
Health Council of the Netherlands Reports 2009

Executive summaries



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Health Council of the Netherlands

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The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport, Housing, Spatial Planning & the Environment, Social Affairs & Employment, Agriculture, Nature & Food Quality, and Education, Culture & Science. 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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Preface

The Health Council of the Netherlands (Gezondheidsraad) is the scientific advisory body on health and health care to the Dutch Government. Since the integration, in February 2008, of the Advisory Council on Health Research (RGO), the Health Council also advises on health (services) research. Its recommendations cover fields which relate to the health of the population, such as clinical medicine, public health, environmental protection, food and nutrition and occupational hygiene. The Council's advisory reports are usually drawn up by independent, multidisciplinary committees of experts.

The present volume is a compilation of the executive summaries of reports published in 2009. Other publications without a summary are mentioned in Annex A. Copies of all reports, however, can be downloaded from our website: www.healthcouncil.nl or www.gr.nl. When ordering please mention the publication number.



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Contributing to optimum health care

Autism spectrum disorders: a lifetime of difference

Health Council of the Netherlands. Autism spectrum disorders: a lifetime of difference. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/09E. ISBN 978-90-5549-775-1 (in Dutch and English)

Autism Spectrum Disorders

Autism Spectrum Disorders (ASD) are developmental disorders characterised by limitations in social interaction, communication and imagination. They are often associated with stereotypical or rigid behaviour patterns. The term 'spectrum' is used to reflect the fact that the disorder takes different forms in each individual with ASD. Most ASD cases can be classified into one of the following three groups: childhood autism, PDD-NOS (pervasive developmental disorder – not otherwise specified) and Asperger's disorder. In childhood autism, depending on their age, affected individuals make little or no contact with the outside world. Conversely, those with PDD-NOS or Asperger's disorder are characterised not so much by a lack of contact, but more by dysfunctional interactions with those around them.

The causes of ASD are unknown. What is clear, however, is that ASD is largely hereditary, with a higher incidence among boys/men than among girls/women. Environmental factors also appear to be implicated in these disorders, but the exact mechanism involved has yet to be elucidated. Approximately half of those with ASD also suffer from some form of intellectual disability.

Request for advice

In recent years, there appears to have been an increase in the number of children diagnosed with ASD. This is mainly reflected in an increase in the number of applications for care under the terms of the Exceptional Medical Expenses Act (AWBZ)/client-linked budgets (PGB), or indications for special education/pupil-specific funding (LGF) associated with the diagnosis of ASD. There has also been an increase in the number of claims for incapacity benefit for young people with ASD.

In response to this development, the Minister of Youth and Families, together with his counterparts at the ministries of Health, Welfare and Sport; Social Affairs and Employment; and Education, Culture and Science, formally requested the Health Council of the Netherlands to produce an advisory report on autism spectrum disorders. They asked the Council to address issues relating to: the occurrence of ASD; the possible relationship between the observed increase in occurrence and indication processes for care and funding; the problems encountered by those with ASD; and the integrated approach required to enable children and adults to participate in society and to function as effectively as possible in everyday life.

Detection

Autism is not something that can be detected by a simple blood test or scan. A diagnosis of ASD is made on the basis of behavioural characteristics. A good diagnosis includes two important factors. The first is a classification in which the core symptoms (limitations in social interactions and communication, together with rigidly stereotypical behaviour) are scored according to the Diagnostic and Statistical Manual of Mental Disorders (DSM). The second involves a dimensional diagnosis, which addresses the subject's context, as well as their individual potential and limitations. Together, these separate aspects of the overall diagnosis form the basis for the action-oriented diagnosis, which indicates the treatment and counselling needs of the individual in question, taking into account their potential and limitations. The classification will remain the same throughout the life of the individual in question. This is not true of the dimensional diagnosis and the action-oriented diagnosis, however, as they are partially dependent on the development of the individual and their social context. Accordingly, the latter two types of diagnosis must be repeated at regular intervals.

Childhood autism can be detected before the second year of life, on the basis of developmental characteristics. PDD-NOS and Asperger's disorder often do

not cause problems until children are of school-going age, sometimes not even until they reach adolescence or adulthood.

While there are a sufficient number of valid tools for detecting these conditions in young children, this is not the case for older children, young adults, and older age groups. Diagnostic tools are available for very young children and for children of school-going age. As yet, there are few such tools for young adults and older age groups, but this situation is expected to improve in the not-too-distant future.

One difficulty with identifying ASD is that generalists such as GPs, physicians at post-natal clinics, occupational health physicians and insurance physicians lack the equipment needed to detect these disorders. This also applies to professionals in other 'lookout' positions (teachers and youth-care workers, for example). Even professionals working in the mental health care service (GGZ) cannot automatically be assumed to have a knowledge of autism.

Treatment

ASD is incurable. While various therapies are used to treat the effects of the disorder, their effectiveness is still somewhat limited. Presently, the most effective form of treatment involves early, intensive behavioural interventions. As yet, however, there is only limited evidence to support the effectiveness of this approach.

In the Netherlands, there is consensus about which elements must be included in the treatment and supervision of individuals with ASD. One is psycho-education and the dissemination of information about the disorder, and about how it affects ASD sufferers' ability to function as well as other aspects of their lives. A second element involves treating the somatic symptoms presented by such individuals (such as visual and hearing problems). Then there is the treatment of comorbidity, such as ADHD and motor problems. Finally there are psychosocial interventions such as behavioural interventions and family support, as well as support in education and employment.

Prevalence

There are no figures for the prevalence of ASD in the Netherlands. According to estimates published in the international scientific literature, the prevalence of ASD is currently 60 to 100 per 10,000 individuals. No differences have been found between ethnic groups or between groups with a different socio-economic status. Accordingly, there is no reason to suppose that prevalence in the Nether-

lands differs from that found elsewhere in the world. Well over thirty years ago, the reported prevalence was 2 to 5 per 10,000 individuals. The observed increase can be attributed to a number of factors. In the 1980s and 1990s not only were the criteria for classic autism broadened, but Asperger's disorder and PDD-NOS were included as classifications in the autism spectrum. Effectively, therefore, the diagnosis of autism was expanded. Another important factor is a society that places much greater demands on social and communicative skills, flexibility, and independence than was the case thirty years ago. As a result, the disorder causes problems more often now than it did at that time. In other words, people with this condition have always been with us, but improved diagnosis and the greater demands being placed on individuals are now making them much more noticeable. One factor that might be involved in the Netherlands in particular is that anyone wishing to apply for care funding or educational assistance must first obtain a classification.

Problems encountered

From the initial suspicion that something is wrong with a child, youth or young adult, the route to diagnosis and, ultimately, appropriate treatment and support is an excessively long and complicated one. A wide range of professionals working in many different domains (families, school, work) encounter people with ASD. If treatment and rehabilitation are to be successful, then thorough consultation and effective cooperation are of pivotal importance. The current funding system for the many and varied types of care does not always provide sufficient incentive, or adequate facilities, for cooperation. As a result, these children and their parents are all too often repeatedly sent from pillar to post.

Within the families concerned, life often centres around the child with ASD. This generally imposes a heavy burden on the parents, so much so that working mothers often feel compelled to give up their jobs. Given that autism has a pronounced genetic component, other family members are also likely to exhibit autistic characteristics or to suffer from a disorder. This affects the family's ability to maintain financial independence and the type of treatment/counselling being offered, as well as support measures both for the family and for childrearing.

In the area of education, their anomalous methods of information processing and language acquisition mean that ASD sufferers are unable to study 'normally'. Furthermore, their social and communicative constraints and rigid behaviour patterns make it difficult for them to work and collaborate with others.

These same constraints at the social and communicative level make it very difficult for those with ASD to work in our modern, service-oriented economy.

In general, people suffering from ASD find it difficult to cope with changing circumstances (transitions) that affect their lives. Examples of such circumstances include: starting school, the transition to secondary education, or the transition to work. Transitions involve the disruption of an existing equilibrium, resulting from the sudden introduction of different, possibly more demanding tasks. A new equilibrium has to be found, which always involves the risk that the specific characteristics of the individual disorder in question will make it impossible to meet the new requirements. This in turn further aggravates the symptoms. Assistance given to children, adolescents or young adults with ASD can, to some extent, help to prepare them for such situations. All that remains then is to wait and see how they handle these transitions in practice.

Integrated approach

It is not enough simply to explore the specific, individual characteristics of the disorder and how it affects the ability to function of those with ASD. When assisting or collaborating with these individuals, it is also important to examine their social and functional context. This requires a tailored approach that is focused on the individual's specific phase of life. Furthermore, wherever possible, an attempt must be made to anticipate possible future changes (transitions).

The Committee calls for a uniform procedure to be adopted for the early detection of ASD in children aged 0-4 and in children of school-going age. Tools should be developed to enable these conditions to be detected in adults. Research is needed into ways of effectively treating and supervising the disorder from childhood to adulthood. Furthermore, with regard to the general research effort, an effective balance has to be achieved between supply and demand. The Committee takes the view that, in the area of education, tailor-made procedures are vital. Education has an important part to play in preparing individuals as effectively as possible for the transitions that they will encounter before, during and after their years spent in the educational system. The aim here is to restrict the adverse effects of the disorder as much as possible. Measures to facilitate entry to the labour market are required, and these must be implemented in good time. A job coach will be needed to provide guidance in the workplace. This individual should always be available to deal with any problems that may arise. With regard to continuity of care, the Committee would like to see permanent arrangements put in place to provide the services of life coaches. Such people would be capable of providing guidance in the areas of health, education, employment and

municipal services, and possibly direct practical assistance for short periods of time (MEE social workers are already performing this role to some extent, and the Youth and Families Centres are assigned similar tasks). Cooperation between those offering treatment and those providing guidance should be encouraged and rewarded. The autism covenant can contribute to this, provided that the national coordinating effort is given an adequate mandate and sufficient resources, at least until such time as the regional organisations are up and running.

People with an ASD are different. They stay that way throughout their lives. Some individuals with ASD will need very intensive care, in institutions for example. Others are capable of living independently, without assistance. Given the right facilities, a significant proportion of the remaining individuals with ASD are capable of participating and performing fairly well (in some cases, very well indeed) in contemporary society.

The hospital as a healing environment

Health Council of the Netherlands. The hospital as a healing environment. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/14. ISBN 978-90-5549-774-4 (in Dutch)

In addition to providing optimal care, new style hospitals also aim to provide a healing environment for their clients. Can the architectural features of such hospitals really make patients feel more comfortable, and help them recover more rapidly? If this is indeed the case, then what architectural characteristics and environmental variables have the greatest effect? These are the main issues dealt with in this horizon scanning report, which was drawn up by the Central Committee on Medical Technology Assessment (MTA) of the Health Council of the Netherlands.

In the Committee's view, scientific research in this field is both heterogeneous and fragmented. Furthermore, the methodology employed often does not stand up to close scrutiny. Despite these reservations, however, some useful results have been obtained. Of these, the finding with the best supporting evidence is that good natural ventilation with fresh air does indeed promote healing. There is also substantial evidence that 'views of (real or depicted) natural landscapes', together with building measures to combat noise nuisance and hospital-acquired infections, have beneficial effects in terms of patients' healing and recovery. However, it is not always clear which of these measures is most effective in this respect.

Things are less clear-cut, however, in the case of numerous other environmental variables. People appear to differ substantially in terms of their preferences for certain factors (or combinations thereof), such as light, colour and sound. Moreover, there is insufficient evidence that preferences of this kind are

associated with beneficial health effects. In addition, no definitive conclusion has yet been reached concerning the potential benefits of single rooms.

Further research may help to clarify this situation. In this context, the Committee has raised several important points. Methodological quality has the highest priority, both for studies into the impact of design variants and for research into possible correlations between environmental variables and health effects. Furthermore, greater efforts must be made to distinguish between the actual (and potential) impact of such factors in terms of (1) patient health and (2) patient wellbeing. Each type of effect is valuable in its own way. The two can co-occur, but this need not be the case.

In practice, the architectural features of hospitals (or of individual wards) are also primarily aimed at facilitating and encouraging new developments in the provision of healthcare itself. These include partnerships between different medical professions and auxiliary services, or between caregivers and researchers. In this connection, there is also a need for analyses in which the various objectives being pursued are evaluated in terms of their cost-effectiveness.

Finally, the Committee indicates the importance of something that, to date, has not traditionally featured in hospital construction: the effective exchange and dissemination of tried and tested concepts. It takes the view that the Architecture in Health innovation platform can be an effective player.

Proton radiotherapy

Health Council of the Netherlands. Proton radiotherapy. Horizon scanning report. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/17. ISBN 978-90-5549-776-8 (in Dutch and English)

What is proton radiotherapy?

Treatment with protons (a kind of charged particles) is a promising development in the field of modern radiation oncology. The physical properties of protons allow a better dose distribution as compared to current photon (X-ray) radiotherapy. This has the potential to minimize the dose to normal tissues and significantly reduce acute and late side effects. The result may be a more effective and less toxic radiation technique.

