Screening: between hope and hype

Gezondheidsraad **President**
Health Council of the Netherlands

To the Minister of Health, Welfare and Sport

Subject : Presentation of advisory report *Screening: between hope and hype*
Your reference: PG/Zp-2.747.737
Our reference : I-182/WD/mj/808-E
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Date : April 1, 2008

Dear Minister,

On 12 March 2007 you asked the Health Council to investigate a number of questions relating to scientific and other developments in the area of screening and their implications for the role and responsibility of the government. I set up a committee to look into these questions, and it has produced an advisory report entitled: *Screening tussen hoop en hype* [Screening between hope and hype]. The advisory report has been reviewed by four standing committees of experts within the Health Council: the standing committees on Medicine, Medical Ethics & Health Law, Genetics and Social Health Care.

The committee has concluded that the rate at which useful new screening opportunities become available is not as rapid as reports in the media might sometimes indicate. It has also found that cultural, social and economic factors contribute to a situation in which various types of screening (including self-testing kits) are placed on the market without any proper investigation having been conducted to ascertain whether the benefits for those affected outweigh the disadvantages that always also exist.

What does this mean for the government? A fresh approach is needed to encourage sensible screening and to protect individuals against the risks of unsound screening. Extending regulations does not seem to be the most suitable way of achieving this in the first instance. Rather, the committee would be in favour of creating an independent body to deal with the whole issue of screening, along the lines of the UK National Screening Committee. A key element of this would be to establish a quality-mark for responsible screening, based on scientific assessments of new developments and aimed at promoting responsible provision and responsible choices.

P.O.Box 16052
NL-2500 BB The Hague
Telephone +31 (70) 340 65 75
Telefax +31 (70) 340 75 23
E-mail: wj.dondorp@gr.nl

Visiting Address
Parnassusplein 5
NL-2511 VX The Hague
The Netherlands
www.healthcouncil.nl

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I support the committee's conclusions and recommendations, and have pleasure in submitting its advisory report to you.

Your sincerely,
(signed)
Prof. J.A. Knottnerus

P.O.Box 16052
NL-2500 BB The Hague
Telephone +31 (70) 340 65 75
Telefax +31 (70) 340 75 23
E-mail: wj.dondorp@gr.nl

Visiting Address
Parnassusplein 5
NL-2511 VX The Hague
The Netherlands
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to:

the Minister of Health, Welfare and Sport

No. 2008/05E, The Hague, April 1, 2008

The Health Council of the Netherlands, established in 1902, is an independent scientific advisory body. Its remit is “to advise the government and Parliament on the current level of knowledge with respect to public health issues...” (Section 22, Health Act).

The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport, Housing, Spatial Planning & the Environment, Social Affairs & Employment, and Agriculture, Nature & Food Quality. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

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Executive summary

New forms of screening raise new issues

Screening (or population screening) involves the medical examination of individuals who exhibit no health problems with the aim of detecting disease, or an hereditary predisposition to disease, or risk factors that can increase the risk of disease. The government has great expectations of screening, as do caregivers, private individuals, and other groups within the healthcare sector. Developments appear to be moving fast: new forms of screening are either being brought on line within the healthcare sector or are being marketed by commercial organisations.

The focus on novel screening techniques is tied in with changes within the healthcare sector itself. It is also in keeping with many people's need for reassurance on matters of personal health. The rapid growth in the range of various health checks and self-testing kits is also in keeping with a health service that is determined by market forces, with an emphasis on freedom of choice and individual responsibility.

These developments involve both opportunities and threats. The opportunities derive from the fact that new forms of screening can help people to live more healthily, and avoid symptoms and consequences of disease. There are also threats, because it is by no means a foregone conclusion that the benefits of screening will always outweigh the ever-present drawbacks. There is a tendency to introduce screening before it has been properly researched.

It was in this regard that the Minister of Health, Welfare and Sport approached the Health Council of the Netherlands for advice. There are three central issues. The Minister wants a clear idea of forthcoming developments in the area of screening over the next few years. He would also like to know whether the existing criteria for responsible screening still form a sound basis for the evaluation of those developments and of how they are dealt with in other countries. Finally, he has asked for an indication of the significance of developments in this area, in terms of the role and responsibility of government.

The range of screening techniques will expand and diversify

What about scientific developments in this area? Firstly, there has been a rapid generation of new knowledge concerning the genetic backgrounds of many diseases. This often involves common diseases such as cardiovascular diseases, diabetes and certain psychological disorders. These 'multifactorial diseases' involve a variety of genes, which together produce a more or less increased risk of developing the disease in question. The same effect may result from these genes' interaction with external factors such as diet, smoking, or exposure to hormones. A second, partly overlapping development involves the use of biomarkers. These are characteristic abnormalities in DNA, RNA and proteins, which are also associated with a risk of disease. Thirdly, imaging techniques are improving all the time. This can sometimes enable certain diseases (such as cancer) to be detected at an early stage. Fourthly, new questionnaires are being developed for purposes such as the detection of psychological disorders. Finally, there are great expectations for the potential benefits to be gained by the combination of various screening techniques.

Despite the great pace of new scientific and technological developments, this is not necessarily reflected by the rate at which worthwhile new screening options become available. While we have only just started to elucidate the genetic background of many common diseases, it is important to note that responsible screening requires more than just the early detection of disease, or the charting of predisposition or risk factors. To start with, there must be a suitable test for discriminating between those who have the characteristics in question and those who do not. Furthermore, early detection only makes sense if it has been established that those involved can derive health gains or other benefits, and that these advantages outweigh the drawbacks.

This does not detract from the fact that the range of screening options is expected to grow over the course of the next five to ten years. Aside from an increase in the screening options for monogenic disorders (in genetically loaded

families, in newborns, and prior to conception), the main area of development is expected to involve new forms of screening for risk factors for common multifactorial disorders. However, it is not simply a question of increased volume. In a parallel development, the range of screening options is also expected to become more diverse. This will include not only new types of classic population screening, but also screening of risk groups in the border area of regular care, and checks and self-testing kits offered via private channels to consumers. A third development that can be cited in this connection is a blurring of the line between collective prevention and individual care.

Responsible screening criteria remain valid

At international level, there is a broad consensus regarding the criteria to be met by responsible screening. The major conditions involve the required degree of usefulness of such screening for participating individuals, its scientific basis, and the voluntary nature of screening. That normative framework stems from 'Principles of screening for disease', which was published forty years ago by J.M.G. Wilson and G. Jungner. In the intervening years it has been further developed and modified by various institutions associated with screening, also in response to new scientific developments in the field of genetic and prenatal screening. While some elements are currently the subject of debate, there is no reason to suppose that this normative framework is not entirely 'future proof'.

Since these criteria were primarily developed for classic, government-backed large-scale population screening, not all of them are automatically applicable to private sector screening. Accordingly, the requirement that screening must target major health service problems is tied to the use of public (or collective) funding. Obviously, it does not always apply to private screening that is paid for directly by the individuals in question. However, the core of the normative framework: the principle that the provision of screening can only be justified if it has been established that the benefits to the participants outweigh the ever-present drawbacks, applies regardless of whether this is being provided through public or private channels. That principle requires continual, active confirmation.

The government must ensure the availability of screening worthwhile to all

In this area, the government's duty is twofold. On the one hand, it must ensure that worthwhile screening is available and accessible to everyone. On the other hand, it must protect people from the risks inherent in unsound screening.

The government fulfils the former duty by itself making certain types of screening available. In this connection, it operates mainly via the National Screening Programme and the screening part of larger programme for child healthcare. Which types of screening are eligible for inclusion in those programmes and which are not? In any event, the government clearly must not provide screening that is scientifically unsound, or which in any other respect fails to meet the conditions of responsible screening. Conversely, it is not the case that the government should be expected to provide any and all types of screening that do meet those conditions.

There are good grounds for limiting the range of screening variants that are funded from public or collective resources to those that are capable of generating actual health gains. Thus, screening where this is not the case should be excluded as a matter of principle. One exception is screening (not aimed at generating health gains) in de context of reproduction, including existing screening for Down's syndrome and other severe foetal abnormalities. Whether this takes place via the National Screening Programme or (as is currently the case) via basic cover health insurance is not a matter of principle.

Beyond that, it is inevitable that there be some sort of priority setting. This involves the same sort of decisions as those associated with the issue of which amenities should be included in (or removed from) basic cover health insurance. There is a consensus that, in that case, the factors of disease burden and cost effectiveness should be examined. However, the applicability of these criteria (also with regard to screening) is a topic for research and debate.

The government's duty of care also requires it to ensure that any screening which is not offered by the government itself but which is (via public health insurance cover) part of the public health service, is qualitatively sound. Furthermore, the government is also required to foster research that can lead to worthwhile new screening options, whether or not these are to be incorporated into the range of screening provided by the government.

The current level of protection against the risks of unsound screening is inadequate

Screening almost always has some drawbacks. It is not merely that false-positive test results ('false alarms') and over-diagnosis (an anomaly is identified, but it is not one that without screening would have led to symptoms of disease) are associated with unnecessary feelings of fear and uncertainty, they can also result in damage to health from high-risk follow-up tests or therapeutic interventions. False-negative results may lead to unfounded reassurance.

Accordingly, the Population Screening Act (WBO) was introduced to protect the public against risks of this kind. The WBO dictates that some types of screening that are considered to involve a significant degree of risk must first be subjected to independent quality testing. In this connection a check is made to see whether provision and implementation are in keeping with the above-mentioned conditions for responsible screening. The screening in question can only be performed once the Minister has granted a permit. The use of self-testing kits for materials produced by the body is, to some extent, governed by different legislation based on a European Directive for in-vitro diagnostic medical devices (IVD Directive).

In addition to a debate about whether the WBO meets current needs, there are problems with compliance. The fact that certain forms of screening (such as total-body scans and prostate cancer screening) are prohibited in the Netherlands, even though their use is permitted elsewhere, is seen by many people as unwanted state intervention. Nevertheless, evidence gathered both in this country and elsewhere clearly underlines the WBO's importance, as an indispensible instrument of protection.

The WBO's biggest problem is that the scope of the protection it offers is determined by the rigid and somewhat arbitrary demarcations imposed by the permit requirement. All other types of screening require no assessment whatsoever. There is another way, however, in which the protective effect of the IVD Directive is found wanting. It cannot effectively prevent the marketing of risky DIY test kits that have not been subjected to adequate quality reviews. Furthermore, the range of self-testing kits that are marketed from outside Europe, via the Internet, is largely beyond the reach of EU legislation.

Finally it is worth considering that, even if people pay for the initial test themselves, unsound screening can have adverse repercussions for the collectively supported health service system. This derives from the fact that a (false-)positive result can give rise to a chain of events that imposes an unnecessary burden on caregivers and resources.

The added value of an active approach

How can the government meet its responsibility in such a way that it covers the entire dynamic arena of publicly and privately available screening and self-testing kits?

Organise continually proactive intervention spanning all areas of screening

It appears that there are better ways of doing this than by simply imposing addition regulations. One such approach would involve continual proactive intervention spanning all areas of screening. The goal would be to identify opportunities for the development of worthwhile new screening options, enhancing the quality of existing options, and enabling people to make well considered choices by equipping them with the requisite knowledge. This will only succeed if the task of active intervention were to be assigned to an independent and authoritative central institution capable of conducting such dealings with the necessary degree of transparency.

Develop a quality mark for responsible screening

Not only would the creation of a ‘quality mark’ enable people to sort the wheat from the chaff, it would also discourage the provision of unsound screening. A basic variant of this would involve the use of on-line reviews of various types of screening which would be available to the public. A quality mark for screening providers will first have to be devised, however, if this alternative to further regulation is to successfully drive quality improvements in this area. The success or failure of any such quality mark system is largely dependent on the authority of the institution behind it, and upon support from the various parties involved.

Link the quality mark to standards of professional conduct

Wherever possible, use can be made of existing professional guidelines and standards in the area of screening. Conversely, a forceful boost to the development of such quality documents can be linked to the quality mark and to the reviews upon which it is based. Professionals should neither offer nor perform any type of screening that has not been granted a quality mark. This requires the existence of a close relationship between the quality mark and the professional standard. While this cannot be imposed from above, it can grow of its own accord.

Transform the WBO into a flexible safety net

If the categories for which a permit is mandatory were no longer set out in the law itself (but instead in an Order in Council) this would facilitate a more flexi-

ble use of the WBO. The quality mark system would require a more prudent application of the permit requirement. Only where the admission of screening involves a substantial risk (either for the participants or for the health service system) that could not be adequately or fully alleviated by means of the quality mark, would there be a need to introduce a mandatory permit for that form of screening. If used in this way, the permit requirement would operate as an effective 'safety net' for the quality mark system. In advance of such a development, it would seem wise not to make radical changes to the current scope of the permit requirement. Yet it would also be useful to enable the permit requirement to be applied where necessary to prevent the health service system from becoming overloaded by unsound types of screening.

Ensure central control

That continually proactive intervention spanning all areas of screening can best be entrusted to an independent and authoritative institution (a 'Standing Committee on Screening'), which would be charged with:

- Implementing systematic scientific assessments of newly developed screening options, at international level wherever possible;
- Promoting research into worthwhile screening and encouraging population screening trials;
- Contributing to critical reflections on the normative framework itself, and on its further development;
- Advising on the incorporation (or removal) of screening from the range of such services offered by the government or via basic cover health insurance;
- Control over the information and quality mark system;
- Encouraging the development of professional guidelines and standards;
- Pointing out any sticking points that impact the government's duty of protection and giving advice on the scope of the WBO permit requirement;
- Assessment of WBO permit requests.

In addition to independent expertise in all relevant areas, the implementation of these duties requires focused funding and the broadest possible support. In view of its duties in this regard, the government can be expected to make substantial financial commitments. Other parties (insurers, scientific associations) should also be called to account with respect to their own responsibilities in this matter. Additional efforts are required to work out the precise details of embedding and design.

Chapter 1

Introduction

The existing range of screening techniques targeted at early detection of disease or at charting health risks is increasing both inside and outside the public health-care sector. The aim of this advisory report is to discuss the significance of this phenomenon to public health and government policy in that regard.

1.1 Request for advice

The Minister of Health, Welfare and Sport (HWS) approached the Health Council of the Netherlands and the Council for Public Health and Health Care (RVZ) on 12 March 2007 with a request for an advisory report to be used in updating government policy on population and other screening. The background to the advisory report (see annex A) is as follows:

Science offers ever-increasing insights into the opportunities and risks of diseases. This is likely to result in a shift from the focus on clinical medicine related to existing health problems to predictive medicine not related to existing health problems. Newly developed techniques offer previously unknown opportunities for determining individual and other risks of a condition and for taking preventive action against actual or potential conditions. These developments give rise to opportunities and threats to individual citizens and society as a whole, and pose fresh challenges to government policy.

The Minister has asked the Health Council to provide him with more detailed information about new screening opportunities that are likely to be developed over the next five to ten years. He also wishes to know whether the current normative framework for assessing new types of screening is still fit for purpose, and what approach is taken by other countries. Finally, he has asked to be informed of the significance of developments in this area for the role and responsibility of the government. The questions put to the RVZ relate mainly to how new forms of screening can be integrated into society.

Additional advice

Both councils selected an approach that fits in well with their own area of work, and consulted each other closely while preparing the advisory report. The Health Council's report emphasises the state of scientific knowledge, while that of the RVZ, which is the strategic advisory body to the Ministry of HWS, concentrates on implications for the healthcare system, financial issues and the position of individual citizens. The advisory reports of both councils complement each another.

1.2 Committee and review

The Chairman of the Health Council set up a committee to address the issue. It was made up of experts in the field (or epidemiology) of various forms of screening, operations research, paediatric medicine, general practice medicine, internal medicine, community genetics, medical sociology, psychology, medical ethics and medical law. This committee, 'Predictive medicine: population screening and government' (hereinafter referred to as 'the committee') was set up on 28 June 2007. A list of the committee members can be found in annex B.

As is the Health Council's usual practice, a number of permanent internal groups of experts were also consulted to provide a form of peer review. It is in this context that the advisory report was submitted to the standing committees on Medicine, Medical Ethics & Health Law, Genetics and Social Health Care.

1.3 Terms and definitions

Screening

Rather than addressing all possible forms of predictive medicine, this advisory report focuses exclusively on screening and population screening. The

committee does not draw a distinction between the two latter terms. It understands them to mean: offering medical tests to individuals who are not known to have any health problems with a view to detecting (or excluding) at an early stage a latent condition that may already be present, an inherited predisposition to disease, or risk factors that increase the possibility of disease.[1,2]

A distinguishing feature of screening (or population screening) is that the test is provided without being requested to people who do not yet have any symptoms of illness. Predictive medical tests performed on people who have sought medical help because of health problems is diagnostic or prognostic in nature, but is not a form of screening and so does not fall within the remit of this advisory report. Nor are medical examinations for employment and insurance covered, because they are not really being offered to the people undergoing them.

In this context, 'provision' not only means specific individuals being invited to undergo a medical test, but also highlighting the opportunity to be tested in brochures or in the press, via advertising or promotion by commercial providers.

Screening can take the form of large-scale programmes for which all pregnant women, all newborn babies, or all men or women in a particular age group are eligible. But it can also entail patients (or a certain group of patients) being invited to a preventative examination by their GP, employees being offered tests by their companies, or people responding to an advertisement or a website offer for a health check with a clinic or a health organisation.

Self-testing kits

Predictive medical examinations that are provided or sold in the form of self-testing kits are also discussed in this advisory report as a form of screening. In strictly legal terms, this is only true of self-testing kits that are associated with a service, such as home collection tests. In these tests, users must take a sample of body tissue and send it to an organisation that then gives them the result. Self-testing kits that consumers can use without external help (DIY self-testing kits) are legally speaking only products, and so are not covered by the rules governing the provision of screening.[3]

Nevertheless, the committee is of the opinion that these DIY kits form part of the trend that sets the background against which the advisory report was requested: the creation of new opportunities for early detection and risk-determination, which are increasingly available to citizens outside the conventional State provision. Furthermore, there are important factors shared by the provision of medical tests to a population that, in theory, has no particular health problems and the sale of DIY self-testing kits. Not only are these tests sometimes carried

out to detect the same conditions, but there are also common features with regard to the consequences, both for the individual (reassurance and possible health benefit versus worry and possible health damage) and for the healthcare system. It is also important to bear in mind that someone whose DIY test result shows that something is wrong will visit their doctor, who may have to arrange further tests and support.

1.4 Structure of this advisory report

This advisory report addresses the following issues in turn:

- what social developments affect the role of screening? [chapter 2]
- what scientific developments will affect the role of screening over the next five to ten years? [chapter 3]
- are the current criteria for responsible screening sufficiently future-proof? [chapter 4]
- how can the government ensure that the public provision of screening is worthwhile and responsible? [chapter 5]
- how can the government ensure that there is adequate protection against dangerous forms of screening? [chapter 6]
- what measures should be introduced over the next few years to enable the government to fulfil its duty of care and responsibility to protect the public in respect of screening? [chapter 7]

The key outcomes of the international comparison that was requested are discussed in chapters 4 and 6. A report of the findings is to be found in annexes C, D and E.

Chapter 2

Social developments

Scientific progress and technological innovation have made new and better tests possible, but that alone does not explain the dynamics in the area of screening. Supply and demand are also driven by developments in healthcare and medicine itself, and by cultural, social, economic and political factors. In this chapter, the committee sets out the situation, the main elements and the interplay between the various factors involved.

2.1 New relationship between parties involved in healthcare

Healthcare is going through a process of profound change in many countries. It is taking place at different speeds, but the main thrust is always the same: moving from a government-regulated healthcare sector to one which is driven to a greater or lesser extent by market forces. In the Netherlands, the launch of the new healthcare system on 1 January 2006 should be regarded as an important milestone, but by no means as the end of this process.[4] The introduction of market forces has not only brought about significant changes in the structure of the healthcare system, but also challenges the parties involved in healthcare to re-define their own roles and responsibilities and to distinguish where the boundaries between each group lie. This entails more than simply considering the question of what should be done and by whom. The matter of how and why things are done also needs to be addressed. What exactly is good healthcare, and from whose point of view should this question be answered? Traditionally, the

medical profession exercised this 'defining power'[5], with the government monitoring quality and costs. The involvement of the market is intended to lead to better quality and a greater response to patients' needs, but it also sheds new light on how various groups (such as insurance companies, 'consumers' of care, etc.) would like healthcare to evolve. The consequence of that for this advisory report is that there is not necessarily a single vision, shared by all parties, as to what contribution screening can make to better healthcare and how and by whom this can best be achieved.

2.2 New relationship between collective prevention and individual care

Scientific developments and technological innovation (see chapter 3) offer new opportunities for identifying at-risk groups and early detection, with more tests being available for use at the point of care (at the bedside, in the consulting room, at home). Demand for this is also fed by a shift in emphasis in healthcare itself, with a general trend to blurring the familiar distinction between collective prevention and individual client-focused care.[6]

One important factor is that better treatment options and demographic trends (ageing population) has led to an increased focus on chronic diseases and risk factors that are relevant to them.[7,8] GPs' surgeries are seen as a particularly important setting for screening for such conditions. One of the models with which practical experience has been acquired involves using the GP information system to invite people who might be at high risk of cardiovascular disease for further screening.[9] People who are found to be at high risk can then be given lifestyle advice in addition to any treatment or further tests that are required.

At the same time, in the context of individual care, there is a growing awareness of the importance of regular medical examination of people who are at greater risk of contracting a specific (other) condition because of a health problem (a chronic illness, a congenital genetic or chromosomal defect, or a predisposition that has been identified from family tests).[10] These include life-long medical check-ups for people who underwent treatment for cancer at a young age.[11] They are no longer patients, but the primary therapy they have undergone means that they do have a greater chance of health damage later in life.[12] These check-ups are in fact more of an investigation into indications ('integral care') than screening, defined as providing predictive testing to a population that does not currently have any particular medical problem.[13] But the two procedures are not dissimilar, and this shows that it is not always easy to draw a clear distinction.

The grey area between collective prevention and testing for indications also covers predictive testing for (a tendency to) monogenic conditions in families with a genetic problem. Clinical genetic family testing that arises from a request for help is testing for an indication. But family testing offered systematically to all individuals on a family tree that has been traced both vertically and horizontally is a form of screening (cascade screening).[2] Screening for familial hypercholesterolaemia (FH), which is already carried out in the Netherlands, is an example of this approach.

2.3 Need for reassurance

In its report entitled *Gezondheidspolitiek in een risicocultuur* [Health policy in a risk culture], the Rathenau Institute places the development of predictive medicine in a broader cultural and historical context.[14] A more secular society and the fading away of a deterministic philosophy have made managing uncertainty a structural element in the way we order our lives. The report refers to modern society as a 'risk culture', a phrase coined by the German sociologist Beck.[15] As part of this, attitudes to illness and health have shifted to lay more emphasis on the importance of prevention both for the individual and for society as a whole. Looked at from this perspective, the rise of predictive medicine meets a deep-rooted need and goes beyond simply making use of new knowledge and opportunities. The message of the aforementioned report is that this makes it harder to produce a critical assessment of what is worthwhile and what is not. Uncertainty as to health in the future, experienced as a threat, together with the nature of the risk, which is often hard to understand and needs to be explained by experts, will make people receptive to anything that promises to eliminate that threat or at least make it manageable.[14]

This is also the thrust of *Humane genetica en samenleving* [Human genetics and society], a report by the Council for Social Development (RMO).[16] While the Rathenau report emphasises what it sees as the largely artificially created and to that extent improper demand for predictive tests ('hardly an autonomous demand'), the RMO stresses what it regards as the often irrational nature of decisions concerning participation in screening. The report refers to a study conducted a few years ago into attitudes to cancer screening in the United States. Questioning a representative sample (women aged over 40 and men aged over 50), Schwartz *et al* found great faith in the benefit of early detection of cancer, with hardly any attention to what doctors and scientists see as the downside.[17] A total of 87% of the respondents said they thought that routine cancer screening was 'almost always a good idea', and 74% thought that it could prove life-saving

‘in most or all cases’. Two-thirds of them said that they would be willing to undergo tests for an untreatable form of cancer.

Screening as a system without negative feedback

The need for reassurance appears to be an important reason for undergoing screening.[18-22] There is however no reason to describe this as an improper or irrational motive, as the aforementioned reports do. People go for screening because they hope to find out that nothing is wrong. Or if something should be amiss, then they certainly hope to hear that fortunately it has been picked up in time. One important point to make is nevertheless that screening can function as a ‘system with no negative feedback’.[23,24] In an article about why it is that American men (and many doctors) are so enthusiastic about screening for prostate cancer, since the potential health benefit is uncertain and the health risk (impotence, incontinence) is considerable, it is underlined that every possible outcome of every further step in the screening process appears to confirm the wisdom of deciding to undergo screening:

> A patient who is impotent and incontinent after a decision for curative treatment may attribute his survival to surgery and be grateful for having his cancer cured. Individual experience provides almost no negative feedback that early detection and aggressive treatment may not work. Although reinforcement operates similarly in other medical decisions, the example of prostate cancer provides insight into the strength of the forces at work because the personal harms, which are relatively common and dramatic, are readily discounted or explained away.[23]

The problem is not that the need for reassurance is an irrational motive. If someone is willing to accept the risk of considerable health damage in return for this reassurance, that is not necessarily irrational. But one of the problems is that the mechanism we are looking at here can impede a balanced weighing-up of the benefits and drawbacks of undergoing screening. As the negative effects of screening do not actually come to light, it appears as if screening has only benefits.[25] This is a misunderstanding that is not reserved to the lay population; many doctors also think that early detection of illness is always beneficial or in any case can do no harm.

Importance of being well informed

Being well informed can help people gain a better understanding of what they can really expect from screening. And is essential if they are to take well-

considered decisions. In the research by Schwartz *et al* referred to above, 73 percent of respondents said that, given the choice, they would rather have a total-body scan than be given a thousand dollars.[17] But in another study in which the participants were well informed about the actual benefits and drawbacks of this type of scan, the willingness to pay fell to 68 dollars.[26]

Research into breast cancer screening has shown that women severely overestimate the sensitivity and efficacy of screening mammography.[27,28] For that reason, good information is also essential to help people understand that a normal result may provide unjustified reassurance. If pregnant women know that a screening test for Down's syndrome is an assessment of probability, and that a normal result does not exclude the possibility of their unborn child having that condition, then reassurance is mentioned much less often as a reason for taking part in screening.[29]

2.4 Growing market value of screening

In the aforementioned articles on cancer screening in the United States[17,23], the enthusiasm for screening in that country is linked to years of promotional activity by public health officials, doctors and patient associations and marketing campaigns by commercial providers. The latter group in particular often puts across a simplistic message playing on emotions of fear, guilt and uncertainty. An important difference between the United States on the one hand and the Netherlands and other European countries on the other is that the healthcare sector in the US has been more commercialised for much longer. The recent change in the Dutch system has reduced this gap, and we will also be faced with ever more types of screening available on the free market. The request for this report mentions some potential benefits of this (such as cost savings and a more patient-friendly system), but also raises the risk of screening taking place in response to the pressure of commercial interests that has no certain benefit and results in unnecessary consumption of healthcare.

As can be seen from the Health Council's annual reports on population screening, this risk is at least conceivable.[2,3] A classic example by now is the total-body scan promoted in the Dutch media and carried out in German hospitals. This example also shows that commercialisation and globalisation go hand in hand, a phenomenon that is boosted by the role of the Internet. The Web offers new opportunities for commercial provision of DIY self-testing kits or lab services (home-collection tests) outside the institutional healthcare sector.[30-32] A recent review of the products and services provided by seven Internet firms active in this area concluded that the self-test kits they sell and the claims made

for them have insufficient scientific foundation and can have harmful consequences for users.[33]

The activity of the market has now also given groups traditionally involved in healthcare additional motives to offer screening. Dutch GPs, who have always questioned the benefits of health checks, but now see themselves increasingly faced with rising demand for healthcare generated by the provision of tests by other parties, would rather perform these tests themselves. Then at least they can give patients the benefit of their expertise and exert some measure of control over how many tests are done.[34] Pharmacists can find the provision of self-testing kits (also via the Internet) a lucrative way of boosting the sales of drugs such as cholesterol inhibitors. Insurance companies can find screening an attractive tool to stand out from the competition, and charities can see it as a way of maintaining their public profile and encouraging donations. But in none of these cases is it obvious that these activities, aimed at increasing market share, are actually beneficial to the health of the individuals concerned.

The new system does not give insurance firms sufficient incentive to offer their customers useful forms of prevention. That is because this involves long-term investment, and it is not certain, given the mobility of policyholders, whether the insurance firm that makes the investment would benefit from it.[35,36] Until that problem has been solved, insurance firms will tend to assess their prevention initiatives mainly on the basis of their promotional value.

