



Targeted screening in the UK: A narrow concept with broad application

Anna Bobrowska,^{a,1} Molly Murton,^{a,1} Farah Seedat,^b Cristina Visintin,^b Anne Mackie,^b Robert Steele,^{b,c} and John Marshall^{b*}

^aCostello Medical, 50/60 Station Road, Cambridge CB1 2JH, UK

^bUK National Screening Committee, Southside, 39 Victoria Street, London SW1H 0EU, UK

^cCentre for Research in Screening and Prevention, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK

Summary

A recent report on screening in the UK proposed that the responsibility for recommendations on population and targeted screening programmes should be held by one new integrated advisory body. There is no wide international consensus on the definition of targeted screening. Our review identified and compared the defining components of screening terms: targeted, population, selective, and cascade screening, and case finding. Definitions of targeted screening and population screening were clearly demarcated by the eligible population; targeted and selective screening were found to be conceptually interchangeable; cascade screening, whilst conceptually similar to targeted screening across several components, was only used within the context of genetic diseases. There was little consensus between different definitions of case finding. These comparisons contributed to an updated definition of targeted screening. Considerable overlap between definition components across terms implies that a broad range of disease areas may fall into the remit of the new advisory body.

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Introduction

A recent review of screening in the UK, commissioned by National Health Service (NHS) England, proposed that the responsibility for making recommendations on population and targeted screening programmes should be held by one new integrated advisory body.¹ This would differ from the current UK system, where the UK National Screening Committee (NSC) is responsible for reviewing evidence and making recommendations on population screening programmes, and the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), and professional medical bodies are responsible for issuing guidance on targeted screening and other tested interventions in routine clinical practice.

In the most general terms the concept of screening has been used in the UK and throughout Europe since the early 20th century.^{2–4} It was recently described by the UK NSC as the process of identifying healthy people who may have an increased chance of a condition and offering them information, further tests, and treatment,

in order to reduce associated problems or complications. In addition to information as an outcome of screening, the principle of personal informed choice is also central to the offer of the initial screening test.^{5,6} The assumption that ‘screening’ is synonymous with ‘population screening’ is reflected in the UK NSC’s primary focus on screening within large, asymptomatic, and demographically defined populations, and the Committee’s close association with the principles of mass screening established by Wilson and Jungner in 1968.^{3,4,7,8}

The NHS England review proposing the reorientation of UK screening policy-making structures and processes did not discuss the concept of targeted screening in detail.¹ There is a lack of clarity on the terminology relating to targeted screening; this may impact decisions on which programmes and conditions might be considered, and which organisation is responsible for the evaluation of candidate screening interventions. This, ultimately, impacts health outcomes for patients.⁹ Reaching consensus on the definition and features of targeted screening is therefore of great relevance to European, Australasian and Canadian audiences, as many screening decision-making bodies share a similar conceptual framework with that used in the UK.¹⁰ In this article, we present the results of a literature review

* Corresponding author.

E-mail address: john.marshall@dhsc.gov.uk (J. Marshall).

¹ Joint first authors.

which was prepared as a discussion document to aid a multi-agency Chief Medical Officer (CMO) Working Group tasked with establishing the new advisory body's role and remit. The Working Group benefited from the input of patient and public voice partners who had been involved in preliminary discussions of the concept of targeted screening within the UK NSC's structures. We explore the defining components of targeted screening, in order to develop a clear and practical definition that allows differentiation from population screening and clinical management. We also consider potential applications of the definition of targeted screening, with an aim to inform discussions around the remit of the new integrated advisory body.

Methods

Framework for developing, refining, and testing definitions of targeted screening

During its formative period, the UK NSC established a definition for population screening using a framework of seven structured components: population (identification, characteristics, and health status), test (purpose, initiation, and speed), and organisation. Using this framework as a reference point, we proposed a set of components for targeted screening which functioned as a working definition. This working definition was a practical tool which was used in the evolving discussions of the CMO Working Group (Table 1). We then conducted a literature review to assess and update the components of the working definition of targeted screening against existing definitions found in the literature. The updated components of targeted screening were subsequently compared with the literature definitions of population screening and three other screening terms, which had been selected *a priori* based on the authors' experience of the field: selective screening, cascade screening, and case finding. On the basis of this work a narrative summary statement was developed as an 'updated definition' of targeted screening.

