World Health Organization
REGIONAL OFFICE FOR Europe

Screening programmes: a short guide

Increase effectiveness, maximize benefits and minimize harm

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Abstract

The purpose of screening is to identify people in an apparently healthy population who are at higher risk of a health problem or a condition, so that an early treatment or intervention can be offered and thereby reduce the incidence and/or mortality of the health problem or condition within the population. There appears to be a growing trend in the WHO European Region towards more screening for noncommunicable diseases and health checks. However, in too many cases, a clear evidence base for effectiveness is missing. Policy-makers, health professionals and the public often seem unaware of the potential harm of screening, its cost and burden on the health system and the need for strong quality assurance. This guide is designed for policy-makers and public health leads involved in planning, designing and implementing screening programmes in the WHO European Region. It describes various aspects policy-makers should consider before starting, continuing or stopping a screening programme and the operational, monitoring and evaluation aspects of implementation. This guide forms part of WHO's efforts to increase the effectiveness of screening programmes within the Region, maximizing benefits and minimizing harm.

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This guide is an output of an initiative of the WHO Regional Office for Europe, strategically coordinated by Jill Farrington, WHO Regional Office for Europe, that aims to improve screening practice through the life-course to increase effectiveness, maximize benefits and minimize harm.

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Foreword

Evidence-based screening programmes have great potential to improve public health outcomes and advance universal health coverage. When organized effectively, they can prevent disease, reduce disability and cut mortality. Such programmes are at the core of public health services, bringing together the best of science and innovation for the public good.

In the WHO European Region, screening programmes are part of a long public health tradition, recognized and valued by citizens as an essential part of health care. Yet as screening programmes proliferate, the public, health professionals and policy-makers are giving less consideration to whether "doing more" actually means "doing better". Questions such as: How strong is the evidence base? What is the balance of benefit versus harm? Are there potential ethical dilemmas? Are commercial interests involved? Will this exacerbate inequities? often remain unanswered. Implementation requires a well-functioning health system to ensure that screening programmes are well organized and fit for purpose.

This short guide offers operational advice for designing and managing screening programmes. It seeks to support and equip policy-makers, public health professionals and clinicians with a clear overview of evidence, examples and factors to consider when providing high-quality screening programme services.

As we embark on implementing my vision for health across the Region, United Action for Better Health, which seeks to apply practical solutions to health challenges together, this publication serves as a timely and necessary resource. I encourage you to read on, using this guide to inform your initiatives, helping you to achieve the best possible health outcomes and leave no one behind.

Hans Henri P. Kluge
WHO Regional Director for Europe

Preface

This guide is an output of a cross-programmatic initiative of the WHO Regional Office for Europe aiming to improve screening practices through the life-course and thereby to increase effectiveness, maximize benefits and minimize harm. This is especially important since Member States requested it to better inform their decision-making and implementation of screening programmes.

This guide comes at an important time, since the WHO European Region is observing a growing trend towards more screening for noncommunicable diseases and health checks throughout the life-course. However, many of these screening programmes are not based on available scientific evidence, and policy-makers, health professionals and the public are often unaware of the potential harm of screening and its cost and burden. As Raffle & Gray wrote, "All screening programmes do harm. Some do good as well and, of these, some do more good than harm at reasonable cost." It is therefore important to identify what the benefits and harm are and assess the balance between the two before deciding to implement a screening programme. This guide aims to capture the challenges policy-makers may face and lays out the important steps that should be considered. It covers planning, designing, implementation, monitoring and evaluating screening programmes.

We hope that it will raise awareness of the complexities surrounding the implementation of screening programmes and how making the decision to start or stop a screening programme is not easy. It highlights the importance of evaluating the strength of the evidence supporting each screening programme and considering the capacity and resources that each country has available. The WHO Regional Office for Europe will continue to support Member States in strengthening the effectiveness of their screening practices, and we hope that this guide proves to be useful in this endeavour.

Jill Farrington
Coordinator, Division of Noncommunicable Diseases and Promoting Health through the Life-course, WHO Regional Office for Europe

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Introduction

This guide is designed for policy-makers involved in planning, designing and implementing screening programmes in the WHO European Region.

Why do a guide for the WHO European Region?

Countries in the WHO European Region have increased their focus on preventive measures in recent years. As part of this approach, there has been considerable interest in introducing new screening programmes for various conditions along the life-course. Although policy-makers, health professionals and the public may be aware of the evidence that well-run screening programmes for some conditions can improve public health, there is less understanding of the potential harm of screening and the costs of and requirements for implementing an effective screening programme.

This guide is designed to increase understanding of this topic. It is relevant to countries at different stages in developing and implementing screening programmes and should be equally applicable for a range of conditions that are commonly screened for, such as cancer and antenatal and neonatal conditions.

It is not intended to be comprehensive guidance on policy-making and implementation for screening programmes but rather indicates what should be thought about when considering whether screening should be used as a public health intervention to improve population health.

Other books and documents provide detailed guidance on the theory and practice of screening programmes and technical guidance for individual screening programmes. Readers who want further information are directed to these in Annex 2.

A note on terms

Screening is commonly used in everyday language and has a scientific meaning. The technical definitions of screening and its subtypes are debated. This publication defines the terms but recognizes that these might not always align with the definitions that appear in other texts.

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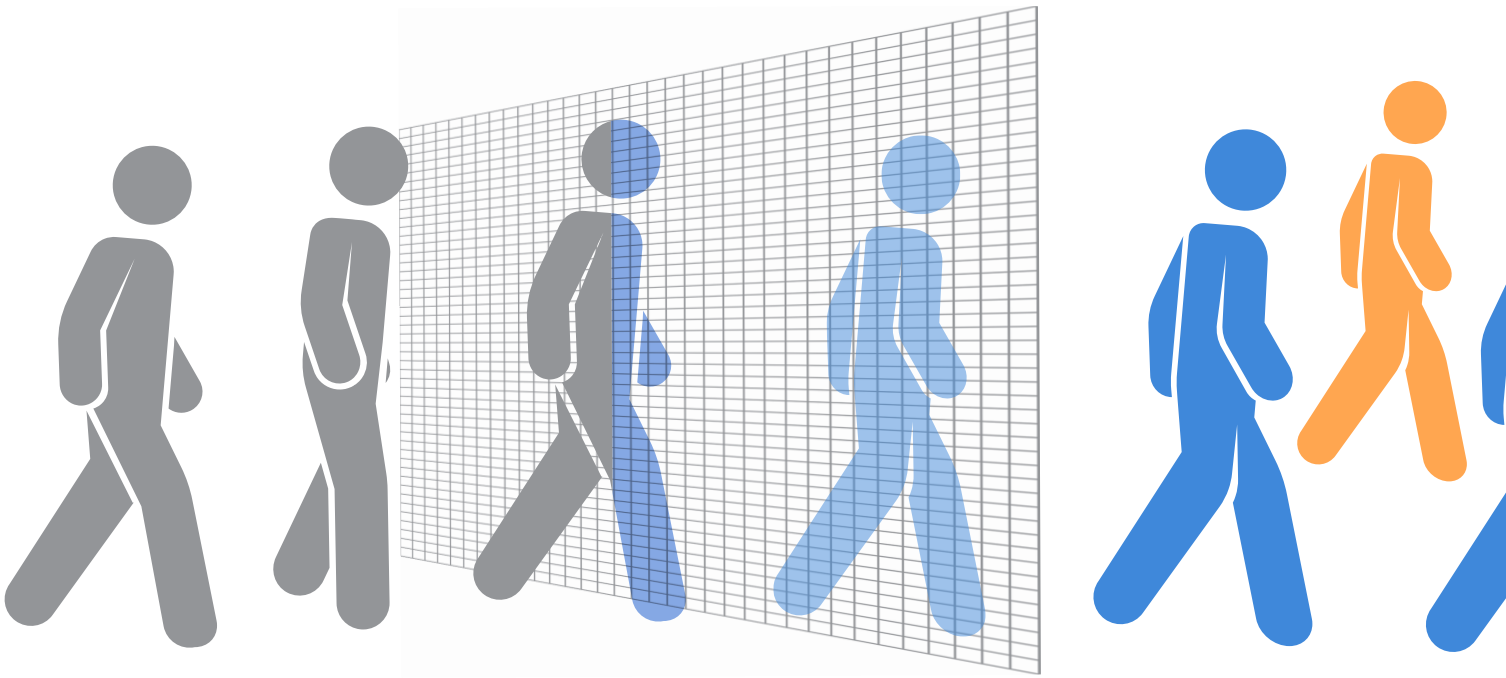
What is screening?

Screening is a rough sorting process. It operates like a sieve (Fig. 1), separating the people who probably do have the condition from those who probably do not. A screening test is never 100% accurate; it does not provide certainty but only a probability that a person is at risk (or risk-free) from the condition of interest.

Fig. 1. Screening as a sieve



Screened positive Screened negative

The purpose of screening is to identify people in an apparently healthy population who are at higher risk of a health problem or a condition, so that an early treatment or intervention can be offered. This, in turn, may lead to better health outcomes for some of the screened individuals *(1)*.

In some cases, such as antenatal screening, the purpose of screening is to give people information about an increased risk or condition to help them make an informed decision about their care or treatment.

Screening is not the same as early diagnosis. Screening invites people who do not have symptoms to undergo testing, whereas early diagnosis is intended to detect conditions as early as possible among people with symptoms.

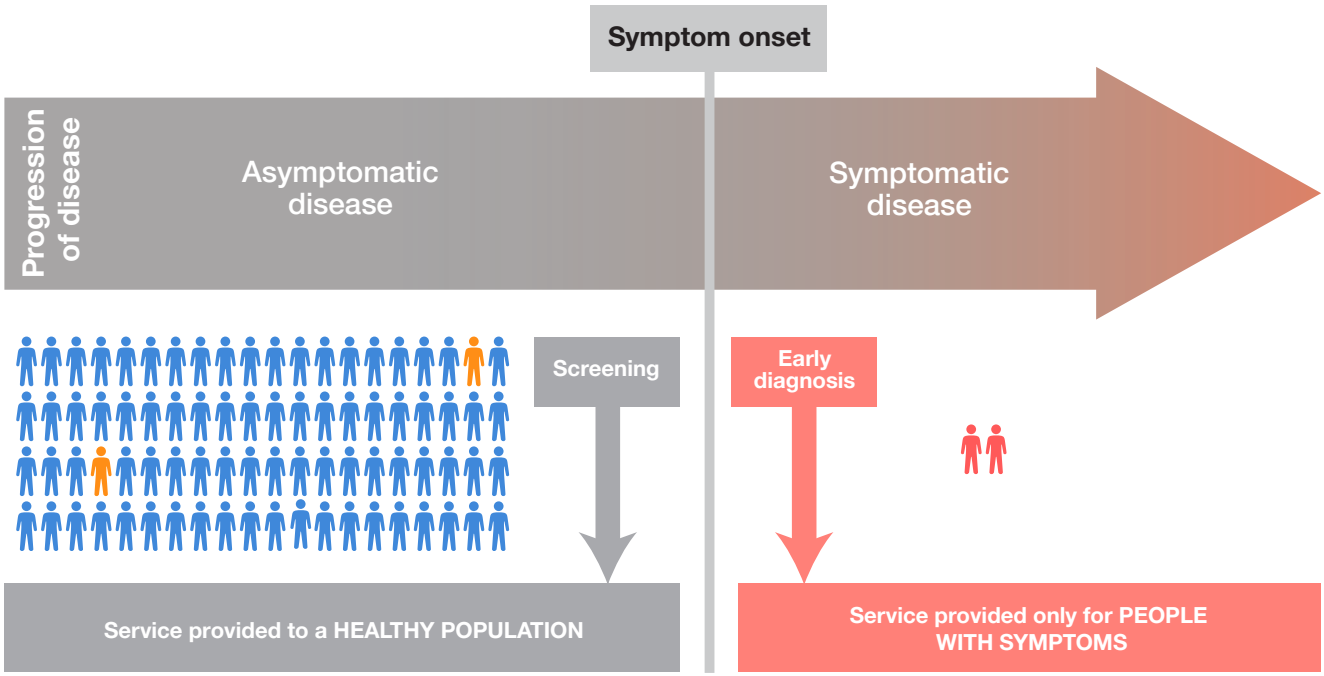
Fig. 2 illustrates an early diagnosis programme. The following are important features of this approach.

- An early diagnosis programme identifies and addresses barriers to diagnostic and treatment services in the population and among service providers. It builds service capacity and quality and establishes referral pathways. These are all essential preparatory steps before starting a screening programme.

- Screening programmes test large numbers of people. This requires considerable investment in equipment, personnel and information technology, which can strain a health system. In contrast, early diagnosis is a strategy focusing just on the people with symptoms, which is a much smaller number and therefore uses fewer resources.

- Where late diagnosis of cancer is a feature of a health system, screening is unlikely to be effective as an initial strategy since both coverage and service capacity will be inadequate to reduce mortality. In these circumstances, an early diagnosis programme is a more cost-effective strategy *(2)*.

Fig. 2. Distinguishing screening from early diagnosis in cancer according to symptom onset



Aims of screening programmes

Screening programmes exist for a range of conditions. The aim of each programme should be clearly stated and understood. This will influence the design of the programme and will be used to evaluate its effectiveness.

The aims of screening programmes include (Fig. 3):

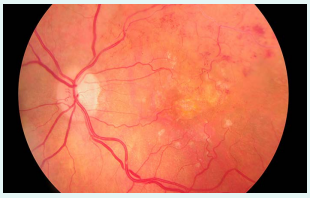
- to reduce mortality by early detection and early treatment of a condition;
- to reduce the incidence of a condition by identifying and treating its precursors;
- to reduce the severity of a condition by identifying people with the condition and offering effective treatment; and
- to increase choice by identifying conditions or risk factors at an early stage in a life-course when more options are available.

The aims of the screening programme should be stated in a public screening policy documented in law or an official regulation, decision or directive.