A telling example is the ‘Stop kidney disease in the early stages’ campaign run by the Netherlands Kidney Foundation in autumn 2006, offering people free self-testing kits. By April 2007, this ‘kidney check’ had been requested by or on behalf of 1.1 million people (8.7 percent of the adult Dutch population). An evaluation study carried out by the Netherlands Institute for Health Services Research (NIVEL) concluded that ‘in terms of public awareness, the campaign was certainly a success’.[37] But the question remained whether the campaign was based on a screening strategy with a solid scientific foundation. The Health Council found that it was not.[3]

Mechanisms of this kind may proliferate as a result of greater commercialisation. Examples might include the incorporation of screening activities into the pay-for-performance schemes dictated by insurance firms (under which healthcare providers are paid for meeting agreed targets), policy discounts for policyholders who undergo regular medical check-ups (or fines for those who fail to do so), or agreements between employers and insurance firms. Researchers and universities also feel that they are coming under increasing market pressure. They are expected to contribute to the ideal of the knowledge economy by ‘valorising’ new scientific insights wherever possible. This can lead to pressure to launch

tests on the market too soon, as was seen in the case of G-nostics, a spin-off business of the University of Oxford. In 2004, a home-collection test available via the Internet was introduced on the back of insufficiently validated results of research into genes thought to increase the risk of nicotine addiction. Users sent in blood taken from a finger-prick and once the results had been determined were supposed to receive a personalised, and therefore more effective, offer of drugs to help them give up smoking.[38] The test is still available, but the University has pulled out of the business following criticism of its scientific validity.[39]

2.5 Emphasis on the individual as a 'consumer of healthcare'

The new system addresses the individual in the first instance as a 'consumer of healthcare with the ability to choose'.[40] The idea is that the provision of healthcare should match his or her needs better, and that this can only be done if there are actually options to choose from. This fits in with the modern ideal of self-determination, but is also and above all aimed at achieving a more cost-effective provision of care.[41] Critical choice behaviour on the part of consumers and insurance firms should keep healthcare providers (and providers of other forms of social services) 'on their toes' by forcing them to compete on the basis of quality.[42,43]

Of course, there is less opportunity for critical choice behaviour in the context of a screening test offered routinely to a particular group of the population. But it is not surprising that, as patients increasingly take on the role of critical consumers in the healthcare system, the call for as much individual choice as possible also seems to get a response here.[44] A telling example is the legal action taken against the State in October 2007 by three elderly women, with the support of the Clara Wichmann Foundation, for age discrimination. They applied for a temporary injunction against the policy of imposing an upper age limit of 75 for breast cancer screening. The initiative had the support of the patients' association. The plaintiffs lost their case, but have said that they will go to appeal.

There is no scientific reason for abandoning this age limit.[2,45] The benefits of continuing screening are outweighed by the disadvantages (over-diagnosis and over-treatment of breast cancer, which grows more slowly in older patients). However, in the light of the comments made above on the need for reassurance as an important reason for taking part in screening, it is understandable that women who are no longer invited for screening because they are too old see this as something being taken away from them: the loss of an acquired right. They find the fact that the likelihood of developing cancer increases with age a more important argument, and that even if you are over 75 you would like to know as

soon as possible. The idea that screening is always useful is difficult to correct by means of technical information on distorting effects such as lead time bias, over-diagnosis, and the possibility that even if an individual dies from a particular condition, he or she would otherwise have died from something else. In addition, consumers may indeed understand all this but still not be convinced. After all, they can argue that it is up to them to decide whether the advantages of screening outweigh the disadvantages.

The currently limited screening provision available outside the context of collective prevention seems to fit better into the concept of quality improvement by critical choice behaviour. This naturally depends on consumers having the information they need to really be able to make a choice on the basis of quality and that they do indeed do so.[41] The question of whether the system can function like this in practice is still hotly debated.[46-48] Given the comments made above on screening as a system without negative feedback, this is not necessarily the case for this part of the healthcare system.[49] Consumers of healthcare with the ability to choose are likely to demand increasing amounts of screening tests, but this is unlikely to push provision towards cost-effectiveness and quality.

In the American study referred to above, most of the respondents said that they would not simply accept the advice of a doctor not to undergo a particular screening test.[17] Canadian researchers found that, in contrast, doctors tended to order screening tests for worried patients who requested them even if they themselves did not think these were useful.[50]

2.6 Emphasis on individual responsibility

Individual responsibility is the moral counterpart to freedom of choice. Individuals as consumers have more opportunities to choose, but at the same time are urged to accept their civic duty to stay as healthy as possible.[40] This can be defined as including a particular lifestyle (not smoking, drinking responsibly, eating a healthy diet, getting enough exercise) as well as undergoing those screening tests that are regarded as useful.

Since 1988 this has been an explicit part of German Federal health legislation, with the provision that those covered by health insurance are ‘co-responsible’ for their own health and that they can be expected, among other things, to take part in good time in the forms of disease prevention offered to them by their insurers. A recent change in the law, introduced on 1 April 2007, gives insurance providers the opportunity to offer financial incentives to policyholders who always attend the screening test appointments to which they are invited (see

annex C). Individuals who fail to do so and fall ill have to pay a higher contribution to their medical care.[51,52]

But even without legally based directive measures, the (internalisation of the) message that people are responsible for their own health can be another impulse to people's willingness to undergo screening. Respondents to the aforementioned American study seemed to subscribe to this sense of social responsibility. They regard failing to undergo regular screening (especially among older people) as irresponsible behaviour.[17]

2.7 Conclusion: new contexts are boosting screening

The committee has two observations to make in relation to the situation described above. Firstly, new forms of screening are now being offered in addition to the government-funded population screening (recently restructured as the National Population Screening Programme). Details of these new opportunities are given in the table below. In the public healthcare sector (i.e. funded from public or collective resources), these are forms of screening that border on client-focused individual healthcare, such as preventive tests of at-risk groups in GP practices. Private provision has also appeared, ranging from health checks offered by GPs to 'uncontrolled screening' in the form of total-body scans and DIY self-testing kits available via the Internet.

The second observation is that this new situation offers both opportunities and threats. Opportunities because screening can bring about significant advantages in terms of health benefits, worthwhile treatment options, or information that is valuable to those concerned. Screening that is not offered by the government or in basic healthcare provision can be obtained privately by anyone who wants to avail themselves of it for personal reasons (treatment options, information).

Screening in new contexts.

Public	National population screening programme (see chapter 5): • population screening • systematic family screening (cascade screening) Other forms of screening in the healthcare/public healthcare sector: • preventive screening of at-risk groups in standard treatment practice • screening in the context of scientific research
Private	Private provision by doctors/general practitioners: • health checks Uncontrolled screening, usually in a commercial context: • general medical check-ups and body scans • home-collection lab tests DIY self-testing kits available for purchase

But there are threats as well. The description in this chapter shows that the demand for new tests and the growth of provision are not always, and certainly not for all parties concerned, accompanied by the thought (or even just the awareness) that screening can be harmful too.[2] The psychology of the modern risk culture, the interests of commercial providers, and the new emphasis on individual self-determination and responsibility do not offer a propitious environment for caution, especially since all these factors boost one another. An inevitable conflict arises between a professional and scientific (evidence-based) assessment of the benefits of screening and an attitude based on the views of the market and consumers.[53]

Both observations are important to the question of what the government's role should be (to be discussed later on in this advisory report). This role is less than self-evident and needs to be re-assessed. What does the government itself offer, and what is left to other parties (inside and outside the healthcare system)? And how can the government ensure that provision in these differing contexts meets minimum standards of quality and care?

Chapter 3

Scientific developments

What scientific developments might influence the role of screening inside and outside the healthcare sector over the next five to ten years? In this chapter, the committee looks at relevant developments in a number of scientific domains that may overlap to a greater or lesser extent. The focus lies on identifying new possibilities for screening rather than on assessing their potential benefit and value in the first instance.

3.1 Genes and the environment

Powerful analytical techniques and other new developments are now allowing us to find out much more about the structure and function of the human genome and therefore about the genetic background to an increasing number of medical conditions. This has been best charted for monogenic diseases, most of which are rare. These are conditions with a pattern of inheritance that is largely predictable ('Mendelian') and are caused by one or more mutations on a single gene. They are characterised by the fact that the inherited predisposition is very likely to be expressed.

Multifactorial conditions such as cardiovascular disease, certain mental conditions, rheumatism, dementia, diabetes, asthma, COPD and cancer are much more common and arise as a result of a complex interaction of genetic and environmental factors. Various genetic mutations are involved, and even if all of them are present they usually only slightly increase the likelihood of developing

the condition, probably if external factors such as diet, smoking and hormonal exposure are also involved. This situation is described as aetiological heterogeneity, which means a disease that can be caused by various combinations of risk factors. Furthermore, a single gene can be associated with more than one condition. There are also genetic variants that do indeed increase the chance of a particular illness (such as the likelihood of having a stroke) but that at the same time reduce the risk of another one (such as dementia).[54,55] We are only at the start of unravelling these complex interactions.[56,57] The development of automated genomics techniques has enabled scientists to quickly compare the inherited characteristics of large numbers of people. It can be used to detect subtle differences and look at them in the context of environmental factors.[58,59]

As far as genomic screening is concerned, the committee sees three possible trends: (1) new screening for a propensity to monogenic conditions, (2) screening for genetic sensitivity to multifactorial conditions and (3) as an extension to the first two, mapping someone's entire genome.

3.1.1 New screening for a propensity for monogenic conditions

The first of these trends is the least revolutionary, as the models and contexts already exist. Looking at the relatively rare dominantly inherited conditions, it would be possible (under the conditions discussed in chapter 4) to introduce a system similar to the model of cascade screening among families affected by familial hypercholesterolaemia (FH). Examples of new screening of this kind could include testing for monogenic conditions such as hereditary cardiac dysrhythmia (including long QT syndrome[60]) or certain types of hereditary cancer. Though these are not strictly speaking monogenic diseases, they are conditions in which a monogenic factor does determine a considerable proportion of the risk. Such 'Mendelian variants of complex diseases'[61] have a certainly incomplete but often high penetrance.[62-65]

In the same way, new information about the treatment of congenital metabolic disorders and other recessively inherited conditions that manifest in childhood could put the issue of expanding existing neonatal screening on the agenda. Though the debate on the pros and cons of such proposals needs to be thorough, they are simply an extension of what already exists in this area. This is not necessarily the case for any neonatal screening for untreatable conditions. The committee returns to this question in chapter 4.

The Health Council has recently suggested to the Minister that he should consider offering pre-conception screening to all couples planning to have a child to find out whether they are carriers of common recessively inherited con-

ditions such as cystic fibrosis and haemoglobin diseases (sickle-cell anaemia, thalassaemia).[66] The burden of such conditions is so great that couples who find out that they are both carriers (in which case there is a one in four chance that a pregnancy will result in a child with the condition) may decide to revise their plans for having children. Possible options include: not having any or any more children, donor insemination, in-vitro fertilisation and pre-implantation genetic diagnosis, or conception and prenatal diagnosis possibly followed by termination.[67] It is likely that if this pre-conception screening is introduced, it will give rise to a debate on expanding the system to include other conditions such as Tay-Sachs disease[66,68] and fragile X syndrome.[69,70] Some metabolic disorders may eventually be added to the list as well. An important point for debate is whether risk differentiation by population of origin is acceptable.[59]

3.1.2 *Screening for genetic sensitivity to multifactorial conditions*

Screening for genetic sensitivity to multifactorial conditions is a new development. Though these tests are already on sale,[3] the scientific foundations of most of them is by no means adequate.[3,56,71,72] It is true that scientists are increasingly finding associations that explain part of the risk, especially for breast cancer, macular degeneration and type 2 diabetes.[73-75] It is therefore legitimate to expect that in the medium to long term this research will be able to show that more and more genetic variants (DNA polymorphisms) are associated with a greater than average chance of developing a particular condition. The idea is that, given this knowledge, people with a particular genetic sensitivity can be offered tailor-made lifestyle advice.[76] Examples might include intensive support in giving up unhealthy habits, such as smokers with a genetic constitution associated with a greater chance of lung cancer[77] or obese individuals at greater risk of cardiovascular disease.[71,74] Research into the effects of tailor-made risk information shows that the combination of this information and advice customised to match the individual risk is very effective in changing behaviour.[78-81]

Further research is needed to show what this approach can add to the main preventive strategies that currently apply to everyone: exercise, a varied and sensible diet, and not smoking. Even without genetic information, anyone can get some idea of their risk based on their family history. This reflects the complex interaction between genes, behaviour, culture and the environment, and is so far the most consistent risk factor for the relevant conditions.[82] There is also a risk that the group found to have a lower than average risk might unjustifiably feel that they are protected, and so be less motivated towards healthy behaviour.[56,83,84] So not everything that might result from new screening opportunities in this area

is necessarily beneficial. However, the concept of individualised preventive medicine captures the imagination and is easy to sell.[3,33]

3.1.3 *The 'thousand dollar genome'*

The third trend is a continuation of the previous one. It is as yet prohibitively expensive to determine the complete sequence (three billion base pairs) of an individual's genome. If this process eventually becomes much cheaper, then mapping the whole genome could become a routine part of medical care. This is the background to hunt for the 'thousand dollar genome' sponsored by the American National Institutes of Health. In 2005 it was predicted that it would be at least another 15 years before determining this complete profile would be affordable to public healthcare budgets. At that time, the cost was estimated at around 10 million dollars.[85] This estimate has since fallen dramatically: to around one million dollars in mid-2007, when Craig Venter's genome was published, [86,87] and to 350,000 dollars in December that year.[88]

It has been suggested that, once complete sequencing of individual genomes becomes relatively inexpensive, screening of newborn infants would be a good time to obtain this information. The idea was discussed at length a few years ago in a report by the British Human Genetics Commission (HGC).[85] The aim of 'newborn profiling' would be to acquire an individual genomic database that could be consulted at all stages in later life where screening, diagnosis or individualised therapy or medication (pharmacogenomics) was needed.

The HGC report highlights the complex ethical, legal and social aspects of this idea. There are issues around privacy, data protection and data access, and also the psychosocial impact. What will having all this information available mean? How will people handle it? What social consequences might result? Furthermore, it is clear that some conflict exists with internationally recognised conditions for responsible screening (see chapter 4). The test is not looking for a specific and clearly described illness, obtaining informed consent (from the parents) is scarcely possible, and inevitably information will also become available on high or low risks of contracting serious untreatable conditions that only manifest later in life. This runs counter to current guidelines on testing children.[89,90]

In addition, it is conceivable that complete genome mapping would be conducted primarily as part of prenatal care rather than on infants, i.e. on individuals as yet unborn. This will then perhaps also be done as part of screening of embryos within the context of in-vitro fertilisation.[91] Women who are deciding whether to continue with a pregnancy or terminate it (or whether to place embryos in the womb) and are receiving counselling as part of the decision-mak-

ing process will be faced with information about a wide range of conditions and health risks that they might find hard to digest, and with information whose clinical significance is unclear.[92]

It is already anticipated that the karyotyping carried out in the context of chorionic villus sampling or amniotic fluid tests (which detect only chromosomal abnormalities that show up under the microscope) could be replaced by chromosomal testing using microarray technology (the 2007 Trend Analysis reports that large-scale implementation is not unlikely within the next five years, provided that the advantages and disadvantages are clarified).[59] This would not only lead to faster and cheaper prenatal chromosomal tests, but would also allow a larger number of subtle chromosomal abnormalities (deletions and insertions) and associated genetic syndromes to be detected.[93] Looked at from a theoretical perspective, creating a complete genome profile is not a very big step further down the line. Now that it is also possible to obtain DNA using non-invasive techniques by isolation from maternal plasma, eventually all pregnant women could theoretically be offered screening for thousands of genetic variations at the same time.[94,95] A recent comment warned that this development threatened to undermine the rationale and purpose of prenatal screening.[92,96] Even if producing a complete genome profile becomes affordable in the long run, the actual costs, particularly that of the counselling that would be required, will be high and may continue to prove a significant barrier. Obtaining information is a one-off process, but the subsequent pattern of events is not. The HGC speaks of an ‘ongoing duty of care (…) to regularly check the profile against developing knowledge of health related risks and to advise accordingly’.[85]

Another alternative that could be introduced sooner but provides less information would be to map only those parts of the genome that are known to be closely correlated with disease and the effects of medication at the time the test is carried out. At present, this type of testing often makes use of single nucleotide polymorphisms (SNPs, pronounced ‘snips’) that are stored in a variety of databases (such as Hapmap). Some commercial companies, such as 23andme, Navigenics and deCODE, already offer this service. They charge between 1,000 and 2,500 dollars to test the DNA in an individual’s saliva or mucus taken from the inside of the cheek against around a million markers. They interpret the findings using the latest information about associations with common diseases and other characteristics.

The risks of illness associated with these SNPs are usually very small. At present, only common SNPs are found, as the technique cannot detect rare ones. It is also starting to become clear that structural variation, such as variation in location and variations in the number of copies of genes (copy number variation,

CNV) plays an important part in someone's risk of disease[97-100], which depends on the combination of different SNPs. Much research is still needed before these general genetic profiles can add anything to the existing possibilities of early detection and prevention of disease.[33,101] What is certain is that premature introduction can have harmful consequences: large numbers of false positives, much unnecessary follow-up research, damage to health and high social costs.[101,102]

3.2 Biomarkers

Biomarkers are characteristic deviations in DNA, RNA and proteins that are used in determining the likelihood of disease, the nature of the disease, the choice of therapy and the individual's response to it, the progress of the disease and whether or not it is hereditary. The characteristics involved are germline-specific or tumour-specific properties such as multiplication, loss or translocation of chromosomes or parts of chromosomes, mutations, polymorphisms or modifications of genes, and also levels of expression of individual genes or groups of genes measured in RNA or protein. Biomarkers can also be functional proteins found in abnormal concentrations in bodily fluids such as plasma, brain fluid or urine.[59,103]

The word 'biomarker' is quite new, but the process of measuring various substances in blood, urine and other body material has been around for a long time. One example relevant to screening is PSA for prostate cancer. There is some common ground with the subject of the previous section: genome analysis ('genomics') also uses biomarkers.

If we have information about the make-up of someone's genome, we can say something about his or her chance of illness. Whether that person does indeed become ill depends on whether certain genes are expressed. This process is affected by interaction with other genes and environmental factors. Certain substances involved in it can be measured. This is another and in fact more accurate way of hunting down diseases. 'Proteomic' testing, looking at the expression profile at protein level, is therefore a rapidly growing area of investigation, as are 'transcriptomics' (looking at mRNA activity) and 'metabolomics' (investigating metabolic processes). Neonatal screening, mentioned above, is an example of the latter approach. Though most of what is tested for in this screening concerns hereditary conditions, the screening method used (MS/MS, HPLC etc.) detects abnormal metabolic products, not mutations.

Developments in genomics, proteomics, transcriptomics and metabolomics will lead to possibilities for screening for multifactorial conditions coming closer. Multiplex testing (testing a sample of tissue for various conditions - such

as hypertension, diabetes, obesity - in a single procedure) is likely to become commonplace in the long term. But the committee does not expect this to lead to a dramatic rise in population screening within the next five years.

Developments in microarray technology ('biochips'), mass spectrometry and bioinformatics have improved the speed and quality of analyses. It will become easier and cheaper to accurately measure large numbers of DNA fragments, proteins, mRNA and similar material. A lot of scientific research is being carried out into biomarkers that can easily detect disease or preliminary stages of disease. The 2006 annual report on population screening gave examples of tests that are already about to be introduced, such as urine tests for Chlamydia infection or prostate cancer.[2] In its second annual report, the Health Council described the dramatic developments in the area of self-testing kits.[3] The committee believes that the trend will continue. More and more fast, cheap diagnostic tests will become available, allowing people to test themselves. There will also be a rise in the provision of tests in which people take samples of body material (urine, saliva, mucus from the inside of the cheek) and send these to a laboratory, which then returns the results by post or e-mail.

3.3 Imaging techniques

3.3.1 Structural imaging

Conventional radiology (X-rays), echography, CT and MRI are tried and tested methods for displaying the location, size and structure of organs and other body parts. In screening, the only significant use of conventional radiology is for early detection of breast cancer. But this method is less suitable for women aged under 50: breast tissue is denser, which means that many tumours go undetected. Women with breast cancer in the family, or who have been found to have a BRCA1- or BRCA2 mutation, are at greater risk of developing breast cancer at a younger age. Research is being conducted into the use of MRI for the early detection of breast cancer in this high-risk group.[62,104] The Netherlands is about to become the first country to move to digital mammography for the national population screening programme. Other digital techniques are also being developed, such as digital tomosynthesis and stereo mammography.[2,105]

The question of whether echographic screening for abdominal aorta aneurysm (AAA, a local widening of the large artery that runs through the body) will be useful in the future is currently a matter of discussion.[2,106] Surgical mortality from the treatment used up to now for AAA, which involves opening up the abdomen, is around 7 percent. Surgical mortality is lower in the case of endovas-

cular treatment, but with the vascular prostheses currently available, this benefit is lost within a year or two.[107,108]

Approximately 2.5 percent of people who have a brain scan done are found to have a cerebral artery aneurysm. This percentage far exceeds the risk of an aneurysm of this kind ever bursting and causing a subarachnoid haemorrhage (0.6 percent). The possibility of over-diagnosis is therefore high. Furthermore, treatment is risky and the long-term effects of endovascular therapy ('coiling') are unknown. The benefits of screening are not expected to outweigh the risks.[25,109]

We are moving closer to a situation where imaging techniques will replace more invasive procedures such as colonoscopy. Considerable progress has already been made towards 'virtual CT colonoscopy'.[2,110-113] There is less experience with virtual MR colonoscopy, but this approach also appears promising, especially because it avoids exposure to radiation.[2,114]

Imaging techniques (MRI, CT) are likely to play an increasingly important role in the diagnosis of cardiovascular defects and perhaps also in screening for risk factors for cardiovascular conditions.[113] It is already possible to use advanced CT techniques without a contrast agent to produce a reliable estimate of the amount of calcium in the walls of blood vessels (coronary arteries, aortic arch, carotid arteries). But the question remains whether the results of such tests have any added value and whether these will motivate individuals to change their behaviour.[115]

The Health Council has already expressed its views on the body/total-body scans that some firms are now offering directly to consumers.[2] There is no proof that preventive scans are useful, and they can have serious drawbacks, such as the high chance of false-positive results and over-diagnosis leading to invasive procedures and (often unnecessary) expense. Having a scan once a year triples the likelihood of a 'lung cancer' diagnosis, for which surgical mortality is around five percent and the chance of serious complications is 20 to 44 percent.[116] But a beneficial effect on mortality and metastised lung cancer has not (yet) been established. Also worth mentioning is the high number of defects that are detected but whose significance is unclear.[25,117,118]

Exposure to radiation

The dose of radiation administered per image is on a downward trend. At the same time, however, the total exposure to radiation is increasing because the number of images taken per session is rising (partly due to multislice CT, used to create three-dimensional reconstructions) and because CT is being used more

often. This is because it is now more easily available, and so doctors are more likely to order a CT scan, and because consumers ask for preventive screening, sometimes on the prompting of their medical insurance company.

A total-body CT scan involves an effective radiation dose of up to 22 mSv, though the exposure is of course lower if only part of the body is scanned. A low-dose CT scan of the lungs involves an effective dose of 0.3-0.6 mSv.[119] The amount of radiation administered in a scan of the heart or the large intestine is around 2-7 mSv[120,121], depending on the type of scan and the patient's weight and gender. It is widely agreed that rising radiation exposure rates are a cause for concern.[122-124]

3.3.2 *Functional imaging*

The functional imaging techniques currently in clinical use are PET and SPECT. Both of these techniques use radioactively marked substances that are absorbed in the metabolism. They can reveal processes such as persistent bleeding, oxygen consumption, oxygen deficiency and glucose metabolism, and detect abnormal metabolic processes. They are used mainly in the diagnosis of common tumours such as lung cancer, breast cancer and colon cancer, and sometimes also to assess response to therapy. It is expected that these techniques will be used at earlier stages in the course of disease[125] and might eventually be considered for use as screening instruments.[113]

It appears likely that functional imaging will continue to evolve towards representation of biological processes at molecular level, using techniques such as MRI or CT. This combination of biomarkers and imaging, referred to as molecular imaging technology, will probably make the move from the research lab to the hospital within the next few years.[125-129] But this does not mean that their use as worthwhile screening instruments is imminent. It is however true that PET and PET/CT are already used widely to screen for cancer in Japan and Taiwan, and to a lesser extent in the United States as well.[130]

It is anticipated that combinations of structural and functional (molecular) imaging techniques will improve their predictive value and so make them more valuable as screening instruments. Dementia is one example of this. Though no treatment is available (other than perhaps relieving the symptoms), there is a demand for risk profiling for dementia. This may eventually become possible thanks to a combination of structural and functional information. The test criteria for diagnosing Alzheimer's disease are already based on this approach.[131] The committee expects the debate on the desirability of screening for Alzheimer's disease to continue.[132-135]

3.3.3 *Long-term developments*

Nanotechnology, which is developing fast[136,137], is almost certain to offer new applications for molecular imaging.[129,138,139] But structural imaging in medicine is making progress as well. Try to imagine a disposable video camera/transmitter/light source combination the size of a pill that sends colour images to a receiver/recorder around the patient's waist while the camera is passing through his or her digestive system and detecting tumours or other abnormalities. It sounds like science fiction, but the PillCam has already been invented.[129]

Developments in bio-informatics and the creation of new hardware and software for performing complex calculations should improve the opportunities for computer pattern recognition. This should clear the way for automated assessment of screening resultats.[129]

Finally, technical research is being carried out into the use of various new, harmless sources of radiation, such as visible and infra-red light, microwaves, very high-frequency vibrations (tetrahertz), and so on. However, it is very unlikely that these will be available within the next few years.

3.4 Questionnaire-based tests

Screening that makes use of written questionnaires can offer major practical advantages. It is not very time-consuming, does not need any special premises (can be done via the Internet) and analysis is often quick. Questionnaire-based tests are therefore a cheap, relatively straightforward instrument, and are also suitable for use in self-testing. Concise screening instruments are available for various conditions.

3.4.1 *Questionnaires for mental disorders*

There are many questionnaires used in detecting mental disorders, and most of these tests are easily accessible via the Internet. Examples include depression, anxiety disorders, ADHD and alcoholism. They are short, simple questionnaires that can pick up disorders in a sensitive and specific manner, though this does not automatically mean that systematic screening is effective too. For example, the efficacy of interventions following systematic screening for depression of patients in GPs' practices has been found to be low, probably because the people who are picked up in this way have little need for help because their symptoms are mild and they are likely to recover without intervention.[140-143]

The efficacy of systematic screening for anxiety and alcohol-related disorders has not been established either, and it is not effective at population level. But it is not impossible that written questionnaires could become useful in the future, for example in the diagnosis of people with a suspected mental problem or as an instrument for selective use among high-risk groups.

In addition to questionnaires that people fill in themselves, there are standardised lists for use by trained professionals, for example in detecting cognitive decline and early dementia among elderly people, mental disorders that could cause problems for women during pregnancy or labour[144], or learning difficulties or autism among children. These tests are increasingly being used both in screening and diagnosis. For example, it has been found that early detection and treatment of dyslexia improves performance at school.[145]

3.4.2 *Questionnaires for other conditions*

Questionnaires are rarely used as the only instrument in detecting conditions. But their importance as part of the screening process is increasing. It is anticipated that written questionnaires will identify people with particular psychosocial risk patterns that increase their risk of certain somatic conditions such as cardiovascular disease. One example could be people with a neurotic or type D personality, or people who have a poor social network because of certain conditions.[146,147] It remains to be seen whether this approach is effective.

3.4.3 *Points to bear in mind*

The provision of self-testing kits in the form of questionnaires, especially via the Internet, is expected to rise in coming years. But the Internet also offers many questionnaires of dubious validity. It is becoming increasingly difficult for lay people to distinguish the wheat from the chaff. In addition, Internet self-tests and the associated care in the case of a positive result are often offered by the same individual or organisation. It is not impossible that the interests of the provider (classifying as many people as possible as patients) could take precedence over those of the person completing the test.

And the risk that people might give the answers they know to be socially desirable should not be ignored. This limits the usefulness of questionnaires.

3.5 Integrated risk profiling

Combining the results of various types of tests is referred to as risk profiling. This is not entirely new; 60 years ago it was described as ‘multiphasic screening’.[148] Risk profiling can be used to pre-select a high-risk group. This allows screening to be performed on a tighter group than if pre-selection were based only on age and sex. It mainly uses a combination of questionnaires, lab results and functional tests. An example of this kind of approach is the current research being done in the Rijnmond region into the benefits of screening for type 2 diabetes. Offering people over the age of 40 a questionnaire and a tape measure to determine their waist size produces a high-risk group that might benefit from being screened for diabetes.

A process known as ‘integrated risk profiling’ could also be applied in an attempt to devise a more targeted approach. This uses the fact that some chronic diseases have common risk factors. The NDDO Institute for Prevention and Early Diagnosis (NIPED) has compiled a list of questions relating to topics such as medical history, family diseases, general health, mental state and lifestyle. These are combined with findings for blood pressure, weight, waist size and height, and the results of lung function, urine and blood tests to create a medical profile and an associated health plan. This involves not only lifestyle advice but also targeted screening for particular conditions.

Further research is needed into the added value claimed for such an approach. At the end of 2006, NIPED was granted a permit under the Population Screening Act to carry out scientific research into colonoscopic screening for intestinal cancer using individual risk profiling comprising a digital questionnaire, physical examination and lab tests on blood, urine and faeces (FOBT). The report of findings emphasises that this kind of approach can have a ‘downside’ in terms of the possible psycho-social impact of some elements of risk profiling and the possibility of over-diagnosis and over-treatment.[149]

3.6 Conclusion: high expectations, rapid developments, uncertain clinical benefit

Developments in genomics and associated areas, nanotechnology and imaging techniques in combination with developments in bioinformatics, computer science and, not forgetting (the use of) the Internet, will have a decisive impact on what happens in the future. New technological developments are usually first applied in the treatment of patients as a diagnostic method or as an instrument to

monitor the effect of the therapy that is being administered. They are normally extended to screening of healthy populations later on.

Expectations are high and scientific and technological developments follow each other in quick succession. But this does not mean that useful new screening opportunities will rapidly become available. Firstly, the process of unravelling the genetic background to common diseases is in the very early stages. Secondly, responsible screening involves more than simply identifying or mapping disease, predisposition or risk factors at an early stage. To start with, it is essential to have a suitable test that can be administered to a population that is currently healthy and distinguish between individuals who do have the relevant characteristics and those who do not. In addition, early detection only makes sense if it is certain that those affected can have some health gain or other benefit, and that these advantages outweigh the disadvantages.

