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Dietary Reference Values for thiamin

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Abstract

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) derived Dietary Reference Values (DRVs) for thiamin (vitamin B1). The Panel considers that data from depletion–repletion studies in adults on the amount of dietary thiamin intake associated with erythrocyte transketolase activity coefficient (αETK) < 1.15, generally considered to reflect an adequate thiamin status, or with the restoration of normal (baseline) erythrocyte transketolase activity, without a sharp increase in urinary thiamin excretion, can be used to estimate thiamin requirement. In the absence of new scientific evidence, the Panel endorses the Average Requirement (AR) of 0.072 mg/MJ (0.3 mg/1,000 kcal) for all adults proposed by the Scientific Committee for Food (SCF) in 1993 on the basis of one depletion–repletion study, in which both αETK and urinary thiamin excretion were measured. Results from other depletion–repletion studies are in agreement with this value. The Panel agrees on the coefficient of variation of 20% used by the SCF to cover uncertainties related to distribution of thiamin requirements in the general population, and endorses the Population Reference Intake (PRI) of 0.1 mg/MJ (0.4 mg/1,000 kcal) set by the SCF for all adults. The same AR and PRI as for adults, expressed in mg/MJ, are proposed for infants aged 7 to 11 months, children aged 1 to < 18 years, and during pregnancy and lactation, under the assumption that the relationship between thiamin requirement and energy requirement is the same in all population groups.

Keywords: thiamin, Average Requirement, Population Reference Intake, Dietary Reference Value

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Summary

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver a Scientific Opinion on Dietary Reference Values for the European population, including thiamin (vitamin B1).

Thiamin is a water-soluble vitamin composed of a thiazole and a pyrimidine ring linked by a methylene group. In human tissues thiamin occurs mostly in phosphorylated forms as thiamin monophosphate (TMP), thiamin diphosphate (TDP, called also thiamin pyrophosphate), thiamin triphosphate (TTP), as well as its non-phosphorylated form ("free thiamin"). Free thiamin functions as the precursor for TDP, which acts as coenzyme for enzymes involved in carbohydrate and branched-chain amino acid metabolism, and in energy-yielding reactions. Thiamin deficiency leads to disorders that include several forms of beriberi, with mostly neurological and cardiovascular manifestations.

Thiamin in food exists mainly in phosphorylated forms in animal products, and in free form in foods of plant origin. Upon ingestion, thiamin phosphate esters are hydrolyzed in the intestinal lumen by phosphatases. Free thiamin is taken up through the mucosal membrane by a specific saturable transport system. In healthy subjects, thiamin absorption is above 95% at usual intakes. Alcohol and anti-thiamin factors (such as some phenolic compounds, sulfites and thiaminases) can reduce thiamin bioavailability. Thiamin in blood is mainly found in erythrocytes (> 80% of total thiamin in the blood) in the form of TDP and TTP, while low amounts of the vitamin are present in plasma, as free thiamin, TMP and protein-bound TDP. Thiamin in the body is mostly located in skeletal muscles, heart, brain, liver and kidneys.

Urine is the main route of thiamin excretion, mainly in the form of free thiamin and thiamin metabolites. 24-hour urinary thiamin excretion is related to thiamin intake, particularly to short term intakes, in thiamin-replete individuals. However, the thiamin intake cannot reliably be estimated from the urinary excretion of the vitamin. Determination of 24-hour urinary thiamin excretion is not a reliable marker of thiamin body stores and cannot, on its own, be used as a biomarker of the thiamin status of individuals. Still, in experimental studies where 24-hour urinary thiamin excretion is assessed in response to various intakes of the vitamin, a sharp increase in thiamin excretion is considered to be indicative of the saturation of the thiamin body stores.

Measurement of erythrocyte transketolase activity (ETKA), a TDP-requiring enzyme, is a functional test of thiamin status. Erythrocyte transketolase activity coefficient (αETK, also called "TDP effect") represents the degree to which ETKA rises in response to addition of TDP. This test can discriminate low ETKA due to thiamin deficiency from a lack of the apoenzyme. A value of αETK < 1.15 is generally considered to reflect an adequate thiamin status. The concentrations of total thiamin (free thiamin and its phosphate esters) in whole blood, serum and erythrocytes have also been investigated as biomarkers of thiamin status. Erythrocyte TDP concentration was found to have similar performance as the erythrocyte transketolase activation assay for assessment of thiamin status. The Panel notes, however, the lack of established cut-offs for these biomarkers.

The Panel considers that data from depletion–repletion studies in adults on the amount of dietary thiamin intake associated with αETK < 1.15 or with the restoration of normal (baseline) ETKA, without a sharp increase in urinary thiamin excretion, can be used to estimate thiamin requirement. In the absence of new scientific evidence, the Panel endorses the average requirement (AR) of 0.072 mg/MJ (0.3 mg/1,000 kcal) for all adults set by the Scientific Committee for Food (SCF) in 1993 on the basis of one depletion–repletion study in seven healthy males, in which both αETK and urinary excretion of thiamin were measured. Results from other depletion–repletion studies are in agreement with this value. The Panel notes that the AR was based on data on a small number of men and agrees on the coefficient of variation of 20% used by the SCF, to cover uncertainties related to distribution of thiamin requirements in the general population. The Panel endorses the Population Reference Intake (PRI) of 0.1 mg/MJ (0.4 mg/1,000 kcal) set by the SCF for all adults. No new evidence has become available that the relationship between thiamin requirement and energy requirement differs between men and women, or between younger and older adults.

The Panel proposes the same AR and PRI as for adults, expressed in mg/MJ, for infants aged 7 to 11 months, children aged 1 to < 18 years old, and during pregnancy and lactation, under the assumption that the relationship between thiamin requirement and energy requirement is the same in all population groups.

Based on data from 13 dietary surveys in nine countries of the European Union, average thiamin intakes across countries ranged between 0.31 and 0.65 mg/day (0.11 to 0.21 mg/MJ) among infants (< 1 year old), between 0.58 and 0.98 mg/day (0.12 to 0.21 mg/MJ) among children aged 1 to < 3 years old, between 0.68 and 1.29 mg/day (0.10 to 0.21 mg/MJ) among children aged 3 to < 10 years old, between 0.93 and 1.92 mg/day (0.11 to 0.20 mg/MJ) among children aged 10 to < 18 years old and between 0.88 and 1.99 mg/day (0.11 to 0.24 mg/MJ) among adults (≥ 18 years old).

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BACKGROUND AS PROVIDED BY THE EUROPEAN COMMISSION

The scientific advice on nutrient intakes is important as the basis of Community action in the field of nutrition, for example such advice has in the past been used as the basis of nutrition labelling. The Scientific Committee for Food (SCF) report on nutrient and energy intakes for the European Community dates from 1993. There is a need to review and if necessary to update these earlier recommendations to ensure that the Community action in the area of nutrition is underpinned by the latest scientific advice.

In 1993, the SCF adopted an opinion on the nutrient and energy intakes for the European Community.[1] The report provided Reference Intakes for energy, certain macronutrients and micronutrients, but it did not include certain substances of physiological importance, for example dietary fibre.

Since then new scientific data have become available for some of the nutrients, and scientific advisory bodies in many European Union Member States and in the United States have reported on recommended dietary intakes. For a number of nutrients these newly established (national) recommendations differ from the reference intakes in the SCF (1993) report. Although there is considerable consensus between these newly derived (national) recommendations, differing opinions remain on some of the recommendations. Therefore, there is a need to review the existing EU Reference Intakes in the light of new scientific evidence, and taking into account the more recently reported national recommendations. There is also a need to include dietary components that were not covered in the SCF opinion of 1993, such as dietary fibre, and to consider whether it might be appropriate to establish reference intakes for other (essential) substances with a physiological effect.

In this context the EFSA is requested to consider the existing Population Reference Intakes for energy, micro– and macronutrients and certain other dietary components, to review and complete the SCF recommendations, in the light of new evidence, and in addition advise on a Population Reference Intake for dietary fibre.

For communication of nutrition and healthy eating messages to the public it is generally more appropriate to express recommendations for the intake of individual nutrients or substances in food–based terms. In this context the EFSA is asked to provide assistance on the translation of nutrient based recommendations for a healthy diet into food based recommendations intended for the population as a whole.

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

In accordance with Article 29(1)(a) and Article 31 of Regulation (EC) No. 178/2002,[2] the Commission requests EFSA to review the existing advice of the Scientific Committee for Food on population reference intakes for energy, nutrients and other substances with a nutritional or physiological effect in the context of a balanced diet which, when part of an overall healthy lifestyle, contribute to good health through optimal nutrition.

In the first instance the EFSA is asked to provide advice on energy, macronutrients and dietary fibre. Specifically advice is requested on the following dietary components:

- Carbohydrates, including sugars;
- Fats, including saturated fatty acids, polyunsaturated fatty acids and monounsaturated fatty acids, *trans* fatty acids;
- Protein;
- Dietary fibre.

[1] Scientific Committee for Food, Nutrient and energy intakes for the European Community, Reports of the Scientific Committee for Food 31st series, Office for Official Publication of the European Communities, Luxembourg, 1993.

[2] Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety. OJ L 31, 1.2.2002, p. 1–24.

Following on from the first part of the task, the EFSA is asked to advise on population reference intakes of micronutrients in the diet and, if considered appropriate, other essential substances with a nutritional or physiological effect in the context of a balanced diet which, when part of an overall healthy lifestyle, contribute to good health through optimal nutrition.

Finally, the EFSA is asked to provide guidance on the translation of nutrient based dietary advice into guidance, intended for the European population as a whole, on the contribution of different foods or categories of foods to an overall diet that would help to maintain good health through optimal nutrition (food-based dietary guidelines).

ASSESSMENT

1. Introduction

In 1993, the Scientific Committee for Food (SCF) adopted an opinion on the nutrient and energy intakes for the European Community (SCF, 1993). The SCF set an Average Requirement (AR) and a Population Reference Intake (PRI) for thiamin, expressed in µg/MJ, which applied to all age and sex groups. PRIs expressed in mg/day were also derived, considering the average energy requirements of infants, children, adults, and pregnant and lactating women. A Lower Threshold Intake (LTI) expressed in µg/MJ was set for all age and sex groups, and converted to mg/day for adults, again using the values for average daily energy requirements for men and women.

2. Definition/category

2.1. Chemistry

Thiamin, also called vitamin B1 or aneurine, is a water-soluble vitamin. Thiamin is chemically defined as 3-[(4-amino-2-methyl-5-pyrimidinyl) methyl]-5-(2-hydroxyethyl)-4-methyl-1,3-thiazol-3-ium, with molecular formula $C_{12}H_{17}N_4OS$ and a molecular mass of 265.35 Da. Thiamin is composed of a thiazole and a pyrimidine ring linked by a methylene group.

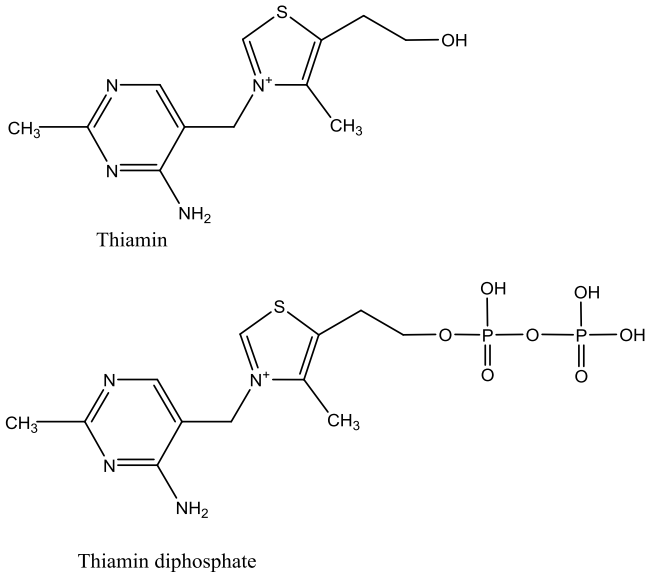

Figure 1: The thiamin and thiamin diphosphate molecules

In human tissues thiamin occurs mostly in phosphorylated forms as thiamin monophosphate (TMP), thiamin diphosphate (TDP, called also thiamin pyrophosphate) (Figure 1), thiamin triphosphate (TTP), as well as its non-phosphorylated form ("free thiamin"). Adenosine thiamin triphosphate (ATTP) is also found in some tissues (Gangolf et al., 2010) (Section 2.3.3.).

There are different methods of measurement of thiamin content in foods and biological samples (urine, blood and other tissues), such as high performance liquid chromatography (HPLC) followed by fluorescence or ultraviolet detection, fluorometry and microbiological assay (Icke and Nicol, 1994; Lynch and Young, 2000; Talwar et al., 2000; Mickelsen and Yamamoto, 2006). Techniques based on fluorimetric detection involve the oxidation of thiamin into thiochrome (Fayol, 1997). These methods showed comparable performance in foods (Hollman et al., 1993). The analytical procedure may comprise a step of enzymatic hydrolysis of phosphorylated thiamin, allowing the quantification of total thiamin content. The amounts of the respective forms of thiamin (i.e. free thiamin and its phosphate esters) can be determined after separation by HPLC (Gangolf et al., 2010).

2.2. Function of the nutrient

2.2.1. Biochemical functions

Free thiamin functions as the precursor for TDP, which acts as coenzyme for enzymes involved in carbohydrate and branched-chain amino acid metabolism, and in energy-yielding reactions. TDP is needed for the activity of pyruvate dehydrogenase responsible for the conversion of pyruvate to acetyl-coenzyme A, α-ketoglutarate dehydrogenase converting α-ketoglutarate to succinyl-coenzyme A within the Krebs cycle, and branched-chain α-keto acid dehydrogenase involved in the oxidation of the α-keto acids from branched-chain amino acids. These enzyme complexes play a key role in processes related to mitochondrial energy metabolism. TDP is also the coenzyme for transketolase in the pentose phosphate pathway, which is essential for the generation of pentoses and nicotinamide adenine dinucleotide phosphate (NADPH) (Singleton and Martin, 2001; Combs, 2008; Lonsdale, 2012; Manzetti et al., 2014). TDP is required for the function of the brain and nervous system as acetyl-coenzyme A and α-ketoglutarate are involved in the production of the neurotransmitters acetylcholine and gamma-aminobutyric acid.

TDP may be further phosphorylated to TTP. TTP is able to phosphorylate proteins and to activate large conductance anion channels as e.g. a chloride channel in nerves (Bettendorff et al., 1993; Nghiem et al., 2000; Bettendorff and Wins, 2009). The precise physiological role of TTP has not yet been elucidated (Bettendorff et al., 2014).

2.2.2. Health consequences of deficiency and excess

2.2.2.1. Deficiency

Thiamin deficiency usually presents with symptoms of peripheral neuritis, cardiac insufficiency and a tendency for oedemas and may be accompanied by extreme fatigue, irritability, forgetfulness, poor coordination, gastrointestinal disturbances, constipation, laboured breathing, loss of appetite and weight loss (WHO, 1999).

Thiamin deficiency leads to disorders that include several forms of beriberi, with mostly neurological and cardiovascular manifestations. Dry beriberi is predominately a neurological disorder with a sensory and motor peripheral neuropathy. Wet beriberi is the term used for thiamin deficiency that, in addition to the presence of peripheral neuropathy, involves cardiovascular manifestations that include congestive heart failure, cardiomegaly and tachycardia. A rapidly developing form of wet beriberi refers to the acute fulminant cardiovascular beriberi (Shoshin beriberi), or acute pernicious beriberi. Infantile beriberi can occur in breastfed infants of thiamin-deficient mothers at the age of two to six months and may be characterized by both neurologic and cardiac signs with lethal outcome due to heart failure (Roman-Campos and Cruz, 2014; Abdou and Hazell, 2015). Infantile thiamin deficiency was described in infants fed a soy-based thiamin deficient infant formula (Fattal-Valevski et al., 2005). Lack of thiamin impairs metabolic functions of the brain and can lead to Wernicke's encephalopathy, which is clinically characterized by ocular abnormalities, ataxia, and disturbances of consciousness, and to Korsakoff's syndrome (psychosis) resulting in amnesia, disorientation and often confabulation (Harper et al., 1986; Gui et al., 2006; Sechi and Serra, 2007; Kopelman et al., 2009).

Thiamin deficiency occurs predominantly in populations whose diet consists mainly of poor sources of thiamin (as milled white cereals, including polished rice and white wheat flour). It can also be related to diets that are rich in thiaminase, a natural thiamin-degrading enzyme, which is abundantly present in some raw or fermented fish, ferns and insects consumed primarily in Africa and Asia (WHO, 1999). In Western countries, thiamin deficiency is associated with alcoholism and drug abuse, and can occur in other risk groups including subjects after bariatric surgery, gastrectomy, or with chronic gastrointestinal and liver disorders (Lonsdale, 2012; Crook and Sriram, 2014).

2.2.2.2. Excess

Reviewing the evidence to set a Tolerable Upper Intake Level (UL) for thiamin, the SCF noted that data on adverse effects of oral intake of thiamin in humans were limited and that dose–response

studies were lacking (SCF, 2001). The SCF also noted that thiamin absorption declines for an intake higher than 5 mg/day and absorbed thiamin is actively excreted in the urine. No lowest-observed-adverse-effect level (LOAEL) or no-observed-adverse-effect level (NOAEL), and therefore, no UL, could be set for thiamin.

