
**Towards an adequate intake
of vitamin D**

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To the Minister of Health, Welfare and Sport

Subject : Presentation of advisory report *Towards an adequate intake of vitamin D*
Your reference: VGP/VV 2646726
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Dear Minister,

On 28 January 2006, your predecessor requested the Health Council to review the policy on micronutrients. We are pleased to present the accompanying advisory report on one of those micronutrients: vitamin D. The advisory report on iodine is also being published today. The Health Council provided you with information on folic acid earlier this year. Further advisory reports on vitamin A and other micronutrients are scheduled for publication in 2008 and the beginning of 2009.

To advise you on optimum vitamin D intake, a Committee of Experts considered recent research and its policy implications, also in the light of new European regulations. The findings have been checked by two permanent advisory and consultative bodies in the Council, namely the Standing Committee on Medicine and the Standing Committee on Nutrition.

The Committee has concluded that a section of the population needs extra vitamin D, in addition to the vitamin D obtained from food (including margarine, low-fat margarine and products used in baking and frying) and that produced by the skin through exposure to sunlight. The specific groups concerned are children under the age of 4, dark-skinned people, women who are pregnant or are breastfeeding, women who wear a veil, women from the age of 50 and men from the age of 70. The Committee recommends streamlining information on the importance of extra vitamin D obtained from supplements.

Although unable to meet the full requirement for extra vitamin D, fortified foods could provide a partial alternative for people who take too few, if any, supplements. It is therefore important for specifically those products that are frequently used by risk groups to be fortified.

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The Committee therefore recommends that vitamin D continues to be added to margarine, low-fat margarine and products used in baking and frying, and to regulate that vitamin D may further only be added to milk, milk substitutes and oil, rather than allowing it to be added to any product without restriction, as is currently the case. Agreements will have to be made about this at the European level. The Committee concludes by recommending a review of the dietary reference values for vitamin D which were established in 2000.

This new advisory report on vitamin D provides you with details of the most recent scientific findings and the state of affairs in other countries. It also includes considerations that are important for policy measures. I fully support the Committee's conclusions and recommendations.

Your sincerely,

(signed)

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to:

the Minister of Health, Welfare and Sport

No. 2008/15E, The Hague, September 30, 2008

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

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

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



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Brief outline of the advisory report

Vitamin D and calcium are important for strong bones. People obtain this essential micronutrient through intake and through production in the skin during exposure to sunlight. This advisory report is concerned with how people in the Netherlands can achieve an adequate vitamin D intake.

Vitamin D deficiency occurs in all sections of the population

Vitamin D deficiency occurs in dark-skinned people (for example those of Turkish, Moroccan and Surinamese extraction), people who do not spend enough time outdoors, women who wear a veil, are pregnant or are breastfeeding, and elderly people. People at the highest risk are residents of nursing homes or care homes. Young children not receiving a vitamin D supplement or infant formula are also at risk of developing a vitamin D deficiency.

Clear information is required to improve the present situation

With the exception of that provided for young children, information currently available on the importance of vitamin D is unclear. Within the context of this report, light-skinned people aged from 4 to 50 (females) or 70 (males) need at least a quarter of an hour a day out of doors and healthy diet (including intake from margarine, low-fat margarine, and products used in baking and frying). It should be explained to other groups that, in addition to this, they need 10 micrograms extra vitamin D per day from supplements. Elderly people with osteoporosis or who live in a care home or nursing home and people from the age of 50 (females) or 70 (males) who are dark-skinned or who do not spend enough time outdoors, and veiled women from the age of 50 need 20 micrograms extra vitamin D per day. Within the context of these measures, calcium intake must also be sufficient.

Arrange at the European level to restrict the type of food that may be fortified and prevent excessive intake

Fortified foods, although unable to meet the full requirement for extra vitamin D, could provide a partial alternative for people who do not wish to take supplements. It would be advisable to agree at the European level that vitamin D may only be added to products that people in high-risk groups tend to use more, such as margarine, low-fat margarine and products used in baking and frying, as well as oil, milk and milk substitutes, rather than allowing it to be added to any product without restriction as is the case at present. To prevent excessive intake, it would be advisable to register fortified products and to monitor intake.

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Executive summary

What is the background to this advisory report?

Regulations and research undergo rapid development

European regulations, legislation and research in the field of vitamins, minerals and trace elements, known as micronutrients, undergo rapid development. It is for this reason that the Minister for Health, Welfare and Sport has asked the Health Council of the Netherlands for advice on reviewing its policy in this area in the light of new scientific developments.

The aim of the new 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 advisory report, the committee set up to address this issue indicates the requirements for vitamin D.

Vitamin D is essential to the body

Vitamin D can be obtained from food, but strictly speaking it is not a true vitamin. That is because between April and October it can be produced in our skin thanks to the action of sunlight (ultraviolet radiation).

The amount of vitamin D produced in the skin depends not only on exposure to daylight but also on skin colour: less vitamin D is produced in dark skins than in pale skins. Vitamin D is important for strong bones, along with calcium. Insufficient vitamin D is also associated with muscle weakness and muscle cramps. A severe deficiency leads to weak, painful bones in children and the elderly. An excessively high vitamin D intake causes excessively high blood calcium levels, which gives symptoms of poisoning such as loss of appetite, weakness, fatigue, disorientation and vomiting. If this persists, calcium is deposited around organs such as the kidneys, the urinary tract, blood vessel walls, muscles and tendons.

What are the main scientific developments?

The amount of vitamin D in the body can be measured by means of an indicator: blood serum calcidiol levels. In 2000 the Health Council established dietary reference values for vitamin D on the basis of a serum calcidiol level of 30 nmol per litre. In this advisory report the committee sets a higher target figure (at least 50 nmol per litre of blood) for women aged 50 and over and men aged 70 and over.

This conclusion is based on recent research into the effects of vitamin D and calcium on bone quality, the risk of fracture and the risk of falling in the elderly. The effects are the largest among post-menopausal women who are institutionalized. As bone loss accelerates around the menopause, the committee assumes that the higher target is appropriate for women aged 50 and over.

A good vitamin D supply is known to be important for bone quality and has recently been linked to a lower risk of many other conditions as well, such as cardiovascular disease, auto-immune diseases, infectious diseases and type 2 diabetes. However, the committee finds that the evidence for these effects is not yet strong enough to allow it to issue recommendations.

What is the position with regard to vitamin D supply?

Vitamin D deficiency occurs in all sections of the Dutch population

Inadequate vitamin D status is observed in all sections of the Dutch population. The proportion is higher at the end of winter than at the end of summer (table 1). The figures for pregnant women are probably also applicable for women who are breastfeeding. Vitamin D intake is also too low among children aged up to four who are not receiving follow-on milk or a vitamin D supplement (about four per cent of children aged one year and twelve per cent of children aged eighteen months).

Table 1 The occurrence of vitamin D deficiency among the Dutch population.

Population group	Serum calcidiol criterion	Percentage throughout the year ^a	Percentage in summer	Percentage in winter
Newborn infants with light skin	< 30 nmol/l	15		
Newborn infants with dark skin	< 30 nmol/l	65		
Children with light skin	< 30 nmol/l	5	0	
Children with dark skin	< 30 nmol/l	15-30		40
Children on a macrobiotic diet	< 30 nmol/l		10	80
Adults with light skin	< 30 nmol/l	5-10		
Adults with dark skin	< 30 nmol/l	15-60		
Pregnant women with light skin	< 30 nmol/l	5-10		
Pregnant women with dark skin	< 30 nmol/l	55-65		
Elderly people living independently	< 50 nmol/l	50	35	50
Residents of care homes	< 50 nmol/l	0-85		

^a The percentages are rounded to the nearest 5, as different cut-off points were used in the various studies.

What is the best way of improving vitamin D supply?

Provide more information about the importance of vitamin D, and make the message consistent

The committee feels that the current information is not altogether clear. It is important that the various official bodies involved in the provision of information about boosting vitamin D intake by means of supplement or diet should give the same advice.

A positive exception is the provision of advice on supplements for children aged up to four, where new actions have been taken to increase the use of supplements. Pre-conception care units and infant welfare centres could be involved in recommending additional vitamin D intake during pregnancy and while women are breastfeeding.

Underline the importance of spending at least a quarter of an hour a day out of doors

The committee recommends that people should spend at least a quarter of an hour a day out of doors to help vitamin D production in the body, while taking care to avoid sunburn. The committee feels that exposing at least the head and hands should not be emphasized in the information, because it is actually brief exposure of larger parts of the body, such as the arms and legs, that boosts vitamin D production. But this exposure only generates vitamin D between April and

October. During the winter, people rely on the physical reserve of vitamin D they have built up over the summer in combination with dietary vitamin D.

Also stress the importance of supplementing intake through diet

A healthy diet should provide enough vitamin D (and calcium) for people aged between four and 50 (women) or 70 (men) with light skin who spend enough time outdoors. All other groups need additional vitamin D from supplements.

People who do not take supplements would benefit from eating foodstuffs fortified with vitamin D, but very few such foodstuffs are currently available. And even if there were enough products on the market, their consumption would not provide all the additional vitamin D needed.

The information should contain clear recommendations for additional vitamin D

The committee believes that the currently recommended additional vitamin D levels for certain groups are too low. It advises the following targets:

- an additional 10 micrograms of vitamin D a day for:
 - children aged up to four*;
 - people aged between four and 50 (women) or 70 (men) who have dark skin, who do not spend enough time outdoors;
 - women aged up to 50 who wear a veil;
 - women who are pregnant or are breastfeeding;
 - people aged over 50 (women) or 70 (men) who have light skin and who spend enough time outdoors.
- an additional 20 micrograms of vitamin D a day for:
 - people who have osteoporosis, who live in a care home or nursing home, people aged over 50 (women) or 70 (men) who have dark skin or who do not spend enough time outdoors, and women aged over 50 who wear a veil.

The committee assumes hereby that calcium intake is adequate.**

* This advice does not apply to children consuming more than half a litre of infant formula or follow-on formula a day.

** 'Adequate' in the sense that it is at the level of the dietary reference value.

Importance of preventing excessively high vitamin D intake from supplements and/or dietary sources

The committee emphasises that it is essential for vitamin D intake to remain below the safe upper intake limit when people are taking supplements and/or eating fortified foodstuffs. Dietary supplements that contain more than the quantities of vitamin D given above in a daily ration must therefore be taken with caution. Children are at the greatest risk of exceeding this limit. The committee advises addressing this issue by registering the composition of fortified foodstuffs: at the moment it is not known precisely which foodstuffs are fortified with vitamin D and how much they contain. This information is however available for supplements.

It is also important that dietary vitamin D intake and the vitamin D status of the Dutch population as a whole and of high-risk groups in particular are monitored. Policy may be adjusted in the light of the results.

Measures can also be taken at European level

The committee thinks that vitamin D should continue to be added to margarine, low-fat margarine, and products used in baking and frying. It also recommends that the type of foodstuffs to which vitamin D can be added in Europe should be restricted to milk, milk substitutes and oil, rather than allowing it to be added to any product without restriction as is the case at present. The advantage of these products is that they are consumed in large quantities by high-risk groups. The advisory report contains proposed fortification levels for these products, which do not put children or adults at risk of excessively high intake when they are consumed in combination with supplements.

Introduction

Vitamin D occurs naturally in foods. Although it can be obtained from food, it is not a true vitamin in the strictest sense because it can also be produced by the skin itself from April to October (in the northern hemisphere) through exposure to the sun's ultraviolet rays. The amount of vitamin D produced in this way depends not only on exposure to sunlight but also on skin colour: dark skin produces less vitamin D than light skin. Vitamin D plays a role in bone mineralisation. Insufficient vitamin D is associated with muscle weakness and muscle cramps. A severe deficiency leads to weak, painful bones in children and the elderly.

Within the scope of European regulations, the Ministry of Health, Welfare and Sport would like to develop a new policy to ensure that as many people as possible in the population have an adequate intake of vitamin D and other micronutrients. However, at the same time it is important to minimise the risk of people's intake exceeding the established safe upper level of intake. The ministry has asked the Health Council of the Netherlands for advice on reviewing its policy on fortifying foods with micronutrients, such as vitamins, minerals and trace elements (annex A). The Health Council has also received an additional request following questions in parliament concerning vitamin D deficiencies in various population groups in the Netherlands (annex B).

This advisory report is the third in a series of five. The first advisory report, on folic acid¹, has been published and that on iodine² is being published simulta-

neously with this report, while work is underway on the other two scheduled reports, namely one on vitamin A and one on other micronutrients.

1.1 Original policy on vitamin D

The addition of vitamin D to dietary supplements in the Netherlands was not statutorily regulated until 1994. Its addition to foods was permitted to a very limited degree.³ For example, vitamin D could only be added to margarine, low-fat margarine, and products used in baking and frying. Fortification of other foods with vitamin D was prohibited.

The Dutch government was forced to review its policy in the early 1990s. This was primarily because of the pressure resulting from free trade. Other European countries had been permitting vitamin additions to foods for longer. Another reason for revising the policy was that a habitual diet* proved inadequate in the supply of a number of micronutrients. On the other hand, it was necessary to prevent an excessive intake of certain micronutrients. This was particularly the case for micronutrients with a 'narrow margin', for which the dietary reference value or recommended dietary allowance and the safe upper intake level were relatively close.

These developments led to the introduction of the Commodities Act Exemption for Vitamin Preparations in 1994⁴ and the Micronutrient Additives (Commodities Act) Decree in 1996.⁵ The Commodities Act Exemption for Vitamin Preparations sets a limit for the amount of vitamin D that may be added to vitamin preparations.⁴ The Micronutrient Additives (Commodities Act) Decree continues to prohibit the fortification of foods with vitamin D but does permit restoration or substitution**.^{5,6} In 1999, the government concluded an agreement with producers of margarine, low-fat margarine and products used in baking and frying, thereby enabling these alternatives for butter to be fortified with at least 75 per cent of the amount permitted by law, namely 7.5 micrograms of vitamin D per 100 grams. The agreement will apply until new European legislation on fortification enters into force.⁷

* Unless further specified, diet means intake from foods and supplements.
** Annex H provides a list of definitions.

1.2 Developments that call for a new policy

Nutritional necessity

There have been further developments this year (2008) that necessitate a review of the policy on vitamin D. Since 1996, fortification of foods with vitamin D, vitamin A, folic acid, copper and selenium was only permitted if there was a nutritional necessity. Such a necessity has no longer been required since 2004.⁸ Requests for the discontinuation of the prohibition on the addition of micronutrients may now only be refused if it can be demonstrated that marketing the specific product would pose a public health problem. Within the scope of this, the Netherlands must discontinue the absolute prohibition on fortification with vitamin D. Pending new European legislation, an exemption has been in place since 2007 for the addition of up to 4.5 micrograms of vitamin D per 100 kcal. Individual applications for exemptions can be submitted for the addition of higher amounts of vitamin D.⁹

European harmonisation

The policy on supplements and food fortification will be harmonised in the European Union between 2008 and 2012. In the same period, a European Union Supplements Directive from 2002 and a European Union Regulation from 2006 on voluntary fortification of food will have been given shape in national legislation^{*,13,14} Both cases are concerned with framework legislation, in which the principles are laid down but not the details. The Regulation and Directive already stipulate that vitamin D, in the form of vitamin D₂ or D₃, may be added to supplements and foods. Information on the minimum and maximum vitamin D dose that may be added to supplements and foods was not available at the time of writing this advisory report. Nor had the recommended dietary allowance to be stated on the label been determined.

* The Directive on dietary supplements and the Regulation on fortified foods have already been incorporated in the Food Supplements (Commodities Act) Decree and the Commodities Act Exemption for Vitamin Preparations.¹⁰⁻¹²

A regulation is scheduled to govern this, as well as the minimum dose required to state on the label a food contains or is rich in vitamin D*. The regulation is concerned with voluntary fortification, which does not necessarily solve the problem of possible deficiencies.¹⁴ However, the regulation enables the European Union's member states to maintain or introduce mandatory fortification of staple foods, if deemed necessary for public health reasons.

New insights

The Dutch policy needs to be reviewed not only in connection with changing European regulations but also in the light of recent scientific developments. Sections of the population could derive considerable health benefits from taking vitamin D, of which the required intake is, in fact, far above the level of the present dietary reference values. However, high doses of this kind could lead to adverse side-effects. It is essential to balance the positive and negative effects on health for groups that benefit from a higher vitamin D intake as well as for those who do not.

1.3 Several measures with the same aim

Several measures exist for ensuring that as many people as possible in the population have an adequate intake of micronutrients, within safe margins. A healthy diet is at the top of the list. If this proves inadequate, either one or a combination of several of the following additional measures could be considered: restoration, substitution, fortification and supplementation¹⁵:

- Restoration involves adding micronutrients that are lost during the production process, storage and/or sale of food stuffs. Additions are made up to the level that was originally present in the edible part of the food or the raw material from which it was made.
- Substitution is the replacement of a food with another food that is as similar as possible in appearance, consistency, taste, colour and odour or serves the same purpose in its use.

* The new European regulation on nutrition and health claims includes provisions for stating on the label that a food is a source of a micronutrient if it contains 15% of the recommended dietary allowance for the micronutrient per 100 g, or per 100 ml or per packaged portion, and that it is rich in a micronutrient if it contains a level of at least 30%. For as long as the transitional period stipulated in the European regulation applies, it is still permissible under the Dutch legislation based on the regulation to claim that a food is rich in a micronutrient if it has more than 20% of the recommended dietary allowance per daily portion.

- Fortification involves adding to foods one or more micronutrients to a level that is higher than that which occurs naturally in the food or the raw material used to produce the food, in aid of preventing or correcting a demonstrated deficiency in one or more micronutrients in the population or population groups. Generally speaking, fortification may be voluntary or mandatory. The decision of whether or not to fortify a product in the case of voluntary fortification is left to the manufacturer, which therefore means that specific products are fortified. The government may consult producers to encourage voluntary fortification. Mandatory fortification is concerned with staple foods. Mandatory fortification is not legally feasible in the Netherlands. The government can however regulate mandatory fortification on the basis of an agreement with manufacturers. The Commodities Act also stipulates how much of a given micronutrient may be added to which products.¹⁶
- Supplementation involves taking a supplement containing micronutrients in addition to intake from foods.

1.4 Issues addressed

The ministry's request to the Health Council for an advisory report (see annex A) originally asked for a survey of (1) essential micronutrients that are not found in adequate amounts in the habitual diet, (2) the level at which those nutrients need to be supplied, and (3) the best way of achieving that supply level, e.g. through restoration, substitution, fortification or supplementation, with a consideration of any associated health effects.

Consultation between the Health Council and the Ministry of Health, Welfare and Sport has led to a more specific request for an advisory report to cover those for which the supply might be inadequate if they are not added to the habitual diet. This applies to vitamins A and D, iodine and folic acid. An active substitution policy has already been adopted for vitamins A and D. A limited degree of fortification with iodine is permitted.^{15,17} There have been indications since as far back as the 1990s that the folic acid intake of more than half of the adult population may be inadequate.¹⁸ There are no clear indications that the population's general intake of the other micronutrients is too low.^{19,20} However, the situation is different in specific population groups. The Committee (annex C) will therefore have to indicate in the final advisory report of this series of five, which other micronutrients ought to be given priority.

The minister's questions have been put into effect as follows for this advisory report, which is the second in the series:

- 1 Do any recent scientific developments call for a review of Dutch policy?
- 2 What is the vitamin D intake and nutritional status of population groups in the Netherlands?
- 3 If the supply is inadequate, how much vitamin D could the various population groups safely take (in addition to that contained in the habitual diet, which only includes vitamin D additions in connection with restoration or substitution) to guarantee or continue to guarantee an adequate supply of vitamin D?
- 4 What is the best way to achieve this guarantee?

1.5 Methodology

The background information for this advisory report has been systematically assessed and categorised according to the degree of supporting evidence (see annex D). The Committee also organised a working conference with other experts on vitamin D (see annex E). The Committee has not restricted itself to scientific knowledge but has also considered experiences with fortification and supplementation in other countries, as well as European developments.

Answering the questions involved describing the vitamin D supply, discussing the impacts of various policy measures, and, amongst other things, using an assessment of the possibilities available within the scope of European legislation for the formulation of the recommendations. No risk-benefit analysis was available at the time of drafting this advisory report.

The Committee submitted its advisory report for review by the Health Council's Standing Committee on Nutrition and Standing Committee on Medicine.

1.6 Structure of the advisory report

Chapter 2 discusses the physiological role of vitamin D and the consequences of intake being too high or too low. Chapter 3 describes the dietary reference values for vitamin D. In chapter 4 the Committee examines whether recent scientific insights concerning vitamin D have any bearing on the recommendations. This chapter therefore answers the first question in the request for an advisory report. Chapter 5 outlines the present vitamin D supply, thereby addressing the second question in the request for an advisory report. Chapter 6 describes policy measures in other countries. Chapter 7 focuses on current Dutch policy measures and

the benefits and disadvantages of possible policy changes. This forms the basis for answering the third and fourth questions of the advisory report request. The Committee presents its conclusions and recommendations in chapter 8.

Introduction to vitamin D

This chapter describes the various types of vitamin D and vitamin D's role in the body. It also discusses the effects of excessive or inadequate vitamin D intake and the various sources of vitamin D.

2.1 Types of vitamin D and its physiological role

Vitamin D is a generic name for steroids with the same biological activity as fat-soluble vitamin D₃ (cholecalciferol). Vitamin D can be obtained through intake and through production in the skin during exposure to sunlight or when using a sunbed. Vitamin D is therefore not strictly a vitamin but a prohormone.

It stimulates the absorption of calcium and phosphorus from the diet and the mineralisation of bones. The process of absorbing calcium in the intestine is partially vitamin-D dependent and partially vitamin-D independent. In the case of a high calcium intake, absorption through the latter process is high in absolute terms and the need for vitamin D is low. The vitamin D requirement is therefore inversely proportional to calcium intake. The Committee's recommendations primarily apply when calcium intake is adequate.

There are also suggestions that vitamin D plays a role in other physiological processes, such as cell growth and development, muscle functioning, and the immune system.^{21,22}

The following designations are used in this advisory report for the different vitamin D variants:

- *Vitamin D2*, ergocalciferol, is a form of vitamin D that is found in foods such as certain fungi.
- *Vitamin D3*, cholecalciferol, is found in foods of animal origin and is also produced by skin as follows: upon exposure to ultraviolet light, 7-dehydrocholesterol is converted into pre-vitamin D3, or pre-cholecalciferol, which is converted, under the influence of heat, into vitamin D3.
- *Calcidiol*, 25-hydroxyvitamin D is the inactive or only very slightly active metabolite of vitamin D produced in the liver from vitamin D2 or D3. Calcidiol is a good indicator of vitamin D status. Because serum and plasma calcidiol levels do not differ, the term serum calcidiol level is used throughout the advisory report, also when referring to the determination of the calcidiol level in plasma.
- *Calcitriol*, 1,25-dihydroxyvitamin D, the active metabolite of vitamin D produced in the kidneys, stimulates calcium absorption in the intestine. This metabolite is also produced by other tissue, and this appears to be important for cell development and growth and the immune function.²¹⁻²³

2.2 Consequences of a deficiency or an overdose

A lack of vitamin D* through insufficient exposure to ultraviolet radiation in combination with inadequate intake is associated with muscle weakness and muscle cramps. A severe lack of vitamin D causes rickets in children and osteomalacia in adults. In people suffering from rickets and osteomalacia the newly formed matrix of bone tissue (the osteoid) is not mineralised, which makes the bone weak and painful. A lack of vitamin D can also lead to loss of bone mass and osteoporosis, through secondary hyperparathyroidism**. This applies especially in the case of elderly people.²²

Exposure to ultraviolet radiation cannot lead to an excess of vitamin D but excessive intake can. Prolonged exposure to ultraviolet radiation does not lead to vitamin D poisoning because in such cases pre-vitamin D3 is converted into sterols with no vitamin D activity. However, a vitamin D intake of more than 60 micrograms per day can be toxic.²² An overdose of vitamin D results in an excessive calcium level in the blood (serum calcium level > 2.75 mmol per litre). When the kidneys are unable to eliminate a sufficient amount of the surplus cal-

* A calcidiol level below 30 nmol per litre.
** An over-active parathyroid gland.

cium, overdose symptoms, such as anorexia, weakness, tiredness, disorientation, vomiting and constipation, appear. In the long term, excessive calcium deposits can occur in soft tissue, especially around the kidneys (nephrocalcinosis) and urinary tract, vascular walls, muscles and tendons.²⁴ Sections 7.2 and 7.3 discuss the consequences of fortification and supplementation for the risk of exceeding the safe upper intake level or tolerable upper intake level.

2.3 Sources of vitamin D

Foods that naturally contain vitamin D are mostly of animal origin. For example, fatty fish is rich in vitamin D. Eggs, liver, meat and milk products also contain small amounts. The addition of vitamin D to margarine, low-fat margarine and products used in baking and frying is also permitted in the Netherlands.

Another important source of vitamin D is its production by skin during exposure to ultraviolet radiation, especially radiation at wavelengths between 290 and 320 nanometres*, either from sunlight or a sunbed. Exposure to this light converts 7-dehydrocholesterol into pre-vitamin D₃, which spontaneously isomerises into vitamin D₃. As mentioned, an advantage of ultraviolet radiation is that it never leads to excessive vitamin D production. A short period of exposure is all that is required for skin to attain maximum vitamin D production. In the summer, light-skinned people who spend at least 15 minutes outside during the day with their hands and face exposed will have adequate vitamin D levels. The estimated average amount of vitamin D produced by this type of exposure throughout the year is 2.5 to 5.0 micrograms per day. Actual vitamin D production is difficult to determine because it depends on numerous factors, such as the amount of cloud, duration of exposure, skin colour and the use of sunscreen lotions. For example, dark-skinned people need a longer period of exposure.²² Sunscreen lotions prevent ultraviolet radiation from reaching the skin and can therefore considerably reduce the skin's vitamin D production.²⁵ In the winter in the Netherlands (52nd degree of latitude), there is insufficient ultraviolet radiation at the right wavelength for the skin to produce significant levels of vitamin D.²⁵

However, excessive exposure to ultraviolet radiation is related to an increased risk of skin cancer and suppression of the immune system and can be a contributory factor in eye disorders such as cataracts.²⁶

* Ultraviolet B radiation has a wavelength of 280 to 315 nanometres, and ultraviolet A radiation a wavelength of 315 to 400 nanometres.

Dietary reference values

This chapter describes the dietary reference values and the tolerable upper intake level for vitamin D and the biochemical and physiological factors, environmental factors and effects on health they are based on.

3.1 Application of dietary reference values

The term 'dietary reference values' is a generic name for various reference values for energy and nutrients. Dietary reference values apply to healthy people and are mainly concerned with preventing diseases. They are used for:

- programming dietary supplies for healthy groups;
- drafting dietary guidelines for healthy people;
- assessing dietary intake data of healthy groups;
- evaluating the dietary intake of people who have been shown to have an inadequate nutritional status on the basis of biochemical parameters;
- drafting the so-called Guidelines for a Healthy Diet.