The committee nonetheless expects the range of screening provision to become broader and more diverse over the next five to ten years. Examples include:

- an increase in the number of dominantly inherited monogenic conditions that are suitable for cascade screening;
- an increase in the number of monogenic conditions that are suitable for neonatal screening;
- an increase in the number of monogenic conditions that are suitable for preconception carrier screening of couples wishing to have children;
- screening for genetic sensitivity for common multifactorial conditions with test panels of genetic variants;
- detection of diseases at an earlier stage thanks to the use of biomarkers and imaging techniques, either in isolation or in combination;
- extending the practice of identifying and selectively screening at-risk groups, especially by means of questionnaire tests and in combination with one or more of the aforementioned screening methods. It is likely that this will increasingly happen by means of a single procedure creating risk profiles for a range of common conditions, which may or may not be carried out as part of routine patient care;
- an increase in the provision of self-testing kits.

Chapter 4

Criteria for responsible screening

The Minister wants to know whether the normative framework for population screening is sufficiently future-proof. By this he means the conditions for responsible population screening formulated for the World Health Organization by Wilson and Jungner in the 1960s[150] and further refined and adapted by various authors and organisations later on, particularly with a view to developments in genetic and reproductive screening (see annex D). Examples of such refinements include the work done in the Netherlands by the Health Council[1], in the United Kingdom in the more recent reports of the National Screening Committee[151,152], in Canada (Quebec) by the HTA advisory board AETMIS.[153] Significant international contributions have been made by the Council of Europe (recommendations R(92)3 and R(94)11), the European Society for Human Genetics [154] and participants in the ACCE project.[155] All this work has produced a normative framework for the assessment of population studies that has broad international support, although some elements remain the subject of debate.

When we look at the question of whether this framework is future-proof, we need to examine two perspectives. Firstly, the question of how it relates to the new scientific developments described in the previous chapter. Is it able to adequately guide the responsible introduction of the new screening opportunities that are likely to be created? The second perspective is linked to the observation (at the end of chapter 2) that, for a considerable time now, screening has no longer been merely a matter of the conventional population screening offered by the government. The fact that the current framework was devised primarily for

that conventional population screening approach raises the question of which parts of it are of importance in other contexts and which are not.

4.1 Principles of the current normative framework

The general principles in the aforementioned framework can be summarised as follows:

- screening must be focused on a *significant health problem*;
- *benefit*: it must be clearly established that early detection of the illness(es) or condition(s) in question (or: detection of medical conditions such as carrier status or risk factors) can lead to a significant reduction in the burden of disease in the target group in question, or to other outcomes useful to the participants in the context of the medical problems to which the screening relates; these advantages must clearly outweigh the disadvantages that screening can always have (for themselves or for others);
- *reliable and valid instrument*: the screening method must have a solid scientific basis and the quality of the various parts of the screening process must be guaranteed;
- *respect for autonomy*: participation in screening and follow-up tests must be based on an informed and free choice; supply and performance must respect patients' rights (in the case of services offered outside the healthcare system: consumers' rights);
- *appropriate use of resources*: the use of available healthcare resources in connection with and because of the programme must be clearly shown to be acceptable in terms of cost-effectiveness and justice.

These general principles need to be fleshed out before they can serve as a practical guide, both in general terms and for specific forms of screening, as has been done for neonatal screening[156] and screening for hereditary bowel cancer[157,158]). This advisory report is not the proper setting for a detailed examination of these issues.

4.2 Significant health problem

Contrary to popular opinion, screening does have a down side and does not usually save on the healthcare budget. Looking at the social justification of screening offered in the public sector (i.e., paid for from public or collective funds), it is therefore essential that the test relates to a significant medical problem.[6] That does not mean that the condition in question must always be a

public health problem with a high prevalence. The classic example, already mentioned by Wilson and Jungner, is neonatal screening for phenylketonuria (PKU). This condition is 'extremely uncommon but warrants screening on account of the very serious consequences if not discovered and treated very early in life'.[150] Reformulations of the criteria have often emphasised that 'significance' can relate both to prevalence (common illnesses or conditions) and to severity (see annex D).

This condition does not apply to private-sector screening carried out by doctors, laboratories or commercial firms. Screening for a propensity to baldness has no part in a government programme or the basic healthcare package, but if people wish to pay for it themselves, that is not a problem. Grosse and Khoury express this as follows:

> we agree that consumers have a legitimate interest in obtaining access to services that they consider to provide good value for money, and we believe that they should have the freedom to use their own resources in this way. Nevertheless, it is questionable that third-party payers, public or private, should be obligated to pay for services that lack a demonstrable health impact.[159]

4.3 Benefit: ratio of advantages to disadvantages

It is not enough for screening to lead to early detection of disease or to information about carrier status or risk factors. After all, the purpose of screening is not the actual outcome of the test, but rather the ensuing health gain or other benefit to the person being tested. The American literature uses the term 'clinical utility' in this context.[159] In a more limited sense, this term refers to the extent to which the use of a test or screening method can help prevent or reduce the burden of disease in terms of mortality, illness, or quality of life. In a broader sense it means whether, all things considered, the benefits that screening can offer those affected outweigh the drawbacks that always exist as well.[155,159] In this broader sense, this condition applies both to public-sector and private-sector screening, including the sale of DIY self-testing kits.

4.3.1 Screening must produce a health gain

One of the conditions put forward by Wilson and Jungner is that there must be an acceptable treatment for people in whom early-stage disease is found. It is consequently essential that this treatment leads to a better prognosis than would have existed without early intervention. After all: 'unless this is so, there can be no advantage to the patient and, in fact, in alerting him or her to a condition that

has not been shown to benefit by treatment at an earlier stage, actual harm may be done'.[150]

This assumes not only that the screening test is for a condition with a recognisable latent or early stage; it also involves knowledge of the natural course of the disease and a clear policy as to who should be regarded as a patient on the basis of a particular test result, as otherwise over-diagnosis and over-treatment would result.[150]

Newer wordings of these conditions take account of the fact that, unlike in the time of Wilson and Jungner, screening can also look at hereditary predisposition to illness or genetic variations that play a part in the development of multifactorial conditions (see annex D). In the case of this type of screening as well, the benefit does not come purely from the test results but depends on how the information can subsequently be used. The requirement for a solid scientific foundation (see annex D), which some texts include as a separate criterion, is also mentioned in Wilson and Jungner's document in the statement that 'accepted treatment' must improve the health prognosis for the group that has undergone screening: 'It is clearly vital to determine by experimental surveys whether a better prognosis is given by treating the conditions found at an earlier stage than was previously the practice'.[150]

4.3.2 *The ratio of advantages and disadvantages must be positive*

Some more recent texts describing the normative framework include the fact that there must be a favourable ratio of advantages to disadvantages of screening for participants in the form of a separate requirement.[1,153] This requirement, which is also implicitly to be found in Wilson and Jungner's work, can be regarded as the core of the normative framework we are discussing here. It is too often assumed that early detection always leads to a better prognosis. Or that, even if that is not necessarily the case, 'being informed as soon as possible' cannot do any harm. But the truth is that screening can do harm, and in most cases it does. False-positive test results and over-diagnosis lead to unnecessary tests, interventions, anxiety, physical health damage and costs. False-negative results can produce unjustified reassurance. Offering screening is only responsible if it has been ascertained that the individuals being tested will definitely benefit.

For example: even under the existing system of screening for breast cancer, if population screening is applied in the optimum manner and all appropriate follow-up treatment is given, 'only' 27 percent of women found to have breast cancer will benefit. For the other 73 percent, the disease is indeed picked up a few years earlier, but this has no effect on survival rates (53 percent would have been

treated early enough to prevent metastisation even without screening; 13 percent die from breast cancer in spite of early detection; 7 percent would never have known that they had breast cancer if they had not been screened because they would have died from some other cause before the symptoms of the disease appeared).[160]

Genetic screening

Partly as a consequence of the introduction of genetic screening, and reproductive screening which overlaps it to some extent, more recent documents on the normative framework are starting to pay more explicit attention to the possible negative psychosocial consequences of screening. This includes not only the feelings of anxiety and uncertainty produced by an abnormal result, but also undesirable social effects such as stigmatisation, exclusion or discrimination. These psychosocial effects, too, must be included in the assessment of advantages and disadvantages, and based on the strongest possible evidence. Of course, genetic screening also affects the interests of the blood relatives of participants.

Concern as to the possible social consequences of genetic screening would appear in the first instance to arise mainly in the context of screening for a hereditary predisposition to a monogenic disease (including the 'Mendelian variants of common diseases') and less so in the case of screening for genetic 'sensitivity' to certain common diseases ('susceptibility testing'). The predictive value of the results of this type of screening is generally low, and the likelihood that relatives will have exactly the same genetic profile as the person being tested is very small.[161] Nevertheless, it is true to say that if a large number of high-risk genes are present in combination, a small group of individuals may be faced with a very high risk of a certain condition.[162] These can include serious conditions for which no treatment (or no proper treatment) is available, such as Alzheimer's disease. If integrated risk profiling is performed, a process which often tests for a large number of conditions at the same time, it is conceivable that people will not be sufficiently prepared for such an outcome.

Screening for untreatable conditions

But the situation has become more complex in respect of possible benefits as well. Wilson and Jungner assume that screening for untreatable conditions can be of no benefit to participants, and so should not be offered. But some later texts defining the normative framework, including that produced by the Health

Council, explicitly allow for the possibility of screening for conditions for which no treatment (or in the case of genetic screening, no prevention) is possible , arguing that there can still be a favourable advantage/disadvantage ratio, namely when an abnormal result leads to (other) useful outcomes for the participants.[1,152,163] It must also be borne in mind that 'treatability' is certainly not always a simple 'yes or no' question.[164] In an earlier report, the Health Council stated that there must be 'a favourable effect caused by therapeutic or preventive intervention that has a relevant impact on clinical outcome measures, i.e. mortality, illness or quality of life'.[165]

4.3.3 There must be practical courses of action open to the participants

The broadening of approach from the principles initially laid down by Wilson and Jungner followed the introduction of prenatal screening for foetal conditions such as Down's syndrome and neural tube defects. The specific aim of screening for those conditions is to give information to pregnant women who want to have it, so that if the test results turn out to be abnormal they can decide whether or not to terminate the pregnancy.[166] How does this fit in with the idea that screening must open the way to treatment or prevention? Treatment is not an option here. And prevention? If a foetus is found to have Down's syndrome or another condition, and the pregnant woman decides to terminate the pregnancy, she does so - however difficult and distressing that decision is - in order to avoid having a child that may be seriously ill or handicapped. But because this decision can only be justified as the highly personal choice of the pregnant woman (and her partner), the term 'prevention' must be used very cautiously in this context. Selective abortion is not a normal preventive measure, and must not be presented as such.

Options for reproductive choice

The following quotation shows clearly what is at stake here. According to the authors of a British HTA study, the aim of prenatal screening is: 'to reduce the birth prevalence of the disorder (…) by identifying (….) couples who can have prenatal diagnosis and selective termination of pregnancy'.[167] Of course, this does not clearly state that pregnant women must decide to have an abortion if the test results are bad, but the fact that they are likely to do so is a condition for achieving what is regarded here as the aim of screening provision: reducing the number of children born with the condition in question. That makes this formulation problematic, because what is and must remain a highly individual

decision by the pregnant woman is presented as an obvious and socially desirable choice. There is a danger here that expectant parents are put under pressure to take the 'right' decision and perhaps even held responsible for the outcome if they fail to do so. It might also be thought as implicit in this aim that people with such conditions have no place in society.

In order to avoid these moral pitfalls, there is a broad international consensus that the aim of prenatal screening for foetal abnormalities such as Down's syndrome must not be worded in terms of prevention or health gain, but as giving those concerned worthwhile options from which to choose.[1,166,168] This approach is in line with the normative principles of clinical genetics and hereditary counselling, the context from which this form of screening actually evolved.[169]

The normative framework criterion discussed in this section relates not to the purpose of screening provision but to its possible benefit to participants. But as is clear from the discussion above, these perspectives lie close together. The reformulation proposed by the Health Council's Committee on Genetic Screening aims to rule out any misunderstanding as to the aim of prenatal screening by laying down the (general) condition that there must be 'practical courses of action for participants'.[1] The explanatory notes to the document emphasise that this includes 'the choice between continuing with or terminating a pregnancy'.[1] The recent document drawn up by the Canadian HTA organisation AETMIS actually states that, in addition to health gain as a consequence of treatment or prevention that has been proven to be effective, the benefit of screening can also lie in 'reproductive choice based on an improved risk assessment'.[153] The criteria of the British National Screening Committee refer to 'effective treatment or intervention', but at a later point in the document it is stated that the only aim of prenatal screening for conditions such as Down's syndrome is to enable the pregnant woman to make an informed choice.[152]

Timely decisions concerning further life-plans

The wording 'practical courses of action' indicates that screening for serious conditions for which there is no effective treatment or prevention can take place in contexts other than pregnancy and reproduction. This is explicitly emphasised in the recommendations and criteria drawn up by the European Society of Human Genetics: it can involve 'health-related reproductive or life-style choices.[154] Another example is the wording used by the French *Agence nationale d'accréditation et évaluation en santé* (ANAES) [French National Agency for Accreditation and Evaluation in Healthcare]. The requirement for effective intervention to be available has been expanded by adding a definition of

‘intervention’, which should be understood to mean: ‘a treatment, a preventive measure or information that is felt to be important for the individual with the disease’.[163]

The room that these wordings create in terms of screening for non-treatable conditions signifies a break with Wilson and Jungner’s initial approach. It is defended by referring to the key principle that the benefits for participants must outweigh the drawbacks. These benefits need not necessarily involve only treatment, prevention and health gain. Where this is not possible, or not to a sufficient degree, other factors come in to play such as taking timely decisions about how to spend the time remaining (relationships, where to live, working, healthcare, saying goodbye to loved ones, etc.). In the case of serious untreatable conditions, the balance will, for that matter, not easily shift to the ‘benefits’ side.

One example of this is the current debate on early detection of dementia.[135,170,171] As very little treatment is currently available, and as the relationship between benefits and drawbacks is not clearly understood, systematic early detection has been rejected.[172-174] This decision expressly takes account of the question of possible benefits other than treatment or prevention:

> Individuals identified with early dementia by screening may have the opportunity to discuss the nature of the syndrome, its prognosis, and future planning with regard to health care, safety, and finances. They may be able to formulate advance directives; choose a person to exercise power of attorney for financial and personal care decision making; consent to participate in research; and contemplate issues such as motor vehicle driving, self-neglect, financial victimization, and housing relocation. Screening may also permit earlier and more effective treatment of co-existing conditions by improving medication adherence and avoiding drug interactions. No high-quality study has been done to verify, quantify, or refute these potential benefits.[172]

A recent American trial population screening programme into dementia among elderly people (aged over 65) without symptoms attending their GP clinic found not only a considerable percentage of false-positive results, but also discovered that almost half of those who tested positive did not want to undergo any further diagnostic testing.[175] This result not only emphasises the importance of better test methods, but also of further research into public attitudes to the possible advantages and disadvantages of early detection of dementia.[171] Further investigation of the ethical and legal implications is also necessary.[135] Although such screening is therefore premature at the moment, there is no good reason why it should be excluded from the normative framework at this stage.

4.3.4 *Useful information*

The wording ‘practical courses of action’ is on the one hand narrower but on the other hand broader than the French wording referred to above (‘information that is regarded as being important to the sick person’). ‘Courses of action’ means that something can be done, while information can be useful because it meets the need of the individuals affected to know what they can expect, for example so that they can prepare for it emotionally. This is a justified addition that is also in line with the thinking behind the criterion of ‘practical courses of action’.

On the other hand, the phrase ‘sick person’ seems to imply that the French wording can apply only to early detection of a disease that is already present in latent form, rather than to screening in the sense of detecting carrier status or a higher genetic risk of contracting a serious and untreatable condition later in life. No reasons are given in the document for this limitation. Is the thinking that early detection of an untreatable condition can lead to useful information for the person affected, but that this is not the case for a predictive test or risk assessment? It would seem difficult to uphold such an argument.

Emotional preparation

In this context it is interesting to consider the results of a prospective randomised trial population study into the psychosocial aspects of screening for genetic sensitivity to Alzheimer’s disease (REVEAL study).[176-180] This type of screening cannot predict whether or not someone will develop dementia in later life, but can indicate whether they are at greater risk. Adult children of patients with Alzheimer’s disease were invited to take part in the study. They were given comprehensive information about the nature, limitations and possible implications of a genetic sensitivity test and about the lack of effective methods of treating or preventing Alzheimer’s disease. During the explanation, they were told about information obtained from association studies regarding the life-time risk of Alzheimer’s disease among first-degree relatives with various genotypes (combinations of alleles of the APOE gene), ranging from 13 to 57 percent. As a basis for comparison, they were told that the general risk among first-degree relatives was 20 percent, and that of the general population was 10 percent. Given this information, a quarter of the group which responded to the invitation decided to have the test.

The study had various aims, including mapping their motives. Important motives included being able to settle personal affairs, achieving certain life plans

earlier than they would otherwise have done, and emotional preparation of the individual or his or her relatives.[176,180] So far, no significant negative psychosocial effects have been found.[177,181]

The conclusion is not that screening for genetic sensitivity for untreatable conditions such as Alzheimer's disease can be responsibly offered, but rather that when assessing the benefit that such screening can have for the participants, consideration of the benefits should not be limited to ascertaining whether treatment or prevention is available: attention should also be paid to the possible importance of other action options, or even just receiving information in good time, for those affected. The normative framework must therefore offer space for this.

'The value of information per se'

A recent American discussion has made the point that 'demand from consumers and marketing by commercial laboratories and test developers have emphasized the value of information per se'.[159] This seems to follow naturally from the expansion of the utility criterion discussed here: 'In its broadest sense, clinical utility can refer to any outcomes considered important to individuals and families'[159]. It is worthwhile noting here that only accurate and reliable information can be useful to those concerned, and that the greater the disadvantages of screening are, the less likely it is that the possible 'value of information per se' will outweigh them.

4.3.5 Useful for whom?

As the interests of third parties may also be affected by genetic screening, the question of how a possible conflict of interest should be handled arises. The principle that the advantage/disadvantage ratio must be favourable to the participants implies that people cannot be required to undergo screening purely in the interests of others (or purely with a view to achieving social objectives).[1] But in recent years a debate has begun on whether this principle is too stringent in the context of neonatal screening.[182]

The interest of the child as the conventional aim of neonatal screening

The conventional aim of neonatal screening is to prevent damage to the health of infants by detecting conditions that can be effectively treated at an early stage.[183-185] In the days of Wilson and Jungner, the only such condition was phenylketonuria (PKU), but the range of illnesses that can be detected has grown

dramatically especially since the invention of tandem mass spectrometry (MS/MS). In the Netherlands, the heel prick test now screens for sixteen extremely rare but serious and treatable childhood conditions. But carrying out an MS/MS test in the same procedure to detect a number of other conditions for which there is (as yet) no treatment or prevention would pose no technical difficulties. This does not necessarily mean that screening for such conditions cannot confer any benefit on the child (early detection can certainly avoid the diagnostic long-haul through the healthcare system and enable optimum care to be given as soon as the first symptoms appear), but the question then is whether these benefits are enough to justify screening.[186,187]

Interests of parents and the family

The situation appears rather different if we look at it not only from the point of view of the benefits to the child, but also take account of the interests of parents and the family as a whole. As most of the conditions in question are (recessively) hereditary, parents (and their blood relatives) also have an interest in untreatable conditions being brought to light through screening. This will enable them to take the likelihood of recurrence into account if they intend to have more children.

Contrary to what is sometimes suggested in the debate, we are not talking here about the general question of whether screening for untreatable conditions can be acceptable.* This question has already been adequately answered above: further to the health gain, providing practical courses of action can also be an acceptable goal of screening. It is obvious that neonatal screening for untreatable conditions can lead to practical courses of action. The question here is not whether such outcomes are useful, but rather: useful for whom? Can additional screening of newborn infants also be acceptable if it only serves the interests of parents or the rest of the family?

Some commentators consider that this problem has been superseded.[189] Developments in this field should lead the situation to be regarded from another point of view, in which the interests of the person (the infant) being screened are not necessarily paramount: ‘in neonatal screening, the beneficiary is the family’.[190] This does not appear to be a good proposal. Firstly, it merely covers the possible divergence of the interest of the child and of the parents. Secondly, if the benefit to the family as a whole takes precedence, it has already been decided

* This suggestion is also implicit in the letter sent to the committee by the Biotechnology and Genetics Forum on 10 January 2008.[108]

that, in the event of a conflict of interest, those of the infant that has undergone screening can be overridden. The reformulation of 'Wilson & Jungner' by the Canadian HTA body AETMIS is unsatisfactory as well. It emphasises that there must be a favourable ratio of advantages to disadvantages for 'individuals and families', but fails to address the question of whose interests have priority when it comes down to it.[153]

'No disadvantage to the child' as a justifiable criterion

It would seem more fruitful to investigate whether the principles underlying the normative framework do not leave any room for additional neonatal screening that is not also in the interests of the child. From an ethical point of view, it is vital that the person undergoing screening is respected as an individual and not simply treated as a means to meet the needs of others. It can be argued that it is not necessarily a case of unacceptable 'instrumentalisation' for the child to be screened for certain conditions if this would be beneficial to the parents but not to the child, but it would be considered unacceptable if the child might suffer disadvantage by it.[90,182,191] As this involves additional screening carried out using the same heel-prick blood that is used to screen for treatable conditions, it must concern disadvantages related to the information obtained. One example of this would be the psycho-social impact of an unfavourable result on the parent-child relationship.[192] If it is sufficiently clear that no such disadvantage is to be feared, then additional neonatal screening that is purely in the interests of the parents (bearing the conditions of proportionality and subsidiarity in mind) might well be acceptable. But further discussion on this is needed.

The recent draft additional protocol to the convention on human rights and biomedicine concerning genetic testing for health purposes drawn up by the Council of Europe does leave somewhat more space for this: the expected benefit to the parents must 'significantly outweigh' the risks associated with collecting, processing or sharing the information.[193]

4.4 Reliable and valid instrument

Test methods used for both public-sector and private-sector screening must be reliable and valid. The former means that repetition of the test must give the same outcome (reproducibility); the latter means that the test must measure what it is supposed to measure.

4.4.1 *Analytical and diagnostic validity*

Analytical validity is a description of the performance in a trial design in the laboratory, for example how often a test produces a positive (abnormal) result in the presence of the genetic mutation which is being sought (the genotype). Clinical or diagnostic validity goes a step further: how often does the test give a positive result for individuals who have or develop the condition in question (the phenotype) and how often does it produce a negative (normal) result for people without that phenotype? A test can accurately indicate the presence or absence of a genetic mutation, for example, but if people with that mutation hardly ever develop the disease, the test serves no purpose. So looking at analytical validity alone is not enough.[155]

The validity of a test is determined by the test properties of sensitivity and specificity. The (diagnostic) sensitivity of a test is its ability to identify all individuals with the disease in question, or the number of true positive test results divided by the total number of people with the disease (true positives plus false negatives). A highly sensitive test produces few false-negative outcomes. (Diagnostic) specificity is the ability of a test to identify *only* people who actually have the disease in question, or the number of true negative test results divided by the number of people who do not have the disease in question (true negatives plus false positives). A highly specific test produces few false-positive outcomes.

Contrary to popular opinion, the degree of sensitivity and specificity depends not only on the test but also on the clinical spectrum of the disease among the individuals being tested. A test is normally first 'calibrated' among a set of patients who are referred to a hospital. They will frequently already have a serious, pronounced form of the disease. People with an earlier stage of the disease will be present in the general population, and in this group it is much harder to distinguish between those who do and those who do not have it.

4.4.2 *Predictive value*

The predictive value of the test result is the most important factor in deciding whether a particular screening method is useful in practice. This depends on the validity of the test and also on the percentage of cases of illness among the individuals tested (the prevalence of the disease). A test that performs well in a group with many cases of disease may be unsuitable for use in the general population. The positive predictive value indicates how likely people with a positive (abnormal) test result are to actually have the disease in question. The

negative predictive value indicates how likely a negative (normal) test result is to be correct.

4.4.3 *Overall quality of the programme*

An effective screening programme needs to be properly planned in terms of design, implementation and evaluation. Key components in this are a centralised system for inviting target groups for screening, providing clear, standardised information and reports, quality monitoring and assessment.[194] In the Netherlands, annual assessment of population screening for breast cancer reveals significant (sub)regional avoidable differences in detection, interval cancer and hospital referrals.

Systematic investigation of the functioning of screening programmes shows that there is much room for improvement in this area. A study by the European Cervical Cancer Screening Network and the International Agency for Research on Cancer (IARC) of 25 programmes in 18 countries found that the number of smear tests a woman is offered during her lifetime ranges from seven (in Finland and the Netherlands) to 50 or more (Germany, Luxembourg, Austria). Screening is registered in only 13 programmes, and only eight record detection figures for cervical cancer and its precursor stages.[195]

The way that diagnosis is arranged following an abnormal screening result is a vulnerable point. In the case of population screening for breast cancer in countries such as Britain, Finland and Sweden, diagnosis takes place in assessment centres within the screening organisation. But in the Netherlands this is done outside the screening organisation in whichever hospital the GP refers the patient to. The advantage of assessment centres is that the entire course of screening and diagnosis takes place under one roof, and the radiologist working in the screening programme has a direct feedback from his or her original screening assessment. In the system applied in the Netherlands, the surgeon and hospital radiologist may lack experience and specific training in breast diagnosis. This means that abnormalities that might point to cancer could incorrectly be regarded as not suspicious. Consequently, the diagnosis would then only be established a year or two later when the tumour is causing symptoms.[196]

4.5 Respect for autonomy

Although Wilson and Jungner made it a condition that screening methods must be acceptable to the target group, informed consent is not specifically addressed in the original formulation of the normative framework. But the subject is clearly

dealt with in a number of recent reformulations. This reflects the increasing focus since the 1960s on the autonomy of individuals as a key notion in medical ethics and health law.

Participation in screening must be voluntary, and provision must be accompanied by balanced, adequate information that can be understood by the target group. This information must relate to all aspects that are of importance in allowing individuals to reach a well-considered decision on whether or not to take part. It must always include: information about the condition for which the screening would be performed, the nature and design of the screening test, the reliability of the test and the predictive value of a normal or abnormal result, possible implications for relatives and other (different) advantages and disadvantages of participation for those concerned.[1]

The requirement of informed consent applies to all screening offered in the public or private sector. Particularly in the case of tests that may have far-reaching consequences, it can be desirable for providers to ensure that the person concerned has really understood the information. In the case of self-testing kits, this may be difficult to achieve. A further problem is that it is impossible to guarantee that people who buy self-testing kits are only going to use them on themselves rather than to obtain information about other people who may not have consented or been able to consent. This applies not only to DIY self-testing kits but also to tests in which body material has to be sent off for analysis. Examples might include parents wanting to use this kind of test to obtain information about the health prospects of their children, or about health risks to which their children are particularly susceptible.[38,90]

4.5.1 *Informed consent and complexity*

Screening makes use of risk-assessment tests. They require considerable amounts of information and counselling, given the inability of many people (not only patients and consumers, but also professionals) to deal with probability information.[197]

In the case of escalated screening, the ‘innocent’ nature of the first step (such as a blood test for PSA or for the risk of Down’s syndrome) can conceal the sometimes risky or otherwise invasive nature of the follow-up test if the first test produces an abnormal result (prostate biopsy, amniotic fluid sample) or the action and treatment options available if a definitive diagnosis is established (surgery and the possibility of distressing complications, decision to have an abortion). In order to prevent those concerned feeling forced at any point in the trajectory to take a decision that they would have preferred not to take (‘screen-

ing trap'), potential participants must be informed of the possible subsequent developments and their implications at the start of the process. On the other hand, it is important not to flood people with information, as this can hinder rather than help them in their decision-making process. Avoiding both these risks is the challenge.[166] Participants must also clearly understand that they can decide not to take any future part in the process at any time during the screening trajectory.

In the case of screening that tests for diverse conditions at the same time, and sometimes for a very large number of such conditions (multiplex testing), it soon becomes unfeasible to provide information about the individual conditions and results. This is not only for practical reasons, but also because of the problem of information overload alluded to above. The strategy of generic consent has been put forward as a way round this problem.[198] In this approach, the information given is of a more general and summary nature. The question is, how to avoid people being faced with results that they would rather not know or being exposed to risks which they would not have chosen. Little if any empirical research has been done into the feasibility of actual informed consent for multiplex screening. It has been argued, by the European Society of Human Genetics among other groups, that 'screening packages' should be available only for conditions that are sufficiently similar in terms of their nature, severity and implications.[154] In the context of neonatal screening, this would mean for example that screening for treatable conditions would be separated from screening for untreatable conditions.

Screening can sometimes identify conditions which it was not designed to detect. In practice, such 'ancillary findings' can lead to difficult decision-making situations, in which participants' right to know and their right not to know come into play. Respect for autonomy means that participants should wherever possible not be confronted with results that they would rather not have had. But in practice it will be very difficult to reach clear agreement on this beforehand.[166] It is certainly important for participants to be given general information beforehand as to the possible nature, severity and implications of any ancillary findings.