2.3. Physiology and metabolism

2.3.1. Intestinal absorption and bioavailability

Thiamin in food exists mainly in phosphorylated forms in animal products, and in free form in foods of plant origin. Thiamin phosphate esters are hydrolyzed in the intestinal lumen by phosphatases, mainly the alkaline phosphatase associated with brush-border membranes. Free thiamin is taken up through the mucosal membrane by a specific saturable transport system (Laforenza et al., 1997; Reidling et al., 2002). Two transporters, ThTR-1 and ThTR-2, encoded by *SLC19A2* and *SLC19A3* genes, are involved in intestinal thiamin uptake (Said et al., 2004). In case of low dietary thiamin intake, an enhanced expression of ThTR-2 is induced, but not of ThTR-1 (Laforenza et al., 1997; Reidling et al., 2002; Said et al., 2004).

When two healthy young men received an oral dose of 0.67 mg 2-^{14}C-thiazole-labelled thiamin (50 µCi) and a controlled diet providing a constant thiamin intake (range 1.35–2.10 mg/day, mean 1.75 mg/day), less than 1% of the radioactivity dose was found in the 1st and 2nd day faecal samples (Ariaey-Nejad et al., 1970). Overall, less than 5% of the labelled dose was found in the 5-day faecal collection. In another study which involved 10 healthy individuals who received a dose of 1 mg of 2-^{14}C-thiazole-labelled thiamin (10 µCi), mean faecal excretion was 4 ± 6.1% during the first 24 hours after administration (Tomasulo et al. (1968).

The efficiency of thiamin absorption is reduced upon consumption of thiamin above 5 mg/day, (Friedemann et al., 1948; Davis et al., 1984). When thiamin was infused directly into the lumen of the small intestine of humans and animals, it was absorbed by an active process at low concentrations (0.2 to 2.0 µM (0.05 to 0.50 mg/L)) and by a passive process at higher concentrations (5.0 to 50.0 µM (1.3 to 13 mg/L)) (Hoympa, 1975; Hoympa, 1982; Hoympa et al., 1982).

Chronic alcohol consumption impairs the intestinal absorption of thiamin, possibly through the inhibition of thiamin transporters (Subramanya et al., 2010). In the above-mentioned study from Tomasulo et al. (1968), significantly lower absorption of thiamin was found in 20 chronic alcoholic individuals (mean faecal excretion of labelled thiamin 21 ± 13.9%), compared to the 10 healthy controls.

Bioavailability of dietary thiamin can also be impaired by different types of anti-thiamin factors present in some foods. These factors degrade or modify thiamin so that it cannot be absorbed or loses its function. Sulfites, which are added to foods as a preservative, destroy thiamin at the methylene bridge. Thiamin can also be degraded by thermolabile thiaminases present in some raw or fermented fish, ferns and insects (Combs, 1992; WHO, 1999). Plants may contain heat-stable thiamin antagonists such as some aromatic acids (e.g. caffeic acid, chlorogenic acid, and tannic acid), which can oxidize the thiazole ring, making thiamin absorption impossible. Flavonoids, quercetin and rutin, have also been implicated as thiamin antagonists (Kositawattanakul et al., 1977; Hilker and Somogyi, 1982; Vimokesant et al., 1982). The bioavailability of thiamin was found to be reduced in controlled studies comparing diet with and without tea (Wang and Kies, 1991; Saeed and Zaheer-ud-Din, 1996).

Microbiota of the large intestine can synthesize thiamin in the form of TDP. *In vivo* experiments suggested that thiamin derived from bacterial synthesis is not used as a source of the vitamin (Alexander and Landwehr, 1946; Denko et al., 1946). More recently, free thiamin was found to be taken up by isolated human colonic epithelial cells via a process similar to the one occurring in the small intestine. A specific regulated high-affinity carrier-mediated uptake system (encoded by *SLC44A4* gene) for TDP was also identified (Nabokina et al., 2015). Further studies are needed to determine whether TDP synthesised by microbiota may be used by colonocytes.

The Panel notes that data on the efficiency of thiamin absorption are limited. In healthy subjects, thiamin absorption was found to be above 95% of daily thiamin intake lower than 2 mg, as determined

by the absorption of ^{14}C-labelled thiamin. The Panel notes that alcohol and anti-thiamin factors (such as some phenolic compounds, sulfites and thiaminases) can reduce thiamin bioavailability.

2.3.2. Transport in blood

Thiamin is transported by a high-affinity transporter into erythrocytes, where it is phosphorylated to TDP, a fraction of which is further converted to TTP (Gangolf et al., 2010). As a result, thiamin in blood is mainly found in erythrocytes (> 80% of total thiamin in the blood) in the form of TDP and TTP, while low amounts of the vitamin are present in plasma, as free thiamin, TMP and protein-bound TDP (Gangolf et al., 2010).

2.3.3. Distribution to and content in tissues

Thiamin is taken up by cells of the blood, liver, heart and other tissues, including placenta and brain, by active transport, mostly through thiamin transporters ThTR-1 and ThTR-2. In addition, the reduced folate carrier-1 (encoded by *SLC19A1* gene) provides a minor access route for TMP, TDP and TTP but not free thiamin. Members of the human extraneuronal monoamine transporter proteins, including the organic cation transporter proteins, are active in the transport of amine forms of nutrients and neurotransmitters, including thiamin, to the neurons (Zhao and Goldman, 2013; Manzetti et al., 2014).

The total thiamin content of the adult body has been estimated to be about 25–30 mg, located mostly in skeletal muscles, heart, brain, liver and kidneys (Ariaey-Nejad et al., 1970; Manzetti et al., 2014). Analysis of biopsies from various human tissues shows that TDP is the most abundant thiamin compound, with the highest content in heart and skin, followed by kidney, lung, colon, adipose tissue, skeletal muscle and vascular samples (content from 9 ± 6 to 66 ± 44 pmol/mg protein). The content of other forms is low: TMP content ranged from 0.7 ± 0.4 to 3.6 ± 0.8 pmol/mg protein in most tissues except kidney with a content of 80 pmol/mg protein; TTP content ranged from 0.3 ± 0.2 to 3 ± 4 pmol/mg protein; and free thiamin content ranged from 0.07 pmol/mg protein in colon to 3.5 pmol/mg protein in kidney (Gangolf et al., 2010). In some tissues (lung, thymus, skin, skeletal muscle, adipose tissue, arteries and veins), ATTP has also been found (0.13 ± 0.05 to 7 ± 9 pmol/mg protein). Analysis of distribution between subcellular fractions has shown that in most tissues, about 50% of the total thiamin occurs in the soluble fraction, 35% in mitochondria, 10% in the nuclei, and 5% in the microsomal fraction (Zempleni J., 2007). Free thiamin or TMP cross the cell membranes and can be found in extracellular fluids including cerebrospinal fluid (Manzetti et al., 2014).

The biological half-life of the vitamin was found in the range of 9 to 18 days (Ariaey-Nejad et al., 1970; Manzetti et al., 2014).

2.3.4. Metabolism

In cells, two enzymes phosphorylate thiamin: thiamin diphosphokinase, which catalyses the formation of TDP from free thiamin using adenosine triphosphate (ATP), and TTP-ATP-phosphoryltransferase, which catalyses the formation of TTP from TDP and ATP. TTP and TDP are catabolised by thiamin pyrophosphatase yielding TMP. TMP can be recycled to free thiamin or is excreted in the urine. Free thiamin as well as numerous thiamin metabolites formed in liver are also excreted via urine (Combs, 2008; Ross et al., 2014) (Section 2.3.5.1.).

2.3.5. Elimination

2.3.5.1. Urine

Thiamin is excreted in urine as free thiamin, small amounts as TMP and TDP, the oxidation product thiochrome, and more than 20 metabolites such as acid metabolites (2-methyl-4-amino-5-pyrimidine carboxylic acid, 4-methylthiazole-5-acetic acid, and thiamin acetic acid) and a 25-kDa thiamin containing peptide (Ariaey-Nejad et al., 1970; Combs, 2008; Ross et al., 2014). Thiamin that is not bound to plasma proteins is rapidly filtered in the glomerulus and excreted (Bender, 2003).

Urinary excretion varies with the level of thiamin intake. Thiamin depletion is associated with a marked decrease in thiamin excretion (Ziporin et al., 1965a, 1965b; Kraut et al., 1966; Bamji, 1970; Sauberlich et al., 1979), while the urinary excretion rate increases with increasing thiamin intakes (Alexander et al., 1946; Mickelsen et al., 1947; Kraut et al., 1966; Davis et al., 1984; Shibata et al., 2014) (Section 2.4.3). An enzyme which rapidly dephosphorylates unbound TDP was identified in human plasma, and this may facilitate excretion of an excess of the vitamin (Thom et al., 1985).

The Panel notes that urine is the main route of thiamin excretion, mainly in the form of free thiamin and thiamin metabolites.

2.3.5.2. Faeces

Significant amounts of thiamin are excreted in faeces (in the order of 0.10 to 0.40 mg/day) (Alexander, 1943; Hathaway and Strom, 1946; Boyden and Erikson, 1966). At usual levels of intake, faecal excretion of thiamin is not related to thiamin intake (Hathaway and Strom, 1946; Boyden and Erikson, 1966); an increase in thiamin excretion in the stool was observed with thiamin intakes above 5 mg/day (Schultz et al., 1938; Alexander, 1943). Thiamin in faeces arises mainly from its biosynthesis by gut microorganisms, and is largely present within bacterial cells (Najjar and Holt, 1943; Alexander and Landwehr, 1946). Upon parenteral administration of thiamin, no significant increase in faecal thiamin was observed, which indicates that thiamin is not secreted into the gastrointestinal tract (Alexander, 1943).

The Panel notes that faecal thiamin is not related to thiamin intake in the usual range of intake. Significant amounts of thiamin are synthesised by gut microorganisms, which are not bioavailable and are excreted in faeces.

2.3.5.3. Sweat

Sweat may contain up to 8–16 µg/L of thiamin (Bender, 2003).

The Panel notes that sweat does not represent a significant route of thiamin loss.

2.3.5.4. Breast milk

Thiamin is present in breast milk mostly as TMP (about 70%) and free thiamin (about 30%), while a negligible amount of TDP has been reported (less than 1%) (Stuetz et al., 2012a; Stuetz et al., 2012b). The concentration of thiamin is lower in colostrum (1–5 days) and transitional milk (5–13 days) than in mature milk, and the concentration remains constant during the rest of the lactation (Roderuck et al., 1945; Ford et al., 1983; Dostalova et al., 1988). Maternal thiamin intake does not significantly affect the thiamin concentration in breast milk, except in women deficient in the vitamin (Picciano, 1995; Coats et al., 2013). Nail et al. (1980) and Thomas et al. (1980) found about 10% difference in thiamin breast milk concentrations between supplemented (1.7 mg/day of thiamin as part of a multivitamin supplement) and non-supplemented mothers.

Thiamin concentrations in breast milk from healthy mothers of term infants in Western countries are shown in Appendix A. The mean thiamin concentrations in mature breast milk ranged from 0.14 mg/L to 0.22 mg/L (midpoint 0.18 mg/L) (Roderuck et al., 1945; Nail et al., 1980; Thomas et al., 1980; Ford et al., 1983; Dostalova et al., 1988; Ortega et al., 2004).

Considering an average milk transfer of 0.8 L/day during the first six months of lactation in exclusively breastfeeding women (Butte et al., 2002; FAO/WHO/UNU, 2004; EFSA NDA Panel, 2009), and a concentration of thiamin in mature breast milk of 0.18 mg/L, the secretion of thiamin into milk during lactation is estimated to be 0.15 mg/day.

2.3.6. Interaction with other nutrients

TDP is involved in many metabolic processes in which it serves as a coenzyme (Section 2.2.1.). The three dehydrogenases for which TDP acts as a cofactor require other cofactors derived from pantothenic acid, riboflavin, and niacin (Frank, 2015). Transketolase activation depends on thiamin as

well as divalent cations, such as Ca^{2+} and Mg^{2+} (Kochetov, 1982; Ospanov et al., 2007). Magnesium deficiency has been reported to aggravate thiamin deficiency in humans (Dyckner et al., 1985).

Thiamin is involved in carbohydrate metabolism (Section 2.2.1.). In an intervention study, the influence of a stepwise increase of carbohydrate contribution to energy intake on urinary and blood thiamin concentration and erythrocyte transketolase activity (ETKA) was studied in 12 healthy volunteers (six men and six women, aged 25–30 years) consuming defined isocaloric diet (9.1 ± 3.0 MJ/day) and with a constant level of physical activity (Elmadfa et al., 2001). During a four-day adaptation phase (period I), the carbohydrate intake was 55% of total energy intake and thiamin intake was 0.13 mg/MJ. During the subsequent intervention periods, carbohydrate intake was increased to 65% of total energy for four days (period II) and to 75% for another four days (period III), and thiamin intake was 0.10 mg/MJ and 0.11 mg/MJ, respectively. No significant differences in transketolase activity were found in periods II and III compared to that measured in period I, while the mean blood thiamin concentration and urinary excretion of thiamin decreased significantly.

The Panel notes that there are limited data on the relationship between thiamin requirement and carbohydrate intake in humans.

2.3.7. Energy intake and expenditure

In two studies, which compared thiamin status in physically active subjects and less active controls, no difference between groups was found in erythrocyte transketolase activation coefficients (Fogelholm et al., 1992; Malara et al., 2013). In these studies, energy intakes were significantly higher in the active groups than in the less active groups, while thiamin intakes, expressed in mg/MJ, were comparable. The Panel notes that in these studies no alteration in erythrocyte transketolase activation coefficient (αETK) was found when enhanced energy expenditure was accompanied with increased thiamin intake. In a longitudinal study in swimmers, a significant decline in blood thiamin concentrations (by 13% in men and 19% in women, respectively) after an intensive training associated with enhanced energy expenditure, as compared to the control period, was observed (Sato, 2011). There was no significant difference in mean dietary thiamin intakes between the study periods (1.28 vs 1.54 mg/day, assessed by three-day food records). When expressed in mg/MJ, women had a lower thiamin intake during the training period than during the control period (control vs training: 0.131 vs 0.107 mg/MJ, $p = 0.033$), while intakes were similar in the two periods in men (control vs training: 0.105 vs 0.109 mg/MJ). The Panel notes that no other marker than thiamin blood concentration was measured in this study, which makes the study difficult to interpret.

The depletion-repletion study by Sauberlich et al. (1979) aimed at relating thiamin requirement to energy utilisation (Section 5.1.1.). Seven subjects were assigned to diets providing controlled intakes of thiamin and either 2,800 or 3,600 kcal, and constant weights of the subjects were maintained by adjusting daily activity and exercise schedules. Thiamin requirements were evaluated in terms of αETK and urinary excretion of the vitamin (see Sections 2.4.2. and 2.4.3.). A daily intake of 0.84 mg thiamin/day failed to restore normal αETK in subjects with an energy intake of 3,600 kcal/day, while this amount was associated with adequate αETK in subjects with 2,800 kcal/day. At this level of intake, subjects with an energy intake of 3,600 kcal/day had lower urinary excretion of thiamin than subjects with 2,800 kcal/day. When both groups received a similar amount of thiamin per energy unit (0.072 mg/MJ, corresponding to 0.84 mg/day and 1.08 mg/day in the respective groups), no difference in urinary thiamin excretion between groups was found and adequate αETK were achieved in both groups. The Panel notes that this study indicates a positive relationship between thiamin requirement and energy intake and expenditure.

The Panel notes that thiamin is involved in energy-yielding reactions (Section 2.2.1.). The Panel also notes that data on the relationship between thiamin requirement and energy requirement are limited, however, available data indicate a positive relationship between thiamin requirement and energy requirement.

2.4. Biomarkers of intake and status

2.4.1. Whole blood, serum and erythrocyte thiamin concentrations

The concentrations of total thiamin (free thiamin and its phosphate esters) in whole blood, serum and erythrocytes have been investigated as biomarkers of thiamin status. In Western healthy populations, concentrations of total thiamin in whole blood are typically in the range of 70–190 nmol/L (Schrijver et al., 1982; Schrijver et al., 1985; Laschi-Loquerie et al., 1992; Lu and Frank, 2008). The major part of thiamin is present in erythrocytes. Concentrations of total thiamin in the serum fraction are between 10 and 20 nmol/L. Whole blood TDP concentration in the range of 90–220 nmol/L, TMP 1–10 nmol/L, TTP 1–13 nmol/L and free thiamin 2–15 nmol/L have been reported (Warnock et al., 1978; Lu and Frank, 2008; Gangolf et al., 2010). Lower total thiamin concentrations have been reported in whole blood of beriberi patients (Kawai et al., 1980; Kuriyama et al., 1980) and in erythrocytes of alcoholic subjects (Mancinelli et al., 2003; Ceccanti et al., 2005), compared to healthy individuals. In a longitudinal study in which four young adults were maintained on a constant diet for 60 days (1.55 mg thiamin/day), within-subject variation in whole blood total thiamin concentration in the order of 8–10% were reported (van Dokkum et al., 1990). In this study, mean (± standard deviation (SD)) total thiamin concentrations varied between 130 ± 11 and 166 ± 19 nmol/L across subjects, indicating substantial between-subjects variation with a similar level of thiamin intake.