Search strategy and selection criteria

We conducted pragmatic literature searches of PubMed, Web of Science, Google Scholar, and Google. Literature was gathered on definitions of the five screening terms: targeted screening, population screening, selective screening, cascade screening, and case finding. Initial searches for these five terms and 'screening' were supplemented by search strings containing combinations of terms: 'definitions AND criteria AND screening', 'principles AND screening OR surveillance', and 'validation AND screening procedures'. Additionally, we identified further relevant publications using a 'Similar articles' or equivalent search function, and by hand searching the reference lists of relevant articles.

Studies were included if they contained definitions of population screening, targeted screening, selective screening, cascade screening or case finding. Studies were also included if they described aspects of these screening terms with regards to the intended population (identification and characteristics, health status), test (purpose, initiation, speed) or organisation. In instances where the primary references for relevant information described in narrative reviews were unavailable, the information was attributed a lower weighting of relevance when compared with information directly available from primary sources. Titles and abstracts were reviewed by one independent reviewer and a second reviewer was consulted in cases where relevance was uncertain. The same approach was used for reviewing full texts. All searches were conducted in an iterative manner during March and April 2020.

Data extraction and synthesis

The resulting data for each of the five screening terms were extracted and compiled into a mind map using Docear software, in order to group together definitions and characteristics of specific screening terms.¹⁴ Passages of interest were then indexed into the framework of the seven pre-specified set of components, enabling a qualitative synthesis of the data into distinct definition components.

Role of the funding source

Authors from the funding organisation contributed to the development of the study design, the interpretation of data, and manuscript editing.

Results

Definitions of screening terms

In total, 61 full texts were reviewed for relevant information and of those, 20 publications were identified as reporting one or more definitions of any of the pre-specified screening terms, or of general screening. There was broad consistency within the descriptions of each of the targeted, population, selective, and cascade screening terms as described across the publications. The exception to this was case finding, which was described in ways which approximated to both targeted and population screening. A full list of relevant texts is presented in Table 2.

Development of the updated definition for targeted screening

The findings of the literature search corroborated the core elements of the working definition of targeted screening, across the pre-specified seven-component framework. Ultimately, the essential elements of the

Component	Population Screening	Targeted Screening
POPULATION		
Identification and Characteristics	Population in which the test is undertaken, which is large rather than an evaluation of an individual.	Population is large but defined by a recognised, above average risk (which could be determined by: family history, e.g. genetic risk; behaviour, e.g. smoking; or established disease, e.g. diabetes) for the condition for which screening is being offered.
Health status	Health status of the individuals comprising the population, which is asymptomatic.	Population is asymptomatic for the condition for which screening is being offered.
TEST		
Purpose	Purpose of the test, which is primarily to establish risk rather than diagnosis.	The purpose of the test is primarily risk refinement rather than either to establish risk or diagnosis.
Initiation	Mode of testing's initiation, which is offered by the health service rather than sought by a patient.	This remains the same for both population and targeted screening. In targeted screening the population should be identifiable in the community.
Speed	Speed of test delivery, which should be rapid and episodic rather than part of an ongoing encounter with the health service.	Rapid does not necessarily apply to targeted screening. Episodic applies to targeted screening but frequency may be increased compared to population screening (e.g. diabetic eye screening is offered annually).
ORGANISATION		
	<p>Organisation of test delivery, which is systematic rather than ad hoc or opportunistic.</p> <p>This is extrinsic to the 'nature' of the testing and represents a strategic component, something which is related more closely to a business model rather than 'screening' in and of itself. In population screening it was applied on the grounds of service quality and patient safety and this was underpinned by an ethical obligation to a healthy population.</p> <p>In UK NSC terms, systematic is synonymous with 'nationally managed'.</p>	<p>This should remain the same for both population and targeted screening.</p> <p>However, a further strategic component is required. This is that the test is of a level of complexity that it requires a nationally managed approach to ensure high quality delivery e.g. blood pressure readings would not fit this criterion, whereas CT scans or colonoscopy would.</p> <p>This is a functional consideration which can help distinguish the new body's remit from the mass of NHS practice. Component six might be: "The testing technology is complex and requires a nationally managed, rather than ad hoc or opportunistic, approach to roll out and subsequent management."</p>
<p>Table 1: Components of population screening and the working definition for targeted screening initially compiled by the UK NSC.</p> <p>CT: computed tomography; NHS: National Health Service; NSC: National Screening Committee.</p>		