4.5.2 Provision and autonomy

In the preceding sections, the principle of 'respect for autonomy' has been discussed as a condition of duty of care: the party providing screening must ensure that the informed consent requirement is met. But respect for autonomy is also important in terms of the screening provision itself. There are two sides to this. On the one hand, it is essential to prevent the provision alone from already

forcing people to make choices that do not chime with their personal view of life. The Health Council's recent advisory report on pre-conception care made the point that it is conceivable that, when making reproductive decisions, people might 'want to avoid a medical perspective'. Recognising that this possibility exists means that a cautious approach should be taken and information should be given in multi-layered form.[66]

On the other hand, screening produces knowledge about an individual's health that will be useful to them in terms of the way they want to live their life. Looked at from this point of view, the value of screening is not limited to the health gain or other benefits that may result. From a broader perspective, another aspect of screening is that it increases individual autonomy.

This idea was expressed in the work done by the Health Council's genetic screening committee, which stated that a condition of screening must be: 'to enable the participants to determine the presence or the risk of a disorder or carrier status, and [to enable them] to take a decision on the basis of that information'.[1] This phraseology makes respect for autonomy much more than a condition of duty of care: it is the very purpose of screening, and so at the heart of the normative framework. We do not find this emphasis in Wilson and Jungner or in other reformulations of the normative framework. But this refinement is an extension of the central tenet, which is implicitly present in Wilson and Jungner's work, that screening must on balance be favourable to the participants. The question is whether this should also have consequences for defining screening provision. Would it not be better for citizens to be able to decide for themselves the conditions for which they would like to be tested?*

It is important here to draw a distinction between the various contexts in which screening is offered. In the public domain, these are screening tests offered by the government or by practitioners and paid for from public or collective funds. This provision must in principle be potentially useful for everyone. So it would be difficult to argue that any screening for Alzheimer's disease (until such time as there is an effective treatment for or prevention of this condition) should be incorporated into the national population screening programme or the basic package of health services, even if such screening could offer courses of action for some individuals that (for them) outweigh the disadvantages of such screening.

What is not available in the public sector may, if the demand exists, become available in the private sector in the form of services or DIY self-testing kits. In

* This question was put before the committee in the letter it received from the Biotechnology and Genetics Forum on 10 January 2008.[108]

this respect, there is more room for freedom of choice in that sector. Private-sector provision must of course, in terms of this normative framework, also meet the requirement that the benefits to the participants clearly outweigh the drawbacks. Still, there is more room here for people to decide for themselves what they regard as advantages and disadvantages from their own point of view.

4.6 Responsibility in terms of cost-effectiveness

Screening that is funded from public or collective resources must not only address a significant health problem, but the costs incurred must also be justified in the context of the total healthcare budget. The opportunity costs must also be taken into consideration: introducing an expensive screening programme might mean that other forms of screening cannot be carried out, or that care funded by the government or in the basic package of health services will have to be cut. In this context, it is important that the balance between the proceeds of a screening programme, in terms of health gain or other worthwhile courses of action for those affected, and the costs incurred comes down on the positive side. These costs must be defined not only as the cost of the (initial) screening test but must also cover the costs of all follow-up tests and ensuing interventions. The costs should be considered as net costs, i.e. after deducting any savings made. A screening method that produces a high proportion of false-positive results soon generates considerable unnecessary cost down the line, and therefore the cost-effectiveness profile of the entire screening process becomes unfavourable.

It is incorrect to think that these considerations are irrelevant to screening offered in the private sector because people pay for it themselves. After all, what they pay for themselves is only the initial screening test and not the subsequent treatment they need if the result is abnormal. All these costs are paid for from the basic package of health services covered by State health insurance. The costs of follow-up care for each person tested may be rather more than the cost of the screening test for which they have paid. To that extent, we can say that all screening tests that are commercially available are also part of the basic healthcare package. Consequently, private providers also bear some social responsibility. Screening that leads to extensive unnecessary follow-up testing or intervention should be avoided for that reason among others.[102]

4.7 Conclusion: the normative framework requires active validation

The committee concludes that there is little reason to doubt that the normative framework is future-proof. Though new developments will always require the

system to be adjusted and made more concrete, this in itself does not mean that the normative framework will not continue to be able to guide the responsible use of new screening options.

Three observations are important here. Firstly: the normative framework formulates principles for assessing the value of screening; however, it is not a decision-making model that simply needs to be 'applied' in order to produce the right result. Assessment of screening remains a complex issue which certainly offers room for differing views and interpretations. The fact that the implementation of certain elements is still the subject of debate (for instance, the acceptability of screening for untreatable conditions) does not detract from the relevance of the normative framework; rather, it emphasises how vital it is. Reflection and debate are essential to make this framework future-proof.

Secondly: the central requirement that the ratio of advantages to disadvantages should be favourable relates to the benefit of screening for individual participants (or users) and not in the first instance to any social benefit. The perspective of the normative framework is individual, not collective. Only when the question of whether a certain form of screening, which has been assessed and found to be beneficial, should be paid for by the government does the collective perspective come into focus. This raises the issue of whether the condition for which the screening method tests is sufficiently significant, whether provision can be justified in terms of cost-effectiveness and how, given limited funding, priorities should be set. These questions are addressed in the next chapter.

Finally: the most important challenge to the normative framework lies not so much in new scientific developments as in the shift in context referred to above (Chapter 2). We can expect the government to continue to orient its own screening provision by the normative framework discussed here. But what about new providers in other contexts? Seen in this light, the question of whether the normative framework is future-proof refers to how, in the new situation, the idea of 'responsible population screening' can be upheld. The next chapters of this advisory report address this issue.

Chapter 5

Ensuring worthwhile screening

What is the government's responsibility here? We need to distinguish between two important tasks: ensuring that high-quality, responsible forms of screening are available and (financially) accessible, and protecting the population against health damage that might result from risky or unsound screening. Both these tasks arise from the obligation imposed on the government in the Constitution to take steps to promote public health (article 22, paragraph 1, of the Constitution). This chapter discusses the government's duty of care; the duty of protection is addressed in chapter 6.

The Minister wants to know what the development of new screening options means for the future of the National Population Screening Programme. What forms of screening may be suitable for inclusion in that programme? Should it include screening for non-treatable conditions? And how can responsible provision take account of the 'stages of life perspective'?

5.1 Existing public provision

The government can comply with its duty of care in two ways. It can provide certain facilities itself, or it can ensure that they are available and accessible by incorporating them in the basic healthcare package. The first of these is the only choice in the case of facilities that would probably not otherwise be available, or where their quality cannot otherwise be guaranteed. This is why large-scale

collective screening programmes tend to be provided by the government itself, both in the Netherlands and abroad.

The National Screening Programme is a recent accumulation of screening programmes that have themselves long been publicly funded. It comprises:
- cervical cancer screening;
- breast cancer screening;
- screening for familial hypercholesterolaemia (FH);
- prenatal screening for infectious diseases and erythrocyte immunisation (PSIE);
- the neonatal heel-prick test for treatable childhood diseases, which has recently been considerably expanded;
- neonatal screening for perceptive hearing loss.

Other forms of screening are offered to certain high-risk groups as part of public provision outside the National Screening Programme. These include screening for tuberculosis and various forms of screening included in the basic list of infant and child health services (early detection of developmental disorders). This list refers to the tasks local authorities are required to perform in addition to vaccination, reporting and providing advice.[199] They include, inter alia:
- hearing and sight screening;
- for boys: checking that the testes are descending at the right time;
- screening for speech and language disorders.

The quality of the screening offered as part of the National Screening Programme is assured by the central coordinating role of the Centre for Population Screening (CvB), which is part of the National Institute for Public Health and the Environment (RIVM). The tasks carried out by the CvB in this context include funding (apart from the heel-prick test), giving guidance to bodies responsible for implementation, providing information to the public, monitoring and evaluation. The Child Health Platform is responsible for monitoring and improving the quality of the screening activities carried out in the context of the basic list of infant and child health services.

5.2 Limits to public provision

As the National Screening Programme was created as a collection of existing forms of screening, it does not have a specific set of underlying criteria. It is however quite clear that screening which does not meet the requirements laid

down in chapter 4 for ‘responsible population screening’ has no place in the National Screening Programme.or the basic list of infant and child health services. But some questions do remain to be answered. Firstly: what definition of the ‘clinical benefit’ criterion should be used when drawing the limits of public provision? Should it include screening for non-treatable conditions? Secondly: where should the line between public provision and individual care be drawn in terms of screening? And finally: in the light of the ‘appropriate use of resources’ criterion, how should priorities be set?

5.2.1 *Public provision must be limited to screening that can produce a health gain*

It was argued in chapter 4 that the utility of screening can be defined in broader terms than health gain alone. Screening for untreatable conditions can also be responsible if it leads to courses of action or other outcomes that are worthwhile for those concerned. But here we are discussing the question of what screening the State should offer. In principle, the criterion of health gain must be upheld in this context. The basis of public provision is, after all, the government’s duty under the constitution to promote public health.

It can of course be debated how broadly or narrowly the term ‘health’ should be defined in this respect. If we follow the line laid down by the WHO in its well-known definition*, and make health synonymous with well-being, then ‘promoting public health’ must also include creating action options that are relevant to the well-being of those concerned. In contrast, earlier advisory reports produced by the Scientific Council for Government Policy[200] and the Health Council[201] have stressed that realistic objectives for public health policy should be based on a definition of health that is not too broad, for example in terms of ‘absence of disease and other health problems, both physical and mental’.[200]

Screening that only creates action options that add something to the well-being of those concerned should in that case form no part of public provision, however useful they may be in themselves.

The argument for this is however not purely a matter of budgetary realism and spending choices that must be democratically justified. Another reason for avoiding an excessively broad definition is that we could otherwise lose sight of the fact that health is important as a necessary condition for the various ways people want to live their lives. The government can be expected to do what it can to achieve this condition, but the way people then live their lives is up to them.

* A condition of complete physical, mental and social well-being (WHO 1948).

This includes taking their own steps to achieve what they want. Screening that cannot produce a health gain should therefore be left out of public provision.

An example would be the (possible) screening for genetic risk of Alzheimer's disease referred to in the previous chapter. The research mentioned at that point indicates that some people would like to undergo this screening so that they can adjust their future life plans if they find that their risk is (much) higher than average. But it also found that most people were not interested in having this type of risk information. What is regarded in this context as a useful outcome depends very much on someone's personal values and ideals. Even if offering screening of this kind is not necessarily irresponsible, it seems hard to argue that the government (or the basic package of medical services) should provide it.

5.2.2 *Exception for reproductive screening*

Public provision should in principle be restricted to screening that can produce health gains. And there is a good reason for this qualification ('in principle'). It could be argued that the government does indeed have a role to play in screening that offers choices which are regarded as important not only by some people but by a large proportion of the population. The committee is thinking here of reproductive screening, including existing screening for Down's syndrome and other serious foetal abnormalities.

Countries such as France and the United Kingdom include this in public provision. In the Netherlands, it has a special position. In contrast to prenatal screening for infectious disease and erythrocyte immunisation (PSIE), it is not part of the National Screening Programme but is (in most cases) paid for via the basic package of medical services. To be precise: pregnant women aged under 36 have to pay for screening for Down's syndrome (but not for any follow-up tests); for older pregnant women, this screening is part of the basic package of medical services. All pregnant women have access to structural echoscopic examination (SEO) without having to pay for it via this route. So screening for foetal abnormalities does not come under public provision. The government has however agreed to set up a national programme governing the organisational and quality aspects of this screening (run by the CvB).

The previous Secretary of State repeatedly emphasised that government policy on screening of this kind must be 'cautious'.[202] After all, selective abortion is a morally burdened option, with widely varying views in society as to its acceptability. The Secretary of State was of the opinion that the government must avoid giving the impression that it wanted to become involved in the decision. For that reason, it would be better for such screening not to be offered 'by the State'.[203]

But if we look at the situation in terms of government commitment, there is very little difference between incorporating something in the National Screening Programme and placing it in the basic package of medical care covered by social insurance as defined by the government. The government does ensure that screening for Down's syndrome and other foetal abnormalities is available by this indirect route involving the basic package of medical services. Moreover, the national programme set up by the CvB to monitor aspects such as quality, evaluation and explanation of screening is funded directly from the national budget. We must therefore conclude that if the moral sensitivity of the issue did not stand in the way of the government's current involvement, there would be no real argument about incorporating this screening into the National Screening Programme.

This does not mean that the National Screening Programme ought to be the route of choice here; the choice between the two approaches is in the final analysis a matter of pragmatism rather than principle. Secondly: the difference between a morally acceptable provision and a morally dubious provision depends not on who the provider is, but on whether the matter is handled in such a way that there can be no misunderstanding as to the purpose of the screening in question. The aim must be to provide worthwhile options and not to encourage selective abortion in the case of Down's syndrome or other serious conditions or handicaps. This is a very sensitive issue. The provision needs to be presented in a very careful way, with high-quality information and diligent counselling and support.[166] It is good that the government wants to keep a grip on these aspects through the national programme, not in spite of but rather because of the moral sensitivity of this form of prenatal screening.

Another consideration is that prenatal screening for foetal abnormalities, especially those techniques that involve echoscopy, are likely to be increasingly focused on achieving health gains as well. Examples that spring to mind here include cases where echoscopic results lead to a change in support or perinatal policy. In future it will also be possible to treat foetuses for certain conditions prior to birth (while they are still in the womb).[204-206] The more that such findings are likely to be observed, the more prenatal screening will come to have a dual objective. This will certainly not make counselling any easier.

The exception to the health gain rule referred to here can also include other forms of reproductive screening. Examples include possible pre-conception screening to ascertain whether people are carriers of recessively hereditary conditions such as cystic fibrosis (CF) or haemoglobinopathies[66] and screening newborn infants for untreatable conditions because the hereditary information could be useful to the parents in making decisions as to whether to have more children.[187]

5.2.3 *The grey area between screening and individual care*

In its recent report entitled Van preventie verzekerd [On Prevention Insurance], the Health Care Insurance Board drew a distinction between collective, indicated, and care-related prevention.[207] The aim of collective prevention is to stop people becoming ill, or to detect people at high risk (or with an early stage of a condition) and direct them towards care. The aim of indicated prevention is to prevent the development of an illness in an individual with a higher than average risk of it. Finally, the purpose of care-related prevention is to prevent complications, aggravation or handicap in people with a certain condition. The Board concludes that the latter two forms of prevention should be considered as care which is insured under the Healthcare Insurance Act and the Exceptional Medical Expenses Act, although the opportunities this approach offers are still not used widely enough by insurers. In contrast, collective prevention does not come into the category of insured care, and cannot be put into this category. The report's comments on this are:

> Identifying groups of people at high risk of disease and guiding them towards care is essential, but cannot be carried out under the Healthcare Insurance Act as this is focused on individual care. The Board is therefore of the opinion that the ministries and authorities concerned must accept their responsibilities in this respect.[207]

The reason why this report concludes that care-related and indicated prevention can be incorporated into the basic package of medical services, but that this is not true for collective prevention, is a technical matter related to the principles of insurance: entitlement to insured care depends on whether the insured risk has manifested itself. If there is no indication, there is no entitlement. By definition, no such indication can exist in the case of collective prevention aimed at early detection. Therefore, screening in this category must be offered directly by the government and funded from the national budget.[207]

The situation discussed above shows at least that this reasoning need not be compelling. Prenatal screening for foetal abnormalities is performed not on the basis of an indication but is nonetheless funded via the basic package of medical services. As has been pointed out, this is ultimately a pragmatic choice. Nevertheless, the general rule of thumb is that collective prevention falls into the government provision category and indicated prevention into the basic package category.

This latter category includes, for example, the risk-specific medical checks offered to former patients or to people who have a greater risk of contracting a (different) condition because of earlier medical treatment, as described in chapter 2. At present there is often insufficient funding for such (lifelong) monitoring.

The National Screening Programme is the right setting for cascade screening

Cascade screening, such as the screening for familial hypercholesterolaemia which is part of the National Screening Programme, is not offered to the population as a whole or to a particular age group or gender, but to people coming from a family with a genetic problem. This could be seen as an argument for including this type of screening in the basic package of insured care, as a form of indicated prevention. But it is not the only possible approach. One reason not to go down this route is that funding for programme quality aspects is not necessarily available. Separate provision would have to be made for this, as in the case of the prenatal screening offered via the basic package of medical services discussed above.

Screening on the basis of risk profiling is still collective prevention

One development that could be looked at in this context is selective screening on the basis of individual risk profiles. A topical example is the trial population screening for bowel cancer carried out by NIPED.[149] It is based on 'integrated' risk profiling, which should allow selective screening to be offered for various conditions with common risk factors. The investigators expect that this approach could be more effective than conventional population screening, which is offered for particular conditions on the basis of general characteristics such as age and gender. It remains to be seen whether this is the case (see chapter 3). The question is: what would such a development mean for the National Screening Programme? Does screening based on individual risk move us away from the idea of collective prevention? Of course not. After all, it would be a form of graduated screening in which the first step (risk profiling) is still offered to a group of the population selected by general characteristics. The fact that this first step makes targeted provision of follow-up testing possible does not mean that the entire screening programme can no longer be considered as a form of collective prevention that should be part of the National Screening Programme.

5.3 Screening at various stages of life

How can responsible screening provision take account of the 'stages of life perspective'? It is obvious that people should be offered screening at the stage in their lives when it can really be of use to them. That is the underlying principle behind the current provision:

- all newborns are eligible for neonatal screening;
- the screening techniques designed to detect developmental disorders and other conditions are offered to children and adolescents as part of the basic list of infant and child health services;
- all pregnant women are given information about the opportunity to undergo screening for Down's syndrome (and other chromosomal abnormalities) in the first trimester of pregnancy; women aged 36 and over do not have to pay for it. All pregnant women undergo a structural echography examination (SEO) which picks up many foetal abnormalities later in pregnancy (around 20 weeks). Prenatal screening for infectious diseases and erythrocyte immunisation (PSIE) is also offered to all pregnant women;
- Screening aimed at early detection of disease later in life is offered at the stage of life where this provision can do more good than harm to those undergoing it. Women are invited for cervical cancer screening between the ages of 30 and 60, while breast cancer screening is offered to women between 50 and 75. If bowel cancer screening is introduced, it will be offered to men and women from the age of 50 or 55.

It is likely that screening will in future be offered to people at other stages of life. If screening for Chlamydia trachomatis is introduced, it will target adolescents and young adults. Other possible forms of screening include pre-conception screening to ascertain carrier status of recessively hereditary diseases such as cystic fibrosis and haemogloblinopathies. This form of screening would be offered to couples wishing to have children, and therefore would have to be available to all men and women of reproductive age.

Premature health information can be distressing

Screening can sometimes produce medical information that will only be relevant to the person concerned when he or she is older, but that can be distressing in the meantime. It is important to consider the effect of such premature information on the well-being of participants when weighing up the advantages and

disadvantages of screening provision. This is particularly important in the case of children who cannot decide for themselves whether to undergo screening.

For example, neonatal screening for recessively hereditary conditions can sometimes reveal that the infant in question is an otherwise healthy carrier of the condition in question. This is particularly relevant in the case of neonatal screening as presently offered for sickle-cell anaemia and cystic fibrosis. This information will only be relevant to the child once he or she is thinking about having children. The question of how distressing this premature carrier status information might be in the meantime is an important point to bear in mind when assessing these forms of neonatal screening.[191]

The (hypothetical) proposal put forward in chapter 3 to map the entire genome of all newborn infants would produce all sorts of information about health prospects and health risks. This information would in the vast majority of cases be premature, could be extremely distressing, and the individuals concerned would not be able to decide whether or not they want to receive it: these are all important arguments against that idea of 'newborn profiling'.[85,187]

Fragmentation of provision and information must be avoided

It is also important to coordinate the various types of screening that people are offered at various points in their lives. Fragmentation of provision and information must be avoided as far as possible. This applies, for instance, to screening around the time of pregnancy. If pre-conception screening is introduced, couples will be faced with various types of screening within a short period, carried out for different purposes but sometimes focusing on the same conditions. Timely and integrated information and good support are essential.

For example, it is conceivable that screening for sickle-cell anaemia will shortly be carried out both after birth and before conception.[187] The screening of infants is carried out for other reasons (to improve the child's health outlook) than screening for carrier status performed before pregnancy (offering the parents worthwhile reproductive options). In the United Kingdom, screening for sickle-cell anaemia (and thalassaemia) is carried out not before pregnancy (pre-conception) but during pregnancy (prenatal).[208] The benefit of this approach is that it is easier to reach the target group, but the drawback is that if the result is unfavourable the only decision is whether to continue with the pregnancy or have an abortion.[67] But the two approaches can complement each other. For instance, it is conceivable that in future couples who were not offered pre-conception screening (because the pregnancy was unplanned, for example) might be offered prena-

tal screening for the condition in question. This type of chain approach expands the choices available to the couples concerned.

The importance of coordinating screening options is also relevant to the current system of prenatal screening for Down's syndrome. Pregnant women aged under 36 have to pay for the 'combination test' performed in the first trimester. As this is not the case for the structural echography carried out later in pregnancy, it is not impossible that some younger women might wait for the echography, assuming that if anything is wrong it will be picked up then. But the structural echography is not the best test for Down's syndrome. In the case of women who would have liked to have the combination test but did not want to pay for it, this situation can lead to sub-optimum screening practice, with Down's syndrome often being missed and detected later than it need have been. This would be an undesirable effect of an age limit which is in itself difficult to justify.[166]

Clustering screening does not necessarily improve provision

It is possible that if new forms of screening for cancer (currently being trialled as a population screening approach) are incorporated into the National Screening Programme, it will be argued that target groups should be invited to undergo screening for various forms of cancer at the same time where this is possible, in order to improve efficacy and prevent fragmentation. But as there are optimum screening intervals and age limits for the various techniques used to screen for different conditions, this will not always be feasible. Adjusting these intervals and age limits in order to facilitate clustering (as is done in the French region of Isère, see annex E) is not a good idea as it actually makes screening for cancer less effective. Therefore, the aim of preventing fragmentation of screening provision must be pursued primarily by coordinating and integrating information.

5.4 Setting priorities

The government's responsibility to ensure good quality healthcare provision (including screening) is a duty that is limited by the funds available, bearing in mind the other tasks that the government is (constitutionally) required to perform. This means that priorities have to be set, a process that involves the same kinds of decisions as those that have to be taken when deciding what services to include in (or remove from) the basic package of medical services.

The criteria that should be used in this had long been a matter for debate. It is now agreed that they should be the burden of disease and cost-effectiveness.[201]

The burden of disease is defined as 'reduced quality of life or life span as a result of a disease or some other somatic or mental health problem in cases where no health care service would be utilized'. Cost-effectiveness means the relationship between how effective a form of care is (the extent to which it reduces the burden of disease) and its cost (in money, human resources, equipment and time). Taken together, these criteria determine for what medical provision citizens are willing to excercise solidarity with one another[201], but they can be extrapolated to answer the question of what government spending is justifiable in this area. The applicability of both criteria depends on:

- practicability: is there a valid method of measurement to determine the criterion in question?
- availability of data: is there enough (reliable) data to determine, for example, the burden of disease, costs, or efficacy?
- availability of decision-making rules: what thresholds or limit values are used in applying the criteria?
- availability of suitable (national) testing procedures.

All these aspects remain the focus of continued research and debate.[201,209,210] In addition to the necessary scientific foundation,[211] social attitudes and choices play a crucial role here. For example, where does the lower limit of the burden of disease lie? And when are the costs unacceptably high compared with the efficacy of a form of care?

In the context of screening (and prevention in general), the costs must be assessed, taking the savings made into account as well.

5.5 International differences

Many countries indicate that they use a version of the criteria laid down by Wilson and Jungner, with refinement or updating of certain parts, when deciding whether to introduce population screening (see annex D). But there are significant differences between countries in respect of the conditions for which screening is performed (see annex E).[212] Some of these differences can be traced back to the observations made at the end of chapter 4: that differences of interpretation are inevitable in complex situations, and that there is still some debate over certain elements of the normative framework. For example, the fact that neonatal screening for Duchenne's muscular dystrophy is only offered in a

few regions of Europe (Wales, Antwerp) is related to the current discussion on what exactly neonatal screening should cover. It is also important to bear in mind that individual countries may set priorities differently, partly because the pattern of disease and the costs of care can vary widely from one country to the next. For example, incidence and mortality figures for breast cancer in the Netherlands are relatively high, and those for cervical cancer are low. This can mean that the health gain (in terms of additional years of life per thousand individuals undergoing screening) and the costs of each screening session can vary by a factor of two. As a consequence, the same screening programme can result in costs per additional life year that in one country are three times as high as the costs of healthcare per head of population, but 21 times as high in the other.[213]

5.6 Future of the National Screening Programme

At present there are few forms of screening that meet the stated criteria for inclusion in the National Screening Programme, though the number may rise in the near future. The value of population screening for bowel cancer using the faecal occult blood test (FOBT) has been established.[214] Feasibility studies are taking place, and are expected to lead to its inclusion in the National Screening Programme. Trial population screening studies are also being conducted to ascertain the value of screening for lung cancer, prostate cancer, Chlamydia trachomatis infection and diabetes. It is also conceivable that new forms of cascade screening might be included in the National Screening Programme once their value has been established. The same applies to any pre-conception screening to ascertain carrier status of recessively hereditary conditions, including cystic fibrosis and haemoglobinopathies in particular.[66] Neonatal screening is also likely to be expanded. The Health Council submitted an advisory report on the expansion of that programme in 2005. It concluded that early detection could produce a health gain in around 17 conditions. Three years later, developments in the treatment of rare metabolic diseases indicate that the desirability of further expansion should be investigated, leaving aside the question of neonatal screening for untreatable conditions, which has still to be discussed.

Ongoing assessment and provision of advice

The abovementioned developments in the treatment of metabolic disease emphasise the importance of regular independent scientific assessment of current

and future screening opportunities, and providing advice on the National Screening Programme on the basis of this assessment.

What kind of screening is suitable for inclusion in these programmes? And what kind of screening can be done away with? The United Kingdom has a permanent National Screening Committee that, among other tasks, advises on the inclusion of various types of screening in the National Health Service (NHS). This could also be a useful model for the Netherlands. Ad-hoc advisory reports produced by the Health Council, and the population screening annual reports, could be seen as a basis for this type of approach. The committee returns to this question in chapter 7.

5.7 Promoting worthwhile screening in the public healthcare sector

The government's responsibility to ensure the provision of worthwhile screening goes beyond deciding what it should itself provide in two respects. Firstly: screening that the government does not provide itself but that is part of public healthcare provision because it comes under the package of services covered by social insurance must be of acceptable quality. Integrated professional guidelines and standards in line with the principles of the normative framework discussed in chapter 4, and the requirements of the Healthcare Facilities Quality Act, need to be devised to ensure that this is the case. The scientific associations of the relevant professional groups are responsible for developing these quality standards.[215] Professional education on screening also requires attention. The government's main role here is to encourage such activities.

Secondly, concern for worthwhile screening also means concern for such screening to be developed irrespective of whether or not it should at present be included in government provision. This depends on targeted encouragement of research into forms of screening that could have public health benefits. The committee returns to this question as well in chapter 7.

5.8 Conclusion: concern for worthwhile screening goes beyond the National Screening Programme

One of the government's important tasks is to ensure that worthwhile screening is available and accessible. Whether this is achieved via the National Screening Programme or the basic package of services is a pragmatic question rather than a matter of principle. There are good reasons for restricting provision paid for from public or collective funds to forms of screening that can produce health gains. Screening which does not fulfil this criterion should therefore in principle be

excluded from public provision. An exception could be made for reproductive screening that is not carried out with a view to health gains, including current screening for Down's syndrome and other serious foetal abnormalities. It is unavoidable that priorities will have to be set within government provision.

But the government's duty of care in this area is not limited to making decisions on its own provision. The government can also be expected to encourage high quality of screening offered by other parties in the public healthcare sector, and to stimulate useful innovation.

Chapter 6

Protection against risks of unsound screening

In addition to the duty of care referred to in the previous chapter, the government also has a duty of protection: it must guard its citizens against health damage that might result from risky or unsound forms of screening. This task also arises from article 22, paragraph 1, of the Constitution, which was referred to above. Neither the duty of care nor the duty of protection is however absolute. This is because the government must also protect citizens' right to privacy (article 8 of the ECHR, and article 10 of the Constitution). Protective measures that run counter to this principle can be justified, but must then meet requirements of necessity, proportionality (the extent to which they run counter to the principle must be proportionate to the importance of the objective) and subsidiarity (there must not be any less invasive way of achieving the same objective).

In this chapter, the committee discusses the question of whether existing protection is adequate in the light of the developments in screening discussed earlier in this advisory report. This relates not only to the new screening opportunities that can be offered by scientific developments, but also to changes in the social embedding: new contexts, new providers, emphasis on freedom of choice and responsibility for oneself.

6.1 Examples of unsound screening

For decades, women have been encouraged to examine their own breasts and mass screening programmes have been conducted for tuberculosis,

neuroblastomas and scoliosis without their usefulness having first been examined. Research has since showed that this screening was scientifically unsound and actually harmful to those who took part.[216-219]

The total-body scan, advertised as 'a MOT for your body' is also unsound and harmful. There is no scientific evidence that this type of screening improves the health prospects of the individuals who undergo it.[2] It is however clear that the screening has a high chance of producing false-positive outcomes (false alarms) and over-diagnosis (something is picked up, but the abnormality in question would never have led to symptoms or to the disease being diagnosed if screening had not taken place).[25,109] Abnormal outcomes not only cause fear and uncertainty, but also lead to iatrogenic health damage as a result of risky follow-up tests or therapeutic interventions.[116] The use of CT scanning apparatus also exposes people to radiation.[122,124]

Another example is prostate cancer screening through pharmacies and drug-store chains that offer DIY self-testing kits on the Internet to look for prostate-specific antigen (PSA) in blood taken from a finger prick. This form of screening is being offered in advance of the results of two large trials investigating whether screening involving a PSA test can actually reduce prostate cancer mortality. Until we know that, the only thing that is certain is that screening for prostate cancer can cause significant health damage (impotence, incontinence, intestinal problems) because of the often unnecessary invasive procedures that are carried out. Half of all prostate cancers picked up via screening would never have caused symptoms if screening had not taken place.[220,220] Another problem with the DIY self-testing kits is that there is no independent scientific information about the diagnostic value of a PSA test carried out by consumers themselves and that the quality of the information provided with the test is often seriously deficient.[3]

6.2 Existing protective instruments

The government's duty of protection relates both to public and private screening provision. Various instruments are at the government's disposal for this purpose. Statutory rules govern medical intervention in the case of screening services offered in the public or private sector. The Population Screening Act (WBO) is the most important source of regulation. Self-testing kits using body tissue are governed by slightly different regulations.