Particular attention has been paid to the use of TDP concentrations in erythrocytes as a marker of low thiamin status. In rats on a thiamin deficient diet, erythrocyte and liver TDP concentration begun to be depleted before any change in erythrocyte transketolase activity was detected, suggesting that erythrocyte TDP levels may be a more sensitive indicator of thiamin status (Warnock et al., 1978). In humans, Talwar et al. (2000) found that measures of TDP concentrations in erythrocytes compared well with the erythrocyte transketolase activity. The two methods were in agreement for 58 of 63 individuals. Fourteen individuals were considered to be thiamin deficient by the transketolase activation test (cut-off value: > 1.25), and 13 of them also had erythrocyte TDP concentrations lower than the reference range established in the study (95% reference interval: 280–590 ng/g Hb). Four individuals with low TDP concentrations had αETK ≤ 1.25, although they were close to the cut-off (1.21–1.23). Measures of TDP in erythrocytes or whole blood have been used to assess thiamin status in populations (Hanninen et al., 2006; Brough et al., 2007; Stuetz et al., 2012a; Whitfield et al., 2015), with different cut-off values applied by the respective research groups. Wilkinson et al. (2000) reported lower mean (95% CI) erythrocyte TDP concentrations in 221 older healthy subjects (149 (137–160) nmol/L) compared to 100 younger adults (224 (213–235) nmol/L) and erythrocyte TDP concentrations were found to decrease as age progressed (−20 (−14.5–−24.5)% over 3 years).

In the usual range, these biomarkers are not related to observed habitual thiamin intake and their response to thiamin supplementation is modest. In observational studies in populations with mean thiamin intake between 0.9 and 1.2 mg/day, no significant correlations between thiamin intake and total thiamin concentrations were found in whole blood, serum or erythrocytes (Bailey et al., 1994; Hiraoka, 2001) and no or poor ($r = 0.268$; $p < 0.05$) correlations were found between thiamin intake and TDP concentration in whole blood (Fidanza et al., 1989; Ihara et al., 2005). A study in pregnant women who received thiamin supplementation (n = 41; 3 mg thiamin/day for around 20 weeks) or a placebo (n = 25) showed no significant difference in mean concentration of TDP in whole blood (mean (± SD) 100.3 ± 41.6 nmol/L vs 88.7 ± 36.8 nmol/L) (Brough et al., 2007). In healthy adults (aged 20–55 years), high intake of thiamin (5–15 mg/day) resulted in modest increases in serum or whole blood concentrations of thiamin, while an active excretion of the vitamin in urine was observed (Davis et al., 1984; Shibata et al., 2014), indicating that blood thiamin concentration is regulated by the urinary excretion of the vitamin, besides reduced intestinal absorption.

The Panel notes that thiamin deficiency is generally associated with “low” total thiamin or TDP concentrations in whole blood and erythrocytes. The Panel also notes that the determination of TDP concentration in erythrocytes had similar performance as the erythrocyte transketolase activation assay

to assess thiamin status. The Panel notes, however, the lack of established cut-offs for these biomarkers. In the usual range of intake, total thiamin or TDP concentrations in whole blood and erythrocytes are not valid markers of thiamin intake.

2.4.2. Erythrocyte transketolase activity (ETKA) and erythrocyte transketolase activity coefficient (αETK)

Erythrocyte transketolase is a TDP-requiring enzyme. Measurement of its activity (ETKA) is a functional test of thiamin status. Different methods of determination can be used (McCormick and Greene, 1994), based on the rate of substrate utilised (e.g. ribose-5-phosphate) or product formed (e.g. fructose-6-phosphate, sedoheptulose-7-phosphate) in the two reactions catalyzed by the enzyme (Section 2.2.1.). ETKA can be measured without (basal) or with (stimulated) added TDP. αETK (also called "TDP effect") represents the degree to which ETKA rises in response to addition of TDP and corresponds to the ratio of stimulated to basal enzyme activity, sometimes expressed as a percentage (i.e. percentage of activation when TDP is added). This effect can discriminate low ETKA due to thiamin deficiency from a lack of the apoenzyme (Sauberlich, 1999).

The erythrocyte transketolase activity coefficient may be regarded as a continuum with αETK value increasing progressively from values close to 1, when the level of saturation of the enzyme with its cofactor is high, to higher values as thiamin deficiency develops, until severe deficiency symptoms occur (Lonsdale, 2012). Based on experimental thiamin deficiency studies in which αETK and urinary excretion of thiamin were assessed in individuals maintained on controlled intakes of thiamin (Brin, 1962; Sauberlich, 1967; Wood et al., 1980), classifications have been proposed for the interpretation of results of αETK in the assessment of thiamin status. In these studies, αETK in control subjects were typically below 10%, while in individuals receiving a thiamin depleted diet αETK was found to progressively increase by up to more than 30% after several weeks of depletion. In general, αETK ≤ 1.15 (≤ 15%) is considered as indicative of an adequate thiamin status, αETK values 1.15–1.25 (15–25%) as marker of insufficiency, while αETK > 1.25 (> 25%) is considered as an indicator of thiamin deficiency (IOM, 1998; WHO, 1999). These cut-off values have been applied to assess thiamin status of population groups (Duffy et al., 1981; Mataix et al., 2003; Wolters et al., 2003; Yang et al., 2005; Shaw et al., 2007). In eight infants aged 2.5 to 12 months who had consumed a thiamin free soy-based formula for some months, αETK were between 13.8 and 37.8% (Fattal-Valevski et al., 2005). In the VERA (Verbundstudie Ernährungserhebung und Risikofaktoren Analytik) nationally representative survey of the German adult population (n = 2,006 adults), median thiamin intakes of 1.36 mg/day in men and 1.1 mg/day in women were associated with median αETK of 1.11 and 1.10, respectively (Heseker et al., 1992). In the UK National Diet and Nutrition Survey (NDNS) (n = 6,828), mean thiamin intakes in adults were 1.44 mg/day (19–64 years) and 1.43 mg/day (≥ 65 years) and in children 0.94 mg/day (1.5–3 years), 1.27 mg/day (4–10 years) and 1.38 mg/day (11–18 years) (Bates et al., 2014). In blood samples obtained from 2,671 participants, mean αETK in adults was 1.12 (19–64 years) and 1.11 (≥ 65 years), in children 1.07 (1.5–3 years), 1.10 (4–10 years) and 1.12 (11–18 years).

Inter-individual variabilities of ETKA and αETK are large. In a study in Japanese subjects aged ≥ 15 years, mean (± SD) ETKA were 374 ± 135 µg/mL erythrocytes/hour (range 150–650) in 21 patients with diagnosed beriberi compared to 461 ± 61 µg/mL erythrocytes/hour (range 250–850) in 674 control subjects ($p < 0.01$) (Kuriyama et al., 1980). Measures of αETK were 34.6 ± 18.4% (range 8–85%) and 11.6 ± 11.5% (range −10–55%), in the respective groups ($p < 0.001$). The two groups could not be reliably separated by using a single biomarker because of significant overlaps. Several factors may affect the specificity of these assays, such as the unstability of the enzyme during sample storage (Puxty et al., 1985), altered binding of apoenzyme and coenzyme because of the presence of transketolase isoenzymes (Warnock et al., 1978; Baines and Davies, 1988; Talwar et al., 2000), as well as reduced synthesis of the apoenzyme in patients with diabetes and liver disease (Talwar et al., 2000). Prolonged thiamin deficiency also induces a reduction in the apoenzyme level so that both basal and stimulated eythrocyte transketolase activities are low, resulting in a misleading "normal" αETK value (Bamji, 1976; Schrijver, 1991). Notable inter-individual variation in the time required for formation of fully functional holoenzyme have been reported, in particular at low TDP concentrations

(Singleton et al., 1995). The status of other nutrients which contribute to the enzyme activity (Section 2.3.6.), such as magnesium, has also been reported to affect the assay (Lonsdale, 2007).

In depletion–repletion studies, measures of basal ETKA (Ziporin et al., 1965b; Bamji, 1970; Wood et al., 1980) and αETK (Kraut et al., 1966; Sauberlich et al., 1979; Wood et al., 1980) were found to be sensitive to large changes in thiamin intake levels (Section 5.1.1.). These markers have also been found to respond to thiamin supplementation (Reuter et al., 1967; Asciutti-Moura et al., 1993). In contrast, in observational cross-sectional studies in children (Jung et al., 2003), adolescents (Bailey et al., 1994) and adults (Gans and Harper, 1991; Nichols and Basu, 1994) on their usual diet (thiamin intake range: 1.07–1.7 mg/day), no significant relationships between thiamin intakes and measures of ETKA and αETK were found.

The Panel notes that ETKA and αETK are sensitive markers of thiamin function and status. ETKA decreases and αETK increases following depletion of the vitamin. A value of αETK < 1.15 (i.e. < 15% increase in ETKA upon addition of TDP) is generally considered to reflect an adequate thiamin status. Several factors may affect the specificity of these assays and confound their interpretation, so that their combination with other biomarkers (Sections 2.4.1. and 2.4.3.) is required to reliably assess the thiamin status of individuals. In the usual range of intake, no relationships have been found between thiamin intake and both ETKA and αETK.

2.4.3. Urinary excretion of thiamin

In studies using controlled diets, linear relationships between thiamin intake and 24-hour urinary excretion of free thiamin were describe over a wide range of thiamin intakes (0.03 and 10 mg/day) (Mickelsen et al., 1947; Reuter et al., 1967; Fukuwatari and Shibata, 2008; Tasevska et al., 2008; Shibata et al., 2014). In a controlled study in seven male and six female healthy participants consuming their usual diet for 30 days (mean ± SD thiamin intake: 2.22 ± 0.55 mg/day), large intra- and inter-individual variability in 24-hour urinary excretion of thiamin was found (32.5% and 36.7%, respectively) (Tasevska et al., 2008). In a multiple regression model controlled for body weight and age, thiamin intake was a significant predictor of thiamin urinary excretion (adjusted $r = 0.51$; $p < 0.001$), with almost half of the variance left unexplained. The percentage of thiamin intake recovered in urine showed large inter-individual variability (11.9–41.5%). In a longitudinal study in which four young adults were maintained under a constant diet for 60 days (1.55 mg thiamin/day) (van Dokkum et al., 1990), within-subject variation in urinary thiamin excretion of 11 to 13% was found and the variability was similar when the results were expressed per mmol creatinine. Mean 24-hour urinary excretion ranged from 0.43 to 0.67 mg/day across subjects. The levels of carbohydrates consumption (Elmadfa et al., 2001) (Section 2.3.6.) and energy expenditure (Sauberlich et al., 1979) (Section 2.3.7.) have been found to affect urinary excretion of thiamin. Variability in thiamin absorption (Section 2.3.3.) as well as genetic variability in thiamin metabolism (Section 2.3.7.) and other factors may also influence urinary excretion of thiamin, although experimental data are lacking.

The correlations between thiamin intake, estimated through 4-day weighted food record, and 24-hour thiamin urinary excretion were assessed in cross-sectional studies in Japanese populations (Tsuji et al., 2010a, 2010b, 2011). Correlations were $r = 0.42$ ($p < 0.001$) in 114 male and female children aged 10–12 years, $r = 0.42$ ($p < 0.001$) in 156 male and female adults aged 18–27 years and $r = 0.62$ ($p < 0.001$) in 37 women aged 70–84 years.

When tissues are depleted, urinary thiamin excretion is decreased. In depletion-repletion studies, urinary excretion of the vitamin was observed to decrease progressively down to 0.04–0.07 mg/24 hours with thiamin intakes between 0.036 and 0.048 mg/MJ (0.15 and 0.20 mg/1,000 kcal) for a few weeks (Kraut et al., 1966; Bamji, 1970; Sauberlich et al., 1979; Wood et al., 1980) (Section 5.1.1.). In these studies, thiamin urinary excretion rapidly increased upon repletion with the vitamin. In the study by (Ziporin et al., 1965a, 1965b), where thiamin intake was restricted to 0.009–0.015 mg/MJ (0.039–0.064 mg/1,000 kcal) for 30 days, thiamin was not detected in urine at the end of the depletion period. The mean amounts of thiamin metabolites (sum of pyrimidine and thiazole moieties) excreted in urine increased from 0.588–0.748 mg/24 hours during the control period to 0.747–0.965 mg/24 hours during the depletion period. In this study, urinary excretion below

0.03 mg/24 hours persisted during the 12-day "low level" repletion period (0.046–0.052 mg/MJ (0.19–0.22 mg/1,000 kcal)), while the clinical symptoms and biochemical impairment (decline in ETKA), which had developed during the depletion phase, progressively disappeared. In patients with beriberi, reported urinary thiamin excretion was < 0.015 mg/24 hours (Robinson et al., 1940; Sauberlich, 1967). Urinary free thiamin excretion < 0.04 mg/24 hours may be used as an indicator of low thiamin intake associated with high risk of thiamin deficiency (WHO, 1999).

The Panel notes that 24-hour urinary thiamin excretion is related to thiamin intake, particularly to short term intakes, in thiamin-replete individuals. However, the thiamin intake cannot reliably be estimated from the urinary excretion of the vitamin. Determination of 24-hour urinary thiamin excretion is not a reliable marker of thiamin body stores and cannot, on its own, be used as a biomarker of the thiamin status of individuals. In experimental studies where 24-hour urinary thiamin excretion is assessed in response to various intakes of the vitamin, a sharp increase in thiamin excretion is considered to be indicative of the saturation of the thiamin body stores.

2.5. Effects of genotypes

Rare mutations in genes encoding thiamin transporters, ThTR-1 and ThTR-2, cause tissue-specific (i.e. localised) deficiency of thiamin. This occurs in patients with thiamin-responsive megaloblastic anemia (TRMA) and patients with thiamin-responsive Wernicke's-like encephalopathy and Leigh syndrome (Diaz et al., 1999; Kono et al., 2009; Ortigoza-Escobar et al., 2014). The autosomal-recessive disorder TRMA is caused by mutations in the *SLC19A2* gene coding for ThTR-1 (Diaz et al., 1999). The thiamin-responsive Wernicke's-like encephalopathy and Leigh syndrome can be caused by mutations in the *SLC19A3* gene coding for ThTR-2 (Kono et al., 2009; Ortigoza-Escobar et al., 2014). Mutations in the *SLC25A19* gene resulting in a diminution of mitochondrial TDP transporter have also been described. Mutations in the thiamin diphosphokinase gene (*TPK1*) were found to reduce TDP concentrations in blood and muscles, and decreased the activity of TDP-dependent enzyme complexes, especially pyruvate dehydrogenase and α-ketoglutarate dehydrogenase (Brown, 2014).

The Panel considers that, although the effect of rare mutations affecting thiamin transport and metabolism have been characterised, no genotypes have been identified that would require consideration with regard to the estimation of DRVs for thiamin in the general population.

3. Dietary sources and intake data

3.1. Dietary sources

Thiamin is present in all plant (as free thiamin) and animal tissues (in phosphorylated forms). The principal food sources of thiamin include whole grains, pulses, meat, liver and fish. Food processing (alkaline pH, high temperatures, exposure to sulphites) contributes to significant thiamin loss (Bentreud, 1977; Clydesdale et al., 1991; Ball, 2005; Damodaran et al., 2007).

Currently, thiamin hydrochloride and thiamin mononitrate may be added to both foods[3] and food supplements,[4] and 'thiamin monophosphate chloride' and 'thiamin pyrophosphate chloride' may be also added to food supplements.[6] The thiamin content of infant and follow-on formulae and of processed cereal-based foods and baby foods for infants and children is regulated.[5]

3.2. Dietary intake

EFSA estimated dietary intakes of thiamin from food consumption data available through the EFSA Comprehensive Food Consumption Database (EFSA, 2011a), classified according to the food

[3] Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods, OJ L 404, 30.12.2006, p. 26.

[4] Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements, OJ L 183, 12.7.2002, p. 51.

[5] Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC, OJ L 401, 30.12.2006, p.1. and Commission Directive 2006/125/EC of 5 December 2006 on processed cereal-based foods and baby foods for infants and young children, OJ L 339, 06.12.2006, p. 16-35.

classification and description system FoodEx2 (EFSA, 2011b). Data from 13 dietary surveys in nine countries of the European Union (EU) were used. The countries included were Finland, France, Germany, Ireland, Italy, Latvia, Netherlands, Sweden and the UK. The data covered all age groups from infants to adults (Appendix B).

Nutrient composition data for thiamin were derived from the EFSA Nutrient Composition Database (Roe et al., 2013). Food composition information of Finland, France, Germany, Italy, the Netherlands, Sweden and the UK were used to calculate thiamin intakes in these countries, assuming that the best intake estimate would be obtained when both the consumption data and the composition data were from the same country. For nutrient intake estimates of Ireland and Latvia, food composition data from the UK and Germany, respectively, were used, because no specific composition data from these countries were available. The amount of borrowed values for thiamin (i.e. values taken from other tables or databases) varied between 15% (Germany) and 85% (Sweden) in the seven composition databases. The food composition data available in the EFSA Nutrient Composition Database for the respective countries include the effect of processing on thiamin content. EFSA estimates are based on consumption of foods, either fortified or not, but without taking dietary supplements into account.

Data on infants (1–11 months old) were available from Finland, Germany, Italy and the UK. The proportions of breast-fed infants were 58% in the Finnish survey, 40% in the German survey, 44% in the Italian survey and 21% in the UK survey. For the Italian and German surveys, breast milk intake estimates were derived from the number of breastfeeding events recorded per day multiplied by standard breast milk amounts consumed on an eating occasion at different ages. For the UK survey, the amount of breast milk consumed was either directly quantified by the mother (expressed breast milk) or extrapolated from the duration of each breastfeeding event. In the Finnish survey, information was limited to whether infants were breastfed or not, and the contribution of breast milk to thiamin intakes could not be taken into consideration. The Panel notes the limitations in the methods used for assessing breast milk consumption in infants and related uncertainties in the intake estimates for infants (Appendices C and D).