Fig. 3. Aims of screening programmes

The breast cancer screening programmes aims to reduce the ***mortality*** from breast cancer by the ***early detection*** and ***early treatment*** of asymptomatic cancers.

The cervical cancer screening programme aims to reduce the ***incidence*** and mortality of cervical cancer through the identification and treatment of precancerous stages of cervical cancer.



The diabetic retinopathy screening programme aims to ***reduce the severity of*** diabetic eye disease by early detection and treatment to prevent blindness.

One aim of antenatal screening is to detect conditions in the fetus and provide information to parents so that they can make an ***informed choice*** about whether to continue or end a pregnancy.

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Wilson & Jungner's principles of screening

The era of modern screening began in 1968 with a landmark publication by Wilson & Jungner for WHO *(3)*, which stated:

> ***Screening is the presumptive identification of unrecognized disease or defect by the application of tests, examinations, or other procedures which can be applied rapidly. Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment.***

Wilson & Jungner stated 10 principles that should be used to assess whether screening is an appropriate course of action to improve public health (Box 1)**.**

These principles laid the foundation for a scientific debate about the benefits, harm, costs and ethics of screening programmes.

Box 1. Wilson & Jungner's principles of screening

1. The condition should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic phase.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including a diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuous process and not a "once and for all" project.

Source: Wilson & Jungner *(3)*.

Screening programmes as pathways

A screening programme is not just a single test but rather a pathway that starts by identifying the people who are eligible for screening and stops when the outcomes are reported. Fig. 4 is a simplified pathway that shows the essential steps. A screening programme will only be effective if all parts of the screening pathway are provided.

Fig. 4. Steps in a simplified screening pathway

Understanding how screening tests work in practice

An ideal test would perfectly separate those who do have the condition from those who do not. However, tests in real life cannot do this. The values of the screening test always overlap for people who are healthy and people who have the condition.

Measuring test performance

This means some of the healthy people will receive an abnormal or positive test result (false positive) and some people with the condition will receive a normal or negative screening result (false negative).

Measurements of screening test performance indicate how good the test is at distinguishing the people who do have the condition (true positives) from those that do not have the condition (true negatives). Measures of test performance (Fig. 5) are:

- sensitivity: the ability of the screening test to identify people with the condition as positive; and

- specificity: the ability of the screening test to identify healthy people as negative;

The threshold value of a test is the value chosen as the cut-off between values determined to be screen positive (with the condition) and screen negative (without the condition). Altering the threshold value can change whether a screening test is more sensitive and less specific or less sensitive and more specific.

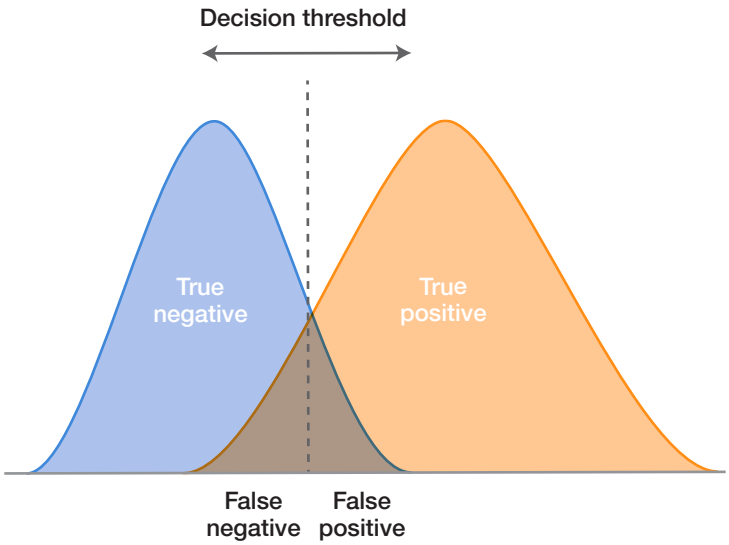
Some screening programmes choose a highly sensitive threshold for the screening test at the expense of lower specificity. This means that there will be very few false negatives but more false positives. In these circumstances, all the positive results are then investigated with a further test with high specificity to exclude the false positives *(1)*.

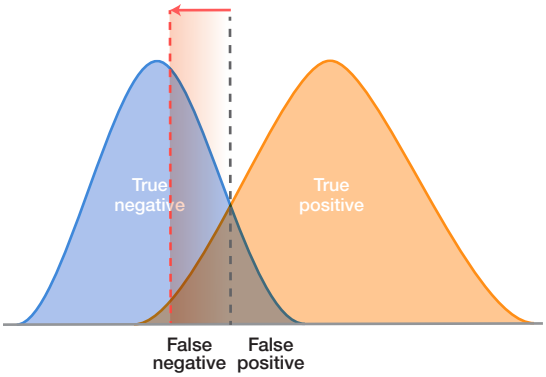
Sensitivity and specificity indicate how well a test performs. Two other measures used in screening indicate the likelihood of having the condition with an abnormal result or not having the condition when the result is normal.

Positive predictive value is the likelihood that the screening participant has the condition that screening targets when the test is positive. Negative predictive value is the likelihood that the screening participant does not have the condition that screening targets (the person is healthy) when the test is negative.

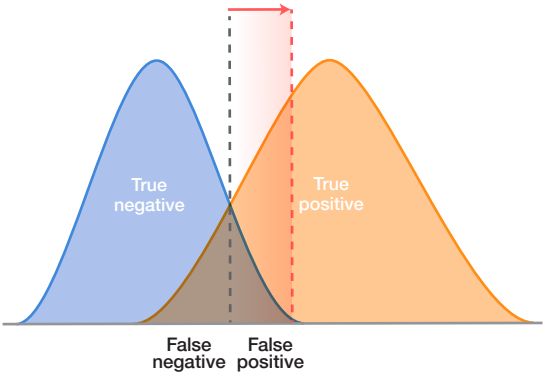
Both the positive predictive value and the negative predictive value of a test depend on the prevalence of the condition (how common a condition is in the screened population) and the distribution of the severity of the condition in the population receiving screening (Fig. 6). Using the same type of screening test in different populations will therefore give different results.

Fig. 5. Measuring the performance of screening tests





To increase the sensitivity, shift the threshold to the left. However, this will increase the false positives and reduce the specificity.



To increase the specificity, shift the threshold to the right. However, this will increase the false negatives and reduce the sensitivity.

Test result	Has the condition (cases)	Does not have the condition (healthy)
Positive	True positive	False positive
Negative	False negative	True negative

These values can be used to calculate:

Sensitivity = $\frac{\text{true positive}}{\text{true positive + false negative}}$

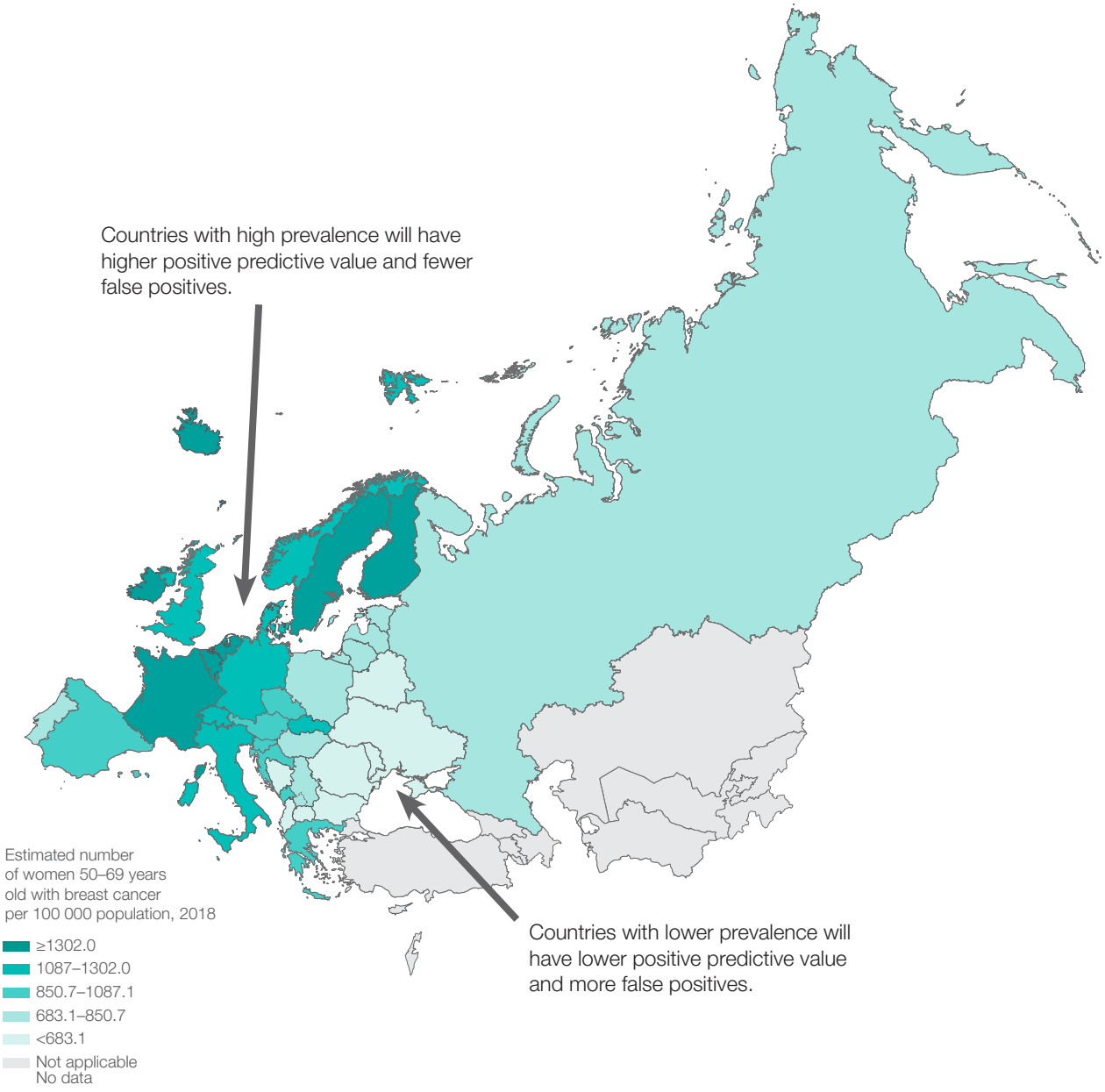
Specificity = $\frac{\text{true negative}}{\text{true negative + false positive}}$

Positive predictive value = $\frac{\text{true positive}}{\text{true positive + false positive}}$

Negative predictive value = $\frac{\text{true negative}}{\text{true negative + false negative}}$

Fig. 6. How prevalence affects the positive predictive value

The positive predictive value and the numbers of false positives vary according to the prevalence of the disease in each country (the sensitivity and specificity remain the same).



In this case, the positive predictive value is the proportion of women with a positive mammogram who have breast cancer.

Source: Global Cancer Observatory [online database].

When a condition is less common in a country (low prevalence), the positive predictive value is lower. This means that there will be more false positives than in a country with a higher prevalence of the condition, even though the sensitivity and specificity are the same.

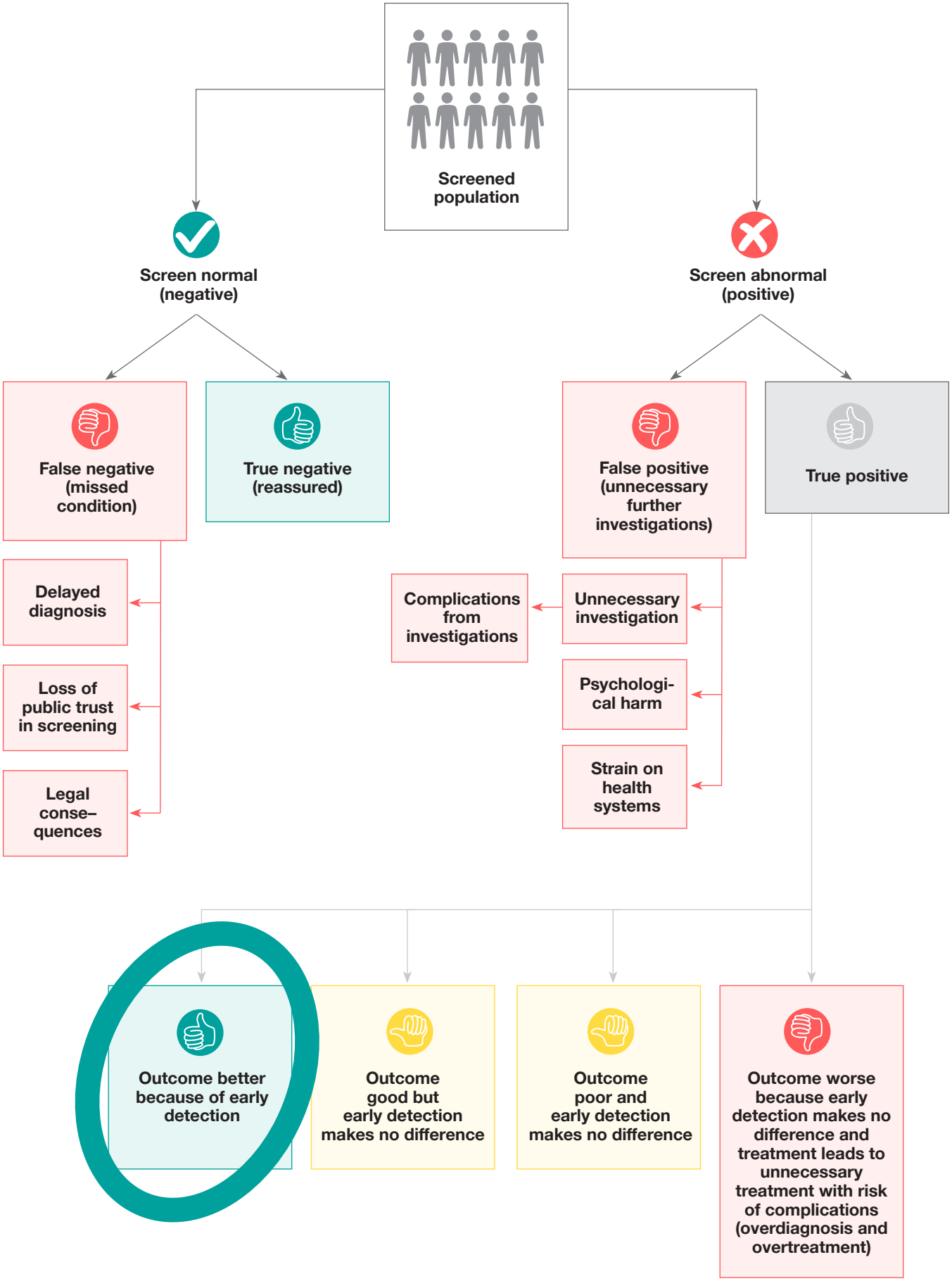
Measuring outcomes from screening programmes

In real life, screening programmes may involve multiple tests and follow-up investigations. Different test thresholds might be used according to a person's age and/or sex. This may lead to a complex pathway with multiple outcomes.