6.2.1 *General statutory rules*

The general statutory rules here are those laid down in the Medical Treatment Contracts Act (WGBO), the Individual Healthcare Professions Act and the Healthcare Facilities Quality Act. The Special Medical Treatments Act (WBMV) is also relevant, as it is this piece of legislation that restricts complex clinical genetic tests and the provision of hereditary advice to the eight licensed academic centres. One of the consequences of this is that 'DNA testing for use in diagnosing congenital and hereditary abnormalities' cannot be performed by other laboratories except under contract to a licensed centre. The licence is conditional on a protocol laying down rules on the quality of the test, its performance, support and advice, and follow-up.

6.2.2 *Population Screening Act (WBO)*

The Population Screening Act (WBO) was created specifically to protect the population against physical or mental risks associated with screening. This protection consists of ensuring that some forms of screening referred to in the Act must first undergo an independent quality test. The relevant forms of screening can only be carried out once the Minister has issued a licence following favourable review of the screening protocol submitted. The review is carried out by the Health Council's WBO committee. The WBO currently specifies that three types of population screening require licensing:

- population screening using ionising radiation;
- population screening for cancer;
- population screening for serious diseases or abnormalities for which no treatment or prevention exists.

It has to be screening that is covered by the statutory definition of population screening (article 1c of the WBO). An offer of testing that is made after a patient seeks help, or that is sufficiently related to someone's medical condition, is not population screening in the sense of the law and therefore cannot require a licence[13].

Licences are refused if the screening is scientifically unsound, contrary to statutory rules for medical intervention, or if the expected benefit is outweighed by the risks to the individuals undergoing screening. The WBO does not currently impose any requirements on screening that does not fall into one of the three categories that require licensing.

6.2.3 *Rules for self-testing kits*

The provision of self-testing kits using body tissue falls partly inside and partly outside these regulations*. It is important to draw a distinction between self-testing kits that are associated with a service (for example, when people take samples of their own body tissue and have to send it to a laboratory) and self-testing kits that people can perform without outside assistance. Legally speaking, the latter (DIY self-testing kits) are 'products' and the former are also 'services'.

In the case of services carried out to assess someone's state of health, the activities performed are medical interventions and are therefore subject to the relevant regulations (see above), including the requirements of the WBO. It must be pointed out here that the Healthcare Facilities Quality Act does not necessarily apply to all providers of such services. Whether or not this is the case depends on whether the services they provide are sufficiently similar to healthcare as 'defined in or by virtue of the Medical Insurance Act or the General Act on Special Medical Expenses'. That is the factor that triggers application of the Quality Act.

DIY self-testing kits fall outside the aforementioned regulations and so also outside the WBO. Tests of this kind are subject both to general consumer legislation (which is not discussed further in this advisory report) and to the In-Vitro Diagnostics Decree (IVD decree). This decree, an Order in Council under the Medical Devices Act, implements European Directive 98/79/EC of the European Parliament and Council dated 27 October 1998 on in-vitro diagnostic medical devices (IVD Directive).

European IVD directive

The core of the IVD directive are the 'essential requirements' which in-vitro diagnostic medical devices have to meet in order to obtain the CE marking which is necessary for them to be placed on the market. The aim of these essential requirements is to ensure that the purpose of the device is clear, that it works as it is supposed to, and that it does not endanger the health or safety of patients and users. Additional requirements apply to DIY self-testing kits. The purpose of these is, among other things, to limit the risk of error and to ensure that the

* For a more detailed discussion of this issue, see the 2007 Population Screening Annual Report[3] and a legal background study (by prof. J.K.M. Gevers) to the advisory report Screening and the role of the government by the Council for Public Health and Health Care.[221]

instructions for use are comprehensible by lay people. These instructions must clearly state that users must consult a doctor before taking any decisions of a medical nature.

The IVD directive distinguishes between various risk classes (high, medium, low) for the CE marking assessment. Products in the high and medium risk classes must be assessed by a notified body, while low-risk products can be assessed by the manufacturer personally. The assessment looks at whether a product meets the aforementioned 'essential requirements'. In the case of DIY self-testing kits, this assessment procedure to ascertain compliance with the relevant additional requirements must always be performed by a notified body.

Marketing channel regulations

Member States may not interfere with the marketing or use of any products that bear CE marking. However, member states do have the freedom to make arrangements for how in-vitro diagnostic devices are sold (supply restrictions, promotion) within the limits of the directive. The Netherlands has adopted the IVD in order to make use of this opportunity. The 'marketing channel regulations' specify that high-risk diagnostic devices (defined in these regulations as: tests for detecting HIV infection or tumour markers, for diagnosing hereditary diseases and for predictive genetic testing) may only be supplied to users via a professional intermediary (a doctor or pharmacist). Additional requirements are also laid down with regard to the information that pharmacists must give users before supplying a high-risk diagnostic device and in terms of the content of the pack insert leaflet that accompanies the product.

6.3 Debate on the Population Screening Act (WBO)

6.3.1 Bottlenecks observed in the evaluation report

The WBO evaluation report published in 2000 concluded that this Act had markedly improved the quality of population screening carried out in the Netherlands.[215] But it also remarked that it was not yet as effective as it could be in achieving its intended target of protecting the population. The authors were critical of the delineation of the license requirement, which they regard as arbitrary and (because it is part of the Act itself) insufficiently flexible. They also pointed to the problem that some categories of population screening are intensively tested while others are not tested at all.[215]

The evaluation report argues that in future all screening (that falls under the legal definition of population screening) should undergo some form of assessment before being introduced. This would involve two assessment regimes: one that is less stringent (authorisation) and one that is more stringent (licensing). Screening techniques that are neither authorised nor licensed would be prohibited. Authorisation would automatically be granted for population screening that had already been assessed and authorised (for a first provider), while, in the case of screening that comes into a category requiring licensing, each separate provision would have to be tested before being placed on the market.

The evaluation report also recommended that the text defining categories requiring licensing should, in order to increase flexibility, be part of an Order in Council rather than part of the Act itself. The scope of the licensing requirement can then be adapted in the light of circumstances without the WBO always having to be amended. Licensing would be required if, in view of the nature of the test, the specific way in which the screening programme is intended to be offered needs to be examined. A decision to grant authorisation would be sufficient for all other forms of screening. This would depend on 'whether it is likely on balance to contribute to the health of the target group and, if so, what requirements should apply to implementation'. Examination of this issue would have to be based as much as possible on the guidelines developed by the professional group(s) responsible for the area in question.[215]

Though the Minister of HWS welcomed the evaluation report in principle, no further work has yet been done on the proposals put forward in the report with a view to possible changes in the legislation.

6.3.2 *Problems reported with enforcement*

The Healthcare Inspectorate has encountered a problem with the enforcement of the WBO, in that it appears that prosecution is only an option for parties who carry out population screening requiring a licence without having applied for or received a licence, and not to parties that offer it. This loophole is exploited by two companies that carry out screening scans in clinics just over the German border, because they do not have a licence to conduct these scans in the Netherlands. No action can at present be taken against the active promotion of these scans in the Dutch media.

Another problem is that the legal definition of population screening and the wording of two of the three categories assume that screening is always directed at one or more specific conditions, while providers can easily be vague about the

actual target condition(s) in the information they provide. It is therefore not always clear whether the screening in question requires a licence. Another topical question is whether the licence requirement should be upheld in the case of conditions that cannot be screened for without a licence but for which consumers can easily obtain DIY self-testing kits via the Internet or from a pharmacist. This is already the case with tests for prostate, bladder and bowel cancer.

6.3.3 *Implication of the ban perceived as a restriction on freedom*

One argument that has in recent times been put against the WBO with increasing vigour is that the implication of the ban associated with the licensing requirement restricts citizens' freedom of choice. Screening that requires a licence but has not obtained one cannot be carried out in the Netherlands and so is not available to those who would like to access it. People who want to have a total-body scan have to go to Germany, men who would like to be tested for prostate cancer will find it more difficult in the Netherlands than in many other countries, and a request for a licence to carry out screening for osteoporosis was recently turned down.[222]

Screening that is licensed is often limited to particular age groups. For example, only women aged between 50 and 75 are invited for breast cancer screening, and then only every other year. Women who would like to be screened before or after the cut-off age limits, or who would like to have more frequent tests, are unable to do so in the Netherlands. Commercial providers advertise unlimited breast cancer screening, but those who want to avail themselves of this service have to travel to a scanning unit in another country.

Heel-prick screening tests currently look only at conditions where significant, irreparable damage to the newborn child can be avoided.[187] Screening for untreatable conditions requires a licence. Until such a licence has been granted, the heel-prick test cannot look for such conditions in the Netherlands, even if the parents request it*.

The criticism that the WBO restricts freedom is not entirely new, but used to apply only to the question of prenatal screening for Down's syndrome and neural tube defects, where the Act has long been used to stop provision being updated to

* The letter sent to the committee by the Biotechnology and Genetics Forum on 10 January 2008 described this as a serious restriction on citizens' freedom of choice: 'A greater focus on autonomy should also mean that the possibility of screening for an untreatable condition should not be ruled out in advance'.[188] The committee points out that there is no question of 'ruling something out in advance'. The debate on the possible expansion of the heel-prick test is still to be conducted.[182,187]

take account of scientific developments. That debate related not to the WBO itself, but to its improper use.[166] Now we are dealing with an argument based more on principles: the protection that the WBO is intended to offer is regarded as unjustified government interference.[44]

The committee sees a clear link here with the trends and shifts described in chapter 2. The introduction of market forces into healthcare, the new role that this creates for 'healthcare consumers with the power to choose', the strong emphasis on the importance of prevention and a healthy lifestyle, the new focus on everyone taking responsibility for their own health, the promotion of all types of health checks and predictive tests, the widespread misconception that early detection is always useful or at least can do no harm: all these factors make the WBO and its licensing requirement look utterly anachronistic.

In the remainder of this chapter, the committee first discusses the issue of whether the WBO is in fact necessary to protect people from the risks of unsound screening. It then returns to the problem of freedom of choice and paternalism.

6.4 Value of the Population Screening Act (WBO)

The WBO is an unusual piece of legislation. Except in Flanders, the committee is not aware of any other country among those it investigated (see annex C) that has similar legislation imposing licensing requirements on the provision of (risky) population screening. We could ask ourselves why this is. Does the fact that hardly any other country appears to see any need for legislation along the same lines as the WBO mean that such legislation is actually superfluous? Is it obvious that the aims pursued by the legislator (quality, protection) can be sufficiently achieved by other types of legislation and regulation, such as general quality legislation, laws on patients' and consumers' rights, and legislation on product safety? If so, then would it not be simple to resolve the problems mentioned in the evaluation report and the difficulties encountered by the Healthcare Inspectorate with the WBO by abolishing the law?

The committee does not come to this conclusion. The fact that broadly similar instruments exist hardly anywhere else (though there are many examples of statutory rules governing specific population screening or certain aspects of screening) does not mean that scrapping the WBO would only do away with various bureaucratic issues of definition and enforcement. The potential problems relating to the quality of screening are simply too great for this to be the case. The committee would like to illustrate this by way of a few examples.

6.4.1 *Problems with screening quality in other countries*

1 German law requires screening provision accessible to people covered by statutory health insurance to comply with a number of general requirements, most of which relate to the 'validity' of the test rather than addressing the broader question of whether the benefits for those concerned outweigh the disadvantages of screening (clinical utility). Attempts to broaden the requirements along these lines have so far failed. A screening programme that is systematically offered and assessed has recently been introduced for breast cancer (mammography); this is the only condition for which such a programme exists. A recent publication described other forms of cancer screening in Germany as being opportunistic and of inadequate quality.[194] In a more general sense, this is also the conclusion reached by a working party of the joint committee of doctors and insurance companies that is responsible for the screening provision (Gemeinsamer Bundes-ausschuss; G-BA).[223]

2 There has been criticism of the quality of the informed consent in France's national programme for serum screening for Down's syndrome ever since it was introduced in 1997.[224] Recommendations for 'improving information to pregnant women' (drafted by a working party of the professional groups concerned and published by the Haute Autorité de Santé, HAS) did not appear until 2005. But a recent publication indicates that information is still not up to standard, and since a high-profile 'wrongful birth' case ('affaire Perruche'), medical practitioners may have been tempted to 'play safe' by presenting screening and any follow-up testing to pregnant women as a matter of course.[225]

3 Japan regards screening as much more important than primary prevention. Screening was introduced by law for stomach cancer (in 1966), neuroblastomas (1985) and lung cancer (1987), even though it had not been proved to be useful.[226] Japan was the only country with a national screening programme for neuroblastomas in infants. Similar programmes have been introduced in various regions of countries such as Britain, France, Austria and the United States. Two large-scale trials showed that screening more than doubled the number of cases diagnosed without reducing the number of metastised tumours or death from neuroblastomas.[218,227] The initial assumption that early diagnosis is always beneficial ignored the fact that this form of cancer can disappear spontaneously. The Japanese screening programme was terminated in 2004, thirty-two years after it was launched in Kyoto. The Canadian/American trial cost 8.8 million dollars, but waiting for

its findings meant that Canada and the US saved 575 million dollars in screening costs, 5,000 false-positive screening outcomes and unnecessary treatment (surgery, chemotherapy) on at least 9,200 children.[228]

4 In the United Kingdom, the National Screening Committee (NSC) has an important role in monitoring the quality of screening offered by the National Health Service (NHS). The NSC advises on what forms of screening should be included in or removed from NHS provision, and on implementation and investigation. It acts on the basis of the same criteria for responsible population screening that are used by the WBO Commission in the Netherlands.[151,152] As the NHS cannot introduce any screening without it being first reviewed by the NSC, the system is de facto a licensing system. The NHS website contains a list of screening techniques that the NSC has indicated should not (yet) be offered, either because there is not yet enough evidence or because it is clear that such provision would do more harm than good. But this system applies only to NHS provision. Various forms of private medical screening, for which there is less scientific evidence, are available outside the NHS. Examples include total-body scans and other health checks, screening for various forms of cancer, including prostate cancer and breast cancer (targeted specifically at women aged between 40 and 50), screening for osteoporosis, cardiovascular disease, etc. In spring 2007, following the alarm call sounded by the British Medical Association[229], the NSC's programme director, Sir Muir Gray, highlighted the urgent need for additional regulation of screening in the private sector: 'We are thinking of how we control private testing because it's an example of low value activity which generates work for the health service, may cause harm and does not benefit the individual'.[230] The NSC is preparing an advisory report on this issue for the UK Ministry of Health. Furthermore, the Committee on Medical Aspects of Radiation in the Environment (COMARE) recently recommended an immediate ending of the practice of commercial provision of total-body scans using CT.[124] Another signal that unsound private screening is a growing cause for concern is the recent initiative aimed at creating a Medical Screening Code of Practice that would inform medical practitioners and other providers what is responsible in this area and what is not. Professor Wald, who was behind the initiative, commented as follows in the Journal of Medical Screening:

> There is, emerging in Britain, a culture in which judgments on medical screening practice are being made in the absence of evidence that a particular screening method is an effective and safe way of reducing morbidity and mortality from a specific disorder. (…) The present culture

appears unaware of publications on the principles of screening and the criteria for a worthwhile screening test. The culture needs to change, so that screening is subject to professional scientific assessment before it is promoted to the public.[118]

5 Healthcare policy is decentralised in many countries, or there are other barriers in the way of a nationally organised screening programme. Fragmentation can make screening much less efficient.[213,231] Well-organised population screening offers more health gain than opportunistic screening, and is less expensive.[232-234]

6.4.2 *Reasons for keeping the WBO*

These examples from other countries show that, in the committee's opinion, the WBO has significant added value[235] in three respects: Firstly, it has an educational significance that goes further than the limits of the licensing requirement.[236] Contrary to the situation that pertains in some other countries, doctors in the Netherlands agree that screening can be harmful, should only be offered if the ratio of advantage to disadvantage is favourable for those concerned, and that it stands or falls by the quality of actual provision. The committee takes the view that the WBO has made a major contribution to this by clearly 'setting standards' for the quality of screening programmes.

Secondly: the licensing requirement for forms of screening that are regarded as risky means that carrying out a concrete programme can be made conditional on specific quality standards that arise from an independent assessment of the entire proposed screening trajectory. The example of screening for Down's syndrome shows how important this is. The quality of information provision is critical in determining whether this form of screening gives the pregnant women taking part in it more advantage than disadvantage. In the Netherlands it is possible to make high-quality information provision a requirement.[237]

The ability to set quality standards is very important. Screening is a complex procedure in which four or more medical professions can easily be involved. It is vital that the same criteria are used throughout the country on important issues such as information, the screening test, the definition of what result is regarded as positive, intervals between tests, and the target group, as only then can sufficient quality of provision be guaranteed and the screening programme be evaluated. High quality of provision is crucial if population screening is to be efficient.

Thirdly: the WBO can prevent forms of screening that are regarded as risky and for which there is insufficient scientific evidence from being offered. This is

also possible in the United Kingdom, but only for state (NHS) provision. The debate currently taking place in the UK over unsound screening in the private sector is taken by the committee as an important argument against too readily calling the WBO into question. Without the WBO, the government would face much more difficulty in protecting the population against risks of screening.

The committee believes that the fact that this protection does not extend beyond national borders and that self-testing kits can be purchased via the Internet for conditions for which no unlicensed screening is permitted in the Netherlands does not detract from the continued importance of the WBO.

6.5 The paternalism of the Population Screening Act (WBO)

But this does not answer the key objection of principle. The fact that some forms of screening (for which a WBO licence is required but has not been obtained) are not easily accessible in the Netherlands can be regarded as a form of state paternalism: limiting the freedom of citizens while claiming that this is being done in their own interests. Is the government not going too far in its attempt to protect citizens? Should well-informed people not be able to decide for themselves whether they want to undergo a particular test at their own expense, even if this puts them at some risk?

6.5.1 The WBO as an instrument of 'hard paternalism'

The literature draws a distinction between hard and soft paternalism.[238,239] Soft paternalism means the government being allowed to stop people engaging in activities that would harm them if these are not based on a (sufficiently) free choice. These could include action under force, action based on inaccurate or incomplete information, or action by incapacitated people. The aim is not in the first instance to prevent people harming themselves, but to prevent them doing so on the basis of what are not really their own choices. Hard paternalism does have the first of these aims in view. The government removes certain choices, even if these meet all the conditions of free will, in order to prevent people from harming themselves. An example of a soft-paternalist measure is the requirement proposed in the 2007 Population Screening Annual Report that providers of DIY self-testing kits must enclose with their products information that is comprehensible to lay people about the performance of the test in relation to the aim of the test.[3] This should put people in a better position to take their own decision as to the use of such tests. It is easy to argue why this is justified. However, the WBO licensing requirement goes a step further. The consequence

of this measure is that certain forms of screening are not available in the 'best interests' even of people who clearly understand the risks and drawbacks but still want to undergo testing. This is hard paternalism, which is much more difficult to justify.

6.5.2 *First justification: no significant restriction of autonomy*

Can the restriction on freedom that arises from the licensing requirement be justified? The committee sees two possible arguments. Firstly, it could be argued that the self-determination of most people, in the sense of realising certain ideals of life to which they themselves adhere, is not significantly restricted by the licensing requirement. This view can be explained by the following analogy. The law requires people to wear seat belts and motorcycle helmets. People who do not wear a seat belt or who leave their helmet at home do not generally do so because using these devices is contrary to important aspects of their belief of what constitutes a good life ('living on the edge'), but because they are weak-willed or careless. People find safety more important than comfort, but do not necessarily always draw the logical conclusions from this. So they should appreciate the little nudge that a legal obligation provides,[239] as it helps them act in accordance with what they really do want. The requirement to wear a seat belt or helmet can be justified as a form of self-binding that can only be organised collectively. The few individuals for whom being able to drive a car or ride a motorbike without wearing a seat belt or helmet forms part of the good life can be asked to accept this obligation in the interests of everyone else.

Restriction of freedom as a form of collective self-binding

The restriction on freedom of choice that is the consequence of the WBO licensing requirement can also be regarded as a form of collective self commitment. Chapter 2 points out that the need for reassurance is an important reason why people want to undergo screening. This is psychologically understandable in the light of the high value that people put on their own health and the belief that it is vulnerable. It is for this very reason that it is implausible to expect people to put their own health knowingly and deliberately at risk if this is the price for the reassurance that any screening test, however good or bad it is, will usually offer most participants. Though the way people actually choose to behave suggests otherwise, this is probably because if you want reassurance, you will probably allow yourself to be reassured too easily.

Most people who go to Germany to have a total-body scan that is not permitted in the Netherlands do not do so because they find the disadvantages on balance to be acceptable, but because besides giving reassurance, they expect the scan to be purely beneficial. It is hard to understand that just finding out that 'something's wrong' does not by any means imply that you will benefit from that knowledge, and that it can also lead to a trajectory that may entirely unnecessarily lead to serious health damage. Because this information is at odds with the deep-rooted need for reassurance, it is also hard to accept. This makes people vulnerable to the often incomplete information in the advertisements of commercial providers.

Against this background, it could be argued that the licensing requirement plays a similar role to the requirement to wear a seat belt or helmet as described in the previous example. It is true that it restricts freedom (certain forms of screening that are hazardous to participants' health are not available), but the actual aim of this is to stop people making a choice that is contrary to their real priorities (i.e.: health rather than reassurance).

Individuals who would rather make another choice can be asked to pay a price

The question then is whether or not there might be people for whom more is at stake than the freedom to act against their actual priorities. This is not to say that it could be seriously considered whether for some people reassurance would be more important than health. It is, however, conceivable that someone might come to a conclusion about the utility of a particular form of screening for themselves that differs from the the assessment underlying the decision not to grant a WBO licence.

Clearly, we are dealing here not with the anticipated health effects or other outcomes of screening, as these can only be determined for groups rather than for individuals. The chances facing individual participants are only those that can be derived from this group information. The possibility of a different conclusion is only expressed in terms of advantages and disadvantages when the possible outcomes are weighed up. The evaluation performed with a view to granting or withholding a licence must at this point focus on quality-of-life research or be based on the criterion of the 'reasonable person'. Even if most people support the result of this assessment, that will not necessarily apply to everyone.

It is conceivable that individual men, having weighed up the pros and cons for themselves, may wish to undergo screening for prostate cancer. Anyone who concludes that any chance of living longer is more important than the possible

risks of considerable health damage should not be swayed by the fact that it is still unknown whether screening can produce a health gain. Just like individual motorcyclists who do not see the requirement to wear a helmet as a nudge, someone in this situation could assert that the WBO licensing requirement robs him of significant choices.

This assumes that this choice does reflect that individual's actual priorities and is based on a good understanding of the implications of the often complex probability information that is important in making the decision. But the number of people who would (be able to) take a decision on whether to undergo screening under these circumstances is probably quite small. That is precisely why something like collective self-binding can be a rational instrument for most people. But can the individual who rejects this be asked to accept the much greater restriction on freedom that this constitutes for him in the general interest?

The point at issue here is the right to private life, as laid down in the Constitution and in the European Convention on Human Rights and Fundamental Freedoms. It could be argued that one aspect of this includes the right to obtain information about oneself with a view to taking personal decisions, or in any case the right not to be unnecessarily impeded in attempting to do so. The question is whether the latter principle (being unnecessarily impeded) applies here. The greater the interest of all others in the enforcement of the licensing requirement, the more important it is for this question to be answered at an early stage. It flows from this that the justification being investigated here (in terms of collective self-commitment) is more convincing if the instrument in question is used more sparingly.

6.5.3 *Second justification: commitment to professional standards*

A second basis for justifying the licensing requirement is that, in contrast to the requirement to wear a seat belt or helmet, this is a form of 'indirect paternalism'. The ban does not directly interfere with the liberty of people to undergo a form of screening that they would like to have, but with the freedom of others (doctors) to carry out this screening and thereby fulfil the wishes of those concerned. In most legal systems, indirect paternalism is accepted if someone's right to life, physical integrity or personal freedom is at stake. The mere consent of the person whose rights are involved cannot offer carte blanche to someone who undermines, or wants to undermine, those rights on his or her request.

Untested or unsafe drugs are not available either

As an extension of this, it is accepted that drugs cannot be put on the market if they have not been shown to be safe and effective. It is also accepted that doctors (and other professionals) cannot treat someone, even at their own request, if that treatment does not come up to professional standards, i.e. is indicated in the interests of the patient or client. There is no good reason why the same principle should not apply to screening. Doctors and other medical professionals are not required to comply with requests for screening that are not demonstrated to confer health gains or other significant benefits on those affected. Nor do they have to offer such screening.

Looked at from this perspective, the licensing requirement does not actually add anything to what would already happen even if the WBO did not exist. The restriction on freedom that this entails for people who want to undergo screening found to be unsound is similar to that resulting from inability to access unindicated treatment or untested, unsuitable or unsafe drugs.

As long as the link to professional standards is less robust than it is in curative medicine, the WBO is not superfluous. Some doctors may occasionally need to be reminded that screening is subject to the same principles of qualitatively responsible medical care. Where the risks are too great to let things run their course, the licensing requirement offers an important safety net. Nevertheless, this link can offer a critical foundation for achieving the desired protection without licensing and bans wherever possible. The committee returns to this question in the final chapter.

6.6 The burden on others must also be taken into account

Pure paternalism is not the issue in situations where the measure restricting freedom also protects the interests of third parties. That is the case here, as with the requirement to wear a seat belt or helmet. The freedom to undergo screening in order to obtain knowledge about oneself, even by means of unsound tests, puts a financial burden on others who have to contribute to the costs of any follow-up tests via their social insurance contributions.

It is of course acceptable for the follow-up costs of private screening to be paid from public funds in the case of outcomes that enable effective treatment or secondary prevention. But if the value of the screening (diagnostic validity and clinical utility) has not been demonstrated, while it is indeed known to lead to a high proportion of false-positive outcomes and over-diagnosis, this leads to unnecessary costs that are passed on to all who contribute to the social insurance

system. This eventually affects everyone's interest in good, affordable health care. This issue has also been raised in the UK debate on improving the quality of screening in the private sector by means of regulation or a code of practice.

At present, the level of costs passed on to third parties seems low, simply because relatively few people make use of private screening or DIY self-testing kits.[31] This might change, but whether this will definitely happen and how quickly the change will occur is impossible to predict. A striking conclusion from the evaluation of the recent screening programme conducted by the Renal Foundation ('Kidney Check') is that only a quarter of those who had an abnormal result went to see their GP.[37] Further research should be carried out into the (likely) effects of unsound private screening on publicly funded health care. It should cover all forms of screening (from prostate cancer screening to DIY self-testing kits) that are of unproven value but can lead to often expensive follow-up tests.

It has recently been decided in Germany that anyone wishing to undergo treatment for a disease contracted as a result of a non-medically-indicated procedure (such as cosmetic surgery, tattooing or piercing) must pay a considerable proportion of the cost themselves. By analogy with this, might it be conceivable to consider recovering the social costs of unsound screening from those who are so keen on using it? This might initially sound attractive ('the polluter pays'), but if you think about it for a moment it becomes clear that this is not an option for moral, legal and practical reasons – leaving aside the question of how tenable the German precedent is.[51]

If it is therefore inevitable that the costs will be passed on to the community at large, then from that point of view as well it becomes legitimate to ask whether and how unsound screening can be prevented. Though the WBO was not designed to protect society from unnecessary costs, the current definition of the licensing requirement does (to some extent) meet that need. The committee considers it desirable that when the WBO is revised, a section should be included specifically stating that screening which passes on unnecessary high subsequent costs to society may be licensed. This is an expansion of the factors that can be taken into account in assessing the need for the licensing requirement: not only the likelihood of health damage to participants, but also social harm.

6.7 Regulation of self-testing kits can be improved

In its 2007 annual report on population screening, the Health Council noted that regulations for self-testing kits should be tightened up.[3] The UK Human Genetics Commission made the same point in the reports entitled Genes Direct (2003) and

More Genes Direct (2007).[240,241] This section summarises the key conclusions and recommendations from the annual report.

6.7.1 *Improving self-testing kits as products*

The options for altering the rules governing self-testing kits as products are largely determined by the European IVD Directive, which will be reviewed in a few years' time.

Improvements to the IVD directive (proposals for the upcoming review)

- It is not sufficiently clear whether self-testing kits also need to be assessed for diagnostic validity and clinical utility in order to obtain CE marking. The 'essential requirements' should be clarified or adjusted along these lines;
- It must be made easier to adapt regulations to take account of rapid technological and commercial developments. One of the main problems is that the current system of risk classes in the CE assessment process is insufficiently flexible; tests which are not specifically named end up in the low-risk group and so can be assessed by the manufacturer. Tests for cancer and genetic tests must be added to the high- or medium-risk group as quickly as possible;
- Manufacturers of DIY self-testing kits applying for CE marking assessment must be required to have these kits tested with inexperienced users;
- The credibility of the CE marking assessment system needs to be made more transparent.