The dietary reference values were previously always drafted by the Dietary Reference Values Committee of the Netherlands Nutrition Council/Health Council of the Netherlands. A micronutrient's recommended dietary allowance was derived from figures on the average requirement for that micronutrient. When figures were unavailable, as was the case for vitamin D, the Committee only stated a value for adequate intake. Recommended intake and adequate intake

have the same practical significance: both indicate the level of intake which is desirable on health grounds.²⁷

3.2 Adequate intake

The adequate intake is the lowest intake level that appears to be adequate for the entire population. Adequate intakes are estimated if insufficient research data are available to determine an average requirement and a recommended dietary allowance.

The vitamin D requirement depends on skin colour and the level of exposure to ultraviolet radiation. The Health Council therefore specifies dietary reference values not only for various age groups and for pregnant or breastfeeding women but also for light-skinned people and those who have sufficient exposure to sunlight and for dark-skinned people and those whose exposure to sunlight is insufficient (figure 3.1 and table 3.1). Taking the relationship between vitamin D intake and the serum calcidiol level as its basis, the Dietary Reference Values Committee has determined adequate intake levels for children, adults up to the age of 50 and pregnant or breastfeeding women.

Adequate intake for people from the age of 51 is based on the vitamin D/serum calcidiol level relationship and bone density, and for people from the age of 71 the figure is based on the vitamin D/serum calcidiol level relationship, bone density and the risk of fractures.

As no vitamin D deficiency occurs in people with a serum calcidiol level of 30 nmol per litre or higher, this figure has been used as a target value for determining standards. It is unclear whether the target value has been adopted as an average or minimum level. This figure has been adopted in the present advisory report as the minimum level for an individual throughout the year.

The advisory report on dietary reference values does not provide a more precise definition of what is meant by dark skin.^{22,28,29} The advisory report sometimes refers to the skin of people with a Mediterranean background as dark and sometimes as slightly darker. The present Committee believes that the group of dark-skinned people should also include people with slightly darker skin. This means that the definition also covers people from countries like Turkey, Morocco, India, Indonesia and Surinam.

A distinction is also made in the dietary reference values between sufficient and insufficient exposure to sunlight, whereby sufficient exposure to sunlight is defined as at least 15 minutes outdoors every day with at least the hands and face uncovered. To avoid confusion with information on skin-cancer prevention, the

present advisory report does not refer to sufficient exposure to sunlight but rather to spending enough time outdoors.

The Committee sees no reason for changing the guideline of 15 minutes per day, as there are major uncertainties about the estimated effect of being outdoors on the production of vitamin D (see section 2.3 Sources of vitamin D).

However, the present advisory report does not stress the importance of exposing at least the head and hands but rather short-term exposure of larger parts of the body, such as the arms and legs, as this leads to a higher level of vitamin D production.³⁰

The dietary reference values further state that vitamin D production is lower in the winter than in the summer. However, the skin's vitamin D production is negligible in the winter (October to April).²⁵ Vitamin D levels in this period therefore depend on reserves built up in the summer and through intake.

The starting point in the dietary reference values for vitamin D was adequate calcium intake. This was because low calcium intake probably results in a higher vitamin D requirement. Adequate calcium intake has been established at 1.0 grams of calcium per day for the 19- to 50-year-old age group.*²²

3.3 The tolerable upper intake level

The tolerable upper intake level is the highest intake level at which no harmful effects occur. In the case of vitamin D, the figure has been established on the basis of the lowest intake level at which no effects of overdosing are observed (NOAEL, no observed adverse effect level).

When determining the acceptable vitamin D upper intake limit, the Dietary Reference Values Committee's starting point was the tolerable upper intake level determined by American researchers.^{22,31}

* Adequate calcium intake has been established at 0.21 grams per day for breastfed infants up to the age of 6 months; 0.32 grams per day for bottle-fed infants up to the age of 6 months; 0.45 grams per day for children from 6 to 12 months; 0.5 grams per day for children aged 1 to 3; 0.7 grams per day for children aged 4 to 8; 1.2 grams per day for children aged 9 to 18; 1.1 grams per day for girls aged 9 to 18; 1.1 grams per day for the age group from 51 to 70; 1.2 grams per day for the age group from 71 upwards and 1.0 grams per day for pregnant or lactating women.²²

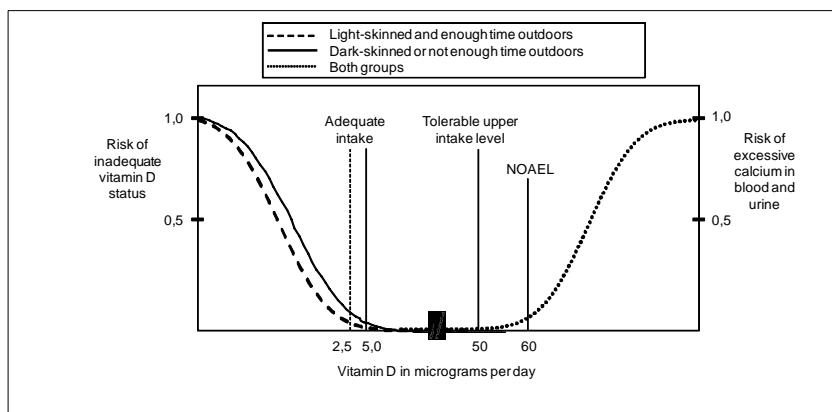


Figure 3.1 The dietary reference values for vitamin D for people aged 11 to 50. Adequate intake = The lowest intake level that appears to be adequate for the entire population. Adequate intakes are estimated if insufficient research data are available to determine an average requirement and a recommended dietary allowance. Tolerable upper intake level = highest intake level at which no adverse effects are observed or expected. This is determined on the basis of a NOAEL (no observed adverse effect level), the lowest intake level at which no harmful effects occur. The figure is based on figure 1.3 of the Health Council's advisory report entitled 'Dietary reference intakes: calcium, vitamin D, thiamine, riboflavin, niacin, pantothenic acid, and biotin'.²²

The principal adverse effect of a vitamin D overdose is excessive calcium levels in the urine (hypercalciuria, molar ratio of calcium: creatine > 1.0) and in the blood (hypocalcaemia, serum calcium level > 2.75 mmol per litre). The lowest vitamin D intake at which this effect is not observed (NOAEL) is 60 micrograms per day. Likewise for children aged up to 19, there are no indications that intakes of up to 60 micrograms per day are harmful. Children are possibly relatively less susceptible to a high vitamin D intake because of their high bone development rate. The Institute of Medicine makes allowances for uncertainties in the NOAEL by adopting an uncertainty factor of 1.2. The tolerable upper intake level for children older than 12 months and all adults has therefore been established at 50 micrograms per day. Research into effects on growth rate formed the basis for establishing a NOAEL of 45 micrograms per day for children up to 12 months old. A higher uncertainty factor (1.8) was adopted for this group, partly because rate of growth is not a sensitive measure of results and because of the small number of children studied. The tolerable upper intake level for this group was therefore established at 25 micrograms per day (Table 3.1).³¹

Table 3.1 Adequate intake, original supplementation advice^a and the tolerable upper intake level for vitamin D in micrograms per day.²²

	Adequate intake ²²		Original supplementation advice ^a	Tolerable upper intake level
	Light-skinned and enough time outdoors ^b	Dark-skinned and/or not enough time outdoors ^c		
0 to 11 months old	5	10	+5	25
1 to 3 years old	5	10	+5	50
4 to 50 years old	2.5	5		50
51 to 60 years old	5	10	Women +2.5	50
61-70 years old	7.5	10	Men +2.5	50
From 71 years old	12.5	15	Women +5	50
			Men +7.5	
Pregnant women	7.5	10	Women +10	50
			Men +5	
Lactating women	7.5	10	+5	50

^a The recommendations on supplements were compiled by the Netherlands Nutrition Centre.^{28,29}

^b Light-skinned and at least 15 minutes outdoors every day with at least the hands and face uncovered.

^c For people who do not spend enough time outdoors during the day and/or dark-skinned people.

Recent scientific developments

In this chapter, the Committee assesses which recent scientific insights it wishes to take into account in the recommendations. Insights have been categorised according to the effect of vitamin D on bone density; falls; fractures; cancer; and other disorders. The Committee has taken this as the basis for examining whether the present minimum level for serum calcidiol should be increased. It concludes by discussing recommendations for increasing the tolerable upper intake level. Details of individual studies of the effect of vitamin D on the risk of falls or fractures are available in a web annex, which includes web tables 1 and 2*.

4.1 Bone density

4.1.1 *Systematic review articles on the effect of vitamin D intake*

Two systematic review articles found that taking vitamin D with calcium had a protective effect on bone density compared to placebo but the studies were largely limited to post-menopausal women.^{32,33}

Most of the studies reviewed in the two articles lasted 2 to 3 years and were conducted using daily doses of up to 20 micrograms of vitamin D and at least 500 milligrams of calcium. One review article found a minor increase in bone density of around 1.4 per cent per year. However, the estimation of the effect is

* The web annex is available online at www.healthcouncil.nl.

limited by heterogeneity as a result of differences in treatment duration and in places in the body where bone density was measured.³² The other review article found that vitamin D with calcium counteracted losses in bone density compared to the results for a placebo.³³ Interpreting this meta-analysis was also made more difficult because of heterogeneity, which appeared to influence the level of calcium supplementation, amongst other things.

Both articles concluded that vitamin D supplements alone had no effect on bone density compared to placebo. This may be connected with the relatively low dose of 7.5 to 10 micrograms of vitamin D per day but also with the low calcium intake in many of the studies. For post-menopausal women with adequate calcium intake, 10 micrograms of vitamin D per day or 0.5 microgram of calcitriol per day appeared to inhibit bone loss in the hip.^{34,58}

The effect of vitamin D and calcium intake on bone density in other groups could not be determined using meta-analysis owing to a lack of data.

4.1.2 *Intervention research into the effect of vitamin D intake*

Little intervention research has been conducted into the effect of vitamin D supplements on bone density of children and adult males. However, it is clear in the Netherlands and other European countries that the introduction of vitamin D supplementation for infants and young children has resulted in the almost total eradication of rickets.²²

Two studies of pre- and peri-pubescent children showed no difference in bone density between a group given a placebo and groups given 10 micrograms of vitamin D₂ or 5 micrograms of vitamin D₃ in combination with calcium. In one study, bone density was not adjusted for bone size³⁵ and, in the other study, differences in growth rate during puberty could have masked the effect of the supplement.³⁶ A third study of girls aged 10 to 17 found that a significantly higher vitamin D₃ dose of 350 micrograms per week (equivalent to 50 micrograms per day*) improved bone density compared to the placebo group and the group given 35 micrograms of vitamin D₃ on a weekly basis, which is equivalent to 5 micrograms per day. The effect was greatest for girls who had not yet started to menstruate. The researchers stated in the report that supplements given to boys had no effect on bone density but failed to present any data on this.³⁷

Milk fortified with calcium and vitamin D₃ (20 micrograms per day) given to elderly men inhibited loss of bone density compared to a control group that received no treatment.³⁸

* This is the same amount as the tolerable upper intake level for people from the age of 11.

Despite the lack of hard evidence, these limited data, when taken as a whole, suggest that high doses of vitamin D, whether or not in combination with calcium, may improve bone density in teenagers and counteract bone loss in elderly men.

4.1.3 *Vitamin D status*

The protective effect on bone density of supplying vitamin D is backed by research into the effect of the vitamin D status. There are indications that a high serum calcidiol level is linked to achieving a higher peak bone density among teenagers and young adults. In elderly people, this is linked to a higher bone density.^{22,32,39,40} The results of studies of a relationship between vitamin D status and bone density in children are unclear, and insufficient studies of any such relationship have been conducted among pregnant or breastfeeding women. However, there are indications that a high serum calcidiol level in these groups is related to a lower parathyroid hormone level* in serum.³²

Little research has been conducted into whether a threshold level exists for an optimum serum calcidiol level in relation to bone density. The National Health and Nutrition Examination Survey (NHANES III) of adults (aged 20-49) and older people (aged 50) of various ethnic backgrounds associated a high serum calcidiol level with higher bone density across the entire range from 22.5 to 94 nmol per litre. In adults with a Western or Mexican-American background, a higher serum calcidiol level, also in excess of 100 nmol per litre, was likewise associated with higher bone density.⁴¹ It is unclear whether this association also applies in the Netherlands, as calcium intake in the United States is approximately half that of the Netherlands. Previous studies in the Netherlands only indicated a link between bone density and serum calcidiol levels when levels were below 30 nmol per litre and this applied to both adults and newborn children.²² In the United Kingdom, teenage girls with a serum calcidiol level below 45 nmol per litre had lower bone mass in the forearm than girls with higher serum calcidiol levels. However, there was no difference in bone density between teenage boys with a low or high serum calcidiol level.⁴² Likewise in Finnish adults (aged 31 to 43), no link was found between serum calcidiol levels and bone density in the forearm.⁴³

A limiting factor in interpreting studies of vitamin D status is that there is no standardised way of determining the serum calcidiol level. This calls for caution

* Parathyroid hormone = parathormone.

in interpreting absolute values.⁴⁴⁻⁴⁶ Moreover, it is unclear whether variations in serum calcidiol levels throughout the year affect bone density.⁴⁷

4.1.4 *A broader look at the effects of vitamin D and calcium*

Bone mass reaches its peak between the age of 25 and 30. Thereafter bone mass gradually declines. The pace accelerates around the time of the menopause. Achieving a high peak bone mass is linked to a lower risk of osteoporosis. To achieve the highest possible peak bone mass, it is important to have an adequate* intake of calcium – and probably also vitamin D – at a young age.²²

It is difficult to separate the effects of calcium and vitamin D on the basis of the studies described but they can be deduced on the basis of metabolism. The process of absorbing calcium is partially vitamin-D dependent and partially vitamin-D independent. Given an adequate calcium intake, the absorption which occurs independently of vitamin D is high in absolute terms. The vitamin D requirement in such situations is therefore low. Given an adequate calcium intake, an inadequate supply of vitamin D therefore leads to low absorption of calcium less quickly than when calcium intake is inadequate.²²

It has also been suggested that adequate calcium and vitamin D intake could counteract excessive bone renewal.⁴⁸

4.1.5 *Conclusion*

There are indications that vitamin D supplements combined with calcium counter bone loss in elderly people and especially in post-menopausal women compared to placebo. The maximum vitamin D dose in most studies was 20 micrograms per day. There are also indications that bone loss in elderly people is counteracted when vitamin D is taken without extra calcium, provided calcium intake is in line with the dietary reference values.

Although there is a lack of hard evidence, there are suggestions that vitamin D, whether or not in combination with calcium, could improve bone density in teenagers and counter bone loss in elderly men.

There are also indications that the serum calcidiol level is linked to higher bone density in teenagers and older women. Results in children are unclear and there has been a lack of research into any such link in the case of men and young women. However, it is clear that the introduction of vitamin D supplementation

* An intake in line with the dietary reference value.

for infants and young children in the Netherlands and other European countries has resulted in the almost total eradication of rickets.

4.2 Falls

4.2.1 Systematic review articles on the effect of vitamin D intake

Some studies found a link between a relatively low serum calcidiol level and muscle weakness* and reduced physical performance**, although the evidence is not always consistent.^{32,49,50} However, there are no clear indications that vitamin D supplements alone can improve muscle weakness or reduced physical performance. However, it has been demonstrated that vitamin D supplements taken in combination with calcium lead to better neuromuscular function, a better sense of balance and improved body sway, which are linked to an increased risk of falls.^{51,52}

Five meta-analyses exist of the effect of vitamin D supplements on the risk of falls (table 4.1).^{32,51,53-55}

The most recent and largest systematic review article – by Cranney and colleagues – concluded that the 12 studies of the effect of vitamin D and possibly calcium on the risk of an initial fall were inconsistent. The studies varied with regard to the type and dose of vitamin D and the method of determining falls. Subgroup analyses showed that the combination of vitamin D3 and calcium resulted in a 15 per cent lower risk of falls compared to placebo in post-menopausal women.³²

None of the other meta-analyses studied the effect of vitamin D and calcium compared to placebo. However, two other meta-analyses found that vitamin D supplements, whether or not in combination with calcium, resulted in a reduced risk among elderly people of 12 per cent⁵⁴ and 22 per cent respectively.⁵⁵ One of the studies, which investigated the effect of vitamin D3 alone, found a borderline non-significant effect.⁵⁴ The other study, which also took into account calcidiol and calcitriol in addition to vitamin D3, took the number of falls as its measure of results.⁵⁵ The Committee believes that the number of falls can be determined less precisely as a measure of results than the figure for the number of people who have had a least one fall. On the other hand, a fourth study found no effect.⁵¹

Cranney's systematic review article found no significant effect for vitamin D compared to placebo but did find an effect for vitamin D and calcium compared

* A relatively low calcidiol level is defined as a serum calcidiol level below 25 nmol/l.

** A relatively low calcidiol level is defined as a serum calcidiol level below 50 to 87 nmol/l.

to calcium.³² The latter finding was supported by two previous meta-analyses, although the reduced risk in these was not significant.^{51,53} In all five meta-analyses, researchers adopted the starting point that the effects of vitamin D and calcium are independent and do not reinforce or weaken each other.

4.2.2 *Dose-response relationship*

The effect of vitamin D on the risk of falls may depend on the dose but too few studies have been conducted of relatively low vitamin D doses to enable a statement on this. In one study, 124 relatively healthy, white, nursing home residents took a daily vitamin D₂ supplement of 0, 5, 10, 15 or 20 micrograms over a five-month period. Forty-four per cent of participants in the placebo group suffered a fall, compared with 60 per cent in the groups taking vitamin D doses of 5-15 micrograms per day and 20 per cent in the group taking 20 micrograms per day (RR 0.28, 95% confidence interval 0.11-0.75). Owing to the relatively small size of the study group, it is unclear whether doses lower than 20 micrograms per day have no effect or a relatively lower effect on the risk of falls.⁵⁶

4.2.3 *Vitamin D status*

In intervention studies that found a significant effect on the risk of falls, the average serum calcidiol level at the end of treatment with vitamin D varied, insofar as reported, from 43 to 61 nmol per litre (web table 1).⁵⁷⁻⁶⁰

A cohort study supports these indications. For example, a lower serum calcidiol level* in Dutch elderly people was associated with an increased risk of repeated falls (at least 2 falls OR 1.78, 95% confidence interval 1.06-2.99 and at least 3 falls OR 2.23, 95% confidence interval 1.17-4.25).⁶¹ As mentioned earlier, determining the number of falls is less reliable than determining whether a person has suffered one or more falls.

4.2.4 *Conclusion*

There are indications that vitamin D supplements combined with calcium can reduce the risk of falls in post-menopausal women by 15 per cent compared to placebo (OR=0.85, 95% confidence interval 0.76-0.96) (table 4.1). The daily vitamin D₃ dose used in most studies was between 10 and 20 micrograms.

* A low calcidiol level is defined as a calcidiol level below 25 nmol per litre.

However, owing to a lack of studies, it is not possible to say whether a dose-response relationship exists. Vitamin D supplements alone are not effective.

4.3 Fractures

4.3.1 *Systematic review articles on the effect of vitamin D intake*

In 2000, the advisory report entitled ‘Dietary reference values: calcium, vitamin D, thiamine, riboflavin, niacin, pantothenic acid and biotin‘ concluded that it was likely that the risk of fractures could be reduced in people aged 51 to 70 if they take at least 10 micrograms of vitamin D per day and in people aged over 70 if they take 15 micrograms of vitamin D per day.²²

Since then, seven systematic review articles have been published on the effect of vitamin D on the risk of fractures (table 4.2).^{32,54,62-66} Cranney and colleagues concluded that supplementation with vitamin D3 and calcium reduces the risk of fracturing a hip or non-vertebral bone by 17 and 13 per cent respectively compared to placebo, while vitamin D3 alone was ineffective compared to placebo. The effect appears to be limited to elderly people not living independently: supplementation with vitamin D and calcium results in a 31 per cent lower risk of fractures compared to placebo (OR=0.69, 95% confidence interval 0.53-0.90). Elderly people not living independently go outside less often than those living independently and therefore have a lower serum calcidiol level. They also eat less and consequently have a lower vitamin D intake. The idea is therefore that a protective effect can only be demonstrated for people with such a low calcidiol level* that supplements result in a reduction in the level of parathyroid hormone.^{32,66} Cranney and colleagues found no evidence that the effect depends on the vitamin D dose taken.³²

Previous meta-analyses largely found similar effects.^{54,62-66} An exception was that both Bischoff-Ferrari and colleagues and Tang and colleagues found indications that vitamin D’s protective effect was limited to high doses of vitamin D.^{62,66}

* A low calcidiol level is defined as a calcidiol level below 25 nmol per litre.

Table 4.1 Systematic review articles on the effect of vitamin D supplements on the risk of falls.

Meta-analysis	N study summarized	Control	N	RR/OR at least one fall, unless stated otherwise	95% confidence interval	Quality study ^a
Vitamin D and possibly calcium versus placebo or calcium						
Cranney 2007 ³²	12, 10-20 micrograms of vitamin D or active analogue and possibly calcium	Placebo or calcium	14 101	0.89 ^b	0.80-0.99	A1
Bischoff-Ferrari 2004 ⁵⁵	5, ^c 10-20 mcg/d of vitamin D3 or active analogue and possibly calcium	Placebo or calcium ^d	1 237	0.78 (number of falls)	0.64-0.92	A1
Jackson 2007 ⁵⁴	5, vitamin 7.5-40 mcg/d of vitamin D3 and possibly calcium	Placebo or calcium ^d	3 776	0.88	0.78-1.00	A1
Latham 2003 ⁵¹	4, 10-40 mcg/d of vitamin D3 or active analogue and possibly calcium	Placebo or calcium	1 317	0.99	0.89-1.11	A1
Vitamin D and calcium versus placebo						
Cranney 2007 ³²	5, 10-20 micrograms of vitamin D and calcium	Placebo	7 056	0.85	0.76-0.96	A1
Vitamin D versus placebo						
Cranney 2007 ³²	4, 10-20 micrograms of vitamin D	Placebo	5 958	1.03	0.91-1.17	A1
Vitamin D and calcium versus calcium						
Cranney 2007 ³²	4, 10-20 micrograms of vitamin D and calcium	Calcium	3 512	0.81	0.68-0.97	A1
Latham 2003 ⁵¹	1, 20 mcg/d of vitamin D3 and calcium	Calcium	148	0.55	0.29-1.08	A1
Gillespie 2004 ⁵³	3, 10-20 mcg/d of vitamin D3 and calcium	Calcium	461	0.87	0.70-1.08	A1

^a See appendix D for a description of the codes.

^b Indication of heterogeneity.

^c A supplementary sensitivity analysis included 5 additional studies.

^d Studies in which vitamin D was supplemented with calcium have only been included if a control group existed that only received calcium.

Table 4.2 Systematic review articles on the effect of vitamin D supplements on the risk of fractures.

Meta-analysis	N studies and Intervention	Control	N persons	Type of fracture	RR	95% confidence interval	Quality ^a
Vitamin D and possibly calcium versus placebo or calcium							
Jackson 2007 ⁵⁴	6, 10-20 mcg/d of vitamin D3 and possibly calcium ^c	Placebo or calcium	8 524	non-vertebral	0.96	0.84-1.09	A1
	2, 15-20 mcg/d of vitamin D3 and possibly calcium ^b	Placebo or calcium	902	vertebral	1.22	0.64-2.31	
Bischoff-Ferrari 2005 ⁶²	5, 17.5-20 mcg/d of vitamin D3 and possibly calcium	Placebo or calcium	6 098	1st non-vertebral	0.77	0.68-0.87	A1
Papadimitropoulos 2002 ⁶⁵	3, 10-20 mcg/d of vitamin D and possibly calcium	Placebo or calcium	5 399	non-vertebral	0.78	0.55-1.09	A1
Vitamin D and calcium versus placebo, calcium or no treatment							
Avenell 2005 ⁶³	7, 20 mcg/d of vitamin D and calcium	Placebo, calcium or no treatment	10 376	1st hip	0.81	0.68-0.96 ^b	A1
	2.20 mcg/d of vitamin D and calcium		2 708	1st non-vertebral	0.87	0.78-0.97 ^b	
				1st vertebral	0.34	0.01-8.34	
Boonen 2007 ⁶⁴	6, 10-20 mcg/d of vitamin D and calcium	Placebo, calcium or no treatment	45 509	hip	0.82	0.71-0.94	A1
Vitamin D and calcium versus placebo							
Tang 2007 ⁶⁶	8, 5-20 mcg/d of vitamin D and calcium	Placebo	46 108	1st	0.87	0.77-0.97	A1
Cranney 2007 ⁷²	7, 10-20 mcg/d of vitamin D and calcium	Placebo	46 072	1st	0.87	0.76-1.00	A1
				1st hip	0.83	0.68-1.00	
				1st non-vertebral	0.87	0.75-1.00	
Vitamin D versus placebo							
Cranney 2007 ⁷²	3, 10-20 mcg/d of vitamin D	Placebo	7 939	1st	0.98	0.79-1.23	A1
				1st hip	1.11	0.86-1.44	
				1st non-vertebral	0.99	0.83-1.17	
Bischoff-Ferrari 2005 ⁶²	2, 10 mcg/d of vitamin D3	Placebo	3 722	1st hip	1.15	0.88-1.50	A1
				1st non-vertebral	1.03	0.86-1.24	

Vitamin D versus placebo or no treatment							
Avenell 2005 ⁶³	7, 10-20 mcg/d of vitamin D only	Placebo or no treatment	18 668	1st hip	1.17	0.98-1.41	A1
	4, 15-20 mcg/d of vitamin D only		5 698	1st vertebral	1.13	0.50-2.55	
	8, 10-20 mcg/d of vitamin D only		18 935	1st	1.02	0.93-1.11	
Boonen 2007 ⁶⁴	4, 10-20 mcg/d of vitamin D	Placebo or no treatment	9 083	hip	1.10	0.89-1.36	A1
Vitamin D and calcium versus calcium							
Cranney 2007 ³²	3, 7.5-20 mcg of vitamin D and calcium	calcium	2 997	1st	0.92	0.74-1.25	A1
Avenell 2005 ⁶³	3, 20 mcg/d of vitamin D and calcium	calcium	6 866	1st hip hip	0.91 0.81	0.61-1.36 0.60-1.10	A1
	4, 7.5-20 mcg/d of vitamin D and calcium		3 061	non-vertebral	0.96	0.79-1.16	
	2, 20 mcg/d of vitamin D and calcium		2 681	vertebral	0.14	0.01-2.77	

^a See appendix D for a description of the codes.

^b The protective effect was limited to elderly people who no longer lived independently.

^c Studies in which vitamin D was supplemented with calcium have only been included if a control group existed that only received calcium.