Working through all the potential outcomes is an important step in developing a reasonable estimate of the true effect of a screening programme. It is important to consider all the potential outcomes of screening, both benefits and harm, along the entire screening pathway (Fig. 7) *(1)*.

Even when a person gets a true positive result, this does not always mean that early detection will improve their outcome. For some people, early detection will not make any difference in improving the outcome from treatment. In some cases, they can be harmed because the true positive is in fact overdiagnosis. The next section examines these situations in more detail.

Fig. 7. Possible outcomes from a screening programme



Benefits and harm of screening

Benefits

An effective screening programme can deliver significant public health benefits.

Examples of benefits include:

- reduction in the incidence and mortality of cervical cancer;
- early intervention for newborns with hearing loss to support speech and language development; and
- providing parents with information in the antenatal period so they can make an informed choice about whether they wish to continue with a pregnancy if they know that the fetus has a higher risk of having a serious condition.

Not only individuals may benefit but also the family and society. Economic analysis has shown how antenatal and neonatal screening can save society the costs of lifetime support into adulthood by preventing long-term disabilities *(4)*.

Detecting the condition at an early stage provides other benefits, including using a less-toxic treatment or intervention, such as reducing the use of chemotherapy for people with breast cancer.

Lastly, introducing a new screening programme can drive changes within a health system that have wider benefits. For example, introducing technical quality control for mammography benefits all women using the service or improving the care pathway and quality of surgery for colorectal screening programmes can improve services overall.

Maximizing the benefits of screening programmes

Although good-quality evidence may show that screening can deliver benefits, these will only be delivered if the programme is run effectively. This is discussed further on. Here are two important ways to maximize the benefits of screening programmes.

- The most important step is to make sure the screening programme is operating high-quality services through a quality assurance system.
- The technology or test used should be appropriate for a country's health system. This may not be the same test in each country.

Harm

Screening can also lead to harm. Three characteristics of screening programmes, when acting together, mean that harm is more significant than often appreciated.

- Because most people who are screened do not have the condition, more people can be exposed to the harm of screening than may be able to benefit from it.

- Because screening tests are not 100% sensitive or specific, there will always be false positives and negatives.

- Earlier detection of conditions can lead to overdiagnosis: detecting conditions that would never cause that individual harm in their lifetime *(5)*.

Because the benefits are intended and the harm is unintended, professionals and the public may have less information or understanding of the harm of screening.

Understanding harm

Harm from screening is unintended and inevitable. It is the totality of all the possible adverse consequences of the entire screening pathway *(6).* This can result from unwanted effects or complications of the screening test, further investigations or the treatment. It can also arise because of how the screening programme affects the health system.

Some types of harm may occur multiple times: for example, anxiety before and after testing and during investigations or treatments *(7,8)*. Harm may be underreported in clinical trials compared with the actual occurrence in real-world screening programmes *(9)*.

Consequences of false-positive results

All screen-positive (abnormal) results require further investigation to distinguish false-positive from true-positive results. People who have false-positive results are therefore subjected to unnecessary investigations and their potential complications.

Complications of investigations that are carried out following a screen-positive result can be devastating, such as a miscarriage after amniocentesis for a screen-positive test for Down's syndrome or perforation of the bowel after a colonoscopy *(10,11)*.

A false-positive result can also lead to psychosocial effects, such as anxiety, sadness, sleep problems or frustration, which persist for some people for up to three years and possibly longer *(7,12,13)*.

A screening programme with many false positives can strain the health system because they need to be investigated and use already stretched diagnostic services such as endoscopy. This, in turn, can make people with symptoms wait longer to be treated by general services.

Consequences of false-negative results

False-negative (normal) results always occur in screening programmes, because no programme is 100% sensitive.

People who receive a negative test result may ignore important symptoms, resulting in delayed diagnosis *(14).* Some people may file lawsuits because they received a false-negative screening result and potentially had their diagnosis

delayed. Legal claims as a result of false-negative results can be very costly for a screening programme *(15)*.

False-negative screening results may also lead to the public having decreased trust and confidence in the screening programme *(14).*

Overdiagnosis

Overdiagnosis identifies a condition or problem that would never cause a person harm during their lifetime *(16)*.

Box 2 describes the reasons why overdiagnosis may occur *(5)*.

Box 2. Reasons for overdiagnosis

Many conditions resolve spontaneously, and some do not progress at all or they progress too slowly to cause symptoms.

There is always a competing risk of dying from something other than the condition detected by screening. The higher the risk of dying from something other than the condition screened for, the higher the risk that the screening-detected condition is overdiagnosed.

High-resolution technologies such as sensitive biomarkers or imaging technologies, which can detect very small occurrences of a condition, lower the detection threshold of the screening tests, leading to detection of smaller, and often more benign, instances of a condition.

Overdiagnosis is recognized as a problem in cancer screening (see the section on monitoring and evaluation) but quantifying its exact impact is often difficult *(17)*. This is because the methods for calculating overdiagnosis are complex and can depend on contextual factors. This means that countries often quote different values or ranges for overdiagnosis.

For example, in the United Kingdom, estimates indicate that, for every 1000 women 50–70 years old invited to screening for breast cancer every three years, 4 women will have their life saved from breast cancer but 13 women will be diagnosed with cancer that would not have harmed them *(18)*. In Belgium, a similar approach estimated that for every 1000 women 50–59 years screened every two years, 3 women will have their life saved from breast cancer and 3 women will be overdiagnosed; for those aged 60–69 years, the figures are 4 and 4 *(19)*.

These estimates indicate the amount of overdiagnosis in a screened population. However, at the individual level, identifying who has been overdiagnosed and who was correctly diagnosed with a condition that, if untreated, would have led to a poorer outcome is not possible. This means that, once a screening programme starts, everyone who is found to have a condition such as cancer has to be offered treatment – even though some of these people would not have needed treatment *(16)*.

Overdiagnosis is a complex topic to explain to people who are considering whether to be screened. Infographics can really help (see the section on information and communication).

Overtreatment

Overtreatment means that people receive more extensive or invasive treatment than is required to improve health outcomes. In screening, overtreatment can occur alongside overdiagnosis. For example, in countries with prostate screening programmes, men are subject to surgery and radiotherapy for prostate cancer with concomitant problems such as impotence and urinary incontinence in circumstances in which the cancer may not have caused them any harm in their lifetime *(20)*. Overtreatment can also occur because benign conditions found as part of screening are treated unnecessarily, such as surgical removal of small benign breast lumps.

Use of health resources

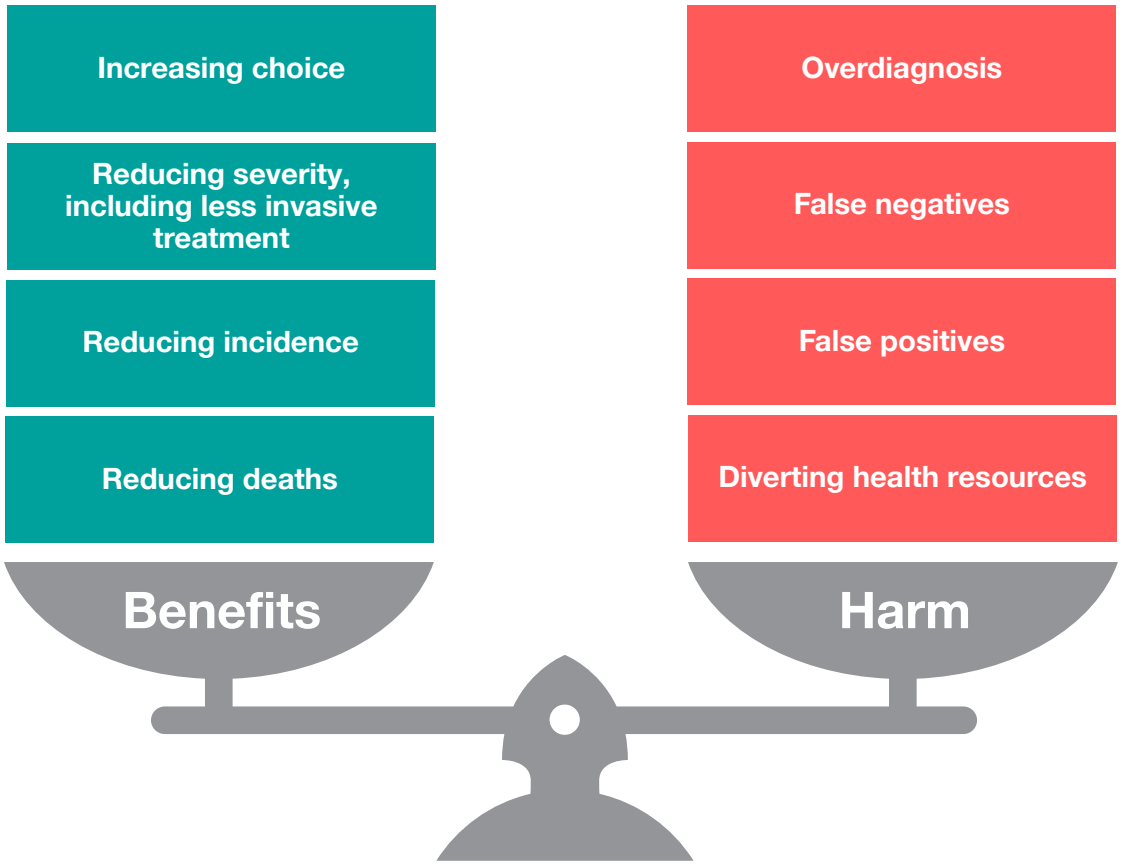
Screening programmes usually require considerable investment in equipment, personnel and information technology. This can strain a health system, resulting in reallocation of resources (such as funding, time or personnel) to the screening programme and away from symptomatic care, delaying care for people with symptoms and potentially leading to greater inequalities.

Balancing benefits and harm

The challenge for policy-makers is to consider all the potential benefits and harm and decide in the context of their health system and their values or ethics whether the screening programme is expected to produce benefits at a reasonable cost.

This analysis is not easy, and fig. 8 considers some of the challenges.

Fig. 8. Balancing benefits and harm



How are benefits and harm compared?

The benefits and harm of screening are difficult to compare because they differ in nature and are measured and valued differently. For example, comparing the mortality reduction (benefit) with the number of people with false-positive results or overdiagnosed people is difficult *(21)*.

In comparing, the ability to benefit versus the risk of harm should be presented in the same way. For example, if a person's ability to benefit from colorectal cancer screening is measured across their lifetime after being screened 10 times, then this must be compared to their risk of harm when they have been screened 10 times. This means that the risk of harm at each screening, including complications, anxiety etc. should be added together to fairly compare harm versus benefits.

Valuing benefits and harm is also affected by such things as the number of years an individual can benefit from screening. For example, neonatal screening for phenylketonuria can lead to a lifetime benefit through adulthood, whereas harm such as anxiety from a false positive may be short-lived.

Who benefits?

Evidence indicates that people with high socioeconomic status and a low risk of having severe conditions tend to participate more in screening than do socioeconomically deprived people, who have a higher risk of disease *(22–24)*. This can lead to increasing health inequalities.

Does the context affect the balance between harm and benefits?

Each screening programme has different benefits and harm, and the balance between these depends on the screening technology, the quality of delivery of the screening services and other contextual factors such as the health of the invited population and the prevalence of the condition in the screened population.

This means that a randomized control trial conducted in one country that is considered to demonstrate an overall benefit or harm for the screened population cannot necessarily be replicated when the screening programme is transposed to another country or setting.

Ethics of screening

Policy-makers may use different ethical frameworks to help them decide whether to proceed with a screening programme.

Using a utilitarian position, policy-makers could justify introducing a screening programme when its benefits outweigh its harm at a reasonable cost *(25)*.

Alternatively, a deontological perspective would state that some things cannot be morally justified regardless of their outcome; that is, harm to healthy people is not justified even though it might benefit others.

A principlism perspective uses a set of principles to guide decision-making *(26).* A WHO consultation examining the ethics of individual health assessments presented a pragmatic set of values for consideration *(27)*.

Respect for dignity and autonomy. Autonomy is the capacity to make an informed and uncoerced decision.

Non-maleficence and beneficence. Non-maleficence means doing no harm to people; beneficence aims to do good for people *(28)*.

Justice and equity. In health care, justice concerns fair allocation of resources and that resources are allocated proportionate to the need.

Prudence and precaution. The precautionary principle requires foresight, planning for the potential outcomes of screening and making wise judgements based on these future concerns.

Honesty and transparency. This requires clear and transparent communication, thus promoting accountability.

Box 3. Occupational health checks

Occupational health checks or assessments describe a variety of employee health screenings required by employers. In principle, the primary purpose is to prevent work-related injuries and disease and may be used, for example, before employment to determine whether individual people are fit to perform their job without risk to themselves or others.