Why a horizon scanning report on protons?

In 2008 the Health Council of the Netherlands published an advisory report on the future need and planning of radiotherapy at the request of the Minister of Health, Welfare and Sports (WVS).^{*} The Advisory Committee that prepared the report, concluded, among others, that the clinical introduction of proton radiotherapy, an emerging radiation delivery technique using heavy charged particles will require special attention in the near future. This was underlined by the fact that, in comparison to the currently used photon radiation, the clinical introduction of proton radiotherapy calls for complex infrastructural requirements with,

^{*} Health Council of the Netherlands. *Searchlight on radiotherapy. A vision for 2015*. The Hague: Health Council of the Netherlands, 2008; publication no. 2008/27.

in addition, special expertise and far greater financial investments resulting in higher costs per treatment. Apart from the financial aspects, there is also discussion concerning the scientific validation of new radiation delivery technology in general and proton radiotherapy in particular. This debate focuses primarily on the role and feasibility of randomised controlled trials (RCT's) to demonstrate the clinical value of proton radiotherapy. Because of this, it was felt that a separate and more comprehensive advisory report on proton radiotherapy was called for.

Potential benefits of proton radiotherapy

The use of proton radiation may result in significant benefits over current radiation techniques. First, radiotherapy with protons is associated with a substantial reduction of the integral dose deposited in tissues and organs both in the vicinity and at a distance of the primary target volume, as compared to photon radiotherapy. This benefit, based on the physical properties of proton beams, may clinically translate into a significant reduction of serious and frequently irreversible late side effects, and of the long-term risk of induction of (secondary) cancer. The lower radiation exposure to normal tissues with protons complies with the fundamental basis of safe radiation delivery, known as the 'ALARA'-principle ('as low as reasonably achievable'). Randomized controlled trials however may not be the most suitable approach to demonstrate this clinical advantage. Instead, clinically validated 'Normal Tissue Complication Probability' (NTCP) models and 'dose planning comparative studies' offer a more appropriate methodology in this case.

Second, in those cases where current radiation techniques do not achieve the delivery of higher doses due to unacceptable toxicity, proton radiotherapy, by virtue of its superior dose distribution, does permit dose escalation aiming to increase local control rates and improve survival without enhancing side effects. Assessment of this type of clinical advantage requires robust comparative studies, preferably RCT's.

Scientific validation of proton beam therapy

Evidence-based medicine has become the cornerstone in the clinical introduction of new treatment strategies. In this context, RCT's are generally considered the gold standard for assessing differential benefits in clinical outcome between competing therapies. Thus an RCT approach is undoubtedly needed to demonstrate the potential and efficacy of a novel radiation technique, such as proton

therapy, to improve local tumour control and patient survival. However, when translating these requirements to the validation of new radiation technologies that primarily aim to reduce side effects and secondary tumours, one is confronted with certain methodological, practical and ethical problems. This is particularly the case for proton radiotherapy. Therefore, the critical assessment of the clinical benefits of proton radiotherapy requires an alternative methodological approach in addition to RCT's. For the purpose of the current report, the committee decided to use the approach and criteria as proposed in a (recently published) advisory report by the Dutch Health Care Insurance Board (*College voor Zorgverzekeringen - CVZ*), for the purpose of determining "the current status of science and clinical practice of proton therapy".*

Current and future indications for proton radiotherapy

On the basis of prospective phase I and II trials and observational and case-control studies, it has become clear that for some well-defined indications the benefit of proton radiotherapy over conventional photon treatment is substantial enough for proton radiotherapy to be considered an 'accepted' therapy, in addition to currently existing treatment options. And in selected cases there may even be a surplus value over conventional (radio)therapy, which could make proton radiotherapy the treatment of choice. These so called 'standard' indications include: intraocular melanoma, tumours of the skull base and paraspinal tumours (chordoma, chondrosarcoma), and some paediatric tumours. In the Netherlands this group of patients will total around 252 annually.

Next, there is a relatively large and diverse group of tumours, where protons may be used to achieve dose escalation and subsequent improvement of local tumour control, resulting in increased treatment efficacy. This category includes lung cancer and prostate cancer. Proper RCT's should be performed to demonstrate the potential benefit of protons for these indications. These tumours can be indicated as 'potential indications'.

Another large group of indications comprises tumours for which protons can be used with the aim to reduce acute and late side effects of radiation (resulting in improved treatment quality). This consideration is based on (computer-based) individual planning comparative studies, simulating dose distributions of photons versus protons, and estimating and comparing the respective risk of side effects of these techniques. These so called 'model-based' indications include:

* CVZ Report 'Protonentherapie', Publication nr. 273, March 9, 2009.

head and neck tumours, urologic tumours, breast and lung cancer as well as gynaecological cancers.

Finally, there is a relatively small category of cancer patients, for whom proton radiotherapy is expected to reduce the incidence of radiation-induced secondary tumours. These indications include breast cancer and haematological malignancies in young patients, as well as testis tumours (seminoma) in young males.

Estimated total number of patients for proton radiotherapy in the Netherlands

On the basis of the cancer incidence data available from the Dutch Cancer Registry (IKC), and data from Australian* and Swedish studies** on the percentage of cancer patients eligible for radiotherapy, it can be estimated that in total around 7,000 cancer patients in the Netherlands could potentially benefit from receiving proton radiotherapy (based on 2005 figures). This estimate is based on currently available in-silico studies and relevant expert opinion. Assuming that a proton facility in the Netherlands could be operational at the earliest by 2015, this number may have increased by then to around 9,400. The estimated numbers of patients eligible for proton therapy, as presented in chapter 6 of this report, should be interpreted – as is stressed by the committee – as maximum numbers. The actual number to be treated with protons will probably turn out to be less, one of the reasons being that patients are not willing to travel longer distances for obtaining this specific treatment. In addition, it should be considered that, after starting up a proton facility, it will usually take a minimum of 3 years to reach its maximum capacity. The clinical introduction of proton radiotherapy in the Netherlands will therefore be a gradual process.

Current and future facilities for proton radiotherapy in Europe

In all there are now eight operational centres for particle therapy (protons and ions) in Europe. These centres have already treated more than 15,000 patients in the past years, and worldwide this number exceeds 50,000. Some centres (with low-energy accelerators) are dedicated to treatment of eye melanomas only,

* Deleany G, Jacob S, Featherstone C, et al. The role of radiotherapy in cancer treatment – estimating optimal utilization from a review of evidence-based guidelines. Collaboration for Cancer Outcomes Research and Evaluation – CCORE. *Cancer* 2005; 104: 1129-37.

** Möller TR, Einhorn N, Lindblom C, et al. Radiotherapy and cancer care in Sweden. *Acta Oncologica* 2003; 42: 366-75.

while others perform treatments (with both protons and carbon-ions) for a wider range of indications, using high energy accelerators. Most centres devote considerable time to research activities, apart from providing clinical treatment.

There are over ten initiatives in European countries today for additional proton/ion centres; some already under construction, others have been approved or are in the early stage of planning. Additional centres are planned in Germany (5), France (2), Italy (3) and Austria (1). Realization of these plans will eventually result in an eight-fold expansion of the capacity for patient treatment in Europe.

In the Netherlands there are at present explorative plans for proton radiotherapy facilities in Maastricht, Groningen and a proposal by a consortium including Leiden/Delft/Amsterdam/Rotterdam.

Prerequisites for a well-controlled introduction of proton therapy in the Netherlands

Based on the above mentioned considerations, and assuming that further validation studies prove successful, it is concluded that a substantial number of Dutch cancer patients could potentially benefit from future treatment with proton radiotherapy, resulting in less clinically relevant side effects, improvement of local tumour control, and prevention of secondary cancers. Well-planned and timely investments in proton radiotherapy in the Netherlands are called for to enable the future treatment of these patients and achieve the potential benefits. A number of prerequisites will have to be fulfilled to let this become a reality. The most important are:

- The centres that will take up proton radiotherapy must be embedded in an environment where clinical care, clinical research and technological development are naturally well-integrated.
 - During the initial investigational phase an important part of activities should be focused on the clinical validation of potential and model-based indications for proton radiotherapy, besides the treatment of patients with 'standard' indications.
 - Future capacity for proton radiotherapy should be sufficient to allow treatment of both patients with 'standard' indications and patients with potential and model-based indications who will participate in validation studies, either observational studies or RCT's. In a scenario favouring gradual and controlled introduction, proton facilities in the Netherlands could – in the longer run – reach a capacity to treat approximately 7,000 patients per year. In the initial phase however, emphasis should be on clinical validation involving prospective controlled and observational studies, where an important part of the
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patients eligible for proton treatment will take part in RCT's comparing protons with photons. Therefore one can realistically expect that the capacity for proton therapy during this phase will show a gradual increase to finally reach a maximum of 4,000 patients annually at the end of this period.

- From the very start of the introduction of proton radiotherapy there should be reasonable prospects that the treatment cost of both patients with 'standard' indications, patients treated with the intention to prevent secondary tumours, as well as patients enrolled in clinical validation studies of 'potential' and 'model-based' indications, will be covered.
- The introductory phase should see a well-controlled start, with proton therapy facilities in the Netherlands highly concentrated, if necessary on the basis of the Specific Medical Procedures Act. Efficient referral of patients by Dutch hospitals is important to guarantee good utilization of the available capacity and sufficient enrolment in the validation studies.
- The Dutch Health Council committee that has prepared this horizon scanning report does not see pronouncement upon the number of proton facilities needed, or making recommendations on specific locations or centres as part of its assignment.

Contributing to prevention

General vaccination against hepatitis B revisited

Health Council of the Netherlands. General vaccination against hepatitis B revisited. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/03E. ISBN 978-90-5549-764-5 (in Dutch and English)

The question is: should we retain the existing vaccination of high-risk groups, or implement supplementary general vaccination against hepatitis B?

In its 2007 report *The future of the National Immunisation Programme: towards a programme for all age groups* the Dutch Health Council carried out a preliminary selection from a large number of candidate vaccines. Further analysis was recommended for a limited number of vaccines, and for vaccination against hepatitis B the Council recommended that the effectiveness and appropriateness of directed hepatitis B vaccination programmes be evaluated and compared with a general vaccination programme. The present advisory report is the result of this evaluation and comparison.

Between 1983 and 2003 the Health Council advised on several occasions on vaccination against hepatitis B within the framework of public health programmes. As a result of its advisory reports, vaccination programmes have been set up to protect social groups having a raised risk of contracting hepatitis B: the children of mothers carrying the hepatitis B virus (HBV), certain patient groups, behavioural risk groups, medical and paramedical staff, and others running the risk of infection as a result of their professional work. After it had become clear during the 1990s that these various directed programmes did not have the reach that had been hoped for, implementation of the programme was intensified in a number of phases. In 2003 the package was extended to include the vaccination

of infants whose parents came from countries having intermediate or high levels of endemic disease.

The main reason that the Netherlands has opted for this 'risk group'-oriented approach is the relatively low incidence of hepatitis B compared with other parts of the world, and the fact that hepatitis B occurs with greatest frequency within specific social groups which – up to a point – can be targeted. Other countries in North-Western Europe (the United Kingdom, the Scandinavian countries and Finland) operate similar policies; in this they depart from the advice given by the World Health Organization (WHO), which has recommended general vaccination.

Directed vaccination programmes have an expanded, but still inadequate range

In recent years the range of these directed programmes was expanded, particularly in order to include people in behaviour-linked risk groups: homosexual men, injecting drug users, heterosexual prostitutes and their clients and, until recently, heterosexuals undergoing sexually transmitted disease (STD) diagnosis and treatment. In Amsterdam the intensification of the direct approach method towards people in these risk groups led to a clear drop in the number of new and acute cases of hepatitis B. At the same time, it became clear that the reach of that programme as well was still limited with respect to the total numbers of people in these behavioural risk groups: in fact more than half of them turned out not to have been vaccinated.

The number of new infections and mortalities is not falling

In the Netherlands the number of reported cases of acute hepatitis B is at least three times as high amongst men as it is amongst women. In both groups the early 1980s saw a decline in incidence levels, with numbers stabilising over the following years. In the early 2000s there was a limited rise in incidence in men, and in recent years this has once again been followed by a decline to previous levels.

At national level, the intensification of this direct approach to people in high-risk groups has resulted in a slight fall in the number of new, acute cases of hepatitis B. At the moment the Netherlands deals with 200 to 300 reported cases of acute hepatitis B per year; and every year there are a few deaths from acute hepatitis B, and an average of 23 deaths as a result of chronic hepatitis B reported. However, these reported numbers are subject to underreporting. Most cases of

chronic hepatitis B concern infections which were contracted abroad and which would not have been prevented by a Dutch national vaccination programme; those carrying the disease are nonetheless contagious to others.