The starting point adopted by the authors of the meta-analyses was that the effects of vitamin D and calcium are independent and do not reinforce or weaken each other. Boonen and colleagues showed that vitamin D3 supplements in combination with calcium were effective in reducing the risk of a fractured hip compared to vitamin D3 supplements alone (RR 0.76, 95% confidence interval 0.58-0.96).⁶⁴

The question is therefore whether vitamin D supplements in combination with calcium provide added value compared to calcium alone. Previous meta-analyses found no significant effect of calcium alone on the risk of fractures compared to a placebo.^{67,68} On the contrary, Tang and colleagues found a risk-reducing effect for calcium alone compared to placebo.⁶⁶ In subgroup analyses they found no clear difference in risk-reduction between studies examining the use of calcium in combination with vitamin D and those examining the use of calcium alone, which had also been the case in earlier meta-analyses.^{32,63} However, Tang and colleagues found a 3 per cent lower risk in studies examining a daily vitamin D dose of 20 micrograms or more compared to those examining lower doses. They cannot therefore exclude the possibility that vitamin D is protective at doses of 20 micrograms per day or more, although data are still too sparse on the effects of such doses. To obtain the maximum preventive effect

they therefore recommend calcium in combination with a vitamin D dose of 20 micrograms per day.

4.3.2 *Intervention research into the effect of vitamin D intake*

Because some of the meta-analyses contained indications of data heterogeneity, the original publications of the studies referred to were also examined. Web table 2 provides a description of intervention studies that examined the effect on the risk of fractures of taking extra vitamin D, whether or not in combination with calcium. The conclusions correspond with those in the systematic review articles. Studies of the effect of vitamin D2 on the risk of fractures are not altogether clear.⁶⁹⁻⁷⁴

Hardly any studies have been conducted to determine whether extra vitamin D and calcium also help prevent fractures in younger people. The possibility that it might do so was indicated by a study conducted in the United States of women soldiers who were given 20 micrograms of vitamin D in combination with 2 grams of calcium per day during an eight-week training period. The placebo group included 170 women who suffered stress fractures during the training period, which was 20 per cent more than in the group of women who had taken extra vitamin D and calcium.⁷⁵

4.3.3 *Vitamin D status*

In four studies in which 17.5-20 micrograms of vitamin D3 per day in combination with a calcium supplement or a high dietary calcium intake reduced the risk of fractures compared to placebo, the average serum calcidiol level varied after intervention with vitamin D from 74 nmol per litre to 112 nmol per litre (web table 2).⁷⁶⁻⁸⁰ This amounts to a minimum serum calcidiol level of around 50 nmol per litre. Bischoff-Ferrari even concluded in her review article that supplementation with vitamin D would have to produce a serum calcidiol level of at least 75 nmol per litre to reduce the risk of fractures.⁸¹

On the other hand, cohort studies of the relationship between vitamin D status and the risk of fractures do not provide a clear indication of the minimum serum calcidiol level required to reduce the risk of fractures. Elderly Dutch people aged 65 to 75 only had a higher risk of fractures if their serum calcidiol level was lower than 30 nmol per litre (HR=3.1, 95% confidence interval 1.4-6.9), whereas there was no increased risk of fractures as a result of a low serum calcidiol level for people from the age of seventy-five.⁸² Another study found increased risk at a serum calcidiol level below 50 nmol per litre but no corrections were

made in this study for confounding factors such as age.⁸³ Cohort studies that did take these factors into account did not find an increased risk at serum calcidiol levels below 30, 50 or 75 nmol per litre.^{84,85}

4.3.4 *Conclusion*

Vitamin D3 in combination with calcium can reduce the risk of fractures by 13 per cent in elderly people (RR 0.87, 95% confidence interval 0.77-0.97) (table 4.2). This conclusion is based on studies in which the vitamin D3 dose was 10 to 20 micrograms per day. Supplementation appears to be most effective in elderly people not living independently. Taking such a dose of vitamin D3 on its own does not appear to be effective in people with an inadequate calcium intake. Whether this also applies to people with an adequate calcium intake* could not be determined as this has not been studied sufficiently. Studies of the effect on fracture prevention of vitamin D2, whether or not in combination with calcium, are not unequivocal.

4.4 **Cancer**

Vitamin D may play a role in the prevention and treatment of various types of cancer and in the patient survival rate.^{86,87}

4.4.1 *Systematic review articles on the effect of vitamin D*

The World Cancer Research Fund concluded on the basis of 11 cohort studies that there is only limited evidence of Vitamin D having a protective effect on the risk of colorectal cancer. Data from observational studies of vitamin D intake are of limited use because serum calcidiol levels are not only dependent on intake but also on exposure to ultraviolet radiation (table 4.3).⁸⁸

Another systematic review article concluded that vitamin D intake had no effect on the risk of breast cancer.⁸⁹

4.4.2 *Intervention research into the effect of vitamin D intake*

An intervention study found a 60 per cent lower risk of cancer in post-menopausal women who were given vitamin D and calcium compared to women given a placebo (table 4.3). The risk of the occurrence of any type of cancer dur-

* A calcium intake in line with the dietary reference value.

ing 4 years of follow-up was a secondary outcome measure. The effect was even greater when all cases of cancer in the first year were excluded.⁹⁰

On the other hand, the Women's Health Initiative study found that daily supplements of 10 micrograms of vitamin D3 and 1 gram of calcium had no impact on the risk of developing colorectal cancer, but this is possibly explained by the relatively low dose of vitamin D3, poor compliance and the fact that many women in the control group were already taking vitamin D supplements.⁹¹

The Women's Health Study, which was published after the aforementioned meta-analyses of vitamin D intake in relation to the risk of breast cancer⁸⁹ found a weak association between high vitamin D and calcium intake and a lower risk of breast cancer in premenopausal women but not in post-menopausal women.⁹²

4.4.3 Vitamin D status

There are indications that a good vitamin D status is linked to a lower risk of colorectal cancer and possibly also to a lower risk of other types of cancer (table 4.3).

One meta-analysis found that people with a very high serum calcidiol level had a 50 per cent lower risk of colorectal cancer than people with a relatively lower serum calcidiol level.⁹³ Similar effects were found in the Health Professionals Follow-up study and in the Third National Health and Nutrition Examination Survey.^{94,95} Because physical activity is linked to a higher serum calcidiol level and a lower risk of colorectal cancer, it may be a confounder of the relationship between vitamin D status and the risk of this type of cancer. This hypothesis is not confirmed by the aforementioned studies. There was no effect on risk estimates when adjustments for physical activity were made in the Health Professionals Follow-Up study and the Third National Health and Nutrition Examination Survey.^{94,95} This was not specifically examined in the aforementioned meta-analysis.⁹³ Another possibility is that the relationship between physical activity and the risk of colorectal cancer comes partially through calcidiol.

Another meta-analysis of a nested case-control study and a normal case-control study found that a very high serum calcidiol level protected against the risk of breast cancer compared to a low serum calcidiol level^{**}.⁹⁶ Women with a very high serum calcidiol level have a 50 per cent lower risk of breast cancer than women with a low serum calcidiol level.

* A very high calcidiol level is defined as a serum calcidiol level of 82 nmol per litre or more and a low calcidiol level as a calcidiol level of no more than 30 nmol per litre.

** A very high calcidiol level is defined as a serum calcidiol level of 124 nmol per litre or more and a low calcidiol level as a calcidiol level of no more than 25 nmol per litre.

A nested case-control study – using data from Nurses’ Health Studies I and II and the Women’s Health Study – of the effect of vitamin D status on the risk of ovarian cancer found a non-significant reduction in the risk of ovarian cancer.⁹⁷

Studies are not unequivocal with regard to the relationship between serum calcidiol levels and death resulting from any type of cancer. Analyses of data from the Third National Health and Nutrition Examination Survey did not indicate that serum calcidiol levels had a protective effect in relation to death from cancer in general.⁹⁵ On the other hand, based on the Health Professionals Follow-up study, the researchers estimated that an increase of 25 nmol per litre in the serum calcidiol level was associated with a 17 per cent reduction in the total number of new cancer cases and a 29 per cent reduction in death from cancer. However, these effects should be treated with caution because the serum calcidiol level was only measured in 1,095 men. The serum calcidiol level was estimated for the remaining 47,800 participants on the basis of six important determinants, with the aid of regression techniques.⁹⁴ In another cohort study of 3,299 patients, it was estimated that an increase of 25 nmol per litre in the serum calcidiol level was linked to a 34 per cent lower risk of death from cancer.⁹⁸

Garland and colleagues concluded on the basis of three studies^{93,96,97}, two of which were conducted by the authors themselves, that, to prevent cancer, the serum calcidiol level would have to remain higher than 137 nmol per litre throughout life.⁹⁹ However, an argument against this is that too few studies have been conducted to determine which phase in the disease process exposure to vitamin D can reduce the risk of cancer and at what time exposure is most effective.^{100,101}

Table 4.3 Studies of the effect of vitamin D supplements on the risk of cancer.

Meta-analysis or pooled analysis	N studies	N persons	Type of cancer	Comparison	OR	95% confidence interval or P value	Quality ^a
Gorham 2007 ⁹³	5 nested case-control studies	1 448 men and women	Colorectal cancer	Calcidiol \geq 82 nmol/l versus \leq 30 nmol/l	0.49	0.35-0.68	B1
Garland 2007 ⁹⁶	1 nested and 1 'normal' case-control study	1 760 women	Breast cancer	Calcidiol \geq 124 nmol/l versus \leq 25 nmol/l	0.50	P trend < 0.001	B2
Tworoger 2007 ⁹⁷	2 nested case-control studies	827 women	Ovarian cancer	Calcidiol \geq 74 nmol/l versus \leq 47 nmol/l	0.83	0.49-1.39	B2
World Cancer Research Fund 2007 ⁸⁸	9 cohort studies	n.d. ^b	Colorectal cancer	Vitamin D intake	0.99 ^c	0.97-1.00	B1
Intervention study	Duration and intervention	Control	N, gender, average age	Type of cancer	RR	95% confidence interval	Quality ^a
Lappe 2007 ⁹⁰	27.5 micrograms vitamin D per day and calcium for 4 years	Placebo	1 179 women aged 55+	All	0.40	0.20-0.82	A2
Women's Health Initiative ⁹¹	10 micrograms vitamin D and calcium for year	Placebo	36 282 women	Colorectal	1.08	0.86-1.34	B2
Cohort study	Follow-up duration	N, gender, age	Type of cancer	Comparison	HR/RR	95% confidence interval	Quality ^a
Women's Health Study ⁹²	10 years	276 premenopausal women	Breast cancer	\geq 14 mcg vitamin D/day versus < 4 mcg/day	0.65	0.42-1.00	B2
		743 postmenopausal women aged 45+		\geq 14 mcg vitamin D/day versus < 4 mcg/day	1.30	0.97-1.73	B2
Health Professionals Follow-Up Study ⁹⁴	6 years	47 800 men aged 40-75	All types	25 nmol per litre increase in calcidiol	0.83	0.74-0.92	B2
Third National Health and Nutrition Examination Survey ⁹⁵	6-12 years	16 818 men and women aged 17+	Death from all types	Calcidiol \geq 80 nmol/l versus < 50 nmol/l	1.00	0.71-1.40	B2
			Death from colorectal cancer	Calcidiol \geq 80 nmol/l versus < 50 nmol/l	0.28	0.11-0.68	B2
Ludwigshafen Risk and Cardiovascular Health Study ⁹⁸	8 years	3 299 men and women with an average age of 60-65	Death from all types	Calcidiol \geq 58 nmol/l versus \leq 25 nmol/l	0.45	0.22-0.93	B2

^a See annex D for a description of the codes.

^b N.d., not described.

^c The estimate is restricted by a (moderate) degree of heterogeneity.

4.4.4 *Exposure to sunlight*

Exposure to sunlight stimulates vitamin D production by the skin, without leading to too high levels of vitamin D in the blood.²⁶ As with exposure to sunlight,¹⁰²⁻¹⁰⁴ there are also indications that an extremely high serum calcidiol level – as discussed above – may be linked to a lower risk of internal types of cancer. However, exposure to ultraviolet radiation increases the risk of skin cancer.²⁶ Evidence for the relationship between exposure to sunlight and the increased risk of skin cancer is considerably stronger than the evidence for the relationship between a very high serum calcidiol level or exposure to sunlight and the reduced risk of other types of cancer.¹⁰⁵

4.4.5 *Conclusion*

There are indications, but no hard evidence, that a serum calcidiol level of 82 to 124 nmol per litre is related to a reduced risk of certain types of internal cancer. Whether a change in vitamin D intake or exposure to sunlight could indeed play a role in preventing or treating these types of cancer has not been studied in sufficient depth.

4.5 **Other disorders**

4.5.1 *Findings*

Vitamin D may also play a role in auto-immune diseases, tuberculosis, diabetes type 2 and cardiovascular diseases.^{30,106,107} Moreover, both a high vitamin D status as well as vitamin D supplements have been linked to a lower risk of death.^{108,108,109} The indications for a relationship between a high serum calcidiol level or vitamin D supplements and a lower risk of auto-immune diseases such as diabetes type 1 and multiple sclerosis primarily come from ecological, casecontrol, genetic, and in-vitro studies and intervention studies in animals.¹¹⁰⁻¹¹² However, practically no cohort or human intervention studies are available.

The same applies to the relationship between a high serum calcidiol level and a lower risk of tuberculosis.^{113,114}

Indications that a low serum calcidiol level is a risk factor for diabetes type 2 and cardiovascular diseases are primarily based on cross-sectional studies. These studies were often inadequately adjusted for confounding factors. Moreover, the indications for this risk factor are based on short-term intervention studies or

studies with a small number of participants, in which various vitamin D and calcium supplements were used or post-hoc analyses were carried out.^{106,107,115}

Researchers in the Women's Health Initiative study found that a vitamin D and calcium supplement had no effect on the risk of cardiovascular diseases or diabetes type 2. As mentioned earlier, the vitamin D dose and therapy compliance were relatively low.^{116,117} On the other hand, in a cohort study, people with a low calcidiol level had a higher risk of dying from cardiovascular diseases.¹⁰⁸

The Framingham Offspring study reported a link for participants with high blood pressure between a low serum calcidiol level and a higher risk of cardiovascular diseases. This link did not exist for participants with low blood pressure.¹¹⁸ There are also indications of a link between a high serum calcidiol level and lower blood pressure. It is true that cohort studies found no relationship between vitamin D intake and the number of new cases of high blood pressure,¹¹⁹ but did find a link between a high serum calcidiol level and lower blood pressure^{120,121}, a lower number of new cases of high blood pressure¹²² and a lower age-related increase in blood pressure,¹²³ although not all studies point in the same direction.¹²⁴ Moreover, in one intervention study, 20 micrograms of vitamin D3 per day in combination with calcium reduced systolic blood pressure in older women with an inadequate vitamin D status* by 9.3 per cent within eight weeks compared to calcium alone.¹²⁵

One cohort study found that people with a high calcidiol level had a lower risk of death.¹⁰⁸ This appears to be confirmed by the finding in a meta-analysis that taking 7.5 to 50 micrograms of vitamin D per day – in most of the studies a dose of 10 to 20 micrograms per day – was linked to a 7 per cent lower risk of death within six years (RR=0.93, 95% confidence interval 0.87-0.99) compared to the control group. The risk was not affected by taking a supplement with calcium. However, none of the studies in the meta-analysis had been specially designed to study mortality rates and most of the participants were middle-aged or older, with an increased risk of fractures or, in one study, heart failure. Nevertheless, this study showed that there appear to be no unexpected adverse effects from taking an average of 13 micrograms of vitamin D per day over a period of from six months to 7 years.¹⁰⁹

4.5.2 Conclusion

Too few high-quality studies have been conducted of the relationship between vitamin D and auto-immune diseases, tuberculosis, diabetes type 2 and cardio-

* An inadequate vitamin D status is defined as a serum calcidiol level below 50 nmol per litre.

vascular diseases. However, there are indications that a high serum calcidiol level is linked to lower blood pressure and that taking an extra 20 micrograms of vitamin D per day is linked to a lower mortality risk.

4.6 Minimum serum calcidiol level, effect of spending time outdoors and vitamin D intake

4.6.1 Determining vitamin D status: the minimum serum calcidiol level

The Dietary Reference Values Advisory Report of 2000 adopted a serum calcidiol level of 30 nmol per litre as an indicator of an adequate vitamin D status.²² This was because there were insufficient indications that increasing the serum calcidiol level to more than 30 nmol per litre would affect bone density or the risk of fractures. The Dietary Reference Values Committee did not specifically discuss the question of whether this was intended as a minimum level or whether it applied for the entire year. The present advisory report considers the serum calcidiol level as a minimum level applicable at the individual level* and throughout the year.

Light-skinned women from the age of 50

The Committee believes that the minimum serum calcidiol level should be increased to 50 nmol per litre for women from the age of 50. As already mentioned in this chapter, studies published since 2000 have shown that increasing the serum calcidiol level to more than 50 nmol per litre can reduce the risk of fractures in post-menopausal women by 10 to 20 per cent. Moreover, it is likely that it can counteract the reduction in bone density in older women and that it can further reduce the risk of falls. Only protective effects were found for vitamin D in combination with calcium. However, there are indications that bone loss in elderly women is counteracted when vitamin D is taken without extra calcium, provided calcium intake is in line with the dietary reference values. The Committee assumes on the basis of this that, for an adequate calcium intake of this level, extra vitamin D would also have a positive effect on the risk of falls and fractures, without extra calcium being taken.

These protective effects are highest in post-menopausal women not living independently. Because the decrease in bone density accelerates in women

* This means that 97.5 per cent of the population ought to have a calcidiol level of at least 30 or, as the case may be, 50 nmol per litre.

around the time of the menopause, the Committee believes they would benefit from a higher serum calcidiol level from the age of fifty, although no proper study of this has been conducted.

A protective effect on the risk of fractures was found for average serum calcidiol levels of 74 to 112 nmol per litre and a protective effect for bone density or the risk of falls was found for levels of 35 to 67 nmol per litre. Caution should be exercised when comparing these figures, owing to a lack of standardisation in determining serum calcidiol levels.⁴⁴⁻⁴⁶ It is also unclear whether variation in the serum calcidiol level throughout the year affects bone density and the risk of falls or fractures.⁴⁷

For cases in which the vitamin D supply for the skeleton* is optimal, other authors state various minimum values for the serum calcidiol level, such as 50 nmol per litre, 75 to 80 nmol per litre and as high as 90 to 100 nmol per litre.^{126,127} An argument against stipulating a serum calcidiol level higher than 50 nmol per litre serum is that the greatest effects of vitamin D on bone quality are found among post-menopausal women not living independently, who generally have a low calcium and vitamin D intake. Moreover, achieving a level of at least 75 to 80 nmol/l requires a vitamin D intake that has not been extensively studied and which may exceed the tolerable upper intake level of 50 micrograms per day for a percentage of the population.^{128,129} Given the risk of excessive calcium levels in blood and urine and of kidney stones, the EU Scientific Committee on Food only recommends such an intake level under medical supervision.²⁴

Dark-skinned women from the age of 50

The Committee assumes that dark-skinned women from the age of 50 would likewise benefit from an increase in the minimum serum calcidiol level to 50 nmol per litre. Studies of the relationship between vitamin D and bone quality were mainly conducted among light-skinned women. Insufficient studies have been conducted to determine whether the results also apply to women with an Asian or African background.

There is no difference in the bone density of people with an Asian background living in the West and that of people with a Western background.¹³⁰ However, people with an Asian background are less likely to suffer fractures.¹³¹ This is possibly partially explained by locomotor differences.

* Authors adopted criteria such as the calcidiol level associated with maximum repression of the parathyroid hormone level, the highest calcium absorption, highest bone density, a lower bone loss rate, and a lower fall and fracture frequency.

On the other hand, people with an African background have a different calcium metabolism from that of people with a Western background. For example, in spite of a lower calcium intake and lower serum calcidiol level, they have a stronger skeleton and a lower risk of fractures than people with a Western background. Differences in sensitivity to parathyroid hormone and calcitriol and differences in calcium absorption may play a role in this.¹³²⁻¹³⁴ There are suggestions from epidemiological research that these differences are not sufficient to protect elderly people with an African background against a reduction in bone density^{41,135}, although an intervention study among post-menopausal women found no protective effect for extra vitamin D in combination with an intake of 1.2 to 1.5 milligrams of calcium per day.¹³⁶

Women up to the age of 50 and men

The Committee sees no clinical advantage in increasing the minimum serum calcidiol from 30 nmol per litre to 50 nmol per litre for women up to the age of 50 and men up to the age of 70. It is not known whether a higher serum calcidiol level for these people would affect the risk of fractures at a later age. A minimum serum calcidiol level of 30 nmol per litre is sufficient to prevent rickets, a deficiency disease. The Committee believes that men would benefit from a higher target value from the age of 70. The limited research results that are available suggest that the effects of extra vitamin D in older men are comparable with those for older women. Because men do not experience menopausal changes, the Committee sees no reason to reduce the age limit from 70 to 50.

Effects on health not considered

In determining the optimum serum calcidiol level, the Committee has not taken into account how increasing serum calcidiol levels might affect internal types of colorectal cancer, auto-immune diseases, tuberculosis, diabetes type 2 and cardiovascular diseases because the indications for any such effects currently lack strength (see section 4.1.4 Vitamin D and the risk of other disorders). Nevertheless, these effects have been observed for serum calcidiol levels varying from more than 30 or 50 nmol per litre to – in most cases – more than 80 or 100 nmol per litre.

Conclusion

Since the publication of the dietary reference values for vitamin D in 2000, new scientific insights have indicated that extra vitamin D in combination with extra calcium reduces the risk of fractures. There are also indications that extra vitamin D in combination with extra calcium counteracts bone loss and reduces the risk of falls. The studies concerned were mainly of light-skinned, post-menopausal women from the age of 70 and the effect was most clear for women not living independently.

In the studies in which vitamin D was found to have a protective effect against fractures, the average serum calcidiol level was 74 to 112 nmol per litre, in participants receiving supplements of 10 to 20 micrograms per day. In the case of effects that protected bone density and the risk of falls, the serum calcidiol level varied from 35 to 67 nmol per litre. The interpretation of the aforementioned data is limited by the absence of standardisation in the determination of calcidiol levels.⁴⁴⁻⁴⁶ Moreover, it is unclear whether variation in the serum calcidiol level throughout the year affects bone density.⁴⁷ On the basis of these findings, the Committee believes that the minimum serum calcidiol level for women from the age of 50 should be increased from 30 to 50 nmol per litre.

Protective effects were only found for vitamin D in combination with calcium. However, there are indications that bone loss in elderly women is counteracted when vitamin D is taken without extra calcium, provided calcium intake is in line with the dietary reference values. The Committee assumes on these grounds that, given this adequate calcium intake, vitamin D alone could reduce the risk of fractures or falls.

Because the decrease in bone density accelerates in women around the time of the menopause, the Committee believes they would benefit from a higher serum calcidiol level from the age of fifty, although no proper study of this has been conducted. The Committee furthermore assumes that such a serum calcidiol level would also have a protective effect for dark-skinned women from the age of 50, although this has not been studied in sufficient depth.

The Committee also anticipates that men from the age of 70 would benefit from extra vitamin D. The limited research results that are available suggest that the effects of extra vitamin D in older men are comparable with those for older women. Because men do not experience menopausal changes, the Committee sees no reason to reduce the age limit from 70 to 50 in their case.

The target value is not being increased for younger age groups because doing so has not been shown to provide any clinical advantage.

The minimum level applies at the individual level and throughout the year.* In determining this minimum level, the Committee has not taken into account the relationship between the serum calcidiol level and the risk of internal types of cancer, auto-immune diseases, tuberculosis, diabetes type 2 and cardiovascular diseases because the indications for any such relationship currently lack strength.

4.6.2 *Spending time outside in relation to ensuring a minimum serum calcidiol level*

Estimated effect of spending time outdoors

It was assumed in determining the dietary reference values for vitamin D that spending 15 minutes a day outside with at least the hands and head exposed would be sufficient to ensure that the majority of the population would produce an average of 2.5 to 5.0 micrograms of vitamin D per day throughout the year. This is based on research into the effect of sunlight and artificial ultraviolet radiation on the serum calcidiol level in infants, adults and elderly people.²²

The Committee believes that the aforementioned estimated effect of being outdoors during the daytime should be interpreted with caution. The actual effect on vitamin D production is difficult to estimate, as numerous factors affect vitamin D production in the skin during exposure to ultraviolet radiation. For example, the estimate is affected by the time of year, the degree of latitude, the atmosphere, skin pigmentation, age and the amount of unprotected skin that is exposed.

A systematic review article published after the determination of the dietary reference values also concluded that, besides exposure to sunlight, exposure to artificial ultraviolet radiation also increases the serum calcidiol level but the effect could not be estimated accurately owing to a lack of data.³² The increases in the serum calcidiol level varied from less than 10 to more than 100 nmol per litre. However, the eight systematically reviewed articles, four of which examined the effect of sunlight and four the effect of artificial ultraviolet radiation, were limited in terms of their quality. The studies also differed with regard to the age group and gender of the participants, the dose of ultraviolet radiation and the duration of the study. Moreover, the exact dose of ultraviolet radiation could not be properly determined.²⁵

There are indications that vitamin D production is higher in light-skinned people and lower in dark-skinned people than was assumed at the time of deter-

* This means that 97.5 per cent of the population ought to have a calcidiol level of at least 30 or 50 nmol per litre.

mining the dietary reference values.^{30,137,138} This is in line with the conclusion of the UK's Scientific Advisory Committee on Nutrition that most people in the UK obtain most of their vitamin D through exposure to sunlight.²¹ The UK Committee refers to a review article by Holick and colleagues, which showed that exposure of 20 per cent of the body's surface to ultraviolet radiation increases the serum calcidiol level in young adults as well as elderly persons.³⁰ The article also indicates that serum calcidiol levels in the summer are linked to the degree of exposure to sunlight and that the level is primarily affected by the time spent outdoors and the amount of skin exposed. The article also suggests that exposure to sunlight for around 5 to 15 minutes between 10:00 and 15:00 during spring, summer and autumn, at locations above the 37th degree of latitude is sufficient for light-skinned people.³⁰ In the winter, the population in the Netherlands is dependent on vitamin D stored in the body and vitamin D from food and dietary supplements. This is confirmed by studies indicating that serum calcidiol levels in children and elderly people in the UK are only linked to dietary vitamin D intake in the winter and not in the summer.^{139,140} The relative contribution from exposure to sunlight and intake varies seasonally but cannot be determined precisely.²¹

It is therefore not possible to determine exactly how much time should be spent outdoors for the skin to produce a given amount of vitamin D and thereby guarantee a serum calcidiol level of 30 or 50 nmol per litre.

Effect of skin colour and the effect of spending time outdoors

None of the studies included in the aforementioned systematic review article examined the extent to which the effect was influenced by skin colour.³² Studies published after the systematic review article found that the effect of artificial/natural ultraviolet radiation (280 to 315 nanometres) on serum calcidiol levels was 4 to 6 times less in people with very dark skins than it was in light-skinned people. The intensity of ultraviolet radiation required to increase the serum calcidiol level by 30 nmol per litre for exposure three times a week over a four-week period was 6.5 times higher for Africans from the sub-Saharan and 4.5 higher for Afro-Americans than the intensity required for white people from Northern Europe.¹⁴¹ These figures correspond with another study in which the percentage increase in serum calcidiol levels through exposure to artificial ultraviolet radiation was five times greater for people with light skin (type 2) than it was for people with very dark skin (type 5).¹⁴² Precisely how much time dark-skinned people from various groups need to spend outdoors to produce a given amount of vitamin D in the skin and thereby ensure a serum calcidiol level of 30 or 50 nmol per litre was not determined.