working definition for targeted screening (Table 1) were retained. However, some literature sources provided slightly different perspectives, or additional details, for targeted screening. Some extra nuances within the *identification* and *health status* components were elicited from the literature and are presented in Tables 3 and 4. These additional details were based on literature from Brown et al., who described the population as the group for whom screening would provide maximal benefit, which may indicate those in the early stages of disease.¹²

We additionally considered two statements from the WHO regarding the *initiation* and *characteristics* of the screening test, but did not incorporate them into the

updated components (Tables 3 and 4).¹³ The WHO noted that targeted screening could be considered at either the community or individual level and for those seeking healthcare for a different condition.¹³ This draws a parallel between targeted screening and routine clinical practice, as it is not unusual for clinical encounters between patients and healthcare professionals to lead to the offer of tests for other conditions. However, this focus on testing at the individual level departs from the other definitions of screening identified in the literature, which place a larger emphasis on populations or groups. The WHO's definition may therefore highlight a different concept of, or approach to, targeted screening.

Source	Definition
Population screening	
Last 1991 ¹⁶	Population-based screening describes the activities of community-based professionals. They identify a population of people who are at risk of developing a certain condition and then invite them for examination to detect this disease or pre-disease condition. The results are then compiled based on the findings and outcomes of all those invited for screening, whether or not they attended.
Speechley 2017 ⁹	The key feature is that eligibility is very broad and not based on factors associated with increased risk of the health condition of interest.
Targeted screening	
Brown 2003 ¹²	There is an idea that targeted screenings identify a greater number of individuals at risk than a general public screening.
Gray 2004 ¹⁵	This concept of screening focuses more closely on populations at risk rather than on risk factors. This concept for disease control is also relevant when screening for infectious diseases.
Speechley 2017 (Friis and Sellers 2009; Oleckno 2008) ⁹	Selective and targeted screening are used synonymously. The key distinguishing feature from mass screening is that eligibility is based on a characteristic associated with increased risk of the condition being detected such as occupation or ethnicity.
Selective screening	
Wilson and Jungner 1968 ⁸	The screening of selected high-risk groups in the population. It may still be large scale and can be considered as one form of population screening.
Whitby 1974 ¹⁹	Screening can be carried out on selected subgroups of the population (selected as being at relatively high risk on the basis of epidemiological research) when it is called selective screening (e.g., selected by age, sex, genetic history, occupation).
Hakama 1979 ¹⁸	Successful selective screening is based on the assumption that there is a subpopulation with a high risk of the disease and that these people can be identified. In principle, the screening of those with a high risk of disease only is recommended because of the reduction in cost, or because this helps to avoid the adverse effects of screening.
Szklo 1990 ¹⁷	Screening high-risk subjects to detect early disease is known as selective screening. The main objective of selective screening is to identify the smallest subgroup of the total reference population that will yield a substantial proportion of the total number of cases while concurrently keeping the false-positive rate at its lowest possible level.
Speechley 2017 (Friis and Sellers 2009; Oleckno 2008) ⁹	Selective and targeted screening are used synonymously. The key distinguishing feature from mass screening is that eligibility is based on a characteristic associated with increased risk of the condition being detected such as occupation or ethnicity.
Cascade screening	
Super 1994 (context of cystic fibrosis) ²¹	Index families with affected members are contacted by the fieldworker, often at visits to cystic fibrosis clinics, and arrangements are made to draw up formal family trees.
Knowles 2017 (context of FH) ²⁰	Cascade screening relies on identifying an FH patient (proband) and active cholesterol testing, genetic testing, or both for all potentially affected relatives—a cycle that is repeated (cascaded) for each relative diagnosed with FH, thereby expanding the number of potential cases detected.
Case finding	
Wilson and Jungner 1968 ⁸	That form of screening of which the main object is to detect disease and bring patients to treatment, in contrast to epidemiological surveys.
Wald and Morris 1996 ²⁷	The term case-finding is widely used, but it is unsatisfactory. Its meaning is unclear, and this has encouraged its use in different ways. A problem with the term case-finding is that it carries an implication that one has identified a case of the disorder for which one is screening, while in fact one has usually identified an individual with a positive screening test for that disorder. The term case-finding avoids any obligation to specify the conditions under which the screening activity should operate and the expected improvements in health that will arise from it. It evades the need to demonstrate net benefit.

