Open Access Protocol

BMJ Open The characteristics of national health initiatives promoting earlier cancer diagnosis among adult populations: a systematic review protocol

Natalia Calanzani, David Weller, Christine Campbell

To cite: Calanzani N. Weller D. Campbell C. The characteristics of national health initiatives promoting earlier cancer diagnosis among adult populations: a systematic review protocol. BMJ Open 2017;7:e015922. doi:10.1136/ bmjopen-2017-015922

Prepublication history and additional material are available. To view these files please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2017-015922).

Received 10 January 2017 Revised 31 May 2017 Accepted 5 June 2017

ABSTRACT

Introduction The increasing burden of cancer morbidity and mortality has led to the development of national health initiatives to promote earlier cancer diagnosis and improve cancer survival. This protocol describes a systematic review aiming to identify the evidence about such initiatives among the adult population. We will describe their components, stakeholders and target populations, and summarise their outcomes.

Methods and analysis We will search databases and websites for peer-reviewed publications and grey literature on national health initiatives in high-income countries as defined by the World Bank. Quantitative, qualitative and mixed-methods studies will be included and assessed for their methodological quality. Study selection, quality assessment and data extraction will be carried out independently by two reviewers. Narrative synthesis will be used to analyse the findings.

Ethics and dissemination This systematic review analyses secondary data and ethical approval is not required. Review findings will be helpful to researchers, policy makers, governments and other key stakeholders developing similar initiatives and assessing cancer outcomes. The results will be submitted to a peerreviewed journal in order to reach a diverse group of healthcare professionals, researchers and policy makers. This systematic review protocol is registered at PROSPERO (CRD42016047233).

INTRODUCTION

Cancer imposes a significant public health burden worldwide; in 2012, there were over 14 million diagnoses and 8.2 million cancer deaths.1 Cancer incidence has increased over time,² partly due to population ageing and lifestyle factors such as diet, tobacco use, alcohol consumption, obesity and physical inactivity. In the UK, it is estimated that one in two people born after 1960 will be diagnosed with cancer at some time in their lives.4

Furthermore, the number of people surviving cancer is increasing, mainly as a result of improvements in early detection and treatment.⁵ In 2012, there were

Strengths and limitations of this study

- ▶ To our knowledge, there are no other studies systematically reviewing national cancer strategies promoting the earlier diagnosis of cancer and describing their characteristics, populations and overall outcomes.
- Limitations include challenges related to wide heterogeneity in the composition and intensity of initiatives, populations and contexts, and carrying out comprehensive literature searches in such a broad area.

32.6 million 5-year cancer survivors worldwide. There is, however, a wide survival gap between different countries.8 In Europe, England and Denmark have been identified as having poor survival rates compared with other Western European countries.⁵ Late cancer stage at diagnosis and quality of treatment have been described as important explanatory factors for international variation in cancer survival. 10-12

The increased burden of cancer and the opportunity to improve survival have driven the development of organised health system level initiatives related to early cancer detection. In 2002, the WHO recommended the development of national cancer control programmes adopting 'strategies for prevention, early detection, diagnosis, treatment, and palliation' of cancer. Suggested early detection strategies included promoting the awareness of cancer signs and symptoms and training health professionals. 13 Acknowledging resource variation across countries, the WHO recommended the adoption and implementation of nationwide strategies in countries with high level of resources and community approaches in countries where resources are limited. ¹³ In 2005, the WHO approved a resolution on Cancer Prevention and Control¹⁴; one of its recommendations



University of Edinburgh, Centre For Population Health Sciences. The Usher Institute of Population Health Sciences and Informatics, Edinburgh, UK

Correspondence to

Natalia Calanzani; natalia. calanzani@ed.ac.uk

1

was to reduce late presentation for cancers that are amenable to early detection and treatment. 15

In the UK, the National Awareness and Early Diagnosis Initiative (NAEDI) was launched in 2008, led by the Department of Health and Cancer Research UK (a leading cancer charity) with the aim of improving cancer outcomes. A similar initiative (the Detect Cancer Early Programme) was launched by the Scottish government in 2012, aiming to improve overall 5-year survival for patients with lung, breast and colorectal cancers. In Denmark, a novel strategy focusing on different pathways for patients presenting with a range of symptoms was established with the aim to expedite early diagnosis and treatment.