Exposure to sunlight to attain optimum vitamin D production and optimal protection against skin cancer

The recommended period of exposure to sunlight for light-skinned people at seven locations in Australia was determined for each month, subject to the head, arms and hands being exposed. The duration of exposure is based on ultraviolet radiation measured over a 12-month period, the estimated vitamin D production and the estimated risk of the skin turning red. A distinction was made between three different times of the day, namely 10:00, 12:00 and 15:00. In the Australian summer (January), depending on the location, 2 to 14 minutes in the sun, at around 12:00 is sufficient to produce vitamin D in an amount equivalent to 5 to 15 micrograms of vitamin D, whereas red skin can occur within 8 to 27 minutes. Exposure of 3 to 16 minutes is required at the same time in the winter, whereas red skin can occur within 12 to 28 minutes. However, these researchers commented that the final level of production is affected by physiological and behavioural factors. They concluded that it is not possible to provide uniform advice for the whole of Australia on the optimum length of exposure to sunlight in minutes, owing to the large number of factors that affect the figure. They also stated that spending time in sunlight in order to produce vitamin D unavoidably increases the risk of skin cancer.¹⁴³

Conclusion

Spending time outdoors during the day can help ensure that at least the minimum serum calcidiol level is achieved. The Dietary Reference Values Committee assumed that spending 15 minutes a day outside with at least the hands and head exposed would be sufficient to ensure that the majority of the population would produce an average of 2.5 to 5 micrograms of vitamin D per day throughout the year. However, the estimate should be interpreted with caution, as numerous factors affect the final amount of vitamin D produced. The amount of vitamin D produced by being outdoors is higher for light-skinned people and lower for dark-skinned people. For example, under the same exposure conditions, vitamin D production was around five times lower in dark-skinned people than in light-skinned individuals. It is therefore not possible to determine precisely how much time people from various skin-colour groups need to spend outdoors to produce a given amount of vitamin D in the skin and thereby ensure a serum calcidiol level of 30 or 50 nmol per litre.

4.6.3 *The minimum amount of vitamin D required to avoid serum calcidiol levels below the minimum level*

Experts estimate that a vitamin D intake of 10 to 15 micrograms per day would result in an average serum calcidiol level of 50 nmol per litre, whereas an intake of 25 to 40 micrograms per day would lead to an average serum calcidiol level of 75 nmol per litre.¹²⁶

A meta-analysis based on 16 intervention studies estimated that an increased vitamin D3 intake of 2.5 micrograms would lead to a 1,0 to 2,0 nmol per litre increase in the serum calcidiol level. However, following adjustment for the vitamin D3 dose, there were still indications of significant heterogeneity.³² People therefore vary widely with regard to the amount by which vitamin D supplements increase serum calcidiol levels. This may also be connected with the absence of standardisation in the determination of calcidiol levels.⁴⁴⁻⁴⁶ Between laboratories, the coefficient of variation for calcidiol varies from 20 to 30 per cent.¹⁴⁴ In spite of these limitations, it is possible to determine the average serum calcidiol level at the population level. However, drawing comparisons between groups is not possible.

People aged 4 to 50

The minimum serum calcidiol level for young age groups remains the same as the level adopted at the time of drawing up dietary reference values for vitamin D. Nevertheless, new research has since been conducted that suggests that the dietary reference values and therefore the recommendations for taking extra vitamin D are on the low side.

For example, the average vitamin D intake by teenage girls in Northern Europe was 3.2 micrograms per day and in the winter 37 per cent of them had a serum calcidiol level below 25 nmol per litre.¹⁴⁵ In Ireland, median vitamin D intake among teenagers with a serum calcidiol level below 25 nmol per litre was 1.5 micrograms per day and among teenagers with a higher serum calcidiol level the figure was 2.6 micrograms per day.¹⁴⁶ Average vitamin D intake in Germany was 2.8 micrograms for men and 2.3 micrograms for women. Approximately 10 per cent had a serum calcidiol level below 25 nmol per litre at the end of the summer and the figure at the end of the winter was around 20 per cent.¹⁴⁷ In a Danish study, vitamin D intake by women who did not wear a veil was 7.5 micrograms per day, while the average serum calcidiol level was 47 nmol per litre. Vitamin D intake by white women who wore a veil was 13.5 micrograms

per day. In spite of this high intake, the average serum calcidiol level was only 17 nmol per litre.¹⁴⁸

Daily vitamin D supplements of 10 micrograms were insufficient in 11 per cent of dark-skinned teenage girls and adults to ensure a serum calcidiol level of more than 30 nmol per litre. Serum calcidiol levels were too low in 6 per cent of participants when daily supplements of 20 micrograms were taken (table 4.4).¹⁴⁹ Even in a study in which a dose of 25 micrograms vitamin D per day was given, the serum calcidiol level of around 13 per cent of participants was below 30 nmol per litre.¹²⁸

The Committee assumes on the grounds of these suggestions that people aged from 4 to 50 who are dark-skinned or who do not spend enough time outdoors and women up to the age of fifty who wear a veil require 10 micrograms of vitamin D per day extra to maintain a serum calcidiol level higher than 30 nmol per litre throughout the year. Light-skinned people who spend enough time outdoors are unlikely to need extra vitamin D, apart from that obtained from margarine, low-fat margarine and products used in baking and frying.

Men from the age of 50 to 70

The Committee also assumes that light-skinned men from the age of 50 to 70 who spend sufficient time outdoors do not require extra vitamin D. A higher intake has not been shown to offer any clinical benefit for them.

Women from the age of 50 and men from the age of 70

It is clear that intakes of 2.5 to 5 micrograms vitamin D per day are insufficient to enable women from the age of 50 and men from the age of 70 to achieve a serum calcidiol level of at least 50 nmol per litre. Vitamin D intake of elderly women in Northern Europe was 4.1 micrograms per day and, at the end of the winter, 67 per cent of them had a serum calcidiol level below 50 nmol per litre.¹⁴⁵ Average vitamin D intake in Germany was around 2.5 micrograms per day and around 42 per cent of people aged over 65 had a serum calcidiol level below 50 nmol per litre.¹⁴⁷

Few intervention studies report the percentage of participants that had a serum calcidiol level of at least 50 nmol per litre after receiving vitamin D supplements. However, the average effects of supplements in doses varying from 10 to 50 micrograms of vitamin D per day overlap each other (table 4.4). For example, one study found that serum calcidiol levels increased to more than 40 nmol per litre in residents of old-people's homes and nursing homes who

received 10 or 20 micrograms of vitamin D per day. The same study found a relatively minor difference (10 nmol per litre) in the increase in serum calcidiol levels between the group of people who received 10 micrograms of vitamin D per day and the group that received 20 micrograms of vitamin D per day.¹⁵⁰ In another study, vitamin D supplements of 15 micrograms per day resulted in serum calcidiol levels higher than 50 nmol per litre in 90 per cent of the nursing home residents.¹⁵¹

The extent of the increase in the serum calcidiol level depends on the initial level: the lower the initial level, the greater the effect. For example, a vitamin D supplement of 10 to 15 micrograms per day given to people with a serum calcidiol level below 25 nmol per litre led to a four times greater increase in serum calcidiol levels than it did in people with a serum calcidiol level of more than 50 nmol per litre.¹⁵² The increase in a study among people with a relatively low serum calcidiol level¹⁵⁰ was greater at doses of 10 and 20 micrograms per day than that in studies among people with higher serum calcidiol levels who received higher doses of 25 micrograms per day.^{128,153-155} A study to determine the dose required to raise the serum calcidiol level above 75 nmol per litre also found a wide variation in the doses required. To achieve this level, people with a serum calcidiol level below 55 nmol per litre need an estimated 125 micrograms vitamin D per day and people with a calcidiol level above 55 nmol per litre need an estimated 95 micrograms per day.¹⁵⁶

Studies of dark-skinned people showed that a vitamin D dose of 20 micrograms per day resulted in comparable effectiveness with that mentioned above for light-skinned. The effect is also inversely proportional to the serum calcidiol level at baseline.^{149,156,157}

On the basis of these indications, the Committee assumes that women from the age of 50 and men from the age of 70 who are dark-skinned or who do not spend enough time outdoors need 20 micrograms of vitamin D extra per day to maintain a serum calcidiol level above 50 nmol per litre throughout the year. The Committee also assumes that this amount applies to women older than 50 who wear a veil and people who live in a care home or nursing home or suffer from osteoporotic disorders.

Light-skinned people who spend enough time outdoors probably need an extra 10 micrograms of vitamin D per day after the age of 50 (women) or 70 (men).

Conclusion

There are suggestions that current recommendations for extra vitamin D may be too low to ensure a serum calcidiol level of at least 30 nmol or, in women from the age of 50 and men from the age of 70, 50 nmol per litre . The Committee assumes on these grounds that:

- children up to the age of 4, women up to the age of 50 who wear a veil, pregnant or breastfeeding women, people from the age of 4 to 50 (females) or 70 (males) who are dark-skinned or who do not spend enough time outdoors, other women from the age of 50 and other men from the age of 70 need an extra 10 micrograms per day;
- light-skinned people from the age of 4 to 50 (females) or 70 (males) who spend enough time outdoors are probably not in need of extra vitamin D from supplements or fortified foods, with the exception of the vitamin D intake from margarine, low-fat margarine and products used in baking and frying;
- People with osteoporosis or who live in a care home or nursing home and people from the age of 50 (females) or 70 (males) who are dark-skinned or who do not spend enough time outdoors and women from the age of 50 who wear a veil probably need an additional 20 micrograms of vitamin D per day.

Table 4.4 Study of the effect on serum calcidiol levels of a daily dose of vitamin D3 of up to 50 micrograms (see annex D for a description of the quality).

Studies	N, gender, age	Duration (months)	Vitamin D dose (mcg/day)	Average serum calcidiol level (nmol/l)				Quality
				Starting value	Increase	Final value	% < 30 nmol per litre	
Persons < 50 years old								
Heaney 2003 ¹⁵⁴	67 men, average age 39,	5	25	72	13	85	n.r. ^a	A2
Holick 2007 ¹⁵⁵	68 men and women aged 18-84	2.5	25	49	23 ^b	72	n.r.	A2
Barger-Lux 1998 ¹⁵³	116 men, average age 28,	2	25	67	29	96	n.r.	B2
Vieth 2001 ¹²⁸	15 men and women, average age 41,	3	25	41	28	69	~13%	B2
Harris 2002 ¹⁵⁸	25 men aged 18-35	2	20	60	26	n.r.	0	B2
Andersen 2008 ^{149c}	26 girls aged 10-15, 89 women aged 18-52, 84 men aged 18-63, dark-skinned	12	10	15	25 ^b	40	~11%	B2
			20	15	25 ^b	50	~6%	

People aged ≥ 50 , living independently, partially independently or details not reported								% < 50 nmol per litre	
Dawson- Hughes 1997 ⁷⁹	389 men and women, average age 71	36	17.5	75	37 ^b	112	n.r.	A2	
Chapuy 2002 ⁷⁶	583 women, average age 85	24	20	22	64 ^b	78	n.r.	A2	
Bischoff-Ferrari 2006 ⁵⁷	445 men and women, average age 71	36	17.5	30	12 ^b	43	n.r.	A2	
Talwar 2007 ¹⁵⁷	208 dark-skinned women, average age 60	3 ^d	20	47	28 ^b	71	n.r.	A2	
Pfeifer 2000 ¹⁵⁹	137 women, average age 74	2	50	47	38 ^b	87	n.r.		
Lips 2001 ¹⁵²	2,529 women, average age 66	6	20	25	22 ^b	66	n.r.	B2	
		6	10-15	<25	58	n.r.	n.r.	B2	
		6	10-15	25-50	39	n.r.	n.r.		
Harris ¹⁵⁸	25 men aged 62-79	2	10-15	>50	14	n.r.	n.r.		
Larsen 2004 ¹⁶⁰	114 men and women aged 66+ ^e	2	20	61	26	n.r.	0	B2	
Grant 2005 ¹⁶¹	60 men and women, average age 77 ^e	42	10	35	5 ^b	47	66	B2	
		24-60	20	38	20 ^b	62	n.r.	B2	
People aged ≥ 50 , not living independently								% < 50 nmol per litre	
Lips 1988 ¹⁵⁰	112 men and women, average age 81	3	10	24	36	60	> 40 nmol/l	A2	
Chapuy 1992 ⁷⁷	142 women, average age 84 ^e	3	20	24	46	70	> 40 nmol/l		
Lips 1996 ¹⁶²	96 men and women, average age 80 ^b	18	20	36	70 ^b	105	n.r.	A2	
Chel 2007 ¹⁵¹	112 men and women, average age 84	42	10	27	38 ^b	62	n.r.	A2	
Meyer 2002 ¹⁶³	65 men and women, average age 85 ^e	6	15	22	17 ^b	60	11	A2	
Bischoff 2003 ¹⁶⁴	122 men and women, average age 85	24	10	49	22 ^b	64	n.r.	B2	
		2.5	20	30	35 ^b	65	n.r.	B2	

^a N.r. not reported.

^b Corrected for changes in the placebo group.

^c Average of the median serum calcidiol level of men and women.

^d Female participants received 20 micrograms of vitamin D per day during the first two years and 50 micrograms during the third year. The serum calcidiol level was determined after three months' intervention.

^e The subgroup of participants whose serum calcidiol level was determined.

4.7 Tolerable upper intake level

4.7.1 *Tolerable upper intake levels for children in Europe and the United Kingdom*

When determining the tolerable upper intake levels for vitamin D, the Dutch Dietary Reference Values Committee adopted those of the Institute of Medicine in the United States.^{22,31}

However, for children from 1 to 10 years of age, these limits are twice the upper limits recently determined in Europe and the United Kingdom.^{24,165} The EU Scientific Committee on Food has set a tolerable upper intake level of 25 micrograms for children aged up to 2 years. They based this figure on the adverse effect of a vitamin D overdose on the amount of calcium in urine and blood and the highest reference value for the serum calcidiol level. The Scientific Committee on Food decided that a tolerable upper intake level for children and young people aged 2 to 17 could not be determined owing to a lack of data on the effects of excessive vitamin D intake. In view of the low weight of children up to the age of 10, the Scientific Committee on Food therefore exercised caution by adopting a tolerable upper intake level of 25 micrograms per day for children up to the age of 10 and a limit of 50 micrograms per day from the age of 11.²⁴ The Committee believes this lower tolerable upper intake level should be adopted (table 4.5).

The UK-based Expert Group on Vitamins and Minerals decided that a tolerable upper intake level could not be determined owing to a lack of data. They consequently set a guidance level of 25 micrograms of vitamin D per day extra, which is in addition to the vitamin D produced by the skin during exposure to ultraviolet radiation.¹⁶⁵

A risk assessment made in 2007 by Hathcock and colleagues based on studies of good quality vitamin D doses of from 50 to 2,500 micrograms per day suggested that vitamin D is non-toxic at intakes of up to 250 micrograms per day.¹⁶⁶ The risk assessment mainly concerned short-term studies not exceeding 6 months. Vitamin D poisoning often occurs only after excessive intake of vitamin D for several years. Hardly any long-term studies of excessive vitamin D intake are available.

4.7.2 Conclusion

The tolerable upper intake levels determined in 2006 by the EU Scientific Committee on Food will be adopted in this advisory report. This means that the tolerable upper intake level adopted for children from 1 to 10 years of age is not 50 micrograms vitamin D per day but 25 micrograms vitamin D per day (table 4.5).

Table 4.5 The acceptable upper vitamin D intake limit in micrograms per day adopted in this advisory report.²⁴

Group	Tolerable upper intake level
0 to 11 months old	25
1 to 10 years old	25
11 to 50 years old	50
50 to 60 years old	50
61-70 years old	50
From 71 years old	50
Pregnant women	50
Lactating women	50

4.8 Conclusion

Since the publication of the dietary reference values for vitamin D in 2000, new scientific insights have indicated that extra vitamin D in combination with extra calcium reduces the risk of fractures. There are also indications that vitamin D in combination with calcium counteracts bone loss and reduces the risk of falls. The studies concerned were mainly of light-skinned, post-menopausal women from the age of 70 and the effect was most clear for women not living independently.

In the studies in which vitamin D was found to have a protective effect against fractures, the average serum calcidiol level was 74 to 112 nmol per litre. In the case of effects that protected bone density and the risk of falls, the serum calcidiol level varied from 35 to 67 nmol per litre. The interpretation of the aforementioned data is limited by the absence of standardisation in the determination of calcidiol levels.

On the basis of these findings, the Committee believes that the minimum serum calcidiol level for women from the age of 50 should be increased from 30 to 50 nmol per litre.

Only protective effects were found for vitamin D in combination with calcium. However, there are indications that bone loss in elderly women is counteracted when vitamin D is taken without extra calcium, provided calcium intake is

in line with the dietary reference values. The Committee assumes on the basis of this that, for an adequate calcium intake of this level, extra vitamin D would also have a positive effect on the risk of falls and fractures, without extra calcium being taken.

Because the decrease in bone density accelerates in women around the time of the menopause, the Committee believes they would benefit from a higher serum calcidiol level from the age of 50, although no proper study of this has been conducted. The Committee assumes that such a serum calcidiol level would also have a protective effect for dark-skinned women from the age of 50, although this has not been studied in sufficient depth.

The Committee also anticipates that men from the age of 70 would benefit from extra vitamin D. The sparse research results that are available suggest that the effects of extra vitamin D in older men are comparable with those for older women.

The target value remains 30 nmol per litre for younger age groups, as a higher target value has not been shown to provide any clinical advantage.

This minimum level applies at the individual level and throughout the year.* In determining this minimum level, the Committee has not taken into account the relationship between the serum calcidiol level and the risk of internal types of cancer, auto-immune diseases, tuberculosis, diabetes type 2 and cardiovascular diseases, because the indications for any such relationship currently lack strength.

The serum calcidiol level can be increased by spending time outdoors during the day and by a vitamin D intake. Spending time outdoors in the summer (April to October in the northern hemisphere) can considerably increase the skin's production of vitamin D. It was assumed in determining the dietary reference values that spending 15 minutes a day outside with at least the hands and head exposed would be sufficient to ensure that the majority of the population would produce an average of 2.5 to 5 micrograms of vitamin D per day throughout the year. However, the estimate should be treated cautiously, as numerous factors affect the final amount of vitamin D produced. The amount of vitamin D produced by being outdoors is higher for light-skinned people and lower for dark-skinned individuals. It is therefore not possible to determine precisely how much time people from various skin-colour groups need to spend outdoors to produce a given amount of vitamin D in the skin and thereby ensure a serum calcidiol level of 30 or 50 nmol per litre.

* This means that 97.5 per cent of the population ought to have a calcidiol level of at least 30 or 50 nmol per litre.

With regard to intake, there are suggestions that current recommendations for extra vitamin D may be rather low to ensure a serum calcidiol level of at least 30 nmol in women up to the age of 50 and men up to the age of 70, or 50 nmol per litre in women from the age of 50 and men from the age of 70.

The Committee assumes on these grounds that children up to the age of 4, women who wear a veil, are pregnant or breastfeeding, and people from the age of 4 to 50 (females) or 70 (males) who are dark-skinned or who do not spend enough time outdoors need an extra 10 micrograms per day from supplements or fortified foods to ensure a serum calcidiol level of at least 30 nmol per litre. Light-skinned people from the age of 4 to 50 (females) or 70 (males) who spend enough time outdoors are probably not in need of extra vitamin D from supplements or fortified foods, with the exception of the vitamin D intake from margarine, low-fat margarine and products used in baking and frying.

There are also indications that people from the age of 50 (females) or 70 (males) who are light-skinned and spend enough time outdoors need an extra 10 micrograms of vitamin D per day. People with osteoporosis or who live in a care home or nursing home, people from the age of 50 (females) or 70 (males) who are dark-skinned or who do not spend enough time outdoors and women from the age of 50 who wear a veil probably need an additional 20 micrograms of vitamin D per day.

The Committee adopted the new tolerable upper intake levels for vitamin D, as determined by the EU Scientific Committee on Food in 2006 (table 4.5).

Table 4.6 Overview of evidence of recent scientific developments (see annex D for a description of categorisation and codes).

Convincing

Vitamin D3 supplements in combination with calcium can reduce the risk of a fractured hip or non-vertebral bone by 13 per cent (95% confidence interval 0.77-0.97) in light-skinned people from the age of 70 and especially in post-menopausal women. The effect is most clear in the case of elderly people not living independently. The vitamin D3 dose in the studies concerned was 5-20 micrograms per day.

A1^{32,54,62-66}

Probable

Vitamin D3 supplements in combination with calcium mitigate bone-density decreases in light-skinned elderly people and especially in post-menopausal women compared to placebo. The vitamin D3 dose in the intervention studies was 5-20 micrograms per day, with the exception of one study of a dose of 50 micrograms per day.

A1^{32,33}

A high serum calcidiol level is linked to high bone density in teenagers and older women.

B1^{22,32}

Vitamin D supplements reduce bone loss in post-menopausal women with an adequate calcium intake.^a

A2³⁴ B2⁵⁸

Vitamin D3 supplements in combination with calcium reduce the risk of falls in elderly people by 15 per cent (95% confidence interval 0.76-0.96). The vitamin D3 dose in the intervention studies was 10 to 20 micrograms per day.

A1^{32,51,53-55}

An extremely high serum calcidiol level (> 75 nmol per litre) is linked to a lower risk of internal types of cancer.

B1^{93,96}

A high serum calcidiol level (> 80 nmol per litre) is linked to lower blood pressure.

B2^{120-123,125}

A serum calcidiol level of at least 50 nmol per litre is required to maintain good bone density and to reduce the risk of falls or fractures.

B1^{126,127}

The effect of vitamin D intake on vitamin D status is greater for people with a low serum calcidiol level.

A2¹⁵², B2^{128,150,153,154}

Insufficient

Vitamin D supplements in combination with calcium improve bone density in children and teenagers.

A2³⁵⁻³⁷

Vitamin D2 supplements, whether or not in combination with calcium, reduce the risk of fractures in elderly people.

A2⁷⁰

Vitamin D3 supplements in combination with a high dietary calcium intake reduce the risk of fractures in elderly people.

A2⁸⁰

Vitamin D3 supplements in combination with a high dietary calcium intake mitigate bone-density decreases in elderly people.

D

A high vitamin D intake is linked to a lower risk of cancer.

A2⁹⁰, B1⁸⁸, B2⁹¹

A high serum calcidiol level or supplementation with vitamin D is linked to a lower risk of autoimmune diseases.

C^{87,112,113}

A high serum calcidiol level is linked to a lower risk of tuberculosis.

C^{110,111}

A high serum calcidiol level is linked to a lower risk of diabetes type 2 and cardiovascular diseases.

C^{106,107,115}

Taking 10 to 20 micrograms of vitamin D per day is linked to a lower risk of death.

A1¹⁰⁹

^a Adequate in the sense that it is at the level of the dietary reference value.

Vitamin D intake in the Netherlands

This chapter discusses the amount of vitamin D received by the population of the Netherlands through diet and through exposure to ultraviolet radiation, otherwise referred to collectively as the vitamin D supply. The Committee first discusses how the vitamin D supply is determined. It then assesses the values found. The Committee also describes the main sources of vitamin D in the Dutch diet and considers vitamin D supplements separately. The chapter concludes by examining the extent to which excessive vitamin D intake occurs in the Netherlands.

5.1 Methods for assessing supply

Three steps are required to determine whether the vitamin D supply is adequate. The first step is to collect intake data: what do people in the Netherlands eat and drink and how much vitamin D do those foods and dietary supplements collectively contain? Step two involves a comparison with dietary reference values, which indicate the vitamin D requirement to maintain the health of people of different genders, skin types, periods of exposure to sunlight, and of various ages. This information makes it possible to assess vitamin D intake for various groups of people. Step three therefore serves to provide a final answer regarding the estimate in step two, in combination with the vitamin D produced during exposure to ultraviolet light; the vitamin D status of a particular group of people is assessed. Examinations may also be made of disorders that are suspected of being linked to an excessively low or high intake.

5.1.1 *Intake data*

Most of the intake data on which this advisory report is based were taken from Dutch National Food Consumption Surveys. Up to 2000, these intake data were collected on two consecutive days. The data are therefore not independent but do provide an insight into day-to-day variations. Adjustments can be made for the variations. The term ‘observed intake’ refers to the unadjusted intake data and the term ‘habitual intake’ refers to intake after adjustment. The habitual intake average is comparable with the observed intake average but the variation is smaller.¹⁶⁷ Data on habitual intake are preferable for determining the number of people with an excessively high or low intake.

5.1.2 *Methods for comparing intake data with dietary reference value*

The Health Council has set an adequate intake for vitamin D. This means that only a global, qualitative assessment of the intake data is possible. The percentage of people with an insufficient intake cannot be estimated on the basis of an adequate intake, because the distribution of the vitamin D requirement is unknown. The percentage of people with an intake below the adequate intake is therefore of little significance. In a situation in which the median intake equals the adequate intake, half the people will, by definition, have an intake below the adequate intake. However, it is not possible to determine the section of the group concerned for which intake really is below par. Nevertheless, if the median intake is higher than the adequate intake, there is little likelihood of intake being insufficient.²² Dietary reference values take into account the extent to which vitamin D can be produced by the skin during exposure to ultraviolet light. However, because this production is dependent on numerous factors, some people may have an extremely low vitamin D intake but still have an adequate vitamin D supply thanks to sufficient exposure to ultraviolet radiation. An examination of the status and possible physical problems provides a definite answer as to whether people actually have a vitamin D deficiency.

5.2 **Vitamin D supply**

5.2.1 *Comparison of intake data with dietary reference values*

Average vitamin D intake by young adults in 2003 was 4.1 micrograms per day for males and 2.9 micrograms per day for females.¹⁶⁸ Dutch National Food Con-

sumption Surveys indicate that vitamin D intake fell by 2.6 per cent in the period from 1988 to 1998.¹⁶⁹⁻¹⁷¹ Dutch National Food Consumption Survey did not pay particular attention to residents of care homes or nursing homes, members of population groups who are dark-skinned or who do not spend enough time outdoors, people following a vegan or macrobiotic diet, or pregnant or breastfeeding women. Other studies among these risk groups were therefore taken into account. The Committee is not aware of data on the vitamin D intake of breastfeeding women.