Table 2 (Continued)

Source	Definition
NHS England 2015 ²⁶	A systematic or opportunistic process that identifies individuals (e.g. people with COPD) from a larger population for a specific purpose (e.g. 'flu vaccination').
Fell 2016 (Raffle and Gray 2009; Last*) ²⁴	Case-finding is rather more "difficult to define [than screening] as it tends to be used rather vaguely. It can mean finding cases in known high risk individuals." (Raffle and Gray, 2009). Last* defines case finding as a concept either applying to control of infectious disease – seeking persons who may have been exposed (often referred to as contact tracing) or one of early clinical detection of disease (or risk) in persons using health services for other reasons (for e.g. opportunistic blood pressure checking as part of a visit for another reason).
Mackenzie 2017 ²²	Case finding is a strategy for targeting resources at individuals or groups who are suspected to be at risk for a particular disease. It involves actively searching systematically for at risk people, rather than waiting for them to present with symptoms or signs of active disease. Note the similarities to screening – both seek to risk stratify the population for further investigation.
Speechley 2017 (Cassen; Sackett 1991; Porta 2008; Raffle and Gray 2009) ⁹	The common characteristic of case finding mentioned by most authors is that it is usually done as part of a clinical encounter for some other health condition, although the provided examples differ. Raffle AE and Gray JAM stated it is "difficult to define as it tends to be used rather vaguely. It can mean finding cases in known high risk individuals".

Table 2: Full list of definitions of screening terms identified from literature searches.

* Sources drawn on within Fell 2016 ('Raffle and Gray' and 'Last') were not adequately referenced so the primary sources could not be checked. COPD: chronic obstructive pulmonary disease; FH: familial hypercholesterolaemia; NHS: National Health Service.

Comparison of the components of population screening with the updated components of targeted screening

Table 3 shows components of definitions found in the literature on population screening, compared with the updated components of targeted screening. The most significant distinction between the terms was identified in the *population* components: population screening characterises populations by demographics, in which risk of the disease is low, whereas targeted screening characterises populations by heightened risk of the disease.^{9,12,14,15} This suggests that targeted screening strategies aim to focus testing in groups in which cases are more likely to be concentrated,¹² whereas population screening identifies risk amongst broader populations, or major demographic subgroups.^{9,14,15}

Grootendorst et al. provided an interesting rationale for this difference by comparing the *purpose* of population and targeted screening: they argued that population screening should aim to detect as many cases as possible, whilst targeted screening should aim to reduce the number who need to be screened to detect a case compared with population screening.¹⁴ A related point was raised by Brown et al., who stated that targeted screening may save cost and resource compared with population screening.¹² In this way, targeted screening might be considered to strike a more preferential balance between screening programme performance and health system resource use.

Within the *speed* component, population screening was described as rapid and episodic, not implying

ongoing clinical management of the affected person, with Last suggesting that screening must also be frequent enough to achieve efficacy.¹⁶ No further sources reported on *speed* for targeted screening or *organisation* for targeted or population screening.