Improving marketing channel regulations

- The efficacy of marketing channel regulations needs to be examined. The weak points of the system include the definition of high-risk diagnostic products, the role of Internet-based pharmacies, and the fact that users do not receive the pack insert information until they have bought the test;
- This information should enable consumers to come to a considered decision as to whether or not to buy the test in the first place.

6.7.2 *Improving self-testing kits as services*

Bringing the self-testing process under the Quality Act

- Doubts as to the applicability of the Healthcare Facilities Quality Act to institutions or laboratories offering self-testing kits that include a service element (home collection, street-corner testing) must be eliminated (see 6.2.3).

Developing a quality policy for providers

- Within the framework of the Quality Act, providers of self-testing kits that include a service element will have to pursue a quality policy, which can be examined by the Inspectorate. The annual report recommends that the diagnostic industry should help devise such a policy, based on the code of conduct of the umbrella organisation Diagned;
- Within the framework of the Medical Treatment Contracts Act (WGBO), the professional groups concerned should consider what constitutes 'care provided by a good medical practitioner' in this context (art. 7:453 of the Civil Code). If they do not yet have a professional standard that covers this point, they should rapidly produce one.

6.7.3 *Improving information about self-testing kits (services and products)*

Users should be given appropriate information

- The user information must describe the purpose of a test in terms of the disease or condition for which it is designed.
- Providers must undertake (or be required) to indicate in their promotional material whether their tests are CE marked.
- By analogy with the requirements that currently apply to promotional statements for products for which a health claim is made, providers of self-testing kits must be required to make their promotional statements evidence-based.

6.8 Conclusion: protection is still necessary, but the tools are limited

The availability of new screening possibilities both inside and outside the public healthcare system and sometimes in the form of DIY self-testing kits can be regarded as strengthening the position of citizens and consumers of healthcare. They are given new opportunities for self-determination and responsibility for their own health. However, it is difficult to get across the message that in many cases it is not certain that this improves health prospects, and that screening almost always entails some risk. Taken together, these factors make the government's duty of protection both more important and more difficult. More important because provision is becoming more ubiquitous, and more difficult because it is hard to explain that some forms of screening (such as total-body scans and prostate cancer screening) that are available abroad cannot be carried out in the Netherlands because they do not have a WBO licence. This can easily be seen as unwanted State interference.

The scope of the licensing requirement is limited

One important message to emerge from this advisory report is that protection against risky screening remains important and that the WBO is essential for that reason. It is also clear that the scope of this instrument is limited. Population screening that requires a licence must first undergo thorough testing, but forms of screening that do not come into this category are not investigated in any way.

The rules for self-testing kits are of limited effectiveness

A significant part of the aforementioned recommendations for tightening up regulations governing self-testing kits can only be implemented in a European context, when the IVD Directive comes up for review. The most far-reaching, and probably therefore also the most controversial, recommendation relates to the clarification or adaptation of the 'essential requirements' for CE evaluation, so that these essential requirements also include investigating the diagnostic validity and clinical utility of a test. The plea for a change to the risk classification system is less controversial. Along with the proposed changes to the requirements laid down in the IVD Directive on user information and promotional statements, these proposals could improve the protective efficacy of the current regulations. If however it proves impossible to incorporate the clarification of the 'essential requirements' in the IVD Directive, as was argued

for in the annual report, then the protective effect of CE marking will remain inadequate.

Internet provision from outside Europe can evade all the rules

Self-testing kits offered via the Internet from outside Europe are also supposed to be CE marked before they can be supplied. But it is difficult to take action against providers that ignore this requirement.

Need for a different approach

The committee concludes that the instruments available to the government, however important they may be, only provide limited protection. In the following chapters, it outlines an approach based on an additional instrument: a quality-mark for responsible screening.

Chapter 7

The benefit of an active approach

It is not becoming any easier for the government to fulfil its responsibilities with regard to screening. The principal challenge is not necessarily the rate of scientific development referred to in chapter 3. If we look at how long it actually takes for worthwhile new screening opportunities to become available, this process is much slower than you might think from reports in the media. A far greater challenge is presented by the interplay between the various cultural, social, political and economic factors described in chapter 2, and the pressure exerted by them to make all kinds of screening available even if it has not been shown that it could make a positive contribution to the health outlook of those concerned.

The government can use the National Screening Programme or the basic package of medical services to ensure that responsible screening is available and accessible. It can also act to promote the quality of screening that it does not offer itself but that is part of public medical care through the package of services covered by statutory medical insurance (see chapter 5). Of course, it has less control over screening offered in the private sector. But this does not mean that it has no role whatsoever there. It certainly has a duty to protect citizens against the risks of unsound screening (see chapter 6). But the government can be expected to do more here than simply ensure that minimum standards are upheld. It should also do as much as it can to promote responsible provision and responsible use of screening, in accordance with the normative framework discussed in chapter 4.

Information and education (of both the general public and professionals) are important instruments here.

7.1 Towards an integrated approach

The committee proposes a system combining these various elements. This is an ambitious proposal as it requires a strong, proactive engagement with the whole area of screening. Engagement not primarily in the sense of regulation, though the WBO will still have a role to play, but in the sense of monitoring and assessing scientific and other developments, identifying opportunities for new forms of screening that can be worthwhile, promoting quality of provision and arming citizens with the knowledge they need in order to make responsible choices on the screening and self-testing kit market. The success of this depends on active engagement being placed in the hands of an independent, authoritative central body (a 'screening standing committee') that can act transparently to flesh out this idea. In the final chapter of this report, the committee examines the key tasks that would be transferred to this central body.

7.2 Identifying and using opportunities

Two of these tasks have already been referred to in chapter 5: advising on the content of state provision and encouraging research into new forms of screening that are important to public health.

This advisory work should be carried out on an ongoing basis. Chapter 5 mentioned developments in the treatment of metabolic conditions as relevant to neonatal screening. It is important to have a central body able to take the initiative of regularly investigating, by means of systematic assessments, whether these developments have progressed sufficiently for new screening opportunities to be eligible for inclusion in the heel-prick programme. This method can ensure that the government's screening provision follows the latest scientific developments as closely as possible.

In a more general sense, it is important to have a a central body encouraging research into worthwhile screening opportunities. It is true that a large amount of work is being done to investigate genetic variants, risk factors and associations, but the validation and systematic assessment of the advantages and disadvantages of screening developed as a result, which should be the next step, is a slow process. A recent report by the British Royal College of Pathologists (2008) referred to the need for adequate funding for this evaluation research, which is often expensive, and to the lack of any control function in this area. It is

as yet unclear who is responsible for ensuring that significant gaps in the development of knowledge are filled.[242]

Another important point is that new tests should be developed in the light of whether the greatest need lies from a public health standpoint, not just with a view to generating the greatest commercial demand.

7.3 Granting a quality-mark for responsible screening

For the past two years, the Health Council has been issuing annual reports on the screening situation. These contain brief assessments of current and new forms of screening based on scientific literature and the normative framework discussed earlier in this advisory report. These assessments show which forms of screening (including self-testing kits) have been found to be capable of producing health gain or other benefits to those concerned, which forms of screening are still being investigated in this respect, and which forms of screening have been found to confer no benefits on those concerned, and so are on balance likely to do more harm than good. Independent scientific assessments of (new) forms of screening are also carried out in other countries. Examples include the reviews and recommendations of the US Preventive Services Task Force, the (revitalised) Canadian Task Force on Preventive Health Care, and the Health Technology Assessment Programme of the British National Institute for Health Research.[243]

Like all the Health Council's advisory reports, the annual reports are intended to inform the government and parliament on the state of scientific knowledge. They are not intended in the first instance for a broader audience. But these regular independent reports could be regarded as a basis for a 'quality-mark' system of responsible screening that would be accessible to all citizens. The committee thinks that it would be useful to explore how this model could be developed. At this point it will simply set out a few principles.

7.3.1 Aim of the quality-mark: information, education, exposure, trust

The proposed system has four aims. Firstly: to offer users (and professionals) simple and comprehensible information that will enable them to sort the wheat from the chaff. Secondly: to put across the fundamentals of responsible screening to professionals and other providers. Medical professionals also need to be constantly reminded that early detection does not necessarily lead to health gain, and that screening can turn out to be harmful for those concerned. A third purpose of the quality-mark is to highlight irresponsible screening (bring it into the spotlight) and therefore make its provision less attractive. And fourthly, as

the reverse of this, to bolster public trust in screening that meets the requirements of the quality-mark.

Whether this can work in practice depends largely on the authority of the body involved and the support the system gains among the various parties involved (professional groups, patient and consumer organisations, insurance firms). The integrated approach for which the committee is arguing must consist as much as possible of a combination of existing and new initiatives.

A vital difference to something like the CE marking system is that this quality-mark is not intended to be used as an instrument of prohibition. The idea is not to ban the provision of screening that does not have a quality-mark, but that the quality-mark would promote responsible screening and discourage unsound screening. So we are certainly not talking about expanding the regulations, but about an instrument that, provided it gains sufficient support, would act as an alternative to more stringent rules (in particular: extending the licensing requirement under the WBO). This chimes with the ideas behind the recent British argument for a code of practice referred to in chapter 6:

> Education and self-regulation are probably the preferred approaches, since these encourage responsibility while retaining valuable flexibility that can be lost with governmental regulation. But if governmental regulation is to be avoided, health service providers, insurers and scientists in medical screening need to work together and prepare a Medical Screening Code of Practice. Demonstrating compliance with such a Code of Practice would go a long way towards securing public trust and reassuring people of the value of the value of screening services that are offered.[118]

7.3.2 *Possible features of the quality-mark*

The quality-mark may be conceived, for a start, as involving a positive or negative assessment of various forms of screening (breast cancer screening with mammography, prostate screening with the PSA test, total-body scans, self-testing kits which can be used to produce a partial or complete genome profile, etc.). In addition to this, the system could also involve awarding a quality-mark to providers who offer and carry out approved forms of screening in a responsible manner.

Basic version: assessment of forms of screening

The basic version consists of making the type of information that is given in the annual reports available on-line, but systematically revised to make it accessible to a broader public, regularly updated and with a conclusion in the form of an

evaluation. People who read about health checks or self-testing kits in the newspaper or on the Internet, or who are offered screening by their employer or health insurance firm, will be able to access independent information here that clearly shows whether the provision in question is worthwhile or not.

A negative evaluation (no quality-mark) means that a certain form of screening may have significant negative consequences for participants without any obvious benefits (in terms of health gain or otherwise) in return. Forms of screening that are shown to be beneficial on balance for participants will receive a positive evaluation (quality-mark). There is a possible intermediate category: no significant benefits, but no major drawbacks either. An important condition for the success of the system proposed here is that it should look only at the possible advantages and disadvantages to participants themselves, and not take social considerations (such as cost-efficacy) into account as well. If people want to use the quality-mark information, it must be clear that the evaluation has been carried out from the point of view of their own position as participants.

As was emphasised at an earlier stage in this advisory report, the effects of screening (in terms of the likelihood of particular outcomes) can only be established for groups. When assessing the importance of the benefits and drawbacks of screening for participants, the outcomes of quality-of-life research or the criterion of the 'reasonable person' will have to be taken into account, as is done with current WBO assessments. This approach can allow the quality-mark to show clearly to a broad audience what forms of screening are worthwhile or not in the light of the preferences of most people. But the underlying considerations must be put across in a transparent manner and in a form comprehensible to lay people in order to reflect the possibility that individuals will sometimes make different choices. Issues should be presented in the most neutral way possible in the cases of screening that focuses on benefits other than health gain (for example, in the context of reproduction).

Screening that is part of public provision and all forms of screening that are licensed under the WBO are always eligible for a quality-mark in the sense used here (positive evaluation). But forms of screening that do not fall into these categories may also receive a quality-mark if this is justified by independent scientific assessment. The reviews in recent annual reports indicate that this is not likely to be the case at present for many forms of screening. The assessments underlying the quality-mark must be updated at regular intervals. Quality-marks may be withdrawn in the light of new information.

One aspect of the proposal outlined here is that all newly submitted forms of screening should, in principle, be accompanied by an assessment. This is close to the proposal made in the WBO evaluation report that all forms of screening

should undergo an ‘authorisation test’.[215] But there are two differences. Firstly, the quality-mark is not limited to screening in the sense of the legal definition of population screening, but is meant to apply to the entire spectrum of possible screening activities. The proposed system could also assess DIY self-testing kits. The second difference is that, except in the case of population screening requiring a licence, a negative assessment or absence of assessment does not lead to the form of screening being banned.

Quality-mark for providers

In the basic version described above, a negative evaluation provides most information. The absence of a quality-mark tells people which forms of screening and self-testing kits they would be best advised to avoid. In contrast, a positive evaluation of a particular form of screening does not say anything about the quality of performance (including information, counselling and arranging suitable follow-up) by a particular provider. But these are the factors that can often determine the advantage to disadvantage ratio for users. In order for the quality-mark system to really improve quality and give people information which they can use to decide whether or not to take up a particular screening offer, a quality-mark for providers is vital too. Of course, this can only apply to providers of services (including home-collection kits and street-corner tests), not to providers of DIY self-testing kits.

This quality-mark would have to be based on the same assessment of the complete screening process to which population screening requiring licensing is also subject. Providers must submit an application in order to obtain a quality-mark. Whether they do so will of course depend on how important they feel it is to obtain such a quality-mark at the time.

Quality-mark for providers of screening in the research stage

Another possibility is for separate quality-marks to be granted to providers of screening that has not yet been proven to be useful but that is undergoing scientific research that has been approved by a medical ethics committee or under the WBO (in the case of population screening requiring licensing) to ascertain its utility. Of course, no further evaluation would then be necessary.

7.4 Involving professionals in the quality-mark system

The aim of the quality-mark is also to improve the quality of provision. In the light of this, it is very important that, in addition to other parties, the various professional groups and their scientific associations are closely involved in the development and implementation of the quality-mark. This involvement will not happen spontaneously, but will have to be actively encouraged. This can only be achieved by a powerful central body.

7.4.1 Quality-mark as catalyst for the development of guidelines and standards

This issue relates primarily to the relationship between the quality-mark on the one hand and, on the other hand, the development of (integrated) guidelines and standards for screening, something that is in the very early stages. Naturally, it is important that quality-mark evaluations are based as much as possible on existing professional documents relating to quality of screening (where they exist and are good enough). In turn, the development of such guidelines and standards, which is to be strongly encouraged, could take account of the quality-mark and its underlying evaluations. In this way the quality-mark will be able to send out an important signal on quality. International rapport should be the starting point for this.

7.4.2 Quality-mark as a norm for professional conduct

Secondly, it is important that the quality-mark and individual professionals are putting across the same message as far as possible. This means that professionals should not offer or carry out screening that does not have a quality-mark. It should also be possible to call them to account in that regard. This would require a close relationship between the quality-mark and professional standards – something that cannot be imposed but that needs to evolve. It could be a (desirable) outcome of the process of mutual adjustment referred to above.

Work on developing this aspect of the proposed quality-mark needs to examine whether a close relationship with professional standards as described might give rise to legal pitfalls, and how they can be dealt with. One clear advantage is that it can, in practice, have an important protective effect without any need to expand the WBO instruments of licensing and prohibition. This also makes a difference from the perspective of the objection of paternalism referred to in chapter 6. After all, if there is a close relationship between the quality-mark

and professional standards, it will be possible in specific cases to take account of the fact that individuals may come to a judgement of their personal advantage to disadvantage ratio that differs from the evaluation underlying the quality-mark. Professionals would not be prevented from responding to such requests for screening, as would be the case with a legal prohibition.

7.5 Providing advice on flexible application of the licensing requirement

In the previous chapter it was pointed out that the WBO is a useful protective instrument and must be retained, but also that the extent of the protection it affords depends on the rigid and somewhat arbitrary definition of the licensing requirement. Some aspects of the legislation do need to be changed in order for this instrument to become a useful complement to the quality-mark system proposed here. It must also be borne in mind that the WBO can only apply to forms of screening that incorporate a service, and so does not apply to DIY self-testing kits (see chapter 6).

7.5.1 Amendment of the WBO

Following on from the evaluation report, the committee argues that the three categories for licence requirement that are currently included in the law should be replaced by a more flexible system of designation by Order in Council. This was also the intention of the original bill. A more flexible system of decision-making on licensing requirements will make it easier to respond to needs at the time, and if necessary to bring forms of screening temporarily into the scope of licensing. Decisions on changing the licensing requirement would best be made on the basis of advice from the same authoritative independent body that operates the quality-mark system and is able to assess the risks of screening.

Legislative history shows clearly the kinds of risks against which the licensing requirement is intended to offer protection. In any case the issue must be risks pertaining to the users themselves. They may relate to the screening technique used, to the need for follow-up testing or suitable treatment if an abnormal result is found, or to possible psycho-social risks. Further to this, the committee would support a clause in the Act referring to the possibility of making forms of screening subject to the licensing requirement in order to guard against serious damaging consequences (financial and otherwise) to the healthcare system if this should prove necessary.

Changes are also needed to the legislation in order to make it quite clear that not only carrying out but also offering population screening that is subject to the licensing requirement without holding such a licence is a criminal act.

Finally, the committee raises the possibility that the WBO could be amended to include a requirement for the provision and conduct of screening to meet professional standards, and suggests that investigations should be carried out to ascertain whether, alongside the licensing requirement, the law could contain other, less invasive, protective instruments such as the ability to impose certain conditions on advertising for screening*.

7.5.2 *Licensing requirement as a safety net*

A restrained approach to use of the licensing requirement would be appropriate to the quality-mark system we are proposing here. Forms of screening should only be made subject to the licensing requirement if authorising them would entail a substantial risk (to participants or to the healthcare system) that cannot be (sufficiently) warded off by means of the quality-mark. The licensing requirement would then act as a 'safety net' below the quality-mark system.

Time will tell what this eventually means for the definition of the licensing requirement. This will depend partly on how the situation evolves: what forms of screening become available, how and to whom they are offered, what the risks are and whether they cannot be avoided in some other way (by the quality-mark system). If as a consequence the scope of the licensing requirement needs to be expanded in order to guard against significant risks, it is at least clear that the requirement of subsidiarity has been met alongside those of necessity and proportionality. But if the quality-mark appears to work, it may be possible to limit the scope of the licensing requirement as a result.

Provisional enforcement of the existing categories

There would not appear to be much point in making any fundamental changes to the current system of three categories before the more flexible approach to the licensing requirement is introduced in connection with the quality-mark system. Abolishing one or more of the existing categories would not make sense as the quality-mark system still has to prove its worth, while adding any new categories could interfere with the development of that system. Furthermore, the current

* See the legal background study (by prof. J.K.M. Gevers) to the advisory report Screening and the role of the government by the Council for Public Health and Healthcare.[221]

categories have enough good points to make it worthwhile keeping them in place for the time being at any rate. This is true of ‘screening for cancer’ and ‘screening for serious diseases or abnormalities for which no treatment or prevention is available’, and given the growing concern over radiation exposure caused by screening by CT scans (see chapter 3), also for ‘screening using ionising radiation’.

No licensing requirement for genetic screening at present

It has been argued that genetic screening should become subject to the licensing requirement, or at least that such a move should be considered.[3,244] The committee does not consider such a move expedient in advance of the quality-mark approach recommended in this chapter. Looking at the mental and social risks involved, both for the individual undergoing screening and his or her blood relatives, it is especially important to bear in mind the possibility of being faced with the prospect, or strong probability, of contracting a serious condition for which there is no treatment or prevention. However, screening for such conditions already requires a licence.

Loophole needs to be closed off

A solution needs to be found to a previously mentioned difficulty that leads to serious problems with the enforcement of the law: the fact that providers of (broad, multiplex) forms of screening, for example those using imaging techniques or DNA panels, can be deliberately vague as to the conditions on which the test is focused, even if it is clear that some of the conditions in question are (or are likely to be) cancer or serious untreatable conditions. The committee is of the opinion that when the current categories are transferred from the text of the Act to an Order in Council, an effort should be made to find a form of words that effectively closes this loophole without as a result making too many forms of screening subject to the licensing requirement again.

7.6 Monitoring practice

The system outlined here requires constant monitoring of tangible developments. Will the quality-mark work, and can the role of the WBO be further limited? Or will new developments rather provide grounds for further expansion of the licensing requirement? How can information provision be improved in the context of the quality-mark? How will the use of screening without a quality-

mark evolve, and how much burden will the resulting follow-up work place on the healthcare system? How will the field of genetic screening evolve, and will the quality-mark be able to cope with the risks it might present? Are there any indications that self-testing kits are being used to obtain medical information about third parties (especially children)?

7.7 Debate on the normative framework

The approach recommended by the committee also requires further debate on the normative framework discussed in chapter 4. If it is to continue to show the way in the future, it is important firstly that its role is confirmed in practice (by means of the quality-mark and public information) and secondly that it is kept appropriate and up to date by means of critical reflection and debate. One aspect that we could mention here as an example is the feasibility of informed consent to screening for several conditions at the same time.

7.8 Standing committee on screening

A standing committee on screening, partly similar to the UK National Screening Committee, should be charged with overseeing the integrated approach we are arguing for. It would then be perfectly logical for this committee to be made responsible for assessing WBO licensing applications as well.

Independent expertise

If it is to perform its duties properly, the standing committee will need the expertise required to oversee the entire sphere of screening, proactively assess new developments on their merits, pick up on hiatuses in the development of knowledge, identify risks of screening and produce comprehensible and accessible public information. It will need contributions from experts in particular fields (not only medical specialists, GPs and epidemiologists but also communications experts), representatives from other disciplines (law, philosophy/ethics, psychology) and experts invited from patient and consumer organisations in a personal capacity.

Support

It is essential that the system enjoys the widest possible support among all interested parties. These could include both medical professionals (professional

groups and organisations) and other groups such as insurance firms and patient and consumer organisations. In order that this support is generated, it is important that all relevant parties are involved in the running of the system outlined here, without undermining the independence of the standing committee and consequently the authority of its controlling function.

Funding

The standing committee and the quality-mark system that it will operate need appropriate funding. The government can be expected to make a significant investment in view of its duties, but other parties should also be reminded of their responsibilities. These would certainly include insurance firms, given their interest (and that of their policyholders) in a properly functioning quality-mark system, and scientific associations.

Embedding

The precise embedding and shape of this system remain to be determined. The standing committee itself could be set up as part of the Health Council to some extent, except for its operational tasks. This would be logical not only because of the Council's independent status and its expertise in assessing WBO licence applications and the annual reports, but also because of the overlap with the area of activity of the Advisory Council on Health Research (RGO), which is part of the Health Council. Obviously important would be close relationships with the Centre for Population Screening (CvB), which is responsible for the organisation and quality assurance of population screening currently offered in the public sector, and with the College of General Practitioners, specialists' organisations and the Institute for Healthcare Improvement (CBO).

International coordination and cooperation

Finally, international exchanges of views and coordination are important. This is because the challenges facing governments, professionals and society in this area arise in other countries too, even though they do not always enjoy the same priority yet. Where possible, international cooperation should take place in the assessment of new screening opportunities, in defining research priorities and in undertaking research.

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Annexes

Annex **A**

Request for advice

Letter dated 12 March 2007 (reference PG/ZP-2.747.737) from the Minister for Health, Welfare and Sport to the president of the Health Council and the president of the Council for Public Health and Health Care.

The Ministry for HWS requires an advisory report with a view to updating the policy on (population) screening*. Rapid scientific developments and their application have led to a dramatic increase in the provision of (population) screening in recent years, and this trend is expected to continue over the coming years. The topic is also high on the political and social agenda.

Advice is needed on two closely related points.

Firstly, the content of the national population screening programme over the next ten years in the light of the state of scientific knowledge and expected developments, and in view of a future-proof normative framework for government provision. This calls primarily on the expertise of the Health Council.

The Ministry also needs strategic advice from the Council for Public Health and Health Care as to the social effects and significance of the general increase in (commercial) screening provision available to the population from the point of view of citizens, healthcare providers and funding bodies, and

* The phrases ‘screening’ and ‘population screening’ are often used interchangeably and with different interpretations. ‘Screening’ in this context refers to the entire range of opportunistic early detection through to programmed detection of predisposition to a condition, the presence of risk factors for a condition, or the detection of an early stage of a condition, as is done in the national population screening programme provided by the government. Population screening in the context of Medical Help in Accidents and Disasters is not covered by this request for an advisory report.

from the perspective of government policy. The emphasis here is mainly on the contribution to prevention, quality aspects, funding/cost aspects, including the effects on the healthcare chain, and the relationship between healthcare and public health.
The main focus of the advisory report should lie on the role and responsibility of the government.
In view of the tasks and areas of activity of both the Health Council (GR) and the Council for Public Health and Health Care (RVZ), I am of the opinion that both Councils can work together to contribute their respective knowledge and expertise to the advisory report. The specific questions on which I would like the advice of both the GR and the RVZ, which cannot be answered in isolation, are set out below. Please discuss how this work can best be coordinated and notify me of your plans by 1 March. I should like to receive your advisory report by the end of 2007.

Health Council

The state of scientific knowledge, the likely new scientific developments, possible applications and ethical aspects in the field of population screening are matters that are always on the Health Council's agenda. For example, the Council has published various advisory reports on topics such as genetic screening, prenatal screening and neonatal screening, and reports in connection with the Population Screening Act (WBO). It also produces regular reports on developments in the area of population screening: the first of these was the 2006 annual report on population screening and the next one is due in the last quarter of 2007. In connection with horizon scanning and early warning systems, the Council is also tasked with producing reports on healthcare innovations that have been placed on the market or are likely to be placed on the market within the foreseeable future.
I should like the Health Council to address the following questions in addition to its ongoing advisory work:

1 What are the medium-term trends in the scientific development of new forms of screening and their practical application? What will this mean for the content of the national population screening programme over the next decade?
2 What criteria could the government use in deciding whether or not to add particular forms of screening to the national population screening programme or to remove them from it?
3 Given relevant social developments such as attitudes to health and illness, medicalisation, freedom of choice and individual responsibility, and how people deal with risks, is the normative framework based on the criteria set down by Wilson and Jungner for population screening sufficiently future-proof? Please consider the following issues:

3a. Can screening for untreatable conditions be a desirable or responsible part of public provision, and if so, under what conditions?
3b. What principles should be applied in dealing with information about both treatable and untreatable conditions that fall outside the remit of screening but that may become available as a

result of the tests used in screening? How should the interests of the individuals undergoing screening, of parents, of third parties and of professionals be balanced?

4 In working towards a responsible screening provision, how can the ‘stage of life perspective’ be taken into account?

5 I assume that you will also look at the international dimension in your advisory report. What are the criteria for government programmes in adjacent countries, do they meet the criteria laid down by Wilson and Jungner, and is the matter covered by regulations?

I also intend to ask the Health Council to produce a separate advisory report on the proposed changes to the WBO, addressing issues such as which categories of population screening should be subject to the WBO licensing requirement.

Council for Public Health and Health Care

These are the questions I am putting to the Council for Public Health and Health Care: (RVZ)

1 What are the opportunities and threats of the developments in (population) screening for individual citizens and for society as a whole?

2 What are the social effects and the significance of the general increase in (commercial) screening provision available to the population from the point of view of citizens, healthcare providers and funding bodies, and from the perspective of government policy? This is particularly in respect of prevention, quality aspects, funding/cost aspects throughout the healthcare chain, and the relationship between healthcare and public health.

3 What is the government’s role/responsibility in relation to the provision and funding of population screening, and what responsibility is borne by third parties, such as professionals, providers and funders of healthcare?

4 What instruments, such as information and explanation, do citizens need to deal with screening provision? and

5 What general requirements should the performance of screening provision in practice meet, especially such provision that is not covered by the PSA licensing requirement?

I should like the RVZ to focus on:

- the potential health gain;
- how expensive and cost-effective screening is from the point of view of social and economic returns;
- employment and access to insurance;
- risks of social exclusion;
- the international and legal dimensions.

I am sending this letter for information to the Chairman of the Lower House of the States-General.
The Minister of Health,
Welfare and Sport,
[signed] dr. A. Klink

Explanatory notes to the request for an advisory report

Science offers ever-increasing insights into the opportunities and risks of diseases. This is likely to result in a shift from (focus on) clinical medicine related to existing health problems to predictive medicine not related to existing health problems. Newly developed techniques offer previously unknown opportunities for determining (individual) risks of a condition and for taking preventive action against (potential) conditions. These developments give rise to opportunities and threats to individual citizens and society as a whole, and pose fresh challenges to government policy.
Understanding the risks of contracting disease can encourage people to make efforts to avoid the disease or to postpone it by changing their lifestyle. This can increase citizens' autonomy and freedom of choice. Another effect can be an increase in prevention opportunities. Screening does have drawbacks, such as medicalisation, over-consumption of healthcare and the suggestion that it guarantees good health, etc.
The opportunities for early detection and screening are likely to become cheaper, more accurate and more suitable for large-scale use, and more widely available. These factors and medical technological developments will lead to an increase in demand, putting huge pressure on supply and the use of diagnostic devices. Recent experience shows that people do generally tend to respond to the offer of screening.

Political context

Protecting citizens' health and preventing ill health are among the main responsibilities of the Ministry of HWS under the constitution. Population screening is one of the instruments in the field of public health that can contribute to both of these tasks. The aim is to reduce morbidity and mortality, and in the longer term perhaps also to reduce the burden on the healthcare budget and cut social costs.
Coping with rapidly rising healthcare expenditure is a major challenge for the government. It is sometimes cheaper and usually more effective to invest in preventing disease at the start of the healthcare chain than to pay for additional and expensive care at its end; prevention pays. On the other hand, preventive interventions can lead to an increase in demand for healthcare. Screening has drawbacks as well as benefits.
The number of (freely accessible) tests is rising; the DIY medical market is experiencing a sharp increase in turnover. The slogan 'prevention is better than cure' is used to offer citizens a choice of commercial and non-commercial health tests and check-ups. At one end of the spectrum are home-testing kits offered by chain stores. Consumers can use these kits to test for things such as pregnancy, ovulation, cholesterol or menopause, and also simple tests carried out in supermarkets. At the other

end are the ‘total-body scans’ which are conducted in specialised clinics or centres using high-tech equipment to look for serious conditions such as various forms of cancer.