Average thiamin intakes across countries ranged between 0.31 and 0.65 mg/day (0.11 to 0.21 mg/MJ) among infants (< 1 year old), from 0.58 to 0.98 mg/day (0.12 to 0.21 mg/MJ) among children aged 1 to < 3 years old, between 0.68 and 1.29 mg/day (0.10 to 0.21 mg/MJ) among children aged 3 to < 10 years old, from 0.93 to 1.92 mg/day (0.11 to 0.20 mg/MJ) among children aged 10 to < 18 years old. The average thiamin intake ranged between 0.88 and 1.99 mg/day (0.11 to 0.24 mg/MJ) among adults (≥ 18 years old). Average daily intakes were in most studies slightly higher among males compared to females mainly due to larger quantities of food consumed per day.

The main food groups contributing to thiamin intake were grain and grain-based products in most population groups, or food products for young population for infants and meat and meat products for pregnant adolescents from Latvia. Beside grain and grain-based products, meat and meat products and milk and milk products were also important contributors to thiamin intake in adults. Differences in main contributors to thiamin intakes between genders were minor.

EFSA intake estimates were compared with published intake estimates from the same national surveys and age ranges (Appendix G). The EFSA estimates differed at maximum around 14% from the published values, although in several cases differences were less than 5%. Uncertainties in the estimates of all countries may be caused by several reasons: inaccuracies in mapping food consumption data according to the FoodEx2 classification, analytical errors or errors in estimating the thiamin content of foods in the food composition tables, the use of borrowed thiamin values from other countries or the replacement of missing thiamin values by values of similar foods or food groups in the thiamin intake estimation process. These uncertainties may, in principle, cause both under- and overestimation of thiamin intake. Taking into account the many uncertainties of the thiamin intake estimation, a difference in a magnitude of up to 15% can be considered acceptable. It is not possible to conclude which of the intake estimates (i.e. those by EFSA or the relevant country) would be closer to the actual thiamin intake.

4. Overview of dietary reference values and recommendations

4.1. Adults

The German-speaking countries (D-A-CH, 2015) used αETK (< 15%) and urinary thiamin excretion (> 66 µg/day) as criteria to set DRVs for thiamin (Finglas, 1993; Bemeur and Biutterworth, 2014). They mentioned data on deficiency symptoms in relation to a thiamin intake of 0.05 mg/MJ during two to eight weeks (Williams et al., 1942; Foltz et al., 1944; Wood et al., 1980), and on adequate ETKA with marginal urinary thiamin excretion at a thiamin intake of 0.07 mg/MJ (Sauberlich et al., 1979). Both ETKA and urinary thiamin excretion were adequate at a thiamin intake of 0.11 mg/MJ (Foltz et al., 1944; Hathaway and Strom, 1946). They considered this intake as the AR for adults. Considering a coefficient of variation of 10%, energy requirements, and data on balance studies and tissue saturation with thiamin (Melnick, 1942), PRIs for adults ranging between 1.0 (women) and 1.3 (men aged 19–25 years) mg/day were set.

For the Nordic Nutrition Recommendations (NNR) 2012, the Nordic countries related the requirement for thiamin to the energy intake (Nordic Council of Ministers, 2014). They considered that data on thiamin intake and health outcomes (Balk et al., 2006; Kabat et al., 2008; Pelucchi et al., 2009; Lu'o'ng and Nguyen, 2011; Key et al., 2012) could not be used to set DRVs. The same reference values as previously published were kept, i.e. an AR for adults of 0.10 mg/MJ (corresponding to 0.9 mg/day for women and 1.2 mg/day for men). The Recommended Intake (RI) was set at 0.12 mg/MJ, and varied between 1.0 (women aged 61 years and over) and 1.4 (men aged 18–30 years) when expressed in mg/day. They noted that thiamin utilisation is impaired among older adults (Nichols and Basu, 1994). A lower intake level of 0.05 mg/MJ, corresponding to 0.5 mg/day for women and 0.6 mg/day for men, was set based on clinical signs of deficiency observed at intakes below 0.5 mg/day (0.05 mg/MJ) (Sauberlich et al., 1979; WHO/FAO, 2004). When planning diets with energy intakes lower than 8 MJ/day, a thiamin intake of at least 0.8 mg/day, or 1.0 mg/day in older adults, was recommended.

The World Health Organization/Food and Agriculture Organization (WHO/FAO, 2004) mentioned the controlled depletion–repletion study by Sauberlich et al. (1979) that suggested an intake of 0.07 mg/MJ as the requirement for thiamin. They also mentioned another study indicating signs of deficiency below this intake (Wood et al., 1980), a study in adults that suggested a requirement of 1.0 and 1.2 mg/day for women and men respectively (Anderson et al., 1985), and data on TDP and αETK in older adults (Hoorn et al., 1975; Nichols and Basu, 1994). The WHO/FAO proposed a Recommended Nutrient Intake of 1.1 mg/day and 1.2 mg/day for women and men, respectively.

The French Food Safety Agency (Afssa, 2001) mentioned the depletion–repletion study from (Sauberlich et al., 1979) and other data on ETKA (Kraut et al., 1966; Reuter et al., 1967; Anderson et al., 1986) and thiamin excretion in urine. Referring to the previous DRV for thiamin set in 1992, i.e. about 0.13 mg/MJ, and considering the revised French reference values for energy, Afssa set a PRI for thiamin of 1.3 mg/day for men (for an energy intake of 9.2 MJ/day) and 1.0 mg/day for women (for an energy intake of 7.5 MJ/day), also noting that thiamin intake should not be below 1 mg/day. Afssa also set a PRI of 1.2 mg/day for adults aged 75 years and over.

The Health Council of the Netherlands (2000) considered a study by Horwitt et al. (1948), which showed that clinical signs of deficiency in adults were observed at a thiamin intake below 0.045 mg/MJ. The Council also considered intervention or observational studies in younger adults measuring urinary excretion of thiamin or αETK (Melnick, 1942; Ziporin et al., 1965a; Reuter et al., 1967; Bamji, 1970; Henshaw et al., 1970; Sauberlich et al., 1979; Wood et al., 1980; Anderson et al., 1986). For the age range 19–50 years, the Council concluded that the AR was about 0.07–0.08 mg/MJ for men and 0.09 mg/MJ for women. Based on an energy intake of 11.2 MJ/day for men and 8.5 MJ/day for women derived from the national food consumption survey (Hulshof et al., 1998), the ARs were 0.84 mg/day for men and 0.77 mg/day for women, averaged to an AR of 0.8 mg/day for both sexes, and the PRI was set at 1.1 mg/day for adults. For older adults aged 51 years and over, the Council considered several intervention or observational studies on thiamin intake and status (thiamin urinary excretion or αETK) (Oldham, 1962; Markkanen et al., 1969; Bowles, 1979; DHSS, 1979;

Schrijver et al., 1985; Löwik, 1986; van der Wielen et al., 1994). For this age group, the Council set an AI of 1.1 mg/day.

The US Institute of Medicine (IOM, 1998) derived Estimated Average Requirements (EARs) and Recommended Daily Allowances RDAs) for adults on the basis of data from 11 metabolic studies on young men and women that used ETKA, urinary excretion and other indicators of thiamin status (Elsom et al., 1942; Foltz et al., 1944; Horwitt et al., 1948; Ziporin et al., 1965a; Kraut et al., 1966; Reuter et al., 1967; Bamji, 1970; Henshaw et al., 1970; Sauberlich et al., 1979; Wood et al., 1980; Anderson et al., 1986). The IOM considered that results from these studies suggest that the average requirement is at least 0.07 mg/MJ or 0.8 mg/day, and that at an intake above 1.0 mg/day, urinary thiamin excretion is 'normal' and ETKA is almost 'normal'. The IOM noted the uncertainty on the dietary intake assessment of two studies (Henshaw et al., 1970; Anderson et al., 1986) and focused on the controlled depletion–repletion study by Sauberlich et al. (1979). For older adults, the IOM noted that limited evidence suggests that the requirements may be higher in older adults than in younger adults (Oldham, 1962; Pekkarinen et al., 1974; Hoorn et al., 1975; O'Rourke et al., 1990; Nichols and Basu, 1994; Wilkinson et al., 1997). The IOM decided to apply the same reference values as for younger adults. The IOM set an EAR for thiamin of 1.0 mg/day for men and 0.9 mg/day for women (i.e. a 10% lower EAR for women based on body size and energy requirements). RDAs were set at 1.2 mg/day and 1.1 mg/day respectively, by applying a coefficient of variation of 10%.

SCF (1993) considered that thiamin is involved in energy-yielding metabolism, in particular carbohydrate metabolism, and related the requirements for thiamin to energy intake. Although the SCF noted that the maximum ETKA and the saturation of the enzyme with its coenzyme are obtained for a thiamin intake of 0.140–0.190 mg/MJ (Brin, 1964), the SCF did not consider this to be a suitable indicator to derive a PRI for thiamin. SCF noted that clinical signs of deficiency are observed with an intake of less than 0.03 mg/MJ, that a long-term intake of 0.045 mg/MJ induced a decline in urinary excretion of thiamin down to 0.015 mg/day after 20 months without signs of deficiency, but with an impairment of metabolism of a glucose test dose after 30 months (Horwitt et al., 1948; Horwitt and Kreisler, 1949). The SCF also noted that an intake of 0.050 mg/MJ maintained urinary excretion of thiamin above 0.015 mg/day in depletion–repletion studies and that an intake of 0.072 mg/MJ maintained a 'normal' αETK (Williams et al., 1943; Sauberlich et al., 1979). SCF considered 0.072 mg/MJ as the AR. Applying a coefficient of variation of 20%, SCF set a PRI at 0.10 mg/MJ. The LTI was set at 0.050 mg/MJ. The SCF considered that thiamin requirement expressed in µg/MJ was the same for men and women or for younger and older adults. The PRI for thiamin corresponded to 1.1 mg/day and 0.9 mg/day for men and women, respectively, based on average energy expenditure of 11.3 MJ/day for men and 8.5 MJ/day for women. SCF also suggested a PRI of 0.8 mg/day for subjects with an energy intake of less than 8 MJ/day.

The UK COMA (DH, 1991) noted that beriberi may occur at thiamin intake of 0.48 mg/MJ (Williams, 1961), with urinary thiamin excretion being below 0.015 mg/day. The UK COMA also noted that 0.4 mg/day thiamin may be the 'absolute minimum' at 'low' energy intakes (Williams et al., 1943), although this value was not confirmed in studies in older subjects (Horwitt et al., 1948). The UK COMA considered the depletion–repletion study from Sauberlich et al. (1979) and set the AR at 0.07 mg/MJ and a Reference Nutrient Intake at 0.09 mg/MJ for adults. They considered that available evidence did not suggest different requirement between men and women (Oldham et al., 1946; Platt, 1958; Bamji, 1970; Ahmed et al., 1975; Lewis and King, 1980; Tang et al., 1989) or between younger and older adults (Horwitt et al., 1948). Based on the AR for energy set for UK, the Reference Nutrient Intake was set at 1.0 mg/day for men aged 19–50 years, 0.9 mg/day for men aged 50 years and over, and 0.8 mg/day for women. The UK COMA considered that thiamin intake should be above 0.4 mg/day for people on 'very low' energy diets. A Lower Reference Nutrient intake was also set at 0.05 mg/MJ for adults.

An overview of DRVs for thiamin for adults is presented in Table 2.

858 **Table 1:** Overview of Dietary Reference Values for thiamin for adults

	D-A-CH (2015)	NCM (2014)	WHO/FAO (2004)	Afssa (2001)	NL (2000)	IOM (1998)	SCF (1993)	DH (1991)
Age (years)	19–25	18–30	≥ 19	19–74	19–50	≥ 18	≥ 18	19–49
Men (mg/day)	1.3	1.4	1.2	1.3	1.1	1.2	1.1	1.0
Women (mg/day)	1.0	1.1	1.1	1.1	1.1	1.1	0.9	0.8
Age (years)	25–65	31–60		≥ 75	≥ 51			≥ 50
Men (mg/day)	1.2	1.3		1.2	1.1[(a)]			0.9
Women (mg/day)	1.0	1.1		1.2	1.1[(a)]			0.8
Age (years)	≥ 65	≥ 61						
Men (mg/day)	1.1	1.2						
Women (mg/day)	1.0	1.0						

859 (a): AI. Adequate Intake.
860 Afssa, Agence française de sécurité sanitaire des aliments; D–A–CH, Deutschland–Austria–Confoederatio Helvetica; DH,
861 Department of Health; FAO, Food and Agriculture Organization; IOM, US Institute of Medicine of the National
862 Academy of Sciences; NCM, Nordic Council of Ministers; NL, the Netherlands; SCF, Scientific Committee for Food;
863 WHO, World Health Organization.

864 4.2. Infants and children

865 D-A-CH (2015) considered the AR set for adults of 0.11 mg/MJ, a coefficient of variation of 10%, and
866 the requirements for energy of infants and children, to set the PRIs ranging from 0.4 mg/day for
867 infants aged 4–12 months to 1.4 mg/day for boys aged 15–19 years.

868 The Nordic countries (Nordic Council of Ministers, 2014) kept the same reference value for infants as
869 previously published, i.e. 0.10 mg/MJ, thus a value of 0.4 mg/day for infants 6–11 months. The AR
870 and RI for children were the same as for adults, i.e. 0.10 and 0.12 mg/MJ respectively. RIs for children
871 ranged between 0.5 mg/day (1–2 years) and 1.4 mg/day (boys aged 14–17 years).

872 WHO/FAO (2004) considered an average thiamin content of human milk of 0.21 mg/L (Committee on
873 Nutrition, 1985) and an average milk intake of infants of 0.75 L/day, which correspond to an intake of
874 0.16 mg/day thiamin for breast-fed infants. The WHO/FAO also mentioned data on blood
875 concentration of thiamin in infants and young children (Wyatt et al., 1991) and data on thiamin intake
876 and status on children aged 13–14 years (Bailey et al., 1994). The RNI for children ranged from
877 0.3 mg/day for infants aged 7–11 months to 0.9 mg/day for children aged 7–9 years. RNIs for boys
878 and girls aged 10–18 years were the same as for adults.

879 For infants, Afssa (2001) mentioned an average thiamin concentration of human milk of 0.15–
880 0.24 mg/L and set a reference value at 0.2 mg/day. For children, the PRIs were scaled down from the
881 PRI for adults using average square height, and ranged from 0.4 mg/day at age 1–3 years to
882 1.3 mg/day in boys at age 16–19 years.

883 For children aged 6 months to 18 years, the Health Council of the Netherlands (2000) noted the
884 limited evidence (Hart and Reynolds, 1957; Bailey et al., 1994), and decided to estimate adequate
885 intakes (AIs) by linear interpolation between the AI for infants aged zero to five months and the AR
886 for adults. The AIs ranged from 0.2 mg/day for infants aged 6–11 months to 1.1 mg/day for children
887 aged 14–18 years.

888 For infants aged 7–12 months, IOM (1998) compared the reference values that would be derived from
889 the upward extrapolation from the AI of infants aged zero to six months, from the downward
890 extrapolation from the EAR of adults (by allometric scaling, using body weights to the power of 0.75
891 and applying growth factors), or from the thiamin content of 0.6 L of breast milk, the average milk
892 volume consumed, and the intake of thiamin via solid foods (Montalto et al., 1985). This last approach
893 was considered to provide a too high value, and the IOM set an AI at 0.3 mg/day by downward
894 extrapolation from adult EARs. For setting RDAs for children and adolescents aged 9–18 years, IOM
895 mentioned studies in children older than 13 years that investigated thiamin urinary excretion or

erythrocyte transketolase activity (Hart and Reynolds, 1957; Dick et al., 1958; Bailey et al., 1994), but did not consider these studies as sufficient evidence. For all children, the IOM derived EARs by downwards extrapolation from adult EARs (by allometric scaling, using body weights to the power of 0.75 and applying growth factors) and RDAs by applying a coefficient of variation of 10%.

SCF (1993) concluded that the requirement for thiamin expressed in µg/MJ does not differ between children and adults, thus set the same AR and PRI in µg/MJ. Expressed in mg/day after calculation considering energy intake, the PRI ranged between 0.3 (infants aged 6–11 months) and 1.2 (boys aged 15–17 years) mg/day.

The UK COMA (DH, 1991) estimated the Reference Nutrient Intake for infants to be 0.07 mg/MJ considering an average thiamin concentration of is 0.16 mg/L in breast milk and a daily breast milk intake of 850 mL/day (0.05 mg/MJ) (DHSS, 1977), with an increase in the breast milk thiamin concentration during the first six weeks post-partum (Nail et al., 1980). For children, the UK COMA considered thiamin intake during the first year of life in the USA without signs of deficiency (0.07–0.16 mg/MJ) (Beal, 1955) and thiamin intake of 0.06–0.09 mg/MJ associated with normal thiamin excretion in girls aged seven to nine years (Boyden and Erikson, 1966). They also refer to a study in boys aged 14–17 years (Dick et al., 1958), which suggested that their minimum requirement was 1.41 ± 0.2 mg/day or 0.09 ± 0.01 mg/MJ (0.38 ± 0.06 mg/1,000 kcal). The UK COMA set for children the same Reference Nutrient Intake of 0.09 mg/MJ as for adults. Based on the AR for energy for UK, Reference Nutrient Intakes in children ranged from 0.2 mg/day at age 7–9 months to 1.1 mg/day in boys aged 15–18 years.

An overview of DRVs for thiamin for infants and children is presented in Table 3.