Vaccination against hepatitis B is effective, safe, and provides long-term protection

In 2006 the general vaccination of children against hepatitis B was carried out worldwide in most WHO member states. This means that there is extensive experience with the use of these vaccines. Large-scale research studies have shown that vaccination against hepatitis B is both effective and safe.

If protection during puberty is seen to be important for a section of the population, then we have to be reasonably certain that vaccination in infancy provides long-term protection. The general vaccination of prepubertal children instead of infants is another option, but this means setting up new contact moments for vaccination at an age for which the National Immunisation Programme (NIP) has, as yet, not been active. For girls, these contact moments could be combined with contact moments for vaccination against cervical cancer, but it is uncertain whether this approach would provide an adequate reach.

Although an increasing amount of data is becoming available on the long-term protection conferred by vaccination, this data does not yet yield absolute certainty. Functional immunity appears to be in place more than fifteen years after vaccination. Moreover, about 26 years after the first use of plasma vaccines and 20 years after the first use of recombinant vaccines, extremely few breakthrough infections have occurred. However, it has been reported that in the long term some individuals, especially if a low vaccine dose was employed, appear to lose immunological memory (as evidenced by the absence of rapid antibody formation after a booster injection). There have been only sporadic breakthrough infections amongst such people, and none has become chronically infected.

New model-based calculations: favourable cost-benefit ratio

In support of the advisory process, staff members of the National Institute for Public Health and the Environment (Rijksinstituut voor Volksgezondheid en Milieu or RIVM) have performed new model-based calculations in which the targeted vaccination programmes and general vaccination of infants or pre-teens are compared to each other. Estimates of the potential health gains show that the incidence of new hepatitis B infections may decrease by 44 percent in 50 year's time if the high-risk group policy is followed. A general vaccination strategy

would reduce the incidence over the same period of time by 90 percent. This would prevent an estimated 1,500 deaths in that time frame.

The cost-effectiveness ratio of such a general vaccination when added to the current approach to risk would be about 3,000 euros per Quality Adjusted Life Year (QALY) gained. The cost-effectiveness ratio is hardly dependent on the vaccine being given to infants or pre-teens. The cost-effectiveness ratio of general vaccination of pre-teens *is* dependent on the cost of introducing the necessary new contact moments for vaccination at this age.

RIVM also studied the cost-effectiveness of an eleven-year-long catch-up campaign among twelve year olds in addition to general vaccination of infants. Such a catch-up campaign should be capable of bringing the health benefits forward by more than ten years compared to the situation without a catch-up campaign. In addition, an estimated 500 deaths can be avoided over a period of 50 years. The cost-effectiveness ratio of such a catch-up campaign, if not combined with vaccination against cervical cancer for girls, would be about 8,300 euros per QALY gained. If combined with a vaccination against cervical cancer, the ratio would be approximately 6,875 euros per QALY gained.

Strategy considerations

The decision on which strategy to follow proves to be complex and difficult to make. In addition to scientific aspects, there are also considerations of a practical and moral nature. This is why the committee presents the various options and indicates its preferences, but makes no conclusive recommendations.

Continuation of the current risk policy exclusively

The current high-risk group approach has produced a number of important successes. The corpus of vaccination programmes targeted at specific high risk groups has a long history in the Netherlands, and a considerable reach in comparison with many other countries. Several of these programmes have been intensified to no small degree, especially in recent years. This has helped produce significant health gains through the years. Continuation of only the high-risk group approach would be preferable if it could be established that this approach is sufficiently effective. Despite great efforts, the current approach is still not adequate: there is limited evidence that intensification of vaccination programmes results in a reduction of the disease burden, and the effective range among the high-risk groups is limited, even with an intensive approach. It is uncertain if further intensification will be possible.

Expansion to general vaccination of infants

Far greater health benefits can be achieved through a programme that includes general vaccination of infants than by continuing with the current high-risk group approach only. High-risk individuals are then more likely to be vaccinated, and protection would extend beyond them as well. The hepatitis B vaccine is safe and effective. Expanding the vaccination programme along these lines is also cost effective.

In a practical sense, general vaccination can be easily introduced by replacing the current DPT-polio-Hib vaccine (against diphtheria, pertussis, tetanus, polio and *Haemophilus influenzae* type b) by a combination vaccine including a hepatitis B component. The number of inoculations (two per contact moment) would remain the same. In the short term, the current hepatitis B vaccination could be discontinued for children with one or both parents from medium or high-endemic countries. In the long term, vaccination programmes targeted to people in behavioural risk groups could be discontinued as well. The actual risk reduction, however, will only be truly significant once the vaccinated children grow past the age at which these risks predominantly occur, in other words about twenty to thirty years from now.

Also in the future people will demand individual protection against occupational risks and will want to continue vaccinating those concerned, regardless of their age, if they are not protected by prior inoculation.

Expansion to general vaccination of prepubertals

Expanding current policy to include general vaccination of prepubertals can also produce significant health gains. This strategy is also better suited to reach high-risk individuals and others compared to the current high-risk group approach. Vaccinating people as close as possible to the age at which they become sexually active offers the relevant protection at the most propitious moment, mitigating the concerns about the duration of effective protection that arise where infant vaccination is concerned.

Another advantage of this programme is that vaccination of adults from high-risk groups can ultimately be discontinued. However, vaccination of children with at least one parent from a medium or high-endemic country must be continued if general vaccination of pre-teens is opted. If general vaccination of pre-teens is the option of choice, then the committee recommends a simultaneous vaccination for girls against hepatitis B and cervical cancer.

One problem of the pre-teen approach is that infections that occur between zero and twelve years cannot be prevented. These infections are often asymptomatic. They are therefore not reported and especially young children have a high potential of becoming carrier. The programme also requires establishing new contact moments, and there is some uncertainty about the associated costs. These costs have a significant impact on the overall cost-effectiveness of the programme. Finally, the uptake of vaccination is less certain than in the case of vaccination of infants.

The committee's preference

Both general vaccination scenarios meet the assessment criteria for the National Vaccination Programme. However, the committee would prefer a programme that includes general vaccination of infants. The committee recommends that an eleven-year catch-up campaign be organised for twelve-year-olds, when general vaccination of infants is being implemented. This ensures that, every year, a cohort of twelve-year-olds receives protection against hepatitis B and substantial beneficial effects of vaccination will be obtained earlier.

The current risk policy must be continued

The committee wishes to stress that, when general vaccination is introduced, pregnant women should continue to be screened for carriership of the hepatitis B virus (HBsAg-positive) and the newborn babies of HBsAg-positive mothers should continue to be vaccinated. This protocol is intended for people who have already contracted the virus and who are at serious risk of chronic infection and carriership. It consists of an initial vaccination directly after the birth and the administration – also as soon as possible after the birth – of directly protective antibodies, otherwise known as passive immunisation. It is imperative to vaccinate the children of carrier mothers. The vaccination of adults in behavioural risk groups will also have to be continued for many years after the introduction of the general vaccination until people in these risk groups are protected by the general programme.

A catch-up campaign is relevant

If general vaccination is introduced for infants, the committee recommends that an eleven-year catch-up campaign be organised among twelve-year-olds to raise immunity in the population to a relatively high level. This will also help to real-

ise the anticipated health benefits more than ten years ahead of time and further increase the benefits at relatively minor extra expense. A catch-up campaign would also respond to the crucial need for protection at as young an age as possible; it reduces the chance of carrier ship and chronic infection later in life. Given that the virus in the general population is transmitted mainly through sexual contact, a catch-up campaign would ensure protection relatively quickly in the age groups where sexual transmission is most likely to occur.

The committee recommends that, for girls, the catch-up campaign be carried out at the same time as the vaccination programme against cervical cancer.

Monitoring effectiveness, safety and the immunological memory

As in all public vaccination programmes, it is essential to monitor effectiveness. A monitor should be set up to ascertain the incidence of breakthrough infections among vaccinated children. Besides the usual passive registration of side-effects, the committee advises setting up a link between vaccination registers and disease registers so that any infrequent side-effects can be tracked.

Once the first group of vaccinated infants reaches the age of twelve and their immunological memory clearly points to long-term protection, the catch-up campaign can be terminated. If functional immunity leaves much to be desired eleven years after infant vaccination, the catch-up campaign can be converted into a booster injection for twelve-year-olds. To determine whether vaccination at the age of twelve can be discontinued, in-depth immunological research will have to be performed on some of the twelve-year-olds who were vaccinated as babies. This research will have to look not only at the antibody titres but also at functional immunity – in the form of, for example, the capacity to elicit a fast immune response with a booster injection of the hepatitis B vaccine – in order to demonstrate immunological memory.

Information

The committee advises that an information campaign be set up to communicate the importance of the vaccination. The committee has identified several target groups that require a special approach: parents of newborns, parents of pre-teens, and pre-teens themselves.

It is important for youth healthcare workers to supply parents with proper and adequate information. In order to do so, they need knowledge of hepatitis B and good communicative skills to parents and their children. Training courses and refresher courses should take this into account.

In the Netherlands HBV is often transmitted by sexual contact. Special information kits should therefore be compiled for parents and twelve-year-olds from groups with different cultural, ethnic and religious backgrounds

Pregnancy immunisation by red blood cells

Health Council of the Netherlands. Pregnancy immunisation by red blood cells. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/04. ISBN 978-90-5549-753-9 (in Dutch)

This advisory report concerns pregnancy immunisation by red blood cells – the phenomenon whereby women form so-called irregular erythrocyte antibodies (IEA) against foreign blood cells (erythrocytes). In addition to pregnancy, blood transfusion can cause IEA formation. The distinction between antibodies targeting the Rhesus D antigen (D-IEA) and antibodies targeting other erythrocyte antigens (Non-D-IEA) may also be made.

IEA can lead to severe illness in the unborn or newborn child, namely haemolytic disease of the foetus and newborn (HDFN). Over the past several years, methods have been developed to prevent the formation of IEA and to detect already formed IEA. Dutch research conducted as part of the Identification and Prevention of Pregnancy Immunisation (Opsporing en Preventie Zwangerschapsimmunisatie, OPZI) project has contributed significantly to these developments.

This advisory report addresses the following: screening for non-D-IEA, options for changing transfusion policies for young girls and women of child-bearing age in order to reduce the formation of non-D-IEA, prophylaxis to prevent the formation of D-IEA and ways to ensure this treatment is only given to women who may benefit from it.

Screening for non-D irregular erythrocyte antibodies

In the 18-month OPZI project, all pregnant women in the Netherlands were tested for non-D-IEA during week twelve of their pregnancy and the occurrence of HDFN. Severe HDFN, requiring intra-uterine transfusion or exchange transfusion during the first week after birth, occurred in 21 pregnancies (3.7 percent of pregnancies with clinically relevant non-D-IEA; 0.007 percent of all pregnancies). The HDFN was caused by, in order of decreasing incidence, antibodies targeting the Kell antigen (K-IEA), the rhesus-c antigen (c-IEA), the rhesus-E antigen (E-IEA) or other specific antibodies.

The committee feels the potential health gains of this screening programme are significant: per 100,000 pregnant women screened, four to six cases of foetal death or brain damage are expected to be prevented. The cost per prevented case of prenatal death or perinatal disease with permanent consequences is 500,000 euros, an amount well within generally accepted limits. The committee believes this screening programme meets the generally accepted criteria for responsible screening programmes. It therefore recommends pregnant women be screened for non-D-IEA during week 12 of the pregnancy.

The test for non-D-IEA is performed in all pregnant women in the Netherlands, and follow-up testing is performed in all women testing positive for non-D-IEA. The OPZI project outlines alternative scenarios in which not all women are screened, or follow-up testing is only performed in a specific subset of all non-D-IEA positive women. Regarding these scenarios, the committee recommends the following: it advises selective screening only for those women who have been pregnant before or have received a blood transfusion in the past. The committee also recommends selective follow-up screening for women that have tested positive for c-IEA, E-IEA or K-IEA. For follow-up testing for c-IEA, E-IEA or K-IEA, the committee recommends typing the biological father of the – unborn – child for the specific antigen in question. If the father is homozygous for the antigen, then the child is a carrier and further testing is required. If the father is negative for the antigen, no further follow-up is required. If the father is heterozygous, the committee recommends prenatal testing of the mother's blood to determine whether the child is carrying the antigen in question. If the child tests positive, further follow-up tests are required – this is not necessary if the child tests negative. In the event c-IEA or E-IEA is present, follow-up testing may initially be restricted to laboratory testing. Only if these tests show an increased risk of HDFN does the committee recommend clinical follow-up. For K-IEA, the committee recommends both laboratory and clinical testing in all cases – these antibodies have the potential to cause HDFN in extremely low con-

centrations. When women test positive for another non-D-IEA that may cause severe HDFN it is recommended that the father is typed for the antigen in question. If the father is positive the woman should be re-tested once. Due to the risk of HDFN caused by late formation of c-IEA in particular, the committee's final recommendation is to test all pregnant women for the presence of the c-antigen during week 12 of the pregnancy, and to repeat the test for c-IEA in all c-negative women during week 30.