Another recent phenomenon is ‘direct access testing’ (DAT): laboratories offer various tests that consumers choose and pay for themselves without the intervention of a medical professional being required. More and more genetic tests are becoming available via the Internet.

The entire range of screening options available to consumers can be broken down into the following segments:

1 government provision: the national population screening programme. The benefit of this provision is that it is evidence-based and the quality of performance is guaranteed. Part of this provision comes under the WBO licensing requirement: a licence from the Minister for HWS is needed for it to be carried out. The WBO licence is an instrument aimed at guaranteeing the quality of performance of population screening that can be risky for citizens;
2 third-party provision covered by the WBO licensing requirement (see point 1);
3 third-party provision that the government has decided not to add to the national population screening programme. At present, the government does not interfere with this provision: individuals decide for themselves whether they want to undergo this screening, and they pay for it themselves. But the government does clearly have a duty of information here. It is preparing a policy on this issue in the light of the advisory report. There are two situations to be considered:
   3.a. provision that is not harmful, and
   3.b. provision that is harmful but does not (yet) come under the WBO licensing requirement.

Government policy on population screening

Some of the provision available to citizens is provided by the government itself. These are the national programmes of population screening that are organised and funded by or on behalf of the government: the national population screening programme. Because of the major financial and social implications, the decision on whether to introduce large-scale population screening that entails risk and that is proven to contribute to public health is taken by the government. Prevention programmes serve a public interest that requires the government to play an active role and take responsibility. When the government is considering whether to add a new form of population screening to the national population screening programme, it looks carefully at the medical science, epidemiological, socio-psychological, ethical, economic and legal aspects. There is a broad consensus on the 14* criteria which population screening must meet as a minimum requirement. Population screening is only responsible if it has been proven (evidence-based) that participants are more likely to be helped than harmed by it. This is related to the fact that participants will in theory have no medical symptoms and that the initiative lies with the body performing the screening rather than with the

* Wilson & Jungner laid down ten criteria in 1968 and the (former) National Council for Public Health added four more in 1994.

person undergoing it. A strict system of quality assurance applies to these programmes, covering issues such as information. Individuals must be able to recognise that government provision is ‘safe, useful and responsible’.

In view of the opportunities and developments that are likely to arise, an important political question is whether the principles and criteria underlying the national population screening programmes currently funded and organised by the government need to be revised.

There is also a growing interest in and market for commercial screening outside standard healthcare covered by social insurance. The provision of commercial preventive screening is expanding. Medical insurance firms can also distinguish themselves from their competitors by offering preventive screening to policyholders who take out additional insurance. This free market could lead to lower costs (preventing disease) or to higher costs (increasing medicalisation and consumption of healthcare), but also to health gains and more patient-friendly care. The topic ‘boundaries of healthcare’ is one of the social tasks mentioned by the Ministry for HWS as a key topic for the knowledge and innovation agenda for the healthcare sector*.

Finally, a debate has started in society on the benefits of prevention from a social and economic perspective and the ways in which prevention can be funded via the basic package of medical services. Secondary prevention is the only form of prevention relevant to this request for an advisory report.

* Social Tasks for Public Health and Health Care, The Hague, March 2006, Ministry for Health, Welfare and Sport, page 33.

Annex **B**

The committee

- Prof. H.R. Büller, *chairman*
  Professor of Internal Medicine, Amsterdam University Medical Centre
- Prof. J.M. Bensing
  Professor of Medical Psychology, Utrecht University Medical Centre
- Prof. P.J.E. Bindels
  Professor of General Practice Medicine, Amsterdam University Medical Centre
- Prof. M.C. Cornel
  Professor of Community Genetics, Amsterdam Free University Medical Centre
- Prof. C.M. van Duijn
  Professor of Epidemiology and Biostatistics, Erasmus Medical Centre, Rotterdam
- Prof. J.C.J. Dute
  Professor of Medical Law, Erasmus University, Rotterdam
- Prof. Y. van der Graaf
  Professor of Clinical Epidemiology, Utrecht University Medical Centre
- Prof. J.D.F. Habbema
  Professor of Operations Research, Erasmus Medical Centre, Rotterdam
- Prof. G.A. den Hartogh
  Professor of Ethics, Amsterdam University

- Prof. H.S.A. Heymans
  Professor of Paediatric Medicine, Amsterdam University Medical Centre
- Prof. B.W.J.H. Penninx
  Professor of Psychiatric Epidemiology, Amsterdam Free University Medical Centre
- Dr. D. Stemerding
  Medical Sociologist, Twente University, Enschede
- Prof. F.R. Rosendaal
  Professor of Clinical Epidemiology, Leiden University Medical Centre
- Prof. A.L.M. Verbeek
  Professor of Clinical Epidemiology, St Radboud University Medical Centre, Nijmegen
- Dr. Y.A. van Duivenboden, *advisor*
  Health Council, The Hague (from December 2007)
- P.C. Groeneveld, *advisor*
  Ministry of Health, Welfare and Sport, The Hague
- Dr. P.G. Reulings, *advisor*
  Health Care Inspectorate, Amsterdam
- Dr. W.A. van Veen, *advisor*
  Health Council, The Hague
- Dr. W.J. Dondorp, *scientific secretary*
  Health Council, The Hague
- L.F. Stultiëns, *scientific secretary*
  Health Council, The Hague

The Health Council and interests

Members of Health Council Committees are appointed in a personal capacity because of their special expertise in the matters to be addressed. Nonetheless, it is precisely because of this expertise that they may also have interests. This in itself does not necessarily present an obstacle for membership of a Health Council Committee. Transparency regarding possible conflicts of interest is nonetheless important, both for the President and members of a Committee and for the President of the Health Council. On being invited to join a Committee, members are asked to submit a form detailing the functions they hold and any other material and immaterial interests which could be relevant for the Committee's work. It is the responsibility of the President of the Health Council to assess whether the interests indicated constitute grounds for non-appointment. An advisorship will then sometimes make it possible to exploit the expertise of the specialist

involved. During the establishment meeting the declarations issued are discussed, so that all members of the Committee are aware of each other's possible interests.

Annex **C**

International comparison of criteria and regulations governing screening

Issues addressed, methodology

The request for an advisory report asked the committee to ascertain what the criteria for government programmes were in adjacent countries, whether the criteria for responsible population screening laid down in 1968 by Wilson and Jungner for the WHO were adhered to, and whether there were any regulations governing the area. The committee started by selecting countries to investigate in answering these questions. The international comparison looked at Belgium, Denmark, Germany, Finland, France, Ireland, Norway, Spain, the United Kingdom and Sweden as well as two non-European countries, Australia and Canada.

The committee then produced and discussed a questionnaire, which was sent to contacts in these countries in early June 2007. The contacts were found in national screening advisory bodies (HTA institutes, national screening committees), screening units at ministries and universities, or other relevant establishments. The contacts were asked to provide a range of information, including: what screening programmes are funded/organised by the government in their country; what criteria were used when deciding on whether to introduce new forms of screening; whether these criteria were incorporated in national legislation; what other legislation has an (indirect) impact on screening practice; how screening offered by other parties is handled; and whether in the light of scientific developments the criteria laid down by Wilson and Jungner are thought to be future-proof. The committee then examined the literature (publications, docu-

ments, legal texts), a process that involved consulting various reports on screening.[212, 245-247]

The answers to these questions will be discussed in the context of four principal topics:

1 Screening provided by national/regional authorities: who decides what is provided and what the screening programme contains?
2 Criteria, legislation and regulations: what criteria (Wilson and Jungner or other criteria) underlie a screening programme, and are these enshrined in legislation?
3 Quality assurance and evaluation: what action is taken to ensure that screening programmes meet high quality standards and how are they assessed?
4 Screening outside national/regional programmes: what action does the government take to protect citizens against harmful/unsound forms of screening that are offered outside standard screening programmes?

The committee's findings on this matter do not claim to be exhaustive: the amount of detail presented depends partly on the information provided by our contacts.

Screening provided by national/regional authorities

The national and/or regional authorities in the countries we examined offer a variety of screening programmes (annex E).

The structure of medical care in a country determines whether screening is offered on a national or regional basis. In many countries, medical care is decentralised and the regional authorities have the powers to decide what screening programmes are offered. Some of these countries have adopted legislation specifying what screening programmes must be offered by the regional authorities (see below).

In *Spain*, for example the Minister for Public Health and Consumer Affairs is responsible for defining a basic package of medical services that is part of the state-funded Spanish healthcare system. This package includes, among other services, the following particular forms of screening: neonatal screening, screening for older children, cervical cancer screening and breast cancer screening. The seventeen autonomous communities and regions can decide to add other services to the basic package, funded from their own regional resources.

In *Germany* the government decides, via the Social Legislation Code, what types of screening are available to individuals with statutory health insurance (90

percent of the population).[248] But the government does not organise screening programmes itself, apart from the breast cancer programme which was introduced in 2004.* In contrast to the situation in the Netherlands, collective prevention is covered by social insurance (*Gesetzliche Krankenkassen*). In this way, the national government creates the framework which is further developed and implemented by guidelines created by the self-regulatory body of doctors and medical insurance funds, the *Gemeinsame Bundesausschuss* (G-BA). The G-BA's guidelines are binding on all providers of statutory health insurance.** They apply to a very wide range of screening activities, including, besides various forms of prenatal and neonatal screening, screening for breast cancer (palpation, instruction in self-examination, and mammographic screening since 2004), cervical cancer, prostate cancer (rectal probe), bowel cancer (gFOBT, with the option of a colonoscopy instead since 2002), skin cancer and a check-up every two years (kidney disease, diabetes, cardiovascular disease risk factors).***

The countries investigated have (independent) bodies that advise the government on the desirability of introducing screening programmes by means of national recommendations and guidelines. These are generally based on HTA research that is carried out either by the advisory body itself of by an HTA institute set up for this purpose.

Although health policy is decentralised in many countries, the recommendations of the national advisory bodies still play an important role. For example, the advice and guidelines of the *National Boards of Health* in *Denmark* and *Sweden* are usually accepted. In the *United Kingdom*, the *National Screening Committee* (NSC) has an important role. Though it is left to the *UK Health Departments* (England, Scotland, Wales and Northern Ireland) to decide whether to introduce a particular screening programme, the *National Health Service* (NHS) can only introduce programmes that have been approved by the NSC.****

In other countries, such as *Australia* and *Canada*, we find that various initiatives are developed at national level aimed at improving and implementing screening programmes. The content and quality of screening programmes often vary from one region to another in countries with a more decentralised system, unless there is legislation governing these aspects.

Professional groups often play a key role in advising on various forms of screening. In *Australia*, where there is no national screening programme, the relevant professional groups work at national level to develop policy and issue rec-

* www.g-ba.de/downloads/39-261-33/2003-12-15-Krebs-Mammo.pdf
** http://www.g-ba.de/downloads/17-98-2491/2007-11-Faltblatt_GBA.pdf
*** www.die-gesundheitsreform.de
**** www.nsc.nhs.uk

ommendations on prenatal and neonatal screening.[249-252] And in *Canada* policy on prenatal screening is based on the guidelines issued by the relevant professional groups.[253] In *Germany* the professional groups exert considerable influence via the G-BA.

Criteria, legislation and regulations

Criteria

All the countries we investigated use Wilson and Jungner's criteria – explicitly or implicitly – s a starting point for assessing screening programmes. However, these criteria have over the years been added to and revised in most countries. This has been done partly in the light of new scientific developments (especially in the field of genetics, where the examples of *Canada/Québec* and the *United Kingdom* spring to mind), partly in response to new insights (that screening requires informed consent, or that there may be worthwhile outcomes other than treatment options), and partly in order to lay greater emphasis on elements already contained in the work of Wilson and Jungner or arising from it (such as the requirement for screening provision to be evidence-based, or the central principle that the benefits to those concerned must outweigh the drawbacks).[151-153] In *Australia* there is a national project to develop a 'screening framework' in which a review of Wilson and Jungner's criteria is a priority element.

Legislation and regulations

No country – apart from *the Netherlands* and *Belgium* (Flanders) – has legislation making the introduction of (certain forms of) screening conditional on prior consent/authorisation by the government. Further work is being done on this in Flanders. Further to the Flanders Prevention Decree of 21 November 2003 on preventive health policy, which states that population screening in the context of disease prevention requires the consent of the Flemish government, a draft decree on population screening has been drawn up but not yet adopted.

Legal basis for criteria.[a]

Belgium	Flanders Decree of 21 November 2003 on preventive health policy (art. 31); set out in more detail in the Content and Generalities Memorandum to the decree (http://www.zorg-en-gezondheid.be/preventiedecreet.aspx); the criteria are defined in more detail in the Flanders Draft Decree on population screening in the context of disease prevention - another text based on the Prevention Decree[b]
Germany	Volume V § 25 (3) of the Social Legislation Code (Sozialgesetzbuch (SGB) Fünftes Buch (V) – Gesetzliche Krankenversicherung – of 20 December 1988); defined in more detail in § 17 of the Verfahrensordnung of the G-BA (http://www.g-ba.de/downloads/62-492-83/VerfO_2006-04-18.pdf)
Finland	Government Decree on Screenings (1339/2006) of 21 December 2006 (http://www.finlex.fi/fi/laki/kaannokset/2006/en20061339.pdf). Some of the criteria are contained in the actual text of the government decree, while some are contained in the explanatory memorandum to the decree.
France	Decree of 27 September 2001 (Arrêté du 27 septembre 2001 fixant le modèle de la convention type mentionnée à l'article L. 1411-2 du code de la santé publique) (J.O. du 03/10/2001 Pages: 15582/15583, Annexes: Bulletin officiel du ministère chargé de la santé n° 2001/43 p. 274-318)[c]
The Netherlands	Population Screening Act of 1 December 1992.[d]
Spain	Royal Decree 1030/2006 of 15 September 2006 (based on Act 16/2003 on the cohesion and quality of the National Healthcare System) (http://www.boe.es/g/es/bases_datos/doc.php?coleccion=iberlex&id=2006/16212 - Spanish)

[a] See annex D for an extended summary of the criteria used by the countries in question, which in some cases have been expanded and/or revised.

[b] We have not referred to the actual criteria as this is still a draft.

[c] These are quality criteria for population screening for cancer; the general criteria for assessing screening programmes drawn up by ANAES are not enshrined in law.

[d] It is true that these are not a direct transposition of Wilson and Jungner's criteria (or of those drawn up by the Health Council in 1994), but the three statutory evaluation criteria do cover more or less the same ground.

There are often statutory rules governing some aspects of screening. For instance, the *United Kingdom* has legislation on the use of ionising radiation that applies expressly to screening [*The Ionising Radiation (Medical Exposure) Regulations* 2000]. In addition, as indicated above, some countries have laws making it compulsory for certain forms of screening to be provided. Since 1 January 2007, the regional authorities in *Denmark* have been required to offer breast cancer screening [Health Act of 24 June 2005 (§ 85), which came into effect on 1 January 2007]. Local authorities in *Finland* must offer at least breast cancer, cervical cancer and prenatal screening. The obligation to offer prenatal screening came into force on 1 January 2007, and all local authorities must com-

ply by 1 January 2010 at the latest. This statutory obligation is regarded as essential in order to put a stop to the current chaotic situation (each of the 400 local authorities had the freedom to decide what screening method should be used).[254] Decisions on whether to introduce screening programmes are taken by the Finnish *National Screening Committee* (which is part of the Ministry for Health and Social Affairs) on the basis of a list of criteria drawn up by the Ministry and included in the explanatory memorandum to the *Government Decree on Screenings* (1339/2006). Local authorities can decide whether they wish to offer screening programmes that they are legally required to provide on a broader basis or to introduce screening for other conditions. If they do so, they must respect the criteria laid down in the decree and the explanatory memorandum. This decree requires local authorities to take sufficient account of quality assurance procedures when organising screening programmes. They must also monitor and evaluate the quality of screening and the reliability of tests.

France has very specific legislation on pre- and post-natal screening and on screening for cancer. The provision of some forms of pre- and post-natal screening is compulsory by law (article L2122-1 *Code de la Santé Publique*). The screening of children up to the age of six – the number and nature of tests and the periods in which they must be carried out – is also a matter for legislation (article L2132-2 *Code de la Santé Publique*). A government decree lays down the general principles in which screening programmes for breast cancer, cervical cancer and bowel cancer must be organised (*Arrêté du 27 septembre 2001 fixant le modèle de la convention type mentionnée à l'article L. 1411-2 du Code de la Santé Publique*). It is true that these do not contain the criteria laid down by ANAES (*Agence nationale d'accréditation et d'évaluation en santé*) for assessing screening programmes, but they do specify quality criteria which population screening programmes for cancer must meet. An appendix to the decree contains a very comprehensive and detailed description of the way in which such programmes must be designed and conducted.[163]

In *Spain* various forms of screening (including prenatal, neonatal, cervical cancer and breast cancer screening) are offered to the population through the basic Services Portfolio (SP) funded as part of the national healthcare system. The basic SP is enshrined in law by means of Royal Decree 1030/2006 of 15 September 2006 (which is based on Act 16/2003 relating to the cohesion and quality of the National Healthcare System).

In *Germany* a recent change in the law to § 62 of SGB V means that people who have not made use of screening paid for by insurance have to pay a higher proportion of their healthcare costs if they then contract a disease for which that particular form of screening would have tested. These new regulations relate at

present to breast cancer, bowel cancer and cervical cancer, but the list will be expanded in the future.[52] Since 2004, insurance firms have also had the opportunity, under § 65 a of the SGB V, to award bonuses to policyholders who regularly have themselves screened. The change in the law is controversial, as it touches on various fundamental rights, such as the right to self-determination, the right to take well-considered informed decisions as to whether to undergo screening without pressure, and the right not to know. Other criticisms include: the potential for people who are ill to be stigmatised (the system could give the impression that people who suffer from a particular disease have only themselves to blame), the problem of a causal link (between non-participation and the disease) and the difficulty of the age limit for certain forms of compulsory screening (is it sufficiently justified in the light of the principle of equality laid down in the constitution?).[223]

Quality assurance and evaluation

Various countries have different methods of supervising and monitoring their programmes through specialised institutes in order to ensure that the screening programmes offered by the national and/or regional authorities are of sufficient quality. In the *Netherlands*, the Centre for Population Screening (CvB), which is part of the National Institute for Public Health and the Environment (RIVM), is responsible for ensuring that the national population screening programmes have quality assurance systems and are evaluated. The National Reference Centre for Breast Cancer Screening in Nijmegen has a mandate that includes training and refresher courses for people involved in screening, promoting and checking quality (inspections) and the central physical and technical quality assurance of screening mammography. There is also a National Breast Cancer Screening Evaluation Team which evaluates this form of screening.[255] The National Cervical Cancer Screening Evaluation Team is based at Erasmus Medical Centre in Rotterdam.[256] In *Australia*, the national screening programmes are subject to quality management programmes that relate, among other things, to the accreditation process (for all services offered in the screening programme) and the collection of data for evaluating the results of the programmes. Evaluations and reports by the *Australian Institute of Health and Welfare* (AIHW) and the *Screening Subcommittee* of the *Australian Population Health Development Principal Committee* (APHDPC) ensure that these programmes are conducted in line with national policy.

In *Finland* the screening programmes offered by local authorities are overseen by various bodies: the *Mass Screening Registry* of the Finnish cancer regis-

tration system: planning, evaluation and control of national screening programmes; the *National Research and Development Centre for Welfare and Health* (STAKES): supervision of existing screening programmes and the methodologies used by them; the *National Public Health Institute*: works with STAKES to evaluate existing screening programmes; the *Basic Security Council*: has the power, on instructions from the Minister for Social Affairs and Health, to investigate any irregularities in the provision of healthcare services by local authorities.

In *France*, healthcare provision is monitored at national level by a number of bodies, including the *Haute Autorité de santé* (HAS). The HAS works closely with the *Agence française de sécurité sanitaire des produits de santé* (Afssaps), a body that is responsible for the safety, efficacy, quality and proper use of healthcare products, including the quality of clinical or screening mammographies, and the *Institut de Veille Sanitaire* (InVS), a national body monitoring healthcare. Each region has a *comité régional des politiques de santé* with various duties including quality assurance of screening programmes for breast, cervical and bowel cancer.

In *Ireland*, the new Health Act 2004 created an independent advisory body, the *Health Information and Quality Authority* (HIQA), which monitors quality and safety in healthcare. The HIQA establishes standards, implements a programme of quality assurance reviews, monitors compliance with the standards and investigates any possible violations.

In *Norway* the *Norwegian Board of Health* ensures that services are provided in line with professional standards. At local level, the situation is overseen by regional boards, which report to the *Board of Health*.

In the *United Kingdom*, independent bodies have been set up for monitoring healthcare in England, Scotland, Wales and Northern Ireland: the *Healthcare Commission* (England) – responsible for monitoring NHS services and services provided by independent healthcare organisations; the *Health Inspectorate Wales* – monitors NHS services and the *Care Standards Inspectorate Wales* – monitors independent healthcare; *NHS Quality Improvement Scotland* and the *Regulation and Quality Improvement Authority* (Northern Ireland). Programmes have also been set up for quality management of population screening for breast and cervical cancer: each NHS region has a reference centre with a quality assurance director for the relevant forms of population screening that is charged with ensuring compliance with the standards that have been established.

Screening outside screening programmes

This can be divided into:

- screening offered on an individual basis for conditions for which organised population screening (screening programmes) or at least official recommendations exist. This is referred to below as opportunistic screening;
- the provision of health checks, total-body scans and self-testing kits. This is referred to below as 'unregulated screening'.

Opportunistic screening

Opportunistic screening is more or less the only form of screening available in a number of countries, such as *Germany, Luxembourg, Austria* and the *US*. Consequently, vital components of screening programmes that are important to the quality and suitability of screening provision are absent.[194,257,258] Opportunistic screening can be beneficial if it reaches members of the target group who do not participate in the screening programme. For example, in the *Netherlands* 79 percent of women aged between 30 and 60 have a smear test once every five years if opportunistic screening is included in the figures, but only around 70 percent take part in the population screening programme for cervical cancer. In some countries the figure rises to over 80 percent, but only where the interval between tests is short (as in *Iceland*), where opportunistic screening is widespread (*Finland*) or where both these factors are present (*Germany*).[259,260]

Unorganised screening does however often lead to over-screening and under-screening: In Belgium, where unorganised screening for conditions such as breast cancer and cervical cancer is still common, we find that, despite the guidelines issued by the Federal Healthcare Information Centre (KCE) on the matter, provision varies and there is a discrepancy between the evidence-based recommendations on screening and what actually happens in practice. The proportion of women aged between 25 and 65 attending cervical cancer screening once every three years is only 59 percent. Those who do attend are often over-screened. Half of this 59 percent have another smear test within a year, while the other 41 percent rarely if ever have a smear test.[261]

‘Unregulated’ screening

Individual countries do not always place control of ‘unregulated’ screening equally high on the agenda. Some countries do not (yet) see it as a (common) problem. Other countries are monitoring developments but do not yet have a clear policy. In *Finland*, unregulated screening (PSA tests, for example) is regarded as a problem. The *National Screening Committee* has set out a strategy of taking the first steps towards controlling unofficial screening of healthy, asymptomatic individuals. Specific measures against ‘unregulated’ screening have been taken in the *United Kingdom:* the NSC has drawn up a list of diseases for which screening is not recommended. This list is published on the National Health Service website.*

The site also refers to the dangers of certain unregulated forms of screening that do more harm than good, including total-body scans, ECG screening, prostate cancer screening, breast cancer screening by mammography for women under 50.** The NSC has raised the issue of regulating screening in the private sector and is investigating how this can best be achieved.*** Medical professionals who wish to conduct screening tests outside the NHS framework may do so, but are bound by the guidelines of their regulatory body.

The Human Genetics Commission (HGC), a UK advisory body, published a report on the commercial provision of genetic tests titled *Genes Direct* in 2003.[240] The main conclusion of the report was that an independent body should be set up to assess (claims of) the diagnostic validity and clinical utility of genetic tests. It suggested that all genetic tests offered by commercial providers should be assessed by this body before they could be put on the market. It also advised that predictive genetic tests should generally be undertaken on medical advice. Another recommendation was that no direct advertising be permitted for such tests. It suggested that the *Medicines and Healthcare products Regulatory Agency* (MHRA) should take a leading role in this. It also emphasised the need for training professionals and for public and consumer information (partly with a view to Internet provision). The latter task should be performed by a new independent consumer body that could provide impartial information about direct genetic testing services. The report also recommended that the relevant professional groups be asked to develop codes of practice.

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* http://www.screening.nhs.uk/noscreen/index.htm.
** http://www.screening.nhs.uk/home.htm.
*** http://www.medicexchange.com/mall/departmentpage.cfm/MedicExchangeUSA/_0/1107/departments-content-view.

In December 2007, the HGC published a follow-up report entitled *More Genes Direct* in which it revised and supplemented its 2003 recommendations as follows: it recommended urgent work to revise the risk classification of genetic tests in connection with pre-market review; suggested an alternative regulatory mechanism for genetic tests not covered by the IVD Directive (such as lifestyle tests); recommended the creation of a code of practice for services related to genetic tests (along the lines of existing international standards – OECD, Eurogentest) to be devised and implemented by cooperation between interested parties (such as government agencies, public bodies, charities and the industry).[241]

The Committee on Medical Aspects of Radiation in the Environment (COMARE) was commissioned by the Ministry of Health to investigate the health effects of computer tomography (CT) screening. COMARE produced its report in December 2007, recommending among other things that services offering commercial total-body scans using CT should stop doing so immediately as there was no scientific advice that the benefits outweigh the harmful effects.* It also suggested that the regulations governing commercial CT services (referral procedures, justification and improvement of CT scans) needed to be reviewed.

In *Belgium*, the Advisory Committee on Bioethics produced an advisory report on the free availability of genetic tests (DIY self-testing kits and home-collection tests) in 2004. Its recommendations included providing accurate public information on the opportunities and limitations of genetic tests and ensuring that permanent training is conducted in the relevant professional training courses in the field of genetics (importance of genetic counselling). The report emphasised the importance of freely available genetic tests complying with the statutory minimum quality guarantees (CE label) and of a prohibition on the storage and later use of hereditary data collected from self-testing kits. The Committee was divided on whether a general ban on the distribution of genetic self-testing kits was necessary.

Conclusion

The screening provision in the various countries investigated shares several common features, but there are also considerable differences. We also observed regional differences within some countries where healthcare is organised on a decentralised basis. The extent of decentralisation can influence the organisation, content and quality of population screening programmes even when national pol-

* www.comare.org.uk/documents/COMARE12thReport.pdf

icies or guidelines have been formulated or produced by professional groups or national advisory bodies.

Forty years after Wilson and Jungner established their criteria in 1968, they are still the basis for the normative framework used to assess population screening programmes, but they have been revised and made more specific in almost every country, partly in the light of scientific developments and specific local circumstances. A small number of countries have incorporated (some of) Wilson and Jungner's criteria, or criteria derived from them, in legislation.

Separate legislation making population screening dependent on prior government authorisation/consent exists only in the Netherlands and Belgium. But other countries do often have statutory rules on some aspects of screening. The structure is usually as follows: advice/guidelines on screening is produced by national advisory bodies, which may play a general advisory role in health body issues or work specifically in the field of (cancer) screening, supported by HTA research and guidelines by the relevant professional groups. In these countries, various institutions are responsible for supervising and evaluating screening programmes. Specific quality management programmes for this purpose have been set up in some cases. Healthcare professionals are also required to follow the rules laid down by their regulatory bodies.

The way in which screening is organised (opportunistic screening/organised population screening) is one of the factors affecting the quality and suitability of screening. Opportunistic screening usually reaches a lower percentage of the target group, and there is often unsound screening. This system is still widespread in many countries. Individual countries do not always place the problems of 'unregulated' screening equally high on the agenda. The matter has been the focus of much recent attention in the United Kingdom in particular.[118,124,230,262]

Sources of information

The following contacts were consulted in order to obtain information from the selected countries:

Australia: Kearny B (Medical Services Advisory Committee), Barton B (Screening Section of the Population Health Division of the Department of Health and Ageing); Belgium: Borry P (Katholieke Universiteit Leuven); Canada: Blancquaert I (Agence d'évaluation des technologies et des modes d'intervention en santé – AETMIS), Avard D, Costea I (Universiteit van Montreal); Denmark: Probst H (National Board of Health); Germany: Rosenbrock R (Wissenschaftszentrum Berlin für Sozialforschung gGmbH), Abholz H (Universiteit

Düsseldorf); Finland: Malila N (Finnish Cancer Registry), Autti-Rämö I (Kela – The Social Insurance Institution of Finland); France: Bacou J (La Haute Autorité de santé); Ireland: S Corcoran-Baxter (National Cancer Screening Service), Madden D (University College Cork); Norway: Forland F (Norwegian Directorate for Health and Social Affairs); Segovia C, González J (Institute of Health Carlos III); United Kingdom: Taylor J (UK National Screening Committee); Sweden: Tollin C, Håkansson S (The National Board for Health and Welfare)

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gen, 20 april 2007; 3) Gemeinsamer Bundesausschuss. Richtlinien über die ärztliche Betreuung während der Schwangerschaft und nach der Entbindung ('Mutterschaftsrichtlinien'), 12 juli 2003;

- *Finland:* 1) Järvelin J, Health Care Systems in Transition: Finland. Copenhagen, WHO Regional Office for Europe. European Observatory on Health Care Systems, Vol. 4 No. 1 2002; 2) Malila N, Anttila A, Hakama M. Colorectal cancer screening in Finland: details of the national screening programme implemented in Autumn 2004. J Med Screen, 2005; 12:28-32; 3) Autti-Rämö I, Mäkelä M, Sintonen H, Koskinen H, Laajalahti L, Halila R, *et al*. Expanding screening for rare metabolic disease in the newborn: An analysis of costs, effect and ethical consequences for decision-making in Finland. Acta Paediatrica, Volume 94, Number 8, 2005;
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Annex **D**

Criteria for responsible population screening

Wilson and Jungner 1968

5 The condition sought should be an important health problem
6 There should be an accepted treatment for patients with recognised disease
7 Facilities for diagnosis and treatment should be available
8 There should be a recognisable latent or early symptomatic stage
9 There should be a suitable test or examination
10 The test should be acceptable to the population
11 The natural history of the condition, including development from latent to declared disease, should be adequately understood
12 There should be an agreed policy on whom to treat as patients
13 The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
14 Case-finding should be a continuing process and not a ‘once and for all’ project.