Table 2: Overview of Dietary Reference Values for thiamin for infants and children

	D-A-CH (2015)	NCM (2014)	WHO/FAO (2004)	Afssa (2001)	NL (2000)	IOM (1998)	SCF (1993)	DH (1991)
Age (months)								7–9
Infants (mg/day)								0.2
Age (months)	4–12	6–11	7–12	Infants	6–11	7–12	6–11	10–12
All (mg/day)	0.4	0.4	0.3	0.2	0.2[(a)]	0.3[(a)]	0.3	0.3
Age (years)	1–4	1–2	1–3	1–3	1–3	1–3	1–3	1–3
All (mg/day)	0.6	0.5	0.5	0.4	0.3[(a)]	0.5	0.5	0.5
Age (years)	4–7	2–5	4–6	4–6	4–8	4–8	4–6	4–6
All (mg/day)	0.7	0.6	0.6	0.6	0.5[(a)]	0.6	0.7	0.7
Age (years)	7–10	6–9	7–9	7–9	9-13		7–10	7–10
Boys (mg/day)	0.9	0.9	0.9	0.8	0.8[(a)]		0.8	0.7
Girls (mg/day)	0.8	0.9	0.9	0.8	0.8[(a)]		0.8	0.7
Age (years)	10–13	10–13	10–18	10–12	14–18	9–13	11–14	11–14
Boys (mg/day)	1.0	1.1	1.2	1.0	1.1[(a)]	0.9	1.0	0.9
Girls (mg/day)	0.9	1.0	1.1	1.0	1.1[(a)]	0.9	0.9	0.7
Age (years)	13–15	14–17		13–19		14–18	15–17	15–18
Boys (mg/day)	1.2	1.4		1.3		1.2	1.2	1.1
Girls (mg/day)	1.0	1.2		1.1		1.0	0.9	0.8
Age (years)	15–19							
Boys (mg/day)	1.4							
Girls (mg/day)	1.1							

(a): AI, Adequate Intake.
Afssa, Agence française de sécurité sanitaire des aliments; D–A–CH, Deutschland–Austria–Confoederatio Helvetica; DH, Department of Health; FAO, Food and Agriculture Organization; IOM, US Institute of Medicine of the National

Academy of Sciences; NCM, Nordic Council of Ministers; NL, the Netherlands; SCF, Scientific Committee for Food ; WHO, World Health Organization.

4.3. Pregnancy and lactation

D-A-CH (2015) considered the same AR of 0.11 mg/MJ (0.45 mg/1,000 kcal) as for non-pregnant women, a coefficient of variation of 10% and the increased energy requirement during the second and third trimesters of pregnancy or during lactation, to set the PRIs of 1.2 (second trimester) and 1.3 (third trimester) mg/day for pregnant women and 1.3 mg/day for lactating women.

The Nordic Countries (Nordic Council of Ministers, 2014) followed the approach of the IOM and considered an additional intake of 0.4 mg/day during pregnancy and 0.5 mg/day during lactation, thus a total RI of 1.5 and 1.6 mg/day for pregnant and lactating women, respectively.

In line with the approach by IOM (1998), WHO/FAO (2004) proposed an additional intake of 0.3 mg/day during pregnancy and an additional intake of 0.4 mg/day during lactation, to be added to the RNI for non-pregnant non-lactating women, thus RNI of 1.4 mg/day and 1.5 mg/day for pregnant and lactating women, respectively.

Afssa (2001) mentioned human and animal data on urinary and blood biomarkers of thiamin status during pregnancy, especially during the third trimester (Heller et al., 1974; Dostalova et al., 1988; Roth-Maier et al., 1990; Icke and Nicol, 1994). Afssa set a reference value of 1.8 mg/day for pregnant women. Afssa noted that thiamin content in breast milk is related to thiamin status of the mother (Thomas et al., 1980), that its secretion in breast milk is on average 0.2 mg/day (Nail et al., 1980) and that energy intake increases during lactation. Afssa set a reference value of 1.8 mg/day for lactating women.

The Health Council of the Netherlands (2000) mentioned studies concerning thiamin requirement during pregnancy (Reuter et al., 1967; Sauberlich, 1978; van den Berg and Bruinse, 1983), which could not be used to set reference values. The Council noted the increased energy intake and the growth of maternal and fetal tissues during pregnancy, and estimated the additional requirement to be 0.2 mg/day thiamin. The Council proposed for pregnancy a total AR of 1.0 mg/day and a PRI of 1.4 mg/day. During lactation, the Council considered a secretion of thiamin in breast milk of 0.16 mg/day based on a milk production of 0.8 L/day and an average thiamin concentration in breast milk of 0.2 mg/L (Fomon and McCormick, 1993), and the increased energy requirements of the mothers. After rounding, the Council thus added 0.4 mg/day to the AR of non-lactating women, and set a total AR of 1.2 mg/day and a total PRI of 1.7 mg/day during lactation.

IOM (1998) reported studies in pregnant and non-pregnant women (Toverud, 1940; Lockhart et al., 1943; Hathaway and Strom, 1946; Oldham et al., 1946; Datjm et al., 1948; Slobody et al., 1949; Oldham et al., 1950; Tripathy, 1968; Chong and Ho, 1970; Heller et al., 1974). They could not be used to set DRVs for pregnancy. The IOM set the EARs for pregnant women considering the increased growth in maternal and fetal compartments (20%) and in energy utilisation (10%), leading to a requirement of 0.3 mg/day after rounding, to be added to the EAR for non-pregnant women. The total EARs for the second and third trimesters of pregnancy were set at 1.2 mg/day. The RDA of 1.4 mg/day was derived by using a coefficient of variation (CV) of 10%. For lactating women, taking into account the average volume of milk intake of 0.78 L/day (Hofvander et al., 1982; Chandra, 1984; Neville et al., 1988; Allen et al., 1991; Butte and King, 2002) and an average thiamin content in breast milk of 0.21 mg/L (Committee on Nutrition, 1985), the IOM estimated that 0.16 mg/day of thiamin is transferred in the milk. According to the IOM, these 0.16 mg/day, as well as 0.1 mg/day (to cover the energy cost of milk production) should be added to the EAR for non-pregnant, non-lactating women. The EAR for lactating women was set at 1.2 mg/day, after rounding. The RDA of 1.4 mg/day was derived by using a CV of 10%.

SCF (1993) and the UK COMA (DH, 1991) considered the PRIs set for adults to be sufficient to cover the period of pregnancy and lactation, thus considered that there is no need to increase the PRI for thiamin (expressed in mg/MJ) during a normal pregnancy and that the loss of thiamin in human milk would be compensated by the higher energy intake during lactation. Calculating the PRIs in mg/day considering the increased energy intake during pregnancy and lactation, the PRI set by the SCF was

1.0 mg/day from the 10th week of pregnancy, and 1.1 mg/day for lactation. Considering available data in pregnant women (Oldham et al., 1950; Bagchi and Bose, 1962), and a secretion of 0.14 mg/day of thiamin in breast milk (for a content of 0.16 mg/L and a daily volume of 850 mL), the UK COMA (DH, 1991) set the Reference Nutrient Intake for pregnant or lactating women at 0.09 mg/MJ, as for other women. Expressed in mg/day and considering the AR for energy in the UK, this would lead to an additional 0.1 mg/day thiamin during the last trimester of pregnancy, and an additional 0.2 mg/day thiamin during lactation.

An overview of DRVs for thiamin for pregnant or lactating women is presented in Table 4.

Table 3: Overview of Dietary Reference Values for thiamin for pregnant or lactating women

	D-A-CH (2015)	NCM (2014)	WHO/FAO (2004)	Afssa (2001)	NL (2000)	IOM (1998)	SCF (1993)	DH (1991)
Pregnant women								
(mg/day)	1.2 (2nd trimester) 1.3 (3rd trimester)	1.5	1.4	1.8	1.4	1.4	1.0	0.9
Lactating women								
(mg/day)	1.3	1.6	1.5	1.8	1.7	1.4	1.1	1.0

Afssa, Agence française de sécurité sanitaire des aliments; D–A–CH, Deutschland–Austria–Confoederatio Helvetica; DH, Department of Health; FAO, Food and Agriculture Organization; IOM, US Institute of Medicine of the National Academy of Sciences; NCM, Nordic Council of Ministers; NL, the Netherlands; SCF, Scientific Committee for Food ; WHO, World Health Organization.

5. Criteria (endpoints) on which to base dietary reference values

5.1. Indicators of thiamin requirement

5.1.1. Depletion–repletion studies

A number of depletion–repletion studies have assessed changes in ETKA/αETK and urinary excretion of thiamin in response to controlled dietary intake of thiamin. The Panel considers that taken together these are suitable biomarkers for deriving the requirement for thiamin (Sections 2.4.2. and 2.4.3.). The Panel also considers that there is a positive relationship between thiamin requirement and energy requirement (Section 2.3.8.). Therefore, thiamin intakes are expressed per MJ (per 1,000 kcal) for the assessment.

Williams et al. (1942) reported that a thiamin intake of 0.052 mg/MJ (0.22 mg/1,000 kcal) for up to six months in two healthy subjects caused anorexia and a marked general impairment of mental and physical health. In another study on two healthy subjects, an intake of 0.042 mg/MJ (0.175 mg/1,000 kcal) for three months was accompanied by the development of unspecific clinical signs suggestive of thiamin deficiency (Williams et al., 1943).

On study involved eight healthy young men (age not reported) who were hosted in a metabolic ward for 51 days and received a diet providing 11.71 MJ/day (2,800 kcal/day) and 0.110–0.180 mg thiamin/day (Ziporin et al., 1965b, 1965a). The study was divided into three parts: a control period (thiamin intake 1.71–1.78 mg/day (~0.150 mg/MJ) for 9 days), a depletion period (0.110–0.180 mg/day (0.009–0.015 mg/MJ) for 30 days) and a "low level" repletion period (0.540–0.610 mg/day (0.046–0.052 mg/MJ) for 12 days). Physical activity was performed *ad libitum* with attempts to minimize inter- and intra-individual variations. During depletion, unspecific subjective symptoms (e.g. general malaise, headache, nausea) and physical symptoms (sinus tachycardia at rest (3/8), diminution of muscle strength (2/8) and tendon reflexes (4/8)) developed gradually in five subjects, while three subjects remained asymptomatic throughout the study. Physical symptoms disappeared within one week of thiamin repletion, while subjective symptoms persisted for two weeks, and then gradually disappeared. A progressive decline in ETKA to about 75% of the baseline value was observed during the depletion period, while ETKA returned to baseline value after one week of repletion. Mean (± SD) urinary free thiamin excretion was 0.283 ± 0.071 mg/24 hours at the end of the

control period and decreased to undetectable levels by 18 days of depletion. From then to the end of depletion, urinary excretion of thiamin metabolites (sum of pyrimidine and thiazole moieties) ranged from 0.884 ± 0.217 to 0.913 ± 0.224 mg/24 hours. During repletion, small amounts (0.003–0.013 mg/24 hours) of free thiamin were detected in urine samples, although not in all subjects. The authors assumed that continued excretion of thiamin metabolites during the depletion period indicates that tissue thiamin is used for metabolic purposes, and that metabolites represent a measure of depletion of the vitamin body stores. The authors defined thiamin requirement as the amount of thiamin which would at least equal the amount of metabolites excreted when there is no intact thiamin in the urine: 1) by substracting 0.160 mg of thiamin ingested daily with the diet from a mean thiamin metabolites output of 0.913 mg/24 hours during depletion, a thiamin requirement of 0.753 mg/day, corresponding to 0.064 mg/MJ (0.27 mg/1,000 kcal), was calculated; 2) by considering the total amount of thiamin metabolites excreted, a thiamin requirement of 0.913 mg/day, corresponding to 0.078 mg/MJ (0.33 mg/1,000 kcal), was proposed. The Panel notes that in this study the amount of thiamin required daily to replace the thiamin metabolites was 0.064–0.078 mg/MJ (0.27–0.33 mg/1,000 kcal).

In another study, six healthy adults (four men, two women, aged 22–27 years) were on a diet containing 0.035 to 0.239 mg thiamin/MJ (0.15 to 1 mg/1,000 kcal) for various time intervals during 9 to 10 months (Kraut et al., 1966). ETKA and urinary thiamin excretion were measured. Decrease of thiamin intake from 0.13–0.22 mg/MJ (0.54–0.92 mg/1,000 kcal) to 0.05–0.03 mg/MJ (0.15–0.21 mg/1,000 kcal) was associated with a drop in ETKA, and an increase in thiamin intake in the next study period to 0.07–0.09 mg/MJ enhanced ETKA up to levels similar to baseline. Urinary excretion of thiamin was in the range of 0.053 to 0.507 mg/24 hours. Urinary thiamin excretion was linearly related to dietary thiamin intake (r = 0.9 calculated based on presented data). Subjects had a decreased physical capacity in the bicycle ergometer tests, and one subject complained about lack of concentration and muscle pain with rapid walking over short distances. Complaints disappeared with a thiamin intake of 0.074 mg/MJ. A thiamin intake of 0.07–0.09 mg/MJ resulted in enhanced urinary thiamin excretion, and a further rise in thiamin intake to 0.13–0.19 mg/MJ was associated with a sharp increase in urinary thiamin excretion, suggesting that an intake of 0.07–0.09 mg/MJ may represent the thiamin requirement. Measures of ETKA associated with a thiamin intake of 0.13–0.19 mg/MJ were similar to those observed with thiamin intake of 0.07–0.09 mg/MJ. The Panel notes that maximum ETKA was observed at a daily thiamin intake of 0.17–0.22 mg/MJ. The Panel notes that in this study the measurement of different products to assess ETKA made the results difficult to interpret.

Bamji (1970) measured ETKA and urinary thiamin excretion (expressed in µg/g creatinine) in eight healthy Indian volunteers (four men, four women; age not reported) consuming an experimental diet providing 0.024 mg thiamin/MJ (0.1 mg/1,000 kcal) for two to three weeks (period I), and thereafter 0.048 mg/MJ (0.2 mg/1,000 kcal) and 0.096 mg/MJ (0.4 mg/1,000 kcal) for two 10-day periods (period II and III). An intake of 0.024 mg/MJ for seven days resulted in ETKA decrease by 15%, and after 21 days by 32% in men and by 50% in women. Thiamin intake of 0.048 mg/MJ was associated with EKTA increase to about 88% of the baseline and at intake of 0.096 mg/MJ, EKTA activity was not lower than the baseline value. In men, a continuous decrease in urinary thiamin excretion was observed until about 25% of the baseline values at the end of period I, followed by an increase in periods II (up to 50% of the baseline values) and III (up to 140% of baseline values). In women, urinary thiamin excretion decreased to about 35% of the baseline values at the end of period I, with no apparent change in period II (about 30% of baseline values) and an increase to up to 82% of baseline values at the end of period III. In order to estimate thiamin requirement the logarithm of dietary thiamin intake was plotted against ETKA or against urinary thiamin excretion. Tangents were drawn to the slopes and the points of insertion of these tangents were used to assess the requirement as the turning points at which ETKA had reached a plateau or a sharp increase in thiamin urinary excretion occurred. Based on urinary thiamin excretion, a requirement for thiamin of 0.063 mg/MJ (0.26 mg/1,000 kcal) for women and 0.075 mg/MJ (0.31 mg/1,000 kcal) for men was estimated. Based on ETKA, a thiamin requirement of 0.051 mg/MJ (0.21 mg/1,000 kcal) for women and 0.080 mg/MJ (0.34 mg/1,000 kcal) for men was derived. The Panel notes that these values were estimated from modelling data on a small number of subjects and uncertainties related to these estimates cannot be

assessed from the paper. The Panel notes that in this study, a level of 0.048 mg thiamin/MJ was insufficient to restore baseline ETKA, while a level of 0.096 mg/MJ was associated with a sharp increase in urinary excretion.

In the study by Sauberlich et al. (1979), seven healthy men (age not reported) received a diet free of thiamin for 14 days (depletion period, I). They were then divided in two groups with different levels of energy intake (group A: 11.72 MJ/day (2,800 kcal/day) and group B: 15.06 MJ/day (3,600 kcal/day)). For successive periods of 11 to 14 days, subjects received controlled amounts of thiamin of 0.39 (period II), 0.56 (period III), 0.84 (period IV) and 0.84 or 1.08 mg/day (period V), corresponding to 0.033, 0.048, 0.072 and 0.072 mg/MJ for group A (n = 3) and 0.026, 0.038, 0.055 and 0.072 mg/MJ for group B (n =4), respectively. Finally, an *ad libitum* diet containing > 2 mg thiamin/day (> 0.143 mg/MJ) was provided to both groups (period VI). Constant body weight of the subjects was maintained by adjustment of scheduled daily physical activity and exercise. During periods I (no thiamin) and II (lowest thiamin intake), a progressive decline in urinary thiamin excretion was observed to about 0.025 mg/24 hours in both groups. In periods III and IV, urinary thiamin excretion rose gradually in both groups but urinary thiamin excretion was significantly lower in group B than in group A. There was no difference in urinary thiamin excretion in period V, when both groups received 0.072 mg/MJ (mean ± SD: 0.088 ± 0.009 and 0.090 ± 0.023 mg/24 hours in groups A and B, respectively). Urinary thiamin excretion similar to baseline excretion was reached at the end of the study (0.258 ± 0.010 and 0.302 ± 0.076 mg/24 hours in groups A and B, respectively). Mean baseline αETK level was about 1.02 for group A and 1.03 for group B. In both groups, similar increases in mean αETK were observed during periods I–III, up to above 1.35. In group A, mean αETK decreased to 1.12 in period IV and 1.03 in period V, while in group B the respective figures were 1.22 and 1.07. This indicates that an intake of 0.055 mg/MJ for 11 days was insufficient to restore adequate thiamin status, while an intake of 0.072 mg/MJ was associated with an adequate status of the vitamin (αETK ≤ 1.15, see Section 2.4.2). During period VI (*ad libitum*), mean αETK in both groups was about 1.03. The Panel notes that, contrary to group A, a daily intake of 0.84 mg thiamin/day failed to restore normal αETK in group B, which indicates an increased requirement for thiamin when energy requirement is increased. The Panel notes that αETK returned to normal level (mean αETK about 1.03–1.07) at a thiamin intake of 0.072 mg/MJ and was associated with urinary thiamin excretion of about 0.09 mg/24 hours. On an *ad libitum* diet providing > 0.14 mg thiamin/MJ, a sharp increase (to about 0.3 mg/24 hours) of urinary thiamin excretion occurred, while only slight changes in αETK were noted.

