)
- 48 - Data Extraction
- 49 - Data Analysis
- 50 - Report
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53 **Declaration of Conflict of Interest**

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56 None
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Appendix 2: MEDLINE (Ovid) search strategy

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

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 6 shark or sharks or cod or cods or gadus or morhua or carp or carps or cyprinus or carpio or
 7 killifish or eel or eels or anguilla or zander or sander or lucioperca or stizostedion or turbot or
 8 turbot or psetta or flatfish or flatfishes or plaice or pleuronectes or platessa or tilapia or
 9 tilapias or oreochromis or sarotherodon or common sole or dover sole or solea or zebrafish or
 10 zebrafishes or danio or rerio or seabass or dicentrarchus or labrax or morone or lamprey or
 11 lampreys or petromyzon or pumpkinseed or pumpkinseeds or lepomis or gibbosus or herring
 12 or clupea or harengus or amphibia or amphibian or amphibians or anura or salientia or frog or
 13 frogs or rana or toad or toads or bufo or xenopus or laevis or bombina or epidalea or calamita
 14 or salamander or salamanders or newt or newts or triturus or reptilia or reptile or reptiles or
 15 bearded dragon or pogona or vitticeps or iguana or iguanas or lizard or lizards or anguis
 16 fragilis or turtle or turtles or snakes or snake or aves or bird or birds or quail or quails or
 17 coturnix or bobwhite or colinus or virginianus or poultry or poultries or fowl or fowls or
 18 chicken or chickens or gallus or zebra finch or taeniopygia or guttata or canary or canaries or
 19 serinus or canaria or parakeet or parakeets or grasskeet or parrot or parrots or psittacine or
 20 psittacines or shelduck or tadorna or goose or geese or branta or leucopsis or woodlark or
 21 lullula or flycatcher or ficedula or hypoleuca or dove or doves or geopelia or cuneata or duck
 22 or ducks or greylag or graylag or anser or harrier or circus pygargus or red knot or great knot
 23 or calidris or canutus or godwit or limosa or lapponica or meleagris or gallopavo or jackdaw or
 24 corvus or monedula or ruff or philomachus or pugnax or lapwing or peewit or plover or
 25 vanellus or swan or cygnus or columbianus or bewickii or gull or chroicocephalus or
 26 ridibundus or albifrons or great tit or parus or aythya or fuligula or streptopelia or risoria or
 27 spoonbill or platalea or leucorodia or blackbird or turdus or merula or blue tit or cyanistes or
 28 pigeon or pigeons or columba or pintail or anas or starling or sturnus or owl or athene noctua
 29 or pochard or ferina or cockatiel or nymphius or hollandicus or skylark or alauda or tern or
 30 sterna or teal or crecca or oystercatcher or haematopus or ostralegus or shrew or shrews or
 31 sores or araneus or crocidura or russula or european mole or talpa or chiroptera or bat or bats
 32 or eptesicus or serotinus or myotis or dasycneme or daubentonii or pipistrelle or pipistrellus or
 33 cat or cats or felis or catus or feline or dog or dogs or canis or canine or canines or otter or
 34 otters or lutra or badger or badgers or meles or fitchew or fitch or foumart or foulmart or
 35 ferrets or ferret or polecat or polecats or mustela or putorius or weasel or weasels or fox or
 36 foxes or vulpes or common seal or phoca or vitulina or grey seal or halichoerus or horse or
 37 horses or equus or equine or equidae or donkey or donkeys or mule or mules or pig or pigs or
 38 swine or swines or hog or hogs or boar or boars or porcine or piglet or piglets or sus or scrofa
 39 or llama or llamas or lama or glama or deer or deers or cervus or elaphus or cow or cows or
 40 bos taurus or bos indicus or bovine or bull or bulls or cattle or bison or bisons or sheep or
 41 sheeps or ovis aries or ovine or lamb or lambs or mouflon or mouflons or goat or goats or
 42 capra or caprine or chamois or rupicapra or leporidae or lagomorpha or lagomorph or rabbit or
 43 rabbits or oryctolagus or cuniculus or laprine or hares or lepus or rodentia or rodent or rodents
 44 or murinae or mouse or mice or mus or musculus or murine or woodmouse or apodemus or rat
 45 or rats or rattus or norvegicus or guinea pig or guinea pigs or cavia or porcellus or hamster or
 46 hamsters or mesocricetus or cricetus or cricetus or gerbil or gerbils or jird or jirds or
 47 meriones or unguiculatus or jerboa or jerboas or jaculus or chinchilla or chinchillas or beaver
 48 or beavers or castor fiber or castor canadensis or sciuridae or squirrel or squirrels or sciurus or
 49 chipmunk or chipmunks or marmot or marmots or marmota or suslik or susliks or
 50 spermophilus or cynomys or cottonrat or cottonrats or sigmodon or vole or voles or microtus
 51 or myodes or glareolus or primate or primates or prosimian or prosimians or lemur or lemurs
 52 or lemuridae or loris or bush baby or bush babies or bushbaby or bushbabies or galago or
 53 galagos or anthropoidea or anthropoids or simian or simians or monkey or monkeys or
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	marmoset or marmosets or callithrix or cebuella or tamarin or tamarins or saguinus or leontopithecus or squirrel monkey or squirrel monkeys or saimiri or night monkey or night monkeys or owl monkey or owl monkeys or douroucoulis or aotus or spider monkey or spider monkeys or ateles or baboon or baboons or papio or rhesus monkey or macaque or macaca or mulatta or cynomolgus or fascicularis or green monkey or green monkeys or chlorocebus or vervet or vervets or pygerythrus or hominoidea or ape or apes or hylobatidae or gibbon or gibbons or siamang or siamangs or nomascus or symphalangus or hominidae or orangutan or orangutans or pongo or chimpanzee or chimpanzees or pan troglodytes or bonobo or bonobos or pan paniscus or gorilla or gorillas or troglodytes).ti,ab,kf.) not (human/ or (human\$ or man or men or woman or women or child or children or patient\$).ti,ab,kf.)	
21.	19 not 20	48488
22.	limit 21 to yr="2017 -Current"	15342

Appendix 3: CINAHL (EbscoHOST) search strategy

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

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 4 sheep) OR (MH swine) OR (MH primates) OR (animal OR animals OR pisces OR fish OR
 5 fishes OR catfish OR catfishes OR sheatfish OR silurus OR arius OR heteropneustes OR
 6 clarias OR gariepinus OR "fathead minnow" OR "fathead minnows" OR pimephales OR
 7 promelas OR cichlidae OR trout OR trouts OR char OR chars OR salvelinus OR salmo OR
 8 oncorhynchus OR guppy OR guppies OR millionfish OR poecilia OR goldfish OR goldfishes
 9 OR carassius OR auratus OR mullet OR mullets OR mugil OR curema OR shark OR sharks
 10 OR cod OR cods OR gadus OR morhua OR carp OR carps OR cyprinus OR carpio OR
 11 killifish OR eel OR eels OR anguilla OR zander OR sander OR lucioperca OR stizostedion
 12 OR turbot OR turbots OR psetta OR flatfish OR flatfishes OR plaice OR pleuronectes OR
 13 platessa OR tilapia OR tilapias OR oreochromis OR sarotherodon OR "common sole" OR
 14 "dover sole" OR solea OR zebrafish OR zebrafishes OR danio OR rerio OR seabass OR
 15 dicentrarchus OR labrax OR morone OR lamprey OR lampreys OR petromyzon OR
 16 pumpkinseed OR pumpkinseeds OR lepomis OR gibbosus OR herring OR clupea OR
 17 harengus OR amphibia OR amphibian OR amphibians OR anura OR salientia OR frog OR
 18 frogs OR rana OR toad OR toads OR bufo OR xenopus OR laevis OR bombina OR epidalea
 19 OR calamita OR salamander OR salamanders OR newt OR newts OR triturus OR reptilia OR
 20 reptile OR reptiles OR "bearded dragon" OR pogona OR vitticeps OR iguana OR iguanas OR
 21 lizard OR lizards OR "anguis fragilis" OR turtle OR turtles OR snakes OR snake OR aves OR
 22 bird OR birds OR quail OR quails OR coturnix OR bobwhite OR colinus OR virginianus OR
 23 poultry OR poultries OR fowl OR fowls OR chicken OR chickens OR gallus OR "zebra
 24 finch" OR taeniopygia OR guttata OR canary OR canaries OR serinus OR canaria OR
 25 parakeet OR parakeets OR grasskeet OR parrot OR parrots OR psittacine OR psittacines OR
 26 shelduck OR tadorna OR goose OR geese OR branta OR leucopsis OR woodlark OR lullula
 27 OR flycatcher OR ficedula OR hypoleuca OR dove OR doves OR geopelia OR cuneata OR
 28 duck OR ducks OR greylag OR graylag OR anser OR harrier OR circus pygargus OR red knot
 29 OR "great knot" OR calidris OR canutus OR godwit OR limosa OR lapponica OR meleagris
 30 OR gallopavo OR jackdaw OR corvus OR monedula OR ruff OR philomachus OR pugnax
 31 OR lapwing OR peewit OR plover OR vanellus OR swan OR cygnus OR columbianus OR
 32 bewickii OR gull OR chroicocephalus OR ridibundus OR albifrons OR "great tit" OR parus
 33 OR aythya OR fuligula OR streptopelia OR risoria OR spoonbill OR platalea OR leucorodia
 34 OR blackbird OR turdus OR merula OR blue tit OR cyanistes OR pigeon OR pigeons OR
 35 columba OR pintail OR anas OR starling OR sturnus OR owl OR "athene noctua" OR
 36 pochard OR ferina OR cockatiel OR nymphicus OR hollandicus OR skylark OR alauda OR
 37 tern OR sterna OR teal OR crecca OR oystercatcher OR haematopus OR ostralegus OR shrew
 38 OR shrews OR sorex OR araneus OR crocidura OR russula OR "european mole" OR talpa
 39 OR chiroptera OR bat OR bats OR eptesicus OR serotinus OR myotis OR dasycneme OR
 40 daubentonii OR pipistrelle OR pipistrellus OR cat OR cats OR felis OR catus OR feline OR
 41 dog OR dogs OR canis OR canine OR canines OR otter OR otters OR lutra OR badger OR
 42 badgers OR meles OR fitchew OR fitch OR foumart OR foulmart OR ferrets OR ferret OR
 43 polecat OR polecats OR mustela OR putorius OR weasel OR weasels OR fox OR foxes OR
 44 vulpes OR "common seal" OR phoca OR vitulina OR grey seal OR halichoerus OR horse OR
 45 horses OR equus OR equine OR equidae OR donkey OR donkeys OR mule OR mules OR pig
 46 OR pigs OR swine OR swines OR hog OR hogs OR boar OR boars OR porcine OR piglet OR
 47 piglets OR sus OR scrofa OR llama OR llamas OR lama OR glama OR deer OR deers OR
 48 cervus OR elaphus OR cow OR cows OR "bos taurus" OR "bos indicus" OR bovine OR bull
 49 OR bulls OR cattle OR bison OR bisons OR sheep OR sheeps OR "ovis aries" OR ovine OR
 50 lamb OR lambs OR mouflon OR mouflons OR goat OR goats OR capra OR caprine OR
 51 chamois OR rupicapra OR leporidae OR lagomorpha OR lagomorph OR rabbit OR rabbits
 52 OR oryctolagus OR cuniculus OR laprine OR hares OR lepus OR rodentia OR rodent OR
 53 rodents OR murinae OR mouse OR mice OR mus OR musculus OR murine OR woodmouse
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	<p>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 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#))</p>	
21.	S19 NOT S20	14678
22.	S21 Limiters - Published Date: 20170101-20201231	5333

Appendix 4: Psycinfo (Ovid) search strategy

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

	<p>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 dasyncneme 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 fountmart 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 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.)</p>	
20.	18 not 19	2754
21.	limit 20 to yr="2017 -Current"	608

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

Canada

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

International

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

Appendix 6: Definition for interventions related to the review questions

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5 • *Centralized or coordinated diagnostic service*: Brings together various tests/procedures and care
6 providers needed to determine a definitive diagnosis at one location.
7
- 8
9 • *Interventions in diagnostic services*: An initiative that aims to improve diagnostic services within
10 a jurisdiction.
11
- 12
13 • *Multidisciplinary team*: Working with multiple departments, such as diagnostic imaging,
14 pathology, medical oncology, and research.
15
- 16
17 • *Patient navigation*: A dedicated role to help facilitate the navigation for patients across the
18 cancer journey – helps the patient through testing, appointments, health literacy, etc.
19
- 20
21 • *Rapid referral pathway*: Provides urgent access to specialists and/or diagnostic services for
22 patients.
23
- 24
25 • *Remote or rural populations*: This refers to populations that may live in non-urban areas. They
26 often do not have access to the same services as those who reside in more urban areas.
27
- 28
29 • *Standardized care pathway*: Sets expectations for cancer care based on evidence and shares
30 information about how to provide and what care to provide at each point of diagnosis, treatment,
31 and survivorship. Initiative is often integrated into the current health system.
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34 • *Support for primary care providers*: Initiative focusing on educating and supporting primary care
35 providers on care pathways and how to care for individuals presenting with potential or
36 confirmed cancer symptoms.
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39 • *Target or benchmark*: A figure used as a goal by jurisdictions to measure progress towards the
40 desired outcome of an initiative.
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43 • *Technology to support diagnosis process*: Technological innovations to enhance efficiency of
44 initiatives.
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Appendix 7: Summary of the characteristics of the included published articles that reported data on ineffective interventions

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

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

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

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

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

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

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

UK = United Kingdom; IQR = interquartile range

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

Intervention Type	Performance Metric
Centralized or coordinated diagnostic service	<ul style="list-style-type: none"> • Time from presentation in primary care to diagnosis • Time from referral from primary care to specialist consultation • Time from first abnormal image to biopsy
Interventions to enhance diagnostic services	<ul style="list-style-type: none"> • Time from referral from primary care to specialist consultation • Time from initial specialist consultation to diagnosis • Time from initial specialist consultation to biopsy • Time from first abnormal image to biopsy • Time from presentation in primary care to biopsy • Total diagnostic interval • Turnaround time for diagnosis following histology • Number of urgent referrals to specialist • Cancer detection rate • Patient survival
Multidisciplinary team	<ul style="list-style-type: none"> • Time from referral from primary care to specialist consultation • Time from first abnormal image to diagnosis
Patient navigation	<ul style="list-style-type: none"> • Waiting times from the point of referral from primary care to initial specialist assessment • Feasibility of program/process • Delays in diagnostic resolutions

Summary of findings

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

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

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	4-5
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	7-8
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	8-9
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	9
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	10-11
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	10
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix 2 - 4
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	10-11
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	11-12
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Appendix 6
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Not applicable



SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	11-12
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Table 1
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not applicable
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	14-24
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	13-24
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	25-27
Limitations	20	Discuss the limitations of the scoping review process.	27
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	28
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	2

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

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

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

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

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

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



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BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-055488.R1
Article Type:	Original research
Date Submitted by the Author:	24-Sep-2021
Complete List of Authors:	Okoli, George; University of Manitoba Max Rady College of Medicine Lam, Otto; University of Manitoba Max Rady College of Medicine Reddy, Viraj; University of Manitoba Max Rady College of Medicine Copstein, Leslie; University of Manitoba Max Rady College of Medicine Askin, Nicole; University of Manitoba Prashad, Anubha; Canadian Partnership Against Cancer Stiff, Jennifer; Canadian Partnership Against Cancer Khare, Satya Rashi; Canadian Partnership Against Cancer Leonard, Robyn; Canadian Partnership Against Cancer Zarin, Wasifa; Unity Health Toronto Tricco, Andrea; Li Ka Shing Knowledge Institute, Abou-Setta, Ahmed; University of Manitoba Max Rady College of Medicine; University of Manitoba, Community Health Sciences
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Evidence based practice, Health services research, Patient-centred medicine, Public health
Keywords:	ONCOLOGY, PREVENTIVE MEDICINE, PRIMARY CARE, PUBLIC HEALTH

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3 **1 Interventions to improve early cancer diagnosis of symptomatic patients: A scoping review**
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28 35 **Funding:** This study was funded in part by the Canadian Partnership Against Cancer (the

29
30 36 Partnership) and the Canadian Institutes of Health Research (CIHR) under the Strategy for

31
32 37 Patient Oriented-Research (SPOR) initiative, through the SPOR Evidence Alliance. Andrea

33
34 38 Tricco is funded by a Tier 2 Canada Research Chair in Knowledge Synthesis.

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39 40 **Competing interests declaration:** All authors declare that they have no conflicts of interest: no

40
41 41 financial relationships with any organisations that might have an interest in the submitted work,

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43 42 and no relationships or activities that could appear to have influenced the submitted work.