Comparison of the components of selective screening, cascade screening, and case finding with the updated components of targeted screening

When comparing the updated components of targeted screening to the literature on selective and cascade screening and case finding, we found that selective and targeted screening share many similarities and have typically been used interchangeably in the literature (Table 4).⁹ Like targeted screening and unlike population screening, all relevant sources proposed that selective screening involved a high-risk population,^{8,9,17–19} with Szklo specifying that the risk factors did not need to be causally related to the disease and that patients who are targeted may be asymptomatic for the disease in question.¹⁷ Both Hakama et al. and Szklo also suggested that the process of selective screening should enable detection of a substantial proportion of cases; this reflects Szklo's description of the *purpose*: to identify the smallest subgroup of a reference population that yields a substantial number of the total cases whilst keeping false positive rates to a minimum.^{17,18} This aligns well with the suggestions regarding screening efficiency from Grootendorst et al. on targeted screening.¹⁴

Component	Population Screening	Targeted Screening
POPULATION		
Identification	Entire group <ul style="list-style-type: none"> Populations, not individuals³³ Very broad eligibility⁹ Majority of at-risk population¹⁶ 	Selected high-risk group ¹³ <ul style="list-style-type: none"> Use of risk factors or risk algorithms¹² <u>Group for whom screening would provide maximal benefit</u>^{*;12}
Characteristics	Defined by age, sex, or pregnancy <ul style="list-style-type: none"> Major demographic subgroups⁹ Cover a defined population^{14,15} 	Defined by above-average risk ^{9,12} <ul style="list-style-type: none"> <i>May consider individual- or community-level risk profile</i>^{†;13}
Health status	Apparently healthy, asymptomatic, or unaware ^{15,33,34}	Apparently healthy, asymptomatic, or unaware <ul style="list-style-type: none"> <u>Early stage of disease</u>^{*;12}
TEST		
Purpose	Risk identification, not diagnosis <ul style="list-style-type: none"> Detect as many cases as possible¹⁴ Respond to a recognised need¹⁴ Secondary prevention³⁴ 	Risk refinement <ul style="list-style-type: none"> Reduce the number who need to be screened¹⁴ Save cost/resource compared to population screening¹²
Initiation	Offered, not sought, in community-based setting <ul style="list-style-type: none"> Delivered by clinicians³⁴ 	Offered, not sought, in community-based setting ¹² <ul style="list-style-type: none"> <i>Could target those seeking healthcare for a different health problem</i>^{†;13}
Speed	Rapid and episodic, not ongoing <ul style="list-style-type: none"> Frequent enough to achieve efficacy¹⁶ 	Variable speed and frequency, may be ongoing
ORGANISATION		
	Systematic, not ad hoc	Systematic, not ad hoc

Table 3: Components of population screening and the updated components of targeted screening extracted from the literature review.

* Underlined statements, identified during the literature review, are those incorporated into the updated components, having not been present in the working definition.

† Italicised statements, identified during the literature review, were considered to reflect a different approach to targeted screening and were not incorporated into the updated definition.

Much like population and targeted screening, the frequency of selective screening (*speed* component) was described as being dependent on factors including the duration of the detectable preclinical interval of the disease, severity of the disease, and accuracy and cost of the test.¹⁷ There was no information reported in the literature that could be used to populate the *initiation* or *organisation* components for selective screening.

Definitions of cascade screening also focused on groups with a high risk that pre-exists the offer of a test. However, the origin of this term was found to be specific to particular genetic diseases, such as cystic fibrosis or familial hypercholesterolaemia.^{20,21} The key *population* was described as a cluster of individuals with a genetic connection to a confirmed case: when relatives of confirmed cases are identified, they can be offered a test, a process that can be cascaded (repeated) for each identified case.^{20,21} Therefore, screening is largely based on family tree mapping and *initiation* of testing may be offered or actively sought, in contrast to the updated definition of targeted screening. Within the *organisation*

component, cascade screening was often described as an ad hoc process, perhaps reflecting the unsystematic nature of identification of the index case.^{20,21} Here, the definitions of cascade and targeted screening diverge.^{20,21} Both sources indicated that the test should be used to confirm genetic status, which, depending on disease, could indicate either risk refinement or diagnosis.^{20,21}

