Appendices

Appendix 1: Project work plan

About the Project Team

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

Proposed Method

> **Methods**
>
> Using a team of experienced systematic reviews and methodologists, with expertise in research methodology, knowledge synthesis and implementation science, we will update the 2018 peer-reviewed and grey literature scan by conducting a rapid scoping review to include contemporary, national and international leading interventions for improving accurate and timely cancer diagnosis focusing on the symptomatic population and summarize efficacy, impact and sustainability of identified interventions. We will identify evidence to answer the following key questions:
>
> KQ 1. Are there practice guidelines, care pathways or other initiatives (e.g., benchmarks/ targets for wait times, streamlined or rapid diagnostic services, multidisciplinary teams, patient navigators and/or navigation, etc.) that have been found to streamline and enhance accurate and timely diagnosis in symptomatic individuals?
> – How were patients involved in the design, development and/ or implementation of these initiatives?
> – How were providers (e.g., primary care providers) involved in the design, development and/or implementation of these initiatives?
>
> KQ 2. What are the leading interventions for innovative and/or virtual approaches (e.g., technology-based) to seamless care (i.e., minimally disruptive care that is found to be more convenient/coordinated/timely/less stressful to the patients) in the pre-diagnosis phase within Canada and abroad?
> – How have these interventions been applied, including identification of successes and lessons learned where possible?
> – Were these interventions evaluated and if so, what were the findings?
> – How were patients involved in the design, development and/ or implementation of these interventions?
>
> KQ 3. What are the identified performance metrics that can be used to measure the suspicion to diagnosis phase; and where and how are these metrics used?
> – Are there specific metrics used to measure the patient experience?
> – What data is captured by decision-support systems and how does the data and clinical systems work together?
> – Is there evidence on sustainability of the model?
>
> KQ 4. What are the key points of care in a patient's experience (e.g., diagnostic tests, physician consultations, etc.) as they navigate the system from initial symptoms/ suspicion of cancer to diagnosis?

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

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

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

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

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

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

Knowledge User Engagement Plan

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

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

Declaration of Conflict of Interest

None

Appendix 2: MEDLINE (Ovid) search strategy

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

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

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21.	19 not 20	48488
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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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sheep) OR (MH swine) OR (MH primates) OR (animal OR animals OR pisces OR fish OR fishes OR catfish OR catfishes OR sheatfish OR silurus OR arius OR heteropneustes OR clarias OR gariepinus OR "fathead minnow" OR "fathead minnows" OR pimephales OR promelas OR cichlidae OR trout OR trouts OR char OR chars OR salvelinus OR salmo OR oncorhynchus OR guppy OR guppies OR millionfish OR poecilia OR goldfish OR goldfishes OR carassius OR auratus OR mullet OR mullets OR mugil OR curema OR shark OR sharks OR cod OR cods OR gadus OR morhua OR carp OR carps OR cyprinus OR carpio OR killifish OR eel OR eels OR anguilla OR zander OR sander OR lucioperca OR stizostedion OR turbot OR turbots OR psetta OR flatfish OR flatfishes OR plaice OR pleuronectes OR platessa OR tilapia OR tilapias OR oreochromis OR sarotherodon OR "common sole" OR "dover sole" OR solea OR zebrafish OR zebrafishes OR danio OR rerio OR seabass OR dicentrarchus OR labrax OR morone OR lamprey OR lampreys OR petromyzon OR pumpkinseed OR pumpkinseeds OR lepomis OR gibbosus OR herring OR clupea OR harengus OR amphibia OR amphibian OR amphibians OR anura OR salientia OR frog OR frogs OR rana OR toad OR toads OR bufo OR xenopus OR laevis OR bombina OR epidalea OR calamita OR salamander OR salamanders OR newt OR newts OR triturus OR reptilia OR reptile OR reptiles OR "bearded dragon" OR pogona OR vitticeps OR iguana OR iguanas OR lizard OR lizards OR "anguis fragilis" OR turtle OR turtles OR snakes OR snake OR aves OR bird OR birds OR quail OR quails OR coturnix OR bobwhite OR colinus OR virginianus OR poultry OR poultries OR fowl OR fowls OR chicken OR chickens OR gallus OR "zebra finch" OR taeniopygia OR guttata OR canary OR canaries OR serinus OR canaria OR parakeet OR parakeets OR grasskeet OR parrot OR parrots OR psittacine OR psittacines OR shelduck OR tadorna OR goose OR geese OR branta OR leucopsis OR woodlark OR lullula OR flycatcher OR ficedula OR hypoleuca OR dove OR doves OR geopelia OR cuneata OR duck OR ducks OR greylag OR graylag OR anser OR harrier OR circus pygargus OR red knot OR "great knot" OR calidris OR canutus OR godwit OR limosa OR lapponica OR meleagris OR gallopavo OR jackdaw OR corvus OR monedula OR ruff OR philomachus OR pugnax OR lapwing OR peewit OR plover OR vanellus OR swan OR cygnus OR columbianus OR bewickii OR gull OR chroicocephalus OR ridibundus OR albifrons OR "great tit" OR parus OR aythya OR fuligula OR streptopelia OR risoria OR spoonbill OR platalea OR leucorodia OR blackbird OR turdus OR merula OR blue tit OR cyanistes OR pigeon OR pigeons OR columba OR pintail OR anas OR starling OR sturnus OR owl OR "athene noctua" OR pochard OR ferina OR cockatiel OR nymphicus OR hollandicus OR skylark OR alauda OR tern OR sterna OR teal OR crecca OR oystercatcher OR haematopus OR ostralegus OR shrew OR shrews OR sorex OR araneus OR crocidura OR russula OR "european mole" OR talpa OR chiroptera OR bat OR bats OR eptesicus OR serotinus OR myotis OR dasycneme OR daubentonii OR pipistrelle OR pipistrellus OR cat OR cats OR felis OR catus OR feline OR dog OR dogs OR canis OR canine OR canines OR otter OR otters OR lutra OR badger OR badgers OR meles OR fitchew OR fitch OR foumart OR foulmart OR ferrets OR ferret OR polecat OR polecats OR mustela OR putorius OR weasel OR weasels OR fox OR foxes OR vulpes OR "common seal" OR phoca OR vitulina OR grey seal OR halichoerus OR horse OR horses OR equus OR equine OR equidae OR donkey OR donkeys OR mule OR mules OR pig OR pigs OR swine OR swines OR hog OR hogs OR boar OR boars OR porcine OR piglet OR piglets OR sus OR scrofa OR llama OR llamas OR lama OR glama OR deer OR deers OR cervus OR elaphus OR cow OR cows OR "bos taurus" OR "bos indicus" OR bovine OR bull OR bulls OR cattle OR bison OR bisons OR sheep OR sheeps OR "ovis aries" OR ovine OR lamb OR lambs OR mouflon OR mouflons OR goat OR goats OR capra OR caprine OR chamois OR rupicapra OR leporidae OR lagomorpha OR lagomorph OR rabbit OR rabbits OR oryctolagus OR cuniculus OR laprine OR hares OR lepus OR rodentia OR rodent OR rodents OR murinae OR mouse OR mice OR mus OR musculus OR murine OR woodmouse

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

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Appendix 4: Psycinfo (Ovid) search strategy

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

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

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

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

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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.

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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 ($\chi2(3)=2.6$, p=0.458) and lower gastrointestinal ($\chi2(3)=0.884$, 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

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

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Interventions	Article	Study country (Region)	Study type (Study years)	Cancer type (Population) [Sample size]	Assessment metric	Result
				(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)

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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

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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

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

diagnosis phase

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