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48 44 **Patient consent:** Not applicable

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3 46 **Contributor and guarantor information:** Conceptualization (A Prashad, J Stiff, W Zarin, A
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6 48 Data acquisition (GN Okoli, OLT Lam, VK Reddy, L Copstein, N Askin, & AM Abou-Setta);
7
8 49 Formal analysis (GN Okoli); Draft manuscript (GN Okoli & AM Abou-Setta); Final manuscript
9
10 50 revisions (GN Okoli, OLT Lam, VK Reddy, L Copstein, N Askin, A Prashad, J Stiff, R Khare, R
11
12 51 Leonard, W Zarin, A Tricco & AM Abou-Setta); Guarantor (GN Okoli & AM Abou-Setta). The
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14 52 corresponding author (the manuscript's guarantor) attests that all listed authors meet authorship
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3 69 **Abstract**

4
5 70 **Objectives:** To summarize the current evidence regarding interventions for accurate and timely
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7 71 cancer diagnosis among symptomatic individuals.
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10 72 **Design:** A scoping review following the Joanna Briggs Institute's methodological framework for
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12 73 the conduct of scoping reviews and reported in accordance with the Preferred Reporting Items
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14 74 for Systematic Reviews and Meta-analyses extension for scoping reviews (PRISMA-ScR)
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16 75 checklist.
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20 76 **Data sources:** MEDLINE (Ovid), CINAHL (EBSCOhost) and PsycINFO (Ovid) bibliographic
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22 77 databases, and websites of relevant organizations. Published and unpublished literature (grey
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24 78 literature) of any study type in the English language were searched for from January 2017 to
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26 79 January 2021.
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30 80 **Eligibility and criteria:** Study participants were individuals of any age presenting at clinics with
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32 81 symptoms indicative of cancer. Interventions included practice guidelines, care pathways or
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34 82 other initiatives focused on achieving pre-defined benchmarks or targets for wait times,
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36 83 streamlined or rapid cancer diagnostic services, multidisciplinary teams, and patient navigation
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38 84 strategies. Outcomes included accuracy and timeliness of cancer diagnosis.
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42 85 **Data extraction and synthesis:** We summarized findings graphically and descriptively.
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45 86 **Results:** From 21,298 retrieved citations, 88 unique published articles and 16 unique unpublished
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47 87 documents (on 18 study reports), met the eligibility for inclusion. About half of the published
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49 88 literature and 83% of the unpublished literature were from the United Kingdom. Most of the
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51 89 studies were on interventions in lung cancer patients. Rapid referral pathways and technology for
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53 90 supporting and streamlining the cancer diagnosis process were the most studied interventions.
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3 91 Interventions were mostly complex and organization-specific. Common themes among the
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5 92 studies that concluded intervention was effective were multidisciplinary collaboration and the
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8 93 use of a nurse navigator.
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11 94 **Conclusions:** Multidisciplinary cooperation and involvement of a nurse navigator may be unique
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13 95 features to consider when designing, delivering, and evaluating interventions focused on
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15 96 improving accurate and timely cancer diagnosis among symptomatic individuals. Future research
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17 97 should examine the effectiveness of the interventions identified through this review.
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20 98
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22 99 **Keywords:** Early cancer diagnosis; Symptomatic patients; Interventions; Scoping review
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100 **Strengths and limitations of this study**

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

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123 **Introduction**

124 Cancer is the second leading cause of death globally, with about 1 in 6 deaths attributable to the
125 disease.¹ It was estimated in 2020 that over 19 million new cases and about 10 million deaths
126 were attributable to cancer globally.² This rate is estimated to be over 28 million new cases by
127 2040.² High Human Development Index (HDI) countries such as Canada will likely experience
128 the greatest increase in incidence in absolute cancer burden, with an estimated over 4 million
129 new cases more in 2040 compared with 2020.² This is mostly due to the growth and aging of the
130 population and increasing prevalence of cancer risk factors.² Estimates from Canada alone
131 suggest that every day 617 people in Canada will be diagnosed with cancer, with about 228 also
132 dying from the disease.³

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

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

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3 145 services should be designed to reduce delays in and barriers to diagnosis to allow detection at
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5 146 earlier stages of the disease and commence treatment in a timely manner.
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8 147 Various service-focused interventions to improve early cancer diagnosis of symptomatic
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10 148 patients have been implemented in various jurisdictions with varying levels of success.

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12 149 Knowledge of the available interventions, strategies used to implement them, and how successful
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15 150 they might have been is necessary to inform the development, implementation, and evaluation of
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17 151 effective early cancer diagnosis initiatives.
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153 **Methods**

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

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

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

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

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3 176 ***Search strategy***
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5 177 A knowledge synthesis librarian (NA) designed a search strategy for MEDLINE (Ovid). This
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7 178 search strategy was peer-reviewed independently by another knowledge synthesis librarian using
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9
10 179 the Peer Review of Electronic Search Strategies (PRESS) checklist.⁸ The revised search strategy
11
12 180 was then adapted for Cumulative Index to Nursing and Allied Health Literature (CINAHL)
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14 181 (EBSCOhost) and PsycINFO (Ovid) bibliographic databases. The search strategy for each of the
15
16 182 databases is presented in the appendices (**Appendix 2 - 4**). In addition to searching bibliographic
17
18 183 databases, we searched websites of relevant organizations and professional bodies (**Appendix 5**)
19
20 184 and hand-searched reference lists of potentially relevant publications.
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26 186 ***Study selection criteria and data extraction***
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28 187 We sought to summarize practice guidelines, care pathways and initiatives such as
29
30 188 benchmarks/targets for wait times, streamlined or rapid diagnostic services, multidisciplinary
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32 189 teams, and patient navigation strategies that have been found to enhance accurate and timely
33
34 190 cancer diagnosis in symptomatic individuals. We also sought to summarize the leading
35
36 191 interventions to seamless care in the cancer pre-diagnosis phase, performance metrics that can be
37
38 192 used to measure the suspicion to diagnosis phase and how these metrics have been used. Further,
39
40 193 we sought for specific considerations for underserved populations in studies, including
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42 194 considerations for Indigenous, rural, and remote populations.
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47 195 Published (peer-reviewed) and unpublished (grey literature) articles in the English
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49 196 language from January 2017 to January 2021 were included. The decision to include articles
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51 197 from 2017 was because the Partnership had previously summarized prior evidence, not included
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53 198 in this current report.⁹ Study participants were individuals of any age presenting in any clinical
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3 199 settings with symptoms. Interventions included practice guidelines, care pathways or other
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5 200 initiatives focused on achieving pre-defined benchmarks or targets for wait times, streamlined or
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7 201 rapid diagnostic services, multidisciplinary teams, and patient navigation strategies. Outcomes
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9 202 included accuracy and timeliness of cancer diagnosis.

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12 203 All retrieved citations from the literature search were imported and managed in EndNote
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14 204 (Version X9). One reviewer (GNO or OLTL or VKR or LC) screened each citation for
15
16 205 eligibility. Two reviewers (GNO, OLTL, VKR, and LC in pairs) independently screened the full
17
18 206 texts of relevant citations and reviewed the reference list of the included full-text articles for
19
20 207 potentially relevant citations. Disagreements between the reviewers were resolved through
21
22 208 discussion or involvement of a third reviewer (AMAS). The number of screened citations and
23
24 209 both the number and reason for exclusion of full-text articles were documented. One reviewer
25
26 210 (GNO or OLTL or VKR or LC) performed data extraction and charting, and another reviewer
27
28 211 (GNO or OLTL or VKR or LC) independently checked the extracted and charted data for errors.
29
30 212 Disagreements between the reviewers were resolved through discussion or involvement of a third
31
32 213 reviewer (AMAS).

33 34 35 214 36 37 38 39 40 215 ***Data synthesis and analysis***

41
42 216 Characteristics of the included published articles are presented in a tabular form and descriptive
43
44 217 analysis is reported graphically and descriptively. Characteristics of the included unpublished
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46 218 articles are reported descriptively only. Relevant findings from the review of both published and
47
48 219 unpublished articles are summarized separately and descriptively, by review question, focusing
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50 220 on the interventions related to each question. Interventions are grouped as centralized or
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52 221 coordinated diagnostic service; interventions to enhance diagnostic services; multidisciplinary
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3 222 team; patient navigation; rapid referral pathway; remote or rural populations-focused;
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5 223 standardized care pathway; support for primary care providers; target or benchmark; and
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8 224 technology to support the diagnostic process. These interventions are defined in **Appendix 6**.
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10 225 Effectiveness of an intervention was author-defined.
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15 227 ***Patient and public involvement***

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17 228 There was no active engagement of patients and/or members of the public.
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229 Results

230 Out of a total of 21,298 retrieved citations, 88 unique published articles¹⁰⁻⁹⁷ and 16 unique
231 unpublished (grey literature representing 18 different reports)⁹⁸⁻¹¹³ met the inclusion criteria. The
232 article selection process is detailed below (**Figure 1**). Fifty-seven of the published articles were
233 from Europe, 14 articles from North America, 9 articles from Oceania, 3 articles each from
234 Africa and Asia, and one article each from the Middle East and South America. Almost half of
235 these articles (n = 40) were from the United Kingdom (UK) alone. A geographic map of
236 published articles is shown in **Figure 2**.

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

248 **Figure 4** shows the distribution of intervention types across the published articles. Nearly
249 20% of the published articles were on rapid referral pathway interventions while less than 1%
250 each were on multidisciplinary team, patient navigation, and remote/rural-focused interventions.
251 Of the unpublished articles, half reported on rapid referral pathway interventions, 11% each

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3 252 reported on standardized care pathway, target/ benchmark for wait times, and technology to
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5 253 support the diagnosis process, and 5.5% each reported on centralized or coordinated diagnostic
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7 254 service and interventions to enhance diagnostic services. Most of the published articles (94%; n
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9 = 83) reported a performance metric used to measure an improvement in the suspicion to
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11 255 diagnosis phase of cancer.
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15 257 Eighty-three percent (n = 73) of the articles reported either a practice guideline, care
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17 258 pathway or an initiative such as benchmark/target for wait times, streamlined or rapid diagnostic
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19 259 service, multidisciplinary team development, and a patient navigation strategy to enhance
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21 260 accurate and timely cancer diagnosis. Thirty-one percent (n = 27) of the articles reported (not
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23 261 explicitly) on a key point of care as patients navigate the health system, from initial suspicion to
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25 262 diagnosis of cancer. Twenty-nine percent (n = 25) of the articles reported on a leading innovative
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27 263 intervention or approach to seamless care in the pre-cancer diagnosis phase, while 4.5% (n = 4)
28
29 264 of the articles reported on some form of consideration for underserved populations. Some of the
30
31 265 articles reported on two or more of the above. Details of relevant characteristics of the published
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33 266 articles are presented in **Table 1** (those reporting effective interventions) and **Appendix 7** (those
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35 267 reporting ineffective interventions) and **Appendix 8** (those focused on remote/and rural
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37 268 populations).
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44 270 **Initiatives to enhance accurate and timely cancer diagnosis**

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46 271 This review identified various initiatives to enhance accurate and timely cancer diagnosis. These
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48 272 were often designed, developed, and implemented often with the involvement of primary care
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50 273 providers (physicians and nurses), but not patients. These initiatives are grouped into related
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52 274 interventions and the evidence regarding each intervention is discussed below.
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3 276 ***Centralized or coordinated diagnostic services***
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5 277 Nine published articles on centralized or coordinated diagnostic services for adult lung cancer (n
6 = 5) and breast cancer (n = 4) patients were identified.^{20,23,32,33,44,54-56,93} Five were from
7
8 278 Canada,^{23,33,44,54,55} and there was one each from Denmark,²⁰ New Zealand,⁹³ South Africa,⁵⁶ and
9
10 279 the UK³². The focus and metrics for assessment of the effectiveness of these diagnostic services
11
12 280 varied, but all were found to be effective. These include the rapid access to pulmonary
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14 281 investigation and diagnosis (RAPID) program in Wythenshawe Hospital, Manchester, UK with
15
16 282 expedited (next working day) computed tomography (CT) and reporting in suspected lung cancer
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18 283 cases,³² and the Thoracic Triage Panel in a tertiary care centre in St. John's, Newfoundland,
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20 284 Canada, a multidisciplinary centralized referral program, whose key components include a nurse
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22 285 navigator who coordinates patient care and act as the contact person for patients and clinicians
23
24 286 involved in the program, weekly multidisciplinary (thoracic specialists) meetings, and regular
25
26 287 communications with the primary care provider.²³ The diagnostic services also include the rapid
27
28 288 investigation clinic in a tertiary health centre in Montreal, Canada established to coordinate and
29
30 289 accelerate the workup of patients with suspected lung cancer,³³ the improved respiratory fast
31
32 290 track clinic (RFTC) in Northland district of New Zealand that comprises reserved slots for CT
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34 291 for those referred with a suspicion of lung cancer, bronchoscopy slots and CT-guided biopsy,⁹³
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36 292 and the Danish lung cancer package at the Center for Lung Cancer, Odense University Hospital,
37
38 293 Odense, Denmark, a fast-track diagnostic pathway in the hospital setting.²⁰ Further, there was the
39
40 294 rapid access breast clinic in British Columbia, Canada that provides close collaboration between
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42 295 clinicians and radiologists, facilitated by clinical pathways and nurse navigation,^{54,55} the
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44 296 diagnostic assessment units in Ontario, Canada, focusing on diagnosis at a dedicated breast
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46 297 assessment unit,⁴⁴ and the breast clinic at a tertiary hospital in Western Cape Province of South
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3 299 Africa, an open-access one-stop diagnostic breast clinic where women may present with a letter
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5 300 from a primary level provider (nurse practitioner or doctor) and receive the same day clinical and
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7 301 cytological evaluation with referral to the combined breast clinic if the breast cytology is positive
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10 302 for malignancy.⁵⁶

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12 303 In addition to the above, one unpublished article was identified.¹¹³ This was for the Breast
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14 304 ACCESS Project in Ohio, USA, which scheduled patients for a surgical consult within 2 days
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16 305 and a biopsy within 5 days after the surgical consult, with the aim of reducing wait times
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18 306 between abnormal diagnostic mammogram findings to biopsy from 26 to 7 days (7-day ACCESS
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20 307 goal).

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22 308

23 24 309 *Interventions to enhance diagnostic services*

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26 310 Twelve published articles on interventions to enhance diagnostic services were
27
28 311 identified.^{10,17,24,52,53,64,75,77,78,80,83,94} These articles were focused on varied cancer types; four on
29
30 312 multiple cancers, two on lung cancer, two on skin cancer, and one each on breast,
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32 313 gastrointestinal, haematological and prostate cancers. Four articles were from the UK,^{17,52,53,78}
33
34 314 two articles each from Canada^{24,64} and Sweden,^{10,80} and one article each from Botswana,⁹⁴
35
36 315 Columbia,⁷⁵ Indonesia,⁷⁷ and the USA.⁸³ The focus and metrics for assessment of the
37
38 316 effectiveness of the interventions varied across the publications, and while most were effective,
39
40 317 one intervention for lung cancer and one intervention for skin cancer in the UK⁵³ and Sweden¹⁰,
41
42 318 respectively, were ineffective. The effective interventions were reducing diagnosis through
43
44 319 emergency presentation by improving general practice referral in England, UK,⁵² the guided
45
46 320 personal quality of life (QoL) feedback intervention during the Cancer Research UK's North
47
48 321 West regional summer roadshow in Manchester, UK, aimed at offering guided feedback about
49
50 322 personal QoL to adults with potential cancer symptoms, living in deprived communities to

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2
3 323 promote help seeking in primary care among the communities,⁷⁸ the mandatory primary care
4
5 324 access to faecal immunochemical testing (FIT) in Nottingham, UK, integrated with the 2-week
6
7 325 wait pathway, aimed at improving gastrointestinal cancer diagnosis rather than relying on age
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9
10 326 and symptoms alone,¹⁷ the Stronach Regional Cancer Centre lung diagnostic assessment program
11
12 327 (DAP) at Southlake Regional Health Centre, Ontario, Canada, aimed at using learnings from a
13
14 328 Lean improvement event to provide coordinated, expedited care for all patients undergoing a
15
16 329 possible lung cancer diagnosis and to achieve/improve upon the provincial wait time target from
17
18 330 consultation to diagnosis for lung cancer patients,²⁴ the nurse practitioner-led lymphoma rapid
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20 331 diagnosis clinic in a tertiary care cancer center (Princess Margaret Cancer Centre, part of
21
22 332 University Health Network) in Ontario, Canada, aimed at reducing wait times for a definitive
23
24 333 diagnosis of lymphoma,⁶⁴ the expedited one-stop prostate cancer diagnosis using advanced
25
26 334 imaging and biopsy techniques in a health institution (name not reported) in the USA, aimed at
27
28 335 expediting prostate cancer diagnosis.⁸³ There were also the Swedish Diagnostic Center at the
29
30 336 Central Hospital of Kristianstad, Sweden, introduced as a separate outpatient unit within the
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32 337 Department of Internal Medicine to expedite diagnostics,⁸⁰ the Partners for Cancer Care and
33
34 338 Prevention action plan in Cali, Columbia, aimed at improving access to a coordinated program of
35
36 339 screening and early diagnosis of breast and cervical cancers in three health care centers that serve
37
38 340 subsidized populations,⁷⁵ the dermatology-led quality improvement initiatives in Gaborone,
39
40 341 Botswana, aimed at improving multispecialty care coordination,⁹⁴ and the culturally sensitive,
41
42 342 narrative self-help intervention named PERANTARA (PEngantar peRAwataN kesehaTAn
43
44 343 payudaRA [translated as introduction to breast health treatment]) across four hospitals in
45
46 344 Bandung, West Java, Indonesia, aimed at reducing time to diagnosis in women with breast
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48 345 cancer symptoms.⁷⁷ In addition to the above, one unpublished article on the Accelerate,
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3 346 Coordinate, Evaluate (ACE) program in the UK was identified.¹⁰⁰ This program was an early
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5 347 cancer diagnosis initiative and focused on testing innovations that either identify individuals at
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8 348 high risk of cancer earlier or streamline diagnostic pathways.