We identified more cross-component variation between the identified sources for case finding than for other screening terms. Different sources provided information that was at times consistent with population screening, targeted screening, or both. For example, several articles proposed that case finding could be used on either a selected or broad population,^{22,23} with Fell suggesting that this population would be apparently healthy.²⁴ Similarly to the WHO definition of targeted screening,¹³ some sources considered the relevant population to be individuals seeking healthcare for another condition.^{9,13,25} This feature is further reflected in the consistent finding across most sources that case finding

Component	Targeted Screening	Selective Screening	Cascade Screening	Case Finding
POPULATION				
Identification	Selected high-risk group ¹³ <ul style="list-style-type: none"> Use of risk factors or risk algorithms¹² Group for whom screening would provide maximal benefit^{*:12} 	Selected high-risk group ^{17,18} <ul style="list-style-type: none"> Enable detection of a substantial proportion cases^{17:18} 	Selected cluster of individuals ^{20,21}	Selected population or Broad population ^{22,23}
Characteristics	Defined by above-average risk ^{9,12} <ul style="list-style-type: none"> May consider individual- or community-level risk profile^{1,13} 	Defined by above-average risk ^{9,18} <ul style="list-style-type: none"> Risk factor need not be causally related to disease¹⁷ 	Direct connection to confirmed case or carrier ^{20,21} <ul style="list-style-type: none"> e.g. genetic connection 	Defined by particular characteristic or above-average risk ^{9,22,24}
Health status	Apparently healthy, asymptomatic, or unaware <ul style="list-style-type: none"> Early stage of disease^{*:12} 	Apparently healthy, asymptomatic, or unaware <ul style="list-style-type: none"> Subclinical disease¹⁷ 	Apparently healthy, asymptomatic, or unaware or aware of relation to confirmed case ^{20,21}	Apparently healthy, asymptomatic, or unaware ²⁴ or Suffering from a different condition ⁹
TEST				
Purpose	Risk refinement <ul style="list-style-type: none"> Reduce the number who need to be screened¹⁴ Save cost/resource compared to population screening¹² 	Risk refinement or diagnosis <ul style="list-style-type: none"> Yield large proportion of all cases¹⁸ Identify smallest subgroup of reference population that yields a substantial proportion of the total number of cases while concurrently keeping the false positive rate at its lowest possible level¹⁷ 	Risk refinement or diagnosis ^{20,21} <ul style="list-style-type: none"> Confirmation of carrier status 	Risk identification, not diagnosis ^{24,27} or Stratification or diagnosis ^{8,19,22}
Initiation	Offered, not sought, in community-based setting ¹² <ul style="list-style-type: none"> Could target those seeking health care for a different problem¹³ 	Not defined in literature	Offered or sought, in a community-based setting ^{20,21} <ul style="list-style-type: none"> Actively promoted 	Passive or Active (opportunistic) ¹³ <ul style="list-style-type: none"> Those seeking health care^{9,13,27}
Speed	Variable speed and frequency, may be ongoing	Variable speed and frequency, may be ongoing <ul style="list-style-type: none"> Dependent on factors including duration of detectable preclinical interval, accuracy of screening, severity of disease, and cost of screening¹⁷ 	Sporadic, repeat testing may not be required ^{20,21}	Sporadic, repeat testing may not be required ²⁴
ORGANISATION				
	Systematic, not ad hoc	Not defined in literature	Ad hoc ^{20,21} <ul style="list-style-type: none"> Based on family tree mapping 	Systematic or Ad hoc/opportunistic ^{9,13,22,23,26}

Table 4: Updated components of targeted screening compared with selective screening, cascade screening, and case finding extracted from the literature review.

* Underlined statements, identified during the literature review, are those incorporated into the updated components, having not been present in the working definition.