Light-skinned children and adults

Research on the nutrient intake among young toddlers (2002) showed that young toddlers (9 to 18 months) who are not or no longer receiving breast milk obtain sufficient vitamin D from the combination of foods and the use of a vitamin D supplement or follow-on formula. However, the average intake for young toddlers not given a vitamin D supplement or follow-on formula (4 per cent of toddlers aged 12 months and 11 per cent of those aged 18 months) remained far below the adequate intake level (table 5.1).^{172,173}

In the Dutch National Food Consumption Survey of young children (2005/2006), the median dietary vitamin D intake by children aged 2 to 6 years varied from 1.8 to 2.1 micrograms per day. This is lower than the adequate intake level for all age groups. Taking into account intake from supplements, the median vitamin D intake was around 4.1 micrograms per day for children aged two and three. The figure for children aged four to six was around 2.5 micrograms per day.¹⁷⁴

Median intake for older children and adults in the third Dutch National Food Consumption Survey (1997/1998) was higher than the adequate intake (table 5.1).¹⁷⁰ Vitamin D intake from supplements was not considered in these data. As with the third Dutch National Food Consumption Survey (1997/1998), median vitamin D intake was higher than the adequate intake in the Dutch National Food Consumption Survey of young adults (2003). However, vitamin D intake by young adults who ate margarine and low-fat margarine on sandwiches was significantly higher than the vitamin D intake of young adults who did not do so (table 5.1).¹⁶⁸

Dark-skinned children and adults

Studies of children of asylum seekers showed that 80 per cent of these children had an average vitamin D intake that was lower than 80 per cent of the adequate

intake.¹⁷⁵ Likewise, the study entitled Lifestyle of youth in Amsterdam: Study among Ethnic groups (LASER) found an average vitamin D intake among young adults aged 18 to 30 with Turkish or Moroccan backgrounds that was lower than the adequate intake and also lower than the average intake of young adults with a Dutch background (table 5.2).¹⁷⁶ However, there were suggestions that the average vitamin D intake of people from sub-Saharan Africa who were living in the Netherlands was hardly any lower than the adequate intake, thanks to their high consumption of fish.¹⁷⁷

Calcium intake was also lower among young adults with a Turkish or Moroccan background than among participants in the Dutch National Food Consumption Survey of young adults (2003).¹⁷⁶ A low calcium intake probably increases the vitamin D requirement.

Children and adults with a vegan or macrobiotic diet

Children and adults who follow a strictly vegetarian, vegan or macrobiotic diet have a lower vitamin D and calcium intake than those who do not.^{178,179} For example, the vitamin D intake – excluding supplements – of children who had a vegetarian, anthroposophic or macrobiotic diet was at most half of that of children who did not have such a diet.¹⁷⁸

People from the age of 50

In the third Dutch National Food Consumption Survey (1997/1998), the median dietary vitamin D intake of adults from the age of 50 was below the adequate intake (table 5.1).¹⁷⁰ These data did not take into account any vitamin D intake from supplements.

According to studies among residents of care homes and nursing homes and among fragile elderly people, average vitamin D intake was 3.2 to 3.3 micrograms per day.^{180,181} This is also lower than the adequate intake.

Table 5.1 Average intake (standard deviation) and percentiles of observed daily vitamin D intake in micrograms by infants in 2002, by young children in 2006/2007, by older children and adults in 1997/1998 and by young adults in 2003.^{168,170,172,174a}

	Average intake (SD) ^b	Minimum	P5	P10	P50	P90	P95	Maximum
Infants 9 months	10.9 (4.7) ^c							
Infants 12 months	9.4 (4.2) ^c							
Infants 18 months	3.5 (3.5) ^c							
Infants 9 months	12.5 (4.5) ^d					19.3 ^d		
Infants 12 months	8.9 (3.7) ^d					14.8 ^d		
Infants 18 months	6.7 (1.5) ^d					8.1 ^d		
Boys 2-3 years	1.8		1.0		1.8		3.0	
Girls 2-3 years	1.8		0.9		1.7		3.3	
Boys 4-6 years	2.2		1.1		2.1		3.6	
Girls 4-6 years	1.9		1.1		1.8		3.0	
Boys 2-3 years	4.4 ^e		1.3 ^d		3.9 ^d		8.7 ^d	
Girls 2-3 years	4.7 ^d		1.2 ^d		4.3 ^d		10.0 ^d	
Boys 4-6 years	2.9 ^d		1.0 ^d		2.6 ^d		6.2 ^d	
Girls 4-6 years	2.5 ^d		1.0 ^d		2.3 ^d		4.8 ^d	
Boys 7-9 years	2.9 (1.6)	0.7	1.1	1.3	2.7	4.8	7.3	8.3
Girls 7-9 years	2.8 (1.3)	0.2	1.1	1.3	2.6	4.4	5.1	7.5
Boys 10-12 years	3.6 (2.1)	0.4	1.4	1.6	3.3	6.3	7.2	16.8
Girls 10-12 years	3.1 (1.3)	0.5	1.1	1.4	3.0	4.6	5.2	8.6
Boys 13-15 years	3.9 (1.8)	0.7	1.3	1.8	3.7	6.3	6.9	9.4
Girls 13-15 years	3.4 (1.5)	0.2	1.2	1.6	3.2	5.3	6.4	7.8
Boys 16-18 years	4.6 (2.3)	0.8	1.6	1.9	4.4	7.9	8.9	11.5
Girls 16-18 years	3.2 (1.9)	0.5	1.1	1.5	2.9	5.4	6.1	16.4
Men 19-22 years	4.7 (2.2)	0.1	1.4	2.0	4.5	7.8	8.7	12.4
Women 19-22 years	2.8 (1.4)	0.1	0.9	1.2	2.7	4.6	5.0	7.2
Men 22-49 years	4.4 (2.2)	0.1	1.5	2.0	4.1	7.2	8.5	17.1
Women 22-49 years	3.2 (1.7)	0.0	1.0	1.3	2.9	5.3	6.1	12.9
Men 50-64 years	4.9 (3.2)	0.2	1.3	1.9	4.4	8.1	10.1	27.3
Women 50-64 years	3.3 (2.2)	0.1	0.8	1.2	3.0	5.7	7.0	20.2
Men 65+ years	4.8 (2.9)	0.8	1.6	2.2	4.4	8.0	9.6	22.0
Women 65+ years	3.6 (2.1)	0.6	1.1	1.5	3.2	6.4	7.7	12.2
Men 75+ years	5.0 (3.1)	1.4	1.8	2.0	4.2	8.2	10.8	23.3
Women 75+ years	3.9 (2.4)	0.8	1.2	1.5	3.4	6.1	7.3	21.9

Men 19-30 years	4.1 (2.2) ^c
Women 19-30 years	2.9 (1.7) ^c

- ^a The intake is exclusive of vitamin D intake from supplements, with the exception of the data on infants and young children.^{170,172,174}
- ^b SD, standard deviation.
- ^c Without use of vitamin D supplements.
- ^d With use of vitamin D supplements.
- ^{cc} The average vitamin D intake (standard deviation) by male users of margarine and low-fat margarine was 4.6 (2.2) micrograms per day, whereas the figure for male non-users was 2.9 (2.0) micrograms per day.

Table 5.2 Vitamin D intake by young adults, shown according to gender and ethnic background in 2003 (people with a Dutch background) and 2004/2005 (people with a Turkish or Moroccan background).¹⁷⁶

Group	N	Average vitamin D intake (standard deviation)
Men		
Dutch background	352	3.8 (2.2)
Turkish background	52	2.1 (2.6)
Moroccan background	26	2.6 (1.9)
Women		
Dutch background	398	2.7 (2.0)
Turkish background	42	1.2 (1.3)
Moroccan background	42	1.8 (2.3)

5.2.2 Status data and physiological symptoms

Data on nutritional status and, insofar as available, prevention of symptoms of vitamin D deficiency confirm indications for excessively low intakes and too little exposure to ultraviolet light by elderly people not living independently, children and adults with dark skin or who have a vegan or macrobiotic diet (table 5.3). Studies also indicate that overweight is linked to a lower vitamin D status.¹¹⁴ Limiting factors in interpreting data are that various cut-off values are used for determining an inadequate vitamin D status, that there is a lack of standardisation in the various methods for determining calcidiol levels⁴⁴⁻⁴⁶ and that many studies fail to indicate the season in which the vitamin D status was determined. An inadequate status has been defined for the purposes of this advisory report as a serum calcidiol level below 30 nmol per litre for children and adults, and below 50 nmol per litre for women aged 50 and older and men aged 70 and older. The Committee is not aware of data on the vitamin D status of breastfeeding women.

Light-skinned children and adults

Data on the status of neonatal infants show that around 10 to 20 per cent of them have an inadequate vitamin D status. However, these data are very limited.^{182,183} The vitamin D status of two-year-old children appears to be significantly lower. Moreover, in the winter, the vitamin D status of two-year-old children who had at any time taken vitamin D supplements in the first year of life was slightly higher than the figure for children who had never taken supplements. There was no difference in the summer. It should be noted that these analyses do not take into account vitamin D intake from foods such as follow-on formula and margarine or low-fat margarine.¹⁸⁴ A study of 176 children and young adults between the ages of 7 and 25 found a clear seasonal effect. The average serum calcidiol level was 54 nmol per litre at the end of the winter and 85 nmol per litre at the end of the summer.¹⁸⁵ Around 10 per cent of adults appear to have an inadequate vitamin D status. The percentage of pregnant women with an inadequate vitamin D status is lower in studies in which the level was measured at an early stage of pregnancy^{183,186} than the figure for studies in which it was measured late in pregnancy.¹⁸⁴

Dark-skinned children and adults

Dark-skinned pregnant women and their neonatal infants have a significantly lower vitamin D status than light-skinned pregnant women and their neonatal infants.^{182,183,186} The same applies to dark-skinned children and adults compared to light-skinned children and adults.^{177,187,188} Cases have also been described of convulsions in newborn infants and of severe muscle weakness in the locomotor apparatus of veiled teenage girls as a result of a severe vitamin D deficiency.^{189,190}

Children and adults with a vegan or macrobiotic diet

The incidence of an inadequate vitamin D status is significantly higher in children and adults with a vegan or macrobiotic diet than the figure for people who do not have such a diet.¹⁹¹⁻¹⁹⁴ On the other hand, lacto-ovo vegetarians do not appear to have an increased risk of an inadequate vitamin D status compared to non-vegetarians.¹⁹⁵

Cases of rickets are also known among children with a macrobiotic diet.^{191,192} These cases were caused by a combination of low vitamin D intake and low calcium intake.

People from the age of 50

Among residents of care homes and nursing homes the percentage of people with an inadequate vitamin D status is around 85 per cent, which is approximately twice the percentage for elderly white people living independently.^{180,196-199} Psychogeriatric participants in one study formed an exception to this, as none of them had an inadequate vitamin D status, in spite of their low vitamin D intake.²⁰⁰ The Committee is not aware of studies of the vitamin D status of non-Western elderly people in the Netherlands.

Overweight people

The serum calcidiol level is inversely proportional to body weight. In particular, the amount of fat in the body appears to affect the vitamin D status.²⁰¹ The serum calcidiol level in white elderly people decreased by 5 nmol per litre for every 10 per cent increase in the amount of fat in the body.¹⁹⁷ Various explanations have been put forward to explain the inverse relationship between the amount of fat in the body and the serum calcidiol level. One such explanation is excessive storage of vitamin D in fat tissue, which reduces the serum level. Another explanation is that an inadequate vitamin D status could increase the amount of fat. It may also be the case that overweight people spend less time outdoors.

The Committee does not view overweight people as a separate risk group. It is true that they have a higher risk of falls than people with a low weight but their risk of fractures is lower owing to their higher bone density and the buffering effect of fat around the hips and other areas.²⁰²

Table 5.3 Prevalence of inadequate vitamin D status or rickets in the Netherlands.

Study and year of publication	N, gender, age	Inadequate vitamin D status ^a	
		serum calcidiol level	%
Meulmeester 1990 ¹⁸⁷		< 20 nmol/l	
	79 Dutch children aged 8		0
	80 Turkish children aged 8		31
	80 Moroccan children aged 8		15
Stellinga-Boelen 2007 ²⁰⁸		< 30 nmol/l	End of winter
	112 dark-skinned children aged 2-12		42
Algemene Gezondheidsmonitor Onderzoek Amsterdam 2007 ¹⁸⁸		< 30 nmol/l	
	201 Dutch men aged 18+		6
	189 Turkish men aged 18+		26
	181 Moroccan men aged 18+		13
	289 Dutch women aged 18+		8
	212 Turkish women aged 18+		58
	145 Moroccan women aged 18+		44

Van der Meer 2007 ¹⁷⁷	< 25 nmol/l		
201 Dutch men and women aged 18-65		6	
121 Turkish men and women aged 18-65		41	
96 Moroccan men and women aged 18-65		37	
107 Surinamese men and women with a South Asian background aged 18-65		51	
75 Surinamese men and women with a Creole background, aged 18-65		45	
57 men and women from Sub-Saharan Africa, aged 18-65		19	
Van der Meer 2006 ¹⁸⁶	< 25 nmol/l		
105 pregnant Westerners		8	
79 pregnant Turkish women		66	
69 pregnant Moroccan women		56	
Wielders 2006 ¹⁸³	< 20 nmol/l		
545 pregnant Westerners		5	
131 pregnant non-Westerners		55	
442 newborn Westerners	< 13 nmol/l	6	
81 newborn non-Westerners		54	
Jansen 2007 ¹⁸⁴			
611 pregnant Westerners	< 30 nmol/l	30	
643 Western children aged 2		3	
Dijkstra 2007 ¹⁸²	< 25 nmol/l		
38 newborn Westerners		16	
49 newborn non-Westerners		63	
Manders 2006 ¹⁸⁰	< 30 nmol/l		
43 elderly people not living independently, aged 65+		86	
Veeninga 2004 ¹⁹⁸	< 30 nmol/l		
34 psychogeriatric patients aged 79		82	
Wouters-Wesseling 2002 ²⁰⁰	< 30 nmol/l		
42 psychogeriatric patients aged 60+		0	
Longitudinal Aging Study Amsterdam 2006 ¹⁹⁶	< 50 nmol/l		
1260 elderly people living independently, aged 65+		47	
Hoorn study 2007 ¹⁹⁷	< 50 nmol/l	End of summer	End of winter
538 elderly white people aged 60-87		34	51
Dagnelie 1990 ^{191,192}			
53 macrobiotic children aged 10-20 months	< 20 nmol/l	11	80 ^b
57 non-macrobiotic children aged 10-20 months		0	n.d. ^c
53 macrobiotic children aged 10-20 months	Rickets prevalence	28	55
57 non-macrobiotic children aged 10-20 months		0	n.d. ^c

^a The cut-off value available in the reference was used.

^b Unlike the remaining 20 per cent, none of these children took a vitamin D supplement.

^c N.d. not determined.

5.2.3 Status data from neighbouring countries

Information on the vitamin D status of people in countries bordering the Netherlands was also collected owing to a lack of data on the status of the general population in the Netherlands (table 5.4). The vitamin D status of the general population in Germany between the age of 18 and 79 was surveyed in the late 1990s. A serum calcidiol level below 25 nmol per litre occurred during summer in around 10 per cent of the population, whereas the figure in winter was around 20 per cent. This inadequate status was frequently found among young adults but it was most common among elderly women aged 65 to 79, at a figure of 23 per cent in summer and 31 per cent in winter.¹⁴⁷ A comparable seasonal fluctuation of serum calcidiol levels was found among UK adults aged 43.²⁰³ A more recent study was conducted of the vitamin D status of German children in the age group from 1 to 17. Serum calcidiol levels decreased from an average of 62 nmol per litre in children aged one and two years to around 40 nmol per litre in those in older age groups. The average serum calcidiol level in children of immigrants was 35 nmol per litre, compared with 44 nmol per litre for children of non-immigrants.²⁰⁴

A study of the vitamin D status at the end of summer and winter was also conducted in Ireland among teenage girls and boys, men and older women. At the end of summer, the vitamin D status of teenagers and men appeared to be adequate but at the end of winter more than 30 per cent of the girls and men had an inadequate vitamin D status. The percentage was slightly lower for boys. The percentage for older women was higher at the end of both summer and winter, a fact partially accounted for by the higher cut-off point (50 nmol per litre) for an adequate vitamin D status.^{146,205}

Another study, which compared the vitamin D status of teenage girls and older women living independently in Denmark, Finland, Ireland and Poland, showed that the situation in North European countries is comparable with the aforementioned situation in Ireland.¹⁴⁵

Information on the vitamin D status of Arabic, Danish and Pakistani women also corresponded with data from the Netherlands, regardless of whether or not the women wore clothing that covered the entire body.^{148,206}

Finally, UK citizens with obesity were twice as likely to have an inadequate vitamin D status as UK citizens who were not obese.^{203,207}

Table 5.4 Prevalence of inadequate vitamin D status or rickets in countries close to the Netherlands.

Country and year of study	N, gender, age	Inadequate vitamin D status ^a		
		serum calcidiol level	%	
Germany 1998 ¹⁴⁷		< 25 nmol/l	summer	winter
	541 men aged 18-34		11	21
	630 women aged 18-34		6	19
	977 men aged 35-64		10	22
	1,190 women aged 35-64		11	19
		< 50 nmol/l		
	245 men aged 65-79		52	61
	446 women aged 65-79		75	73
Denmark, Finland, Ireland and Poland 2002 ¹⁴⁵				end of winter
	199 girls aged 11-13	< 25 nmol/l		37
	221 women aged 70-76	< 50 nmol/l		67
Denmark 1996/1997 ¹⁴⁸		< 20 nmol/l		
	60 veiled Arabic women aged 18+		96 ^a	
	9 non-veiled Arabic women aged 18+		89	
	10 veiled Danish women aged 18+		60	
	44 non-veiled Danish women aged 18+		9	
Denmark 2002 ²⁰⁶		< 25 nmol/l		
	37 Pakistani girls aged 10-15			81
	115 Pakistani women aged 18- 55			84
	95 Pakistani men aged 18- 65			65
United Kingdom 2000 ²⁰⁷		< 25 nmol/l		
	322 men living independently, aged 65+		10	
	320 women living independently, aged 65+		15	
	201 men not living independently, aged 65+		30 ^b	
	454 women not living independently, aged 65+		33	
United Kingdom 2002-2005 ²⁰³		< 25 nmol/l	summer	winter
	7,437 white men and women aged 45		3	16
Ireland 2002/2003 ²⁰⁵			end of summer	end of winter
	22 girls aged 11-13	< 25 nmol/l	0	30
	23 women aged 23-50		0	0
	44 women aged 51-69		0	2
	31 women aged 70-75	< 50 nmol/l	19	64
	51 men, aged 20-64	< 25 nmol/l	0	17

Ireland 2000 ¹⁴⁶	1,015 boys and girls aged 12 and 15	< 25 nmol/l	whole year	
		< 50 nmol/l	end of summer	end of winter
			3	
			17	46

^a Data collected between December 1996 and June 1997.

^b 37 per cent of the men who participated in the autumn or winter had a vitamin D deficiency, compared with 22 per cent of the men who participated in the spring or summer. There was no clear difference in the other groups.

5.2.4 Conclusion

The average vitamin D intake for young adult males in the Netherlands in 2003 was 4.1 micrograms per day and the figure for women was 2.9 micrograms per day. Vitamin D intake has decreased slightly in recent years. An inadequate vitamin D status is common in summer as well as winter in people from the age of 50 and especially residents of care homes and nursing homes, dark-skinned people, women who wear a veil or are pregnant and people with a vegan or macrobiotic diet. This probably also applies to breastfeeding women, although no data are available for this group. Calcium intake in these groups is also lower than in other groups, which probably results in an increased need for vitamin D. Some light-skinned people also appear to have an inadequate vitamin D supply at the end of winter. There is also a relationship between excessive body fat and a lower vitamin D status. In countries close to the Netherlands, the percentage of people with a low vitamin D status varies at the end of winter from 10 to more than 30 per cent.

5.3 Dietary sources

5.3.1 Foods

Light-skinned children and adults

In the case of bottle-fed toddlers aged 9 months and 12 months, the product group comprising milk and milk products, mainly in the form of follow-on formula, was the main source of vitamin D intake. The main source of vitamin D in the case of toddlers aged 18 months was the product group comprising fats, oils and savoury sauces, along with the product group comprising milk and milk products. It should be noted that oil does not contain vitamin D.^{172,173} The product groups comprising fats, oils and savoury sauces, meat and meat products, and dairy produce are the main sources of vitamin D for children aged 2 to 6. In 2003, young adults obtained 39 per cent of their vitamin D supply from the prod-

uct group comprising fats, oils and savoury sauces, half to three-quarters of which they ate in the form of margarine and low-fat margarine. Other important sources included product groups comprising meat, meat products and poultry, fish and shellfish, and milk products, including cheese (table 5.5).^{168,209}

Table 5.5 Percentage contribution of the main dietary sources of vitamin D.^{173,174,209}

	Toddlers			Children 2 to 6 years	Young adults	
	9 months	12 months	18 months		Men	Women
Fats/oils/savoury sauces ^a	3	8	35	30	43	33
Meat/meat products/poultry	1	1	7	13	14	14
Fish/shellfish				3	9	12
Milk products including cheese	94 ^b	88 ^c	43	10	9	10
Other	2	3	15	25 ^d	25	31

^a Oil does not contain vitamin D.

^b 91 per cent of vitamin D intake comes from follow-on formula.

^c 83 per cent of vitamin D intake comes from follow-on formula.

^d Intake from supplements was only included for this group: 24 per cent of vitamin D intake came from supplements.

Dark-skinned children and adults

Young Turkish or Moroccan adults use less dairy produce, margarine and low-fat margarine than participants in the Dutch National Food Consumption Survey of young adults (2003) and therefore have a lower vitamin D intake.¹⁷⁶ This was confirmed in another study of determinants of the vitamin D status of people with Dutch, Turkish, Moroccan, Surinamese-Creole, Surinamese-Asian and Sub-Saharan African backgrounds. However, compared to people with a Dutch background, people of Sub-Saharan African background ate twice as much fatty fish, a good source of vitamin D.¹⁷⁷

Children and adults with a vegan or macrobiotic diet

A vegan diet includes no foods of animal origin, whereas a macrobiotic diet may only contain limited amounts of white meat and fish and no dairy produce. In practice, a macrobiotic diet closely resembles a vegan diet and, once a child is no longer breast-fed, a macrobiotic diet contains almost no food of animal origin. It also rejects the use of dietary supplements. Such diets therefore lack a number of important sources of vitamin D and calcium.¹⁷⁸

People from the age of 50

Foods related to a higher serum calcidiol level that are eaten by elderly people include margarine and low-fat margarine, fatty fish and red meat.¹⁹⁷ The Committee is not aware of studies among dark-skinned elderly people.

5.3.2 Supplements

Little information on the use of supplements in the Netherlands is available and the most thorough studies on this subject have been conducted among toddlers and young children.²¹⁰ Preparations that supply vitamin D include vitamin D, vitamin AD, multivitamin and vitamin D with calcium supplements (table 5.6). Data in the Dutch Supplements Database used to estimate the average level of vitamin D in supplements led to a figure of 2.4 micrograms per day for children and 3.5 micrograms per day for adults and elderly people. The P90 of the vitamin D level is 5 micrograms per day for both groups. A range of doses is often indicated on the packaging, for example 1 to 3 tablets per day, which means in the case of the highest recommended dose that both the average level and the P90 are almost twice as high as the aforementioned average level (table 5.7).²¹¹ According to the Dutch National Food Consumption Survey of young children (2005/2006), median intake from supplements was 2.3 to 3 micrograms per day for children aged two and three years, and 0.5 micrograms per day for children aged 4 to 6.¹⁷⁴

Light-skinned children and adults

Estimates based on the Nutrient Intake Survey of young toddlers (2002), the third Dutch National Food Consumption Survey (1997/1998) and vitamin D levels in dietary supplements, indicate that children from the age of 18 months receive an average of around 5 micrograms of vitamin D from dietary supplements.²¹² Use of a vitamin AD supplement by young toddlers is significantly lower than the figure for a vitamin D supplement. This is probably because at the end of the 1990s the recommendation that children up to the age of 4 should be given a vitamin AD supplement was changed to a recommendation that they should only be given a vitamin D supplement.

The Nutrient Intake Survey of toddlers (2002) showed that most bottle-fed toddlers who were not given vitamin D supplements were given follow-on formula. As mentioned, the vitamin D supply was a problem in 4 per cent of children aged 12 months and in 11 per cent of children aged 18 months because they

received neither a vitamin D supplement nor follow-on formula.^{172,173} Sixty-seven per cent of children aged two in the KOALA Survey received a vitamin D supplement. It was not reported whether the remaining children received follow-on formula.¹⁸⁴ Another survey conducted in 1999 of vitamin D supplement use by children up to the age of 4 showed that 57 per cent of them received the recommended vitamin D dose practically every day. However, 15 per cent of the children received no supplements whatsoever. The percentage of non-users increased with age. Of the children who received some form of supplement practically every day, 81 per cent received the recommended dose, 16 per cent received too little and 3 per cent too much.²¹³ According to the Dutch National Food Consumption Survey of young children (2006/2007), 60 per cent of children aged two to three years and 25 per cent of those aged four to six received a daily vitamin D supplement.¹⁷⁴

Table 5.6 Percentage of supplement users on the basis of research conducted since 1998 as reviewed by Ocké and colleagues (2005), nutrient intake study among young toddlers (2002) and the Dutch National Food Consumption Survey of young children (2002/2003)^{172-174,210}

Supplement	Toddlers			Children		Adults ^a	
	9 months	12 months	18 months	2-3 years ^b	4-6 years ^c	19-50 years	50+ years
Vitamin AD	3	7	14	6	1	0.3-0.6	1
Vitamin D	13	40	67	40	2	n.r. ^d	15
Multivitamin	0.3	1	7	22	21	12-22	9-16
Calcium-vitamin D	n.r.	n.r.	n.r.	-	-	0-3	1-2

^a Food consumption survey among young adults (2003), SENECA (1999), CoDAM (1999/2000), Hoorn (1999/2001), Doetinchem (1998-2003), Hartslag (2003).

^b 60 per cent of children aged 2-3 took a vitamin D supplement.

^c 26 per cent of children aged 4-6 took a vitamin D supplement.

^d n.r. not reported.

Table 5.7 Average, median and P90 of the level of vitamin D in supplements per tablet and per highest recommended daily dose.²¹¹

	Micrograms of vitamin D per tablet ^a			Micrograms of vitamin D per highest recommended dose		
	Average	Median	P90	Average	Median	P90
For children	2.4	2.3	5.0	4.6	3.8	9.0
Not specifically for children	3.5	2.5	5.0	4.9	5.0	10.0

^a A total of 63 supplements for children were studied as well as 195 supplements that were not specifically for children.