Transfusion policies for young girls and women of childbearing age

The results of screening for non-D-IEA show that a significant percentage of HDFN is caused by c-IEA, E-IEA or K-IEA. A study showed past blood transfusions to be a risk factor for the development of these IEA. The committee therefore recommends giving young girls and women of childbearing age requiring blood transfusions erythrocytes that are compatible in terms of antigens c, E and K. The committee finds the cost-effectiveness calculations for the introduction of compatible blood transfusions to be convincing.

Antenatal prophylaxis

A programme to prevent D-IEA formation has been in place in the Netherlands for about 40 years. For this postnatal anti-D immunoprophylaxis (postnatal prophylaxis), the D-antigen status of children born to D-negative mothers is determined immediately after delivery. Mothers of D-positive children are given anti-D immunoglobulin (anti-D-Ig) in order to prevent the formation of D-IEA, thereby reducing the chances of HDFN occurring during a subsequent pregnancy.

Despite postnatal prophylaxis, however, HDFN still occurs, albeit less frequently than it used to. One of the reasons for this is that the formation of D-IEA can already take place during pregnancy. In order to combat the occurrence of HDFN caused by this early D-IEA formation, antenatal prophylaxis was introduced alongside postnatal prophylaxis in 1998. In this programme, D-negative pregnant women are given anti-D-Ig during pregnancy (at around week 30 of the pregnancy, in the Netherlands). The effects of antenatal prophylaxis were examined within the framework of the OPZI-project.

Antenatal prophylaxis causes a statistically significant decrease in the incidence of pregnancy immunisation against the rhesus-D antigen. The percentage of women in whom HDFN occurred was also lower in the group receiving antenatal prophylaxis compared to the control group, but the difference was not sta-

tistically significant. The committee is faced with a dilemma: the OPZI-project shows that the introduction of antenatal prophylaxis has met the expectations as far as immunization is concerned. The effect on HDFN is less outspoken, although antenatal prophylaxis does result in a decrease in HDFN which the committee finds clinically relevant. The committee would like stronger evidence for the prevention of HDFN by antenatal prophylaxis, but believes the likelihood of such data, preferably from randomised research, becoming available is essentially none. The committee therefore recommends antenatal prophylaxis be continued.

Prenatal D-typing

Under the current programme, all D-negative pregnant women receive antenatal prophylaxis, while only D-negative women pregnant with a D-positive child benefit from it. Women pregnant with a D-negative child do not form any D-IEA, due to the lack of rhesus-D antigen on the child's erythrocytes. In the Netherlands, this amounts to forty percent of pregnant D-negative women, or about 16,000 per year. The discovery that genetic material from the unborn child can be detected in the mother's blood now allows the determination of the child's rhesus-D status before birth (so-called prenatal D-typing), thereby restricting antenatal prophylaxis to D-negative women pregnant with D-positive children.

The committee feels prenatal D-typing can be used to limit antenatal prophylaxis to those women who may benefit from it, namely D-negative women pregnant with D-positive children. The committee feels this has two advantages: D-negative women pregnant with D-negative children are not unnecessarily exposed to a blood product, and less anti-D-Ig is used. This may allow the use of anti-D-Ig sourced exclusively from unpaid (Dutch) donors. The committee supports this position. The committee therefore recommends adding prenatal D-typing to the programme.

Three of the four studies of prenatal D-typing published to date report discrepancies in test results, in which prenatal D-typing indicated a D-negative child, but postnatal D-typing showed the child to be D-positive. These discrepancies were caused by logistical problems during the screening process. If the decision is made to implement prenatal D-typing, the committee recommends the logistical reliability of the test be further studied. In the committee's opinion, this would best be achieved by maintaining – for an agreed-upon study period – postnatal D-typing for D-negative pregnant women with prenatal D-typing tests indicating they are carrying a D-negative child. If the study shows prenatal D-typing is logistically reliable, postnatal D-typing will no longer be required.

Prevention in the elderly: Focus on functioning in daily life

Health Council of the Netherlands. Prevention in the elderly: Focus on functioning in daily life. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/07. ISBN 978-90-5549-757-7 (in Dutch)

With old age come ailments, and often one or more chronic diseases. In this case treatment does not always mean cure, but often preventing worse, by combating and reducing the effects. This may require different care from what is currently being offered. With this in mind, the Minister of Health, Welfare and Sport asked the Health Council of the Netherlands how ‘prevention and proactivity might play a significant role’ in the effective and efficient care for the elderly. This care must lead to, among other things, ‘a decreased burden of disease, better functioning and less disability’. This advisory report outlines how these questions may be answered. It supports the focus on functioning in daily life, but points out that a great deal is still necessary if this intention is to be realised.

Successful ageing can be compatible with disease

Healthy ageing is a prominent theme in various national and international policy memoranda, plans of action and research programmes. This is not limited to maintaining good physical and mental health, but importantly also promotes a process that enables elderly people to live, and continue to live, lives of good quality, as independently as possible, and to continue participating in society. The latter two points are often referred to as ‘successful ageing’. The committee feels this broader framework is of great importance. As the health of the elderly – medically speaking – eventually proves lacking, values such as functioning in daily life and wellbeing become increasingly important. Health, functioning and

wellbeing are strongly interdependent. The committee therefore interpreted the minister's question about preventive possibilities for the elderly by according these values or outcome measures the central importance they deserve. In other words, healthy and successful ageing is not just about preventing and postponing disease and death, but also about preventing disability and reducing dependency on care. Addressing these issues of functioning also serves the wellbeing of elderly people.

Disabilities are the result of multiple factors

Why is it that people experience greater difficulty when performing regular daily activities – such as caring for themselves, shopping and maintaining social contacts – as they grow older? And why do elderly people experience these problems differently, even when their medical situations are largely similar? Of the partial causes that contribute to the occurrence and development of such limitations, chronic disease and physical and mental impairments are the most important. These become more common with increasing age. Personal factors, such as lifestyle, coping skills in dealing with disease and the motivation to remain socially active, also play a part. The same holds for environmental factors, such as socioeconomic position and living conditions. All of these factors are also closely interrelated.

Prevention in the elderly: a new perspective is needed

In order to fully utilise the potential for healthy ageing, a new perspective on prevention in the elderly is needed. Prevention of limitations to function is necessary in addition to prevention of disease. The committee calls this 'function-oriented prevention'. This form of prevention is not focused on a specific disease and its consequences, but on a problem with functioning; it looks at activities that may prevent disability independently of or in addition to a disease-oriented approach through specific prevention of functional deterioration and limitations, strengthening the individual's potential for maintaining or promoting functioning in daily life, and influencing non-disease linked factors that threaten this functioning.

Function-oriented prevention is important for other reasons as well. For several diseases, no breakthroughs in prevention and treatment are expected in the short term, so function-oriented prevention is the only thing that may add to a better effect. Importantly, it may also limit the need for care.

Function-oriented prevention adds options

The available knowledge of determinants provides a large number of potential starting points for function-oriented prevention; ultimately it is all about identifying which can actually be influenced positively and how. Explicit attention should also be given to influencing personal and environmental factors, not only as determinants for functional limitations but also as sources of motivation for functioning independently in daily life. Examples include general programmes for self-management, stimulation of self-confidence and safety, and improvements around the house. In more general terms, prevention of disability – depending on the nature of the problems – will have to encompass a narrower or broader scale of integrated measures, ranging from medical treatment and rehabilitation to support with activities, devices, care facilities and modifications to the physical and social environment. The function-oriented perspective should also play a greater role in care-related (tertiary) prevention than is currently common.

Measures must address heterogeneity among the elderly

With the advancement of years, while the odds of impairments and functional deterioration increase, the differences between elderly individuals are considerable. At one end of the spectrum is the active, well-off elderly person, at the other the vulnerable geriatric patient. Between these two extremes lie a multitude of profiles, depending on functioning, burden of disease, vulnerability, and the corresponding complexity of care demands. The essential precondition for successful prevention is to tailor the desired goals and planned measures to the individual or target group. Methods to determine risk profiles and identify at-risk groups are essential in this process. A validated, coherent instrument for this does not yet exist, but tools are available for individual elements.

The heterogeneity of the elderly population is reflected by the gains prevention may achieve. In healthy, active elderly people, maintaining health and participation will be the primary concern. It is important to address the need for functional recovery immediately in the event of temporary functional deterioration. For vulnerable geriatric patients, the focus will likely be on wellbeing rather than functioning in daily life. The groups in between will benefit from a variety of forms of prevention focused on maintaining function, depending on their specific risk profiles.

The elderly should have a clear voice in the matter

The committee wishes to emphasise that elderly people can and must play an active part in defining the goals and form of preventive activities. This applies at all levels: from daily practice to government policy. There may well be tension between the propagated promotion of health and social participation on the one hand, and on the other hand the potentially differing desires among elderly people in the face of changing priorities that gain importance as they approach the ends of their lives. Preventive policies should be careful to take this into account.

The committee also feels a client-centred approach and tailoring to the actual needs of the elderly individual must take a central role in the design and implementation of concrete preventive activities. Elderly patients, by learning to deal with all manner of aspects of disease and (potential) disabilities in a individual manner, can contribute to the maintenance of functioning independently as well as to the effectiveness and efficiency of the care provided. Empowering elderly people to sustain this active role is an important social development. Even if an individual's ability to make an active contribution diminishes, determining and realising personal goals remain of major importance.

Solid research into effective prevention of disability is sorely needed

It was not the committee's task to extensively inventory and evaluate the state of knowledge regarding effectiveness and efficiency of specific activities that may be categorised under 'prevention in the elderly'. It did, however, note that we know a great deal about the determinants of limitations and dependency on care, but that knowledge of the effectiveness of preventive interventions is fragmented, heterogenic and still lacking in a variety of areas. It is the opinion of the committee that the following general and specific themes deserve a place on the research agenda:

- To begin with, it is important that various determinants of functional limitations be mapped out systematically. Explicit attention for psychosocial factors is needed. Additionally, there is a need for operationalisation and validation of measurement instruments for functioning in daily life.
- As a follow-up to the study of determinants, research into the development and evaluation of interventions focused on promoting independent functioning in daily life is needed.
- The best way to draw up risk profiles in order to determine the best target group must also be evaluated.

- The necessity, effectiveness, efficiency and most suitable target groups must be assessed for screening programmes targeting functional deterioration.
- Finally, research into organisational design of interventions is crucial, including the examination of the factors that contribute to effective implementation. Potential forms of cooperation between primary and secondary care deserve special attention.

These themes can be implemented as part of the *Nationaal Programma Ouderenzorg* (National Programme for Elderly Care). However, the crucial development of knowledge in this complex field demands a longer term programme.

Better prevention involves all parties

There are numerous indications that there are gains to be made in this broad preventive field, but the committee feels all parties need to do their part. A proactive stance should be expected from care professionals within and outside the medical sector. This means they must actively identify the risks elderly patients run of a cascade of functional deterioration and the associated care needs, by looking beyond the boundaries of their own discipline. Primary care plays a key role in this process, particularly regarding elderly patients whose independent functioning in daily life is threatened or limited. Elements that deserve attention include:

- Profiles for vulnerability and functioning: map risk factor clusters, taking into account an individual's physical, mental and social status.
- Interventions and organisational structures: analyse the competencies required on medical and non-medical levels to help elderly individuals with certain risk profiles. Determine the best management approach through experiments.

The committee recommends explicit attention be paid to functioning in the further creation of professional treatment guidelines. In each case, the relevant professional groups and groups representing the interests of patients or clients must have their say. It is equally important that professionals tailor their actual daily practice to the needs of individual patients or clients. Education and training must take the lead in strongly promoting this perspective on prevention in the care of the elderly.

However, guidelines, daily practice, educational and training also require greater insight into the effectiveness and efficiency of preventive measures and facilities, with indicators for functioning and wellbeing as outcome measures. It is up to the government to stimulate a longer term research programme in this

area. That same government will also have to address involved parties, from umbrella organisations to professional groups, to encourage them to implement preventive measures of proven value.

The importance the government attributes to stimulating independent functioning in daily life is fully supported by this advisory report. However, results require investment in all manner of areas: knowledge, professional development, organisation, legislation and regulation, financing, and last but not least, actual involvement of the elderly themselves.

Vaccination against pandemic influenza A/H1N1 2009: target groups and prioritisation

Health Council of the Netherlands. Vaccination against pandemic influenza A/H1N1 2009: target groups and prioritisation. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/10E. ISBN 978-90-5549-769-0 (in Dutch and English)

This report presents the findings of an expert meeting held on 10 August 2009 to discuss the target groups and possible prioritisation for any vaccination programme against pandemic influenza A/H1N1 2009. Some aspects of the discussion were, of necessity, based on relatively limited knowledge about the patients affected to date and the course of the pandemic. The meeting was nevertheless able to offer the following recommendations.