† Italicised statements, identified during the literature review, were considered to reflect a different approach to targeted screening and were not incorporated into the updated definition.

may be *organised* in either a systematic or ad hoc/opportunistic manner,^{9,13,22,23,26} and that *initiation* can be defined as either passive or active/opportunistic.¹³ By contrast, both population and, usually, targeted screening were described as systematic and offered, not sought. The definition of case finding was further confounded within the *purpose* component, as some sources contended that case finding refines risk but does not allow for the identification of a confirmed case,^{24,27} whilst others noted it can be used for diagnosis.^{8,19,22}

Box 1

Updated definition for targeted screening.

Our updated definition for targeted screening is: 'A systematic process in which testing, of variable speed and frequency, is offered in community-based settings for the purpose of risk refinement, to individuals in groups defined by above average risk but who are apparently healthy, asymptomatic or unaware with respect to the condition being screened for. The aim of this is to improve health outcomes. The updated components of this definition, alongside the literature extracted on targeted screening, are presented in both [Tables 3](#) and [4](#).

Discussion

We proposed a working definition of targeted screening ([Table 1](#)) structured around a framework of seven components: population (identification, characteristics, and health status), test (purpose, initiation, and speed), and organisation. The literature review broadly corroborated this working definition, bringing some additional nuance to the updated components of targeted screening ([Tables 3](#) and [4](#)), but not significantly altering our starting point, the working definition. We therefore consider that targeted screening can be adequately defined with reference to the narrow framework of seven components presented in [Table 1](#). The summary 'updated definition' ([Box 1](#)), developed using the literature, could equally well have been developed from [Table 1](#), the working definition. While this may not be the only possible definition, it has been found to be consistent with published discussions and is proposed as the organising definition for the work of the UK NSC.

Despite the limited volume of relevant publications, clear separation was identified between definitions of targeted and population screening. The most fundamental distinction was found to be the population eligible for screening, with targeted screening focusing on smaller groups with a heightened risk (prior to screening) and population screening focusing on large demographically defined populations with a generally low level of risk. Functionally, both types of screening are similar in their aim of detecting the condition early, or before its onset, in order to intervene to alter its course.

Further, regardless of screening type, it is necessary that there should be clarity about the condition to be detected, and evidence that it can be reliably identified or predicted by an agreed level of risk or marker, so that over-detection can be avoided.

Any distinction between targeted screening and the other screening terms was less obvious; in particular, selective screening was found to be conceptually identical to targeted screening. Cascade screening, despite being exclusively described within the context of genetic diseases, was also found to be conceptually similar to targeted screening. The inconsistency between definitions of case finding was highlighted by the framework approach. This inconsistency limited both comparison with targeted screening and the value of the term itself, compared with the other screening terms considered here. The close conceptual proximity of several of these terms means that the application of the term targeted screening could extend to disease areas in which selective and cascade screening have been applied. This may also be true for other terms which have not been considered directly in this review, but which aim to describe screening in high-risk populations. For example, the National Cancer Forum in Ireland defines "high risk" screening in ways that are differentiated from generalised or population screening and seem to be conceptually similar to targeted screening.²⁸ As such, the scope of operation of a new advisory body addressing targeted screening should be expected to be very broad, including genetic conditions, infectious diseases, and cancers.^{18,21,24}

A considerable strength of the study was the use of the framework of seven components, which enabled a robust comparison between definitions of terms. In most components, we identified sufficient supporting evidence from the literature to facilitate comparisons. However, the terms explored here were a pragmatic selection based on the experience of the authors. It is possible that exploring additional terms such as "high risk" screening may provide further insights. It is also possible that conducting searches in languages other than English may have yielded further results to corroborate these ideas, since only 20 relevant sources were identified. Additionally, there appeared to be little evidence to guide discussion on the effectiveness of different approaches to *organisation*. Therefore, the decision to opt for a systematic approach to programme organisation in the updated definition of targeted screening was based on the Committee's experience of ongoing screening programmes. The paucity of evidence on implementation research is well documented.^{7,29} Of the relevant sources we identified, the WHO definition proposed an opportunistic element to the practical implementation of targeted screening, and several sources proposed an ad hoc approach for cascade screening.^{13,20,21} It was determined that including these ideas in the updated definition of targeted screening