Very little research has been conducted into the use of a vitamin D supplement during pregnancy. A survey covering the period 2004 to 2006 found that 37 per cent of women with a Western background who spent enough time outdoors

(N=30) took a vitamin D supplement during pregnancy.¹⁸² The figure for female participants in the KOALA survey was significantly higher at 63 per cent.¹⁸⁴

Twenty-seven per cent of participants in the Dutch National Food Consumption Survey of young adults (2003) used a dietary supplement. An accurate estimate of the amount of vitamin D obtained from these supplements is not possible. An estimate of the vitamin D levels in over-the-counter dietary supplements indicates that they account for around 30 per cent of total vitamin D intake.^{*210}

Dark-skinned children and adults

The use of vitamin D supplements by dark-skinned people has not been studied in depth. Supplementation in accordance with the recommendations appears to be less common among children of non-European women (43 per cent) than children of European women (60 per cent).²¹³

A survey conducted in the period 2004 to 2006 showed that the use of a vitamin D supplement during pregnancy was 12.5 per cent among women who were dark-skinned or who did not spend enough time outdoors (N=40). This is lower than the figure for other women.¹⁸²

According to a study conducted among adults, 6 per cent of those with a Turkish background and 10 per cent of those with a Moroccan background took a vitamin D supplement. These percentages are significantly lower than the percentage for people with a Dutch background (25 per cent) who take vitamin D supplements. Moreover, 16 per cent of people with a Surinamese-Creole background, 21 per cent with a Surinamese-Asian background and 26 per cent with a Sub-Saharan African background took vitamin D supplements.¹⁷⁷

Children and adults with a vegan or macrobiotic diet

In the 1980s, children who had alternative diets were not given vitamin D supplements, unlike other children. However, they were exposed to sunlight as often as possible.¹⁷⁸ The Committee is not aware of any study to determine whether such children are currently given vitamin D supplements. More recent studies conducted in other countries showed that supplements for vegans form an important source of vitamin D.²¹⁴⁻²¹⁶

* Total vitamin D intake by people who use supplements is 5.6 micrograms per day.

People from the age of 50

Elderly people living independently appear to use multivitamin preparations to an extent that compares with that of young adults but they seem to use slightly more vitamin AD and calcium-vitamin D supplements (table 5.6). The high prevalence of inadequate vitamin D status in residents of care homes and nursing homes indicates that the use of vitamin D supplements is far lower in this group than among elderly people living independently.^{180,198}

5.3.3 Conclusion

The greatest contribution to vitamin D intake among toddlers comes from the product group milk and milk products, especially in the form of follow-on formula. In the case of adults it is the product group comprising fats, oils and savoury sauces*. Margarine and low-fat margarine intake is lower among people with a Turkish or Moroccan background than among people with a Dutch background.

The number of children who receive no extra vitamin D in the form of a vitamin D supplement or follow-on formula increases from around 4 per cent at the age of 12 months to around 40 per cent at the age of three to four years. Relatively more mothers with a Western background give their children vitamin D supplements compared to the figure for those with a non-Western background. A similar difference applies to the use of vitamin D during pregnancy. Around 30 per cent of adults and elderly people living independently take dietary supplements containing vitamin D; this percentage is probably significantly lower for residents of care homes and nursing homes, given the high prevalence of vitamin D deficiency found among them. The percentage of users among other ethnic groups varies from 6 to 26 per cent and appears to be low mainly among people with a Turkish or Moroccan background.

No data are available on breastfeeding women.

5.4 Excessive intake

There are no indications that the upper intake limit for vitamin D intake is being exceeded. In the Dutch National Food Consumption Survey of young adults (2003), the 90th percentile of vitamin D intake from supplements and foods collectively amounted to around 11 micrograms per day.²¹⁰ The maximum vitamin D

* Oil does not contain vitamin D.

intake from follow-on formula and dietary supplements by toddlers aged from 9 to 18 months and children aged from 2 to 6 years was also below the tolerable upper intake level. The highest vitamin D intake among toddlers was found in those given follow-on formula without a vitamin D supplement.¹⁷²⁻¹⁷⁴

At the time of the aforementioned studies, few, if any, products were on the market that had been voluntarily fortified with vitamin D.

In conclusion: there are no indications that young children and adults are structurally exceeding the tolerable upper intake level for vitamin D from supplements and/or foods. Intake from products voluntarily fortified with vitamin D has not been taken into account because few, if any, such products were available on the market at the time of the study.

5.5 Conclusion

An inadequate vitamin D status is common in summer as well as winter in people from the age of 50 and especially residents of care homes and nursing homes, dark-skinned individuals, women who wear a veil or are pregnant and people with a vegan or macrobiotic diet. This probably also applies to breastfeeding women, although no data are available for this group. People with dark skin or who have an alternative diet often also have a low calcium supply, which may increase the vitamin D requirement. Some light-skinned people also appear to have an inadequate vitamin D supply at the end of winter. Overweight is also linked to a lower vitamin D status. Figures from countries close to the Netherlands indicate a low status for 10 to more than 30 per cent of the population at the end of winter and that this is twice as likely to be the case in overweight people.

The greatest contribution to vitamin D intake among toddlers comes from the product group milk and milk products, especially in the form of follow-on formula, whereas among adults the greatest contribution comes from the product group comprising fats, oils and savoury sauces*. Margarine and low-fat margarine intake is lower among people with a Turkish or Moroccan background than among people with a Dutch background.

The number of children who receive no extra vitamin D in the form of a vitamin D supplement or follow-on formula increases from around 4 per cent at the age of one to around 40 per cent at the age of four. More mothers with a Western background give their children vitamin D supplements than do those with a non-

* Oil does not contain vitamin D.

Western background. Women with a Western background also make greater use of vitamin D supplements during pregnancy.

Around 30 per cent of adults and elderly people living independently take a dietary supplement containing vitamin D. The percentage of users is lower among people with a Turkish or Moroccan background and probably also among residents of care homes and nursing homes.

There are no indications that young children and adults are structurally exceeding the tolerable upper intake level for vitamin D from supplements and/or foods.

Policy measures in other countries

In this chapter, the Committee assesses the effects of vitamin D supplementation and fortification in the United Kingdom, Canada, the United States and Finland. A description is also provided of plans for new policy measures concerned with expanding mandatory fortification of staple foods in Australia and New Zealand and scenario calculations from Denmark and the European Optiford project.

6.1 Supplementation

6.1.1 *United Kingdom*

Recommendations have existed in the United Kingdom since the early 1990s that children, elderly people, dark-skinned people and pregnant or breastfeeding women should take vitamin D supplements. The advice was not heeded properly, with the result that a low vitamin D status* is still common. Cases of rickets are also known to occur. It is true that margarines and certain breakfast cereals in the UK are fortified with vitamin D but the recommended dietary allowance can only be achieved when supplements are taken. The recommended dietary allowance for vitamin D in the UK for children up to the age of 4 is between 7 and 8.5 micrograms. The recommended dietary allowance is 10 micrograms per day for elderly people from the age of 65 and for pregnant or breastfeeding women.

* A low vitamin D status is defined as a calcidiol level below 25 nmol per litre.

The requirement may be higher for dark-skinned individuals or people who do not spend enough time outdoors.

The Scientific Advisory Committee on Nutrition stresses the necessity of a clear strategy to increase knowledge among healthcare workers of the benefits of vitamin D supplements, with a view to bringing about improvements in the low use of vitamin D.²¹ At the end of 2007, this resulted in a new information campaign to encourage the use of extra vitamin D doses of 10 micrograms per day to be taken by pregnant or breastfeeding women and children up to the age of 4.

6.2 Voluntary fortification of specific foods

6.2.1 Ireland

Vitamin D may be added to any type of food in Ireland. Fortified foods are used voluntarily by around 65 per cent of Ireland's population. Men using these products obtain around 5 per cent of their total vitamin D intake from them, whereas the figure for women is as high as 11 per cent. Using these products increases the median intake by 0.1 micrograms per day for men and 0.4 micrograms per day for women.²¹⁷

6.3 Mandatory fortification of staple foods

6.3.1 Canada and the United States

Legislation in Canada makes it mandatory to fortify milk* and margarine with vitamin D (table 6.1). The foods to which vitamin D may be added voluntarily are limited to meal replacements, dietary supplements, liquid meals and certain egg products.²¹⁸ Forthcoming legislation in Canada will increase the number of products permitted to be fortified with vitamin D.²¹⁹

In the United States it is only mandatory to add vitamin D to milk if the label states that it is fortified milk (table 6.1). Vitamin D may also be added to a small number of fortified cereal products, instant breakfast cereals, certain milk products and margarine as well as fruit juices and fruit drinks fortified with calcium.

* Liquid milk, dried milk, milk powder and goat's milk.

Table 6.1 Overview of products that are mandatorily fortified with vitamin D in a number of countries.

Country	Product	Level of fortification with vitamin D
Australia	Margarine and low-fat margarine	5.5-16.1 micrograms per 100 g
Canada	Margarine and low-fat margarine	13.25 micrograms per 100 g
	Milk	1.32-1.76 micrograms per 100 ml
United States	Fortified milk	1.05 micrograms per 100 g
Finland	Milk, sour milk and yoghurt	0.5 micrograms per 100 ml
	Margarine and low-fat margarine	10 micrograms per 100 g

Partly as a consequence of this, vitamin D intake in the United States is approximately twice as high as in Europe.^{218, 220}

Cross-sectional studies suggest that the current fortification measures are not effective to assure the vitamin D supply of vulnerable groups, such as elderly people and dark-skinned individuals. This may be because the level of fortification is too low. Moreover, milk is not consumed by everyone and milk consumption has decreased since the 1990s. Vitamin D supplements may be the only effective means for the aforementioned vulnerable groups to obtain sufficient vitamin D.^{135, 218}

On the grounds of these findings, Health Canada recommends everyone over the age of 50 to take a daily vitamin D supplement of 10 micrograms, in addition to drinking two glasses of milk per day. In so doing, Health Canada is following the Canadian Food Guide.²²¹ Recommendations in '2005 Dietary Guidelines for Americans' state that elderly people, dark-skinned people and people who are not exposed to enough ultraviolet radiation should obtain 25 micrograms of vitamin D per day from fortified foods and/or supplements.²²²

6.3.2 Finland

Until 2002, Finland only permitted margarine and low-fat margarine to be fortified (table 6.1).²²³ However, since 2003 it has been mandatory to fortify milk, sour milk, yoghurt, margarine and low-fat margarine with a higher dose of vitamin D.

This new policy measure has resulted in a definite improvement in the vitamin D supply among four-year-old children (table 6.2). In addition, even after the new policy measure's implementation, none of the children had a serum calcidiol level higher than the upper intake limit of 140 nmol/l.²²⁴ Studies among young males indicate that the new policy measure has led to an improvement in the vitamin D supply but that the improvement is insufficient.^{225, 226}

Table 6.2 Percentage of people with a marginal vitamin D status as a result of expanding mandatory fortification of staple foods with vitamin D in Finland

Population group, age	Serum calcidiol limit	Expansion of mandatory fortification	
		Before	After
Children 4 years ²²⁴	20-37.5 nmol/l	N=82 ^a 10%	N=36 ^a 3%
Men aged 19-21 ²²⁵	≤ 20 nmol/l	N=65 34	29%
	≤ 37.5 nmol/l	93	74%
Men aged 19-21 ²²⁶	< 40 nmol/l	N=196 78%	30%

^a The percentages are based on two different cohorts of children.

6.4 Plans for introducing mandatory fortification

6.4.1 Australia and New Zealand

In Australia, it is only mandatory to fortify margarine and low-fat margarine with vitamin D (table 6.1). Modified and low-fat milk products, powdered milk, yoghurt and cheese may also be fortified with vitamin D. In New Zealand, vitamin D may be added to margarine, low-fat margarine, fats and dairy produce. A study commissioned by the predecessor of Food Standards Australia New Zealand, the Australia New Zealand Food Authority, concluded that foods fortified with vitamin D were inadequate for meeting the general population's requirement. It also concluded that the requirement could be met by increasing the number of products fortified with vitamin D. The effect of fortifying milk with 5 micrograms of vitamin D per litre was calculated.²²⁷ Note by way of comparison that the level of fortification in the United States is 10.5 micrograms of vitamin D per litre of milk.²¹⁸ The conclusion drawn from these scenario calculations is that it is extremely unlikely, even with any such increase in the number of fortified foods, that an adequate vitamin D intake could be achieved through diet in groups with a high risk of vitamin D deficiency. It is therefore recommended that a solution be sought for these groups by way of sufficient exposure to sunlight and/or extra vitamin D in the form of a supplement.²²⁷

6.5 Scenario calculations

6.5.1 Denmark and the Optiford-project

Scenario calculations from Denmark concerned a study of how intake is affected by fortifying margarine, milk and a combination of the two with vitamin D. The conclusion was that fortifying milk with vitamin D is not the ideal solution owing to the uneven distribution of milk consumption. The same applied to the intake of margarine in these scenario calculations.²²⁸ However, it could be argued against this that in the Netherlands the product group oil, fats and savoury sauces, including fortified margarine and low-fat margarine, accounts for almost 40 per cent of vitamin D intake.²⁰⁹ The best Danish scenario was combined fortification of margarine (9.5 micrograms per 100 g) and milk (1.1 micrograms per 100 g). At these levels of fortification, more than half of elderly people would have a vitamin D intake of more than 10 micrograms per day and only a few people would have an intake of more than 40 micrograms per day. This does not seem sufficient to tackle existing vitamin D deficiencies.²²⁸ However, higher levels of fortification would lead to excessively high vitamin D intake of 25 micrograms per day or more in around 10 per cent of children aged 4 to 10.¹⁰⁶

Researchers in the European Optiford project concluded with regard to the vitamin D status of children and adolescents that moderate fortification* of milk and margarine could increase vitamin D intake of children and adolescents to a level close to the recommended amounts. However, it is not certain that diet alone is sufficient to maintain a serum calcidiol level above 25 or 50 nmol per litre during the winter. Supplements could increase intake in these groups but the best period for taking supplements (winter months or throughout the year) and the most cost-effective form have not yet been determined.²²³

These findings suggest – as do the findings in the scenario calculations from Australia and New Zealand²²⁷ – that recommending the use of vitamin D supplements is the best way to fully guarantee the vitamin D supply of elderly people, dark-skinned individuals, people whose entire bodies are covered by clothing and persons who spend too little time outside. This does not detract from the fact that lower levels of fortification could help towards achieving an optimum vitamin D status for the entire population, without giving rise to groups that are at risk of having an excessive vitamin D intake.

* Fortification with 0.5 micrograms of vitamin D per 100 millilitres of milk, sour milk and yoghurt and 10 micrograms of vitamin D per 100 grams of margarine and low-fat margarine.

6.6 Conclusion

Advice in the United Kingdom on using vitamin D supplements has thus far not been properly heeded. In Ireland, where voluntary fortification is permitted, products fortified with vitamin D account for 5 to 10 per cent of the vitamin D intake of those who use them, around 65 per cent of the population. Fortification of margarine and low-fat margarine or milk is mandatory in some countries. The vitamin D status of Finland's population was improved by increasing the number of products mandatorily fortified with vitamin D but the level of fortification does not appear to be sufficient to meet the requirement of adult males, not to mention other population groups with a higher risk of vitamin D deficiency. This corresponds with findings based on scenario calculations from other countries, where intake was estimated for various vitamin D fortification strategies.

Dutch policy measures

In this chapter, the Committee discusses current information on using a vitamin D supplement and on exposure to sunlight. It goes on to examine the present exemption policy on vitamin D fortification of specific foods. The Committee concludes with a discussion of the effects of vitamin D fortification and considers the various measures.

7.1 Information

7.1.1 *Current information policy on the use of cooking fats and vitamin D supplements*

Vitamin D is added to cooking fats in the Netherlands but not to oil. The Netherlands Nutrition Centre provides advice in connection with the vitamin D supply on the use of vitamin D supplements for children, pregnant or breastfeeding women and adults aged over 50 (table 3.1).²⁸

The present advisory report indicates that the recommended amounts are on the low side. On the basis of recent scientific developments and the fact that it is not possible to produce too much vitamin D through exposure to sunlight, the Committee recommends that children from aged 0 to 4 years, people aged from 4 to 50 who are dark-skinned or who do not spend enough time outdoors, women who wear a veil, pregnant or breastfeeding women, women older than 50 and men older than 70 should take an extra 10 micrograms of vitamin D per day.* To

keep the advice as simple as possible, the Committee has only opted for one level of supplementation in this advisory report. The only exception to this is the recommendation that people from the age of 50 with osteoporosis or who live in a care home or nursing home and people from the age of 50 (females) or 70 (males) who are dark-skinned or who do not spend enough time outdoors and women from the age of 50 who wear a veil should take an additional 20 micrograms of vitamin D per day.

Child healthcare centres provide similar information to that of the Netherlands Nutrition Centre on the use of extra vitamin D for children up to the age of 4. A new information package for healthcare centre employees will be compiled over the next few years by the Youth Health Centre of the National Institute of Public Health and Environmental Protection (RIVM), on the basis of research into effective information. The aim is to improve the use of extra vitamin D for children up to the age of 4.*

Pregnant or breastfeeding women could be advised via their preconception care units to take extra vitamin D. The latter group of women can also be reached through the child healthcare centre.

However, recommendations of the Dutch College of General Practitioners and the guidelines of the Dutch Institute for Healthcare Improvement on the use of vitamin D for dark-skinned people, elderly persons and pregnant or breastfeeding women differ from those provided by the Netherlands Nutrition Centre. For example, the Dutch College of General Practitioners provides no advice to pregnant or breastfeeding women on the use of extra vitamin D. It does indeed explain in a patient information brochure that in some cases 10 micrograms of vitamin D per day from the fourth month of pregnancy is advised, but that the benefit of doing so is unclear.²²⁹ Moreover, the osteoporosis standard of the General Practitioners provides more limited guidelines on vitamin D supplements than that of the Netherlands Nutrition Centre. The standard addresses patients with questions about osteoporosis who have no complaints, patients with broken vertebrae, women who break a bone after the age of 50 and patients who use Prednison. The advice is to give these patients 10 micrograms of vitamin D per day, if they do not go outdoors or if their serum calcidiol level** is low.²³⁰

On the other hand, the only official Dutch guidelines on vitamin D supplements, namely the second edition of the Osteoporosis Guidelines published by the Dutch Institute for Healthcare Improvement²³¹ and the Guidelines on Fall Pre-

* This advice does not apply to children consuming more than half a litre of infant formula or follow-on formula per day.

* Personal communication, Dr. W.J.G. Lijs 26/02/2008.

** A low calcidiol level is defined as a serum calcidiol level below 50 nmol per litre.

vention for Elderly Persons, published by the same institute²³², advise elderly people to take an extra 10 micrograms of vitamin D per day, if they do not go outdoors. The aforementioned Osteoporosis Guidelines also state that vitamin D supplements for children with pigmentation should be assessed case by case, taking into account their intake of vitamin D and calcium and their exposure to sunlight. Within the scope of this, the guidelines state that people from ethnic minority groups require extra attention.²³¹

The lack of clear advice on supplements may contribute to the low use of vitamin D supplements and the inadequate vitamin D status of dark-skinned children and adults, pregnant or breastfeeding women, women who wear a veil, and elderly people.

7.1.2 *Points for attention in information*

A possible measure is extensive information on the use of foods that are rich in vitamin D. Because diet alone is not sufficient to meet the vitamin D requirement of young children, population groups of people who are dark-skinned or who do not spend enough time outdoors, pregnant or breastfeeding women, women who wear a veil, and elderly people, they also need information on the use of supplements. This means it is important to combine the information campaign with other activities,²³³ and to also involve other parties, such as general practitioners, medical staff in health centres and general practitioners in care homes and nursing homes. The campaign will also have to place the emphasis on positively influencing attitudes towards the use of supplements and towards their anticipated use.²³⁴

Moreover, it will be necessary to take into account cultural and religious convictions and concerns about side-effects. Studies among Turkish women of around the age of 40 in focus group meetings indicated that they have a strong preference for vitamins obtained from 'natural' sources. Concerns about weight gain and overdoses through the use of vitamin supplements regularly emerged. The use of vitamin D supplements was only thought acceptable if prescribed by a doctor. Turkish women were also uncertain about whether margarine fortified with vitamin D contained pork fat and they were worried about whether margarine would make them overweight.²³⁵

7.1.3 *Information on exposure to sunlight*

From the point of view of improving the vitamin D supply, the Committee believes that ideally everyone who is capable should spend at least 15 minutes a

day outside during the day. It must also be ensured that people avoid becoming sunburnt. Exposure of at least the head and hands would be sufficient. The Committee believes that this should not be stressed in the information because a short period of exposure of larger areas of the body, such as the arms and legs, produces a larger amount of vitamin D.³⁰

The Dutch Cancer Society provides information on sensible sunbathing in the summer to reduce the risk of skin cancer. The information is based on the Health Council's advisory report on UV radiation from sunlight.²⁶ The information states that care should be taken not to burn the skin, that the body's exposure to sunlight between 12:00 and 15:00 should be avoided and that it would be advisable for anyone who will be exposed to sunlight for a long time to apply sunscreen.²³⁶ With regard to exposure to sunlight for production of vitamin D, the information corresponds with the Health Council's dietary reference values for vitamin D (15 minutes a day outdoors) and the Netherlands Nutrition Centre's advice on supplements.²²

Updated information on sensible sunbathing will be published in the course of 2008.

7.1.4 Conclusion

Recent scientific developments call for an increase in the level of supplements recommended by the Netherlands Nutrition Centre.

It has emerged that information on the use of vitamin D for children aged 1 to 4 is not reaching the target groups. The information also lacks a clear message for groups of older children and adults with darker skin, for pregnant or breast-feeding women and for elderly people. When providing information on vitamin D in foods or vitamin D supplements it is furthermore important to take into account cultural and religious convictions and living conditions, such as care homes or nursing homes.

Clear information on exposure to sunlight does exist.

7.2 Fortification of specific products

The Netherlands has originally only permitted the addition of vitamin D in a dose of 7.5 micrograms per 100 gram to margarine, low-fat margarine and products used in baking and frying.

In 2004, the Netherlands had to abolish the absolute prohibition on fortification with vitamin D. Pending new European legislation, an exemption has been in place since 2007 for the addition of up to 4.5 micrograms of vitamin D per 100

kcal. Individual applications for exemptions can be submitted for the addition of higher amounts of vitamin D. The exemption is temporary and does not restrict the amount of vitamin D per portion. Although there is no proper registration in place to confirm this, there currently appear to be few products on the Dutch market that have been fortified with vitamin D.

Unlike in the case of fortification of staple foods, fortification of specific foods does not guarantee that they will reach everyone. Nevertheless, risk groups could be provided with information telling them about the products, which could be specially labelled for this purpose.

The tolerable upper intake level for children up to the age of 10, which was established by the EU Scientific Committee on Food, was used in the determination of the value for exemptions.²⁴ It was also assumed that the fraction of the energy intake to be fortified would be 15 per cent and that vitamin D intake from supplements for children and adults would be 10 micrograms per day in the worst-case scenario. If, instead of 15 per cent, 50 per cent of the energy intake came from products fortified with vitamin D, the exemption level would have to be reduced to 0.9 micrograms per 100 kcal.*

The permitted amount of vitamin D is high in comparison with adequate intake because there is some margin for vitamin D between adequate intake and tolerable upper intake level. The starting point was the calculation for children because the margin between adequate intake and safe upper intake level is smallest for children.²¹²

Vitamin D can theoretically be added to all kinds of foods. This is now restricted by a new European regulation that entered into force in 2007. The regulation stipulates that nutritional claims** may only be made in respect of products that comply with the nutritional profile. The nutritional profile still has to be established and is expected to include limits for a small number of nutrients, such as saturated fat, sugar and salt. Nutritional claims are also permitted in respect of products that apply to all but one of the nutrients in the profile, on condition that the exception is stated in the claim on the label. There is therefore a possibility of manufacturers adding extra vitamin D to products that comply with the profile or that depart from it in respect of a single nutrient. This could apply to fruit juice or dairy products, for example. If it is assumed that manufacturers will add the maximum dose (4.5 micrograms of vitamin D per 100 kcal) to their products, a fortified product containing 55 kcal per portion – e.g. 125 ml of semi-skimmed milk or yoghurt or 150 ml of fruit juice – would provide 2.5 micrograms of vitamin D

* Personal communication from J. Verkaik-Kloosterman, 23/04/08.

** For example 'contains vitamin D' or 'rich in vitamin D'.

per day. This is the same as the present adequate intake for light-skinned people aged from 4 to 60 who spend enough time outdoors.²² However, it is unlikely that many manufacturers add the maximum permitted amount of vitamin D to their products. The requirement is less for a nutritional claim, namely 15 per cent (0.75 micrograms of vitamin D per 100 grams of product) or 30 per cent (1.50 micrograms of vitamin D per 100 grams of product) of the recommended daily amount for labelling of 5 micrograms per day. Nevertheless, the adequate intake level would probably be exceeded. Because of the margin between adequate intake and the tolerable upper intake level, the Committee does not think it likely that children would structurally exceed the tolerable upper intake level through consumption of voluntarily fortified foods and a vitamin D supplement of 10 micrograms per day.

In conclusion: the present permitted levels for voluntary fortification of specific foods could easily lead to children and adults having a vitamin D intake in excess of the adequate intake. Because of the certain margin between adequate intake and the tolerable upper intake level, it is unlikely that children will structurally exceed the tolerable upper intake level, as long as less than 15 per cent of energy intake comes from products fortified with vitamin D. If, instead of 15 per cent, the figure was 50 per cent, the exemption level would have to be reduced to 0.9 micrograms per 100 kcal. However, there is no registration of products on the Dutch market that are voluntarily fortified with vitamin D.

7.3 Fortification of a small number of staple food groups

7.3.1 Scenario calculations for the fortification of oil, milk and milk substitutes

RIVM has made scenario calculations containing estimates of changes in the intake of vitamin D as a result of its use in the fortification of oil, milk, milk substitutes, and desserts. Table 7.1 shows various scenarios, the effects on intake from fortified products (the increase) and the risk of the tolerable upper intake level being exceeded. The estimated effect on total intake is described in the following paragraphs and in annex F.

The options for the various levels of fortification are based on policies in the Netherlands and those of other countries. A fortification level of 4.5 micrograms of vitamin D per 100 kilocalories corresponds with the exempted level for voluntary fortification. A fortification level of 10 micrograms per litre is based on milk fortification levels in other countries. The effect of adding 7.5 micrograms of vitamin D to 100 millilitres of oil – the level for cooking fats – is not calculated.

Table 7.1 Effect of various fortification scenarios on vitamin D intake and the risk of exceeding the tolerable upper intake level.

Staple foods	Level of fortification	Increase in intake	Risk of excessive intake
Oil (excluding frying oil)	4.5 micrograms per 100 kcal	0.3-1.0	Absent
Milk and milk substitutes	4.5 micrograms per 100 kcal	5.2-11.2	Children, whether or not in combination with supplement use
Milk and milk substitutes	10 micrograms per litre	2.6-4.7	Absent
And desserts	10 micrograms per litre	2.9-5.3	Children aged 4-6 in combination with supplement with at least 7.5 micrograms of vitamin D per day
And oil	4.5 micrograms per 100 kcal	3.5-5.0	
And desserts and oil	as above	3.7-5.5	

This is because this level is around five times lower than the aforementioned exemption level. This means that the increase in intake would be around five times lower. The use of supplements of up to 10 micrograms per day was taken into account in the calculations. Vitamin D intake from voluntarily fortified foods was not taken into account.