Vaccination is recommended for the following (risk) groups:

- Individuals at medical risk, in line with the existing indication for the annual seasonal flu vaccination, together with all those aged 60 and above, regardless of health status.
- Pregnant women in the medical risk groups, but *only* during the second or third trimester of pregnancy. The experts do not recommend the vaccination of expectant mothers who do not belong to one of the recognised risk groups.
- Healthcare staff who may come into contact with patients belonging to the previously defined medical risk groups.
- Family members and (informal) carers of individuals at extremely high risk of death or serious illness from influenza.

At this time, the experts do not recommend a general vaccination programme for the entire Dutch population.

According to the current delivery schedule, vaccines will be available in sufficient quantities whereby prioritisation will probably not be necessary. If this situation changes, the experts advise that healthy individuals aged 60 and over should be vaccinated *after* the other groups listed above. If further prioritisation within the medical risk groups proves necessary, the experts propose the following order of priority:

- Patients with a serious disorder and functional deficiency of the airways and lungs; patients with a serious (acute or chronic) disorder of cardiac function; patients with insulin-dependent diabetes.
- Patients with a disorder and functional deficiency of the airways and lungs; patients with a chronic disorder of cardiac function which can be stabilised and compensated to a reasonable degree by medication; patients with chronic renal insufficiency (dialysis and kidney transplant patients); children and adolescents aged from 6 months to 18 years who have been taking salicylates on a long-term basis; patients with a non-insulin-dependent form of diabetes; individuals with a mental handicap, in residential care; all other individuals in residential care and having a general predisposition to respiratory infections.
- Individuals aged under 60 with reduced resistance to infections.

Given the current uncertainty with regard to both the course and the seriousness of the pandemic, and the possibility of new knowledge about the specific characteristics of patients and vaccines becoming available in the short term, the experts have decided to reconvene in September 2009. At this next meeting, a possible broadening of the indication for vaccination, perhaps to include children and adolescents, will be discussed.

Note: See for more advisory letters on vaccination against pandemic influenza A/H1N1 2009 Annex A.

A national colorectal cancer screening programme

Health Council of the Netherlands. A national colorectal cancer screening programme. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/13E. ISBN 978-90-5549-780-5 (in Dutch and English)

Conclusion

The Committee has concluded that there is sufficient evidence to justify starting a national bowel cancer screening programme. The most appropriate screening method is an immunochemical Faecal Occult Blood Test (iFOBT). The Committee recommends a programme based on the screening of people between fifty-five and seventy-five years old once every two years. People in the target group would be sent a faecal test sampling kit by the screening organisation. The faecal sample would have to be sent to a laboratory to be tested for invisible traces of blood. Persons with a 'positive' (i.e. abnormal) test result would be referred for colonoscopy, which would take place in an outpatient clinic under sedation and with the aid of pain management.

Recent trials in the Dutch cities of Nijmegen, Amsterdam and Rotterdam suggest that a 60 per cent participation rate may be expected. Under this assumption, modelling indicates that screening will in due course help to prevent an average of 1,428 bowel cancer deaths a year. In 2008, 4,843 people died from the disease in the Netherlands.

Bowel cancer is a serious health problem

Bowel cancer (colorectal cancer) is a common disease. In 2006, 11,231 cases were diagnosed in the Netherlands. In the general population, the lifetime risk of

bowel cancer is 4 to 5 per cent. The average five-year survival is 59 per cent, but an individual's chances of survival depend largely on how extensive the disease is when diagnosed. If the cancer is confined to the inner lining of the bowel (stage I), the five-year survival is 94 per cent; for patients with metastatic bowel cancer (stage IV), the five-year survival is limited to 8 per cent.

Bowel cancer is preceded by a prolonged adenomal state, which is relatively easy to detect and treat. Furthermore, a person who has bowel cancer is unlikely to notice any health problems for several years. These two facts mean that bowel cancer is an ideal 'candidate' for screening. From FOBT-based efficacy trials it has been known for some time that screening can reduce bowel cancer mortality by enabling early detection or prevention through the removal of adenomas. However, the implementation of a screening programme would be responsible only if other internationally recognised criteria are met, such as the availability of adequate manpower for diagnosis and treatment.

Research into possible screening methods

In trials held over the last few years, tens of thousands of Dutch people aged between fifty and seventy-five have been offered bowel cancer screening. Various recruitment strategies and screening methods have been used in these pilot trials, whose aim was to establish whether a national and organized population-based screening programme like those in England, Scotland and Finland would be desirable and feasible in the Netherlands.

In contrast to the situation with most other screenable diseases, there are several screening tests available for bowel cancer. The methods differ in various ways, including the participation rate and the sensitivity (in connection with which some tests need to be repeated annually, while others are needed only once every ten years). The four efficacy trials that have been conducted in other countries were all based on the guaiac (gFOBT) Haemoccult II test, which has been used with limited success for more than forty years. The test involves taking 2 samples from each of 3 consecutive stools. If blood is present, a dye (guaiac) reacts with the haem moiety in haemoglobin (the substance that gives red blood cells their colour), resulting in blue discoloration, which has to be visually assessed.

More recently, a test method has been developed, which involves the immunological analysis of faecal samples for occult blood (iFOBTs). The method has two advantages: the subject only has to provide a single faecal sample, and analysis can be automated, thus increasing quality control and reducing cost.

Another possible screening method is sigmoidoscopy: visual examination using an endoscope inserted through the anus into the distal (left-hand) portion of the large intestine. An enema is required prior to the examination.

A fourth option is colonography ('virtual colonoscopy'). This involves examination of the entire large intestine by means of CT or MRI scanning, preferably after limited bowel preparation (low-fibre diet, oral contrast agent). To achieve colonic distension carbon dioxide (CO₂) is delivered via a rectal catheter. Examinations are performed in both supine and prone position.

With all four methods described above, if any abnormalities are detected, the patient is referred for colonoscopy i.e. visual examination of the entire large intestine (Figure 1). Colonoscopy is a reliable way of detecting most abnormalities. Some screening programmes use colonoscopy as a screening method in its own right.

Finally, screening for molecular biomarkers is under development. Numerous biomarkers might theoretically be used for screening, but it is expected to be another five years before suitable ones can be identified. Even then, it will be necessary to conduct research in unselected populations to establish whether biomarker-based screening offers any advantages over the existing methods.

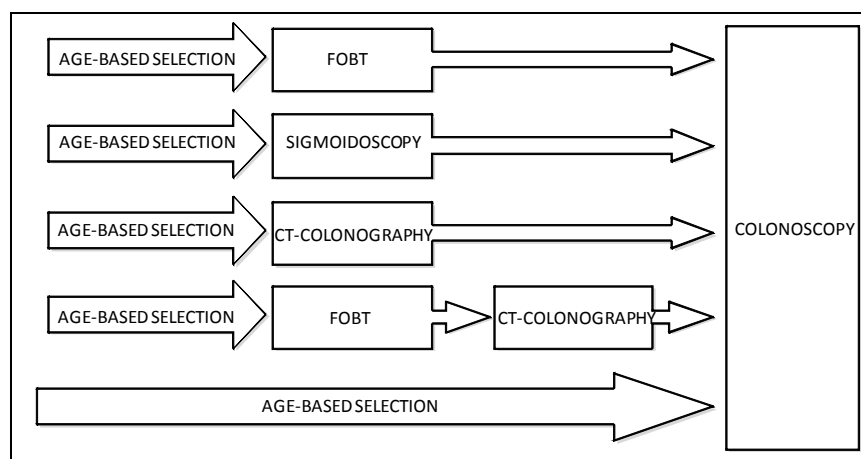


Figure 1 Colonoscopy is the final common pathway of all CRC screening.

Careful assessment is required before introduction of a national screening programme

Assessment of the possible screening methods against the criteria for responsible screening – serious health problem, proven value, suitable screening test, acceptance, cost-effectiveness – reveals the following picture.

As indicated above, it is evident that bowel cancer is a serious health problem. However, it is less obvious which screening method best satisfies the other criteria. It has been demonstrated that gFOBT screening can reduce bowel cancer mortality by 15 per cent. On the other hand, the method is not a very sensitive means of detecting bowel cancer (less than 40 per cent of cases are picked up at first screening). Furthermore, the participation rate is low (47 per cent in the trials).

iFOBT screening is based on the same principle as gFOBT screening: the detection of blood in faecal samples. However, the randomized trials in Amsterdam, Nijmegen and Rotterdam demonstrated convincingly that iFOBT screening yielded better participation and detection rates than gFOBT screening. Furthermore, despite what is often assumed, the cost of iFOBT screening did not prove to be higher. In other words, iFOBT screening is significantly more effective and efficient as a means of reducing both the incidence of bowel cancer and the associated mortality.

The participation rate was significantly higher with iFOBT screening (60 to 62 per cent) than with gFOBT screening (47 to 50 per cent). Moreover, on an intention-to-screen basis (i.e. relative to the number of invitations sent), the number of cases of bowel cancer and advanced adenoma detected was 2.5 times as great. The higher participation and positivity rates do mean that colonoscopy is needed more often (35 cases per thousand invitations). Nevertheless, iFOBT screening is substantially more cost-effective than gFOBT screening.

Compared with a single iFOBT screening, sigmoidoscopy is roughly equally sensitive for bowel cancer, but significantly more sensitive for advanced adenomas. Some studies suggest that re-screening with this method at intervals of five years would be sufficient. However, the level of participation in the Rotterdam trial was low: only 32 per cent. No data are currently available regarding the effectiveness of sigmoidoscopy screening as a means of reducing bowel cancer mortality. It is therefore difficult to draw conclusions regarding its cost-effectiveness. Furthermore, even allowing for a low participation rate, sigmoidoscopy screening requires a great deal of endoscopy capacity (327 sigmoidoscopic

examinations plus twenty-seven coloscopic examinations per thousand invitations). The results of sigmoidoscopy trials in England and Italy are expected in 2010. If they are encouraging, they should be taken into account in modelling of the Dutch situation.

CT colonography is almost identical to colonoscopy in terms of its sensitivity for bowel cancer and polyps measuring ten millimetres or more. However, it is less unpleasant for the subject and less likely to have serious complications. Furthermore, re-screening might not be required for five or ten years. On the other hand, the participation rate associated with colonography is not known, there is no evidence that CT colonography reduces bowel cancer mortality, and it involves exposure to radiation. Colonoscopy is likely to be needed in more than twenty cases per thousand invitations (assuming a 35 per cent participation rate and a referral threshold of ten millimetres).

Colonoscopy is the most sensitive means of detecting bowel cancer (more than 97 per cent) and advanced adenomas (90 to 98 per cent). This form of testing is therefore regarded as the reference standard. Evidence for the timing of colonoscopy screening is limited, suggesting that screening would be needed only once every ten years. No data are available regarding the participation rates and detection rates associated with colonoscopy in the Netherlands. Limited evidence exists on the efficacy of colonoscopy screening on colorectal cancer incidence and mortality. Consequently, it is not possible to calculate its cost-effectiveness. In one of the Dutch pilots, the COCOS trial, the anticipated participation rate is 20 to 25 per cent. Several other factors argue against using colonoscopy as a primary screening method: it is unpleasant for the subjects, there is a risk (albeit a small one) of serious complications and considerable colonoscopy capacity would be required (even assuming a participation rate of 25 per cent, 250 examinations per thousand invitations).

iFOBT screening meets the criteria for responsible screening

A single round of iFOBT testing will pick up 65 per cent of all bowel cancer cases – about the same as five or six rounds of gFOBT testing. The (programme) sensitivity is further boosted by the fact that iFOBT screening is repeated every two years. Assuming that the participation rate associated with iFOBT screening is 60 per cent, while the rate associated with sigmoidoscopy screening is 30 per cent, the effect of iFOBT screening will be one and a half times as great. Screening based only on sigmoidoscopy is not therefore desirable in the Netherlands. In

terms of simplicity, acceptance, performance and safety, iFOBT testing is the best screening method for use in the Netherlands.

Bowel cancer screening is desirable and possible, provided that the required capacity (e.g. colonoscopy) can be realised in the years ahead

The Committee recommends iFOBT-based screening (OC-Sensor, one faecal sample) once every two years for men and women between fifty-five and seventy-five years old. Modelling indicates that a programme designed on that basis would be cost-effective. Assuming a participation rate of 60 per cent, it would be possible to prevent 1,428 bowel cancer deaths each year. This works out at 2,200 euros per life year gained. This is more advantageous than in other cancer screening programmes in the Netherlands – the cost per life year gained being 11,300 euros for cervical cancer screening. For every bowel cancer death prevented, 785 people would need to complete iFOBT tests and 40 would need to undergo follow-up colonoscopy.