These health initiatives are complex, with several interacting components¹⁹ and often require behaviour change from their target population. Furthermore, they may focus on different groups or organisational levels and can change depending on the context.¹⁹ Synthesising results of such initiatives in a systematic way is methodologically challenging, from defining the research questions to discussing the applicability of findings.²⁰ Nonetheless, efforts should be made to review the evidence in order to inform and enhance future initiatives aiming to promote early cancer diagnosis and influence cancer survival. Reporting on their activities and outputs is also important to enhance transparency and accountability, especially when these initiatives are directly or indirectly funded by the public.²¹

Previous reviews have attempted to summarise the evidence on national health initiatives in promoting the early diagnosis of cancer. González-Robledo et al carried out a database and documentary analysis of Latin American governmental actions for early detection of breast cancer and described how these often operated through regulation, design and implementation of early diagnosis programmes, care provided by public and private services and the development of guidelines for early detection.²² Palmer's overview of different UK cancer policies cited a few government interventions aiming to promote the earlier diagnosis of cancer and described factors associated with poor cancer survival, including socioeconomic deprivation.²³ Brown and colleagues investigated how different healthcare system characteristics (several regions in six countries were investigated) could contribute towards a number of cancer outcomes, including early diagnosis. The authors acknowledged that identifying causal relationships between healthcare system characteristics and cancer outcomes was challenging in complex, context-specific systems.²⁴

To our knowledge, there are no existing systematic reviews summarising national cancer initiatives at a health system-level worldwide, describing their characteristics, populations and overall outcomes. This review will add to existing knowledge into the area, systematically reviewing the international literature on national cancer initiatives promoting the earlier diagnosis of cancer.

METHODS AND ANALYSIS

This protocol describes a systematic review that is investigating health system level initiatives promoting the earlier diagnosis of cancer. We are guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) P-checklist, the PRISMA guidelines for reporting systematic reviews, the Cochrane Handbook for Systematic Reviews of Interventions and the Centre for Reviews and Dissemination's guidance for undertaking systematic reviews when developing this protocol. Guidance on reviewing complex interventions has also been consulted. 19 29

Study objectives

The review seeks to identify, describe and categorise the available evidence on national initiatives aiming to promote early diagnosis of cancer among the adult population. Our review methodology was developed in order to answer the following broad research questions:

- 1. What are the key components of these initiatives?
- 2. Who are the target populations and what are their sociodemographic characteristics?
- 3. What are the reported overall outcomes of these initiatives?
- 4. Where reported, what are the perspectives of participants (patients, professionals and policy makers) on these multilevel cancer initiatives?

If available in the included studies, we will also explore relevant contextual issues or any barriers/facilitators that may help to shed light on *how/why* the initiatives' specified objectives were (or not) achieved.

Study selection criteria

Study selection criteria are described in text and summarised in table 1.

Study designs and publication types

We will include experimental and non-experimental (observational) study designs. Quantitative, qualitative and mixed-methods studies are eligible for inclusion.

Study protocols, reviews/overviews, editorials, commentaries, short reports, viewpoints and letters to the editor are eligible for inclusion as these publications can provide important information on the components of national initiatives and their target populations (in addition to contextual information). Theses, government reports and other official documents are also eligible for inclusion.

Conference abstracts are eligible for inclusion provided that full-text about the initiative is also identified. Reviews/overviews are eligible for inclusion if they report on data from a single multilevel initiative (eg, describing its different components/programmes). Those reporting on more than one initiative will be excluded, but their references will be checked in order to identify additional eligible studies. Published guidelines from professional bodies that are not part of a government initiative will be excluded.

Table 1 Inclusion and exclusion criteria

Inclusion criteria

Exclusion criteria

Design and publication types

- ► Experimental and non-experimental studies
- ► Studies using quantitative, qualitative or mixed methods
- ► Protocols, editorials, commentaries, short reports, viewpoints and letters to the editor
- Reviews/overviews and systematic reviews reporting on a number of components from a single national strategy/ initiative
- ➤ Conference abstracts when full-text about initiatives is also available
- Reviews and systematic reviews reporting on more than one national initiative
- ► Conference abstracts when full-text about initiatives is not available
- ▶ Published guidelines/recommendations from professional bodies that are not part of a government initiative
- ▶ Publications without full-text in English

Population and setting

- ► Adults (aged 18 years or older)
- Patients/member of the public with or without medical conditions
- ► Healthcare professionals
- ► Health institutions/settings
- ► High-income countries (World Bank)

- ► Children (aged 17 years or younger)
- Professionals working in an administrative capacity (even if within a health system)
- ► Low-income and middle-income countries (World Bank)

Interventions

- ▶ Initiatives aiming to promote early diagnosis
- ▶ Initiatives addressing the patient/member of the public and at least two more levels of contextual influence (see Taplin et al)
- National level initiatives or equivalent (ie, state or provincial level depending on health system structure and autonomy)
- ▶ Initiatives aiming to support the entire cancer trajectory or to reduce cancer disparities (in which early diagnosis is only a component)
- ▶ Initiatives focusing on primary prevention, surveillance programmes, genetic counselling, cancer recurrence or screening programmes
- ► Cost-effectiveness studies
- ▶ Initiatives addressing the patient/public only
- ► Small, localised research studies and purely academic research studies/projects