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10 349 The ineffective interventions were the standardized care diagnostic pathway at the
11
12 350 Department of Clinical Pathology, Akademiska University Hospital in Uppsala, Sweden
13
14 351 (introduced by the Swedish health authorities to eliminate unwanted delay in the diagnostics of
15
16 352 melanoma)¹⁰ and the 4-week national lung cancer symptom awareness campaign in Wales, UK,
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18
19 353 aimed at increasing urgent suspected cancer referrals and clinical outcomes.⁵³
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22 354

23 355 *Multidisciplinary team*

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25
26 356 Three multidisciplinary team lung cancer approaches were identified from published articles:
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28 357 from the USA^{68,85} and Australia.⁵⁰ The focus and metrics for assessment of the effectiveness of
29
30 358 the approaches varied across the publications. One approach from the USA was found to be
31
32 359 effective,⁶⁸ whereas the others were found to be ineffective. The effective approach was the lung
33
34 360 cancer strategist program, a thoracic surgeon-guided, multidisciplinary (disciplines not reported)
35
36 361 care program in hospitals in Massachusetts, USA, aimed at improving timeliness of lung cancer
37
38 362 diagnosis and treatment.⁶⁸ The ineffective approaches were the pre-diagnosis multidisciplinary
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40 363 tumour board (physicians from radiology, medical and radiation oncology, and
41
42 364 pulmonary medicine) discussions in a clinic in Cleveland, USA aimed at improving the
43
44 365 timeliness of diagnostic evaluation in lung cancer,⁸⁵ and the Victorian lung cancer service
45
46 366 redesign project in Victoria, Australia, which involved multidisciplinary (patients, governance,
47
48 367 administration, clinicians and health information services) evaluation aimed at quality
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50 368 improvement collaborative on timeliness and management in lung cancer.⁵⁰ In addition, nine
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52 369 unpublished articles from the UK were identified.^{99,101-103,106,108,109,112} These included four
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3 370 articles regarding a “straight to CT access” pathway, on community pharmacy direct referral to
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5 371 lung cancer pathway, rapid colorectal diagnostic pathway, and optometrist direct referral to
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7 372 neuroscience pathway. All but the chest x-ray pathway¹⁰⁹ were found to be effective.
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10 373

11 374 *Standardized care pathways*

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14 375 Eleven published articles on standardized care pathways were identified.^{11,12,26,35,39,41,49,59,63,70,71}

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16 376 These articles were focused on varied cancer types (4 each for multiple cancers, and 1 each for
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18 377 ear-nose-throat, urinary tract, and gastrointestinal cancers). Three articles were from

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20
21 378 Denmark,^{26,39,41} two from the UK,^{35,70} and one each from Canada,⁵⁹ Norway,⁴⁹ Sweden,⁶³

22
23 379 Spain,¹² and Saudi Arabia.¹¹ The publications were on adult patient populations with one also

24
25 380 involving paediatric patients. The focus and metrics for assessment of the effectiveness of the

26
27 381 pathways varied across the publications. The main effective pathways were the national

28
29 382 diagnostic cancer pathway in Norway, with recommended maximum limits for time spent in the

30
31 383 diagnostic process as well as mandatory reporting of the actual time intervals for all patients with

32
33 384 suspected lung cancer,⁴⁹ and the standardized triage process in the Southeastern Ontario, Canada,

34
35 385 which entailed a twice-weekly nurse–physician triage, preordered staging tests and scheduling

36
37 386 according to urgency, redirection and recommendations for inappropriate referrals, and new

38
39 387 small nodule clinic.⁵⁹ Other main effective pathways were the standardized diagnostic pathway

40
41 388 for suspected urothelial cancer initiated by primary healthcare providers and specialists in Skane

42
43 389 County, Sweden, and comprises CT urography, urinary cytology and cystoscopy,⁶³ the early

44
45 390 colonoscopy track (within 30 days from referral) in a tertiary referral hospital in Tenerife,

46
47 391 Spain,¹² and the fast-track cancer care pathway in Denmark (national), with maximum acceptable

48
49 392 time thresholds from referral to diagnosis and treatment.³⁹ In addition, two unpublished articles

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2
3 393 from Canada¹¹¹ and the UK⁹⁸ focusing on breast and lung cancers, respectively, were identified.
4
5 394 These were the Alberta Health Services Diagnostic Assessment Pathway and the Somerset
6
7 395 Integrated Lung Cancer Pathway. While the Canadian pathway was found to be effective, the
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10 396 pathway from the United Kingdom was not effective.
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12 397

14 398 ***Support for primary care providers***

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17 399 There were four publications on support for primary care providers (PCP), all from the
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19 400 UK.^{27,31,48,97} Two were focused on multiple cancer types, and one each focused on
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21 401 gastrointestinal and brain cancers. The publications were on adult patient populations with one
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23 402 being also involving paediatric patients. The focus and metrics for assessment of the
24
25 403 effectiveness of the support packages (all educational and informational) varied across the
26
27 404 publications. None of the support packages was found to be effective, with the identified
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31 405 common theme being a lack of awareness of referral guidelines and associated knowledge by
32
33 406 GPs. These ineffective support packages were the use of the Kernick and NICE guidelines as
34
35 407 evidence-based support to assist primary care physicians in identifying patients most at risk of
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37
38 408 having a brain tumour, but also on the fastest route to achieve diagnosis (example, direct access
39
40 409 imaging versus urgent secondary care referral) in Scotland, the UK,⁹⁷ the use of the national
41
42 410 cancer waiting times monitoring dataset for system performance assessment by primary care
43
44 411 physicians in England, the UK,²⁷ and the use of safety netting by primary care physicians in
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47 412 Oxfordshire, UK to ensure that patients are monitored until their symptoms or signs are
48
49 413 explained, and to guard against delays in diagnosis.³¹
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51 414

53 415 ***Target or benchmark for wait times***

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3 416 There were eight published articles related to targets or benchmarks for wait
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5 417 times.^{15,42,43,69,73,81,88,96} Three of these articles were from the UK,^{69,73,81} two articles from
6
7 418 Australia,^{42,88} and one article each from China,⁴³ Sweden,⁹⁶ and New Zealand¹⁵. These
8
9 419 publications were focused on varied cancer types (2 each for multiple, lung and gastrointestinal
10
11 420 cancers, and 1 each for prostate and skin cancers), and were on adult patient populations, with
12
13 421 one publication involving paediatric patients. The focus and metrics for assessment of the
14
15 422 effectiveness of the target or benchmarks varied across the publications, and all but two
16
17 423 targets/benchmarks^{15,88} were found to be effective. The effective targets or benchmarks were the
18
19 424 28-day faster diagnosis standard in the National Health Service England, UK, defined as the time
20
21 425 within which the patient is informed whether they do or do not have cancer,⁷³ the fast-track
22
23 426 diagnostic workup for men with suspected prostate cancer at the Urology Department at Orebro
24
25 427 University Hospital in Sweden, which entailed targeting the shortest possible waiting-time for a
26
27 428 diagnostic workup process,⁹⁶ and the optimal timeframes for referral and diagnosis of lung lesion
28
29 429 at Latrobe Regional Hospital in Victoria, Australia established by the National Cancer Expert
30
31 430 Reference Group as part of the optimal care pathway for people with lung cancer.⁴² The
32
33 431 ineffective targets or benchmarks was the New Zealand Ministry of Health's "faster cancer
34
35 432 treatment" standards of service provision for melanoma patients, with a target of
36
37 433 histopathological diagnosis of melanoma reported within five working days in 80% of cases, and
38
39 434 all cases reported in 10 working days.¹⁵ In addition, two unpublished articles from Canada¹⁰⁵ and
40
41 435 the UK¹⁰⁷ focusing on multiple cancers were identified, and these were the "2-week wait"
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43 436 benchmark in the UK (already discussed under rapid referral pathways) and the Canadian Breast
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45 437 Cancer Screening Network targets for diagnostic intervals: $\geq 90\%$ of abnormal screens to be
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3 438 resolved within 5 weeks if no biopsy is required and $\geq 90\%$ within 7 weeks if a tissue biopsy is
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5 439 required.

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10 441 ***Innovative interventions to enhanced care in cancer pre-diagnosis phase***

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12 442 This review identified 17 published articles related to technological interventions for enhanced
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14 443 care in the pre-diagnosis phase of cancer.^{16,21,22,29,37,38,51,57,58,62,65,66,79,82,87,89,91} Ten of these articles
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16 444 were from the UK,^{22,29,37,38,51,57,62,65,66,91} two articles were from New Zealand,^{79,82} and one article
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18 445 each was from Denmark,⁸⁹ Netherlands,²¹ Italy,¹⁶ India,⁸⁷ and Spain.⁵⁸ These publications
19
20 446 focused on varied cancer types in adult patient populations, with two also involving paediatric
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22 447 patients. The interventions had little patient input in their design, development, or
23
24 448 implementation. The focus and metrics for assessment of the effectiveness of the interventions
25
26 449 varied across the publications. The main identified interventions were the use of teledermatology
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28 450 in skin cancer diagnosis. This involved the taking of images, including dermoscopy by GPs and
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30 451 sending them for evaluation to specialized dermatologists.^{38,62,79,89} The process is embedded in
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32 452 an e-referral system developed in Auckland, New Zealand for suspected skin malignancy,⁸² and
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34 453 included teledermatology images triaged as confirmed, likely or suspected melanoma, the use of
35
36 454 a web-based referral tool for head and neck cancers at two different hospitals in Birmingham,
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38 455 West Midlands, and Wexham, Berkshire, UK.⁵¹ There was also the use of the Digitally
39
40 456 Assembled Referral Toolkit (DART) for 2-week referral, accessible via a cloud-based template,
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42 457 which contained new referral forms native to GP clinical systems in the UK.²⁹ Additionally,
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44 458 there was the use of an electronic straight-to-test pathway at a large tertiary referral hospital in
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46 459 England, UK to remove hospital-based triage from suspected colorectal cancer pathways; this
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48 460 allows GPs to book tests supported by a decision aid based on the NICE guidance, thus,
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3 461 eliminating the need for a standard referral form or triage process.⁶⁵ Further, there was the use of
4
5 462 electronic clinical decision support for melanoma in four general practices in the Southeast of
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7 463 England, UK, which involved the use of an electronic-based 7-point checklist to assess
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10 464 pigmented lesions,⁶⁶ the use of machine learning algorithms in Newcastle, UK to classify
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12 465 patients referred on the 2-week wait pathway for suspected head and neck cancer into different
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14 466 diagnostic groups, albeit very broad ones: cancer and non-cancer,⁵⁷ the use of nurse-led
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16 467 assessments to evaluate certain groups of patients suspected to have bowel cancer in England,
17
18 468 the UK,²² and the use of varied smartphone-based skin and oral self-monitoring and screening
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20 469 applications, in England, UK⁹¹ and in the India,⁸⁷ respectively. In addition, two unpublished
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22 470 articles from the UK were identified.^{106,110} These were for a cancer decision support tool
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24 471 (computer-based programs integrated into a GP's usual patient management system) in
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26 472 Gateshead, London, and a clinical web portal (CWP) electronic system in Manchester, England,
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28 473 with the fundamental part of the CWP being that local clinicians had to take personal
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30 474 responsibility for data input.
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38 476 *Performance metrics to measure improvements in suspicion to diagnosis phase*

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40 477 Varied performance metrics were identified by this review. The main metrics are summarized
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42 478 according to intervention type (**Appendix 9**). While performance metrics appear to be mainly
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44 479 intervention-dependent, time from presentation in primary care to diagnosis and from referral
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46 480 from primary care to specialist consultation, appear to be the most consistent metrics used for
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48 481 evaluation. Performance metrics to measure patients' experience mainly centered on patients'
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50 482 satisfaction and quality of life.
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3 484 ***Specific considerations for underserved populations***
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5 485 Four published articles focused on issues related specifically to underserved populations, with all
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7 486 focused on remote/rural populations.^{18,30,60,88} These publications were from the UK,⁶⁰
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10 487 Australia,^{30,88} and Mexico.¹⁸ A fifth publication only used the patients' area of residence as part
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12 488 of their model.⁹⁵ All of the publications were on multiple cancer types and adult populations,
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14 489 although one included a paediatric population. The specific considerations for underserved
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16 490 populations and the evidence regarding them included a publication from Scotland, the UK, a
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18 491 national audit of cancer diagnosis in Scottish and English general practices, exploring and
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20 492 comparing patient characteristics, diagnostic intervals, and routes to diagnosis,⁶⁰ the publication
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22 493 from New South Wales, Australia on a study that examined geographic variations in time
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24 494 intervals leading up to treatment for head and neck cancer, with assessment of differences based
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26 495 on remoteness of residence (regional/remote or metropolitan) at two tertiary referral centres,⁸⁸ a
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28 496 publication from Mexico City, Mexico on evaluation of a patient navigation program to reduce
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30 497 referral time to cancer centers for underserved patients with a suspicion or diagnosis of cancer at
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32 498 a public general hospital,¹⁸ and a publication from Western Australia, a cluster-randomized
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34 499 controlled trial of a complex intervention to reduce time to diagnosis in rural cancer patients with
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36 500 the aim of measuring the effect of community-based symptom awareness and general practice-
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38 501 based educational interventions on the time to diagnosis in rural patients presenting with breast,
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44 502 prostate, colorectal or lung cancer.³⁰
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504 **Discussion**

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

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

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3 527 The interventions mostly comprised multiple interventions/ changes to the healthcare
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5 528 pathway. As such, the interventions examined varied widely across the studies. This was true
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8 529 even when applied to the same cancer patient populations and in the same jurisdictions/
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10 530 countries, including those where an intervention was part of the standard care pathway. As such,
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12 531 it is difficult, perhaps impossible, to identify one main approach alone that drives an
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14 532 intervention. Methodological approaches also varied significantly with regard to outcome
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16 533 assessment. A common theme among the effective centralized or coordinated diagnostic
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18 534 services, interventions to enhance diagnostic services, patient navigation approaches, and
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20 535 standardized care pathways is multidisciplinary collaboration and the involvement of a nurse
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22 536 navigator.

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26 537 The implications of the findings from this scoping review are that it is difficult to
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28 538 determine a specific intervention, or stand-alone approach to an intervention. It is also difficult to
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30 539 assess the true effectiveness of many of the interventions, especially considering the differing
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32 540 composite nature of the interventions, the fact that the evidence is mostly from observational
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34 541 studies, and the range of outcome measures used to measure effectiveness. While many of the
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36 542 interventions could be adapted to suit different health systems and jurisdictions, emphasis should
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38 543 be on the context and the strengths and limitations of the individual health system, and a clear
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40 544 evidence-based performance metric for appropriate evaluation of effectiveness of an intervention
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42 545 ought to be determined a priority. Diagnosing cancer faster and more accurately at an earlier
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44 546 stage is a key priority of the 2019-2029 Canadian Strategy for Cancer Control.¹¹⁴ Over the next 5
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46 547 years, the Canadian Partnership Against Cancer will leverage findings from this scoping review,
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51 548 as one of several inputs, and partner with Canadian jurisdictions to continue to test innovative
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3 549 models of care that expedite cancer diagnosis, especially for Indigenous and underserved
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5 550 populations.
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10 552 **Limitations and merits**

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12 553 There are some limitations to this study. The literature search was developed by a knowledge
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14 554 synthesis librarian and peer reviewed by an independent knowledge synthesis librarian using the
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16 555 PRESS checklist. We searched appropriate databases and websites for literature, and adhered to
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18 556 known guidelines and standards in the conduct and reporting of the review. Even so, the
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20 557 literature search was limited to evidence from the last 4 years and only evidence from English-
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22 558 language publications and organizational websites. As such, potentially eligible articles could
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24 559 have been missed.
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28 560 The eligibility criteria for inclusion were not limited to only comparative studies. This
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30 561 meant that the focus of some of the included studies was not specifically on the assessment of
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32 562 effectiveness of an intervention, which was based solely on the reported outcome in the articles.
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34 563 As such, an intervention that appeared effective in a study may be ineffective in another study
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36 564 depending on the assessed outcome with no clear reason for this discrepancy. Furthermore, this
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38 565 review did not assess effectiveness of interventions across cancer patient types and
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40 566 jurisdictions/regions. This would have allowed assessment of any differences in intervention
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42 567 effectiveness by patient type and study jurisdiction. Lastly, and in line with the JBI's guidance
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44 568 for the conduct of scoping reviews, we did not attempt to evaluate the quality of the included
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46 569 studies or provide an assessment of the quality of the evidence.
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54 571 **Conclusions**

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3 572 The evidence suggests that interventions focused on improving accurate and timely cancer
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5 573 diagnosis among symptomatic individuals are active topics of research, particularly in lung
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7 574 cancer patient populations, and that the UK is championing this area of research. While the
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10 575 themes of the studied interventions are similar, the interventions differ in many ways within the
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12 576 same intervention group. Multidisciplinary cooperation and involvement of a nurse navigator
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14 577 appeared to be unique features of many of the effective interventions. Canadian and other
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16 578 jurisdictions can leverage these lessons learned to develop and implement strategies adapted to
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18 579 local health system needs to improve the cancer pre-diagnosis phase. Future research should
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20 580 examine the effectiveness of the interventions identified through this review.
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26 582 **Data availability statement:** No additional data are available.
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30 584 **Ethics approval:** Not applicable.
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34 586 **Details of the role of the study sponsors:** The Canadian Partnership Against Cancer (the study
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36 587 commissioner) contributed to specifying the study objectives and questions, and in summarizing
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38 588 the evidence.
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42 590 **Patient and public involvement:** There was no active engagement of patients and/or members
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44 591 of the public.
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For peer review only