The scenario calculations show that for oil (excluding frying oil) fortified with 4.5 micrograms per 100 kilocalories, total vitamin D (median) intake in the various age groups increases to between 2.2 and 5.8 micrograms per day, whereby the increase is higher for adults and elderly people than for children, with the exception of women from the age of 70.

Fortifying milk and milk substitutes with 10 micrograms of vitamin D per litre would increase total vitamin D intake (median) to between 6.0 and 8.2 micrograms per day, and the increase for children in particular would be larger than for adults and elderly people. Also fortifying desserts would increase total intake to between 6.2 and 8.8 micrograms per day.

In the case of milk and milk substitutes fortified with 10 micrograms of vitamin D per litre being used in combination with oil (excluding frying oil) fortified with 4.5 micrograms per 100 kilocalories, total vitamin D intake would increase to between 6.8 and 8.6 micrograms per day. In combination with desserts, total intake would be 7.0 to 9.0 micrograms per day (results not shown). The tolerable upper intake level is only expected to be exceeded in the case of all children having an extra daily intake from vitamin D supplements of 7.5 micrograms.

Fortifying milk and milk substitutes with 4.5 micrograms of vitamin D per 100 kilocalories would increase total vitamin D intake (median) to between 8.6 and 13.8 micrograms per day. This level of fortification alone, apart from vitamin D from supplements, would probably lead to vitamin D intake being several micrograms a day too high in 1 to 5 per cent of children aged between 1 and 10. Fortifying desserts as well as milk and milk substitutes would mean that total

vitamin D intake would exceed the tolerable upper intake level by up to 10 micrograms per day in 4 to 9 per cent of children (results not shown).²¹¹

The scenario for oil has been calculated bearing in mind that people of non-Western cultures use more oil than those with a Western background. As people of non-Dutch background were under-represented in Dutch National Food Consumption Surveys, it is only possible to make limited estimates of the effect that fortified oil would have on the vitamin D intake of people with a non-Western background. However, it is known that the figures for the number of people with a non-Western background who use oil and the amount of oil they use are higher than those for people with a Western background. In comparison with participants in the Dutch National Food Consumption Survey of young adults (2003), around twice as many young adults of Turkish or Moroccan extraction used oil and the amounts they used were around 5 to 10 times higher (table 7.2).¹⁷⁶ A 1998 study of eight-year-old children of Moroccan, Turkish and Dutch backgrounds and their mothers found a similar difference in oil intake.²³⁷ It can be deduced from this that young Turkish or Moroccan adults might have an average vitamin D intake of 6.5 to 9.3 micrograms per day from fortified oil compared to the vitamin D intake of 0.8 to 1.2 micrograms per day of young adults with a Dutch background (table 7.3). However, no information is available to enable an estimate of the effect of fortification on median intake or the distribution of intake.

The scenario for milk and milk substitutes has been calculated bearing in mind that children and elderly people can be reached with these products. A disadvantage of milk and milk substitutes is that they are used less by people with a non-Western background than by their Western counterparts (table 7.2), which means that fortifying these products would have a smaller effect on vitamin D intake (table 7.3). For example, in comparison with participants in the Dutch National Food Consumption Survey of young adults (2003), the percentage of users among young adults with a Turkish or Moroccan background was not much different but the amount used was 3 to 4 times lower.¹⁷⁶ In comparison with this, the intake of milk and milk products by eight-year-old children of Moroccan, Turkish and Dutch backgrounds, and their mothers, differed less.²³⁷

7.3.2 *Scenario calculation for the restoration of milk products made from skimmed and semi-skimmed milk*

In 2003, the Netherlands Organisation for Applied Scientific Research, TNO, calculated for the Dutch Dairy Association that the average vitamin D intake would increase by 0.2 micrograms per day if semi-skimmed and skimmed milk and milk products were restored to the vitamin D level of full-cream milk.

Table 7.2 Use of vegetable oils and milk products by young adults with a Dutch, Turkish or Moroccan background and by Turkish, Moroccan and Dutch eight-year-olds and their mothers.^{176,237}

Background	Milk and milk products and Average standard deviation	% users	Vegetable oils Average and standard deviation	% users
Men				
Turkish	115 (191)	61	21 (23)	70
Moroccan	222 (234)	84	16 (17)	61
Dutch	404 (n.r. ^a)	73	3 (5)	39
Women				
Turkish	133 (254)	70	23 (25)	77
Moroccan	108 (162)	55	16 (16)	68
Dutch	317 (n.r.)	66	2 (4)	39
Boys				
Turkish	254	n.r.	8 (12)	59
Moroccan	279	n.r.	10 (11)	79
Dutch	556	n.r.	2 (5)	17
Girls				
Turkish	251	n.r.	5 (7)	64
Moroccan	197	n.r.	14 (12)	84
Dutch	434	n.r.	2 (4)	25
Mothers				
Turkish	136	n.r.	13 (17)	76
Moroccan	177	n.r.	19 (16)	93
Dutch	321	n.r.	3 (6)	32

^a N.r. not reported.

Table 7.3 Anticipated increase in observed vitamin D intake and the total observed intake among young adults with a Dutch, Turkish or Moroccan background in the case of fortifying oil with 4.5 micrograms of vitamin D per 100 kilocalories and in the case of fortifying milk and milk substitutes with 10 micrograms of vitamin D per litre.^{a 176}

Background	Increase in vitamin D intake		Total intake	
	Milk and milk products	Vegetable oils	from fortified products	from entire diet
Men				
Turkish	1.2	8.5	9.7	11.8
Moroccan	2.2	6.5	8.7	11.3
Dutch	4.0	1.2	5.2	9.0
Women				
Turkish	1.3	9.3	10.7	11.9
Moroccan	1.1	6.5	7.6	9.4
Dutch	3.2	0.8	3.4	6.7

^a Data on median intake and the intake distribution are unavailable.

Restoring reduced-fat cheese to the vitamin D level of full-fat cheese would result in an average increase in vitamin D intake of 0.01 micrograms per day. The effect of restoring these dairy products would therefore have a minimal effect on vitamin D intake.

7.3.3 Conclusion

Scenario calculations show that restoration of milk products could only improve intake to a very limited degree.

On the other hand, low levels of fortification of milk, milk substitutes and oil (excluding frying oil) could contribute to higher vitamin D intake by the entire population, without any groups being at risk of taking too much vitamin D. The advantage of these products is that they are a natural source of vitamin D (milk) or form a substitute product (milk substitutes and oil). These products would also reach risk groups. Use of milk and milk substitutes is particularly high among children and elderly people, whereas use of oil is higher among people with a non-Western background than among their Western counterparts.

If fortified, these products could collectively provide around an extra 5 micrograms of vitamin D per day. This type of fortification sets a base level below the extra requirement for population groups with a high risk of vitamin D deficiency but it is not sufficient to meet the entire extra requirement.

7.4 Vitamin D2 or D3

Vitamin D refers to both vitamin D2 and vitamin D3, which are officially deemed to be equivalent and interchangeable. However, there are three reasons why vitamin D2, which is not produced naturally by the body, is not equivalent to vitamin D3, which is produced naturally by the body:

- vitamin D2 increases the serum calcidiol level less sharply than vitamin D3;
- vitamin D2 metabolites bind less well to the vitamin D-binding protein in plasma;
- vitamin D2 has a non-physiological metabolism.

Moreover, vitamin D2 is less stable in supplements and foods.²³⁸

For these reasons, Houghton and Vieth²³⁸ suggest that vitamin D2 is not suitable for adding to supplements or foods. On the other hand, a study published after the aforementioned overview report indicated a comparable effect on the serum calcidiol level for both types of vitamin D.¹⁵⁵ Nevertheless, an argument against this is that it is uncertain whether vitamin D2 – in combination with calcium – protects against fractures (see chapter 4). However, the European Food Safety Authority concluded that vitamin D3 is (more) toxic than vitamin D2 at a lower intake.²⁴ The type of vitamin D that is most cost-effective has not yet been determined.²²³

In conclusion: vitamin D3 is preferable to vitamin D2 for inclusion in supplements and foods because vitamin D3 is more effective than vitamin D2.

7.5 Consideration of measures

Vitamin D status can be improved by spending time outdoors during the day and by increasing the intake of vitamin D from foods or supplements. The Committee believes that everyone who is capable should spend time outside during the day, whereby guidelines for preventing skin cancer should be followed in accordance with the Health Council's recommendations and as presented by the Dutch Cancer Society.^{26, 236}

However, only spending time outdoors is not enough. To maintain a good vitamin D status, the entire population is dependent for part or for all of the year on the vitamin D supply accumulated in the body during the summer and on vitamin D in food. In the Netherlands during the winter, from October to April, exposure to sunlight does not result in significant vitamin D production because the intensity of the required ultraviolet radiation that reaches the earth's surface is insufficient.²⁵ Moreover, people who are unable to go outside or who wear clothing that covers the entire body cannot benefit by following advice on sensible sunbathing. Present exposure to sunlight in the summer, in combination with vitamin D obtained from foods, seems not sufficient to ensure an adequate vitamin D status in children, adults who are dark-skinned or who do not spend enough time outdoors, women who wear a veil, pregnant or breastfeeding women, women aged over 50 and men from the age of 70. In the case of dark-skinned people, the degree of skin pigmentation and possibly also avoidance of direct exposure to sunlight in the summer also play a role.

Several measures are possible for improving vitamin D intake. Four are discussed below: (1) foods high in vitamin D; (2) restoration of milk products and cheese; (3) fortification; (4) use of supplements.

7.5.1 Use of foods rich in vitamin D

One possibility is to encourage the use of foods that are rich in vitamin D. However, the problem is that few products are good providers of vitamin D: fatty fish is rich in vitamin D, while eggs, liver, meat and milk products contain smaller amounts. Vitamin D is also added to margarine, low-fat margarine, and products used in baking and frying, because these products are used as replacements for butter (substitution). Using these products increases vitamin D intake. The Committee believes that the Guidelines for a Healthy Diet should be followed, as

doing so would result in an estimated vitamin D intake by adult males and females of 6.1 and 5.7 micrograms per day respectively.²³⁹ In such an ideal situation, vitamin D intake would remain below the recommended levels for young children, dark-skinned people, women who wear a veil, women who are pregnant or breastfeeding and elderly people. They would therefore also need a supplement in addition to their intake from foods.

7.5.2 *Restoration of milk products and cheese*

A second option would be a measure to encourage the use of milk products and cheese in which the vitamin D had been restored. Scenario calculations indicate that the effects of restoration on intake would be minimal. The Committee does not therefore see restoration as a serious option.

7.5.3 *Fortification*

A third option would be a measure to encourage the use of fortified products. It is true that major changes in intake could be achieved with fortification but it would still not be possible to meet the entire needs of risk groups. They would need extra vitamin D from supplements. The advisory report distinguishes between two forms of fortification, namely fortification of specific foods and fortification of a small number of staple food groups. From the scientific perspective, fortification of a small number of staple food groups, such as milk, milk substitutes and oil would be preferable. This form of fortification guarantees that almost everyone in the population is reached. This is not the case with the current practice of fortifying specific products. Under current European legislation, fortification of a small number of staple food groups does not seem feasible in the near future (see annex G).

7.5.4 *Supplements*

A fourth option would be a measure to encourage the use of supplements. Supplements offer the advantage that it is possible to specifically improve the vitamin D intake of risk groups. However, there is no guarantee that everyone would receive extra vitamin D who needed it. The groups that are less well reached through information are those with a low level of education, low social-economic status or a non-Western background. Intake of vitamin D supplements by children, adults and pregnant women with a non-Western background is lower than the figure for people with a Dutch background. The low use of supplements is

partially the result of a lack of clear information for these population groups on the use of vitamin D supplements. The Committee thinks it would be advisable to provide a uniform message.

7.5.5 *Monitoring*

Regardless of the policy measure that is finally adopted, the Committee thinks it is important to establish a register of fortified foods, to enable control of whether or not people are at risk of their intake being too high through the use of these and other foods in combination with supplements. Registration would also enable consumers to be informed of which products contain extra vitamin D. It is also important to monitor vitamin D intake and status, regardless of which measure is adopted.

7.5.6 *Conclusion*

The vitamin D supply can be improved by spending enough time outdoors and having a healthy diet*. However, these measures are insufficient for vulnerable groups. They need extra vitamin D from supplements or fortified foods.

A possible measure would be to provide information on obtaining extra vitamin D from supplements or fortified foods. The present information policy on the use of vitamin D supplements reaches children, adults with a non-Western background or people who do not spend enough time outdoors, women who wear a veil, pregnant or breastfeeding women and elderly people insufficiently and is unclear, with the exception of that for young children.

Fortified foods can supply part of the extra requirement and thereby provide a basic level of vitamin D intake. In contrast to the present fortification policy, fortification of a small number of staple foods, such as milk, milk substitutes and oil would offer the advantage that it would cover all risk groups.

An alternative would be restoration of milk products and cheese. Scenario calculations indicate that the effects of restoration on intake would be minimal and that restoration is therefore not a serious option.

7.6 **Conclusion**

There are three sources of vitamin D: production by the skin during exposure to ultraviolet radiation, intake from foods and intake from supplements. Spending

* According to the Guidelines for a Healthy Diet published by the Netherlands Nutrition Centre.

at least 15 minutes a day outside during the day between April and October can improve vitamin D status. However, some people cannot go outdoors and others wear clothing that covers the entire body, thereby cancelling out or reducing the effect of ultraviolet radiation on vitamin D status.

A healthy diet* can also improve vitamin D intake. On its own, a healthy diet is not sufficient for vulnerable groups. They need extra vitamin D from supplements or fortified foods.

A possible measure would be to provide information on obtaining extra vitamin D from supplements or fortified foods. The present information policy on the use of vitamin D supplements reaches children, adults with a non-Western background or people who do not spend enough time outdoors, women who wear a veil, pregnant or breastfeeding women and elderly people insufficiently and is unclear with regard to the last three groups.

Fortified foods can supply part of the extra requirement and thereby provide a basic level of vitamin D intake. In contrast to the present fortification policy, fortification of a small number of staple food groups, such as milk, milk substitutes and oil would offer the advantage that it would cover all risk groups.

Regardless of the measure that is finally chosen, it is important to monitor vitamin D intake and vitamin D status.

* According to the Guidelines for a Healthy Diet published by the Netherlands Nutrition Centre.

Conclusions and recommendations

8.1 Conclusions

8.1.1 *Recent scientific insights*

Women from the age of 50 and men from the age of 70 need a serum calcidiol level of at least 50 nmol per litre

Since the publication of the dietary reference values for vitamin D in 2000, new scientific insights have indicated that the amount of serum calcidiol should be at least 50 nmol per litre* in women from the age of 50, to ensure good bone density and to reduce the risk of falls or fractures. The figure that the Health Council used for this group in 2000 was 30 nmol per litre.

Studies show that extra vitamin D and calcium reduce the risk of fractures and possibly also counteract bone loss and reduce the risk of falls. In the studies in which a protective effect was found for the risk of fractures, the vitamin D dose varied from 10 to 20 micrograms per day and, following supplementation with these doses, the average serum calcidiol level varied from 74 to 112 nmol per litre. The average serum calcidiol level for maintaining bone density and reducing the risk of falls was 35 to 67 nmol per litre.

* This is a minimum level at the individual level, which means that 97.5 per cent of the population ought to have a calcidiol level of at least 30 or 50 nmol per litre.

Protective effects were only found for vitamin D in combination with calcium. However there are indications that bone loss in elderly people is counteracted when vitamin D is taken without extra calcium, provided calcium intake is in line with the dietary reference values. The Committee assumes on the basis of this that, for an adequate calcium intake, extra vitamin D would also have a positive effect on the risk of falls and fractures, without extra calcium being taken.

Studies mainly concerned light-skinned, post-menopausal women from the age of 70 and the effect was greatest for women not living independently. Because the decrease in bone density accelerates in women around the time of the menopause, the Committee believes they would benefit from a higher serum calcidiol level from the age of 50, although no proper study of this has been conducted. The Committee assumes that such a serum calcidiol level would also have a protective effect for dark-skinned women from the age of 50, although this has not been studied in sufficient depth.

The Committee also anticipates that men from the age of 70 would benefit from extra vitamin D. The limited research results that are available suggest that the effects of extra vitamin D in older men are comparable with those for older women. Because men do not experience menopausal changes, the Committee sees no reason to reduce the age limit from 70 to 50.

The target value is not being increased for younger age groups because doing so has not been shown to provide any clinical advantage. However, there are suggestions that current dietary reference values are on the low side.

In determining this level, the Committee did not take into account any relationship between the serum calcidiol level and the risk of internal types of cancer, auto-immune diseases, tuberculosis, diabetes type 2 and cardiovascular diseases because the indications for any such relationship currently lack strength.

Vulnerable groups need extra vitamin D from supplements or fortified foods

A section of the population needs so much extra vitamin D that it cannot all be obtained through a healthy diet in accordance with the Guidelines for a Healthy Diet. The Committee also believes that some of the current recommended levels for extra vitamin D intake from supplements or fortified foods are too low. It advises the following targets:

- an additional 10 micrograms of vitamin D a day for:
 - children aged up to 4 years*,
 - people between 4 and 50 who have dark skin, or who do not spend enough time outdoors,
 - women aged up to 50 who wear a veil,
 - women who are pregnant or are breastfeeding, and
 - people aged over 50 (women) or 70 (men) who have light skin and who spend enough time outdoors.
- an additional 20 micrograms of vitamin D a day for:
 - people with osteoporosis or who live in a care home or nursing home,
 - people from the age of 50 (females) or 70 (males) who have dark skin or do not spend enough time outdoors, and
 - women from the age of 50 who wear a veil.

8.1.2 *Present vitamin D intake*

An inadequate vitamin D status is common

An inadequate vitamin D status is common in summer as well as winter in people from the age of 50 and especially residents of care homes and nursing homes, dark-skinned people, women who wear a veil or are pregnant and people with a vegan or macrobiotic diet. This probably also applies to breastfeeding women, although no data are available for this group. Children up to the age of 4 who do not receive follow-on formula or a vitamin D supplement also run the risk of their vitamin D supply being too low. Some light-skinned people also appear to have an inadequate vitamin D supply at the end of winter. Figures from countries close to the Netherlands indicate that at the end of the winter around 10 to more than 30 per cent of light-skinned people in the population have an inadequate vitamin D status.

Dietary habits affect vitamin D status

The greatest contribution to vitamin D intake among adults comes from the product group comprising fats/oil/savoury sauces, whereby it should be noted that oil does not contain vitamin D. Margarine and low-fat margarine intake is lower among people of Turkish or Moroccan extraction than among people with a

* This advice does not apply to children consuming more than half a litre of infant formula or follow-on formula a day.

Dutch background. People with a non-Western background also have a lower calcium intake, which probably increases the vitamin D requirement.

Use of vitamin D supplements is not optimal

The number of children who receive no extra vitamin D in the form of a vitamin D supplement or follow-on formula increases from around 4 per cent at the age of 12 months to around 40 per cent at the age of four. More mothers with a Western background give their children vitamin D supplements than do those with a non-Western background. Women with a Western background also make greater use of vitamin D supplements during pregnancy.

Around 30 per cent of adults and elderly people living independently take a dietary supplement containing vitamin D. The percentage of users is lower among people with a Turkish or Moroccan background and probably also among residents of care homes and nursing homes.

8.1.3 *Effects of Dutch policy measures*

Information on vitamin D is unclear

There is a lack of clarity in the present information policy on the use of vitamin D supplements for children from the age of 4, adults with a non-Western background, women who wear a veil, pregnant or breastfeeding women and elderly people. Various organisations provide different advice on the use of supplements. A positive exception is the provision of advice on supplements for children up to the age of 4.

Moreover, the effect of information on the use of supplements containing vitamin D is uncertain because there is no guarantee that the information will reach all risk groups and be heeded. However, information is partially effective, for example advice to give young children extra vitamin D, especially during the first year of life, is definitely being heeded.

The effect of current food fortification is uncertain

Food fortification is statutorily regulated by means of a temporary exemption. This provides no guarantee that the risk groups will use the products, as similar unfortified products are also available.

8.2 Recommendations

Increase the range of information and ensure that the message is consistent

The Committee believes that the information on the use of extra vitamin D is unclear. It is important that the various official bodies involved in providing information on boosting vitamin D intake through supplementation or fortified foods should give the same advice.

Preconception care units and child healthcare centres could be involved in recommending additional vitamin D intake during pregnancy and breastfeeding.

Stress the importance of spending time outdoors

The Committee recommends spending at least 15 minutes a day outdoors for vitamin D production in the body. Exposure of at least the head and hands would be sufficient. The Committee believes that this should not be stressed in the information because a short period of exposure of larger areas of the body, such as the arms and legs, produces a larger amount of vitamin D. However it should also be ensured that people avoid getting sunburnt. Instructions on sensible sunbathing could also be followed, such as those published by the Dutch Cancer Society within the scope of preventing skin cancer. An update to these instructions will be published later this year.

Going outdoors only generates vitamin D between April and October. In the winter, the intensity of the required ultraviolet radiation that reaches the earth's surface is insufficient and people rely on the physical reserve of vitamin D they have built up over the summer, in combination with intake of vitamin D.

Also indicate the importance of additional intake from foods or supplements

The Committee believes that a large section of the population needs extra vitamin D from foods or supplements. According to the Guidelines for a Healthy Diet, a healthy diet should provide enough vitamin D (and calcium) for people aged between four and 50 (women) or 70 (men) with light skin who spend enough time outdoors. All other groups need additional vitamin D from supplements.

People who do not take supplements would benefit from eating foods fortified with vitamin D, but very few such foods are currently available. Even if there were more of these foods on the market, their consumption could not provide all the extra vitamin D required.

Preventing excessively high vitamin D intake is of utmost importance

The Committee emphasises that it is essential for vitamin D intake to remain below the tolerable upper intake level when people are taking supplements and/or eating fortified foods. Dietary supplements that contain more than the aforementioned vitamin D quantities in a daily ration must be taken with caution.

Children are at the greatest risk of exceeding the tolerable upper intake level. The limit for children has been derived from that for infants and adults because very little research has been conducted into the possible health risks of excessive doses of vitamin D in this group. Studies of infants and adults indicate that an excessively high vitamin D intake leads to health complaints as a result of an excessive calcium level in the blood and urine and, in the long term, to excessive calcium deposits in soft tissue, such as the kidneys and blood vessels. These disorders definitely constitute a risk for children.

Monitor the effect of policy measures

The Committee recommends monitoring dietary vitamin D intake and the vitamin D status of the Dutch population in general and high-risk groups in particular.

To this end, the composition of fortified foods should be registered. At the moment it is not known precisely which foods are fortified with vitamin D and how much they contain. When fortification with vitamin D was exempted, it was assumed that up to 15 per cent of energy intake came from fortified foods. If registration reveals that this level is being exceeded, it will be necessary to review the exemption policy with regard to the exemption level and the permitted products. The composition and use of supplements are registered.

At the European level, restrict the type of food that may be fortified

Vitamin D can be added to any product without restriction under present legislation. However, there is no guarantee that risk groups will use the products. The Committee therefore believes it would be advisable to only permit vitamin D to be added to a small number of staple food groups that are used by the risk groups

specifically. It therefore recommends maintaining the present addition of vitamin D to margarine, low-fat margarine and products used in baking and frying. The Committee believes it would also be advisable to limit the types of foods that may be fortified with vitamin D to milk, milk substitutes (10 micrograms of vitamin D per litre) and oil (4.5 micrograms of vitamin D per 100 kilocalories). This would have to be regulated at the European level.

Encourage research into the effect of vitamin D intake and spending time outdoors

The Committee also recommends further research into the effect of vitamin D intake on the serum calcidiol level, whether or not in combination with the effect of spending time outdoors. This should involve studies of people with different skin types and of different ages. It would also be advisable to study how much time needs to be spent outdoors and the required intensity of sunlight for vitamin D production for different skin types, and to assess this against the risk of skin cancer.

Evaluate the dietary reference values for vitamin D

The Committee recommends an evaluation of the dietary reference values for vitamin D. There are indications that the present standards are not sufficient to guarantee that women from the age of 50 maintain a serum calcidiol level of at least 50 nmol per litre throughout the year. Likewise, there are suggestions that the standards are also not sufficient to maintain a serum calcidiol level of at least 30 nmol per litre in other groups.

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- A Request for advice
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- B Additional request
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- C The committee
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- D Assessment of methodological quality and level of evidence
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- E Working conference participants
-
- F Scenario calculations for the fortification of oil, milk and milk products with vitamin D
-
- G Fortification
-
- H Definitions

Annexes

Request for advice

Date of request: 26 January 2006

Letter reference: VGP/VV 2646726

It is important for public health that the population has an adequate supply of essential micronutrients. We know that a habitual diet does not contain enough of some of these essential micronutrients to meet the needs of (certain groups of) the population. The Ministry of Health, Welfare and Sport therefore follows an active policy with regard to these essential micronutrients. This policy covers both the use of supplements (vitamin D for young children, folic acid for pregnant women and women who want to have a baby) and fortification of foodstuffs. The addition of vitamins A and D to margarine, butter, and oil is permitted and encouraged under the Agreement on the vitamin fortification of spreadable fats. The addition of iodine to table salt (and alternative products), bread and bread substitutes (via salt used in breadmaking) and meat products (via nitrite pickle) is also permitted.

On the other hand it is important to ensure that people do not consume too much of certain essential micronutrients, as this could be harmful to health. That is why foodstuffs cannot in principle be fortified with essential micronutrients that have a 'narrow margin'. The micronutrients in question are vitamin A, vitamin D, folic acid, selenium, copper and zinc. A 'narrow margin' in this context means that the recommended dietary allowance (RDA) and the safe upper level of intake are relatively close to one another, which means that people can easily run the risk of consuming too much of a certain vitamin, mineral or trace element. The addition of iodine to foodstuffs is prohibited for the same reason. There are however exceptions to these rules: iodine can be added to salt (used in breadmaking

and preparing meat products) and vitamins A and D can be added to spreadable fats. Controlled additions seek to ensure that consumers do not ingest too much or too little. As far as the other essential micronutrients that do not have a narrow margin are concerned, fortification of foodstuffs is permitted up to 100% of the recommended dietary allowance per daily intake.

Three developments are taking place at the moment leading to a need to review micronutrient policy. They are set out below.