Comparators and outcomes

- ► Any comparators (studies without comparators are also eligible for inclusion)
- ► High-level outcomes (national or equivalent) related to the initiatives' main aims (eg, improve awareness and diagnose cancer earlier)
- ► Overall views/experiences about initiatives

- ► Local, setting-specific outcomes
- Outcomes for a single cancer type (when strategies targeted more than one type)

Study population and setting

Initiatives aiming to promote earlier cancer diagnosis for the adult population (aged 18 years and over) will be included due to their relevance regarding the increased burden of cancer incidence and mortality. Initiatives aiming to promote earlier cancer diagnosis for any cancer types are eligible for inclusion. Health status will not be a reason for exclusion; we are interested in early diagnosis initiatives aiming at healthy participants or patients with any underlying medical conditions (provided that the focus is not on these other conditions).

Initiatives may also involve interventions with healthcare professionals. Hence, interventions targetted at general practitioners, other medical doctors, nurses and any allied professionals (such as pharmacists and radiographers) are eligible for inclusion. Initiatives carried out solely with professionals working on an administrative capacity (such as practice managers and hospital administrators) will be excluded. Finally, initiatives may also have healthcare providers, institutions and governments in receipt of an intervention. These groups are therefore also eligible for inclusion.

Initiatives carried out in high-income countries as classified by the World Bank³⁰ are eligible for inclusion. Low-income and middle-income countries are being excluded due to the diversity of health systems, populations and challenges (which would impair the ability to compare review results with activities from the Detect Cancer Early Programme in Scotland—as part of a large study of which this review is a component).

Interventions

We will include national initiatives/strategies with the explicit aim to promote earlier cancer diagnosis at a

health system level. Healthcare delivery occurs in a multilevel system, where multiple levels of contextual influence may affect behaviour. Taplin et al describe seven different levels: (1) the individual patient, (2) family and social supports, (3) provider/team, (4) organisation and/or practice setting, (5) local community environment, (6) state health policy environment and/ or (7) national health policy environment. The authors stipulate that multilevel interventions should address the patient (individual level) in addition to at least two more levels.³¹ All included studies will be required to meet this requirement, although adaptations are possible (eg, a member of the general public may also represent the individual level, and not all countries may have a state level). Interventions will be required to have involvement from governments (at state or national level), although non-governmental organisations may also be involved. Small, localised research studies within a single hospital/ other institution and purely academic research studies are not considered a national initiative and will therefore be excluded. Importantly, we are adopting Taplin et al's definition of interventions, that is, any 'specified strategy or set of strategies designed to change the knowledge, perceptions, skills, and/or behaviour of individuals, groups, or organisations, with the aim of improving patients' health outcomes'. 31 Hence, interventions may refer to trials or observational studies (including natural experiments).

Possible interventions aiming to promote earlier cancer diagnosis include but are not limited to campaigns to increase knowledge/awareness of cancer, training for healthcare professionals and development of care pathways to cancer diagnosis and treatment. We are particularly interested in initiatives that (1) raise awareness of symptoms and encourage prompt presentation by patients; and (2) facilitate timely investigation and referral in primary care. Initiatives focusing solely on primary cancer prevention such as those targeting lifestyle changes, reduction of exposure to environmental factors that may cause cancer or vaccinations (ie, against human papillomavirus), surveillance programmes for patients with Helicobacter pylori (a risk factor for stomach cancer) or Barrett's oesophagus (a risk factor for oesophageal cancer) will be excluded. Studies focusing on patients with genetic susceptibility of cancer, aiming to avoid cancer recurrence or cost effectiveness studies will also be excluded. Likewise, publications solely describing cancer screening programmes will be excluded (as these refer to a different, vast body of literature).

Comparators

Due to our broad aim, the diverse nature of the initiatives and the inclusion of quantitative and qualitative studies, it is likely many included studies will not have comparator populations. When these are present, they are likely to include: (1) indicators before (baseline) and after (one or more time points) at an individual and group level; or at the provider, organisation, local community, state and

national levels; or (2) those in receipt versus those either not in receipt of any initiative or in receipt of a different initiative.

Outcomes

This review aims to provide an overview of different initiatives as opposed to systematically assess all available outcomes for each identified initiative, as this would require a number of different reviews. We will only report overall, high-level outcomes (as the review's aim is to identify, describe and categorise national health initiatives without focusing on the outcomes). The review will summarise key features, target populations and reported measures used to monitor and evaluate different strategies. Local, setting-specific outcomes described in small studies about different initiatives will therefore not be reported. We will identify core publications for each initiative (from which data will be extracted) and list all other relevant, additional publications identified in the searches (categorising them according to the strategies they are referring to). We expect that the search strategy will identify a number of such additional publications.