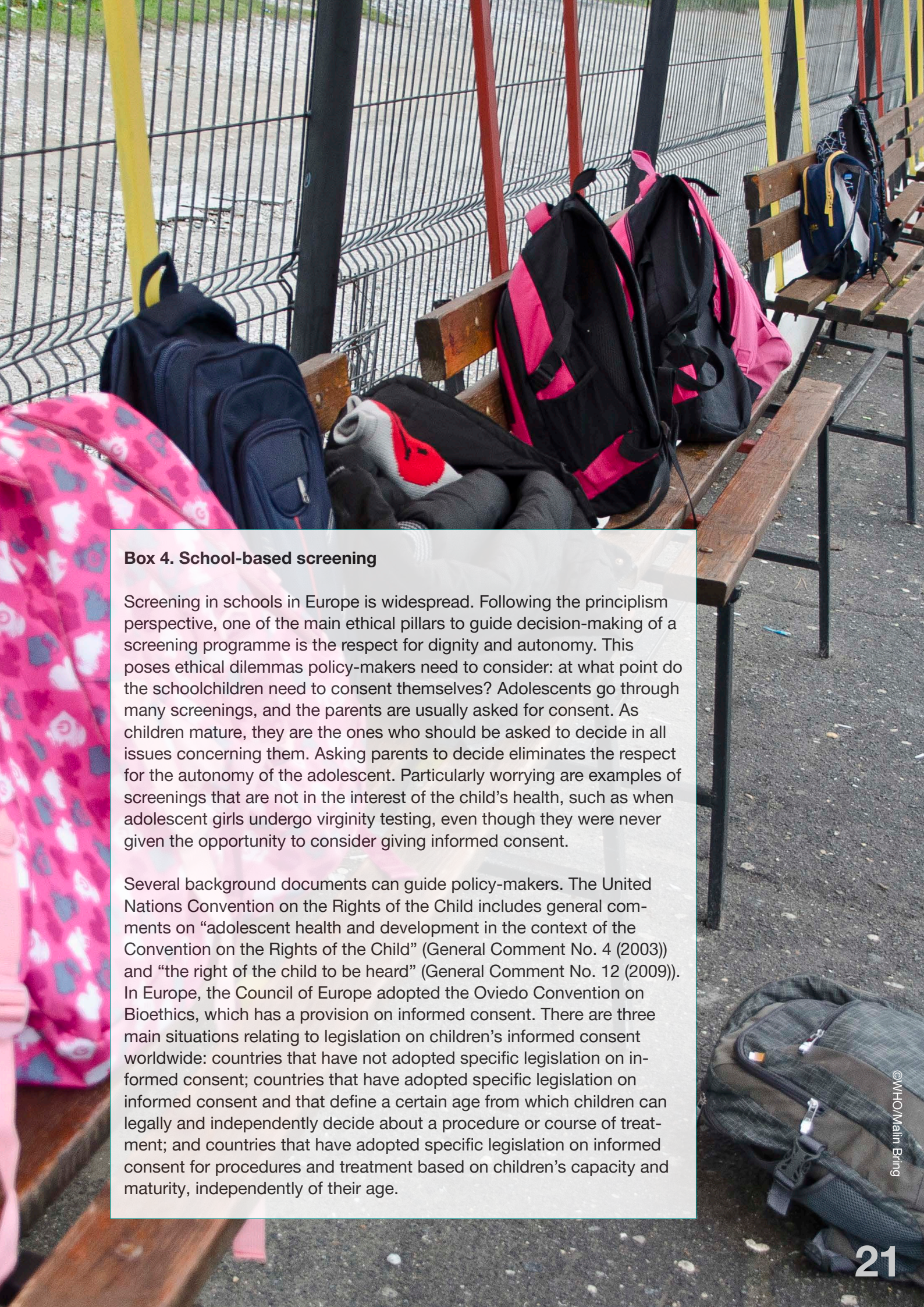
In general, evidence is lacking on the effectiveness of pre-employment health screening in preventing health-related occupational risks.[a] Further, the medical screening may include physical examinations or tests that do not appear to have direct relevance. For example, hypertension screening is commonly included in such screening, but standardized criteria to determine fitness for work are lacking.

Health assessments should only be included when appropriate to the task environment and relevant to fulfilling of the essential job functions. Because the objective of this type of individual screening differs from traditional screening, there are unique challenges. For example, individuals can be put under pressure to undergo screening either to obtain or retain a certain job; this challenges the ethical principle about people's autonomy. Further, the harm and benefits to health need to be balanced: a person may be refused a job because of health issues discovered at screening, but being unemployed can also affect health.

[a]Pachman J. Evidence base for pre-employment medical screening. Bull World Health Organ. 2009;87:529–34.
Schaafsma FG, Mahmud N, Reneman MF, Fassier JB, Jungbauer FHW. Pre-employment examinations for preventing injury, disease and sick leave in workers. Cochrane Database Syst Rev. 2016(1):CD008881.

However, at times these ethical principles can be in conflict. For example, steps to increase the participation rate may threaten the autonomy of individuals to make an informed decision *(29)*.

Each country has its own set of values, which may influence how it balances these ethics and the anticipated harm and benefits from a given screening programme.



Box 4. School-based screening

Screening in schools in Europe is widespread. Following the principlism perspective, one of the main ethical pillars to guide decision-making of a screening programme is the respect for dignity and autonomy. This poses ethical dilemmas policy-makers need to consider: at what point do the schoolchildren need to consent themselves? Adolescents go through many screenings, and the parents are usually asked for consent. As children mature, they are the ones who should be asked to decide in all issues concerning them. Asking parents to decide eliminates the respect for the autonomy of the adolescent. Particularly worrying are examples of screenings that are not in the interest of the child's health, such as when adolescent girls undergo virginity testing, even though they were never given the opportunity to consider giving informed consent.

Several background documents can guide policy-makers. The United Nations Convention on the Rights of the Child includes general comments on "adolescent health and development in the context of the Convention on the Rights of the Child" (General Comment No. 4 (2003)) and "the right of the child to be heard" (General Comment No. 12 (2009)). In Europe, the Council of Europe adopted the Oviedo Convention on Bioethics, which has a provision on informed consent. There are three main situations relating to legislation on children's informed consent worldwide: countries that have not adopted specific legislation on informed consent; countries that have adopted specific legislation on informed consent and that define a certain age from which children can legally and independently decide about a procedure or course of treatment; and countries that have adopted specific legislation on informed consent for procedures and treatment based on children's capacity and maturity, independently of their age.

Deciding whether to start or stop a screening programme

A decision to start or stop a screening programme is complex. It requires carefully considering the current circumstances within a country, evidence of effectiveness, feasibility, stakeholder support, political considerations and the values that inform a country's priorities for health care (Fig. 9).

Leading the process

The decision-making process should start by establishing an appropriate group or committee to lead the process. The group should report to the appropriate national body such as the health ministry and should have representatives who can understand the complexity of the information and command the support of key stakeholders. The processes involved in starting or stopping a programme are similar in principle, but in practice they can be very different.

Recognizing different interests

Many stakeholders may have an interest in screening programmes, such as people with the condition, professional associations, health-care providers or manufacturers of screening equipment. When plans are being made to start or stop a screening programme, identifying the stakeholders, considering their interests and influence and deciding how best to involve and communicate with them are helpful. This is particularly important before deciding to stop or make a major change in a screening programme, since it can meet considerable resistance.

Is screening the answer?

Situational analysis should be undertaken before assuming that screening is the right approach to solve a health problem (Fig. 10).

The analysis assesses the status of the health system, the role screening might play and whether screening is the right course of action compared with alternative strategies such as an early diagnosis programme.

If screening may be considered the right course of action, the evidence related to screening must be examined in detail.

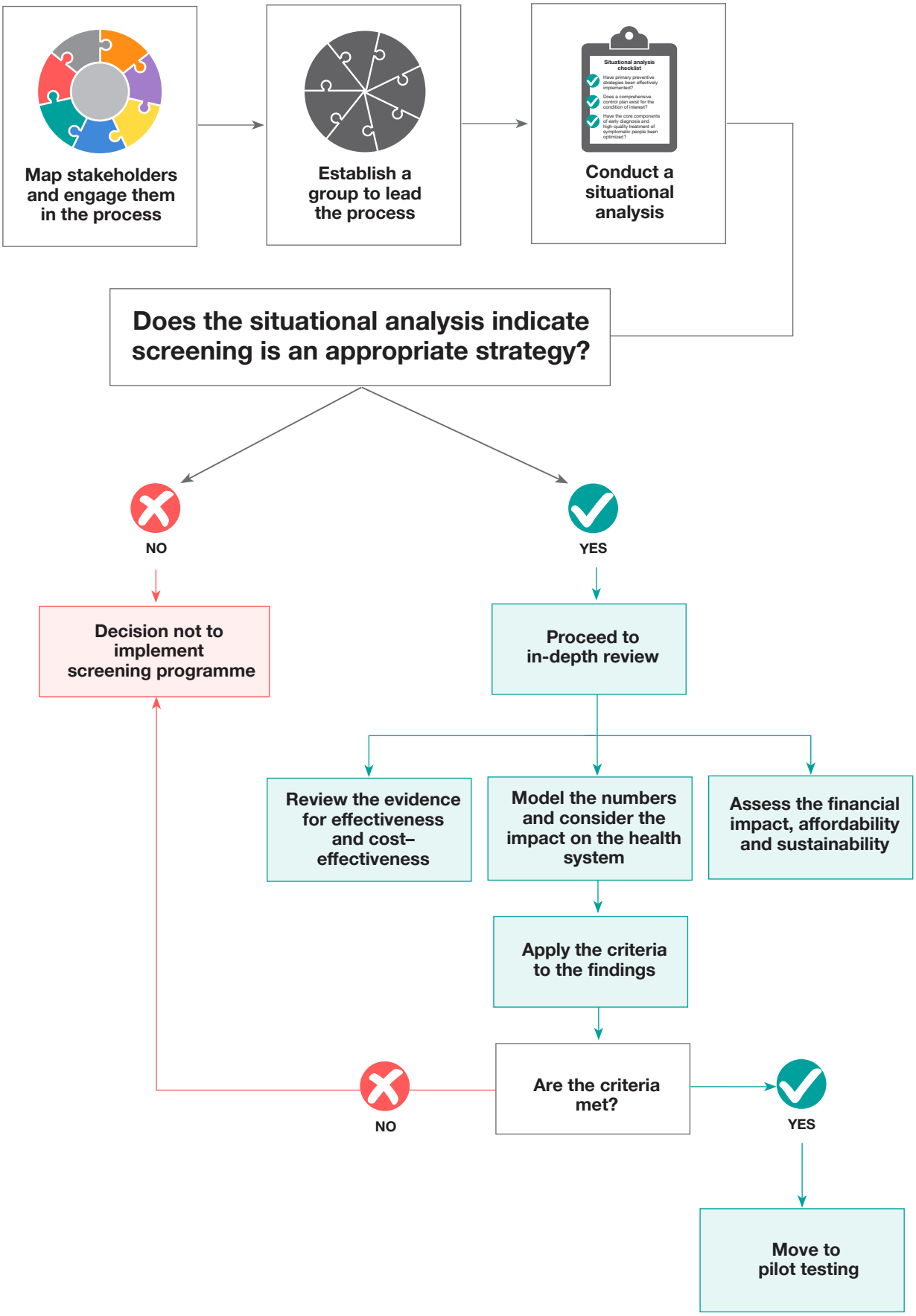
What does the evidence say?

As a rule of thumb, screening programmes in real life often do not deliver the anticipated benefits found in clinical trials.

In examining evidence from clinical trials for both effectiveness and cost–effectiveness, consider using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework *(30)*. With this framework, health authorities can assess the overall quality of the evidence as being high, moderate, low or very low (Fig. 11).

GRADE also supports an evidence-to-decision framework that considers the context in which a decision is made before making a recommendation. Fig. 11 illustrates some of these factors.

Fig. 9. Steps in deciding whether to start or stop a screening programme



Assessing the evidence in this way can help to assess how certain it is that the study results can be applied in a real-life setting. Clinical studies often use the best available diagnostic equipment and highly skilled personnel working under strict protocols for whom to invite and how to treat. Transferring the results from a clinical study to the real-life setting may not produce the same results.