5.1.2. Observational studies

Several observational studies assessed thiamin intake, through dietary questionnaires, and biomarkers of thiamin status in adult populations, particularly older populations.

Using a 7-day dietary recall questionnaire, Anderson et al. (1986) reported mean thiamin intake of about 0.12 mg/MJ (0.5 mg/1,000 kcal) in a group of 11 male and female adults (25–75 years) with αETK > 1.15 compared to about 0.14 mg/MJ (0.6 mg/1,000 kcal) in 31 men and women with αETK < 1.15. High prevalence (> 40%) of αETK > 1.15 were found in two studies which involved older subjects (≥ 65 years) with mean thiamin intake around 0.19 mg/MJ (0.8 mg/1,000 kcal) (30 men and 30 women), assessed by a 3-day food record (Nichols and Basu, 1994) and 0.12 mg/MJ (0.5 mg/1,000 kcal) (80 women), assessed by four 24-hour recall questionnaires (Smidt et al., 1991). The Panel notes that these studies included subjects with health issues and assessed a single biomarker.

In a study in subjects selected to be free of apparent disease, αETK < 15% and similar erythrocyte total thiamin concentrations were found in groups of younger (19–37 years, n = 14) and older (70–82 years, n = 10) people with thiamin intake around 0.17 mg/MJ (0.7 mg/1,000 kcal), assessed by a 3-day weighted record (O'Rourke et al., 1990). Lower ETKA was found in the older compared to the younger subjects (1,287 (1,163–1410) mU/g Hb vs 1,482 (1,320–1,645) mU/g Hb; $p < 0.05$). The authors noted that the actual thiamin intakes were likely to be lower than the estimated intakes as they were derived from food tables that might overestimate the true thiamin content of food by up to 30%.

The Panel notes the methodological limitations of these studies. The Panel considers that these studies do not provide data for deriving DRVs for thiamin in adults. The Panel also considers that these studies do not provide evidence for a different dietary requirement of thiamin in older compared to younger adults.

5.1.3. Conclusions on indicators of thiamin requirements in adults

The Panel considers that results from the controlled experiment by Sauberlich et al. (1979) indicate a positive relationship between thiamin requirement and energy requirement.

The Panel notes that thiamin intake of 0.009–0.014 mg/MJ for about a week resulted in significant reduction in the urinary thiamin excretion and ETKA associated with the development of some unspecific clinical symptoms of thiamin deficiency (Ziporin et al., 1965b, 1965a). The Panel also notes that thiamin intakes of 0.042–0.052 mg/MJ for some months were associated with clinical symptoms suggestive of thiamin deficiency (Williams et al., 1942; Williams et al., 1943).

The Panel considers that the study by Sauberlich et al. (1979) indicates a thiamin requirement of 0.072 mg/MJ for adult men because this thiamin intake was associated with low urinary thiamin excretion (around 0.09 mg/day) and αETK indicative of an adequate thiamin status (< 15%). The Panel also notes that, in this study, increasing the thiamin intake from 0.072 mg/MJ to ≥ 0.14 mg/MJ was associated with a sharp increase in urinary thiamin excretion and only slight changes in transketolase activity, indicating tissue saturation. The Panel notes that the depletion–repletion study by Kraut et al. (1966) supports this value. In this study, ETKA was restored with an intake of thiamin of 0.07–0.09 mg/MJ, while urinary thiamin excretion sharply increased with a thiamin intake of 0.13–0.19 mg/MJ without further change in ETKA. Based on similar criteria, the study by Bamji (1970) indicates that mean thiamin requirement is higher than 0.048 mg/MJ and lower than 0.096 mg/MJ, which is consistent with these findings. The Panel notes that these studies were performed in a small number of subjects and mean values of dietary thiamin intake, ETKA/αETK and urinary thiamin excretion were used to assess thiamin requirement.

The Panel also notes that maximum ETKA was observed at a daily thiamin intake of 0.17–0.22 mg/MJ (Kraut et al., 1966). The Panel considers that the biological significance of maximal stimulation of ETKA and whether it is required for adequate body function is not known.

5.1.4. Infants and children

Some studies attempted to estimate thiamin requirement of infants (Holt et al., 1949) and children (Dick et al., 1958) based on the changes in urinary excretion of thiamin in response to controlled amounts of dietary thiamin. In these studies, the level of thiamin intake associated with "minimal" urinary thiamin excretion was used as a criterion to define thiamin requirement. The Panel notes that a single biomarker was used in these studies, which does not reliably reflect thiamin status.

In an observational study in 19 boys and 35 girls aged 13 to 14 years in the UK, Bailey et al. (1994) assessed thiamin intake, based on 7-day weighed record and direct analysis of duplicate diets, and ETKA, αETK and total erythrocytes thiamin. Mean analysed thiamin intakes were 1.52 mg/day in girls and 1.95 mg/day in boys, corresponding to 0.88 mg/1,000 kcal in both groups. Average 7-day calculated thiamin intake was significantly lower than analysed intakes for both sexes. On an individual basis, calculated intakes ranged from 30 to 143% of corresponding analysed values. Mean (range) αETK were 1.07 (0.86–1.45) in girls and 1.05 (0.69–1.36) in boys. Mean (range) ETKA were 89.66 (54.5–165.74) mU/g Hb in girls and 90.08 (58.33–140.62) mU/g Hb in boys. Mean (range) total thiamin concentrations in erythrocytes were 226.8 (101.0–949.9) nmol/L in girls and 206.1 (119.7–445.7) nmol/L in boys. Overall, 30.8% of children had αETK ≥ 1.15, while 1.9% of children had an analysed thiamin intake < 0.1 mg/MJ (0.4 mg/1,000 kcal). No correlations were found between analysed thiamin intake and any of the markers measured. The Panel considers that no conclusion can be drawn from this study with respect to thiamin requirement in children.

The Panel considers that there are no studies which can be used for deriving requirement for thiamin in infants and children.

5.1.5. Pregnant and lactating women

Some observational studies in pregnant women have reported high prevalence (20–40%) of αETK coefficient > 1.20, taken as indicative of an inadequate thiamin status (Heller et al., 1974; Vir et al., 1980), as well as decrease in ETKA and blood thiamin concentration during pregnancy (Dirige et al., 1978; Vir et al., 1980; Baker et al., 2002). One study found no correlations between αETK and the length, weight and head circumference of the newborns (Dirige et al., 1978). The Panel notes that thiamin intake was not reported in these studies and the cause (e.g. physiological changes, other determinants) and significance of these observations in pregnant women are unknown.

Ortega et al. (2004) examined the relationship between thiamin intake (assessed using a five-day weighted dietary record) and αETK in 51 pregnant Spanish women (aged 18–35 years) in the third trimester. Thiamin concentration in their mature breast milk was also measured. About 13.7% of women had αETK > 1.25, used as a cut-off for thiamin deficiency. Women were divided between those who had thiamin intake > or < 0.4 mg/1,000 kcal + 0.1 mg per day.[6] Mean thiamin intakes of the respective groups were 1.45 ± 0.38 mg/day and 0.87 ± 0.13 mg/day. When expressed on a per MJ basis, mean thiamin intake were similar in both groups (0.16 ± 0.03 mg/MJ vs 0.14 ± 0.04 mg/MJ). Mean αETK value was significantly lower in the first than in the second group (1.01 ± 0.19 vs 1.21 ± 0.30, $p < 0.05$). In the first group, 23.7% of women had αETK > 1.15, and 53.8% in the second group. Thiamin concentrations in mature breast milk were 157 ± 117 µg/L and 66 ± 19 µg/L in the respective groups ($p < 0.05$). The Panel notes that data are presented in aggregated form and that this study cannot be used to assess the level of thiamin intake which would be associated with adequate thiamin status.

The Panel considers that the available data on the relationship between thiamin intake and biomarkers of thiamin status in pregnancy cannot be used for deriving DRVs for thiamin in pregnancy. There are no data on the relationships between thiamin intake and biomarkers of thiamin status in lactating women.

5.2. Thiamin intake and health consequences

A comprehensive search of the literature published between 1990 and 2011 was performed as preparatory work to this assessment in order to identify new data on relevant health outcomes upon which DRVs for thiamin may potentially be based (El-Sohemy et al., 2012). An additional literature search (in Pubmed) was performed to identify new data published afterwards and until September 2016 on thiamin intake and health outcomes.

The relationship between thiamin intakes and health outcomes has been investigated in observational (case–control, cross-sectional, prospective cohort) studies, where an association between thiamin intake and health outcomes may be confounded by uncertainties inherent in the methodology used for the assessment of thiamin intakes and by the effect of other dietary, lifestyle or undefined factors on the health or disease outcomes investigated. No intervention studies are available on thiamin intake and health outcomes.

Available data on the relationship between thiamin intake and mortality (Huang et al., 2012), nuclear cataract (Cumming et al., 2000), squamous intraepithelial cervical lesions (Hernandez et al., 2003), glucose intolerance (Bakker et al., 1998) and premenstrual syndrome (Chocano-Bedoya et al., 2011) are limited and therefore cannot be used to derive DRVs for thiamin.

The relationship between dietary thiamin intake and cognitive function in healthy older adults was assessed in a review by Koh et al. (2015). Nine studies (two cohort studies and seven cross-sectional studies) were included. Among the cohort studies, one examined the relationship between thiamin intake and abstract reasoning and found a positive correlation ($r = 0.29$; $p < 0.01$); there was no significant correlation between thiamin intake and visuospatial skills or nonverbal learning and memory (La Rue et al., 1997). In the other cohort study by McNeill et al. (2011), no association was

[6] Recommended intake for thiamin during pregnancy for the Spanish population Departamento de Nutricion, 1994. Ingestas Diarias Recomendadas de Energia y Nutrientes para la Poblacion Espanola [Recommended Energy and Nutrient Intakes for the Spanish Population] Departamento de Nutricion, Madrid, Spain.

found between thiamin intake and measures of cognitive function. Among the cross-sectional studies, five reported a positive association between thiamin intake and measures of cognitive function (most commonly assessed by Mini Mental State Examination) (Nes et al., 1988; Ortega et al., 1997; Lee et al., 2001; Requejo et al., 2003; Aparicio Vizuete et al., 2010), while two found no association (Shatenstein et al., 2007; Katsiardanis et al., 2013). The Panel notes that there is no consistent evidence for an association between dietary intake of thiamin and cognitive function in healthy older people.

The Panel considers that available data on thiamin intake and health outcomes are either limited or inconsistent and cannot be used for deriving DRVs for thiamin.

6. Data on which to base dietary reference values

The Panel considers that data from depletion–repletion studies in adults on the amount of dietary thiamin intake associated with αETK < 1.15 or with the restoration of normal (baseline) ETKA, without a sharp increase in urinary thiamin excretion, can be used to estimate thiamin requirement (Section 5.1.1.). The Panel considers that thiamin requirement is related to energy requirement (Sections 2.3.7. and 5.1.1.) and decides to set DRVs on a per MJ basis. PRIs for thiamin of particular population groups, expressed in mg/day, can be estimated based on their respective energy requirements. The ARs for energy for various Physical Activity Levels (PAL values) can be found in the Scientific Opinion on Dietary Reference Values for energy (EFSA NDA Panel, 2013). The Panel notes that, as for other nutrient reference values, DRVs for thiamin are set under the assumption that intakes of other essential nutrients and energy are adequate.

6.1. Adults

The Panel considers that no additional scientific evidence has become available since the assessment of the SCF in 1993 which would require to reconsider the DRVs for thiamin set at that time. The Panel endorses the AR of 0.072 mg/MJ (0.3 mg/1,000 kcal) for all adults which was set by the SCF on the basis of the depletion–repletion study by Sauberlich et al. (1979). The Panel notes that the study from Sauberlich et al. (1979) involved a small number of men, however, the Panel considers that results from other depletion–repletion studies (Kraut et al., 1966; Bamji, 1970) are in agreement with this value. The Panel agrees on the coefficient of variation of 20% used by the SCF, to cover uncertainties related to the distribution of thiamin requirements in the general population, and endorses the Population Reference Intake (PRI) of 0.1 mg/MJ (0.4 mg/1,000 kcal) proposed by the SCF for all adults (Table 4). No new evidence has become available that the relationship between thiamin requirement and energy requirement differs between men and women, or between younger and older adults. PRIs for thiamin, expressed in mg/day, are presented in Appendix H.

6.2. Infants

For infants aged 7–11 months, the Panel assumes that the relationship between thiamin requirement and energy requirement does not differ from that of adults. Therefore, the AR and PRI, expressed as mg/MJ, for adults are applied (Table 4). PRIs for children, expressed in mg/day, are presented in Appendix I.

6.3. Children

For children, the Panel assumes that the relationship between thiamin requirement and energy requirement does not differ from that of adults. Therefore, the AR and PRI, expressed as mg/MJ, for adults are applied (Table 4). PRIs for children, expressed in mg/day, are presented in Appendix J.

6.4. Pregnancy

The Panel assumes that the relationship between thiamin requirement and energy requirement in pregnancy does not differ from that of other adults. Therefore, the AR and PRI, expressed as mg/MJ,

for adults apply to pregnancy (Table 4). The Panel notes that the energy requirement in pregnant women is increased by 0.29 MJ/day, 1.1 MJ/day and 2.1 MJ/day, for the first, second and third trimesters, respectively (EFSA NDA Panel, 2013). The PRI for thiamin of pregnant women, in mg/day, is increased compared with that of non-pregnant women, as presented in Appendix K.

6.5. Lactation

The Panel assumes that the relationship between thiamin requirement and energy requirement in lactating women does not differ from that of other adults. Therefore, the AR and PRI, expressed as mg/MJ, for adults apply to lactation (Table 4). The Panel notes that the energy requirement in lactation is increased by 2.1 MJ/day (EFSA NDA Panel, 2013). An average loss of thiamin in breast milk of 0.15 mg/day was estimated during the first six month of lactation (Section 2.3.5.4.). The Panel considers that the extra requirement for thiamin calculated on the basis of the increased energy requirement related to lactation covers the losses of thiamin through breast milk. The PRI for thiamin of lactating women, in mg/day, is increased compared with that of non-lactating women, as presented in Appendix K.

CONCLUSIONS

The Panel concludes that no new scientific data have become available that would require to change the Population Reference Intake (PRI) for thiamin set by the SCF in 1993. The Panel sets a PRI for thiamin of 0.1 mg/MJ (0.4 mg/1,000 kcal) for all population groups (Table 4).

Table 4: Summary of Dietary Reference Values for thiamin

Age	PRI (mg/MJ)
7–11 months	0.1
1–3 years	0.1
4–6 years	0.1
7–10 years	0.1
11–14 years	0.1
15–17 years	0.1
≥ 18 years [(a)]	0.1

(a): including pregnancy and lactation

RECOMMENDATIONS FOR RESEARCH

The Panel recommends:

- Studies to characterise the relationship between thiamin intake and the most informative combination of biomarkers of thiamin status, in different life stages.
- Further investigations of the dose–response relationships between thiamin intake and individual biomarkers.
- Further research on the use of erythrocyte TDP concentration as a marker of thiamin intake and status.
- Further research on the effect of diet composition (e.g. carbohydrates) on the thiamin requirement.
- Further research on the relationship between thiamin requirement and energy requirement.