High-level quantitative outcomes may include but are not limited to measures of knowledge/awareness of cancer, cancer symptoms or cancer screening; proxy measures of survival such as cancer stage at diagnosis may also be available.

Qualitative outcomes of interest include any views or experiences from professionals regarding the initiatives that may shed light on issues regarding implementation, feasibility and acceptability of initiatives. Patients and the public may provide perspectives on the impact of the initiatives and the importance of outcomes. Findings from qualitative studies may also help to shed light on the context (geographical, cultural, social, organisational or political) in which initiatives were implemented. ¹⁹

Some studies may be reporting ongoing interventions and data on health outcomes may not yet be available. It is also possible that some eligible publications will be descriptive in nature, presenting an overview of programmes.

Search strategy

A search strategy has been developed by the authors by making a list of keywords considered to be relevant based on the authors' knowledge of available literature on cancer and early diagnosis and looking at search strategies from specific publications in the area. The search strategy was then refined after discussions with a senior academic liaison librarian experienced with developing systematic review protocols in the field of health sciences. The search strategy was tested to ensure it was identifying relevant publications. It is broad as it was challenging to define specific keywords based on the research questions, and there was the possibility of missing too many relevant studies. It is also likely that national health initiatives are not described as such even when this is the case. We are therefore prioritising sensitivity over precision on the search of the search strategy was tested to ensure it was identifying relevant publications. It is also likely that national health initiatives are not described as such even when this is the case. We are

Table 2 MEDLINE search strategy*

- government or policy\$ or policies or national or regional or multi-level\$ or system-level or whole-system\$ or NAEDI or 'Detect Cancer Early' or 'National Awareness and Early Diagnosis Initiative' or 'Find Cancer Early' or 'Be Cancer Aware' or 'Be Clear on Cancer' or initiative\$ or program\$ or campaign\$ or strateg\$ or engagement or awareness.mp
- 2 health\$ adj2 (care or service\$ or system\$ or seek\$ or provi\$).mp
- 3 surviv\$.mp
- delay\$ adj4 (diagnos\$ or present\$ or treat\$ or consult\$ or patient\$ or doctor\$ or system\$ or refer\$ or therap\$ or care or detect\$).mp
- 5 time adj4 (diagnos\$ or present\$ or treat\$ or refer\$ or care or detect\$).mp
- 6 late adj4 (diagnos\$ or treat\$ or refer\$ or present\$ or detect\$).mp
- 7 earl\$ adj4 (diagnos\$ or present\$ or treat\$ or refer\$ or therap\$ or detect\$).mp
- 8 3 or 4 or 5 or 6 or 7
- 9 Cancer\$ or neoplas\$ or tumour or tumor or malign\$ or oncolog\$.mp
- Randomi\$ or RCT or intervention or trial or cross-sectional or survey\$ or questionnaire\$ or train\$ or 'natural experiment' or interview\$ or 'focus group\$' or 'case study' or observation\$ or time-series or 'time series' or CBA or 'controlled before and after' or 'controlled before-after' or prospective or retrospective or cohort or case-control or cross-over or 'case series' or case-reports or 'case reports' or feasibility or pilot or narrative or qualitative or quantitative or mixed-methods or 'mixed methods' or evaluat\$ or assess\$ or attitude\$ or view\$ or perception\$ or perspective\$ or 'discourse analysis' or 'content analysis' or 'thematic analysis' or 'narrative analysis' or phenomenolog\$ or 'purposive sampl\$' or ethnograph\$ or 'theoretical sampl\$' or 'grounded theory'.mp
- 11 1 and 2 and 8 and 9 and 10
- 12 11 not (child\$ or pediatric\$ or paediatric\$ or adolesc\$ or teenag\$).ti
- 13 12 not (palliative or terminal or 'end of life' or end-of-life or 'advance directive\$' or hospice\$).ti
- 14 13 not (biomarker\$ or molecul\$).ti.
- 15 limit 14 to (english language and humans and yr='2005 -Current')

not to miss important eligible studies. This is especially important when including qualitative studies. ³² Syntaxes/Boolean operators will be changed to meet the requirements of different research platforms. The MEDLINE search strategy is shown in table 2.

A number of databases (such as EMBASE, PsycInfo, MEDLINE and ASSIA; table 3) will be searched electronically, including those focusing on grey literature. Government and charity websites will be searched in addition to different data repositories for randomised controlled trials and studies funded by the European Commission.

We will check the reference lists of all included studies. If relevant references are not available online, we will contact the authors to request these. Finally, the list of included studies will be checked by all authors to verify whether any relevant studies known to them are missing.