Fig. 10. Situational checklist

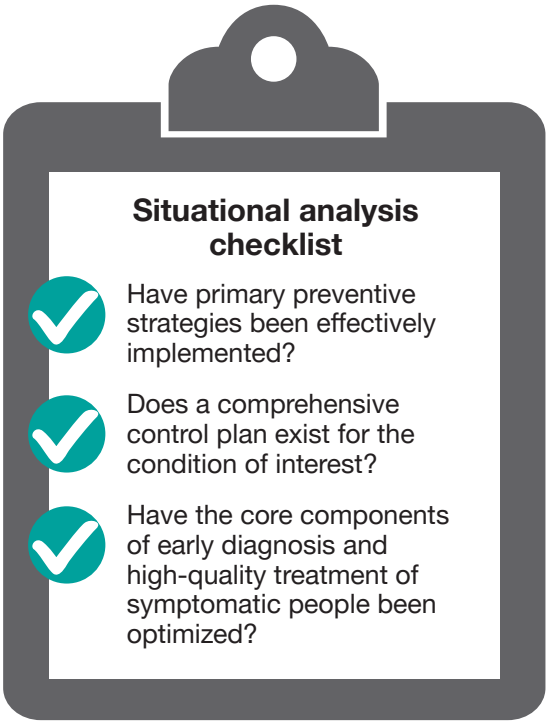
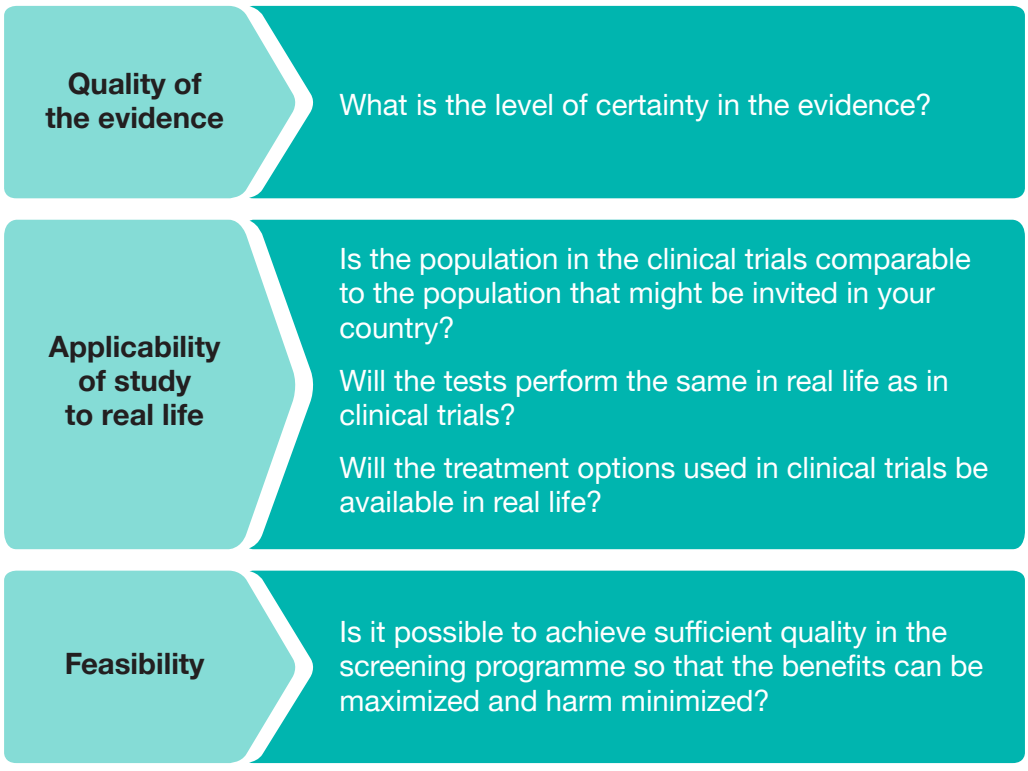


Fig. 11. Using evidence to develop recommendations for screening policy



Modelling numbers and costs

An important step in deciding whether to start a screening programme is to model the number of people who move through the pathway and their outcomes. This should be done using information that is country specific: for example, using the prevalence of the condition in that country.

This information will inform a costing exercise that will be crucial in understanding whether screening will be both cost-effective and affordable.

Using criteria to guide decision-making

Wilson & Jungner's screening principles can preliminarily filter whether a screening programme might end up being effective. Screening criteria serve as a much finer second filter to assess the screening programmes that might be effective within a given country and health system.

The principles are useful in considering all the findings discussed above alongside the values and priorities for the national health of a population.

The United Kingdom provides examples of rigorous sets of screening criteria, with a list of 20 criteria to be considered for screening, as does Sweden, which has a set of 15 criteria (Box 5) *(31)*.

Box 5. Decision pathway for screening in Sweden

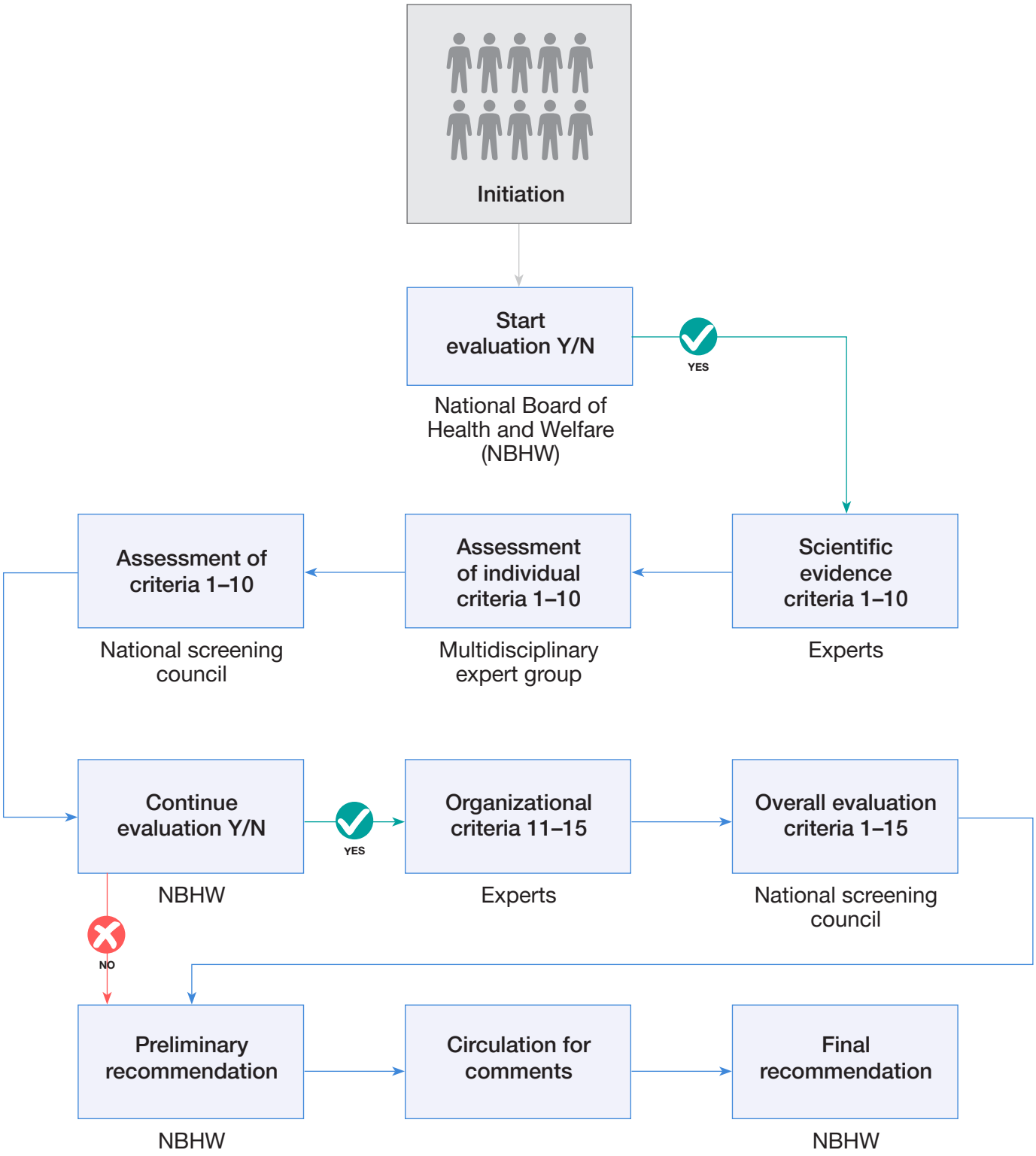
Sweden has implemented a system to support decision-making for screening. The screening programme's evaluation process has three key components: 15 assessment criteria, a defined organization and a systematic work process.

- **Criteria**. The assessment criteria originate from the WHO 10 principles for screening programmes. These have been adapted and expanded to 15 criteria to comply with Sweden's health system. Ten of the criteria demonstrate the scientific evidence for the programme, ethical aspects and the balance between benefits and harm. Five assessment criteria address issues such as organization, resource needs, feasibility, cost–effectiveness information for the participants and possibilities for follow-up, such as the national registries.

- **Organization**. For each screening assessment, a multidisciplinary expert group and patient representatives are recruited to assess whether each scientific assessment criterion is met. The expert group represents the entire care pathway system and the geographical areas of Sweden. In addition, the National Screening Council performs an overall assessment of each programme. The National Screening Council is an advisory board to the National Board of Health and Welfare and comprises politicians from the six health care regions, government agency representatives and experts in screening, medicine and nursing. The Director General of the National Board of Health and Welfare makes the final and formal decision on a recommendation.

- **Work process**. Each evaluation follows the systematic process and takes approximately two years to complete.

Fig. 12. Decision pathway for screening in Sweden



As circumstances change the criteria need to be adapted. In 2008, Andermann et al. warned that the technological advances in genetic screening were outpacing the ability of experts and policy-makers to adequately assess whether these proposed screening programmes should be implemented *(32)*. This work led to the development of a decision-support guide for policy-making about genetic screening *(33)*.

Pilot testing

Once a decision is made in principle that a screening programme is the right intervention, the programme should be tested in practice to determine whether it will deliver the anticipated benefits.

Pilot projects aim to test the feasibility, resource implications and optimal delivery of a large-scale screening programme. Guidance exists on how to set up pilot studies as cluster-randomized pragmatic trials to provide the best evidence on how screening performs under varying circumstances.

Pilot trials should be based on the best evidence demonstrated in clinical trials. These should inform pilot set-up, including which test to use, the age of the participants and the interval of screening.

Pilot projects can be used to test real-life cost–effectiveness and efficiency. Measuring uptake and the numbers of false positives in a pilot project will help authorities in understanding whether a screening programme will deliver the anticipated benefits in their country setting. To be useful, the pilot project should be representative of the average national conditions in which the large-scale screening programme will function.

Pilot testing can be an important preparatory step to scaling up the screening programme to a regional or national level (Box 6).

Box 6. Piloting breast cancer screening in Belarus

Belarus launched a project in 2016 to introduce breast screening, starting with a pilot project. Radiologists who were used to working with people with symptoms were anxious not to miss any cases of cancer and sent about 20% of women through for further assessment. The pilot project therefore recorded a high recall-to-assessment ratio.

The project team realized that this was not going to be sustainable in the future. Working with an experienced breast screening radiologist from the United Kingdom, they audited their mammograms. This showed that the sensitivity was good but the specificity was suboptimal, with lots of false positives. As a result, as they roll out the programme, they are focusing on training and introducing double-reading to reduce the number of false positives being referred for further investigation.

Designing effective screening programmes

Types of screening

How a screening programme is designed can profoundly influence its effectiveness and cost–effectiveness. Understanding how screening tests are offered to a population is therefore crucial.

Unfortunately, the terms used in this field are not consistent, so rather than focus on definitions, Table 1 describes some of the ways screening is carried out and considers their consequences.

For a programme to be effective and reduce incidence and/or mortality, it needs to fulfil the requirements of all the green cells. A screening programme operated this way is often called an organized screening programme or a population screening programme.

Policy-makers can use this table to understand the implications of offering screening tests outside an organized screening programme: that is, in one of the ways described in the blue cells.

For example, the effect of offering a screening test that is not part of a pathway is illustrated in row 1a.

Although there may be a national policy in support of establishing a screening programme, in practice, it may be delivered in an unorganized way within the country. For example, offers of screening are ad hoc (row 3a), there are few protocols and guidelines (row 4a) and standards governing quality are lacking (row 5a).

The effects of this type of design show that this kind of approach is likely to be ineffective in reducing incidence or mortality.

So far in this guide we have considered the circumstances where a screening programme is designed to detect one condition. The next section considers the more complex situation in which more than one screening test is performed simultaneously to detect multiple conditions as part of a bundle of tests.

Multiple screening tests carried out at the same time

There are many examples of screening tests being carried out at the same time:

- newborn physical examination checks;
- newborn bloodspot testing for metabolic or hormonal diseases;
- childhood health checks;
- as part of school health checks; and
- as part of adult health checks or periodic health examination.

Table 1. Dimensions of screening

Dimension	Options	What can happen?
1 Is the test carried out in isolation or is the test part of a pathway of care?	1a The test is carried out in isolation and not linked to a well-defined pathway of care	No guarantee that effective diagnosis and treatment will follow abnormal results (unethical)
	1b The screening test is part of a pathway of care	Makes sure that people with a screen-positive (abnormal) result get referred and treated
2 Who is eligible for screening?	2a Anyone who requests screening	Potential to harm individuals who cannot benefit from screening (wastes resources)
	2b The eligible population is defined according to evidence, based on the balance of benefits versus harm	For the eligible population, the balance favours benefits rather than harm
3 How is the test offered?	3a Offers of screening are ad hoc and rely on individuals to take up the offer or refer themselves	Participation is often poor, and those that use the services tend to have higher socioeconomic status
	3b Systematically, based on a register of the eligible population using a call and recall system	Increases participation and limits inequities linked to socioeconomic level
4 Is the pathway governed by protocols and guidelines?	4a No, clinicians decide about management on a case-by-case basis	Not evidence-based practice; can lead to a drift to higher sensitivity and low positive predictive value as well as overtreatment
	4b Yes, decisions about an individual's care is based on evidenced protocols and guidelines	For the eligible individuals, the balance favours benefits rather than harm
5 Are there quality standards based on evidence that are followed by screening providers?	5a No standards are in place; the screening provider makes decisions on quality locally	Screening can be of poor quality and therefore the harm can outweigh the benefits
	5b All screening services within a screening programme agree on and use the standards	The programme maximizes benefits and minimizes harm
6 Is the screening supported by an information system?	6a No special information system; the test results are recorded as part of routine care	Cannot operate effective call and recall, quality assurance or monitor the programme; also, cannot track people along the pathway for failsafe
	6b Yes, an information system is in place linked to population registries	Enables call and recall, tracking, quality assurance and monitoring

Various terms are used to describe this practice: multiphasic, individual health assessments, health checks or a bundle of tests. Regardless of the term, the important thing is understanding the consequences of organizing screening in this way.

When more than one test is offered as part of a bundle or health check, before it will be an effective screening programme:

- each test should be subject to the same stringent criteria used to determine whether to start a screening programme;
- each test should be part of a pathway of care; and
- each test should be provided in a way that fulfils the requirements of the green cells in Table 1.

Carrying out multiple screening tests at the same time may reduce costs or simplify the programme, but each test needs to be assessed on its own merits.

The following two examples can show the potential consequences.