Following the judgement of the Court (2 December 2004, EC Commission v. Netherlands, C-41 102), the Netherlands has had to give up its absolute ban on fortification with substances such as folic acid. Requests for exemption from the ban on adding micronutrients can only be rejected if it can be demonstrated that placing the specific product on the market would endanger public health. According to the Court's judgement, the absence of a nutritional need for the fortification of foodstuffs, which has in the past been an important argument used by the Netherlands in rejecting requests for exemption, no longer constitutes adequate grounds. The EU regulation on voluntary fortification of foodstuffs with vitamins, minerals and some other substances will take effect in the course of the next year or two. Policy on the fortification of foodstuffs with micronutrients will then be harmonised throughout the EU. This regulation will set minimum and maximum amounts of vitamins and minerals that can be added. The same procedure will be carried out for dietary supplements in order to minimise the risk of overdoses of micronutrients by people consuming fortified foodstuffs and taking dietary supplements. It is true that the regulation deals with voluntary fortification and therefore by definition does not resolve the problem of possible deficits in the supply of essential micronutrients. But the regulation does allow EU member states to continue or introduce mandatory fortification of foodstuffs if this is necessary on public health grounds. The question is whether the Netherlands should maintain its current system of voluntary fortification of spreadable fats with vitamins A and D and the fortification of table salt, salt used in breadmaking and nitrite pickle with iodine or whether it should move to a system of mandatory fortification. Another point is that science is producing new findings. Increasingly, researchers are discovering that the health benefits of a supply of certain micronutrients at levels (far) above the current dietary reference values. As this might also lead to a risk of excessive intake, which needs to be considered in the light of the other effects, the Ministry's policy could be based on a risk-benefit analysis. Risk-benefit analysis models are being devised. One example is the role that folic acid is thought to play in preventing cardiovascular diseases. The United States has examined the advantages and disadvantages of extra folic acid supply and has decided to introduce mandatory fortification of flour (for use in bread making and other applications). Ireland and the United Kingdom are currently considering whether to follow suit.

The challenge facing me is to devise a policy, within the context of the new European regulation, under which the largest possible proportion of the population will receive sufficient essential

micronutrients while the smallest possible proportion of the population will run the risk of consuming more than the safe upper level of intake.

In the light of this, I am asking the Health Council to address the questions set out below.

For what essential micronutrients for which dietary reference values have been established in the Netherlands and in what situation does the habitual diet not offer sufficient guarantees that the population, or groups of the population, will have an adequate supply? Please use food consumption data, nutritional status data and other relevant scientific information when addressing this issue. What is the best way of ensuring an adequate supply of essential micronutrients in these situations? The Council is requested to look at all available policy instruments for each essential nutrient in its deliberations. What might the health benefits of an active fortification policy (whether with mandatory fortification or not) be for (groups of) our population in the light of a risk-benefit analysis for essential micronutrients such as folic acid and vitamin D (and any other relevant vitamins and/or minerals)?

I would very much appreciate receiving your advisory report around the middle of 2007.

(signed)

The Minister for Health, Welfare and Sport

H. Hoogervorst

Additional questions

Date of request: 17 July 2006

Letter reference: VGP/VV 2700094

Dear Professor Knottnerus,

In January 2006, I requested that you draft an advisory report on essential micronutrients (advisory report request VGPIVV 2646726). At the time, in outlining the request, I mentioned various points for attention. Following a question in parliament* concerning vitamin D deficiencies in specific sections of the population in the Netherlands, I now request you to pay particular attention in the aforementioned advisory report to the vitamin D intake of pregnant women and people with a non-Western background.

I trust I have provided you with sufficient information.

The Director-General of Public Health,

J.I.M. de Goeij, M.Sc.

* See annex 1: parliamentary question 2050609210 concerning severe vitamin D deficiency of people with a non-Western background.

Annex 1

Answers to parliamentary questions from Arib (PvdA) on severe vitamin D deficiency of people with a non-Western background (2050609210).

1.

Have you read the article on the severe vitamin D deficiency of people with a non-Western background? 1)

1.

Yes

2.

What is your opinion of the article, which states that half of pregnant women with non-Western backgrounds in the Netherlands and their offspring have a severe vitamin D deficiency? What do you think of the fact that 10% of women with a Dutch background and their offspring had a vitamin D deficiency?

2.

The article concerns a fairly small random sample of Dutch/European and non-Western pregnant women. However, the results of this study conducted in Amersfoort display similarities with a previous study of an midwifery practice in The Hague. As a result of these studies amongst others, a random survey is currently underway of the prevalence of vitamin D deficiency. The aim of these more extensive studies is to achieve a better insight into the factors that have the greatest effect on the occurrence of vitamin D deficiency. The studies are also looking at different ethnic groups separately. The study results are expected this year. Other research has indicated that men and non-pregnant women with a non-Western background are more likely to have a vitamin D deficiency. This is connected with factors that affect vitamin D status, such as skin colour, amount of exposure of uncovered skin to sunlight and dietary patterns. A vitamin D supply below the recommended level has been brought to my attention and needs to be further studied (see the following questions).

3.

Were you aware that a previous study in The Hague of 240 pregnant women also demonstrated similar low vitamin D levels? If so, what did you do with the findings of the study? 2)

3.

Yes, see question 2.

My nutritional policy is based on the Guidelines for a Healthy Diet and the Health Council's dietary reference values (including those pertaining to vitamin D).

New information has recently emerged from studies. This information makes it necessary to review the micronutrients policy. I have requested an advisory report from the Health Council on, amongst other things, which essential micronutrients, such as vitamin D, according to a risk-benefit analysis, would provide health benefits in the event of adopting an active fortification policy, possibly with mandatory addition of nutrients. I also request the Health Council to consider groups of the popula-

tion. In a supplementary letter, I shall specifically refer to pregnant women and groups of the population with a non-Western background as a point for attention in connection with this.

Information on vitamin D intake is currently disseminated via various information media. On its website the Netherlands Nutrition Centre recommends extra vitamin D for certain groups, including children aged 0-4 and pregnant women. The importance of an adequate vitamin D supply is also regularly stressed in news bulletins and other reports on the website and in publications such as the vitamin guide. Within the scope of the folic acid campaign, which is being conducted in cooperation with Erfocentrum (Dutch national genetic resource and information centre) and with funding from the Ministry of Health, Welfare and Sport, a brochure published by the Netherlands Nutrition Centre specifically refers to the use of vitamin D during pregnancy. The brochure specifically targets women from ethnic minorities and women with a low level of education. As part of the same project, to encourage women in ethnic minorities and women with a low socio-economic status to take folic acid, pilots are currently underway in which midwives are actively attempting to provide the women concerned with information via their practices and networks. If the pilots produce good results, I shall certainly be examining the possibility of including information on vitamin D intake in this initiative. Various initiatives are underway at the local level, such as one in which midwifery practices in Amsterdam involve information officials of VETC (which produces information for specific language and cultural groups) to improve communication with women of non-Western background. Pre-conception healthcare is also scheduled to start soon in Amsterdam with the aim of informing women about measures they can take to have a healthy pregnancy, and to aid early identification of women with an increased risk of problems during pregnancy.

Finally, advice on supplements, including vitamin D, for children aged 0-4 already has a firm place in dietary advice provided in child healthcare through child healthcare centres.

4.

What is your opinion of the finding of epidemiological studies that it is likely that a low vitamin D level is one of the factors contributing to the existence of disorders with a long latency period, such as osteoporosis, diabetes mellitus type I, multiple sclerosis, cardiovascular diseases, and prostate, breast and colorectal cancers?

4.

The dietary reference values for vitamin D published by the Health Council in 2000 for the population of the Netherlands had the aim of establishing peak bone mass by the age of 30 and thereafter to delay bone deterioration for as long as possible. At the time of drafting the dietary reference values (2000) there were few indications that vitamin D might have a protective effect against diseases. A recent literature review by the National Institute of Public Health and Environmental Protection, RIVM, has also shown that evidence is only convincing for osteoporosis that a low vitamin D status in men and women older than 50-60 is associated with a higher risk of fractures. The Health Council's advisory report referred to in question 3 will therefore also examine the relationship between vitamin D and various diseases. The Health Council will conduct a risk-benefit analysis taking into

account the achievable health benefits and any adverse effects. This will form the basis for determining the advisable intake for various population groups.

5.

Did you know that it has been scientifically demonstrated 3) that vitamin D deficiency in the last trimester of pregnancy adversely affects bone development in the child? If so, what action did you take in the light of this knowledge? How did you translate the knowledge into your policy on disease prevention in respect of pregnant women?

5.

I am aware of a recent publication in the Lancet concerning a study that showed a definite link between vitamin D status during pregnancy and the bone mass of children aged 9.

I am not aware of what the effect of supplements, as recommended in the Netherlands for children aged 0-4, would be on the child's bone mass at a later age.

Further, see answers to questions 2 and 3.

6.

Why have Devaron tablets, 400 E, and depot injections silently been withdrawn from pharmacies?

6.

The 400 E (10 ug) Devaron tablets and the depot injections (Neo-Dohyfral D3) were withdrawn from the market for economic reasons by the manufacturers concerned. Devaron tablets were mainly used in the indication (prevention of) osteoporosis (brittle bone disease). Sales declined sharply with the arrival of combination preparations that contained calcium and Devaron.

7.

Can you remember the Health Council's advisory report of 2000 4) on dietary reference values?

What did you do with the recommendations made in the advisory report? Could you indicate exactly how you have encouraged vitamin D use in the vulnerable groups?

7.

Further, see my answers to questions 2 and 3.

Elderly people (male and female) may have an increased risk of vitamin D deficiency because reduced mobility prevents some elderly people from going outdoors and because the skin of elderly people is less capable of producing vitamin D when exposed to sunlight. The group is also specifically mentioned in the information produced by the Netherlands Nutrition Centre. Spreadable fats and products used for baking and frying can be fortified with vitamin A and D. Furthermore, the Commodities Act Exemption for Vitamin Preparations has been amended following the Health Council's report. Vitamin preparations containing a higher amount of vitamin D may now be marketed for consumption by people aged 60 and older. This was already possible for children up to the age of 6, pregnant women and breastfeeding women. It may also be clearly stated on the packaging that the product is suitable for people aged 60 and older.

Following the Health Council's advisory report, a number of requests for knowledge were also submitted to RIVM (Ministry of Health, Welfare and Sports, project V/340230: status determination for folate and micronutrients). This concerns research into the vitamin D status of 4,400 pregnant women from various ethnic groups and a status determination of, amongst other things, vitamin D among 1,400 people from various ethnic groups. The results of this will be published before the end of the year.

The results will be included in the review of the vitamin D fortification policy. Following the publication of the Health Council's report on dietary reference values, it was discussed and the possibility was considered of granting permission for the fortification of various products, in addition to spreadable fats and fats used in baking and frying. No priority was stated at the time in connection with scheduled European regulations on the subject. While awaiting the European regulations and the requested advisory report, I have no plans for any voluntary or compulsory fortification of additional products.

The subject has my attention and I will take the appropriate measures in due course.

8.

What specifically will you be doing to motivate general practitioners to take this problem more seriously and actively provide information in their guidance, especially of risk groups, such as pregnant women with a non-Western background, and to enable vitamin D supplements to be provided? Would you be willing to arrange for the Dutch College of General Practitioners to draw up clear guidelines to encourage the use of vitamin D?

8.

See also questions 3 and 7.

I see general practitioners, midwives and gynaecologists as important links in the information chain concerned with pregnancy.

I am therefore eager to hear the response of the Dutch College of General Practitioners (NHG), the Royal Dutch Organisation of Obstetricians (KNOV) and the Dutch Society for Obstetrics and Gynaecology (NVOG) to recent developments (including the article by Wielders of 4 March 2006 in NTVG) and I expect to be able to read their response soon in *Nederlands Tijdschrift voor Geneeskunde* (NTvG).

A request has been submitted to the Health Council for an advisory report on preconception care. The Council will examine whether it would be advisable to integrate preconception care in pregnancy healthcare and child healthcare centres. I look forward to receiving the results and to see whether they jointly lead to a good proposal for information for ensuring vitamin D intake, amongst other things, during pregnancy. My assessment will also include the results of the requests to RIVM for knowledge (see question 7) and other more detailed studies (see question 2). Reports on this will also include information on the determinants of a vitamin D deficiency and on why, for example, women from ethnic minorities do not take supplements during pregnancy.

- 1) Nederlands Tijdschrift voor Geneeskunde, 4 March last. 150 (9).
- 2) Karamali NS, Meer IM van der, Wuister JD, Verhoeven I. Vitamine D-tekort bij zwangere vrouwen: gegevens van een verloskundigenpraktijk uit Den Haag. Epidemiological Bulletin 2004;39:10-4.
- 3) See note 1
- 4) Dietary reference values: calcium, vitamin D, thiamine, riboflavin, niacin, pantothenic acid and biotin. The Hague: Health Council of the Netherlands; 2000.

The committee

-
- Professor G. Schaafsma, *chairman*
Emeritus Professor of Food and Nutrition, Wageningen University / Former director food and health, TNO Quality of Life, Zeist
 - Dr. H. van den Berg
Nutritional expert, Nutrition Centre, The Hague
 - E.N. Blok, *advisor*
Ministry of Health, Welfare and Sport, The Hague
 - Dr. H.J. Blom
Clinical biochemic geneticist, Free University Medical Centre, Amsterdam
 - Professor C.P.G.M. de Groot
Professor of Nutritional Physiology, with a particular focus on the ageing process and elderly people, Wageningen University
 - Dr. M. den Heijer
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 - Professor I.M.C.M. Rietjens
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 - Professor P.J.J. Sauer
Professor of Paediatric Medicine, University of Groningen
-

- Professor P. van 't Veer
Professor of Nutrition and Epidemiology, Wageningen University
- Dr. T. Vulsma
Paediatrician and endocrinologist, Amsterdam University Medical Centre
- Dr. R.M. Weggemans, *scientific secretary*
Health Council, The Hague

The Health Council and interests

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

D

**Assessment of methodological quality
and level of evidence**

In view of the large number of subjects to be examined, the committee decided to select publications with short search actions. They were assessed on the basis of the approach used when drawing up the *Guidelines for a Healthy Diet 2006*.¹⁹ However, the approach is presented more clearly in this advisory report as it incorporates tables in which the conclusions are classified according to their level of evidence, with a reference to the studies on which the classification is based. This is largely in line with the approach used when developing the evidence-based guideline.²⁴⁰ Another feature of the approach taken in this advisory report is that it uses the SIGN grading system, granting the highest level of evidence (A1) only to systematic review articles of good quality.²⁴¹

The aim of the assessment system used is to determine relationships between factors. It is not, or only to a very limited extent, to assess data on the folate supply of the Dutch population or the effects of current Dutch policy, and therefore was not applied to those subjects.

Table D.1 Grades of methodological quality used to classify individual studies into interventions with folic acid or the relationship between folate intake or status and the risk of various conditions.^{240,241}

Grade	Type of study
A1	Systematic review articles of good quality relating to at least two grade A2 studies conducted independently of one another.
A2	Randomised, double-blind, comparative intervention study of good quality and sufficient size.
B1	Systematic review articles of good quality relating to at least two grade B2 studies conducted independently of one another.
B2	Comparative studies, but without all the features referred to under A2 or good-quality cohort studies or patient case studies.
C	Non-comparative studies.
D	Opinion of the committee.

Table D.2 Level of evidence of conclusions.^{19,240}

Level	
1: Convincing	Based on 1 systematic review article (grade A1) or at least 2 grade A2 studies carried out independently of one another.
2: Probable	Based on 1 review article (grade B1) or at least 2 grade B2 studies carried out independently of one another.
3: Insufficient	Based on 1 grade A2 or B2 study or on grade C research.
4: Insufficient	Based on the committee's opinion (grade D).

Working conference participants

The working conference was held on 5 March 2008 and was chaired by Professor D. Kromhout, Vice-President of the Health Council, with secretarial support from Dr. R.M. Weggemans, scientific secretary to the Health Council.

Invitees

- Dr. A.M. Boot
Paediatrician and endocrinologist, Groningen University Medical Centre
- Professor R. Bouillon
Professor of Endocrinology, Catholic University Leuven, Belgium
- Dr. H.J.J. Verhaar
Internist and geriatrician, Utrecht University Medical Centre
- Professor M. Visser
Professor of Healthy Ageing, Free University of Amsterdam
- Professor B.J.C. Middelkoop
Professor of Public Health, Leiden University Medical Centre
- Members of the Committee on Micronutrients (see annex C).

F

Scenario calculations for the fortification of oil, milk and milk products with vitamin D

Table F.1 Habitual daily intake of vitamin D in micrograms when no fortified foods are used.^{a,211}

	P5	P10	P50	P90	P95
Children aged 1-3	0.8	1.0	1.9	3.8	4.9
Children aged 4-6	1.1	1.4	2.3	3.4	3.8
Boys aged 7-10	1.6	1.8	3.0	4.5	5.1
Girls aged 7-10	1.5	1.7	2.7	4.0	4.4
Boys aged 11-17	2.1	2.5	4.2	6.7	7.7
Girls aged 11-17	1.6	1.9	3.2	5.2	6.1
Men aged 18-49	2.3	2.7	4.6	7.5	8.6
Women aged 18-49	1.6	1.9	3.2	5.2	5.9
Men aged 50-59	2.2	2.6	4.8	9.1	11.1
Women aged 50-59	1.5	1.8	3.3	5.8	6.9
Men aged 60-69	2.3	2.7	4.8	8.4	10.0
Women aged 60-69	1.7	2.0	3.3	5.4	6.3
Men aged 70+	2.4	2.8	5.0	9.6	11.9
Women aged 70+	1.7	2.0	3.7	7.1	8.8

^a Intake is exclusive of intake of vitamin D from supplements.

Table F.2 Habitual daily intake of vitamin D in micrograms for oil (excluding frying oil) fortified with 4.5 micrograms of vitamin D per 100 kcal.^{a, 211}

	P5	P10	P50	P90	P95
Children aged 1-3	1.0	1.2	2.2	4.2	5.2
Children aged 4-6	1.4	1.7	2.6	3.9	4.4
Boys aged 7-10	1.8	2.1	3.3	5.1	5.8
Girls aged 7-10	1.9	2.1	3.2	4.6	5.2
Boys aged 11-17	2.4	2.8	4.6	7.6	8.8
Girls aged 11-17	1.9	2.2	3.5	5.6	6.5
Men aged 18-49	3.1	3.5	5.4	8.4	9.5
Women aged 18-49	2.2	2.5	4.0	6.3	7.1
Men aged 50-59	2.7	3.2	5.8	10.9	13.3
Women aged 50-59	2.0	2.4	4.1	7.1	8.3
Men aged 60-69	3.2	3.7	5.6	8.7	9.8
Women aged 60-69	2.1	2.4	3.8	6.1	7.1
Men aged 70+	2.8	3.3	5.7	10.7	13.0
Women aged 70+	2.0	2.4	4.3	8.0	9.6

^a Intake is exclusive of intake of vitamin D from supplements.

Table F.3 Habitual daily intake of vitamin D in micrograms for milk and milk substitutes fortified with 4.5 micrograms of vitamin D per 100 kcal.^{a, b, 211}

	P5	P10	P50	P90	P95
Children aged 1-3	6.4	7.7	13.2	20.0	22.2
Children aged 4-6	5.5	7.1	13.3	21.0	23.5
Boys aged 7-10	5.0	6.7	13.4	22.2	25.2
Girls aged 7-10	6.8	8.1	13.3	19.3	21.1
Boys aged 11-17	5.3	6.7	13.8	22.7	25.7
Girls aged 11-17	4.0	5.2	11.0	19.2	22.0
Men aged 18-49	4.1	5.2	10.6	19.3	22.4
Women aged 18-49	3.5	4.5	9.1	15.6	17.8
Men aged 50-59	4.2	5.2	10.5	19.0	22.2
Women aged 50-59	3.1	4.0	8.6	15.3	17.7
Men aged 60-69	4.5	5.6	10.6	17.3	19.6
Women aged 60-69	3.8	4.8	9.4	16.3	18.7
Men aged 70+	3.9	5.1	10.9	19.9	23.1
Women aged 70+	3.9	5.0	10.0	17.4	20.1

^a Intake is exclusive of intake of vitamin D from supplements.

^b Milk and milk substitutes include milk, milky drinks, yoghurt (including fruit-containing yoghurt), yoghurt drinks, soya milk and soya drinks.

Table F.4 Habitual daily intake of vitamin D in micrograms for milk and milk substitutes fortified with 10 micrograms of vitamin D per litre.^{a, b, 211}

	P5	P10	P50	P90	P95
Children aged 1-3	3.6	4.2	6.7	9.7	10.8
Children aged 4-6	3.2	3.9	6.8	10.2	11.2
Boys aged 7-10	3.5	4.3	7.4	11.0	12.1
Girls aged 7-10	4.3	4.9	7.1	9.6	10.3
Boys aged 11-17	4.0	4.8	8.2	12.6	14.2
Girls aged 11-17	3.0	3.7	6.5	10.4	11.8
Men aged 18-49	3.5	4.2	7.4	11.9	13.6
Women aged 18-49	2.8	3.4	6.0	9.3	10.5
Men aged 50-59	3.6	4.3	7.5	12.7	14.9
Women aged 50-59	2.7	3.3	6.0	9.8	11.3
Men aged 60-69	3.8	4.6	7.7	12.1	13.8
Women aged 60-69	3.3	3.9	6.4	9.9	11.2
Men aged 70+	3.6	4.4	7.9	13.7	16.2
Women aged 70+	3.2	3.9	6.8	11.3	13.3

^a Intake is exclusive of intake of vitamin D from supplements.

^b Milk and milk substitutes include milk, milky drinks, yoghurt (including yoghurt containing fruit), yoghurt drinks, soya milk and soya drinks.

Table F.5 Habitual daily intake of vitamin D in micrograms for milk, milk substitutes and desserts fortified with 10 micrograms of vitamin D per litre.^{a, b, 211}

	P5	P10	P50	P90	P95
Children aged 1-3	4.1	4.8	7.2	10.1	11.1
Children aged 4-6	3.4	4.2	7.2	10.6	11.6
Boys aged 7-10	3.9	4.7	7.9	11.4	12.5
Girls aged 7-10	4.5	5.1	7.6	10.3	11.1
Boys aged 11-17	4.5	5.3	8.8	13.2	14.8
Girls aged 11-17	3.1	3.9	6.9	11.0	12.5
Men aged 18-49	3.7	4.5	7.8	12.5	14.2
Women aged 18-49	3.0	3.6	6.2	9.7	10.9
Men aged 50-59	3.8	4.6	8.0	13.6	15.9
Women aged 50-59	2.8	3.5	6.2	10.2	11.7
Men aged 60-69	4.1	4.9	8.2	12.7	14.4
Women aged 60-69	3.7	4.3	6.8	10.2	11.5
Men aged 70+	3.9	4.7	8.3	14.2	16.7
Women aged 70+	3.5	4.2	7.1	11.6	13.6

^a Intake is exclusive of intake of vitamin D from supplements.

^b Milk and milk substitutes include milk, milky drinks, yoghurt (including yoghurt containing fruit), yoghurt drinks, soya milk and soya drinks, and desserts including custard, soft curd cheese, pudding, mousse and soya-based desserts.

Table F.6 Habitual daily intake of vitamin D in micrograms for milk and milk substitutes fortified with 10 micrograms of vitamin D per litre and oil with 4.5 micrograms of vitamin D per 100 kilocalories.^{a,b,211}

	P5	P10	P50	P90	P95
Children aged 1-3	3.7	4.3	6.9	10.2	11.3
Children aged 4-6	3.7	4.4	7.1	10.4	11.4
Boys aged 7-10	3.9	4.7	7.8	11.4	12.5
Girls aged 7-10	4.6	5.2	7.6	10.3	11.2
Boys aged 11-17	4.3	5.1	8.6	13.5	15.3
Girls aged 11-17	3.3	4.0	6.8	10.8	12.2
Men aged 18-49	4.4	5.1	8.3	12.7	14.3
Women aged 18-49	3.5	4.1	6.8	10.4	11.7
Men aged 50-59	4.0	4.8	8.5	14.7	17.3
Women aged 50-59	3.2	3.9	6.8	11.0	12.7
Men aged 60-69	4.4	5.2	8.3	12.8	14.5
Women aged 60-69	3.8	4.4	6.9	10.4	11.7
Men aged 70+	4.1	4.9	8.6	14.7	17.3
Women aged 70+	3.7	4.4	7.3	11.9	13.9

^a Intake is exclusive intake of vitamin D from supplements.

^b Milk and milk substitutes include milk, milky drinks, yoghurt (including yoghurt containing fruit), yoghurt drinks, soya milk and soya drinks, and desserts including custard, soft curd cheese, pudding, mousse and soya-based desserts.

Fortification

A distinction is made in the advisory report between fortification of specific foods and a small number of staple food groups. This is a somewhat artificial approach because manufacturers can opt (and have opted) to fortify staple foods with vitamin D.

Fortification of specific foods

In the current practice of fortifying specific foods, manufacturers add micronutrients to their own products but non-fortified products are also available in the product category. There is therefore no guarantee of reaching everyone with this type of fortification.

Fortification of staple food groups

Fortification of a small number of staple food groups guarantees that almost everyone will be reached because vitamin D will have been added to practically every product in the category concerned. This type of fortification can meet the requirements of a section of the population, if total daily intake increases to a level of around 7.5 micrograms. Such fortification provides a basic level of the vitamin D intake of vulnerable groups but is not sufficient to meet the entire requirement. This requires supplementation.

However, fortifying staple food groups presents difficulties too. For example, it would be necessary to consider whether the breach of privacy resulting from fortification and substitution under the measure could be justified by the benefits of the measure. This question does not arise when product categories continue to include products that have not been fortified.

The Committee also suggests that fortification of staple food groups such as oil, milk and milk substitutes should be permitted on condition that fortification of specific foods is discontinued. This does not apply to the substitution of margarine, low-fat margarine and products used in baking and frying. It is unlikely that any such discontinuation can be put into effect any time soon, given European Union agreements not to impede free trade. The Committee therefore believes that the government should endeavour to arrange at the European level that vitamin D may only be added to a limited number of staple food groups (margarine, low-fat margarine, products used in baking and frying, oil, milk and milk substitutes).

Definitions

Adequate intake

The lowest level of intake that seems to be adequate for practically the entire population. An adequate intake is estimated if research data is insufficient to allow an average requirement and recommended allowance to be determined.²²

Average requirement

The intake that meets the needs of half the population for a particular nutrient. The recommended dietary allowance is derived from the average requirement, assuming normal distribution of the requirement.²²

Diet

Unless otherwise specified, 'diet' refers to foodstuffs and supplements.

Fortification

Adding one or more micronutrients to a foodstuff, resulting in a concentration higher than that which naturally occurs in the foodstuff or the raw material from which it was made in order to prevent or correct a proven deficit in one or more micronutrients in (parts of) the population.¹⁵

Recommended dietary allowance

The intake that meets the needs of 97.5 per cent of the population for a particular nutrient. It is assumed that this need is distributed normally.²²

Restoration

Adding micronutrients that are lost during the production process, storage and/or sale to foodstuffs. The amount added to the foodstuff restores the level of the micronutrient to the previous concentration in the edible part of the foodstuff or the raw material from which it was made.¹⁵

Safe upper level

Highest level of intake at which no harmful effects are observed or to be expected.²²

Substitution

Replacing a foodstuff with a different foodstuff that is as close as possible to it in terms of appearance, consistency, taste, colour and odour or that serves the same purpose for the consumer.¹⁵

Supplementation

Using a supplement containing micronutrients as an addition to diet.

Threshold method

The threshold method estimates the percentage of people in a population with an intake above or below a particular dietary reference value.