may result in a confusing functional overlap between the respective remits of the new advisory body and those of other bodies. Although nationally organised targeted screening programmes are resource intensive, they may ensure that the quality of targeted screening is consistent across the country, potentially helping to reduce screening inequalities. An example of this, though debatably a routine clinical management programme, may be the NHS diabetic eye screening programme. This programme offers annual screening for diabetic retinopathy to registered diabetics aged 12 years and over, uses a systematic approach and achieves a good level of compliance with nationally monitored key performance indicators.³⁰ Looking ahead, there is still a pressing need for further research into the identification of alternative organisational forms and implementation strategies to support the high-quality delivery of targeted and population screening programmes. This may help find alternatives to the current centralised approach and broaden the organisational options available for screening programmes as well as possibly reducing burden on services.

The proposed definition of targeted screening can be related to existing screening programmes. The NHS England pilot of targeted screening for lung cancer provides a practical example of targeted screening.³¹ The *population* is defined as individuals at increased risk of lung cancer due to a registered smoking history identified in the community via GP records and invited for screening. Once invited, patients undergo a risk assessment, which would function as the primary screening test.³¹ Those above a certain risk threshold would be eligible for a low dose computed tomography (LDCT) scan which functions to stratify those patients further. In this example, a person could either be referred for invasive diagnosis followed by treatment if positive, or scheduled for further LDCT scans at specific intervals, depending on their results.³¹ The applicability of every component of the updated definition of targeted screening to this pilot targeted screening programme provides a model for future reference. This example can be contrasted with a population screening approach. In the UK Lung Cancer Screening Trial all people aged 50–74 in two primary care trusts were approached, regardless of smoking history, with a questionnaire. A five-year risk of lung cancer was calculated and those in the high-risk group were contacted with a second questionnaire for further information.³² Since it is more likely that the complete population of 50–74 year olds will be identifiable than the complete population of ‘ever’ smokers, this is one pragmatic or functional difference between population and targeted screening. More broadly, a consequence of inviting all people within the relevant age range is that screening for lung cancer is made available to the total population, albeit at a particular point in their lives. In a targeted approach, this is not the case, since only inviting people registered as ‘ever’ smokers

means that screening is always confined within a sub-population. A consideration of many factors is crucial, including the balance of benefit and harm of a screening programme. The consequences of using age or behaviour to define a population suggests that there may be a qualitative, as well as a pragmatic, difference between the two types of screening.

The work presented here has important implications for how targeted and population screening programmes are conceptualised in the UK and throughout Europe. Policymakers can use the components of targeted screening identified in this review to develop their policy-making structures and processes. In the UK, the framework of seven components has already been useful for policymakers to bring together an expert advisory body and to inform discussion on the principles and processes for routing proposals for test-based interventions to the appropriate organisation in the UK healthcare system. A checklist enabling consistency in the characterisation of such interventions as targeted screening can be based on the framework considered here. This has the potential to make a practical contribution to efficient and transparent interagency working.

Contributors

Substantial contributions to study conception and design: AB, MM, FS, CV, AM, RS, JM; substantial contributions to analysis and interpretation of the data: AB, MM, FS, CV, AM, RS, JM; drafting the article or revising it critically for important intellectual content: AB, MM, FS, CV, AM, RS, JM; final approval of the version of the article to be published: AB, MM, FS, CV, AM, RS, JM. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. All authors had full access to the data and accept responsibility to submit for publication.

Useful websites

UK National Screening Committee. Screening in the UK: Making effective recommendations [Internet]. 2017 [cited 22 April 2021]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/649986/Screening_in_the_UK_making_effective_recommendation_s_2016_to_2017.pdf.

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Declaration of interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/doi_disclosure.pdf and declare: AB and MM have received grants from the UK NSC for the submitted work; FS, CV, AM, and JM are employed by the UK NSC; no other relationships or activities that could appear to have influenced the submitted work.

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Data sharing

Requests for access to data should be addressed to the corresponding author.

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