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

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

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

					referral to initial clinic assessment	
	Whitley 2017 ⁹²	USA (Boston, Denver, San Antonio, and Tampa)	Case-Control (2007-2011)	Multiple (Adult) [6349]	Delays in diagnostic resolution based on Charlson Comorbidity Index score	Patient navigation reduced delays in diagnostic resolution, with the greatest benefits seen for those with a Charlson Comorbidity Index score ≥ 2 (Effective)
	Antel 2020 ¹³	South Africa (Cape Town)	Before-and-After (2017-2019)	Haematological (Adult) [130]	Diagnostic interval	Compared with a historical cohort, the diagnostic interval (time from first health visit to diagnostic biopsy) for patients with lymphoma was significantly shorter, 13.5 vs 48 days ($p=0.002$) (Effective)
	Arhi 2020 ¹⁴	UK (National)	Case-Control (2000-2013)	Gastrointestinal (Adult) [7130]	Hazard ratios of death	Patients referred between 2 weeks to 3 months, and after 3 months with red-flag symptoms demonstrated a significantly worse prognosis than patients who were referred within 2 weeks (Effective)
	Chng 2020 ¹⁹	UK (Newcastle-upon-Tyne)	Case-Control (2015-2019)	Brain (Adult) [101]	Tumour detection rate	With guideline adherence, the brain tumour detection rate was 3-fold higher (36.0% vs 11.5%, $p=0.02$) (Effective)
	Creak 2020 ²⁵	UK (Brighton; Sussex)	Cross-sectional (2015-2018)	Multiple (Adult) [258]	Time to diagnosis	Direct GP referrals were feasible and manageable within a tertiary clinic and resulted in high rates of cancer diagnoses and early contact with an oncologist and nurse specialist, cutting short the 'limbo' time of high anxiety before diagnosis (Effective)
	Hennessy 2020 ³⁶	Ireland (Dublin)	Case-Control (2012-2018)	Lung (NR) [864]	Time to diagnosis	Time to diagnosis was longer in those who had attended a post Rapid Access Lung Cancer Clinic CT (34.5 versus 21 days) (Effective)
Rapid referral pathway	Jones 2018 ⁴⁵	UK (East Midlands)	Case-Control (2013-2015)	Gastrointestinal (NR) [1401 (340 STTP, 495 traditional pathway, 566 control trusts)]	Time from referral to diagnosis	The pathway saved a mean of 7 days from referral to treatment (with a 95% CI of 3 to 11 days, $p<0.008$) and a mean of 16 days from referral to diagnosis, when compared with a traditional pathway (Effective)
	Joyce 2020 ⁴⁶	UK (National)	Cross-sectional (2017-2018)	Multiple (Mixed age) [NR]	Proportion with emergency diagnosis of cancer	A lower proportion of emergency diagnosis of cancer was found with higher 2 weeks wait referral conversion rate (Effective)
	Pearson 2020 ⁶⁷	UK (National)	Case-Control (2014)	Multiple (Mixed age) [12873]	Primary care interval	Compared with patients with a specific alarm symptom, patients with non-specific but concerning symptoms had higher odds of having longer primary care intervals (adjusted OR: 1.24 (1.11 to 1.36)) (Effective)
	Round 2020 ⁷²	UK (National)	Case-Control (2011-2017)	Multiple (Mixed age) [1469103]	Risk of death	Cancer patients from the highest referring practices had a lower hazard of death (hazard ratio [HR] = 0.96; 95% confidence interval [CI] = 0.95 to 0.97) (Effective)
	Sandager 2019 ⁷⁴	Denmark (National)	Cross-sectional (2010)	Multiple (Adult) [2256]	Patient experience	Overall, pathway referred patients were 21% more likely than non-pathway referred patients to report a positive experience (PR = 1.21 [95% CI: 1.11–1.30]) (Effective)

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

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

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4	Sunderland 2020 ⁸²	New Zealand (Auckland)	Case-Control (2016)	Skin (NR) [809]	Efficacy of diagnostic tool	A positive predictive value (PPV) of 38.1% and number needed to excise (NNE) of 2.6, with less than 10% of referrals triaged for teledermatology confirmed as melanoma (24/264) (Effective)
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6	Uthoff 2018 ⁸⁷	India (Bangalore, Dimapur)	Case-Control (NR)	Oral (Adult) [99]	Diagnostic accuracy	Sensitivities, specificities, positive predictive values, and negative predictive values ranged from 81.25% to 94.94% (Effective)
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8	Vestergaard 2020 ⁸⁹	Denmark (Southern Denmark)	Case-Control (2018)	Skin (Adult) [519]	Percentage of lesions not requiring further in-person assessment	On evaluation by teledermatology, 31.5% of lesions did not need further in-person assessment (Effective)
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13 CRC = colorectal cancer; CT = computed tomography; FIT = faecal immunochemical testing; GP = general practitioner; NR = not reported; RABC = rapid
 14 access breast clinic; RCT = randomized controlled trial; RIC = rapid investigation clinic; STTP = straight to test pathway; TD = teledermatology; TS =
 15 traditional system; UK = United Kingdom; USA = United States of America; * = effective but not applicable; IQR = interquartile range
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3 **Figures**
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7 **Figure 1:** Modified PRISMA flow chart
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10 **Figure 2:** Geographical mapping of the included published articles
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14 **Figure 3:** Summary of cancer types reported by the included published articles
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18 **Figure 4:** Summary of intervention types reported by the included published articles
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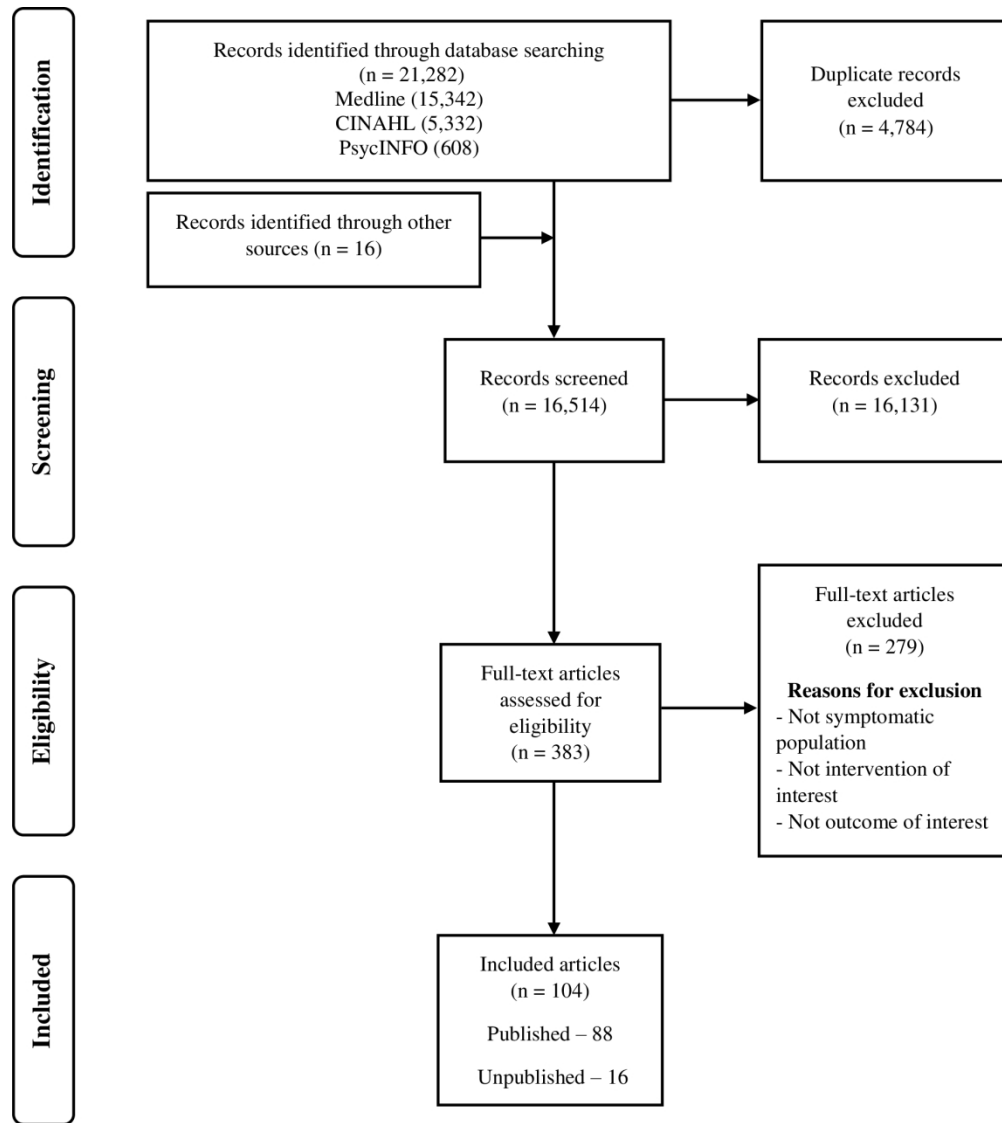
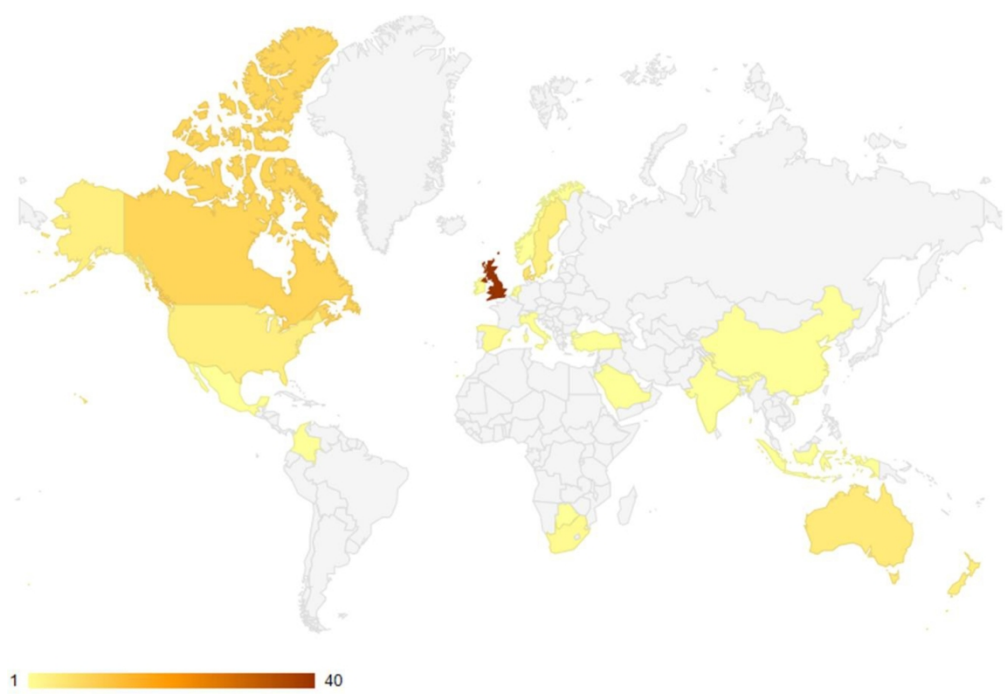


Figure 1: Modified PRISMA flow chart

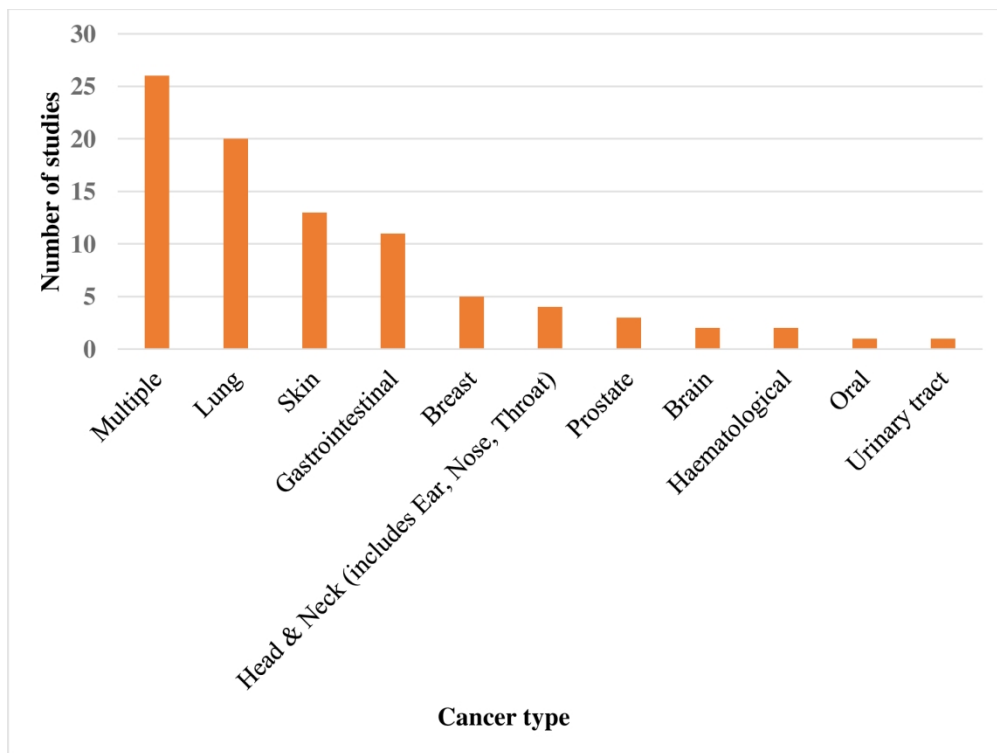
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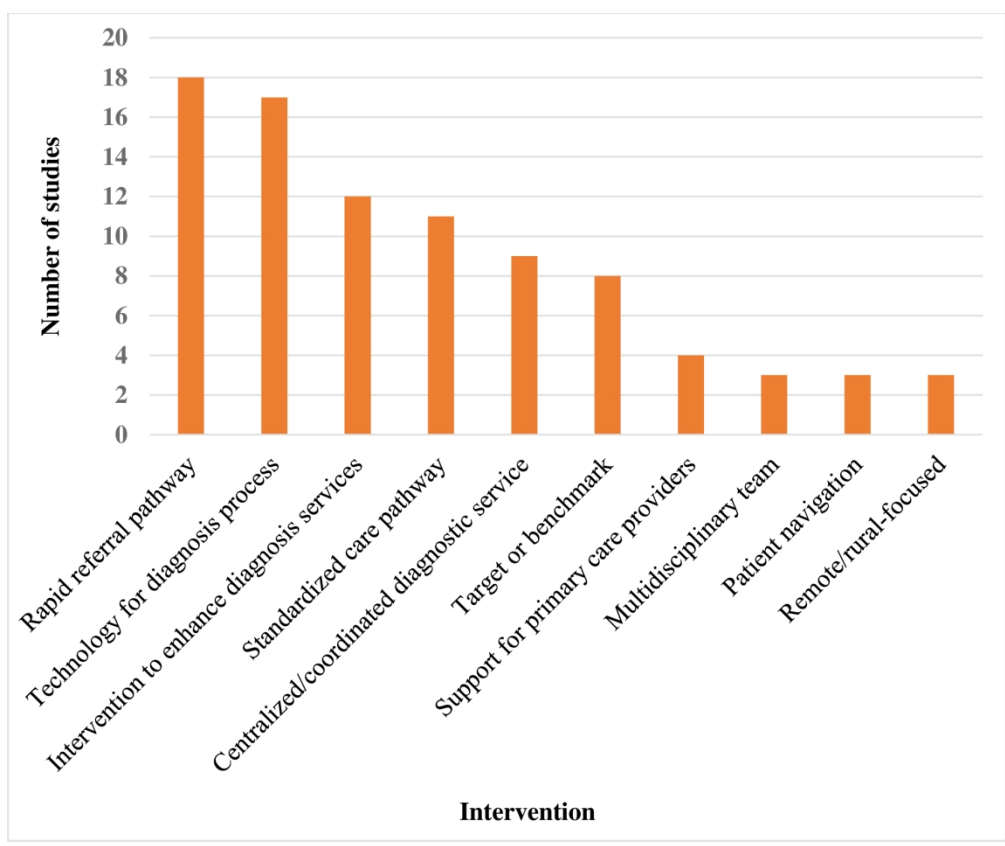
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Appendices

Appendix 1: Project work plan

About the Project Team

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

Proposed Method

Methods

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

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

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

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

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

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

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

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

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4 KQ 5. Have specific considerations been applied to underserved populations including Indigenous,
5 rural, and remote populations within the context of each of the questions above?
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7 **Study eligibility criteria**

8 This review will focus on published and unpublished studies that answer the key questions since 2017.
9 Our focus is on comparative studies that applied a protocol/guideline or a specific intervention or
10 intervention plan. Having said that, we anticipate the need to review lower quality study designs (e.g.,
11 retrospective, and uncontrolled studies). As such, there will be no restriction on the study design, but will
12 be limited to English language publications for feasibility.
13

14 **Search strategy and study selection**

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

26 We will develop data extraction forms and pilot them on a small selection of studies. Extracted data will
27 be stored and managed in MS Excel. One reviewer will independently extract data from included studies
28 and another reviewer will independently check the extracted data for errors. Disagreements will be
29 resolved by discussion between reviewers and/ or by involving a third reviewer, as needed.
30

31 **Data analysis**

32 We will present specific characteristics of all included studies in a tabular form. The analysis of the
33 extracted data will be descriptive.
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35 **Study dissemination**

36 We will submit reports from this study as a technical report to CPAC.
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41 **Knowledge User Engagement Plan**

42 We will be providing a bi-weekly update to CPAC on the progression of the review. Specifically, we will
43 engage during specific time points to review progress and next steps:
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- 45 - Protocol
- 46 - Level I Screening (Title/ Abstract screening phase)
- 47 - Level II Screening (Full-text screening phase)
- 48 - Data Extraction
- 49 - Data Analysis
- 50 - Report
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52 **Declaration of Conflict of Interest**

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55 None
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Appendix 2: MEDLINE (Ovid) search strategy