Health Council Genetic Screening Committee 1994

1 A genetic screening programme must relate to a health problem or to a condition which can lead to such a problem in those being tested or in their descendants.
2 The target group of the screening programme must be clearly defined.
3 The purpose of the programme must be to enable the participants to determine the presence or the risk of a disorder or carrier status, and to take a decision on the basis of that information.
4 Practical courses of action must be open to the participants.
5 Participation in a genetic screening programme should be completely voluntary and should be conditional on consent based on good information.
6 The target group should be supplied with good quality, comprehensible information.
7 A test method should be available which is suited to the objective of the screening.
8 There should be sufficient facilities for follow-up testing, to carry out the selected courses of action and to inform and support the participants.
9 The procedures used for the storage of medical information and cellular material must incorporate adequate measures to protect both the personal privacy of the participants and their rights regarding their personal data and cellular material.
10 If scientific research is carried out within the framework of screening, the participants should be properly informed about this in advance.
11 Provision should be made for continual quality assurance of the effectiveness, efficiency and safety of the test procedure, any follow-up work, as well as information and support given to the participants.
12 When weighing up the benefits and drawbacks for the participants in the programme, the final balance should be clearly biased towards to benefits. To assist with this evaluation, those proposing a screening programme must provide information about:
   a the prevalence of the disease or disorder in the target group;
   b the natural course of the disorder, and the variation in degrees of severity;
   c those target groups which are eligible for testing and the considerations which led to selection of the proposed target group and the proposed time of life for testing;
   d the specificity, sensitivity and predictive value of the test method to be used and the burden which such testing imposes on participants;

e the available courses of action if a health problem or carrier status are revealed;
f the time allowed by the procedure for consideration and possible implementation of the choice made;
g the potential psychological, social and other repercussions (both positive and negative) of an offer and of participation or non-participation in the screening, for the person to be tested and for members of their family or for groups within the community;
h the likelihood of erroneous results, the possible consequences of this for participants and the measures taken to limit any harm which such an error might cause;
i what guarantees there are to prevent participants experiencing unjustified impediments (as a result of their participation or non-participation in the screening programme or follow-up testing) to obtaining employment or private insurance cover;
j the costs which are linked to the screening and to the attainment of the requisite infrastructure.

Countries included in the comparison

All countries included in the comparison use Wilson and Jungner's criteria – explicitly or implicitly – as a starting point for assessing screening programmes. The summary below indicates what additions or changes various countries have made to the original criteria.

Country/criterion	The condition sought should be an important health problem (W & J 1)
Belgium	• Significant morbidity and mortality (Flanders Prevention Decree) • Common in the population undergoing screening (Flanders Prevention Decree)
Canada	• Common and/or serious health problem (AETMIS)
France[a]	• Repercussions on the individual and society should have been measured in terms of morbidity and/or mortality and socioeconomic impact
Norway	• Common enough and serious morbidity or mortality
Spain	• Social need

[a] criteria based on those drawn up by the UK National Screening Committee (NSC), supplemented with criteria from the Canadian and American standards

Country/criterion	There should be an accepted treatment (W & J 2)
Belgium	• Early treatment is more beneficial than later treatment (KCE) • Acceptable, available and effective intervention and treatment (Flanders Prevention Decree)
Canada	• Treatment or preventive measures with a demonstrable evidence based favourable effect on the course of the disease, or a reproductive choice based on an improved risk assessment (AETMIS) • Treatment or intervention that improves survival or quality of life for patients with the disease (*National Committee on Colorectal Cancer Screening)* • Behandeling in presymptomatische fase meer succesvol dan in symptomatische fase (Nationale richtlijnen *Family Centred Maternity and Newborn Care)*
Germany	• Effective, evidence-based treatment possible
France, Ireland, United Kingdom	• Effective treatment or intervention[a] + evidence of earlier intervention leading to better outcomes than later intervention • Evidence based policies on which intervention should be offered to which individuals
Norway	• Effective treatment at an early stage
Spain	• Effective contribution to prevention, diagnosis or treatment of diseases, maintenance or increase of life expectancy, or decrease of pain or suffering

[a] Or: information felt to be important for the individual with the disease (ANAES, France).

Country/criterion	Facilities for diagnosis and treatment should be available (W & J 3)
Canada	• Adequate staffing and facilities for recruitment, testing, diagnosis & follow-up, treatment and programme management (*National Committee on Colorectal Cancer Screening)* • Budget and infrastructure, public information, laboratory, management and professional education and training available prior to the start of the programme (AETMIS)
Germany	• Enough doctors and facilities to establish a thorough diagnosis and treatment of suspected cases
France, Ireland, United Kingdom	• Adequate staffing and facilities available for testing, diagnosis, treatment and administration prior to the commencement of the screening programme
Norway	• Adequate material resources, and skilled professionals to carry out the screening, adequate therapy and post-treatment

Country/criterion	**There should be a recognisable latent or early symptomatic stage (W & J 4)**
Canada	• Or timely detection of an increased risk of disease or of transmitting the disease to one's offspring (AETMIS)

Country/criterion	**There should be a suitable test or examination (W & J 5)**
Belgium	• Sufficient sensitivity, specificity and predictive value in the target group (Flanders Prevention Decree) • Available at a reasonable cost (Flanders Prevention Decree) • Sufficiently standardised so that it can be performed with consistency, accuracy and reproducibility (Flanders Prevention Decree)
Canada	• Safe, usable on a large scale and scientifically based analytical and clinical validity (AETMIS) • Screening procedure has acceptible sensitivity and specificity (National guidelines *Family Centred Maternity and Newborn Care)*
Denmark	• Evaluation of test validity, technical efficiency and predictive value prior to decision on screening programme
Finland	• In terms of sensitivity/specificity and predictive value
France	• Simple, reliable, reproducable and valid screening test (performance in clinical practice must be known, not just laboratory performance)
Ireland	• Simple, safe, precise and validated screening test • Distribution of test values in the target group should be known and a suitable cut-off level defined and agreed
Norway	• Sufficient sensitivity/specificity and safe
United Kingdom	• Simple, safe, precise and validated screening test • Distribution of test values in the target group should be known and a suitable cut-off level defined and agreed

Country/criterion	The test should be acceptable to the population (W & J 6)
Belgium	• Acceptable for those who are at risk of the condition (Flanders Prevention Decree)
Canada	• Both test and further diagnostic investigation (*National Committee on Colorectal Cancer Screening*) • Entire programme must be consistent with the values of the target population (AETMIS)
Ireland, United Kingdom	• Evidence that the complete screening programme (test, diagnostic procedures, treatment/intervention) is clinically, socially and ethically acceptable to health professionals and the public
Norway	• Acceptable to patients and those who carry it out
United Kingdom	• Screening for a mutation: the programme should be acceptable to people identified as carriers and to other family members

Country/criterion	The natural history of the condition, including development from latent to declared disease, should be adequately understood (W & J 7)
Canada	• Epidemiology, natural history of the disease and of risk factors being screened for must be sufficiently well documented in order to demonstrate the efficacy of the intervention and to allow for informed choice (AETMIS)
Germany	• Medical technology must allow a sufficiently unambiguous interpretation of disease symptoms
France	• And epidemiology
Ireland	• And epidemiology • Detectable risk factor, disease marker, latent period or early symptomatic stage
United Kingdom	• And epidemiology • Detectable risk factor, disease marker, latent period or early symptomatic stage • The natural history of people who are carrier of a mutation should be understood, including the psychological implications

Country/criterion	There should be an agreed policy on whom to treat as patients (W & J 8)
Canada	• Evidence-based recommendations for the offering of further diagnostic investigation and/or treatment, and available choices (*National Committee on Colorectal Cancer Screening*)
France, Ireland, United Kingdom	• Consensus within scientific community on further diagnostic investigation of individuals with positive test result and on available choices
Ireland	• Agreed evidence-based policies covering which individuals should be offered treatment and the appropriate treatment to be offered

Country/criterion	The cost of case-finding (including diagnosis and treatment) should be economically balanced in relation to expenditure on medical care as a whole (W & J 9)
Canada	• The programme must not compromise the viability of the health care system (AETMIS) • Opportunity costs of the programme must be acceptable (AETMIS)
Denmark	• Economic assessment of cost-benefit, cost-effectiveness and/or cost-utility and other economic assessments
Germany	• The benefits and harms are assessed in the context of health care as a whole
France	• A screening programme is warranted when it is cost-effective compared to no (systematic) screening and when it is preferred to another health initiative by the financing body
Ireland	• Opportunity cost of the screening programme (including testing, diagnosis and treatment) should be economically balanced in relation to expenditure on medical care as a whole
United Kingdom	• Opportunity cost of the screening programme (including testing, diagnosis and treatment, administration, training and quality assurance) should be economically balanced in relation to expenditure on medical care as a whole

Case-finding should be a continuing process and not a 'once and for all' project (W & J 10)
• This criterion has not been expanded or amended in any of the countries reviewed

Country/criteria	Additional criteria[a]
Belgium	• The interval between having the test and obtaining the result and between having the result and the start of treatment must be as short as possible (KCE) • The invitation must not restrict freedom to participate (KCE) • Potential participants must be adequately informed of the benefits and drawbacks of participation. Medical professionals must also be aware of the benefits and risks (KCE) • The acceptability of the programme should be promoted by public information campaigns, but no moral pressure should be exerted (KCE) • There must be quality assurance and quality control procedures for the entire screening programme (KCE)

Country/criteria	Additional criteria
Canada	• Overall benefit of the screening programme should outweigh the potential harms (*National Committee on Colorectal Cancer Screening)* • Overall benefit should outweigh potential risk for individuals and families (AETMIS) • Clear definition of target group (AETMIS) • Integrated programme that incorporates public information, laboratory and clinical services, as well as programme management (AETMIS) • Quality assurance mechanisms for all levels of the screening programme including an ongoing programme evaluation (AETMIS) • Mechanisms for minimization of risks, including psychological, physical and social harms (AETMIS) • Mechanisms for informed choice and guarantees for respect for the autonomy of individuals and target group (AETMIS) • Programme must be accessible to target group (AETMIS) • Scientific evidence for effectiveness and efficiency of screening programmes (AETMIS)
Denmark	• Assessment of ethical and psychological consequences, stigmatization and consequences of "false positive" and "false negative" results prior to decision on introduction screening programme • Detailed description of the organisation of the programme, steering committee, registration system, visitation plan, information to target group, education of personnel, information on test result
Finland	• Evaluation of ethical and psychological consequences for the examinees, stigmatization and consequences of "false positive" and "false negative" test results • Detailed description of the screening organization: steering committee, quality control and registration system, provision of information to target group, visitation plan, staff training, test result dissemination and consultation • Monitoring and evaluation of the quality of the screening and reliability of the tests • All persons belonging to the target group entitled to participate in the screening on equal grounds • Participation in the screening is voluntary; information on objectives and effectiveness of screening, possible risks and organization • Organization of health services in such a way that there is no discrimination between those who have participated or intend to participate and those who have not participated or do not intend to participate in the screening
France, Ireland, United Kingdom	• Cost-effective interventions aimed at primary prevention should be implemented as much as possible • Evidence from high quality Randomised Controlled Trials or international consensus that the screening programme is effective in reducing mortality or morbidity • The benefit from the screening programme[b] outweighs harm[c] caused by the test, diagnostic procedures and treatment[d] • There should be a plan for managing and monitoring the screening programme + set of quality assurance standards[e]

Country/criteria	Additional criteria[a]
France	• Awareness programmes for both the target population and health professionals • Freedom to accept or refuse the test. Information on advantages and disadvantages of screening prior to consent
Norway	• Clear definition target group • Systematic means of quality Assurance
Spain	• Risk / benefit ratio sufficient • Screening complies with legal requirements for drugs and products
United Kingdom	• Where screening is aimed solely at providing information to allow the person being screened to make an "informed choice" there must be evidence from high quality trials that the test accurately measures risk • Evidence-based information, explaining the consequences of testing, investigation and treatment, should be made available to potential participants to assist them in making an informed choice • If the test is for mutations the criteria used to select the subset of mutations to be covered by screening should be clearly set out

[a] Only the most conspicuous conditions are referred to here.
[b] N.B. Ireland: [screening] test rather than [screening] programme.
[c] N.B. Ireland and the UK add 'physical and psychological' [harm] here.
[d] N.B. France: interventions rather than treatment.
[e] N.B. France adds: 'recognised by the medical community'.

Annex **E**

Screening in other countries

Comparison of national or regional screening in the countries examined.

Country screening-programme[a]	Breast cancer	Cervical cancer	Bowel cancer	Prenatal screening	Neonatal screening[b]	Screening of older children[c]
Australia	Women aged 50-69; interval: 2 years (national)	Women aged 18-69; interval: 2 years (national)	Women and men aged 55-65; interval: 2 years[d] (national)	States/territories have their own programmes and policy (regional)	Number of conditions (over 30, including PKU, CHT, CF, GAL) is decided regionally[e] (regional)	
Belgium[f]	Women aged 50-69; interval: 2 years[g] (national)	Women aged 25-64; interval: 3 years (regional) [h]		No specific programme (in Flanders), but there are national guidelines[i]	At present 11 congenital metabolic disorders[j] (regional)	Various systematic tests of growth and development (regional)
Canada	Women aged 50-69; interval: 2 years (regional)	Women aged 18-69; interval: 3 years (regional)[k]		Pregnant women > 35: Down's syndrome screening (triple test, amniocentesis or CVS test) Also considerable differences between provinces/territories (regional)	Number of conditions varies from 3 to 28 depending on the province/territory. Auditory screening is expanding (regional)	

Country screening-programme[a]	Breast cancer	Cervical cancer	Bowel cancer	Prenatal screening	Neonatal screening[b]	Screening of older children[c]
Denmark	Women aged 50-69; interval: 2 years[l] (national)	Women aged 23-59; interval: 3 years (national)[m]		All pregnant women: - screening for Down's syndrome using the combination test; - SEO[n]; - screening for hepatitis B: trial programme (national)	PKU, CHT and toxoplasmosis (national)	
Germany[o]	Women aged 50-69; interval: 2 years (national)[p]	Women over 19; interval: 1 year	Women and men aged 50-55; interval: every year; > 55 entitled to 2 colonoscopies: at age 55 and 65	All pregnant women: - 3 echoscopy examinations during pregnancy - (including SEO) High-risk pregnancies: - various tests inlcuding CVS/amniocentesis[q]	14 conditions	Children entitled to various tests up to the age of ± 14
Finland	Women aged 50-69; interval: 2 years (national)	Women aged 30-60; interval: 5 years (national)	Women and men aged 60-69; interval: 2 years[r] (regional)	All pregnant women: - screening for Down's syndrome using the combination or triple test - SEO[s] Women > 40: Amniocentesis or CVS (national) [t]	Only CHT (national)	
France	Women aged 50-74; interval: 2 years (national)	In 4 departments. - Target group: women aged 25-65 (3 departments) and 50- 74(1 department)[u] - Interval: 2 years (1 department) or 3 years (3 departments) (regional)	Women and men aged 50-74; interval: 2 years (national)	All pregnant women: - including rubella, toxoplasmosis and hepatitis B - screening for Down's syndrome using the triple test[v] - SEO Women aged 38 or more: amniocentesis (national)	PKU, CHT, AGS, sickle-cell disease and CF (national)	

Country screening-programme[a]	Breast cancer	Cervical cancer	Bowel cancer	Prenatal screening	Neonatal screening[b]	Screening of older children[c]
Ireland	Women aged 50-64;[w] interval: 2 years (national)	Women aged 25-60; interval: 3 years for women aged 25-44; 5 years for women aged 45-60 (national)		No national policy.[x] Amniocentesis, CVS and nuchal translucency measurement are available on request	PKU, GAL, MSUD, homocystinuria, CHT and toxoplasmosis (pilot project) (national)	
Netherlandsy	Women aged 50-75; interval: 2 years (national)	Women aged 30-60; interval: 5 years (national)		All pregnant women: - infectious diseases and blood groups; - information about screening for Down's syndrome using the combination test (only reimbursed for women aged 36+) - SEO (national)	16 conditions (heel prick) + auditory screening (national)	Infant and child health services:[z] - Hearing and sight - Check that testes have descended on time (boys) - Speech and language disorders - Monitoring health status of children (national)
Norway	Women aged 50-69; interval: 2 years (national)	Women aged 25-69; interval: 3 years (national)		All pregnant women: - screening for Down's syndrome using the combination test - SEO (national)[aa]	PKU, CHT and hearing abnormalities (national)	Hearing, sight and speech problems (national)
Spain	Target group varies according to region. Usually: women aged 50-64/ 65[ab]; interval: 2 years (regional)	In some regionsac. Target group: usually: women aged 35-65[ad]; interval: 3 or 5 years (regionaal)		Policy of most regions for Down's syndrome screening: All pregnant women: - nuchal translucency measurement - combination test - SEO Women 35+: amniocentesis/CVS (regional)	In all regions always PKU and CHT[ae] (regional)	Hearing and sight problems, testes descent, hip dysplasia, strabismus, obesity, autism (regional)

Country screening-programme[a]	Breast cancer	Cervical cancer	Bowel cancer	Prenatal screening	Neonatal screening[b]	Screening of older children[c]
United Kingdom[af] E= England W= Wales S= Scotland NI=Northern Ireland UK=E+W+S+NI	Women aged 50-70 (E/W/S); women aged 50-65 (NI) interval: 3 years (regional)	Women aged 25-64 (E); aged 20-64 (W); aged 20-60 (S); aged 20-65 (NI) interval: 3 years (W/S); 3-5 years (E); 5 years (NI) (regional)	Women and men aged 60-69; interval: 2 years (E) [ag] (regional)	All pregnant women: - screening for Down's syndrome (E/W/S; NI not generally offered); - SEO (UK) - thalassaemia + sickle-cell disease (E/W)[ah]; - rubella, hepatitis B, HIV and syphilis (E/W/NI) (regional) [ai]	PKU, CHT, CF(UK); sickle-cell disease (E/W); MCAD (E: full introduction in 2009); DMD (W); hearing test (E/W/S) (regional)	
Sweden	Target group varies according to district (county): 40-74 (11 districts); 50-69 (6 districts); between these 2 target groups in (8 districts); interval: 2 years (regional)	Women aged 23-50; interval: 3 years; women aged 51-60; interval: 5 years (regional)	In the Stockholm district from 2008: men and women aged 60- 64 (later expanding to 65-70) (regional)	- Down's syndrome screening: policy varies according to district[aj]. -SEO (regional)	PKU, CHT and AGS[ak] (regional)	

[a] Screening programmes are regarded as national in this advisory report if the content is determined at national level (perhaps in law) and it is implemented in more or less the same way throughout the country, or whether such a process is being set up. Screening programmes are regarded as regional if the decision whether to introduce a screening programme and/or what its content should be is taken at regional level.

[b] AGS= adrenogenital syndrome; CF= cystic fibrosis; CHT= congenital hypothyroidism; DMD= Duchenne's muscular dystrophy; GAL= galactosemia; MCAD= medium-chain acyl -CoA-dehydrogenase (MCAD) – deficiency; MSUD= maple syrup urine disease; PKU= phenylketonuria.

[c] Insofar as we know from the respondents to the questionnaire.

[d] Work began on a phased introduction of a national population screening programme for bowel cancer in August 2006. It may eventually be expanded to cover the 55 to 74 age range.

[e] The Human Genetics Society of Australasia and the Division of Paediatrics of the Royal Australasian College of Physicians devised a Newborn Screening Policy in 2004. The regions are free to decide what conditions to include in their neonatal screening programme. However, there no longer seem to be any major regional differences as to the conditions for which infants are screened.

[f] In Belgium, the regional governments decide on the conditions to be screened for and the criteria to be used. We only have information on the regional programmes in Flanders.

[g] As far as breast cancer is concerned, the communities and the Federal government signed a protocol in 2000 with a view to organising and funding a national breast cancer screening programme.

[h] Four of the five provinces of Flanders have formal systems for cervical cancer screening.

[i] A national guideline for prenatal care was produced by the Federal Healthcare Information Centre in 2004.
Its recommendations include discussing the risk of Down's syndrome (and other congenital abnormalities) and the advantages and disadvantages of a test and its consequences, and offering one of the following tests on request (ranked in order of efficacy): the combination test, the triple test and the nuchal translucency measurement test. A SEO is also recommended.

A survey of the situation in practice carried out in 2005 revealed a discrepancy with regard to the guideline: overall, more tests are carried out than was recommended (http://www.riziv.fgov.be/news/nl/press/pdf/press20070110.pdf).

[j] The Flanders Agency for Health and Welfare has stated that the number of conditions for which screening is to be carried out will be increased in line with developments in the Netherlands. This body currently screens for the following disorders: PKU, CHT, AGS, biotinidase deficiency, MCAD deficiency, multiple acyl-CoA dehydrogenase deficiency, isovaleriac acidemia, propionic acidemia, methylmalonic acidemia, MSUD and glutaric acidemia. Screening takes place in three recognised screening centres in Flanders. One of these centres (PCMA in Wilrijk) also screens for DMD.

[k] Two provinces currently have well-organised programmes for cervical cancer screening. A number of other provinces have recently launched programmes to boost participation rates.

[l] Although regional and local authorities are in principle autonomous in this area, breast cancer screening is regarded as a national programme, as the obligation to offer breast cancer screening to the relevant target group is enshrined in the new Health Act that took effect on 1 January 2007. Regional governments must comply with it. Breast cancer screening is currently offered in only three of the former 14 districts in Denmark. All regions were supposed to have set up a breast cancer screening programme by 1 January 2008, and all women in the target group must undergo screening for the first time by 1 January 2010.

[m] Although cervical cancer screening is not referred to in the Health Act of 24 June 2005, our respondent stated that there was a national programme and that regions were required to offer cervical cancer screening.

[n] SEO = structural echographic examination, around the 20th week of pregnancy.

[o] In Germany, a wide range of screening tests paid for by insurance is offered to clearly defined target groups. Besides the forms of screening referred to in the table, these tests include prostate cancer (annual rectal probe for men aged over 45), skin cancer (once a year: women aged over 30 and men aged over 45) and cardiovascular, renal disease and diabetes risk factors (every two years for women and men aged over 35). People in the target group are not invited for screening but can decide for themselves whether they want to avail themselves of screening paid for by insurance.

[p] In addition to mammography screening for women aged 50-69, the G-BA also advises that women aged over 29 undergo clinical (palpation) examination once a year.

[q] The forms of prenatal screening referred to here are based on the *Mutterschafts-Richtlinien* and are paid for by insurance firms. In practice, nuchal translucency measurement is becoming an increasingly common part of routine echoscopic examination. The triple test is also offered, but is not paid for by insurance.

[r] Some Finnish local authorities started offering gFOBT testing in 2004. The programme has become sufficiently large for it to be assessed as a randomised trial.

[s] Parents who would be unwilling to consider abortion can be offered the structural echoscopic examination after week 24 instead of between week 18 and week 21.

[t] There is a transitional period of 1 January 2007 to 1 January 2010 for the implementation of these forms of prenatal screening at local authority level.

[u] In the Isère department, this age category is used so that a single target group can be offered screening for three forms of cancer: breast cancer, bowel cancer and cervical cancer.

[v] The *Haute Autorité de santé* issued a recommendation in June 2007, in line with current practice, that the combination test (blood test and nuchal translucency measurement, carried out in the first trimester) should be offered nationally in addition to the triple test carried out in the second trimester.

[w] A report from the National Cancer Forum in 2006 indicated that the age should be raised to 69 in line with the European Council's recommendations on mammography screening.

[x] Abortion can only be performed if there is serious risk to the life of the mother, including suicide. The Constitution also states that the foetus's right to life does not deprive pregnant women of the freedom to travel from one state to another in order to obtain information about or to access services that are legally permitted in another state.

[y] In addition to the forms of screening referred to in the table, there is also a national screening programme for familial hypercholesterolaemia (FH): this is the cascade screening carried out by the Stichting Opsporing Erfelijke Hypercholesterolemie (StOEH) [Foundation for the Detection of Hereditary Hypercholesterolaemia] which involves family testing if an individual is diagnosed (by a GP or specialist) with FH.

[z] These are the services offered in the Basic list of infant and child health services for individuals aged up to 20.

[aa] Though prenatal screening in Norway is only offered to women aged 38 or over, a report published by the Directorate for Health and Social Affairs in 2005 (the National Clinical Guideline for Antenatal Care) indicates that, in the light of the recommendations contained in the report, prenatal screening is now probably being offered to all pregnant women.

[ab] In some regions the lower and upper limits are different (starting from 45 and up to 69).

[ac] Usually opportunistic screening.

[ad] In six regions, women are also invited from the age of 25.

[ae] For example, screening for haemoglobinopathies has also been carried out in the autonomous region of Madrid since May 2003.

[af] The screening programmes referred to are generally regarded as regional in the United Kingdom: The UK National Screening Committee (NSC) is responsible for issuing advice on screening in the United Kingdom. However, it is up to the UK Health Departments of England, Wales, Scotland and Northern Ireland to decide whether to introduce a particular screening programme.

[ag] In Wales, there are plans to introduce a bowel cancer screening programme in phases for women and men aged 50 to 75, at intervals of two years, in 2008; Scotland is currently introducing a bowel cancer screening programme. As soon as the programme becomes operational, bowel cancer screening will be offered at two-year intervals to all women and men aged 50 to 74; Northern Ireland plans to introduce bowel cancer screening in 2009.

[ah] In England, prenatal screening for sickle-cell disease and thalassaemia is being introduced at the moment; in Wales, prenatal screening for sickle-cell disease and thalassaemia is only offered to pregnant women regarded as being at higher risk.

[ai] Scotland and Northern Ireland have yet to decide on whether to screen pregnant women for haemoglobinopathies. In 2006, the national medical ethics council and the Swedish Council on Technology Assessment in Health Care (SBU) recommended screening for Down's syndrome. It is currently offered in six of the 21 counties.

[ak] In addition to the conditions referred to here, Sweden would also screen for GAL and biotinidase deficiency (see Javaher P, Kääriäinen H, Kristoffersson U, Nippert I, Sequeiros J, Zimmern R, Schmidtke J. *EuroGentest: DNA-Based Testing for Heritable Disorders in Europe,* Community Genetics 2008;11 :75-120).

Annex **D**

Abbreviations

ACCE	Analytic validity, Clinical validity, Clinical utility, and Ethical, legal, and social issues
AETMIS	Agence d'évaluation des technologies et des modes d'intervention en santé (Québec)
AGS	adrenogenital syndrome
ANAES	Agence nationale d'accréditation et d'évaluation en santé (France)
CE	European Conformity
CF	cystic fibrosis
CHT	congenital hypothyroidism
COMARE	Committee on Medical Aspects of Radiation in the Environment (UK)
CvB	Centre for Population Screening of the RIVM (Netherlands)
CT	computed tomography
DMD	Duchenne's Muscular Dystrophy
ECHR	Convention for the Protection of Human Rights and Fundamental Freedoms (Council of Europe)
FH	familial hypercholesterolaemia
FOBT	faecal occult blood test
GAL	galactosemia
G-BA	Gemeinsamer Bundesausschuss (Germany)
HGC	Human Genetics Commission (UK)

HPLC	high-performance liquid chromatography
HTA	Health Technology Assessment
HWS	Ministry of Health, Welfare and Sport (Netherlands)
IVD Decree	Decree on in-vitro diagnostic devices (Netherlands)
IVD Directive	European Directive on in-vitro diagnostic devices
KCE	Federal Healthcare Information Centre (Belgium)
MCAD	medium-chain acyl-CoA-dehydrogenase (MCAD) deficiency
MRI	magnetic resonance imaging
MS/MS	tandem mass spectrometry
MSUD	maple syrup urine disease
mSv	micro Sievert Sievert = unit of radiation dose received
NHS	National Health Service (UK)
NIPED	NDDO Institute for Prevention and Early Diagnosis (Netherlands)
NSC	National Screening Committee (UK)
PET	positron emission tomography
PKU	phenylketonuria
PSA	prostate-specific antigen
PSIE	prenatal screening for infectious diseases and erythrocyte immunisation
REVEAL study	Risk Evaluation and Education for Alzheimer's Disease study
RIVM	National Institute for Public Health and the Environment (Netherlands)
RVZ	Council for Public Health and Health Care (Netherlands)
SEO	structural echoscopic examination
SGB	Sozialgesetzbuch (Germany)
SNP	single nucleotide polymorphism
SPECT	single photon emission computed tomography
WBO	Population Screening Act (Netherlands)
WGBO	Medical Treatment Agreement Act (Netherlands)
WHO	World Health Organization