We will include all studies published from 2005 onwards. This cut-off point was chosen as this was the year that the WHO approved its resolution on Cancer Prevention and Control. Broader inclusion criteria will allow for the identification of less well-known initiatives worldwide, with diverse health contexts (such as universal health coverage) and approaching different populations (such as deprived groups, those living in rural areas and ethnic minorities). Due to resource limitations, only publications in English will be included. Initially, we envisioned

to include publications in Spanish and Portuguese (as we have the resources to translate these), but we were concerned that the results would then be biased towards initiatives in countries where these languages are spoken. We do acknowledge, however, that publications will be biased towards studies published in English (implications will be discussed). Full-text publications in any language other than English will be excluded even if the abstracts are available in this language. We will prepare a descriptive supplementary table listing these potentially eligible abstracts that only had full-text in a different language.

Data management, selection and extraction

Citations and abstracts from searches will be exported into EndNote X7 for Windows. After removing duplicates, the studies will be screened using a multistep procedure. First, one author will screen all the titles and abstracts against the inclusion criteria. Another author will screen a random selection (30%) of the excluded studies at this step. Second, two review authors will independently screen the full-text of reports in order to select papers for inclusion. Finally, the two authors will carefully reassess the full-text of all included articles (independently) in order to ensure they have relevant information which could be extracted. Articles that do not have this will be excluded from the analysis. The study selection process will be recorded in SPSS version 22 for Windows. A

^{*&#}x27;.mp' searches automatically for subject heading (MeSH) fields.

Table 3 Electronic data sources	
Search platform/provider	Databases
Cochrane Library (single search)	 ▶ Cochrane Database of Systematic Reviews (CDSR) ▶ Cochrane Central Register of Controlled Trials (CENTRAL) ▶ Database of Abstracts of Reviews of Effects (DARE) ▶ Health Technology Assessment Database (HTA) ▶ NHS Economic Evaluation Database (EED)
Ovid (searching each database independently)	 ► Embase Classic + Embase ► MEDLINE(R) and MEDLINE(R) In-Process & Other Non-Indexed Citations ► PsycInfo ► PsycARTICLES full-text
Web of Science Core Collection (single search)	 ▶ Scielo ▶ Science and Social Sciences ▶ Conference Proceedings in Science and Social Science & Humanities
ProQuest (single search)	 ▶ ProQuest Dissertations & Theses Global ▶ Applied Social Sciences Index and Abstracts (ASSIA) ▶ International Bibliography of the Social Sciences (IBSS) ▶ PAIS International
EBSCOhost (single search)	➤ Cinahl Plus ➤ SocINDEX with full-text
Other sources of data	 ▶ United Kingdom: UK Department of Health Publications and Statistics; The Knowledge Network (NHS e-library); UK Clinical Research Network; Healthcare Management Information Consortium (HMIC) database ▶ United States: Centers for Disease Control and Prevention ▶ International Agency for Research on Cancer ▶ European Commission's Community Research and Development Information Service (CORDIS) ▶ OECD iLibrary
	 ▶ Charities worldwide: Cancer Research UK, Marie Curie, Macmillan Cancer Support, The King's Fund, The Nuffield Trust, National Cancer Research Institute, World Cancer Research Fund International, American Lung Association, American Cancer Society, Cancer Research Institute, National Cancer Institute, Cancer Council Australia, Canadian Cancer Society, Danish Cancer Society, Cancer Society of New Zealand, German Cancer Aid, Irish Cancer Society, Dutch Cancer Society, Norwegian Cancer Society, Portuguese Cancer League, Asociación Española Contra el Cáncer, Swedish Cancer Society, Nordic Cancer Union, German Cancer Society ▶ Theses: EThOS - Electronic Theses Online Service; Dart-Europe ▶ Clinical Trials: U.S. National Institutes of Health's Clinical Trials Database; WHO International Clinical Trials Registry Platform Search Portal; UK Clinical Trials Gateway ▶ Grey literature: Open Sigle

PRISMA flow diagram²⁶ will be developed. Study authors will be contacted if additional information is required to decide eligibility. One reminder will be sent if there are no replies. All disagreements at each step will be solved by consensus; a third review author will be consulted if consensus cannot be obtained.

A data extraction template has been created in Microsoft Word for Windows (see online supplementary file S1). It includes contextual information on the initiatives and a description of its key components, in addition to information on study design, setting, location, other characteristics of the intervention, of study participants and outcomes. Two reviewers will independently extract data from three randomly selected included studies and

compare their forms in order to reduce bias and ensure the forms are being used in a similar manner. Afterwards, one reviewer will extract data from 50% of the included studies and another will extract data from the remaining 50%. The two researchers will compare form content and discuss any disagreements. A third reviewer will be consulted if disagreements cannot be solved by consensus. Extracted data will be described in text, tables and diagrams.