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

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

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

Appendix 3: CINAHL (EbscoHOST) search strategy

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

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 4 sheep) OR (MH swine) OR (MH primates) OR (animal OR animals OR pisces OR fish OR
 5 fishes OR catfish OR catfishes OR sheatfish OR silurus OR arius OR heteropneustes OR
 6 clarias OR gariepinus OR "fathead minnow" OR "fathead minnows" OR pimephales OR
 7 promelas OR cichlidae OR trout OR trouts OR char OR chars OR salvelinus OR salmo OR
 8 oncorhynchus OR guppy OR guppies OR millionfish OR poecilia OR goldfish OR goldfishes
 9 OR carassius OR auratus OR mullet OR mullets OR mugil OR curema OR shark OR sharks
 10 OR cod OR cods OR gadus OR morhua OR carp OR carps OR cyprinus OR carpio OR
 11 killifish OR eel OR eels OR anguilla OR zander OR sander OR lucioperca OR stizostedion
 12 OR turbot OR turbots OR psetta OR flatfish OR flatfishes OR plaice OR pleuronectes OR
 13 platessa OR tilapia OR tilapias OR oreochromis OR sarotherodon OR "common sole" OR
 14 "dover sole" OR solea OR zebrafish OR zebrafishes OR danio OR rerio OR seabass OR
 15 dicentrarchus OR labrax OR morone OR lamprey OR lampreys OR petromyzon OR
 16 pumpkinseed OR pumpkinseeds OR lepromis OR gibbosus OR herring OR clupea OR
 17 harengus OR amphibia OR amphibian OR amphibians OR anura OR salientia OR frog OR
 18 frogs OR rana OR toad OR toads OR bufo OR xenopus OR laevis OR bombina OR epidalea
 19 OR calamita OR salamander OR salamanders OR newt OR newts OR triturus OR reptilia OR
 20 reptile OR reptiles OR "bearded dragon" OR pogona OR vitticeps OR iguana OR iguanas OR
 21 lizard OR lizards OR "anguis fragilis" OR turtle OR turtles OR snakes OR snake OR aves OR
 22 bird OR birds OR quail OR quails OR coturnix OR bobwhite OR colinus OR virginianus OR
 23 poultry OR poultries OR fowl OR fowls OR chicken OR chickens OR gallus OR "zebra
 24 finch" OR taeniopygia OR guttata OR canary OR canaries OR serinus OR canaria OR
 25 parakeet OR parakeets OR grasskeet OR parrot OR parrots OR psittacine OR psittacines OR
 26 shelduck OR tadorna OR goose OR geese OR branta OR leucopsis OR woodlark OR lullula
 27 OR flycatcher OR ficedula OR hypoleuca OR dove OR doves OR geopelia OR cuneata OR
 28 duck OR ducks OR greylag OR graylag OR anser OR harrier OR circus pygargus OR red knot
 29 OR "great knot" OR calidris OR canutus OR godwit OR limosa OR lapponica OR meleagris
 30 OR gallopavo OR jackdaw OR corvus OR monedula OR ruff OR philomachus OR pugnax
 31 OR lapwing OR peewit OR plover OR vanellus OR swan OR cygnus OR columbianus OR
 32 bewickii OR gull OR chroicocephalus OR ridibundus OR albifrons OR "great tit" OR parus
 33 OR aythya OR fuligula OR streptopelia OR risoria OR spoonbill OR platalea OR leucorodia
 34 OR blackbird OR turdus OR merula OR blue tit OR cyanistes OR pigeon OR pigeons OR
 35 columba OR pintail OR anas OR starling OR sturnus OR owl OR "athene noctua" OR
 36 pochard OR ferina OR cockatiel OR nymphicus OR hollandicus OR skylark OR alauda OR
 37 tern OR sterna OR teal OR crecca OR oystercatcher OR haematopus OR ostralegus OR shrew
 38 OR shrews OR sorex OR araneus OR crocidura OR russula OR "european mole" OR talpa
 39 OR chiroptera OR bat OR bats OR eptesicus OR serotinus OR myotis OR dasycneme OR
 40 daubentonii OR pipistrelle OR pipistrellus OR cat OR cats OR felis OR catus OR feline OR
 41 dog OR dogs OR canis OR canine OR canines OR otter OR otters OR lutra OR badger OR
 42 badgers OR meles OR fitchew OR fitch OR fougart OR foulmart OR ferrets OR ferret OR
 43 polecat OR polecats OR mustela OR putorius OR weasel OR weasels OR fox OR foxes OR
 44 vulpes OR "common seal" OR phoca OR vitulina OR grey seal OR halichoerus OR horse OR
 45 horses OR equus OR equine OR equidae OR donkey OR donkeys OR mule OR mules OR pig
 46 OR pigs OR swine OR swines OR hog OR hogs OR boar OR boars OR porcine OR piglet OR
 47 piglets OR sus OR scrofa OR llama OR llamas OR lama OR glama OR deer OR deers OR
 48 cervus OR elaphus OR cow OR cows OR "bos taurus" OR "bos indicus" OR bovine OR bull
 49 OR bulls OR cattle OR bison OR bisons OR sheep OR sheeps OR "ovis aries" OR ovine OR
 50 lamb OR lambs OR mouflon OR mouflons OR goat OR goats OR capra OR caprine OR
 51 chamois OR rupicapra OR leporidae OR lagomorpha OR lagomorph OR rabbit OR rabbits
 52 OR oryctolagus OR cuniculus OR laprine OR hares OR lepus OR rodentia OR rodent OR
 53 rodents OR murinae OR mouse OR mice OR mus OR musculus OR murine OR woodmouse
 54
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 56
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	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 cricetus OR gerbil OR gerbils OR jird OR jirds OR meriones OR unguiculatus OR jerboa OR jerboas OR jaculus OR chinchilla OR chinchillas OR beaver OR beavers OR "castor fiber" OR "castor canadensis" OR sciuridae OR squirrel OR squirrels OR sciurus OR chipmunk OR chipmunks OR marmot OR marmots OR marmota OR suslik OR susliks OR spermophilus OR cynomys OR cottonrat OR cottonrats OR sigmodon OR vole OR voles OR microtus OR myodes OR glareolus OR primate OR primates OR prosimian OR prosimians OR lemur OR lemurs OR lemuridae OR loris OR "bush baby" OR "bush babies" OR bushbaby OR bushbabies OR galago OR galagos OR anthropoidea OR anthropoids OR simian OR simians OR monkey OR monkeys OR marmoset OR marmosets OR callithrix OR cebuella OR tamarin OR tamarins OR saguinus OR leontopithecus OR squirrel monkey OR squirrel monkeys OR saimiri OR "night monkey" OR "night monkeys" OR "owl monkey" OR "owl monkeys" OR douroucoulis OR aotus OR "spider monkey" OR "spider monkeys" OR ateles OR baboon OR baboons OR papio OR "rhesus monkey" OR macaque OR macaca OR mulatta OR cynomolgus OR fascicularis OR "green monkey" OR "green monkeys" OR chlorocebus OR vervet OR vervets OR pygerythrus OR hominoidea OR ape OR apes OR hylobatidae OR gibbon OR gibbons OR siamang OR siamangs OR nomascus OR symphalangus OR hominidae OR orangutan OR orangutans OR pongo OR chimpanzee OR chimpanzees OR "pan troglodytes" OR bonobo OR bonobos OR "pan paniscus" OR gorilla OR gorillas OR troglodytes)) NOT ((MH human) OR (human# OR man OR men OR woman OR women OR child OR children OR patient#))	
21.	S19 NOT S20	14678
22.	S21 Limiters - Published Date: 20170101-20201231	5333

Appendix 4: Psycinfo (Ovid) search strategy

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

	<p>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 fountmart 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 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.)</p>	
20.	18 not 19	2754
21.	limit 20 to yr="2017 -Current"	608

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

Canada

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

International

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

Appendix 6: Definition for interventions related to the review questions

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

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

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

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

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

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

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

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

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

UK = United Kingdom; IQR = interquartile range

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

Intervention Type	Performance Metric
Centralized or coordinated diagnostic service	<ul style="list-style-type: none"> • Time from presentation in primary care to diagnosis • Time from referral from primary care to specialist consultation • Time from first abnormal image to biopsy
Interventions to enhance diagnostic services	<ul style="list-style-type: none"> • Time from referral from primary care to specialist consultation • Time from initial specialist consultation to diagnosis • Time from initial specialist consultation to biopsy • Time from first abnormal image to biopsy • Time from presentation in primary care to biopsy • Total diagnostic interval • Turnaround time for diagnosis following histology • Number of urgent referrals to specialist • Cancer detection rate • Patient survival
Multidisciplinary team	<ul style="list-style-type: none"> • Time from referral from primary care to specialist consultation • Time from first abnormal image to diagnosis
Patient navigation	<ul style="list-style-type: none"> • Waiting times from the point of referral from primary care to initial specialist assessment • Feasibility of program/process • Delays in diagnostic resolutions

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

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	4-5
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	7-8
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	8-9
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	9
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	10-11
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	10
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix 2 - 4
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	10-11
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	11-12
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Appendix 6
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Not applicable

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	11-12
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Table 1
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not applicable
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	14-24
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	13-24
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	25-27
Limitations	20	Discuss the limitations of the scoping review process.	27
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	28
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	2

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

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

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

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

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

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



BMJ Open

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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-055488.R2
Article Type:	Original research
Date Submitted by the Author:	20-Oct-2021
Complete List of Authors:	Okoli, George; University of Manitoba Max Rady College of Medicine Lam, Otto; University of Manitoba Max Rady College of Medicine Reddy, Viraj; University of Manitoba Max Rady College of Medicine Copstein, Leslie; University of Manitoba Max Rady College of Medicine Askin, Nicole; University of Manitoba Prashad, Anubha; Canadian Partnership Against Cancer Stiff, Jennifer; Canadian Partnership Against Cancer Khare, Satya Rashi; Canadian Partnership Against Cancer Leonard, Robyn; Canadian Partnership Against Cancer Zarin, Wasifa; Unity Health Toronto Tricco, Andrea; University of Toronto Dalla Lana School of Public Health, Abou-Setta, Ahmed; University of Manitoba Max Rady College of Medicine
Primary Subject Heading:	Oncology
Secondary Subject Heading:	Evidence based practice, Health services research, Patient-centred medicine, Public health
Keywords:	ONCOLOGY, PREVENTIVE MEDICINE, PRIMARY CARE, PUBLIC HEALTH

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3 **1 Interventions to improve early cancer diagnosis of symptomatic individuals: A scoping**
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26
27 36 **Funding:** This study was funded in part by the Canadian Partnership Against Cancer (the

28
29 37 Partnership) and the Canadian Institutes of Health Research (CIHR) under the Strategy for

30
31 38 Patient Oriented-Research (SPOR) initiative, through the SPOR Evidence Alliance. Andrea C.

32
33 39 Tricco is funded by a Tier 2 Canada Research Chair in Knowledge Synthesis.

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35 40

36
37 41 **Competing interests declaration:** All authors declare that they have no conflicts of interest: no

38
39 42 financial relationships with any organisations that might have an interest in the submitted work,

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41 43 and no relationships or activities that could appear to have influenced the submitted work.

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45 45 **Patient consent:** Not applicable

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7 49 Data acquisition (GN Okoli, OLT Lam, VK Reddy, L Copstein, N Askin, & AM Abou-Setta);
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9 50 Formal analysis (GN Okoli); Draft manuscript (GN Okoli & AM Abou-Setta); Final manuscript
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11 51 revisions (GN Okoli, OLT Lam, VK Reddy, L Copstein, N Askin, A Prashad, J Stiff, SR Khare,
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13 52 R Leonard, W Zarin, AC Tricco & AM Abou-Setta); Guarantor (GN Okoli & AM Abou-Setta).
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15 53 The corresponding author (the manuscript's guarantor) attests that all listed authors meet
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17 54 authorship criteria and that no others meeting the criteria have been omitted.
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49 67 accurate, and transparent account of the study being reported; that no important aspects of the
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51 68 study have been omitted; and that any discrepancies from the study as planned have been
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53 69 explained.
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2
3 **70 Abstract**

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5 **71 Objectives:** To summarize the current evidence regarding interventions for accurate and timely
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7 **72** cancer diagnosis among symptomatic individuals.
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10 **73 Design:** A scoping review following the Joanna Briggs Institute's methodological framework for
11
12 **74** the conduct of scoping reviews and reported in accordance with the Preferred Reporting Items
13
14 **75** for Systematic Reviews and Meta-analyses extension for scoping reviews (PRISMA-ScR)
15
16 **76** checklist.
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20 **77 Data sources:** MEDLINE (Ovid), CINAHL (EBSCOhost) and PsycINFO (Ovid) bibliographic
21
22 **78** databases, and websites of relevant organizations. Published and unpublished literature (grey
23
24 **79** literature) of any study type in the English language were searched for from January 2017 to
25
26 **80** January 2021.
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30 **81 Eligibility and criteria:** Study participants were individuals of any age presenting at clinics with
31
32 **82** symptoms indicative of cancer. Interventions included practice guidelines, care pathways or
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34 **83** other initiatives focused on achieving pre-defined benchmarks or targets for wait times,
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36 **84** streamlined or rapid cancer diagnostic services, multidisciplinary teams, and patient navigation
37
38 **85** strategies. Outcomes included accuracy and timeliness of cancer diagnosis.
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42 **86 Data extraction and synthesis:** We summarized findings graphically and descriptively.
43
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45 **87 Results:** From 21,298 retrieved citations, 88 unique published articles and 16 unique unpublished
46
47 **88** documents (on 18 study reports), met the eligibility for inclusion. About half of the published
48
49 **89** literature and 83% of the unpublished literature were from the United Kingdom. Most of the
50
51 **90** studies were on interventions in lung cancer patients. Rapid referral pathways and technology for
52
53 **91** supporting and streamlining the cancer diagnosis process were the most studied interventions.
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3 92 Interventions were mostly complex and organization-specific. Common themes among the
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5 93 studies that concluded intervention was effective were multidisciplinary collaboration and the
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7
8 94 use of a nurse navigator.
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10 95 **Conclusions:** Multidisciplinary cooperation and involvement of a nurse navigator may be unique
11
12
13 96 features to consider when designing, delivering, and evaluating interventions focused on
14
15 97 improving accurate and timely cancer diagnosis among symptomatic individuals. Future research
16
17
18 98 should examine the effectiveness of the interventions identified through this review.
19

20 99
21
22 100 **Keywords:** Early cancer diagnosis; Symptomatic individuals; Interventions; Scoping review
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3 101 **Strengths and limitations of this study**
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- 5 102 • A knowledge synthesis librarian developed the search strategy for this review and this
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7
8 103 was peer reviewed by an independent knowledge synthesis librarian using the PRESS
9
10 104 checklist.
11
12 105 • The literature search was limited to evidence from the last 4 years and only evidence
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14 106 from English-language publications and organizational websites.
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17 107 • This review did not summarize effectiveness of interventions across cancer patient types
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19 108 and regions.
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22 109 • We adhered to known guidelines and standards in the conduct and reporting of the
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24 110 review.
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27 111 • In line with the JBI's guidance for the conduct of scoping reviews, we did not attempt to
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29 112 evaluate the quality of the included studies or provide an assessment of the quality of the
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31 113 evidence.
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124 **Introduction**

125 Cancer is the second leading cause of death globally, with about 1 in 6 deaths attributable to the
126 disease.¹ It was estimated in 2020 that over 19 million new cases and about 10 million deaths
127 were attributable to cancer globally.² This rate is estimated to be over 28 million new cases by
128 2040.² High Human Development Index (HDI) countries such as Canada will likely experience
129 the greatest increase in incidence in absolute cancer burden, with an estimated over 4 million
130 new cases more in 2040 compared with 2020.² This is mostly due to the growth and aging of the
131 population and increasing prevalence of cancer risk factors.² Estimates from Canada alone
132 suggest that every day 617 people in Canada will be diagnosed with cancer, with about 228 also
133 dying from the disease.³

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

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

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3 146 services.⁵ These services should be designed to reduce delays in and barriers to diagnosis to
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5 147 allow detection at earlier stages of the disease and commence treatment in a timely manner.
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8 148 Various service-focused interventions to improve early cancer diagnosis of symptomatic
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10 149 individuals have been implemented in various jurisdictions with varying levels of success.

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12 150 Knowledge of the available interventions, strategies used to implement them, and how successful
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14 151 they might have been is necessary to inform the development, implementation, and evaluation of
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16 152 effective early cancer diagnosis initiatives.
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154 **Methods**

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

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

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

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

176

177 *Search strategy*

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

187 *Study selection criteria and data extraction*

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

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

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3 200 settings with symptoms. Interventions included practice guidelines, care pathways or other
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5 201 initiatives focused on achieving pre-defined benchmarks or targets for wait times, streamlined or
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7 202 rapid diagnostic services, multidisciplinary teams, and patient navigation strategies. Outcomes
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9 203 included accuracy and timeliness of cancer diagnosis.

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12 204 All retrieved citations from the literature search were imported and managed in EndNote
13
14 205 (Version X9). One reviewer (GNO or OLTL or VKR or LC) screened each citation for
15
16 206 eligibility. Two reviewers (GNO, OLTL, VKR, and LC in pairs) independently screened the full
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18 207 texts of relevant citations and reviewed the reference list of the included full-text articles for
19
20 208 potentially relevant citations. Disagreements between the reviewers were resolved through
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22 209 discussion or involvement of a third reviewer (AMAS). The number of screened citations and
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24 210 both the number and reason for exclusion of full-text articles were documented. One reviewer
25
26 211 (GNO or OLTL or VKR or LC) performed data extraction and charting, and another reviewer
27
28 212 (GNO or OLTL or VKR or LC) independently checked the extracted and charted data for errors.
29
30 213 Disagreements between the reviewers were resolved through discussion or involvement of a third
31
32 214 reviewer (AMAS).

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39 216 ***Data synthesis and analysis***

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42 217 Characteristics of the included published articles are presented in a tabular form and descriptive
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44 218 analysis is reported graphically and descriptively. Characteristics of the included unpublished
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46 219 articles are reported descriptively only. Relevant findings from the review of both published and
47
48 220 unpublished articles are summarized separately and descriptively, by review question, focusing
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50 221 on the interventions related to each question. Interventions are grouped as centralized or
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52 222 coordinated diagnostic service; interventions to enhance diagnostic services; multidisciplinary
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3 223 team; patient navigation; rapid referral pathway; remote or rural populations-focused;
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5 224 standardized care pathway; support for primary care providers; target or benchmark; and
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8 225 technology to support the diagnostic process. These interventions are defined in **Appendix 6**. We
9
10 226 determined the effectiveness of an intervention based on study findings and conclusions reported
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12 227 by the primary study's authors with respect to intervention effect. As such, effective
13
14 228 interventions were those interventions that were found to have had a statistically significant
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16 229 positive effect on an author-determined outcome for effectiveness evaluation. It is important to
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18 230 note that the authors of this scoping review did not assess risk of bias nor rate the quality of
19
20 231 evidence and thus definitive conclusions on effectiveness cannot be drawn.
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26 233 ***Patient and public involvement***
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28 234 There was no active engagement of patients and/or members of the public.
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235 Results

236 Out of a total of 21,298 retrieved citations, 88 unique published articles¹⁰⁻⁹⁷ and 16 unique
237 unpublished (grey literature representing 18 different reports)⁹⁸⁻¹¹³ met the inclusion criteria. The
238 article selection process is detailed below (**Figure 1**). Fifty-seven of the published articles were
239 from Europe, 14 articles from North America, 9 articles from Oceania, 3 articles each from
240 Africa and Asia, and one article each from the Middle East and South America. Almost half of
241 these articles (n = 40) were from the United Kingdom (UK) alone. A geographic map of
242 published articles is shown in **Figure 2**.