If the Committee's recommended screening strategy and the proposed introduction scheme were adopted, the colonoscopic capacity required for full introduction would be no more than 78,000, not 129,000 as previously calculated. The capacity needs can be further limited by updating the surveillance guidelines soon, partly in line with the availability of a screening programme, which will result in the detection of numerous small adenomas.

Alignment of screening with curative care is vital for quality

Experience has shown that the benefits of screening-related early detection are not fully utilised, because referral does not always lead to (prompt) diagnosis and treatment. Furthermore, there are major variations in the quality of colonoscopy among endoscopists. The Committee therefore recommends direct referral by the screening organisation to colonoscopy providers, with GPs playing a supporting role and always being informed. Appropriate arrangements should be made with the health insurers. Such a system would allow for preferential referral to the centres whose colonoscopy services meet the highest quality standards, and which maintain dedicated teams of certified endoscopists and other specialists.

Staged introduction

The implementation of a national screening programme is a major undertaking. The target population would amount to 3.5 million people, who would need to be

invited for screening every two years. Phased introduction is essential; it is expected to take five years to build up the necessary endoscopic capacity. The Committee makes the following recommendations:

- A bowel cancer screening programme should be introduced in phases, with a gradually expanding invitation scheme, as described in subsection 14.8.
 - An organisational structure as described in subsection 14.2 should be adopted, with a view to assuring quality and – if the iFOBT test method is used – sustainability.
 - If it is decided that a screening programme is to be set up, clear arrangements should be made with the relevant professions and care providers regarding:
 - the development of integrated (multidisciplinary) guidelines covering the entire chain from screening to diagnosis, treatment, follow up and surveillance, together with updating the guidelines on surveillance;
 - ways of assuring the quality of colonoscopy, including direct referral by the screening organisation and the creation of a system for on-site audits by a national reference centre; in this context it would seem appropriate for the Centre for Population Screening, as the national supervisory body, to play a supporting role;
 - the provision of data for quality control and evaluation of the screening programme, together with regular reporting;
 - public accountability for work-up, treatment and surveillance within the *Visible Care* programme.
 - From the outset, budgetary provision should be made for monitoring and evaluation, for a reference system and for the promotion of knowledge and innovation-oriented scientific research (necessary to keep the screening programme up to date).
 - The introduction of service screening for bowel cancer should be accompanied by a national public information campaign.
 - To enable people to make informed choices, a system of basic information and supplementary information should be developed, similar to those established in connection with screening for breast cancer and cervical cancer. In this context, particular attention should be given to the national uniformity of information provision in the various phases of the screening process.
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He who pays the piper calls the tune?

Health Council of the Netherlands. He who pays the piper calls the tune? Monitoring Report Ethics and Health, 2009/3. The Hague: Centre for Ethics and Health, 2009. Publicationenumber Health Council of the Netherlands: 2009/18E. ISBN 978-90-78823-12-4 (in Dutch and English)

This advisory report examines the influence of financiers (especially industrial financiers) on the development of medical knowledge, and the ethical questions to which this gives rise. This also especially involves deciding on which fields of knowledge need to be developed and the actual development of that knowledge through research. The words 'sponsoring' and 'sponsor' are used below to refer to research 'funding' and the 'financier'. This advisory report is based on a background study commissioned by the Health Council of the Netherlands which was conducted by Professor R. Bal *et al.*, as well as a study of reference literature and interviews with experts. The Health Council of the Netherlands' Standing Committee on Medical Ethics and Health Law compiled this advisory report. It has been published under the aegis of the Centre for Ethics and Health (CEG), a partnership between the Health Council of the Netherlands and the Council for Public Health and Health Care. The Health Council of the Netherlands is responsible for the content.

Agenda influences

Chapter 1 emphasises that besides industrial sponsors, other parties, such as government and charitable funds, also finance research and therefore influence the research agenda. Particular interests and compromises may also play a role in government decision-making concerned with setting the agenda and priorities for research paid for with public funds (which public interest should be given prior-

ity?). The fact that charitable funds exist for some diseases and not for others may also lead to distortions in knowledge development. Issues of this kind are also worthy of attention but are only discussed briefly in this advisory report.

Industrial sponsoring

Chapter 2 explores the influence of industrial sponsoring on the composition of the research agenda. It is precisely in this initial stage of knowledge development that the prescriptive character clearly comes into focus. Industry especially tends to take an interest in subjects and develop fields of knowledge which can be expected to earn money within the foreseeable future. This is understandable, given that a business has to be profitable to ensure its continuity. The public health knowledge requirement mainly plays a role in the composition of the industrial research agenda where need coincides with commercial feasibility. Commercial feasibility and social importance are compatible but the development of biomedical knowledge would be unbalanced if knowledge development became excessively dependent on industrial research. This would also have adverse consequences for the quality of prevention and care.

The warning against lopsided knowledge development is substantiated by four case studies: drug research; research into diagnostic devices; nutritional research; public health research. Gaps in knowledge developed in these fields are delineated. Possible downsides of increased interrelatedness between industrial and clinical research are also pointed out. There is a risk that the size of the fees paid by industry may carry some weight in the composition of the clinical research agenda and could thereby detract from the attention paid to the social benefit and quality. Possibilities and limitations of Public-Private Partnerships (PPPs) in which research projects are carried out jointly by the public and private sector are discussed. The PPP model is especially suitable for research that is likely to produce economically valorisable results in due course. The model is not a remedy for research for which the results are definitely not commercially marketable, such as research into collective public health interventions.

Unbalanced growth in biomedical knowledge

Chapter 3 summarises the main results of the four case studies. The fields of knowledge studied are subject to all the consequences of the crowding-out effect: in fields of knowledge in which product sales and making profit play little, if any, role, development lags behind that in economically valorisable fields of knowl-

edge, even if society has a definite need for the knowledge concerned. The following factors play a role in this:

- 1 Industry tends not to conduct more research than is required for a new product's registration, as in the case of drugs and diagnostic devices;
- 2 Possibilities for patenting are limited in certain fields, as in the case of research into the effect of foods on health;
- 3 Demand for commercial products is sometimes too low in certain domains, such as public health.

These findings give rise to ethical questions, such as about the extent to which the crowding-out effect leads to imbalances or even unjustifiable choices and results concerning knowledge development, possible restrictions on free choice of research priorities, and the responsibility of government and other parties to make adjustments. This and similar questions would need to be discussed in greater detail.

In the process of knowledge development, the stage of conducting the research follows that of setting the agenda and priorities. International literature has shown that when a company funds research into one of its own products, the results are more favourable for the product concerned than the results of alternatively funded research concerning the same product. This distortion in favour of the sponsor's product is disturbing, also because it can harm trust in research. Explanations of why sponsored research significantly more often produces better results for the sponsor's product are found at three levels: comparisons using a placebo instead of an active drug; selective publication of research results that are favourable for the sponsor; and the selection of a favourable comparison, as when an inadequate dose of the other drug used in the comparison is administered.

The fact that reference literature revealed results favouring sponsors' products also raises ethical questions. What implications do these results have for the conduct of the various actors, such as doctors/researchers and their institutions, science journals and their editorial staff, sponsors/manufacturers and government? The parties concerned will have to engage in debate about this.

Suggested solutions

To conclude, chapter four includes suggestions on how the identified problems could be tackled. The question always revolves around the contribution that the

aforementioned actors can make to possible solutions. Government can direct some aspects but changes in the attitude of professionals and the role of industry are also important.

The potential research capacity and the number of available trial subjects/patients in biomedical research are limited. In view of the results of the case studies and the crowding-out effect, the concern is that the available capacity is not always used to generate the most urgently needed knowledge from the public health point of view. Consequently, the aforementioned actors should jointly reflect on their role and responsibility in funding biomedical research and setting the agenda and priorities. Various options for the parties concerned to combat the crowding-out effect are discussed. The parties must be persuaded that seeding trials (which are sponsored trials with the sole object of getting doctors to prescribe a registered product) produce no new knowledge and cannot therefore be scientifically justified.

Distortions in research results in the case of industrial sponsoring can be combated by preventing any research project intended to find research results that are favourable for the sponsor. The parties concerned can also help with this in their own way. The necessary steps towards achieving this have been made in recent years. If an accepted alternative treatment is available, placebo-controlled trials should be further reduced; research results that are disappointing for the sponsor should also be published; the optimum dose must be administered of the drug with which the comparison is being made.

The main assurance against distortion of this kind is the researcher's independence. Reducing conflicts of interest between the sponsor and the researcher reduces the need for the researcher to be 'agreeable' to the sponsor, which reduces the likelihood of bias in research results. Conflicts of interest may arise through personal reward, for example, or other forms of financial support, such as opportunities to attend congresses and payment of the associated costs. Doctors/researchers should adopt a more assertive and aloof and thereby more independent attitude towards sponsors. Another important development is that ongoing studies are increasingly being made public through trial registers, which have to report conflicts of interest and sponsoring.

Contributing to healthy nutrition

Towards an adequate intake of vitamins and minerals

Health Council of the Netherlands. Towards an adequate intake of vitamins and minerals. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/06E. ISBN 978-90-5549-761-4 (in Dutch and English)

The background to this advisory report

Regulations and research undergo rapid development

European legislation, regulations and research in the field of vitamins, minerals and trace elements, known as micronutrients, undergo rapid development. That is why the Minister for Health, Welfare and Sport has asked the Health Council of the Netherlands for advice in connection with a review of policy in this area.

The aim of the policy is to ensure that as many people as possible consume adequate quantities of micronutrients, while, at the same time, minimising the risk that people exceed the safe upper level of intake.

In this final advisory report, the specially constituted committee (the Micronutrients Committee) presents advice on what is needed for the general, healthy population. The committee takes its earlier advisory reports on vitamins A and D, folic acid and iodine into account. The micronutrient intake of people with medical problems is not covered by this advisory report.

What micronutrients is the daily diet short of, or are supplied in excess?

Some population groups may not obtain adequate quantities of certain micronutrients, although the consequences of this for health are often unclear

The daily diet of most children and adults of Dutch origin supplies enough thiamin, riboflavin, vitamins B₆ and C, phosphorous, potassium, magnesium, copper and zinc.

Much less is known about the micronutrient intake of women who are pregnant or breastfeeding, people of non-Western origin, individuals with a low energy intake or with an unusual dietary pattern. However, there are indications that:

- the riboflavin and calcium intake of people of Turkish, Moroccan or Surinamese background may be too low,
- the vitamin B₁₂ status* of 12 to 25 per cent of elderly people is too low,
- the iron status of 20 per cent of children of asylum-seekers, approximately 35 per cent of women of childbearing age and almost 50 per cent of pregnant women is too low, and
- the vitamin E and selenium intake of young children may be too low.

It is unclear whether excessively low intake or status are associated with adverse effects on health. A low status is not the same as a deficiency of vitamins, minerals or trace elements, which needs to be treated.

There is also a small group of the population who are at risk of having a micronutrient intake above the safe upper level of intake as a result of taking supplements. These levels of intake can have adverse effects on health.

* For example, the concentration of a micronutrient in the blood.

What needs to be taken into account when adopting measures to ensure adequate micronutrient intake?

There is no standard approach. A multi-stage plan can be used to determine how micronutrient intake can be guaranteed

The committee's four previous advisory reports show that it is impossible to devise one standard approach to select the right measure for a micronutrient. Each of the micronutrients examined is unique in respect of excessively low or high intake and associated risks for the various population groups. A multi-stage plan can be followed when considering measures (Figures 1 and 2).

The underlying principle of this plan is that a diet in accordance with the Guidelines for a Healthy Diet supplies enough micronutrients for the general population. However, there are some exceptions to this: women need extra folic acid around the time of conception; young children, people who do not go outdoors enough or who have dark skin, women who are pregnant or breastfeeding, women who wear a veil, women aged 50 and over and men aged 70 and over need extra vitamin D; infants need extra vitamin K; and vegans need extra vitamin B₁₂ (Tables 5 and 6).

The committee is also of the opinion that measures such as advice on supplements or fortification should only be applied if they provide health benefits.

Intake above the recommended dietary allowance does not provide any health benefits

The new European regulations mean that people who consume fortified foods and supplements may in some cases have an intake well above the recommended dietary allowance. There are no indications that intake at these levels is more beneficial to health than the recommended intake.

The current European regulations on voluntary fortification may be a limiting factor with regard to the fortification of staple foods

The advisory reports on folic acid and vitamin D recommended the Minister to consider fortification of only a limited number of staple foods. The European regulations on voluntary fortification may be a limiting factor with regard to the fortification of staple foods with these and other micronutrients where the recommended intake and the safe upper level of intake are relatively close together:

vitamin A, iodine, selenium, copper and zinc. It is not possible at present to prohibit foods that have been fortified on a voluntary basis from the market. In the case of micronutrients with such a narrow margin, the combination of fortified staple foods with products that are fortified on a voluntary basis increases the risk of exceeding the safe upper level of intake.

What measures should be given priority?