Quality assessment

We anticipate that the included studies will be varied in terms of study design and that most will be observational studies.³⁴ This leads to challenges in choosing a quality assessment tool that can be used appropriately for different designs. We will therefore use more than one assessment tool.

Quantitative studies will be analysed using the McMaster Critical Review Form for Quantitative Studies, ³⁵ available in online supplementary file S2. This tool is suitable for different types of quantitative studies (cross-sectional, cohort, case–control, among many others). It contains multiple choice questions regarding the study purpose, literature, design, sample, outcomes, intervention, results, conclusions and implications. The tool also approaches issue of bias, validity and reliability. Percentage agreement between two researchers has been assessed (from 75% to 86%) and guidance on how to assess studies is also provided. ³⁵

Qualitative studies will be assessed using the quality assessment tool from Hawker and colleagues, ³⁶ which was developed to evaluate the quality of heterogeneous studies in systematic reviews. The original tool has nine items and allows for four possible answer options ('good', 'fair', 'poor' and 'very poor'). Item six will be divided into two different items in order to separately assess issues related to ethics and bias as these are shown together in the original instrument (adapted tool is available in online supplementary file S3). This adaptation has been successfully done in a previous systematic review assessing qualitative studies. ³⁷ Study protocols, editorials, commentaries, short reports and viewpoints will also be assessed using this tool (limitations will be acknowledged).

Letters to the editor, conference abstracts and grey literature such as government reports/cancer strategies will not be assessed for quality; potential methodological issues and risks of bias will be discussed. Reviews and systematic reviews will be assessed using the validated Oxman and Guyatt's 10-item checklist (Overview Quality Assessment Questionnaire), as this tool is suitable for both systematic and non-systematic reviews ^{38 39} (see online supplementary file S4).

Mixed-methods studies will be assessed using both the tools for qualitative and quantitative studies; results for both assessments will be reported. For all studies we will report each quality component separately in a supplementary table due to recognised problems with calculating single summed quality scores. 40 41

Each study will be independently assessed by two reviewers, with disagreements solved by consensus. A third reviewer will be consulted if no consensus can be reached. We will report the % agreement and kappa scores using the Landis and Koch guidelines. 42

Data synthesis

We expect wide heterogeneity in the composition and intensity of initiatives, populations and contexts²⁹ ⁴³ and predict that meta-analysis will not be possible nor appropriate considering the review aims. We will carry out narrative synthesis; this is a widely used method when there is heterogeneity.²⁸ ⁴³ Narrative synthesis is an approach that relies on using words and text to 'tell

a story' of findings.⁴⁴ It is useful in reviews investigating questions that are not solely focused on the effectiveness of interventions.⁴³ and well suited for complex interventions.¹⁹ Narrative synthesis has also been described as particularly effective to synthesise qualitative and quantitative evidence⁴⁵ and to make explicit different study designs and contexts.⁴⁶ We will follow published guidelines for using this method⁴⁴ and take into account reported limitations of this approach.⁴⁷

Data will be reported irrespective of the results from the quality assessment; implications will be discussed. Findings will be described in text and in tables and categorised in line with Taplin *et al*'s refined model of multilevel influences on the cancer care continuum. We will provide details of key features of initiatives such as contextual issues (eg, described policies and source of funding), key components (such as relevant guidelines for referring patients to specialist services), target populations and timelines. When reporting outcomes we will take into account the updated NAEDI's hypothesis of factors influencing cancer survival and premature mortality. If feasible, a diagram will be created to summarise these results.

ETHICS AND DISSEMINATION

This systematic review protocol did not require ethical approval as there is no direct contact with research participants. There are also no issues of confidentiality or potential harms. Only secondary data from published studies and grey literature will be analysed.

The review results will be submitted to a peer-reviewed journal in early 2018 in order to reach a diverse group of healthcare professionals, researchers and policy makers.

DISCUSSION

To our knowledge, this is the first systematic review aiming to describe the full breadth of national health initiatives in promoting earlier diagnosis of cancer in high-income countries, exploring their main characteristics (such as key components and target populations) and describing available high-level outcomes. This is an important research area considering the burden of cancer worldwide and the predicted increased number of cancer cases, especially in the context of an ageing population. Furthermore, as health systems, governments and other stakeholders invest in, and develop programmes to tackle the issue, it is paramount that evidence on similar initiatives is made available. This review will provide a more nuanced understanding of the components of such initiatives.

There are challenges to be faced due to the likely complexity of the included interventions, populations and health systems. Furthermore, carrying out comprehensive literature searches in such a broad knowledge area will be time-consuming. We are following several available guidelines and developing strategies to deal with these challenges.

In conclusion, this review addresses a relevant, timely health issue that affects a large proportion of the worldwide population. The findings will be helpful to researchers, policy makers, government departments and key cancer charities developing similar initiatives and assessing cancer outcomes.