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

254 **Figure 4** shows the distribution of intervention types across the published articles. Nearly
255 20% of the published articles were on rapid referral pathway interventions while less than 1%
256 each were on multidisciplinary team, patient navigation, and remote/rural-focused interventions.
257 Of the unpublished articles, half reported on rapid referral pathway interventions, 11% each

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3 258 reported on standardized care pathway, target/ benchmark for wait times, and technology to
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5 259 support the diagnosis process, and 5.5% each reported on centralized or coordinated diagnostic
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7 260 service and interventions to enhance diagnostic services. Most of the published articles (94%; n
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9 = 83) reported a performance metric used to measure an improvement in the suspicion to
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11 261 diagnosis phase of cancer.
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15 263 Eighty-three percent (n = 73) of the articles reported either a practice guideline, care
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17 264 pathway or an initiative such as benchmark/target for wait times, streamlined or rapid diagnostic
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19 265 service, multidisciplinary team development, and a patient navigation strategy to enhance
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21 266 accurate and timely cancer diagnosis. Thirty-one percent (n = 27) of the articles reported (not
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23 267 explicitly) on a key point of care as patients navigate the health system, from initial suspicion to
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25 268 diagnosis of cancer. Twenty-nine percent (n = 25) of the articles reported on a leading innovative
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27 269 intervention or approach to seamless care in the pre-cancer diagnosis phase, while 4.5% (n = 4)
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29 270 of the articles reported on some form of consideration for underserved populations. Some of the
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31 271 articles reported on two or more of the above. Details of relevant characteristics of the published
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33 272 articles are presented in **Table 1** (those reporting effective interventions) and **Appendix 7** (those
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35 273 reporting ineffective interventions) and **Appendix 8** (those focused on remote/and rural
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37 274 populations).
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44 276 **Initiatives to enhance accurate and timely cancer diagnosis**

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46 277 This review identified various initiatives to enhance accurate and timely cancer diagnosis. These
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48 278 were often designed, developed, and implemented often with the involvement of primary care
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50 279 providers (physicians and nurses), but not patients. These initiatives are grouped into related
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52 280 interventions and the evidence regarding each intervention is discussed below.
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282 *Centralized or coordinated diagnostic services*

283 Nine published articles on centralized or coordinated diagnostic services for adult lung cancer (n
284 = 5) and breast cancer (n = 4) patients were identified.^{20,23,32,33,44,54-56,93} Five were from
285 Canada,^{23,33,44,54,55} and there was one each from Denmark,²⁰ New Zealand,⁹³ South Africa,⁵⁶ and
286 the UK³². The focus and metrics for assessment of the effectiveness of these diagnostic services
287 varied, but all were found to be effective. These include the rapid access to pulmonary
288 investigation and diagnosis (RAPID) program in Wythenshawe Hospital, Manchester, UK with
289 expedited (next working day) computed tomography (CT) and reporting in suspected lung cancer
290 cases,³² and the Thoracic Triage Panel in a tertiary care centre in St. John's, Newfoundland,
291 Canada, a multidisciplinary centralized referral program, whose key components include a nurse
292 navigator who coordinates patient care and act as the contact person for patients and clinicians
293 involved in the program, weekly multidisciplinary (thoracic specialists) meetings, and regular
294 communications with the primary care provider.²³ The diagnostic services also include the rapid
295 investigation clinic in a tertiary health centre in Montreal, Canada established to coordinate and
296 accelerate the workup of patients with suspected lung cancer,³³ the improved respiratory fast
297 track clinic (RFTC) in Northland district of New Zealand that comprises reserved slots for CT
298 for those referred with a suspicion of lung cancer, bronchoscopy slots and CT-guided biopsy,⁹³
299 and the Danish lung cancer package at the Center for Lung Cancer, Odense University Hospital,
300 Odense, Denmark, a fast-track diagnostic pathway in the hospital setting.²⁰ Further, there was the
301 rapid access breast clinic in British Columbia, Canada that provides close collaboration between
302 clinicians and radiologists, facilitated by clinical pathways and nurse navigation,^{54,55} the
303 diagnostic assessment units in Ontario, Canada, focusing on diagnosis at a dedicated breast
304 assessment unit,⁴⁴ and the breast clinic at a tertiary hospital in Western Cape Province of South

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2
3 305 Africa, an open-access one-stop diagnostic breast clinic where women may present with a letter
4
5 306 from a primary level provider (nurse practitioner or doctor) and receive the same day clinical and
6
7 307 cytological evaluation with referral to the combined breast clinic if the breast cytology is positive
8
9
10 308 for malignancy.⁵⁶

11
12 309 In addition to the above, one unpublished article was identified.¹¹³ This was for the Breast
13
14 310 ACCESS Project in Ohio, USA, which scheduled patients for a surgical consult within 2 days
15
16 311 and a biopsy within 5 days after the surgical consult, with the aim of reducing wait times
17
18 312 between abnormal diagnostic mammogram findings to biopsy from 26 to 7 days (7-day ACCESS
19
20 313 goal).

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23 24 315 *Interventions to enhance diagnostic services*

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26 316 Twelve published articles on interventions to enhance diagnostic services were
27
28 317 identified.^{10,17,24,52,53,64,75,77,78,80,83,94} These articles were focused on varied cancer types; four on
29
30 318 multiple cancers, two on lung cancer, two on skin cancer, and one each on breast,
31
32 319 gastrointestinal, haematological and prostate cancers. Four articles were from the UK,^{17,52,53,78}
33
34 320 two articles each from Canada^{24,64} and Sweden,^{10,80} and one article each from Botswana,⁹⁴
35
36 321 Columbia,⁷⁵ Indonesia,⁷⁷ and the USA.⁸³ The focus and metrics for assessment of the
37
38 322 effectiveness of the interventions varied across the publications, and while most were effective,
39
40 323 one intervention for lung cancer and one intervention for skin cancer in the UK⁵³ and Sweden¹⁰,
41
42 324 respectively, were ineffective. The effective interventions were reducing diagnosis through
43
44 325 emergency presentation by improving general practice referral in England, UK,⁵² the guided
45
46 326 personal quality of life (QoL) feedback intervention during the Cancer Research UK's North
47
48 327 West regional summer roadshow in Manchester, UK, aimed at offering guided feedback about
49
50 328 personal QoL to adults with potential cancer symptoms, living in deprived communities to

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2
3 329 promote help seeking in primary care among the communities,⁷⁸ the mandatory primary care
4
5 330 access to faecal immunochemical testing (FIT) in Nottingham, UK, integrated with the 2-week
6
7 331 wait pathway, aimed at improving gastrointestinal cancer diagnosis rather than relying on age
8
9 332 and symptoms alone,¹⁷ the Stronach Regional Cancer Centre lung diagnostic assessment program
10
11 333 (DAP) at Southlake Regional Health Centre, Ontario, Canada, aimed at using learnings from a
12
13 334 Lean improvement event to provide coordinated, expedited care for all patients undergoing a
14
15 335 possible lung cancer diagnosis and to achieve/improve upon the provincial wait time target from
16
17 336 consultation to diagnosis for lung cancer patients,²⁴ the nurse practitioner-led lymphoma rapid
18
19 337 diagnosis clinic in a tertiary care cancer center (Princess Margaret Cancer Centre, part of
20
21 338 University Health Network) in Ontario, Canada, aimed at reducing wait times for a definitive
22
23 339 diagnosis of lymphoma,⁶⁴ the expedited one-stop prostate cancer diagnosis using advanced
24
25 340 imaging and biopsy techniques in a health institution (name not reported) in the USA, aimed at
26
27 341 expediting prostate cancer diagnosis.⁸³ There were also the Swedish Diagnostic Center at the
28
29 342 Central Hospital of Kristianstad, Sweden, introduced as a separate outpatient unit within the
30
31 343 Department of Internal Medicine to expedite diagnostics,⁸⁰ the Partners for Cancer Care and
32
33 344 Prevention action plan in Cali, Columbia, aimed at improving access to a coordinated program of
34
35 345 screening and early diagnosis of breast and cervical cancers in three health care centers that serve
36
37 346 subsidized populations,⁷⁵ the dermatology-led quality improvement initiatives in Gaborone,
38
39 347 Botswana, aimed at improving multispecialty care coordination,⁹⁴ and the culturally sensitive,
40
41 348 narrative self-help intervention named PERANTARA (PEngantar peRAwataN kesehaTAn
42
43 349 payudaRA [translated as introduction to breast health treatment]) across four hospitals in
44
45 350 Bandung, West Java, Indonesia, aimed at reducing time to diagnosis in women with breast
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47 351 cancer symptoms.⁷⁷ In addition to the above, one unpublished article on the Accelerate,
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3 352 Coordinate, Evaluate (ACE) program in the UK was identified.¹⁰⁰ This program was an early
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5 353 cancer diagnosis initiative and focused on testing innovations that either identify individuals at
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7
8 354 high risk of cancer earlier or streamline diagnostic pathways.

9
10 355 The ineffective interventions were the standardized care diagnostic pathway at the
11
12 356 Department of Clinical Pathology, Akademiska University Hospital in Uppsala, Sweden
13
14 357 (introduced by the Swedish health authorities to eliminate unwanted delay in the diagnostics of
15
16
17 358 melanoma)¹⁰ and the 4-week national lung cancer symptom awareness campaign in Wales, UK,
18
19 359 aimed at increasing urgent suspected cancer referrals and clinical outcomes.⁵³

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22 360

23 361 *Multidisciplinary team*

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26 362 Three multidisciplinary team lung cancer approaches were identified from published articles:
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28 363 from the USA^{68,85} and Australia.⁵⁰ The focus and metrics for assessment of the effectiveness of
29
30 364 the approaches varied across the publications. One approach from the USA was found to be
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32
33 365 effective,⁶⁸ whereas the others were found to be ineffective. The effective approach was the lung
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35 366 cancer strategist program, a thoracic surgeon-guided, multidisciplinary (disciplines not reported)
36
37 367 care program in hospitals in Massachusetts, USA, aimed at improving timeliness of lung cancer
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39
40 368 diagnosis and treatment.⁶⁸ The ineffective approaches were the pre-diagnosis multidisciplinary
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42 369 tumour board (physicians from radiology, medical and radiation oncology, and
43
44 370 pulmonary medicine) discussions in a clinic in Cleveland, USA aimed at improving the
45
46
47 371 timeliness of diagnostic evaluation in lung cancer,⁸⁵ and the Victorian lung cancer service
48
49 372 redesign project in Victoria, Australia, which involved multidisciplinary (patients, governance,
50
51 373 administration, clinicians and health information services) evaluation aimed at quality
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54 374 improvement collaborative on timeliness and management in lung cancer.⁵⁰ In addition, nine
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56 375 unpublished articles from the UK were identified.^{99,101-103,106,108,109,112} These included four

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3 376 articles regarding a “straight to CT access” pathway, on community pharmacy direct referral to
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5 377 lung cancer pathway, rapid colorectal diagnostic pathway, and optometrist direct referral to
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8 378 neuroscience pathway. All but the chest x-ray pathway¹⁰⁹ were found to be effective.
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10 379

11 380 *Standardized care pathways*

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14 381 Eleven published articles on standardized care pathways were identified.^{11,12,26,35,39,41,49,59,63,70,71}
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16 382 These articles were focused on varied cancer types (4 each for multiple cancers, and 1 each for
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18 383 ear-nose-throat, urinary tract, and gastrointestinal cancers). Three articles were from
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20 384 Denmark,^{26,39,41} two from the UK,^{35,70} and one each from Canada,⁵⁹ Norway,⁴⁹ Sweden,⁶³
21
22 385 Spain,¹² and Saudi Arabia.¹¹ The publications were on adult patient populations with one also
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24 386 involving paediatric patients. The focus and metrics for assessment of the effectiveness of the
25
26 387 pathways varied across the publications. The main effective pathways were the national
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28 388 diagnostic cancer pathway in Norway, with recommended maximum limits for time spent in the
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30 389 diagnostic process as well as mandatory reporting of the actual time intervals for all patients with
31
32 390 suspected lung cancer,⁴⁹ and the standardized triage process in the Southeastern Ontario, Canada,
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34 391 which entailed a twice-weekly nurse–physician triage, preordered staging tests and scheduling
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36 392 according to urgency, redirection and recommendations for inappropriate referrals, and new
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38 393 small nodule clinic.⁵⁹ Other main effective pathways were the standardized diagnostic pathway
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40 394 for suspected urothelial cancer initiated by primary healthcare providers and specialists in Skane
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42 395 County, Sweden, and comprises CT urography, urinary cytology and cystoscopy,⁶³ the early
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44 396 colonoscopy track (within 30 days from referral) in a tertiary referral hospital in Tenerife,
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46 397 Spain,¹² and the fast-track cancer care pathway in Denmark (national), with maximum acceptable
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48 398 time thresholds from referral to diagnosis and treatment.³⁹ In addition, two unpublished articles
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3 399 from Canada¹¹¹ and the UK⁹⁸ focusing on breast and lung cancers, respectively, were identified.
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5 400 These were the Alberta Health Services Diagnostic Assessment Pathway and the Somerset
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7 401 Integrated Lung Cancer Pathway. While the Canadian pathway was found to be effective, the
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9
10 402 pathway from the United Kingdom was not effective.
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14 404 ***Support for primary care providers***

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17 405 There were four publications on support for primary care providers (PCP), all from the
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19 406 UK.^{27,31,48,97} Two were focused on multiple cancer types, and one each focused on
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21 407 gastrointestinal and brain cancers. The publications were on adult patient populations with one
22
23 408 being also involving paediatric patients. The focus and metrics for assessment of the
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25 409 effectiveness of the support packages (all educational and informational) varied across the
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27
28 410 publications. None of the support packages was found to be effective, with the identified
29
30 411 common theme being a lack of awareness of referral guidelines and associated knowledge by
31
32 412 GPs. These ineffective support packages were the use of the Kernick and NICE guidelines as
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34 413 evidence-based support to assist primary care physicians in identifying patients most at risk of
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36 414 having a brain tumour, but also on the fastest route to achieve diagnosis (example, direct access
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38 415 imaging versus urgent secondary care referral) in Scotland, the UK,⁹⁷ the use of the national
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40 416 cancer waiting times monitoring dataset for system performance assessment by primary care
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42 417 physicians in England, the UK,²⁷ and the use of safety netting by primary care physicians in
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44 418 Oxfordshire, UK to ensure that patients are monitored until their symptoms or signs are
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46 419 explained, and to guard against delays in diagnosis.³¹
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53 421 ***Target or benchmark for wait times***

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3 422 There were eight published articles related to targets or benchmarks for wait
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5 423 times.^{15,42,43,69,73,81,88,96} Three of these articles were from the UK,^{69,73,81} two articles from
6
7 424 Australia,^{42,88} and one article each from China,⁴³ Sweden,⁹⁶ and New Zealand¹⁵. These
8
9 425 publications were focused on varied cancer types (2 each for multiple, lung and gastrointestinal
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11 426 cancers, and 1 each for prostate and skin cancers), and were on adult patient populations, with
12
13 427 one publication involving paediatric patients. The focus and metrics for assessment of the
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15 428 effectiveness of the target or benchmarks varied across the publications, and all but two
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17 429 targets/benchmarks^{15,88} were found to be effective. The effective targets or benchmarks were the
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19 430 28-day faster diagnosis standard in the National Health Service England, UK, defined as the time
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21 431 within which the patient is informed whether they do or do not have cancer,⁷³ the fast-track
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23 432 diagnostic workup for men with suspected prostate cancer at the Urology Department at Orebro
24
25 433 University Hospital in Sweden, which entailed targeting the shortest possible waiting-time for a
26
27 434 diagnostic workup process,⁹⁶ and the optimal timeframes for referral and diagnosis of lung lesion
28
29 435 at Latrobe Regional Hospital in Victoria, Australia established by the National Cancer Expert
30
31 436 Reference Group as part of the optimal care pathway for people with lung cancer.⁴² The
32
33 437 ineffective targets or benchmarks was the New Zealand Ministry of Health's "faster cancer
34
35 438 treatment" standards of service provision for melanoma patients, with a target of
36
37 439 histopathological diagnosis of melanoma reported within five working days in 80% of cases, and
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39 440 all cases reported in 10 working days.¹⁵ In addition, two unpublished articles from Canada¹⁰⁵ and
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41 441 the UK¹⁰⁷ focusing on multiple cancers were identified, and these were the "2-week wait"
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43 442 benchmark in the UK (already discussed under rapid referral pathways) and the Canadian Breast
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45 443 Cancer Screening Network targets for diagnostic intervals: $\geq 90\%$ of abnormal screens to be
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3 444 resolved within 5 weeks if no biopsy is required and $\geq 90\%$ within 7 weeks if a tissue biopsy is
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5 445 required.