An annual health check involving women 30–65 years old. Each year, healthy women are invited for a comprehensive check-up that includes blood pressure measurement, blood sugar test, gynaecological examination including cervix, a breast examination and a thyroid ultrasound scan and asked about her mental health, alcohol and smoking habits. If anything is found, the primary care physician decides what to do.

What could be the problems with this kind of approach?

- Tests may be carried out more frequently than the evidence recommends with consequent increased risk of harm, such as annual cervical screening.
- Not all the tests have evidence of effectiveness, such as thyroid screening.
- These tests are not part of a pathway, and if the doctor detects mental health problems or the woman is drinking heavily there are no funded referral pathways in place that can offer evidence-based interventions to support her.
- Because these tests are all carried out at the same time, a woman may have difficulty in providing informed consent for each test or deciding she only wants some of the tests but not others.

Newborn blood spot for multiple conditions. Every newborn baby has a heel prick, and the drop of blood is tested for several conditions such as cystic fibrosis, congenital hypothyroidism, several rare metabolic disorders (phenylketonuria, medium-chain acyl-CoA dehydrogenase deficiency, maple syrup urine disease, isovaleric acidaemia, glutaric aciduria type 1, homocystinuria (pyridoxine unresponsive) and sickle cell disease.

In this example, before each of these screening tests is included in the blood spot, they must meet the country's screening criteria. Only then are they included as part of the blood spot. Before the blood spot screening programme is rolled out, a pathway of care is mapped out for each screening test. So if a baby has an abnormal result for one of these tests, there is a clear referral pathway

and diagnostic and treatment services are available. Bundling up the tests makes the programme more cost-effective and acceptable to the mother and baby, and the programme is effective at reducing the number of cases of disability associated with these conditions.

The newborn blood spot is an example of how bundling tests can be cost-effective, but many other examples of multiple testing or health checks may not be set up with this kind of rigour, and the risk of harm and poor use of resources is considerable.

Given the complexity, cost and consequences of offering multiple screening tests at the same time, policy-makers should ask for an evaluation of each screening test in a bundle to ensure that it meets the screening criteria of a country and is organized such that it can deliver the anticipated benefits.

Operational readiness

Implementing a new screening programme is a major undertaking and requires considerable planning and human and financial resources. This section outlines some of the main workstreams that are part of an implementation plan.

Leadership, coordination and management

Leadership and accountability are key to running an effective and cost-effective screening programme. They need to be in place at all levels of screening provision.

From the outset, there must be a team leading the operation of the programme at either the national or regional level depending on the level of organization. Leadership is also needed at the level of service provision. This might be a senior midwife at a maternal and child health unit or a clinical director of a breast screening service.

Operational policies should outline the responsibilities of the key personnel involved in managing the screening programme at all levels of the system to ensure accountability.

Constructing a pathway

Each country's health system is unique. The screening pathway needs to be mapped on to a country's health system. It describes how people should move through the screening pathway, how they are identified, invited, screened and referred and what further investigations and treatment or intervention they will receive. It should also describe how individuals are given information and receive results from their screening. Fig. 13 provides an example of a screening pathway for a screening programme for newborn hearing.

Each step of the pathway should be supported by standards, protocols and guidance using the best available evidence (see the next section on quality assurance).

The pathway is the cornerstone of developing a screening programme. It is used to design the information technology and information system, to plan who needs to be trained and model the expected numbers, such as the expected proportion of people invited who participate and the number of true positives and negatives and false negatives and positives. This can be used to plan in detail the personnel, diagnostic and treatment capacity and expenditure needed during the coming years.

Trained personnel

The quality of screening largely depends on the skills of those who deliver it. All personnel needed for the screening pathway should be trained. For example, in colorectal screening programmes, additional training may be needed for personnel who run the call and recall system, endoscopists who carry out colonoscopies, pathologists who examine the biopsy specimens and information analysts who interrogate and use the information technology systems for monitoring *(34)*.

Information systems

Information systems are fundamental for organized screening programmes. They are used to identify the people eligible for screening, operate call and recall systems, record who has had the test and support failsafe and tracking systems. Information systems are essential to generate high-quality data for quality assurance and programme monitoring and evaluation.

Funding

To achieve universal health coverage, countries need funding systems that enable people to use all types of health services – health promotion, disease prevention, treatment and rehabilitation – without incurring financial hardship *(35)*.

Identifying adequate funding for all the components needed to run a screening programme is crucial. Ensuring the funding flows for the entire screening pathway is also important.

In some countries, funding for the pathway may come from different sources, which can create barriers to running a cost-effective service.

Policy-makers face common problems in setting up screening programmes.

Capital funding for equipment but no recurrent funding

Countries often receive capital funding to buy equipment for screening such as mammography machines or new laboratory equipment for a screening test or to put in place a new information technology system but then do not have enough funding for other aspects of the programme, such as salaries for trained personnel, maintaining machinery or test kits and reagents. In these circumstances, the money spent on equipment is wasted.

Extra public funding for a screening test but not for further investigations or treatment

Another common scenario is for the health ministry to provide extra public funds for a screening test, but if a person has an abnormal screening result and needs further investigations, they are expected to use usual health-care services.

Within publicly funded health systems, if extra funding only covers the screening test, there may not be enough funding to pay for the increased capacity that will be needed in diagnostic or treatment services such as pathology. This can lead to delays in accessing diagnostic services for people with abnormal screening results and for people with symptoms.

In countries in which health care is paid for by out-of-pocket payments or private or social insurance does not provide universal access, this can lead to delays or even deter people from following up an abnormal screening result. This can cause or exacerbate inequalities in outcomes and a failure to deliver the expected benefits of screening.

Fig. 13. Screening pathway for a screening programme for newborn hearing in the United Kingdom

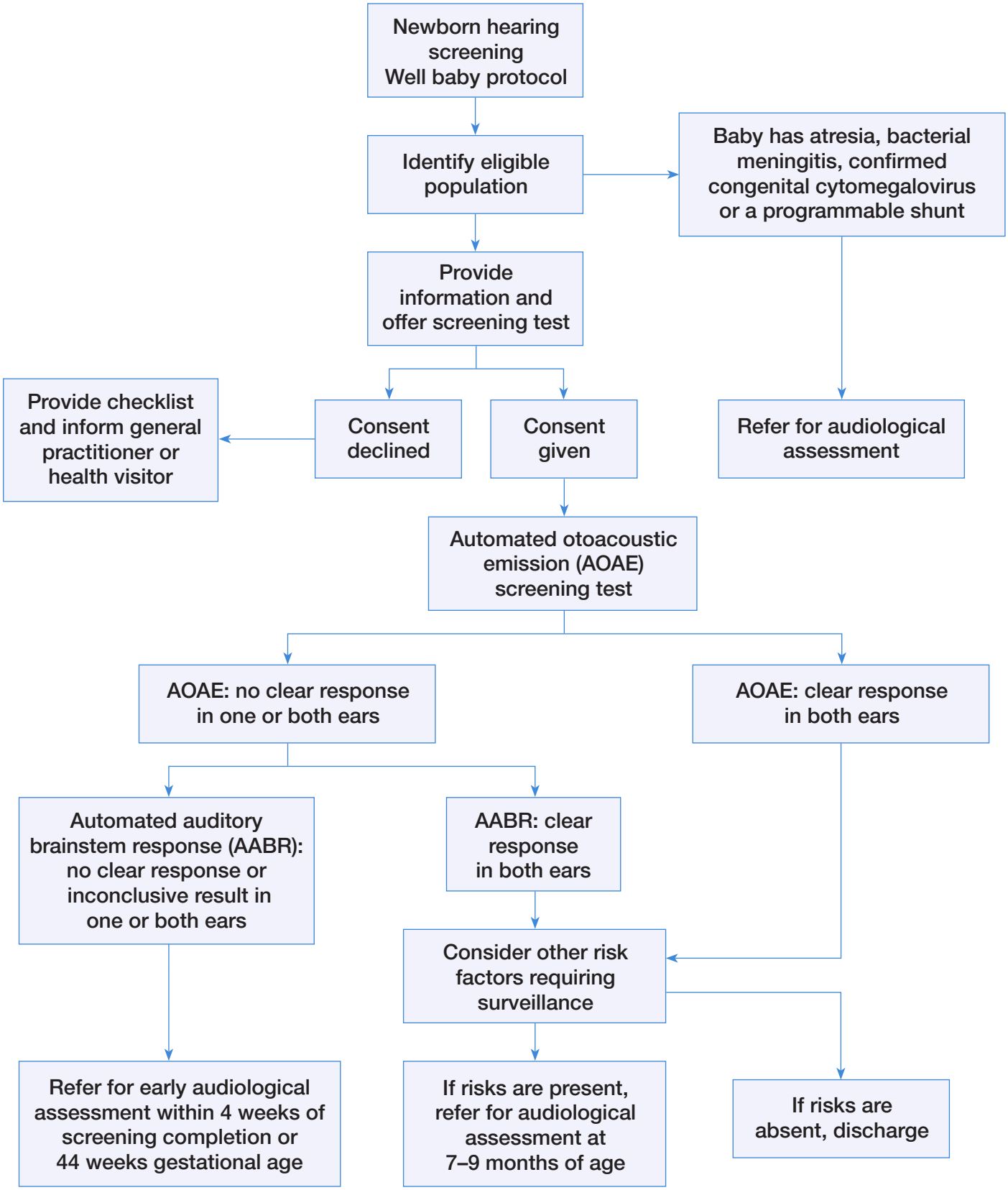


Fig. 14. Examples of information leaflets for screening tests

Inadequate funding for crucial support functions
Some countries may have public funding for the screening pathway but no recurrent funding for:

- national or regional programme coordination, resulting in failure to produce guidelines and protocols and monitor and evaluate the programme;
- quality assurance, leading to poor-quality services with consequent harm to patients and a programme that is not cost-effective;
- health promotion to support people to attend screening, with poor-quality information and engagement resulting in low participation; and
- information analysts to monitor the programme, with no data to monitor the programme and carry out quality assurance.

Without adequate funding for these support functions, the programme is unlikely to be effective.

Health system capacity

Implementing and sustaining a screening programme requires extensive human resources and health system capacity. Screening programmes can cause health-care resources to be reallocated, which can negatively affect other health-care areas and potentially lower the quality of the care for people with symptomatic conditions. Health administrators need to plan adequately to prevent this from happening. If health resources are already scarce and people with symptoms do not receive optimum care because of these constraints, a screening programme might not be the right course of action.

Information and communication

Screening programmes should provide unbiased and easy-to-understand information so that people can make an informed decision on whether to participate in screening.

Information should be accessible to the entire screened population, and materials should be made available in different languages and formats such as large print.

Since health literacy and understanding of complex topics such as risk can vary across a population, information should be carefully developed and tested with different groups to ensure that it is correctly understood (Fig. 14).

This is particularly the case when the implications of screening are complex and require personal choice, such as in antenatal screening.

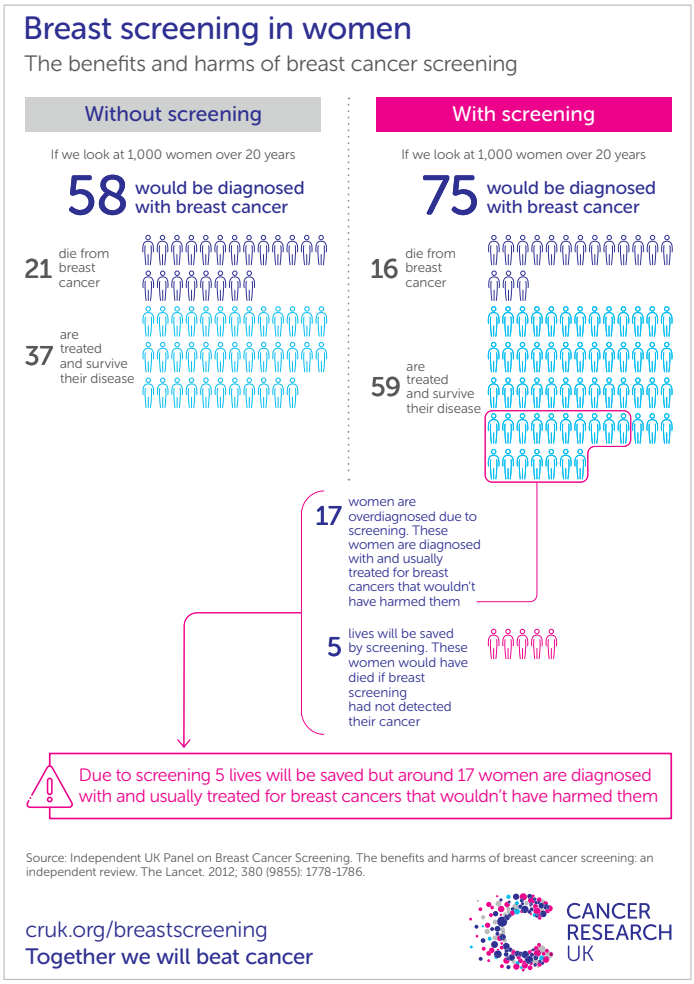
Both laypeople and clinicians tend to overestimate the benefits of screening and underestimate the harm of screening *(36)*. Training personnel on communicating risk and tools such as infographics, videos and decision aids can be used to facilitate understanding and promote informed consent and evidence-informed practice (Fig. 15).

Box 7. Informed consent in antenatal screening

Pregnant women may be offered a screening test during their pregnancy to test the chances of having a baby with certain conditions, such as Down's syndrome, Edwards' syndrome or Patau's syndrome. The results will tell whether the baby has lower or higher chances of having the condition being tested. If the result is the latter, the pregnant woman will undergo a diagnostic test to confirm whether the result is positive. The pregnant woman will then have to decide whether to continue or terminate the pregnancy. In these situations, it is vital for women to receive health and emotional support during the decision-making process and to be directed towards patient associations and other available supportive services.