Acknowledgements We would like to thank Marshall Dozier at the University of Edinburgh for her invaluable advice when developing this protocol. We also thank Leonie Nijenhuis from Radboud University Nijmegen for her help when critically appraising and choosing quality assessment tools to be used in the review. Finally, we thank the reviewers for their comments and recommendations.

Contributors NC, CC and DW developed and refined the systematic review protocol. NC drafted the manuscript, which was then critically assessed by both CC and DW. All authors approved the final version of this manuscript. NC is the quarantor.

Funding This review is supported by the Scottish Government (via the Detect Cancer Early Programme) as part of a PhD study investigating the role of health system level initiatives in promoting the earlier diagnosis of cancer. The PhD is also funded by scholarships from the University of Edinburgh. The supporters had no role in the preparation of this review protocol nor in the decision to publish it.

Competing interests None declared.

Patient consent This systematic review protocol did not require ethical approval as there is no direct contact with research participants, no issues of confidentially or potential harms. Only secondary data from published studies and grey literature will be analysed.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Any data related to this protocol and not published are available upon request to the authors (by email or post). These may include final search strategies for all databases, completed data extraction forms, among others. Please contact the corresponding author (natalia.calanzani@ed.ac.uk) if you would like to obtain these data.

Open Access This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

© Article author(s) (or their employer(s) unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- GLOBOCAN. Cancer fact Sheets. estimated Cancer incidence, mortality and prevalence Worldwide in 2012. 2014. http://globocan. iarc.fr/Pages/fact_sheets_cancer.aspx (accessed Jan 2017).
- Fitzmaurice C, Dicker D, Pain A, et al. The global burden of Cancer 2013. JAMA Oncol 2015;1:505–27.
- Silva I. Cancer epidemiology: principles and methods. Lyon, France: International Agency for Research on Cancer, World Health Organization, 1999. https://www.iarc.fr/en/publications/pdfs-online/epi/cancerepi/CancerEpi.pdf (accessed Jan 2017).
- Ahmad AS, Ormiston-Smith N, Sasieni PD. Trends in the lifetime risk of developing Cancer in Great Britain: comparison of risk for those born from 1930 to 1960. Br J Cancer 2015;112:943–7.
- Walters S, Benitez-Majano S, Muller P, et al. Is England closing the international gap in Cancer survival? Br J Cancer 2015;113:848–60.
- DeSantis CE, Lin CC, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2014. CA Cancer J Clin 2014;64:252–71.
- Centers for Disease Control and Prevention. Global Cancer statistics. number of cases, deaths, and Survivors. 2016. http://www.cdc.gov/cancer/international/statistics.htm (accessed Jan 2017).
- Allemani C, Weir HK, Carreira H, et al. Global surveillance of Cancer survival 1995-2009: analysis of individual data for 25,676,887 patients from 279 population-based registries in 67 countries (CONCORD-2). Lancet 2015;385:977-1010.
- Coleman MP, Forman D, Bryant H, et al. Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK,