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10 447 ***Innovative interventions to enhanced care in cancer pre-diagnosis phase***

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12 448 This review identified 17 published articles related to technological interventions for enhanced
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14 449 care in the pre-diagnosis phase of cancer.^{16,21,22,29,37,38,51,57,58,62,65,66,79,82,87,89,91} Ten of these articles
15
16 450 were from the UK,^{22,29,37,38,51,57,62,65,66,91} two articles were from New Zealand,^{79,82} and one article
17
18 451 each was from Denmark,⁸⁹ Netherlands,²¹ Italy,¹⁶ India,⁸⁷ and Spain.⁵⁸ These publications
19
20 452 focused on varied cancer types in adult patient populations, with two also involving paediatric
21
22 453 patients. The interventions had little patient input in their design, development, or
23
24 454 implementation. The focus and metrics for assessment of the effectiveness of the interventions
25
26 455 varied across the publications. The main identified interventions were the use of teledermatology
27
28 456 in skin cancer diagnosis. This involved the taking of images, including dermoscopy by GPs and
29
30 457 sending them for evaluation to specialized dermatologists.^{38,62,79,89} The process is embedded in
31
32 458 an e-referral system developed in Auckland, New Zealand for suspected skin malignancy,⁸² and
33
34 459 included teledermatology images triaged as confirmed, likely or suspected melanoma, the use of
35
36 460 a web-based referral tool for head and neck cancers at two different hospitals in Birmingham,
37
38 461 West Midlands, and Wexham, Berkshire, UK.⁵¹ There was also the use of the Digitally
39
40 462 Assembled Referral Toolkit (DART) for 2-week referral, accessible via a cloud-based template,
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42 463 which contained new referral forms native to GP clinical systems in the UK.²⁹ Additionally,
43
44 464 there was the use of an electronic straight-to-test pathway at a large tertiary referral hospital in
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46 465 England, UK to remove hospital-based triage from suspected colorectal cancer pathways; this
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54 466 allows GPs to book tests supported by a decision aid based on the NICE guidance, thus,

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3 467 eliminating the need for a standard referral form or triage process.⁶⁵ Further, there was the use of
4
5 468 electronic clinical decision support for melanoma in four general practices in the Southeast of
6
7 469 England, UK, which involved the use of an electronic-based 7-point checklist to assess
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10 470 pigmented lesions,⁶⁶ the use of machine learning algorithms in Newcastle, UK to classify
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12 471 patients referred on the 2-week wait pathway for suspected head and neck cancer into different
13
14 472 diagnostic groups, albeit very broad ones: cancer and non-cancer,⁵⁷ the use of nurse-led
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16 473 assessments to evaluate certain groups of patients suspected to have bowel cancer in England,
17
18 474 the UK,²² and the use of varied smartphone-based skin and oral self-monitoring and screening
19
20 475 applications, in England, UK⁹¹ and in the India,⁸⁷ respectively. In addition, two unpublished
21
22 476 articles from the UK were identified.^{106,110} These were for a cancer decision support tool
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24 477 (computer-based programs integrated into a GP's usual patient management system) in
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26 478 Gateshead, London, and a clinical web portal (CWP) electronic system in Manchester, England,
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28 479 with the fundamental part of the CWP being that local clinicians had to take personal
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31 480 responsibility for data input.
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482 *Performance metrics to measure improvements in suspicion to diagnosis phase*

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38 483 Varied performance metrics were identified by this review. The main metrics are summarized
39
40 484 according to intervention type (**Appendix 9**). While performance metrics appear to be mainly
41
42 485 intervention-dependent, time from presentation in primary care to diagnosis and from referral
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44 486 from primary care to specialist consultation, appear to be the most consistent metrics used for
45
46 487 evaluation. Performance metrics to measure patients' experience mainly centered on patients'
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48 488 satisfaction and quality of life.
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3 490 *Specific considerations for underserved populations*
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5 491 Four published articles focused on issues related specifically to underserved populations, with all
6
7 492 focused on remote/rural populations.^{18,30,60,88} These publications were from the UK,⁶⁰
9
10 493 Australia,^{30,88} and Mexico.¹⁸ A fifth publication only used the patients' area of residence as part
11
12 494 of their model.⁹⁵ All of the publications were on multiple cancer types and adult populations,
13
14 495 although one included a paediatric population. The specific considerations for underserved
15
16 496 populations and the evidence regarding them included a publication from Scotland, the UK, a
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18 497 national audit of cancer diagnosis in Scottish and English general practices, exploring and
19
20 498 comparing patient characteristics, diagnostic intervals, and routes to diagnosis,⁶⁰ the publication
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22 499 from New South Wales, Australia on a study that examined geographic variations in time
23
24 500 intervals leading up to treatment for head and neck cancer, with assessment of differences based
25
26 501 on remoteness of residence (regional/remote or metropolitan) at two tertiary referral centres,⁸⁸ a
27
28 502 publication from Mexico City, Mexico on evaluation of a patient navigation program to reduce
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30 503 referral time to cancer centers for underserved patients with a suspicion or diagnosis of cancer at
31
32 504 a public general hospital,¹⁸ and a publication from Western Australia, a cluster-randomized
33
34 505 controlled trial of a complex intervention to reduce time to diagnosis in rural cancer patients with
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36 506 the aim of measuring the effect of community-based symptom awareness and general practice-
37
38 507 based educational interventions on the time to diagnosis in rural patients presenting with breast,
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40 508 prostate, colorectal or lung cancer.³⁰
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510 **Discussion**

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

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

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3 533 The interventions mostly comprised multiple interventions/ changes to the healthcare
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5 534 pathway. As such, the interventions examined varied widely across the studies. This was true
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8 535 even when applied to the same cancer patient populations and in the same jurisdictions/
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10 536 countries, including those where an intervention was part of the standard care pathway. As such,
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12 537 it is difficult, perhaps impossible, to identify one main approach alone that drives an
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14 538 intervention. Methodological approaches also varied significantly with regard to outcome
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17 539 assessment. A common theme among the effective centralized or coordinated diagnostic
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19 540 services, interventions to enhance diagnostic services, patient navigation approaches, and
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21 541 standardized care pathways is multidisciplinary collaboration and the involvement of a nurse
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23 542 navigator.

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26 543 The findings from this scoping review compare considerably with those of the previously
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28 544 summarized evidence (prior to the ongoing coronavirus disease 2019 (COVID-19) pandemic) not
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30 545 included in this review.⁹ However, while the previous evidence summary identified similar
31
32 546 leading interventions to enhance seamless and coordinated cancer care in symptomatic
33
34 547 individuals, intervention effectiveness was not summarized to enable comparison with the
35
36 548 findings from this current review. As a result, assessment of the potential impact of the COVID-
37
38 549 19 pandemic on intervention effectiveness was not possible; despite reports of decline and delays
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40 550 in cancer diagnosis of symptomatic individuals even in jurisdictions that utilize interventions that
41
42 551 have been found to be effective from this review.^{114,115} A survey by the Canadian Cancer
43
44 552 Survivor Network (CCSN) showed that 54% of those surveyed (with about 75% of pre-diagnosis
45
46 553 and recently diagnosed patients among them) have had their cancer care appointments cancelled,
47
48 554 postponed, or rescheduled because of COVID-19.¹¹⁶ Further, a modelling study in England, by
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50 555 Maringe and colleagues concluded that substantial increases should be expected in the number of
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3 556 avoidable cancer deaths as a result of diagnostic delays due to the COVID-19 pandemic.¹¹⁷ The
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5 557 conclusions of the available evidence reviews suggest that cancer screening programs and
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7 558 diagnoses in symptomatic individuals, have been clearly interrupted since the onset of the
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10 559 COVID-19 pandemic, with delayed diagnosis and marked increases in the numbers of avoidable
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12 560 cancer deaths.^{118,119}

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15 561 It was difficult to determine a specific intervention or a stand-alone approach to an
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17 562 intervention from this scoping review. It was also difficult to assess the true effectiveness of
18
19 563 many of the interventions, especially considering the differing composite nature of the
20
21 564 interventions, the fact that the evidence is mostly from observational studies, and the range of
22
23 565 outcome measures used to measure effectiveness. While many of the interventions could be
24
25 566 adapted to suit different health systems and jurisdictions, emphasis should be on the context and
26
27 567 the strengths and limitations of the individual health system, and a clear evidence-based
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29 568 performance metric for appropriate evaluation of effectiveness of an intervention ought to be
30
31 569 determined a priori. Diagnosing cancer faster and more accurately at an earlier stage is a key
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33 570 priority of the 2019-2029 Canadian Strategy for Cancer Control.¹²⁰ Over the next 5 years, the
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35 571 Canadian Partnership Against Cancer will leverage findings from this scoping review, as one of
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37 572 several inputs, and partner with Canadian jurisdictions to continue to test innovative models of
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39 573 care that expedite cancer diagnosis, especially for Indigenous and underserved populations.
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45 574 46 47 575 **Limitations and merits**

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49 576 There are some limitations to this study. The literature search was developed by a knowledge
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51 577 synthesis librarian and peer reviewed by an independent knowledge synthesis librarian using the
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53 578 PRESS checklist. We searched appropriate databases and websites for literature, and adhered to
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3 579 known guidelines and standards in the conduct and reporting of the review. Even so, the
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5 580 literature search was limited to evidence from the last 4 years and only evidence from English-
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7 581 language publications and organizational websites. As such, potentially eligible articles could
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9 582 have been missed.

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12 583 The eligibility criteria for inclusion were not limited to only comparative studies. This
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14 584 meant that the focus of some of the included studies was not specifically on the assessment of
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16 585 effectiveness of an intervention and therefore, effectiveness may have been underreported for
17
18 586 some interventions. Moreover, an intervention's effectiveness assessment was based solely on
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20 587 author-determined outcome, which may or may not have been an appropriate outcome for
21
22 588 assessing effectiveness of certain interventions. As such, an intervention that appeared effective
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24 589 in a study may be ineffective in another study depending on the assessed outcome, with no clear
25
26 590 reason for such a discrepancy. Furthermore, this review did not assess effectiveness of
27
28 591 interventions across cancer patient types and jurisdictions/regions. This would have allowed
29
30 592 assessment of any differences in intervention effectiveness by patient type and study jurisdiction.
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32 593 Lastly, and in line with the JBI's guidance for the conduct of scoping reviews, we did not
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34 594 attempt to provide an assessment of the quality of the evidence and, as such, the risk of bias in
35
36 595 randomized controlled trials and quality assessment of observational studies, including
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38 596 assessment for important potential biases such as selection, case ascertainment and measurement
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40 597 biases, and potential confounders in studies were not considered in this review; hence, the
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42 598 findings on effectiveness are not conclusive of the performance of the interventions.
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51 600 **Conclusions**
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3 601 The evidence suggests that interventions focused on improving accurate and timely cancer
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5 602 diagnosis among symptomatic individuals are active topics of research, particularly in lung
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7 603 cancer patient populations, and that the UK is championing this area of research. While the
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10 604 themes of the studied interventions are similar, the interventions differ in many ways within the
11
12 605 same intervention group. Multidisciplinary cooperation and involvement of a nurse navigator
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14 606 appeared to be unique features of many of the effective interventions. Canadian and other
15
16 607 jurisdictions can leverage these lessons learned to develop and implement strategies adapted to
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18 608 local health system needs to improve the cancer pre-diagnosis phase. Future research should
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20 609 examine the effectiveness of the interventions identified through this review.
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26 611 **Data availability statement:** No additional data are available.
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31 613 **Ethics approval:** Not applicable.
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33 614

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35 615 **Details of the role of the study sponsors:** The Canadian Partnership Against Cancer (the study
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37 616 commissioner) contributed to specifying the study objectives and questions, and in summarizing
38
39 617 the evidence.
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41 618

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44 619 **Patient and public involvement:** There was no active engagement of patients and/or members
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46 620 of the public.
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Table 1: Summary of the characteristics of the included published articles that reported data on effective interventions

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

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

					referral to initial clinic assessment	
	Whitley 2017 ⁹²	USA (Boston, Denver, San Antonio, and Tampa)	Case-Control (2007-2011)	Multiple (Adult) [6349]	Delays in diagnostic resolution based on Charlson Comorbidity Index score	Patient navigation reduced delays in diagnostic resolution, with the greatest benefits seen for those with a Charlson Comorbidity Index score ≥ 2 (Effective)
	Antel 2020 ¹³	South Africa (Cape Town)	Before-and-After (2017-2019)	Haematological (Adult) [130]	Diagnostic interval	Compared with a historical cohort, the diagnostic interval (time from first health visit to diagnostic biopsy) for patients with lymphoma was significantly shorter, 13.5 vs 48 days ($p=0.002$) (Effective)
	Arhi 2020 ¹⁴	UK (National)	Case-Control (2000-2013)	Gastrointestinal (Adult) [7130]	Hazard ratios of death	Patients referred between 2 weeks to 3 months, and after 3 months with red-flag symptoms demonstrated a significantly worse prognosis than patients who were referred within 2 weeks (Effective)
	Chng 2020 ¹⁹	UK (Newcastle-upon-Tyne)	Case-Control (2015-2019)	Brain (Adult) [101]	Tumour detection rate	With guideline adherence, the brain tumour detection rate was 3-fold higher (36.0% vs 11.5%, $p<0.02$) (Effective)
	Creak 2020 ²⁵	UK (Brighton; Sussex)	Cross-sectional (2015-2018)	Multiple (Adult) [258]	Time to diagnosis	Direct GP referrals were feasible and manageable within a tertiary clinic and resulted in high rates of cancer diagnoses and early contact with an oncologist and nurse specialist, cutting short the 'limbo' time of high anxiety before diagnosis (Effective)
	Hennessy 2020 ³⁶	Ireland (Dublin)	Case-Control (2012-2018)	Lung (NR) [864]	Time to diagnosis	Time to diagnosis was longer in those who had attended a post Rapid Access Lung Cancer Clinic CT (34.5 versus 21 days) (Effective)
Rapid referral pathway	Jones 2018 ⁴⁵	UK (East Midlands)	Case-Control (2013-2015)	Gastrointestinal (NR) [1401 (340 STTP, 495 traditional pathway, 566 control trusts)]	Time from referral to diagnosis	The pathway saved a mean of 7 days from referral to treatment (with a 95% CI of 3 to 11 days, $p<0.008$) and a mean of 16 days from referral to diagnosis, when compared with a traditional pathway (Effective)
	Joyce 2020 ⁴⁶	UK (National)	Cross-sectional (2017-2018)	Multiple (Mixed age) [NR]	Proportion with emergency diagnosis of cancer	A lower proportion of emergency diagnosis of cancer was found with higher 2 weeks wait referral conversion rate (Effective)
	Pearson 2020 ⁶⁷	UK (National)	Case-Control (2014)	Multiple (Mixed age) [12873]	Primary care interval	Compared with patients with a specific alarm symptom, patients with non-specific but concerning symptoms had higher odds of having longer primary care intervals (adjusted OR: 1.24 (1.11 to 1.36)) (Effective)
	Round 2020 ⁷²	UK (National)	Case-Control (2011-2017)	Multiple (Mixed age) [1469103]	Risk of death	Cancer patients from the highest referring practices had a lower hazard of death (hazard ratio [HR] = 0.96; 95% confidence interval [CI] = 0.95 to 0.97) (Effective)
	Sandager 2019 ⁷⁴	Denmark (National)	Cross-sectional (2010)	Multiple (Adult) [2256]	Patient experience	Overall, pathway referred patients were 21% more likely than non-pathway referred patients to report a positive experience (PR = 1.21 [95% CI: 1.11–1.30]) (Effective)