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APPENDICES

Appendix A. Concentrations of thiamin in breast milk from mothers of term infants in Western countries

Reference	Country	Number of women (number of samples)	Maternal thiamin intake (Mean ± SD) (mg/day)	Stage of lactation (post partum)	Thiamin concentration in breast milk (µg/L)		Analytical method
					Mean ± SD	Range	
Ortega et al. (2004)	Spain		During the 3rd trimester of pregnancy:				Oxidation of thiamin to thiochrome and measurement by fluorescent spectrophotometry
		Group L (thiamin intake < RI[a])					
		n = 13	0.87 ± 0.13				
		(3)		13–14 days (transitional)	239 ± 273		
		(5)		40 days (mature)	66 ± 19		
		Group H (thiamin intake ≥ RI[a])					
		n = 38	1.45 ± 0.38[b]				
		(17)		13–14 days (transitional)	234 ± 151		
		(16)		40 days (mature)	157 ± 117		
Nail et al. (1980)[c]	USA	n = 5					Thiochrome assay and fluorometry (Hennessy and Cerecedo (1939))
			not supplemented 5–7 days: 1.33 ± 0.40	5–7 days (transitional)	138 ± 18		
			43–45 days: 1.26 ± 0.17	43–45 days (mature)	220 ± 27		
		n = 7	supplemented				
			5–7 days: 3.40 ± 0.42	5–7 days (transitional)	133 ± 27		
			43–45 days: 3.33 ± 0.77	43–45 days (mature)	238 ± 21		

Reference	Country	Number of women (number of samples)	Maternal thiamin intake (Mean ± SD) (mg/day)	Stage of lactation (post partum)	Thiamin concentration in breast milk (µg/L)		Analytical method
					Mean ± SD	Range	
Dostalova et al. (1988)	Switzerland	n = 26	not supplemented				Fluorometry
		(9)		3–5 days (colostrum)	25 ± 12	15–46	
		(2)		6–10 days (transitional)	20 ± 6	15–24	
		(4)		2 weeks (mature)	169 ± 84	104–290	
		(18)		4 months (mature)	154 ± 42	Foremilk: 65–233 Hindmilk: 104–156	
	Finland	n not reported (57)	supplemented with 2 mg thiamin/day	3 or 4 days (colostrum)	40 ± 25	12–142	Fluorometry
		(57)		8 weeks (mature)	193 ± 40	119–343	
		(57)		4 months (mature)	188 ± 39	107–284	
		(57)		6 months (mature)	199 ± 45	98–396	
		(57)		7.5 months (mature)	204 ± 41	112–296	
Ford et al. (1983)	UK	n = 6 (13)		1–5 days (colostrum)	28.4	13–59	Assayed with *Lactobacillus fermenti* test medium from Banhidi (1958)
		n = 10 (21)		6–15 days (transitional)	64.6	24–106	
		n = 26 (26)		16–224 days (mature)	183	60–360	
Thomas et al. (1980) [(c)]	USA	n = 6	not supplemented 1. 49 ± 0.96	6 months (mature)	208 ± 34		Modification of the thiochrome method (Hennessy and Cerecedo (1939))
		n = 6	supplemented Food: 1.56 ± 0.47 Supplements: 1.7	6 months (mature)	228 ± 26		
Roderuck et al. (1945) [(c)]	USA	2 (2)		Day 1	14.8	9.2–20.5	Tiochrome method adapted from Hennessy (1942)
		5 (5)		Day 2	15.1	12.4–18.4	
		6 (6)		Day 3	16.2	12.3–20.8	

Reference	Country	Number of women (number of samples)	Maternal thiamin intake (Mean ± SD) (mg/day)	Stage of lactation (post partum)	Thiamin concentration in breast milk (µg/L)		Analytical method
					Mean ± SD	Range	
		6 (6)		Day 4	19.6	17.0–24.0	
		6 (6)		Day 5	25.0	17.2–33.9	
		6 (6)		Day 6	35.4	23.2–48.6	
		9 (9)		Day 7	46.5	31.0–62.1	
		7 (7)		Day 8	56.8	32.0–78.7	
		7 (7)		Day 9	77.7	58.0–105.2	
		6 (6)		Day 10	81.2	66.8–102.2	
		10 (90)		45–306 days (mature)[(d)]	148	91–184	
		65 (187)		15–362 days (mature)[(e)]	140	81–227	

Studies were identified by a comprehensive literature search for publications from January 2000 to January 2014 (LASER Analytica, 2014) and additional literature search before these dates.

FFQ, food frequency questionnaire; RI, recommended intake; UPLC–MS/MS, Ultra performance liquid chromatography - tandem mass spectrometry method).
(a): Recommended intake for the Spanish population, for women in the second half of pregnancy: 0,4 mg/4184 KJ + 0,1 mg/day, with a minimum provision of 1 mg/day (Ortega et al., 2014).
(b): One woman took a food supplement which provided 1.57 mg/day.
(c): No information on whether infants were born at term or were preterm. It is presumed that infants were born at term.
(d): 24-hour milk samples.
(e): Complete expressions of milk secreted in 4–8 hours.

Appendix B. Dietary surveys in the EFSA Comprehensive European Food Consumption Database included in EFSA's nutrient intake calculation for thiamin

Country	Dietary survey (year)	Year	Method	Days	Age (years)	Number of subjects						
						Infants < 1 year	Children 1–< 3 years	Children 3–< 10 years	Adolescents 10–< 18 years	Adults 18–< 65 years	Adults 65–< 75 years	Adults ≥ 75 years
Finland/1	NWSSP	2007–2008	48-hour dietary recall [a]	2 × 2[a]	13–15				306			
Finland/2	FINDIET2012	2012	48-hour dietary recall [a]	2[a]	25–74					1,295	413	
Finland/3	DIPP	2000–2010	Dietary record	3	0.5–6	499	500	750				
France	INCA2	2006–2007	Dietary record	7	3–79			482	973	2,276	264	84
Germany/1	EsKiMo	2006	Dietary record	3	6–11			835	393			
Germany/2	VELS	2001–2002	Dietary record	6	< 1–4	158	348[c]	296[c]				
Ireland	NANS	2008–2010	Dietary record	4	18–90					1,274	149	77
Italy	INRAN-SCAI 2005-06	2005–2006	Dietary record	3	< 1–98	16[b]	36[b]	193	247	2,313	290	228
Latvia	FC_PREGNANT WOMEN 2011	2011	24-hour dietary recall	2	15–45				12 [b]	991 [c]		
Netherlands	DNFCS 2007–2010	2007–2010	24-hour dietary recall	2	7–69			447	1142	2,057	173	
Sweden	RISKMATEN	2010–2011	Dietary records (Web)[d]	4	18–80					1,430	295	72
UK/1	DNSIYC-2011	2011	Dietary record	4	0.3–1.5	1,369	1,314					
UK/2	NDNS Rolling Programme (Years 1–3)	2008–2011	Dietary record	4	1–94		185	651	666	1,266	166	139

DIPP, type 1 Diabetes Prediction and Prevention survey; DNFCS, Dutch National Food Consumption Survey; DNSIYC, Diet and Nutrition Survey of Infants and Young Children; EsKiMo, Ernährungsstudie als KIGGS-Modul; FC_PREGNANTWOMEN, food consumption of pregnant women in Latvia; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale des Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia; NANS, National Adult Nutrition Survey; NDNS, National Diet and Nutrition Survey; NWSSP, Nutrition and Wellbeing of Secondary School Pupils; VELS, Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln.

(a): A 48-hour dietary recall comprising two consecutive days.

(b): 5th or 95th percentile intakes calculated from fewer than 60 subjects require cautious interpretation as the results may not be statistically robust (EFSA, 2011a) and, therefore, for these dietary surveys/age classes, the 5th and 95th percentile estimates are not presented in the intake results.

(c): Four children from the VELS study (one aged 1–< 3 and three aged 3–< 10 years) and one adult from the Latvian study were not considered in the assessment as only one 24-hour dietary recall day was available.

(d): The Swedish dietary records were introduced through the Internet.

1939 **Appendix C. Thiamin intakes (mg/day and mg/MJ) in males in different surveys, estimated by EFSA according to age class and country**

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ			
			n	Average	Median	P5	P95	Average	Median	P5	P95
< 1 year[a]	Germany	VELS	84	0.53	0.54	0.32	0.77	0.17	0.17	0.11	0.21
	Finland	DIPP_2001_2009	247[b]	0.39	0.43	0.05	0.68	0.20	0.19	0.12	0.31
	United Kingdom	DNSIYC_2011	699	0.65	0.64	0.32	1.01	0.19	0.19	0.12	0.26
	Italy	INRAN_SCAI_2005_06	9	0.31	0.27	- [c]	- [c]	0.11	0.10	- [c]	- [c]
1–< 3 years	Germany	VELS	174	0.65	0.63	0.40	0.97	0.14	0.13	0.09	0.18
	Finland	DIPP_2001_2009	245	0.75	0.74	0.44	1.12	0.21	0.20	0.15	0.27
	United Kingdom	NDNS-Rolling Programme Years 1–3	107	0.98	0.95	0.64	1.43	0.20	0.19	0.15	0.29
	United Kingdom	DNSIYC_2011	663	0.83	0.82	0.50	1.21	0.20	0.20	0.13	0.27
	Italy	INRAN_SCAI_2005_06	20	0.61	0.59	- [c]	- [c]	0.12	0.13	- [c]	- [c]
3–< 10 years	Germany	EsKiMo	426	1.17	1.12	0.70	1.75	0.15	0.15	0.10	0.22
	Germany	VELS	146	0.75	0.72	0.46	1.12	0.13	0.13	0.09	0.19
	Finland	DIPP_2001_2009	381	1.07	1.01	0.69	1.61	0.18	0.18	0.13	0.24
	France	INCA2	239	1.01	0.95	0.56	1.61	0.16	0.15	0.11	0.24
	United Kingdom	NDNS-Rolling Programme Years 1–3	326	1.29	1.26	0.74	1.91	0.20	0.20	0.14	0.27
	Italy	INRAN_SCAI_2005_06	94	0.95	0.91	0.61	1.43	0.13	0.13	0.09	0.19
	Netherlands	DNFCS 2007-2010	231	0.87	0.82	0.48	1.39	0.10	0.10	0.07	0.15
10–< 18 years	Germany	EsKiMo	197	1.23	1.21	0.74	1.94	0.15	0.15	0.10	0.22
	Finland	NWSSP07_08	136	1.39	1.35	0.92	2.05	0.17	0.17	0.12	0.23
	France	INCA2	449	1.25	1.18	0.73	1.96	0.16	0.15	0.11	0.23
	United Kingdom	NDNS-Rolling Programme Years 1–3	340	1.66	1.60	0.93	2.72	0.20	0.20	0.13	0.29
	Italy	INRAN_SCAI_2005_06	108	1.26	1.21	0.73	2.05	0.13	0.12	0.09	0.19
	Netherlands	DNFCS 2007-2010	566	1.12	1.04	0.64	1.80	0.11	0.10	0.07	0.17
18–< 65 years	Finland	FINDIET2012	585	1.56	1.50	0.77	2.59	0.17	0.16	0.11	0.25
	France	INCA2	936	1.24	1.21	0.69	1.94	0.14	0.14	0.10	0.20
	United Kingdom	NDNS-Rolling Programme Years 1–3	560	1.78	1.72	0.92	2.75	0.21	0.20	0.13	0.31
	Ireland	NANS_2012	634	1.99	1.92	1.06	3.18	0.20	0.20	0.13	0.29
	Italy	INRAN_SCAI_2005_06	1,068	1.13	1.08	0.65	1.75	0.12	0.12	0.09	0.18
	Netherlands	DNFCS 2007-2010	1,023	1.26	1.18	0.66	2.04	0.11	0.10	0.07	0.18
	Sweden	Riksmaten 2010	623	1.52	1.47	0.80	2.37	0.16	0.15	0.10	0.22
65–< 75 years	Finland	FINDIET2012	210	1.40	1.32	0.77	2.30	0.17	0.17	0.11	0.26
	France	INCA2	111	1.19	1.17	0.66	1.78	0.14	0.14	0.10	0.19
	United Kingdom	NDNS-Rolling Programme Years 1–3	75	1.74	1.71	0.74	2.63	0.21	0.21	0.13	0.31
	Ireland	NANS_2012	72	1.87	1.88	1.00	2.73	0.22	0.21	0.14	0.35

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ			
			n	Average	Median	P5	P95	Average	Median	P5	P95
	Italy	INRAN_SCAI_2005_06	133	1.08	1.05	0.70	1.64	0.13	0.12	0.09	0.17
	Netherlands	DNFCS 2007-2010	91	1.16	1.11	0.69	1.96	0.13	0.12	0.08	0.21
	Sweden	Riksmaten 2010	127	1.39	1.34	0.83	2.08	0.16	0.15	0.11	0.23
≥ 75 years	France	INCA2	40	1.06	1.04	- (c)	- (c)	0.14	0.14	- (c)	- (c)
	United Kingdom	NDNS-Rolling Programme Years 1–3	56	1.48	1.44	- (c)	- (c)	0.21	0.20	- (c)	- (c)
	Ireland	NANS_2012	34	1.75	1.69	- (c)	- (c)	0.23	0.22	- (c)	- (c)
	Italy	INRAN_SCAI_2005_06	69	1.03	1.04	0.61	1.54	0.12	0.12	0.09	0.16
	Sweden	Riksmaten 2010	42	1.35	1.29	- (c)	- (c)	0.16	0.16	- (c)	- (c)

n, number of individuals; P5, 5th percentile; P95, 95th percentile.

DIPP, type 1 Diabetes Prediction and Prevention survey; DNFCS, Dutch National Food Consumption Survey; DNSIYC, Diet and Nutrition Survey of Infants and Young Children; EsKiMo, Ernährungsstudie als KIGGS-Modul; FC_PREGNANTWOMEN, food consumption of pregnant women in Latvia; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale des Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia; NANS, National Adult Nutrition Survey; NDNS, National Diet and Nutrition Survey; NWSSP, Nutrition and Wellbeing of Secondary School Pupils; VELS, Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln.

(a): The proportions of breastfed infants were 58% in the Finnish survey, 40% in the German survey, 44% in the Italian survey, and 21% in the UK survey. Most infants were partially breastfed. For the Italian and German surveys, breast milk intake estimates were derived from the number of breastfeeding events recorded per day multiplied by standard breast milk amounts consumed on an eating occasion at different age. For the UK survey, the amount of breast milk consumed was either directly quantified by the mother (expressed breast milk) or extrapolated from the duration of each breastfeeding event. As no information on the breastfeeding events were reported in the Finnish survey, breast milk intake was not taken into consideration in the intake estimates of Finnish infants.

(b): n = 245 for estimated intake expressed in mg/MJ.

(c): 5^{th} or 95^{th} percentile intakes calculated from fewer than 60 subjects require cautious interpretation as the results may not be statistically robust (EFSA, 2011a) and, therefore, for these dietary surveys/age classes, the 5^{th} and 95^{th} percentile estimates are not presented in the intake results.

1956 **Appendix D. Thiamin intakes (mg/day and mg/MJ) in females in different surveys, estimated by EFSA according to age class and country**

Age class	Country	Survey	Intakes expressed in mg per day					Intakes expressed in mg per MJ			
			n	Average	Median	P5	P95	Average	Median	P5	P95
< 1 year[a]	Germany	VELS	75	0.47	0.47	0.29	0.67	0.16	0.16	0.10	0.21
	Finland	DIPP_2001_2009	253[b]	0.36	0.36	0.06	0.67	0.21	0.20	0.13	0.37
	United Kingdom	DNSIYC_2011	670	0.58	0.56	0.28	0.94	0.19	0.19	0.11	0.25
	Italy	INRAN_SCAI_2005_06	7	0.34	0.42	- [c]	- [c]	0.11	0.13	- [c]	- [c]
1–< 3 years	Germany	VELS	174	0.60	0.58	0.38	0.90	0.14	0.13	0.09	0.19
	Finland	DIPP_2001_2009	255	0.69	0.68	0.40	1.05	0.20	0.20	0.14	0.28
	United Kingdom	NDNS-Rolling Programme Years 1–3	78	0.88	0.86	0.61	1.19	0.20	0.20	0.13	0.26
	United Kingdom	DNSIYC_2011	651	0.79	0.77	0.46	1.17	0.20	0.20	0.14	0.27
	Italy	INRAN_SCAI_2005_06	16	0.58	0.57	- [c]	- [c]	0.13	0.12	- [c]	- [c]
3–< 10 years	Germany	EsKiMo	409	1.03	0.98	0.62	1.57	0.15	0.15	0.11	0.20
	Germany	VELS	147	0.68	0.65	0.42	1.04	0.13	0.13	0.09	0.19
	Finland	DIPP_2001_2009	369	0.93	0.92	0.61	1.28	0.18	0.17	0.13	0.23
	France	INCA2	243	0.89	0.85	0.53	1.33	0.16	0.15	0.11	0.22
	United Kingdom	NDNS-Rolling Programme Years 1–3	325	1.24	1.22	0.72	1.82	0.21	0.20	0.14	0.28
	Italy	INRAN_SCAI_2005_06	99	0.93	0.90	0.48	1.42	0.13	0.12	0.09	0.18
	Netherlands	DNFCS 2007-2010	216	0.86	0.82	0.50	1.40	0.11	0.10	0.07	0.16
10–< 18 years	Germany	EsKiMo	196	1.15	1.14	0.67	1.67	0.16	0.15	0.10	0.22
	Finland	NWSSP07_08	170	1.10	1.07	0.63	1.78	0.17	0.17	0.12	0.23
	France	INCA2	524	1.02	1.00	0.52	1.63	0.16	0.15	0.11	0.24
	United Kingdom	NDNS-Rolling Programme Years 1–3	326	1.32	1.30	0.76	1.93	0.20	0.19	0.13	0.28
	Italy	INRAN_SCAI_2005_06	139	1.04	1.02	0.60	1.56	0.13	0.13	0.09	0.18
	Latvia	FC_PREGNANTWOMEN_2011[d]	12	1.92	1.74	- [c]	- [c]	0.19	0.19	- [c]	- [c]
	Netherlands	DNFCS 2007-2010	576	0.93	0.90	0.53	1.45	0.11	0.10	0.07	0.16
18–< 65 years	Finland	FINDIET2012	710	1.19	1.12	0.62	1.96	0.17	0.16	0.10	0.25
	France	INCA2	1,340	0.99	0.96	0.55	1.52	0.15	0.15	0.11	0.22
	United Kingdom	NDNS-Rolling Programme Years 1–3	706	1.38	1.36	0.78	2.05	0.21	0.20	0.14	0.30
	Ireland	NANS_2012	640	1.45	1.39	0.81	2.32	0.20	0.19	0.13	0.30
	Italy	INRAN_SCAI_2005_06	1,245	0.97	0.94	0.56	1.50	0.13	0.13	0.09	0.19
	Latvia	FC_PREGNANTWOMEN_2011[d]	990	1.79	1.72	0.89	2.90	0.21	0.21	0.12	0.32
	Netherlands	DNFCS 2007-2010	1,034	1.02	0.95	0.53	1.68	0.12	0.12	0.07	0.20
	Sweden	Riksmaten 2010	807	1.18	1.14	0.66	1.85	0.17	0.15	0.10	0.23
65–< 75 years	Finland	FINDIET2012	203	1.07	1.04	0.57	1.71	0.17	0.17	0.12	0.25
	France	INCA2	153	0.94	0.89	0.54	1.45	0.15	0.14	0.11	0.21

Age class	Country	Survey	Intakes expressed in mg per day				Intakes expressed in mg per MJ			
			n	Average	Median	P5	P95	Average	Median	P5	P95
	United Kingdom	NDNS-Rolling Programme Years 1–3	91	1.39	1.38	0.93	1.86	0.24	0.23	0.17	0.35
	Ireland	NANS_2012	77	1.55	1.53	0.87	2.18	0.23	0.23	0.16	0.33
	Italy	INRAN_SCAI_2005_06	157	0.94	0.94	0.53	1.37	0.14	0.13	0.09	0.19
	Netherlands	DNFCS 2007-2010	82	0.96	0.95	0.50	1.42	0.13	0.13	0.08	0.21
	Sweden	Riksmaten 2010	168	1.11	1.08	0.65	1.71	0.16	0.15	0.12	0.21
≥ 75 years	France	INCA2	44	0.88	0.87	- (c)	- (c)	0.15	0.14	- (c)	- (c)
	United Kingdom	NDNS-Rolling Programme Years 1–3	83	1.37	1.32	0.87	1.86	0.23	0.23	0.15	0.33
	Ireland	NANS_2012	43	1.45	1.29	- (c)	- (c)	0.23	0.22	- (c)	- (c)
	Italy	INRAN_SCAI_2005_06	159	0.90	0.87	0.54	1.37	0.14	0.13	0.09	0.19
	Sweden	Riksmaten 2010	30	1.08	1.07	- (c)	- (c)	0.15	0.16	- (c)	- (c)

n, number of individuals; P5, 5th percentile; P95, 95th percentile.