Providing information about the risk groups that need extra micronutrients in addition to a varied diet

The committee recommends taking a diet according to the Guidelines for a Healthy Diet as the basis for information, and specifying which population groups need extra vitamins and minerals in addition to this diet.

Preventing excessively high intake of micronutrients

The committee advises people wishing to take supplements or consume fortified foods to ensure that their intake of micronutrients from these products does not exceed the recommended daily intake of micronutrients per day in addition to the micronutrients obtained from the diet. Consuming amounts up to the safe upper level of intake does not offer any health benefits and amounts in excess of the safe upper level can even be harmful in the long term.

Ideally, restrictions should be set at European level on the number of products which can be fortified with micronutrients that have a narrow margin (vitamins A and D, folic acid, iodine, selenium, copper and zinc).

What monitoring activities should be given priority?

High priority should be accorded to determining micronutrient intake by children and adults of Turkish, Moroccan or Surinamese background

The committee recommends that high priority be given to determining the micronutrient intake and status of children and adults of Turkish, Moroccan or Surinamese background. One of the topics that needs to be addressed specifically is the iron intake and status of young children.

Other groups whose micronutrient intake should be investigated

The committee is also of the opinion that it would be desirable for more data to be obtained regarding the micronutrient intake of women who are pregnant or breastfeeding, with investigation into micronutrient status as well where necessary. This also applies to people with a low energy intake, especially elderly people, and individuals whose dietary pattern is unusual. The RIVM (Netherlands National Institute for Public Health and the Environment) will over the coming few years be conducting food consumption surveys of among others individuals of non-western background, women who are pregnant or breastfeeding, and elderly. This may be followed by additional status research.

Monitor the micronutrient intake and the composition of fortified foods continuously

The committee also recommends continuous assessment of micronutrient intake and, where necessary, status, taking account of new developments in science and regulations. It is important to this end to investigate how far fortified products and supplements contribute to the intake of these micronutrients. To this end it is essential that records are kept of the composition and consumption of fortified foods.

What additional research should be given priority?

High priority should be given to research into the effects of low iron status on health among women of childbearing age

The committee recommends giving high priority to investigating whether low iron status among teenage girls and women of childbearing age, whether pregnant or not, is associated with health problems.

Additional research

Other issues which the committee advises putting on the research agenda:

- Investigation as to whether low vitamin B₁₂ status among adults and elderly people is also associated with health problems.
- Investigation as to whether low iron status among children is also associated with health problems.

- Investigation to ascertain whether the possibility that the intake of riboflavin and calcium by people of Turkish, Moroccan or Surinamese background and vitamin E and selenium by children in general is too low is confirmed by status research and, where necessary, research into any health effects.
- Expanding the Dutch food composition database by adding information about the vitamin K content of foods.
- Research into the safe upper intake levels of micronutrients for children (little or no research has so far been carried out into this topic).
- Assessment of the Dutch micronutrient dietary reference values by comparing the current values with those applied in the United States, Australia and New Zealand and with new dietary reference values that may have been established by then in the European Union and Scandinavia. A start has been made on this point in this advisory report, which uses more recent American, Australian and New Zealand dietary reference values for those micronutrients with Dutch dietary reference values which had been drawn up in 1989. The safe upper levels of intake used in this advisory report are those drawn up at European level in 2006.

Contributing to environmental health

Electromagnetic Fields: Annual Update 2008

Health Council of the Netherlands. Electromagnetic Fields: Annual Update 2008. The Hague: Health Council of the Netherlands, 2008; publication no. 2009/02. ISSN 1871-3875 (in Dutch and English)

This is the fifth Annual Update of the Electromagnetic Fields Committee. After a brief overview of the advisory reports that have been published in the period under review, the Committee elaborates upon the approach and methods it uses in analysing scientific data. Following this, two themes are discussed:

- the influence of radiofrequency electromagnetic fields on brain activity and
- the relationship between exposure to such fields and the occurrence of symptoms.

How does the Committee evaluate information

The Committee's conclusions on health effects of exposure to electromagnetic fields are based on scientific data. It is very important for a correct interpretation of these data to have insight into the quality of the research, the way it has been designed and how the data have been collected and analysed. In its evaluation, the Committee puts a lot of weight on the quality of the research. In order to form an opinion on whether or not it is plausible that an association or effect exists, the Committee applies a number of specific criteria.

Epidemiological studies have a special place in the overall analysis because they consider effects in humans. Together with human experimental studies they are therefore very important. However, epidemiological studies suffer from the problem that it is often difficult to establish a causal relationship. One of the reasons for this is that the outcome of an epidemiological study can be distorted for

different methodological reasons. This may lead to a wrongful impression about cause and effect. Therefore, the Committee always considers possible confounders and biases in the evaluation of epidemiological studies; these are discussed in detail in this report.

The Committee bases its overall conclusions on *all* relevant scientific information at its disposal, both epidemiological data and data from human, animal and in vitro experimental studies. The scientific value of the individual studies is taken into account during this process. In that way a judgement is reached that is based upon the weight of evidence, a method that is considered as the most relevant by the scientific community and that is also used by other expert committees.

Biological versus health effects

A multicellular organism such as a human being is not simply the sum of individual cells or tissues, but has an added value that derives among others from the availability of mechanisms that neutralize possible harmful influences and circumstances. These mechanisms maintain the so-called homeostasis, the primary liferegulating function of multicellular organisms.

An effect on a biological system therefore does not necessarily have to lead to an adverse health effect. A health effect will only occur when homeostasis can no longer be maintained, that is, when a biological effect is potentially harmful and cannot or not sufficiently be compensated.

Brain activity

When a mobile phone is held against the head during a call, the brain is exposed to the electromagnetic fields emitted by the device, primarily in the part of the brain closest to the telephone. In recent years many studies have been performed into possible effects of this on the functioning of the brain.

In some studies subtle changes in natural electrical processes in the brain have been observed as a result of exposure to the electromagnetic fields emitted by a mobile telephone. However, these are very minor effects without any health influence on health, according to prevailing knowledge. Studies into effects on cognitive functioning are equivocal: in some studies small and reversible effects have been observed, other studies found no effect. Auditory functioning and body balance do not seem to be influenced by signals from mobile telephones.

In short: some effects on brain functions have been observed, but there are no indications that these indicate, or lead to, health effects.

Symptoms

The number of people attributing a variety of symptoms to various sources of electromagnetic fields in the home and at work seems to increase. They report for instance headache and migraine, fatigue, sleeplessness, concentration problems, itch and sensations of warmth. The number of people that consider themselves to be electrosensitive on the basis of such symptoms seems to be on the increase as well. People particularly attribute their symptoms to mobile phones, base stations, DECT cordless telephones, and now increasingly also to wireless computer network systems.

The prevalence of the symptoms in question within the general population is high. Often no medical explanation can be found, in which case they are generally referred to as medically unexplained physical symptoms.

Both in the living environment and in the laboratory, studies have been performed into a possible link between exposure to electromagnetic fields and the occurrence of symptoms. Several of these studies were not properly designed and cannot be used for the analysis. From the good quality scientific data emerges the picture that there is no causal relationship between exposure to radiofrequency electromagnetic fields and the occurrence of symptoms. However, there is a relationship between symptoms and the *assumption* of being exposed and therefore most likely with the risk perception. Nevertheless, the symptoms do exist and require a solution.

Global environmental impact on health

Health Council of the Netherlands. Global environmental impact on health. Horizon scanning report. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/15E. ISBN 978-90-5549-779-9 (in Dutch and English)

Major environmental changes which are occurring worldwide include global warming and a decline in the diversity of species. These are complicated processes with particular characteristics: they cover a wide area, are insidious, expand in time and space, have numerous causes and impacts and are interdependent. This advisory report from the Health Council of the Netherlands discusses the consequences of global environmental changes for public health in the Netherlands.

More than twenty years ago, the Health Council determined that there were no indications that climate change would have an adverse impact on public health in the Netherlands. The Council's opinion on this subject has changed. This conclusion comes from the advisory report of the Health and Environment Surveillance Committee, which has particular responsibility for identifying important links between environmental impacts and public health.

International reports contain convincing indications that climate change and other global environmental changes pose a health threat. The fact that the Netherlands will not escape the effects is clear from the report published last year on current knowledge of global environmental changes and public health: '*Mondiale milieuveranderingen en volksgezondheid: stand van de kennis*'. The report specifically examines the impact of global environmental changes on the health of the population of the Netherlands and covers the following processes: atmospheric changes (climate change and damage to the ozone layer), changes in land use, depletion of freshwater stocks and a decline in biodiversity. The report

closes with a proposal for a research agenda. The report's publication was a major reason for the Committee deciding to reassess the situation.

The consequences for health of global environmental changes should be paid more attention in policy and research

The Committee notes that in recent decades there has been an increase in knowledge of what the adverse effects of global environmental changes will be on health, both worldwide and in the Netherlands. Climate change in the Netherlands could lead to early death owing to extremely high temperatures and an increase in respiratory complaints and infectious diseases. Additional cases of skin cancer are one of the consequences of damage to the ozone layer. Public health in the Netherlands is also likely to suffer from other environmental changes, such as changes in the use of land, depletion of freshwater stocks and a decline in biodiversity. For example, changes in the use of land and a decline in biodiversity could lead to more infectious diseases. However, indications of the way in which these impacts arise are less direct than in the case of climate change and damage to the ozone layer. The various processes do not usually occur independently but affect each other.

The health effects can be separated into phenomena that probably already occur in the Netherlands and phenomena that may well exist in the future. Examples of the former are the aforementioned increased mortality rate during heat-waves and additional cases of skin cancer attributable to higher levels of UV radiation. An example of the second group of phenomena is an increase in infectious diseases. Also global environmental changes can damage local environments which can lead to conflicts whereby people are forced to flee their homes, and this can have consequences for their health. All these effects are plausible, serious and relevant for the Netherlands. However, they will partially be attributable to other factors, such as an increase in infectious diseases as a result of the growth in international passenger travel and trade.

Health effects still receive little consideration in Dutch policy on global environmental changes. They also receive little attention in the scientific world. As these are plausible, serious and relevant effects and there is still a great deal of uncertainty about how extensive they will be and where and when they will occur, the Committee believes extra policy and research efforts are required.

Policy includes measures for tackling the causes of environmental changes and measures for limiting the adverse effects. Measures in the first category are mainly taken at the international level, as in the case of reducing CO₂ emissions;

measures in the second category generally have a national character; in the Netherlands they are primarily intended to protect the population against flooding.

From the health point of view, the Council believes that it would be advisable to intensify and increase both types of measures.

Research into health threats and protective measures

In the light of this, further research into the health effects of global environmental changes is required. So much is already known about climate change that it would be advisable for part of the research to focus on possibilities for us to adapt, for example by paying more attention to identifying risk groups and how the health threats they face can be reduced. This is less important in the case of damage to the ozone layer because effective global measures have been taken which are expected to result in the ozone layer being restored in due course. Concerning other environmental changes, a lot more research is required into the nature of the health threats, how extensive they will be and where and when they will occur.

Adopt systems thinking

Factors other than global environmental changes also affect public health. Many of them are beyond the scope of the environment. Examples include the quality of education, lifestyle and the level of affluence. Taking the factors as a whole – including global environmental changes – we know or can reasonably assume that some of them are influenced by each other's effects. However, there are still many gaps in our knowledge of how they are interrelated. More detailed information on the connections is required to enable a better assessment of the health effects of global environmental changes and more accurate delineation of the effectiveness of possible measures. It will only be possible to make significant headway by taking these relationships into account. This approach is known as systems thinking.

It involves using knowledge obtained from different fields. Focusing systems thinking on the health effects of global environmental changes requires the integration of disciplines such as epidemiological, biomedical and ecological research into health effects with research in the fields of economics and social science. The strength of systems thinking is that it can help to give structure to available knowledge and to understand the operation of (parts of) the system. The initial aim is a qualitative description of possible processes, links, interactions and feedback. Insofar as components lend themselves to computation, they

are mainly used in aid of the qualitative assessment. Two tools that are commonly used are computer simulation models and scenarios in which possible global developments are described (a free market or a more regulated market, for example). These instruments can be used to make futures studies.

Systems thinking demands the compilation of adequate data. Such data will need to be to some extent specific to the situation in the Netherlands.

Actively encourage research into the health effects of global environmental changes

Systems thinking is becoming established in the field of global environmental changes and their causes and effects. However, there is a blind spot in the area concerned with the effects on public health. System modellers and scientists from various disciplines in the natural and social sciences are involved in the research. Few, if any, doctors and other medical scientists, who familiar with empirical health research, are represented. However, input from this group is essential for public health to have a place in systems thinking about global environmental changes. Dutch scientists have extensive knowledge of systems thinking and it would be advisable to put it to good use. The Committee therefore recommends encouraging systems thinking in the required direction by making grants available to support research that promotes this.