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

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

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

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

Peer review only

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3 **Figures**
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7 **Figure 1:** Modified PRISMA flow chart
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10 **Figure 2:** Geographical mapping of the included published articles
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14 **Figure 3:** Summary of cancer types reported by the included published articles
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18 **Figure 4:** Summary of intervention types reported by the included published articles
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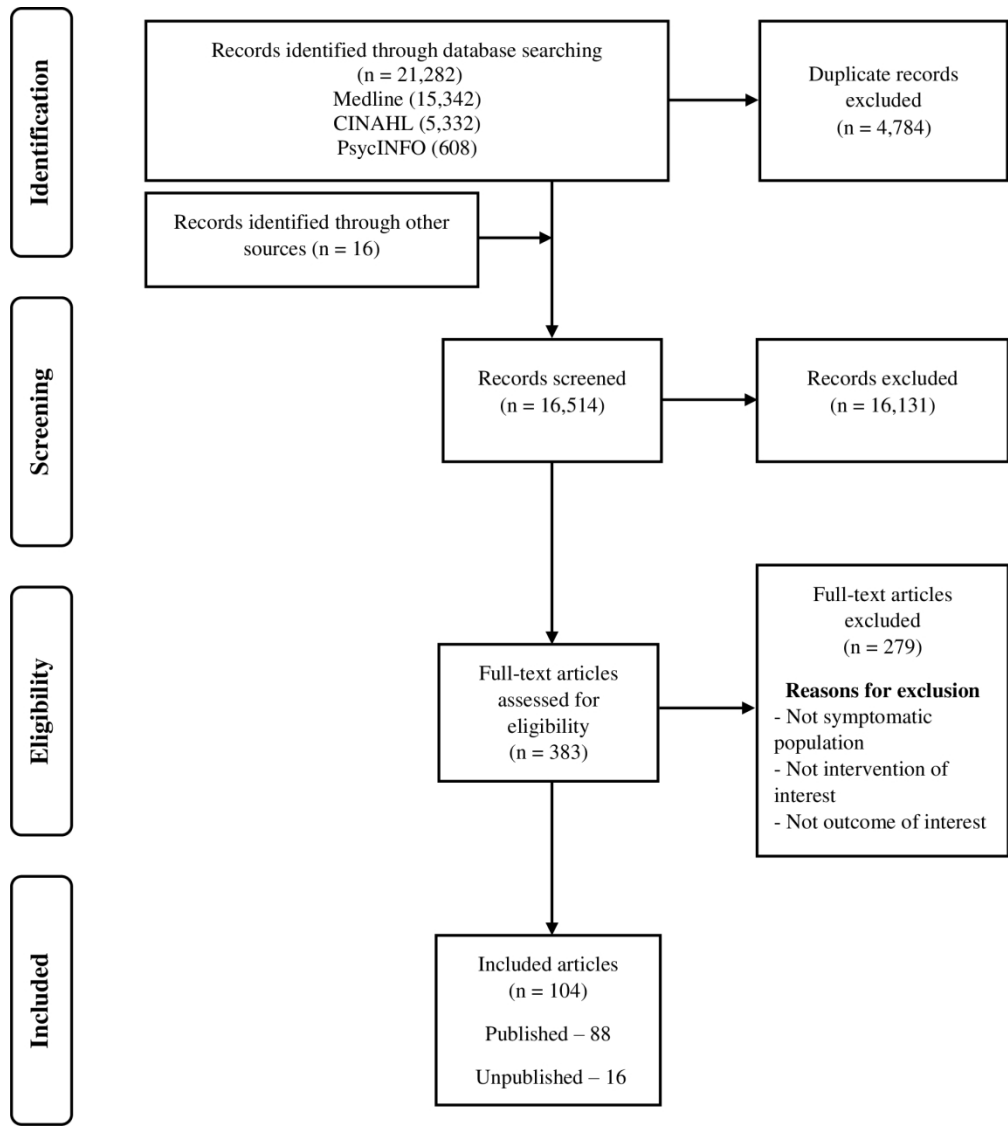
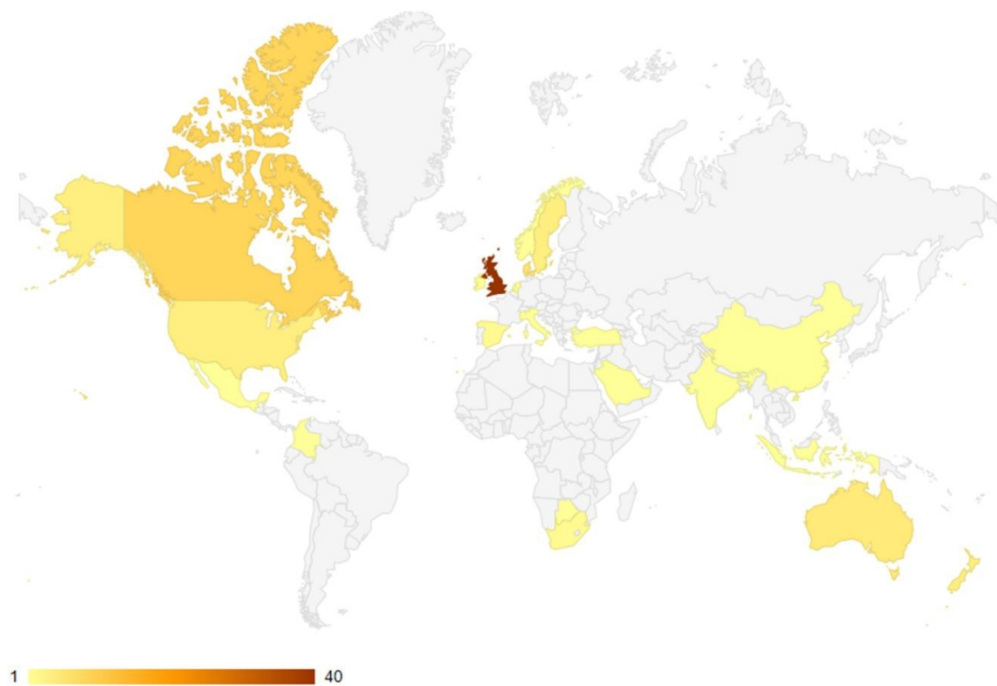


Figure 1: Modified PRISMA flow chart

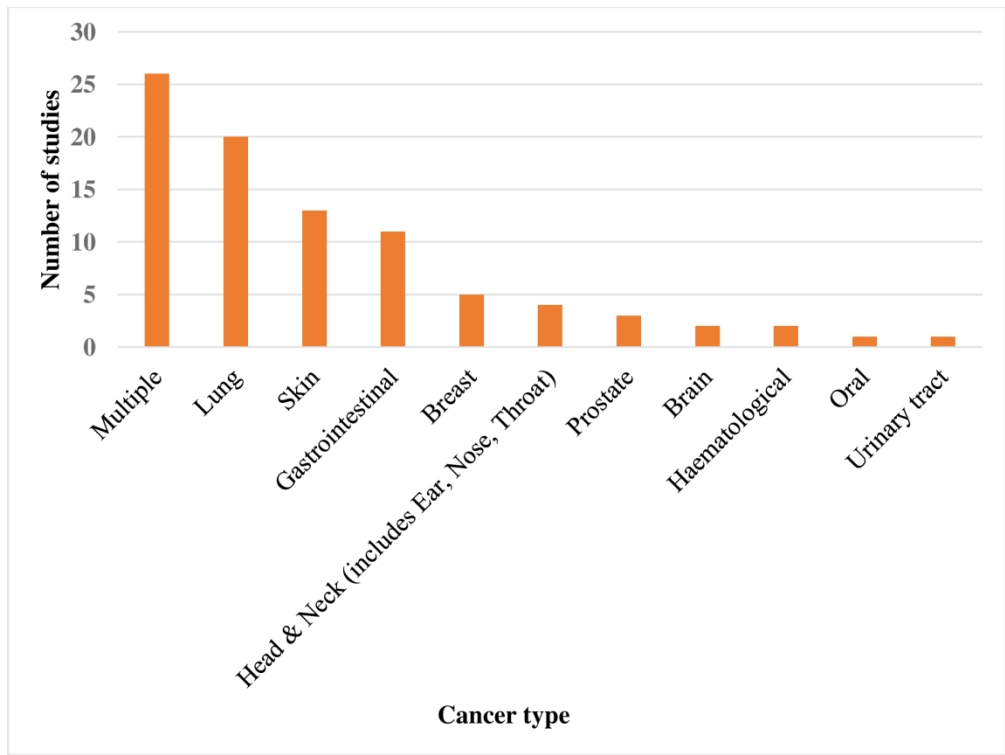
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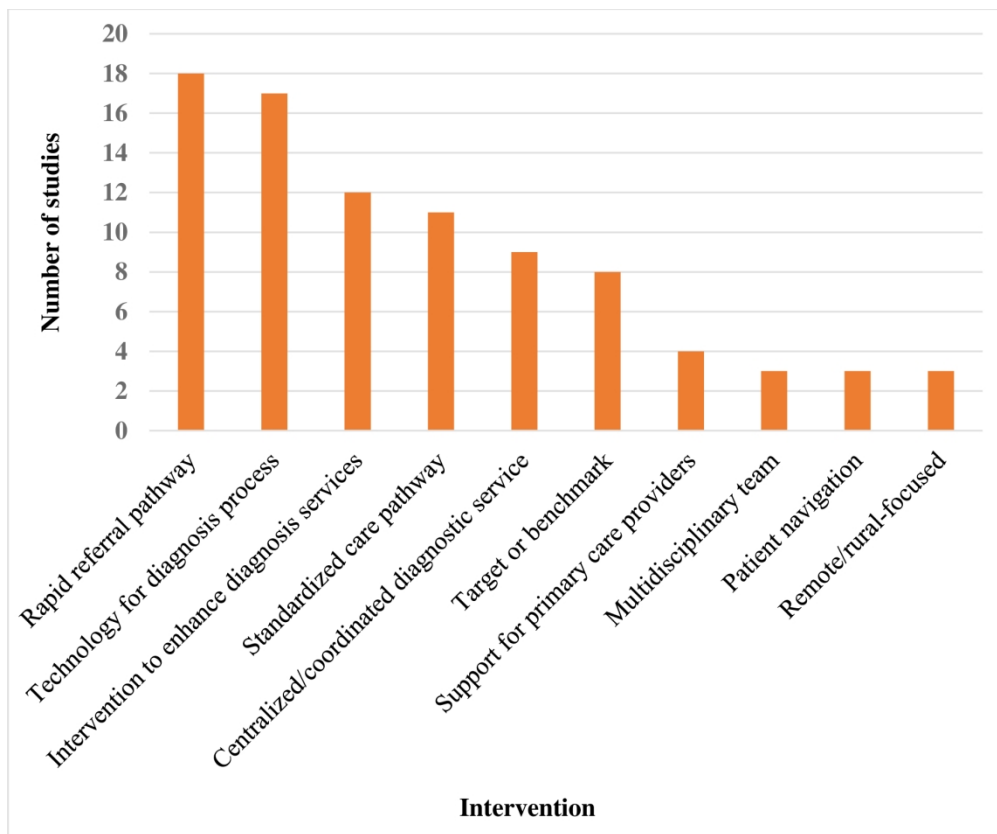
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Appendices

Appendix 1: Project work plan

About the Project Team

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

Proposed Method

Methods

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

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

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

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

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

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

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

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

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4 KQ 5. Have specific considerations been applied to underserved populations including Indigenous,
5 rural, and remote populations within the context of each of the questions above?
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8 **Study eligibility criteria**

9 This review will focus on published and unpublished studies that answer the key questions since 2017.
10 Our focus is on comparative studies that applied a protocol/guideline or a specific intervention or
11 intervention plan. Having said that, we anticipate the need to review lower quality study designs (e.g.,
12 retrospective, and uncontrolled studies). As such, there will be no restriction on the study design, but will
13 be limited to English language publications for feasibility.
14

15 **Search strategy and study selection**

16 A knowledge synthesis librarian has designed and executed a literature search strategy in MEDLINE
17 (Ovid). The search strategy was peer-reviewed by a second librarian and adapted for other bibliographic
18 databases: Cinahl (Ebsco) and Psycinfo (Ovid). Search strategies are presented in Appendix 1. All
19 retrieved records were imported into EndNote for citation management.
20 One reviewer will screen each identified citation for eligibility. Full texts of all relevant citations will be
21 reviewed by two reviewers. All conflicts will be resolved by discussion and/ or a third reviewer, as
22 needed. We will record the number of ineligible citations at the title/ abstract screening stage, and both
23 the number and reason for ineligibility at the full-text articles.
24

25 **Data extraction**

26 We will develop data extraction forms and pilot them on a small selection of studies. Extracted data will
27 be stored and managed in MS Excel. One reviewer will independently extract data from included studies
28 and another reviewer will independently check the extracted data for errors. Disagreements will be
29 resolved by discussion between reviewers and/ or by involving a third reviewer, as needed.
30

31 **Data analysis**

32 We will present specific characteristics of all included studies in a tabular form. The analysis of the
33 extracted data will be descriptive.
34

35 **Study dissemination**

36 We will submit reports from this study as a technical report to CPAC.
37
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39
40

41 **Knowledge User Engagement Plan**

42 We will be providing a bi-weekly update to CPAC on the progression of the review. Specifically, we will
43 engage during specific time points to review progress and next steps:
44

- 45 - Protocol
- 46 - Level I Screening (Title/ Abstract screening phase)
- 47 - Level II Screening (Full-text screening phase)
- 48 - Data Extraction
- 49 - Data Analysis
- 50 - Report
- 51

52 **Declaration of Conflict of Interest**

53
54
55 None
56
57

Appendix 2: MEDLINE (Ovid) search strategy

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

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

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

Appendix 3: CINAHL (EbscoHOST) search strategy

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

1
 2
 3
 4 sheep) OR (MH swine) OR (MH primates) OR (animal OR animals OR pisces OR fish OR
 5 fishes OR catfish OR catfishes OR sheatfish OR silurus OR arius OR heteropneustes OR
 6 clarias OR gariepinus OR "fathead minnow" OR "fathead minnows" OR pimephales OR
 7 promelas OR cichlidae OR trout OR trouts OR char OR chars OR salvelinus OR salmo OR
 8 oncorhynchus OR guppy OR guppies OR millionfish OR poecilia OR goldfish OR goldfishes
 9 OR carassius OR auratus OR mullet OR mullets OR mugil OR curema OR shark OR sharks
 10 OR cod OR cods OR gadus OR morhua OR carp OR carps OR cyprinus OR carpio OR
 11 killifish OR eel OR eels OR anguilla OR zander OR sander OR lucioperca OR stizostedion
 12 OR turbot OR turbots OR psetta OR flatfish OR flatfishes OR plaice OR pleuronectes OR
 13 platessa OR tilapia OR tilapias OR oreochromis OR sarotherodon OR "common sole" OR
 14 "dover sole" OR solea OR zebrafish OR zebrafishes OR danio OR rerio OR seabass OR
 15 dicentrarchus OR labrax OR morone OR lamprey OR lampreys OR petromyzon OR
 16 pumpkinseed OR pumpkinseeds OR lepomis OR gibbosus OR herring OR clupea OR
 17 harengus OR amphibia OR amphibian OR amphibians OR anura OR salientia OR frog OR
 18 frogs OR rana OR toad OR toads OR bufo OR xenopus OR laevis OR bombina OR epidalea
 19 OR calamita OR salamander OR salamanders OR newt OR newts OR triturus OR reptilia OR
 20 reptile OR reptiles OR "bearded dragon" OR pogona OR vitticeps OR iguana OR iguanas OR
 21 lizard OR lizards OR "anguis fragilis" OR turtle OR turtles OR snakes OR snake OR aves OR
 22 bird OR birds OR quail OR quails OR coturnix OR bobwhite OR colinus OR virginianus OR
 23 poultry OR poultries OR fowl OR fowls OR chicken OR chickens OR gallus OR "zebra
 24 finch" OR taeniopygia OR guttata OR canary OR canaries OR serinus OR canaria OR
 25 parakeet OR parakeets OR grasskeet OR parrot OR parrots OR psittacine OR psittacines OR
 26 shelduck OR tadorna OR goose OR geese OR branta OR leucopsis OR woodlark OR lullula
 27 OR flycatcher OR ficedula OR hypoleuca OR dove OR doves OR geopelia OR cuneata OR
 28 duck OR ducks OR greylag OR graylag OR anser OR harrier OR circus pygargus OR red knot
 29 OR "great knot" OR calidris OR canutus OR godwit OR limosa OR lapponica OR meleagris
 30 OR gallopavo OR jackdaw OR corvus OR monedula OR ruff OR philomachus OR pugnax
 31 OR lapwing OR peewit OR plover OR vanellus OR swan OR cygnus OR columbianus OR
 32 bewickii OR gull OR chroicocephalus OR ridibundus OR albifrons OR "great tit" OR parus
 33 OR aythya OR fuligula OR streptopelia OR risoria OR spoonbill OR platalea OR leucorodia
 34 OR blackbird OR turdus OR merula OR blue tit OR cyanistes OR pigeon OR pigeons OR
 35 columba OR pintail OR anas OR starling OR sturnus OR owl OR "athene noctua" OR
 36 pochard OR ferina OR cockatiel OR nymphicus OR hollandicus OR skylark OR alauda OR
 37 tern OR sterna OR teal OR crecca OR oystercatcher OR haematopus OR ostralegus OR shrew
 38 OR shrews OR sorex OR araneus OR crocidura OR russula OR "european mole" OR talpa
 39 OR chiroptera OR bat OR bats OR eptesicus OR serotinus OR myotis OR dasycneme OR
 40 daubentonii OR pipistrelle OR pipistrellus OR cat OR cats OR felis OR catus OR feline OR
 41 dog OR dogs OR canis OR canine OR canines OR otter OR otters OR lutra OR badger OR
 42 badgers OR meles OR fitchew OR fitch OR fougart OR foulmart OR ferrets OR ferret OR
 43 polecat OR polecats OR mustela OR putorius OR weasel OR weasels OR fox OR foxes OR
 44 vulpes OR "common seal" OR phoca OR vitulina OR grey seal OR halichoerus OR horse OR
 45 horses OR equus OR equine OR equidae OR donkey OR donkeys OR mule OR mules OR pig
 46 OR pigs OR swine OR swines OR hog OR hogs OR boar OR boars OR porcine OR piglet OR
 47 piglets OR sus OR scrofa OR llama OR llamas OR lama OR glama OR deer OR deers OR
 48 cervus OR elaphus OR cow OR cows OR "bos taurus" OR "bos indicus" OR bovine OR bull
 49 OR bulls OR cattle OR bison OR bisons OR sheep OR sheeps OR "ovis aries" OR ovine OR
 50 lamb OR lambs OR mouflon OR mouflons OR goat OR goats OR capra OR caprine OR
 51 chamois OR rupicapra OR leporidae OR lagomorpha OR lagomorph OR rabbit OR rabbits
 52 OR oryctolagus OR cuniculus OR laprine OR hares OR lepus OR rodentia OR rodent OR
 53 rodents OR murinae OR mouse OR mice OR mus OR musculus OR murine OR woodmouse
 54
 55
 56
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 58
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	<p>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 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#))</p>	
21.	S19 NOT S20	14678
22.	S21 Limiters - Published Date: 20170101-20201231	5333

Appendix 4: Psycinfo (Ovid) search strategy

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

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

Canada

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

International

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

Appendix 6: Definition for interventions related to the review questions

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

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

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

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

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

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

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

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

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

UK = United Kingdom; IQR = interquartile range

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

Intervention Type	Performance Metric
Centralized or coordinated diagnostic service	<ul style="list-style-type: none"> • Time from presentation in primary care to diagnosis • Time from referral from primary care to specialist consultation • Time from first abnormal image to biopsy
Interventions to enhance diagnostic services	<ul style="list-style-type: none"> • Time from referral from primary care to specialist consultation • Time from initial specialist consultation to diagnosis • Time from initial specialist consultation to biopsy • Time from first abnormal image to biopsy • Time from presentation in primary care to biopsy • Total diagnostic interval • Turnaround time for diagnosis following histology • Number of urgent referrals to specialist • Cancer detection rate • Patient survival
Multidisciplinary team	<ul style="list-style-type: none"> • Time from referral from primary care to specialist consultation • Time from first abnormal image to diagnosis
Patient navigation	<ul style="list-style-type: none"> • Waiting times from the point of referral from primary care to initial specialist assessment • Feasibility of program/process • Delays in diagnostic resolutions

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

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	4-5
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	7-8
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	8-9
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	9
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	10-11
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	10
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix 2 - 4
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	10-11
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	11-12
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	Appendix 6
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	Not applicable



SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	11-12
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	Figure 1
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	Table 1
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not applicable
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	14-24
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	13-24
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	25-27
Limitations	20	Discuss the limitations of the scoping review process.	27
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	28
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	2

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

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

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

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

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

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



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