Importantly, before the screening test can take place, women need to consent to it. It is therefore of paramount importance that pregnant women be aware of the consequences that could derive from a screening test before they authorize it and the possible decisions they might have to face. This is an essential aspect that should be covered by informed consent.

Fig. 15. Use of infographic to illustrate overdiagnosis in breast cancer screening



Source: Cancer Research UK *(37)*.

Operating a screening programme

Ensuring that screening programmes deliver the anticipated benefits

At the outset, every screening programme needs to set the parameters for how it will operate. These should be based on the best evidence, feasibility and cost–effectiveness. These parameters include: who should be invited; how often; what information people should be given to make an informed choice; the threshold for the test and its sensitivity, specificity and positive predictive value; and what diagnostic procedures and treatments should be used.

If screening programmes are going to achieve the anticipated benefits and minimize the harm, they must be operated within these parameters *(38)*. Quality assurance systems enable screening programmes to do this.

Failure to operate a screening programme within accepted parameters can have significant repercussions such as: the expected benefits are not achieved and the programme is no longer cost-effective; the reputation is damaged and the population no longer believes in the benefits of the programmes and fails to attend; and serious incidents occur that harm the population rather than benefit it *(1)*.

Quality assurance is the process of checking that each provider meets national standards, ensuring that screening programmes are safe and effective and encouraging continuous improvement *(39)*.

Quality assurance systems

Quality assurance systems have various components:

- standards based on the parameters of the programme;
- a system to check that standards are being met;
- guidance and operational policies;
- mechanisms to ensure the quality of the testing;
- failsafe systems; and
- quality improvement initiatives to support services to improve their quality.

Box 8. Newborn screening in Germany

In Germany, all newborns are screened for congenital metabolic, endocrine and immune diseases and hearing disorders routinely in the first days of life. The screening protocol, the parental information, declaration of consent and the information about screening results are part of the Paediatrics Directive of the Federal Joint Committee. The screening has high uptake, but a programme to guarantee uptake by tracking all children so that no one is lost is lacking. This has been remedied in Bavaria, where the local health offices track for completeness. There, the screening data of each child is compared with data from the birth registry. The screening centre also tracks the necessary follow-up examinations after a failed screening or a testing result, which indicates the need for a control examination. The low loss to follow-up rate achieved in this way emphasizes the importance of a tracking system with quality assurance characteristics.

Standard setting

Measurable standards are the cornerstone of any quality assurance system. Quality standards can be set for structures, processes and outcomes *(40)*.

Most quality standards measure important processes in the screening pathway such as uptake or positive predictive value. There are several examples of quality standards that have been developed for cancer screening programmes by national or international bodies, such as the European Commission.

Standards must define exactly how something should be measured and usually have an acceptable (or minimum) and desirable level for screening services to meet. For example, the waiting time for referral is the number of people waiting 31 days or less between a positive screening test and having a colonoscopy as a percentage of the number of people referred for a colonoscopy after a positive screening, with 90% being acceptable and 95% desirable *(34)*.

Quality standards are also used for the structural aspects of a programme. For example, a laboratory must carry out a minimum number of tests each year (Annex 2 provides links to international quality assurance schemes and standards).

Checking that standards are being met

After the standards are set, the next step is to check that the standards are being complied with by regularly submitting high-quality data returns. Other ways to check whether standards are being met are self-assessment questionnaires from providers or inspection visits to screening facilities.

Checking might also include ensuring that clinicians working in the screening programme have received training and have the required competence: for example, endoscopists might have to pass a special test to show that the colonoscopies they perform maintain an agreed standard *(41)*.

The oversight for checking quality usually depends on existing systems for regulation or quality assurance within a country. Common examples are voluntary or mandatory accreditation systems or licensing of screening personnel.

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Guidance and operating policies

Guidance and operational policies based on the best evidence describe in detail how the screening should be delivered along the whole pathway, including such considerations as who is eligible to be invited and who is responsible for booking any diagnostic follow-up *(42)*.

Mechanisms to ensure the quality of the testing

Screening programmes also need quality control systems to ensure standardization and the quality of the equipment and tests used in the programme. Examples of these are quality control for laboratory tests for antenatal screening or mammography equipment to limit the harmful effects of radiation. These will have detailed technical standards as part of the quality control scheme *(43)*.

Screening tests that rely on practitioner skill for interpretation; such as reading cytology slides, mammography films or diabetic eye retinal images, require continually checking the performance of the practitioner. Ways of doing this include double-reading of images, peer review of cytology slides and providing standardized test sets of images that practitioners are required to read at regular intervals, such as every six months *(43–45)*. Performance should be regularly checked in a supportive environment with training and feedback to maintain quality.

Failsafe system

Failsafe is a back-up system to stop errors from occurring. In screening, this is very important because many people undergo multiple processes and things can go wrong. Important failsafe actions include tracking people through the pathway and checking that everyone who is screened either receives a normal result or is referred for further investigation or the next step in the pathway. Ideally, failsafe systems are built into information technology systems, although paper-based failsafe systems can be operated.

Quality improvement initiatives

Important measures for improving quality and promoting learning include access to regular training for screening personnel, feedback on performance of services and individual practitioners and regular audits *(46)*.

There are also well-developed continuous quality improvement initiatives such as plan, do, study, act cycles that can be used in screening programmes to improve quality *(47,48)*.

Improving participation

Screening programmes will only make a substantial difference to population health if a sufficient proportion of the eligible population uses them. However, care should be taken to enable informed consent and protect individual autonomy.

Social and cultural factors can influence screening participation, with it being lower among disadvantaged and underprivileged populations and ethnic minorities *(22,23)*.

Terms and definitions of measures for participation may vary between countries. Two common terms are coverage, which is the proportion of the eligible population that has been screened within a defined time period; and uptake: the proportion of the invited population that has been screened.

Box 9. Albania: low uptake in cervical screening has led to rethinking design and delivery

Cervical cancer is the second most common type of cancer among women of reproductive age in Albania, with most cases diagnosed at stages III and IV. So far, the cervical cancer control efforts have been limited to providing opportunistic Pap smear tests, with only a few cytology laboratories located mostly in Tirana, the capital. Most rural health centres do not have qualified personnel, gynaecological beds and equipment for gynaecological sampling. Women often have to travel to an urban health facility, where a vaginal sample can be taken, and then transport the samples themselves to the cytology laboratory. However, uptake is very low: less than 10%. The main reasons for this are inadequate funding and insufficient training of health personnel.

The Ministry of Health decided to rethink their strategy. In 2019, they decided to move to human papillomavirus testing using a free self-administered test. They hope that this strategy will make the test more acceptable to women and increase uptake. They are also taking steps to reduce costs and improve quality. The human papillomavirus tests will be interpreted in a central laboratory, and primary health care personnel will be trained to ensure the quality of the tests.

A country that can only invite people for screening in a small part of the country because of lack of resources may have high uptake (80%) but very low coverage (15%).

There are many reasons why participation in screening programmes might be low *(24)*. Screening sites that are only in towns rather than in rural areas may deter participation. Information about screening may be difficult to understand or not available in local languages, which deters people from attending. The attitudes and behaviour of the population may play a part, such as worrying about the cost of health care or not having time to attend screening. Cultural norms such as family members being expected to accompany individuals to health-care appointments could reduce participation.

Local and trusted health-care professionals such as midwives or primary care doctors can act as important facilitators or barriers to accessing services, depending on their own understanding and support for screening *(49)*.

In general, individual invitations are more effective than open public invitations, such as mass-media campaigns. Other strategies that have been shown to increase participation are postal and telephone reminders and endorsement by primary care doctors *(50)*.

However, since the reasons for low participation are context and country specific, the first step is to understand why participation is low and then try evidence-based initiatives such as reminders and self-collected samples *(51)*. These should be evaluated to assess their impact. Annex 2 provides links to screening-specific resources, including evidence-based strategies to increase participation.

Monitoring and evaluation

Monitoring and evaluating screening programmes at regular intervals are essential.

Monitoring is the process of regularly measuring the outcomes of a screening programme at the national or regional level to ensure that it is meeting its aims.

Monitoring should occur regularly, such as annually, and measure outcomes that are derived from the aims of the programme, such as reduction in blindness from diabetic eye disease.

These data, alongside important key performance indicators such as coverage and uptake, can be used to inform policy-makers whether the screening programme is delivering the expected benefits and, if they are not, why this may be occurring and whether the screening programme needs to be modified in some way *(52)*.

Table 2. Examples of reasons to evaluate a screening programme

Topic	Reason
Population health	Change in the incidence or prevalence of the target condition or its precursor Altered distribution of mild versus severe types of condition
Alternative interventions or technology	New effective primary preventive strategies, such as human papillomavirus vaccination Alternative and more effective screening strategies, such as machine learning and new tests with better sensitivity and specificity
Evidence from scientific studies or monitoring of existing screening programmes	New evidence suggesting that the balance between benefits, harm and costs (value) has changed
Treatments	Effective new treatments reduce the benefit yielded from screening, such as in breast cancer screening
Value	Evidence that modified delivery of screening improves the trade-off between the benefits, harm and costs of screening
Resources	Change in health priorities and/or reduced health resources available for screening
Ethics	Evidence that screening is causing inequality Change in ethical perspective of the public in relation to individual autonomy or harm versus benefits

Evaluation is a periodic review of how the screening programme is working in light of new evidence or changes to the population to check that it continues to be effective and cost-effective. Table 2 provides examples of the kind of reasons that might prompt such an evaluation.

Measures of screening programme performance

Measuring the performance of existing screening programmes is complex. Choosing the right outcome measure is crucial. It should be linked to the aim of the programme.

Appropriate measures include incidence (measuring the number of new cases, such as the number of new cases per year of blindness from diabetic retinopathy) and a reduction in mortality (for example, the number of deaths from colorectal cancer). However, a reduction in mortality may take years to become apparent, and proxy measures such as interval cancers may be used instead. Interval cancer cases are the number of cancer cases occurring between screening episodes. They will always occur because no screening programme is 100% sensitive, but an increase or decrease in numbers at the regional or national level can be an important indicator of the effectiveness or ineffectiveness of a screening programme.

In practice, monitoring outcomes of a screening programme is not always straightforward.

Some of the common problems include the following.

- **Poor-quality data**. Incidence and mortality data rely on accurate and complete reporting of types of conditions and causes of death and registries that can collect and validate the data. Reliable data is required to examine trends and ensure that any change after screening is introduced can be attributed to the screening programme *(1)*.

- **Numbers too small to detect a change**. When a screening programme starts, the numbers may be too small to detect a real difference, and any change can simply result from year-on-year variation. This especially applies to measuring interval cancer cases or events that do not occur very often.

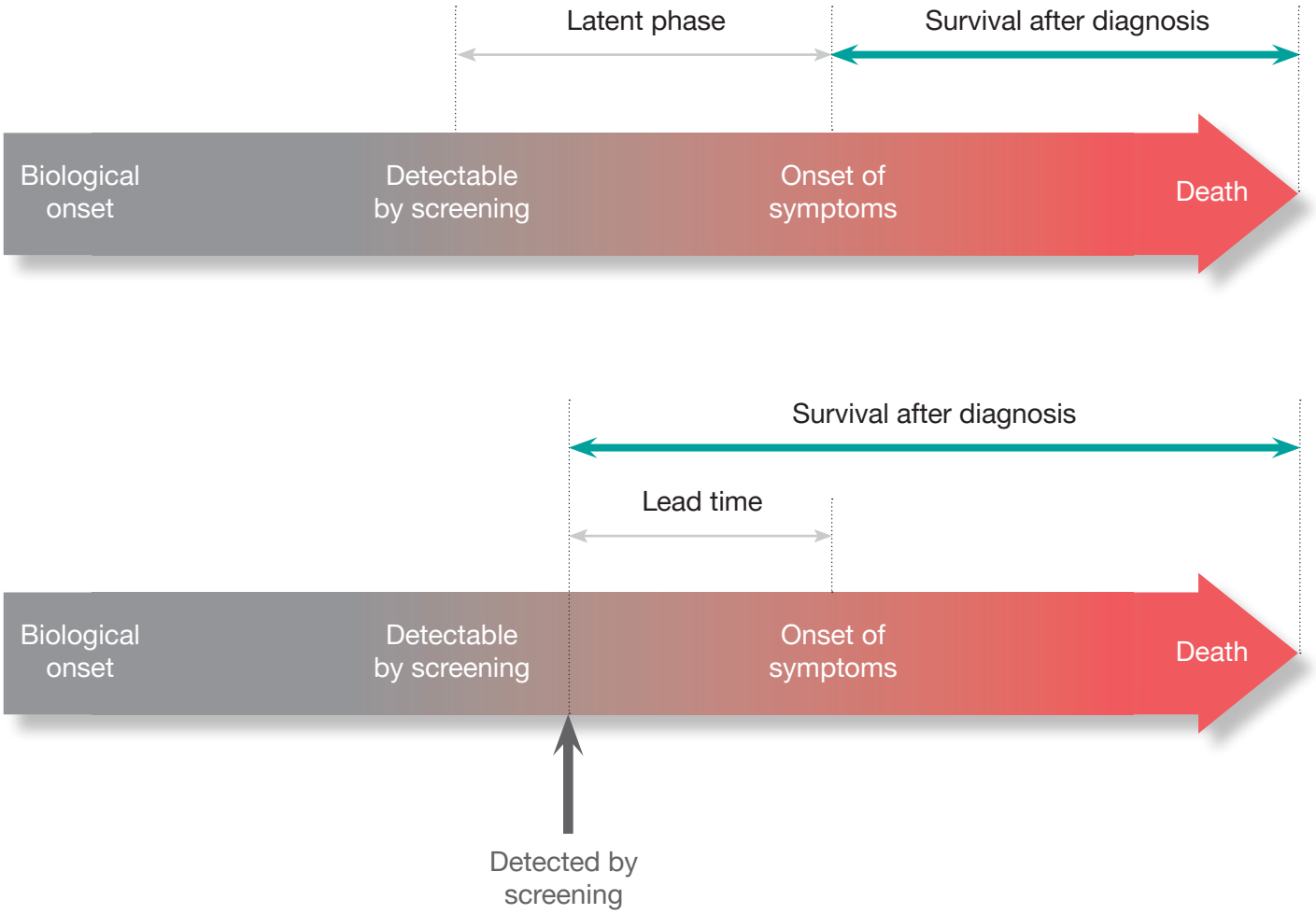
- **Detecting many cases when screening starts**. Introducing a screening programme to a new geographical area often detects many cases (the prevalent or first-round effect). When screening is repeated two or three years later, only new cases since the first screening will be picked up which may well be less (second round dip).