Precautionary action

Paying attention to the health effects in the manner outlined above would be in keeping with a precautionary strategy. Here, the Committee defines 'precautionary' as dealing with uncertainties in a careful, transparent and situation-specific manner. Decision-making concerned with precautionary action should include regular policy evaluation and proper communication. This is all the more important because it concerns an international issue with insidious, far-reaching and irreversible effects which can only be partially described, let alone reliably quantified. The numerous uncertainties and the divergent opinions in society on the urgency of the problem call for participative dialogue with those concerned: authorities, citizens and parties in the community, and experts. The parties include the business community, trade unions and consumer and environmental protection organisations. The Committee sees communication as a two-way exchange of information and discussions between the parties concerned, whereby the importance of information on scientific findings and explanations of policy options should not be underestimated.

The transnational nature of the problem makes international coordination essential for measures and agreements intended to tackle the causes. It will also be possible to take specific measures domestically. A particular aspect of any such measures is that they often have an impact on more than one front simultaneously, which means that they are helpful in tackling more than one environmental issue. For example, energy saving not only reduces the use of natural resources but also emissions, and reducing dependence on fossil fuels for vehicles and transport improves air quality while also reducing greenhouse gas emissions. This is all beneficial to public health.

Finally, the Committee recommends monitoring the effectiveness of policy renewals and examining whether they have any adverse side-effects. The complexity of the problem and the many uncertainties make it difficult to predict the effect of policy. Precautionary action involves assessing policy at set times and more often than in other cases. The findings can be used in combination with new research data to adjust or revise policy.

Contributing to healthy working conditions

Ammonia

Health Council of the Netherlands. Ammonia - Evaluation of the effects on reproduction, recommendation for classification. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/01OSH. ISBN 978-90-5549-755-3 (in English)

In the present report, the Health Council of the Netherlands reviewed ammonia. Eighty percent of all manufactured ammonia is used as fertilizer. A third of this is applied directly to soil as pure ammonia. The rest is used to make other fertilizers that contain ammonium compounds, usually ammonium salts. Ammonia is also used to manufacture synthetic fibres, plastics, and explosives. Furthermore, it is present in refrigeration systems. Many household cleaners and window-cleaning products also contain ammonia in the form of ammonium ions and it is further used in smelling salts.

This report is part of a series in which the Health Council evaluates the effects of substances on reproduction, at the request of the Minister of Social Affairs and Employment. It mainly concerns substances to which man can be occupationally exposed. The Subcommittee on the Classification of Reproduction Toxic Substances of the Dutch Expert Committee on Occupational Safety of the Health Council, hereafter called the committee, evaluates the effects on male and female fertility and on the development of the progeny. Moreover, the committee considers the effects of a substance on lactation and on the progeny via lactation.

The committee recommends classification according to the Directive 93/21/EEC of the European Union. For ammonia, they are:

- for effects on fertility, the committee recommends not classifying ammonia due to a lack of appropriate data
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- for effects on development, the committee recommends not classifying ammonia due to a lack of appropriate data
- the committee is of the opinion that a lack of appropriate data precludes the labelling of ammonia for effects during lactation.

Aluminium and aluminium compounds

Health Council of the Netherlands. Aluminium and aluminium compounds - Evaluation of the effects on reproduction, recommendation for classification. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/02OSH. ISBN 978-90-5549-756-0 (in English)

At the request of the Minister of Social Affairs and Employment, the Health Council of the Netherlands evaluates the effects on the reproduction of substances at the workplace. The evaluation and subsequent classification, according to the Directive 93/21/EEC of the European Union, are performed by the Subcommittee on the Classification of Reproduction Toxic Substances of the Dutch Expert Committee on Occupational Safety of the Health Council, hereafter called the committee. In the present report the committee reviewed aluminium and its compounds.

The committee's recommendations are:

- Metallic aluminium and insoluble (i.e., not soluble in water) aluminium compounds:
 - for effects on fertility, the committee recommends not classifying metallic aluminium and insoluble aluminium compounds due to a lack of appropriate data.
 - for developmental toxicity, the committee recommends not classifying metallic aluminium and insoluble aluminium compounds due to a lack of appropriate data.
 - the committee is of the opinion that labelling of metallic aluminium and insoluble aluminium compounds for effects during lactation is not indicated.
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- Soluble (i.e., in water) aluminium compounds:
 - for effects on fertility, the committee recommends not classifying soluble aluminium compounds due to a lack of appropriate data.
 - the committee recommends classifying soluble aluminium compounds in category 2 (*substances which could be regarded as if they cause developmental toxicity in humans*) and labelling soluble aluminium compounds with T; R61 (*may cause harm to the unborn child*).
 - for effects during lactation, the committee recommends labelling soluble aluminium compounds with R64 (*may cause harm to breastfed babies*).

Ascorbic acid

Health Council of the Netherlands. Ascorbic acid - Evaluation of the effects on reproduction, recommendation for classification. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/03OSH. ISBN 978-90-5549-784-3 (in English)

At the request of the Minister of Social Affairs and Employment, the Health Council of the Netherlands evaluates the effects on the reproduction of substances at the workplace. The evaluation and subsequent classification, according to the Directive 93/21/EEC of the European Union, are performed by the Subcommittee on the Classification of Reproduction Toxic Substances of the Dutch Expert Committee on Occupational Safety of the Health Council, hereafter called the committee. In the present report, the committee reviewed ascorbic acid.

The committee's recommendations are:

- for effects on fertility, the committee recommends not classifying ascorbic acid due to a lack of appropriate data.
 - for developmental toxicity, the committee recommends not classifying ascorbic acid due to a lack of appropriate human data and due to sufficient animal data.
 - for effects during lactation, the committee recommends not labelling ascorbic acid due to a lack of appropriate data.
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Hydrogen fluoride and sodium fluoride

Health Council of the Netherlands. Hydrogen fluoride and sodium fluoride. Evaluation of the effects on reproduction, recommendation for classification. The Hague: Health Council of the Netherlands, 2009; publication no. 2009/04OSH. ISBN 978-90-5549-787-4 (in English)

At the request of the Minister of Social Affairs and Employment, the Health Council of the Netherlands evaluates the effects on the reproduction of substances at the workplace. The evaluation and subsequent classification, according to the Directive 93/21/EEC of the European Union, are performed by the Subcommittee on Classification of Reproduction toxic substances of the Dutch Expert Committee on Occupational Safety of the Health Council, hereafter called the committee. In the present report, the committee has reviewed hydrogen fluoride and sodium fluoride.

The committee's recommendations are:

- for effects on fertility, the committee recommends not classifying hydrogen and sodium fluoride on the basis of a lack of appropriate human data and sufficient animal data which show that classification is not indicated.
- for effects on development of the progeny, the committee recommends not classifying hydrogen and sodium fluoride on the basis of a lack of appropriate human data and sufficient animal data which show that classification is not indicated.
- the committee is of the opinion that sufficient human data regarding effects of hydrogen and sodium fluoride on lactation show that a label is not indicated.

Contributing to innovation and the knowledge infrastructure

Paying upfront

Advisory Council on Health Research. Paying upfront. The problem of matching European subsidies for health research. The Hague: Health Council of the Netherlands, 2009; RGO no. 61. ISBN 978-90-5549-778-2 (in Dutch)

European subsidies for health research cover only part of the total cost of the research. A research institute that accepts a subsidy takes on an obligation to pay the remaining costs, i.e. to match the subsidy by means of co-funding.

This advisory document published by the Advisory Council on Health Research (Raad voor Gezondheidsonderzoek, RGO) deals with the matching of European subsidies for health research. The point of departure was the question that the Ministry of Health, Welfare and Sport placed before the RGO as to whether Dutch participation in European health research programmes could be promoted by establishing a 'matching fund', i.e. a fund from which research institutes that obtain a European subsidy can get co-funding to fulfil their matching obligations.

In preparation for its advice the Council commissioned a check on whether such a matching fund was compatible with European legislation and whether other European countries had taken similar measures. The Council also held talks with executive staff of national knowledge institutes that maintain relationships with the ministry, university medical centres (UMCs) and patients' organisations. This approach was adopted in order to form an impression of the nature and seriousness of the matching problems encountered by these organisations and of the potential solutions that they envisage.

The RGO concluded that a matching fund is permissible under the rules and that similar funds exist (or have existed) in other European countries. The talks

conducted by the RGO revealed that for many years NIVEL (Netherlands Institute for Health Services Research), RIVM (National Institute for Public Health and the Environment), TNO Quality of Life and the Trimbos Institute (Netherlands Institute of Mental Health and Addiction) had been experiencing problems in matching European research subsidies and that they would warmly welcome the establishment of a matching fund. On the whole the matching problems experienced by UMCs appeared slightly less urgent than those confronting the national knowledge institutes. While UMCs felt that matching obligations obstructed the growth of successful research groups they had broadly speaking been able to get by so far thanks to improvisation. Moreover, the problems that UMCs encounter when matching European research subsidies are – more prominently than at the knowledge institutes – part of a wider matching problem whereby roughly speaking Dutch research subsidies account for a far greater share than the European subsidies. The talks conducted by the RGO revealed that patients' organisations regularly identify relevant research questions for which they would like to secure the interest of researchers in Europe and put them in touch with each other. They would benefit greatly from the financing of the preparation of European research projects.

Based on these findings the Council advises the Minister of Health, Welfare and Sport to establish a matching fund. The fund should in any event be open to applications from national knowledge institutes that maintain relationships with the Ministry of Health, Welfare and Sport, on condition that their research proposals are aligned to the 'public interest tasks' formulated by the ministry. The establishment of a matching fund will encourage these institutes to apply for European research subsidies instead of refraining from doing so. As part of the deliberations the Council recommends considering the circumstance that the Dutch investment in the fund will be amply exceeded by the financial benefits in the form of European research subsidies.

The Council further advises the Minister to make it possible for other public knowledge institutes, including UMCs, to seek recourse to the fund, to the extent that their research projects can be expected to contribute directly to ministerial policies aimed at the 'public interest tasks'.

Patients' organisations, which the Council believes should also be considered public knowledge institutes in the present context, would benefit not only from a matching fund, but also from a subsidy scheme that reimburses (in full or in part) the costs that they incur when preparing and writing subsidy applications for submission to European programmes. The Council advises the Minister for Health, Welfare and Sport to create such a scheme.

The advisory document includes two recommendations with a wider scope. The Council advises the Minister for Economic Affairs and the Minister for Education, Culture and Science to examine the desirability and feasibility of stimulating across-the-board Dutch participation in European research programmes by establishing a matching fund usable by research institutes within and outside the health research field.

The advisory document finishes by concluding that the matching of non-cost-covering research subsidies, regardless of the party that provides them, is increasingly causing problems in the health research domain. Sooner or later research groups successful in obtaining such subsidies will be thwarted in their development because of the matching obligations. The Council advises the Minister for Education, Culture and Science to do everything possible to resolve this more general matching problem, which extends beyond the health research field.

A Other publications

Annex

Other publications

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- Care for the unborn child. (2009/01, in Dutch)
 - Advisory letter Power lines and Alzheimer's disease. (2009/05E, in Dutch and English)
 - Advisory letter Vaccination against Mexican flu. (2009/08E, in Dutch and English)
 - Advisory letter UV radiation and sunbeds. (2009/11E, in Dutch and English)
 - Advisory letter Vaccination against pandemic influenza A/H1N1 2009: target groups and prioritisation (2). (2009/12E, in Dutch and English)
 - Advisory letter Vaccination against pandemic influenza A/H1N1 2009: target groups and prioritisation (3). (2009/16E, in Dutch and English)
 - Advisory letter Vaccination against pandemic influenza A/H1N1 2009: dosage. (2009/19E, in Dutch and English)
 - Advisory letter on organically grown foods. (2009/20, in Dutch)
 - Advisory letter on the fourth prevention programme. (60, RGO)
 - Population Screening Act: screening for prostate cancer in BRCA families. (2009/01WBO, in Dutch)
 - Population Screening Act: the HealthRiskTest. (2009/02WBO, in Dutch)
 - Population Screening Act: colonoscopy or colonography for screening; the COCOS trial. (2009/03WBO, in Dutch)
 - Population Screening Act: bottlenecks in enforcement of the law-proposed amendments. (2009/04WBO, in Dutch)
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- Population Screening Act: stepwise screening for fracture risk. (2009/05WBO, in Dutch)
- Annual Report 2008 Health Council of the Netherlands (A09/01, in Dutch)
- Health Council of the Netherlands Reports 2008 (A09/02, in English)
- Plan of activity 2008-2011 of the works council of the Health Council. (A09/03, in Dutch)
- Social Annual Report from the office of the Health Council of the Netherlands 2008 (A09/04, in Dutch)
- Work Programme 2010 Health Council of the Netherlands (A09/05E, in Dutch and English)
- Health Council Lecture for 2009 Gezond aan het werk. (A09/06, in Dutch)