- 1995-2007 (the International Cancer benchmarking Partnership): an analysis of population-based cancer registry data. *Lancet* 2011;377:127–38.
- 10. Richards MA. The size of the prize for earlier diagnosis of cancer in England. *Br J Cancer* 2009;101(Suppl 2):S125–S129.
- Hiom SC. Diagnosing cancer earlier: reviewing the evidence for improving cancer survival. Br J Cancer 2015;112(Suppl 1):S1–S5.
- Maringe C, Walters S, Rachet B, et al. Stage at diagnosis and colorectal Cancer survival in six high-income countries: a populationbased study of patients diagnosed during 2000-2007. Acta Oncol 2013;52:919–32.
- World Health Organization. National Cancer control Programmes. policies and managerial guidelines. Geneva: World Health Organization, 2002. http://www.who.int/cancer/media/en/408.pdf. (accessed Jan 2017).
- World Health Organization. Cancer Prevention and Control Report to the Secretariat by the 58th World Health Assembly. 2005. http:// www.who.int/mediacentre/news/releases/2005/pr_wha05/en/index. html (accessed Jan 2017).
- World Health Organization. WHA58.22 Cancer prevention and control. 2005. http://www.who.int/cancer/media/news/WHA58% 2022-en.pdf (accessed Jan 2017).
- Richards MA. The National Awareness and Early diagnosis Initiative in England: assembling the evidence. *Br J Cancer* 2009;101(Suppl 2):S1–S4.
- The Scottish Government. Detect Cancer Early. 2012. http://www.scotland.gov.uk/Topics/Health/Services/Cancer/Detect-Cancer-Early (accessed Jan 2017).
- Vedsted P, Olesen F. A differentiated approach to referrals from general practice to support early Cancer diagnosis - the danish three-legged strategy. Br J Cancer 2015;112(Suppl 1):S65–9.
- Petticrew M, Rehfuess E, Noyes J, et al. Synthesizing evidence on complex interventions: how meta-analytical, qualitative, and mixed-method approaches can contribute. J Clin Epidemiol 2013;66:1230–43.
- Jackson N, Waters E; Guidelines for Systematic Reviews in Health Promotion and Public Health Taskforce. Criteria for the systematic review of health promotion and public health interventions. Health Promot Int 2005;20:367–74.
- Brinkerhoff D. Accountability and health systems: overview, framework, and strategies. Bethesda, Maryland: Abt Associates, Partners for Health Reform Plus, 2003. USAID Contract No. HRN-C-00-00-00019-00.
- González-Robledo LM, González-Robledo MC, Nigenda G, et al. Acciones gubernamentales para la detección temprana del cáncer de mama en América Latina: Retos a futuro. Salud Publica Mex 2010;52:533–43.
- 23. Palmer SJ. The impact of national policy on the early diagnosis of Cancer. *Br J Nurs* 2013;22:S16–S23.
- Brown S, Castelli M, Hunter DJ, et al. How might healthcare systems influence speed of Cancer diagnosis: a narrative review. Soc Sci Med 2014;116:56–63.
- Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;349:g7647.
- Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535.
- Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. www.cochrane-handbook.org.
- Centre for Reviews and Dissemination (CRD). Systematic reviews. CRD's guidance for undertaking reviews in health care. CRD, University of York, 2008.
- Squires JE, Valentine JC, Grimshaw JM. Systematic reviews of complex interventions: framing the review question. J Clin Epidemiol 2013;66:1215–22.
- World Bank. World Development Indicators. 2013. http://databank. worldbank.org/data/download/WDI-2013-ebook.pdf (accessed Jan 2017).
- Taplin SH, Anhang Price R, Edwards HM, et al. Introduction: understanding and influencing multilevel factors across the Cancer care continuum. J Natl Cancer Inst Monogr 2012;2012;2–10.
- 32. Shaw RL, Booth A, Sutton AJ, et al. Finding qualitative research: an evaluation of search strategies. BMC Med Res Methodol 2004;4:1–5.
- Neal RD, Tharmanathan P, France B, et al. Is increased time to diagnosis and treatment in symptomatic Cancer associated with poorer outcomes? systematic review. Br J Cancer 2015;112(Suppl 1):S92–S107.
- 34. Neal RD. Do diagnostic delays in cancer matter? *Br J Cancer* 2009;101(Suppl 2):S9–S12.



- Evidence-Based Practice Research Group at McMaster University.
 Quantitative review form. http://srs-mcmaster.ca/research/evidence-based-practice-research-group/#OIXEXdby (accessed Jan 2017).
- Hawker S, Payne S, Kerr Č, et al. Appraising the evidence: reviewing disparate data systematically. Qual Health Res 2002;12:1284–99.
- Gomes B, Calanzani N, Gysels M, et al. Heterogeneity and changes in preferences for dying at home: a systematic review. BMC Palliat Care 2013;12:1–13.
- 38. Oxman AD, Guyatt GH. Validation of an index of the quality of review articles. *J Clin Epidemiol* 1991;44:1271–8.
- Oxman AD, Cook DJ, Guyatt GH. Users' guides to the medical literature. VI. how to use an overview. Evidence-Based medicine Working Group. *JAMA* 1994;272:1367–71.
- Whiting P, Harbord R, Kleijnen J. No role for quality scores in systematic reviews of diagnostic accuracy studies. *BMC Med Res* Methodol 2005:5:1–9.
- Jüni P, Altman DG, Egger M. Assessing the quality of controlled clinical trials. BMJ 2001;323:42–6.

- Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–74.
- Michie S, Jochelson K, Markham WA, et al. Low-income groups and behaviour change interventions: a review of intervention content, effectiveness and theoretical frameworks. J Epidemiol Community Health 2009;63:610–22.
- 44. Popay J, Roberts H, Sowden A, et al; Guidance on the Conduct of Narrative synthesis in systematic reviews. A product from the ESRC methods Programme. ESRC Methods Programme, 2006.
- 45. Barnett-Page E, Thomas J. Methods for the synthesis of qualitative research: a critical review. *BMC Med Res Methodol* 2009;9:1–11.
- Lucas PJ, Baird J, Arai L, et al. Worked examples of alternative methods for the synthesis of qualitative and quantitative research in systematic reviews. BMC Med Res Methodol 2007;7:1–7.
- Rodgers M, Sowden A, Petticrew M, et al. Testing methodological guidance on the Conduct of Narrative synthesis in systematic reviews: effectiveness of interventions to promote Smoke Alarm ownership and function. Evaluation 2009;15:49–73.