- **Comparing the number of deaths before and after screening is introduced**. This might be misleading because the improvement could result from other factors such as better diagnosis and treatment in the population rather than the screening programme.

- **Measuring survival time from diagnosis**. Screening can increase survival time from diagnosis but does not necessarily affect when the person will die from the condition, only that they survive longer with a diagnosis. So screening may lead to an increase in survival time but may not change mortality

rates. This is called lead-time bias (Fig. 16) and is the extra time between detection by screening until the condition would have been detected through symptoms and clinical diagnosis.

Fig. 16. Lead-time bias

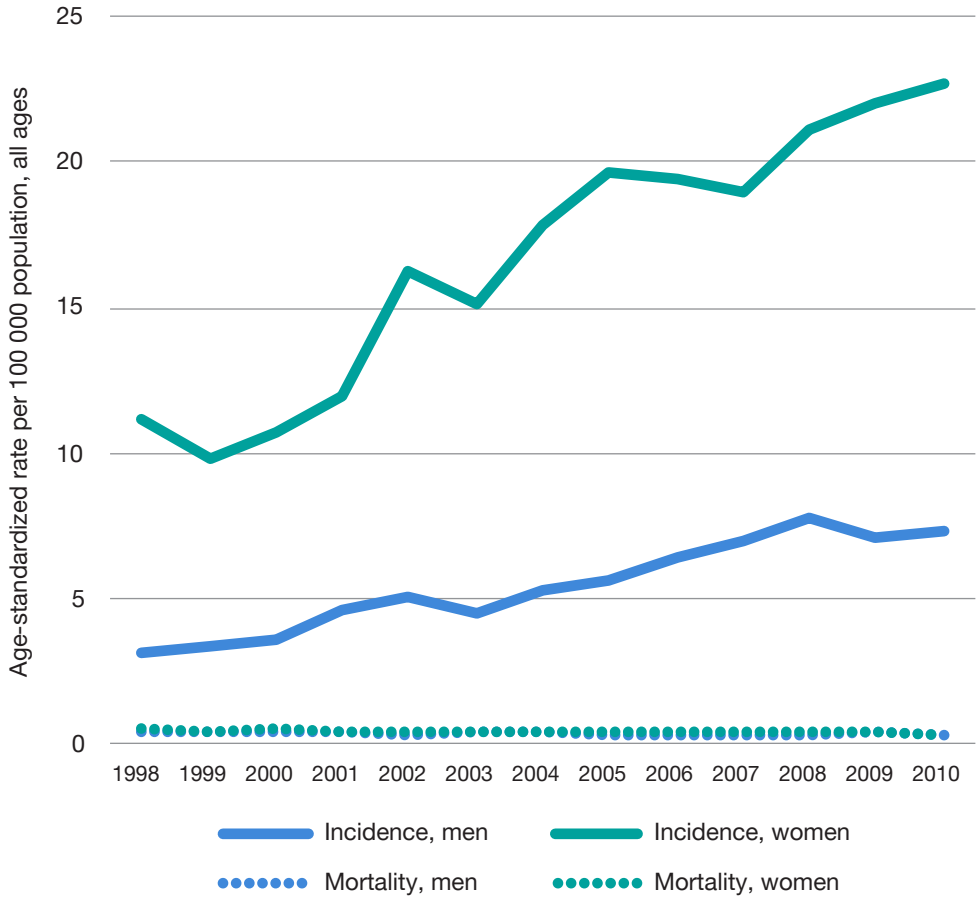


This explains why the survival rate is not a reliable way to measure the success of screening.

An increase in the number of new cases detected in a screening programme may be measured rather than a reduction in mortality. Screening may increase the numbers of cases detected because of overdiagnosis, but these are cases that would not have caused any problem. Unless the increase in detection is associated with a reduction in mortality, it does not demonstrate the effectiveness of a screening programme.

This is illustrated by the example of thyroid screening in Italy (Fig. 17), where opportunistic screening for thyroid cancer has increased, and as a result the number of cases of thyroid cancer detected has increased considerably but the mortality rate has not changed. The most likely reason is overdiagnosis of thyroid cancer.

Fig. 17. Comparison of change in incidence and mortality rates for thyroid cancer in Italy



Source: Global Cancer Observatory [online database] *(53)*.

Outcomes can be compared between screen-detected cases and non-screen-detected cases. Screening tends to pick up slowly progressive conditions that are less aggressive and more amenable to treatment, so these will always do better than cases that are rapidly growing and aggressive. So if outcomes are compared between people whose cancer was screen-detected and those who presented with symptoms, the outcomes for screen-detected cases will usually be better (this is typically the case for breast cancer). This is called length-time bias. However, this may not result in any difference to mortality for a population offered screening.

Annex 2 provides a link to technical documents that discuss these issues in more detail and explains the kind of studies that are needed to measure the performance of screening programmes.

Conclusion

This screening guide has provided an overview of the theory of screening programmes and highlighted some of the issues and dilemmas policy-makers may encounter when deciding whether to implement, stop or change a screening programme.

The guide also outlines how to implement and operate a screening programme. The reason for doing this is to show some of the challenges and considerable resources required to operate an effective programme and, most importantly, to show that, unless screening programmes are done well, they are unlikely to deliver the intended benefits.

The guide does not try to provide detailed guidance on how to carry out these tasks or cover all the aspects of operating a programme. Several areas are not covered and the information is simplified in some cases. However, the guide enables policy-makers to know what questions to ask, where to find further information and when to seek support from experts so that, ultimately, they can make the best decisions for their populations and optimally use the available resources for screening programmes in their countries.

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Annex 1. Explanation of technical terms used in the guide

This annex has been adapted from: Raffles A, Mackie A, Muir Gray JA. Screening: evidence and practice. 2nd ed. Oxford: Oxford University Press; 2019.

AABR and AOAE: automated auditory brainstem response and automated otoacoustic emissions. Tests used in screening programmes for newborn hearing.

Amniocentesis: fine-needle aspiration to remove a sample of amniotic fluid from the womb for examination, enabling cells from an unborn baby to be examined.

Biopsy: a sample of tissue taken for examination.

Bloodspot test: multiple screening tests carried out on a newborn infant by taking a sample of blood by pinprick from the infant's heel.

Cohort: a group of people who share a common characteristic or experience within a defined period.

Colonoscopy: the inspection of the lining of the colon using an endoscope.

Congenital hypothyroidism: a partial or complete loss of function of the thyroid gland (hypothyroidism) that affects infants from birth (congenital).

Coverage: proportion of the eligible population that has been screened within a defined time period.

Cut-off or threshold value: an arbitrary point separating results into abnormal and normal values.

Cystic fibrosis: a genetic disorder in which secretions are of a higher than average viscosity. The lungs are particularly prone to infection.

Cytology: the examination of cells using a microscope (used as part of the cervical screening programme).

Deontological perspective: in which an action is considered morally good because of some characteristic of the action itself, not because the product of the action is good. Deontological ethics holds that at least some acts are morally obligatory regardless of their consequences for human welfare.

Down's syndrome or trisomy 21: a syndrome resulting from having three rather than two chromosomes number 21. The affected individuals may have intellectual impairment, heart defects and other problems.

Edward's syndrome or trisomy 18: a syndrome resulting from having three rather than two chromosomes number 18. The affected individuals are born small, have a range of severe physical and mental disabilities and rarely survive to adulthood.

Eligible population: a defined population that meets the criteria to be offered screening. For example, the eligible population for breast screening is all women 50–70 years old.

Endoscopy: a method of viewing the interior of the body such as the colon or stomach using a fibreoptic tube.

Failsafe system: a back-up mechanism that ensures that, if something goes wrong in a system, then action will be taken to ensure a safe outcome.

False negative: a normal result in a person who does have the condition being tested for.

False positive: an abnormal test result in a person who does not have the condition being tested for.

Glutaric aciduria type 1: an inherited disorder in which the body is unable to process certain proteins properly. The affected individuals can have a mild or severe form that can present in infancy or later in adolescence. It can affect a wide range of organs.

Health checks: a term used to describe a number of screening tests carried out at the same time usually linked to the life-course, such as child health checks.

Health literacy: a term used to describe the cognitive and social skills that determine the motivation and ability of individuals to gain access to, understand and use information in ways that promote and maintain good health.

Homocystinuria: an inherited condition in which the individual is unable to fully break down the amino acid methionine, causing a build-up of methionine and homocysteine. Symptoms develop after the first year of life and can affect a range of organs.

Human papillomavirus: a common virus with numerous types, some of which play a part in cervical cancer.

Incidence: number of new cases occurring within a population during a specified time period.

Interval cancer cases: the number of cancer cases occurring between screening episodes.

Mortality rate: a measure of the frequency of occurrence of death in a defined population during a specified interval.

Multiphasic tests: in which an individual is screened for more than one condition at the same time.

Negative predictive value: the likelihood that the screening participant does not have the condition that screening targets (the person is healthy) when the test is negative (normal).

Overdiagnosis: identifies a condition or problem that would never cause a person harm during their lifetime.

Overtreatment: refers to more extensive or invasive treatment than is required to improve health outcomes. Often associated with overdiagnosis.

Pap smear: abbreviation of Papanicolaou test (named after the doctor who developed the test). A cervical screening test that takes a sample from the cervix for cytology.

Patau's syndrome or trisomy 13: a syndrome resulting from having three rather than two chromosomes number 13. The affected babies have a wide range of serious developmental problems and may not survive more than a few days.

Phenylketonuria: an inherited disease characterized by deficient ability to process phenylalanine, an amino acid.

Positive predictive value: the likelihood that the screening participant has the condition that screening targets when the test is positive (abnormal).

Prevalence: the number of cases of a condition in a given population at a point in time.

Principlism: a system of ethics based on the four moral principles of autonomy, beneficence, nonmaleficence and justice.

Randomized control trial: a research method to assess the effectiveness of an intervention or a service. Participants are assigned randomly either to receive the offer of an intervention or to be in a control group.

Recall-to-assessment ratio: term used in breast screening programmes to refer to the proportion of women who are screened and are sent through for further investigations (assessment). A very high ratio will be associated with a low positive predictive value and a large number of false positives.

Sensitivity: the ability of the screening test to identify people with the condition as positive (abnormal).

Sickle-cell disorders: an inherited condition that affects haemoglobin, the molecule in red blood cells that delivers oxygen to cells throughout the body.

Specificity: the ability of the screening test to identify healthy people as negative (normal).

Screening test: test carried out on someone without symptoms to detect whether they have a condition or risk factor.

True positive: an abnormal result in a person who does have the condition being tested for.

True negative: a normal result in a person who does not have the condition being tested for.

Uptake: proportion of the invited population that has been screened.

Utilitarian: a moral theory that advocates actions that promote overall happiness or pleasure and rejects actions that cause unhappiness or harm.

Annex 2. Resources

General resources

Background information on screening practice and implementation

Sagan A, McDaid D, Rajan S, Farrington J, McKee M. Screening: when is it appropriate and how can we get it right? Copenhagen: WHO Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies; 2020 (Policy Brief, No. 35).

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Guide to cancer early diagnosis. Geneva: World Health Organization; 2017 (https://www.who.int/cancer/publications/cancer_early_diagnosis/en, accessed 27 November 2019).

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Evidence-based practice

GRADE [website]. Grade Working Group; 2019 (http://www.gradeworkinggroup.org).

Evaluation and monitoring of screening programmes

Sankila R, Demaret E, Hakama M, Lynge E, Schouten LJ, Parkin DM, editors. Evaluation and monitoring of screening programmes. Brussels: European Commission; 2000 (http://aei.pitt.edu/42172/1/A6214.pdf).

International screening-specific guidance

Antenatal screening

WHO recommendations on antenatal care for a positive pregnancy experience. Geneva: World Health Organization; 2016 (https://apps.who.int/iris/bitstream/handle/10665/250796/9789241549912-eng.pdf?sequence=1, accessed 27 November 2019).

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Breast screening

Breast cancer screening. IARC Handbooks of Cancer Prevention, Volume 15. Lyon: International Agency for Research on Cancer; 2016 (http://publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Breast-Cancer-Screening-2016, accessed 27 November 2019).

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Cervical cancer screening

European guidelines for quality assurance of cervical cancer screening. Brussels: European Commission; 2015 (https://op.europa.eu/en/publication-detail/-/publication/a41a4c40-0626-4556-af5b-2619dd1d5ddc, accessed 27 November 2019).

Comprehensive cervical cancer control: a guide to essential practice. 2nd ed. Geneva: World Health Organization; 2014 (https://www.who.int/reproductive-health/publications/cancers/cervical-cancer-guide/en, accessed 27 November 2019).

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Colorectal screening

Colorectal cancer screening. IARC Handbooks of Cancer Prevention, Volume 17. Lyon: International Agency for Research on Cancer; 2019 (http://publications.iarc.fr/Book-And-Report-Series/Iarc-Handbooks-Of-Cancer-Prevention/Colorectal-Cancer-Screening-2019, accessed 27 November 2019).

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Diabetic retinopathy screening

TADDS: tool for the assessment of diabetic retinopathy and diabetes management systems. Geneva: World Health Organization; 2015 (https://www.who.int/blindness/publications/TADDS_EN.pdf, accessed 27 November 2019).

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The WHO Regional Office for Europe

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health conditions of the countries it serves.

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