DIPP, type 1 Diabetes Prediction and Prevention survey; DNFCS, Dutch National Food Consumption Survey; DNSIYC, Diet and Nutrition Survey of Infants and Young Children; EsKiMo, Ernährungsstudie als KIGGS-Modul; FC_PREGNANTWOMEN, food consumption of pregnant women in Latvia; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale des Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione - Studio sui Consumi Alimentari in Italia; NANS, National Adult Nutrition Survey; NDNS, National Diet and Nutrition Survey; NWSSP, Nutrition and Wellbeing of Secondary School Pupils; VELS, Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln.

(a) The proportions of breastfed infants were 58% in the Finnish survey, 40% in the German survey, 44% in the Italian survey, and 21% in the UK survey. Most infants were partially breastfed. For the Italian and German surveys, breast milk intake estimates were derived from the number of breastfeeding events recorded per day multiplied by standard breast milk amounts consumed on an eating occasion at different age. For the UK survey, the amount of breast milk consumed was either directly quantified by the mother (expressed breast milk) or extrapolated from the duration of each breastfeeding event. As no information on the breastfeeding events were reported in the Finnish survey, breast milk intake was not taken into consideration in the intake estimates of Finnish infants.

(b): n = 251 for estimated intake expressed in mg/MJ.

(c): 5^{th} or 95^{th} percentile intakes calculated from fewer than 60 subjects require cautious interpretation as the results may not be statistically robust (EFSA, 2011b) and, therefore, for these dietary surveys/age classes, the 5^{th} and 95^{th} percentile estimates are not presented in the intake results.

(d): Pregnant women only

Appendix E. Minimum and maximum percentage contribution of different food groups (FoodEx2 level 1) to thiamin intake estimates among males

Food groups	Age						
	< 1 year	1–< 3 years	3–< 10 years	10–< 18 years	18–< 65 years	65–< 75 years	≥ 75 years
Additives, flavours, baking and processing aids	< 1	< 1	0–1	0–1	0	0	0
Alcoholic beverages	< 1	< 1	< 1	< 1	1–2	< 1–1	< 1–1
Animal and vegetable fats and oils	0	< 1	< 1	< 1	< 1	< 1	< 1
Coffee, cocoa, tea and infusions	< 1–1	< 1–1	< 1–1	< 1–2	1–5	1–6	1–4
Composite dishes	< 1–2	< 1–8	< 1–9	1–12	< 1–15	< 1–13	< 1–14
Eggs and egg products	< 1	< 1–1	< 1–2	< 1–2	< 1–2	< 1–2	< 1–2
Fish, seafood, amphibians, reptiles and invertebrates	< 1	< 1–2	< 1–3	< 1–3	1–4	1–6	1–6
Food products for young population	35–58	3–14	< 1–1	< 1	< 1	–	–
Fruit and fruit products	2–4	3–7	2–5	1–4	2–6	3–7	2–8
Fruit and vegetable juices and nectars	< 1–2	1–7	3–11	2–11	1–7	1–5	1–2
Grains and grain-based products	6–15	24–34	20–38	21–39	20–36	18–33	19–35
Human milk	< 1–20	< 1–1	–	–	–	–	–
Legumes, nuts, oilseeds and spices	< 1–4	1–6	1–6	1–5	2–6	2–7	2–6
Meat and meat products	2–12	8–16	14–25	19–26	21–30	19–29	19–27
Milk and dairy products	5–9	17–22	10–20	6–17	5–14	6–14	7–10
Products for non-standard diets, food imitates and food supplements or fortifying agents	< 1–1	0–1	< 1–1	< 1–1	< 1–1	< 1	< 1–1
Seasoning, sauces and condiments	< 1–3	< 1–2	< 1–3	< 1–3	< 1–3	< 1–2	< 1–5
Starchy roots or tubers and products thereof, sugar plants	1–12	4–12	5–11	5–13	6–12	7–14	7–15
Sugar, confectionery and water-based sweet desserts	0	< 1–1	< 1–2	< 1–2	< 1	< 1	< 1
Vegetables and vegetable products	1–8	4–5	4–7	4–8	3–12	3–12	3–11
Water and water-based beverages	0	0	< 1–3	< 1–3	< 1–1	< 1	< 1

‘-‘ means that there was no consumption event of the food group for the age and sex group considered, while ‘0’ means that there were some consumption events, but that the food group does not contribute to the intake of the nutrient considered, for the age and sex group considered.

Appendix F. Minimum and maximum percentage contribution of different food groups (FoodEx2 level 1) to thiamin intake estimates among females

Food groups	Age						
	< 1 year	1–< 3 years	3–< 10 years	10–< 18 years	18–< 65 years	65–< 75 years	≥ 75 years
Additives, flavours, baking and processing aids	0	0	0–1	0–1	0	< 1	0
Alcoholic beverages	< 1	< 1	< 1	< 1	< 1–1	< 1–1	< 1
Animal and vegetable fats and oils	< 1	< 1	< 1	< 1	< 1	< 1	< 1
Coffee, cocoa, tea and infusions	< 1–1	< 1–1	< 1–1	< 1–2	< 1–6	1–8	1–4
Composite dishes	< 1–3	< 1–9	< 1–9	< 1–13	< 1–16	< 1–14	< 1–16
Eggs and egg products	< 1–1	< 1–1	< 1–2	< 1–2	< 1–2	1–2	< 1–2
Fish, seafood, amphibians, reptiles and invertebrates	0	< 1–3	< 1–2	< 1–3	1–4	1–7	1–7
Food products for young population	35–63	3–14	< 1–2	< 1–1	< 1	–	< 1
Fruit and fruit products	3–5	3–5	2–5	2–6	3–8	4–10	3–9
Fruit and vegetable juices and nectars	< 1–2	1–7	2–11	2–12	1–6	1–5	2–3
Grains and grain-based products	10–16	25–34	21–39	24–38	20–40	19–33	20–37
Human milk	< 1–9	< 1–1	–	–	–	–	–
Legumes, nuts, oilseeds and spices	< 1–4	1–7	1–6	1–5	2–7	2–7	2–6
Meat and meat products	1–10	8–17	14–23	15–39	16–31	18–24	15–23
Milk and dairy products	3–18	15–22	10–22	6–17	5–15	7–16	8–14
Products for non-standard diets, food imitates and food supplements or fortifying agents	< 1	< 1	0–2	< 1–1	< 1–2	< 1–2	< 1–1
Seasoning, sauces and condiments	< 1–3	< 1–2	< 1–3	< 1–3	< 1–2	< 1–2	< 1–2
Starchy roots or tubers and products thereof, sugar plants	3–12	4–11	5–12	5–14	4–12	5–13	6–12
Sugar, confectionery and water-based sweet desserts	0	< 1–1	< 1–2	< 1–2	< 1–1	< 1	< 1
Vegetables and vegetable products	2–9	4–5	4–8	4–9	4–13	4–14	5–12
Water and water-based beverages	0	0	< 1–3	0–2	< 1–1	< 1	< 1

'-' means that there was no consumption event of the food group for the age and sex group considered, while '0' means that there were some consumption events, but that the food group does not contribute to the intake of the nutrient considered, for the age and sex group considered.

Appendix G. Comparison between EFSA intake estimates and published estimates from the same survey

Country	Survey (age range)	Reference	% of published intake[(a)]
Finland	DIPP (1–6 years)	Kyttälä et al. (2010)[(b)]	100–101%
	NWSSP (13–15 years)	Hoppu et al. (2010)[(c)]	100–107%
	FINDIET 2012 (25–74 years)	Helldán et al. (2013)	100–108%
France	INCA2 (3–17 years)	Afssa (2009)	89–98%
Germany	EsKiMo (6–11 years)	Mensink et al. (2007)[(b)]	87–90%
	VELS (< 1–4 years)	Kersting and Clausen (2003)	95–110%
Ireland	NANS (18–90 years)	IUNA (2011)	86–105%
Italy	INRAN-SCAI (1 month–98 years)	Sette et al. (2011)	92–107%
Netherlands	DNFCS 2007_2010 (7–69 years)	van Rossum et al. (2011)	89–101%
Sweden	Riksmaten 2010_2011	Amcoff et al. (2012)	100–109%
UK	NDNS years 1–3 (3–94 years)	Bates et al. (2012)[(d)]	97–108%

DIPP, type 1 Diabetes Prediction and Prevention survey ; DNFCS, Dutch National Food Consumption Survey; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale des Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione - Studio sui Consumi Alimentari in Italia; NANS, National Adult Nutrition Survey; NWSSP, Nutrition and Wellbeing of Secondary School Pupils; VELS, Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln.

(a): Range over different age groups in a specific survey.
(b): For these surveys, published intake values included supplement consumption, while the EFSA estimates are based on food consumption only.
(c): Published values were for two consecutive days of dietary recall, while EFSA data comprised 2 x 48 hour dietary recall
(d): UK-NDNS survey published intake data for three years (2008–2010), while EFSA estimates are based on four years consumption data (2008–2011)

Appendix H. Summary of Population Reference Intakes (PRIs) for thiamin for adults expressed in mg/day

Age	PRI at PAL = 1.4 (mg/day) [(a)]		PRI at PAL = 1.6 (mg/day) [(a)]		PRI at PAL = 1.8 (mg/day) [(a)]		PRI at PAL = 2.0 (mg/day) [(a)]	
	Men	Women	Men	Women	Men	Women	Men	Women
18–29 years	0.99	0.80	1.13	0.91	1.27	1.02	1.41	1.13
30–39 years	0.96	0.77	1.09	0.88	1.23	0.99	1.36	1.09
40–49 years	0.94	0.76	1.08	0.87	1.21	0.98	1.35	1.08
50–59 years	0.93	0.76	1.06	0.86	1.20	0.97	1.33	1.08
60–69 years	0.85	0.69	0.97	0.79	1.10	0.89	1.22	0.98
70–79 years	0.84	0.69	0.96	0.78	1.08	0.88	1.20	0.97

PAL: physical activity level. PAL values of 1.4, 1.6, 1.8 and 2.0 reflect low active (sedentary), moderately active, active and very active lifestyles (EFSA NDA Panel, 2013)

(a): The ARs for thiamin in mg/day were calculated from the AR for thiamin of 0.072 mg/MJ using the ARs for energy for adults according to the Scientific Opinion on Dietary Reference Values for energy (EFSA NDA Panel, 2013). The PRIs were then derived assuming a CV of 20%.

Appendix I. Summary of Population Reference Intakes (PRIs) for thiamin for infants aged 7–11 months expressed in mg /day

Age	PRI (mg/day)[(a)]	
	Boys	Girls
7 months	0.27	0.24
8 months	0.28	0.25
9 months	0.29	0.26
10 months	0.30	0.27
11 months	0.31	0.28

(a): The ARs for thiamin in mg/day were calculated from the AR for thiamin of 0.072 mg/MJ using the ARs for energy for infants aged 7–11 months according to the Scientific Opinion on Dietary Reference Values for energy (EFSA NDA Panel, 2013). The PRIs were then derived assuming a CV of 20%.

Appendix J. Summary of Population Reference Intakes (PRIs) for thiamin for children and adolescents expressed in mg/day

Age	PRI at PAL = 1.4 (mg/day)[(a)]		PRI at PAL = 1.6 (mg/day)[(a)]		PRI at PAL = 1.8 (mg/day)[(a)]		PRI at PAL = 2.0 (mg/day)[(a)]	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
1 year	0.33	0.30	-	-	-	-	-	-
2 years	0.43	0.40	-	-	-	-	-	-
3 years	0.49	0.46	-	-	-	-	-	-
4 years	0.53	0.49	0.60	0.56	0.69	0.64	-	-
5 years	0.56	0.52	0.65	0.59	0.73	0.68	-	-
6 years	0.59	0.55	0.68	0.64	0.77	0.72	-	-
7 years	0.64	0.58	0.73	0.68	0.82	0.76	-	-
8 years	0.68	0.62	0.77	0.72	0.87	0.80	-	-
9 years	0.71	0.67	0.82	0.76	0.92	0.85	-	-
10 years	-	-	0.82	0.77	0.92	0.87	1.02	0.96
11 years	-	-	0.86	0.81	0.97	0.91	1.08	1.01
12 years	-	-	0.92	0.85	1.03	0.95	1.15	1.06
13 years	-	-	0.99	0.89	1.11	1.00	1.23	1.11
14 years	-	-	1.06	0.92	1.19	1.03	1.32	1.15
15 years	-	-	1.14	0.94	1.28	1.06	1.42	1.18
16 years	-	-	1.20	0.96	1.35	1.07	1.50	1.19
17 years	-	-	1.24	0.96	1.39	1.08	1.55	1.20

PAL: physical activity level. PAL values of 1.4, 1.6, 1.8 and 2.0 reflect low active (sedentary), moderately active, active and very active lifestyles. PAL values were selected from the range of PAL values observed in children and adolescents (EFSA NDA Panel, 2013).

(a): The ARs for thiamin in mg/day were calculated from the AR for thiamin of 0.072 mg/MJ using the AR for energy for children and adolescents according to the Scientific Opinion on Dietary Reference Values for energy (EFSA NDA Panel, 2013). The PRIs were then derived assuming a CV of 20%.

Appendix K. Summary of Population Reference Intakes (PRIs) for thiamin for pregnant and lactating women (in addition to the PRI for non-pregnant non-lactating women) expressed in mg/day

	PRI[(a)] (mg/day)
Pregnant women	
1st trimester	+ 0.03
2nd trimester	+ 0.11
3rd trimester	+ 0.21
Lactating women	
0–6 months post partum	+ 0.21

(a): The additional ARs for thiamin in mg/day were calculated from the AR for thiamin of 0.072 mg/MJ using the AR for additional energy for pregnancy or lactation (i.e. in addition to the AR for energy for non-pregnant non-lactating women) according to the Scientific Opinion on Dietary Reference Values for energy (EFSA NDA Panel, 2013). The PRIs were then derived assuming a CV of 20%. These values have to be added to the PRI for non-pregnant non-lactating women.

2020 **ABBREVIATIONS**

Afssa	Agence française de sécurité sanitaire des aliments
AI	Adequate Intake
αETK	erythrocyte transketolase activity coefficient
AR	Average Requirement
ATP	adenosine triphosphate
ATTP	Adenosine thiamin triphosphate
COMA	Committee on Medical Aspects of Food Policy
CV	coefficient of variation
D–A–CH	Deutschland– Austria– Confoederatio Helvetica
DH	Department of Health
DRV	Dietary Reference Value
EAR	Estimated Average Requirement
EC	European Commission
EFSA	European Food Safety Authority
ETKA	erythrocyte transketolase activity
EU	European Union
FAO	Food and Agriculture Organization
FNB	U.S. Food and Nutrition Board
Hb	hemoglobin
HPLC	high performance liquid chromatography
IOM	U.S. Institute of Medicine of the National Academy of Sciences
LOAEL	low-observed-adverse-effect level
LTI	Lower Threshold Intake
NADPH	nicotinamide adenine dinucleotide phosphate
NDNS	National Diet and Nutrition Survey
NNR	Nordic Nutrition Recommendations
NOAEL	no-observed-adverse-effect level
PAL	physical activity level
PRI	Population reference intake
RDA	Recommended Dietary Allowance
RNI	Reference Nutrient Intake
SD	standard deviation
SCF	Scientific Committee for Food
TMP	thiamin monophosphate
TDP	thiamin diphosphate
ThTR	thiamin transporter
TRMA	thiamin-responsive megaloblastic anemia
TTP	thiamin triphosphate

UL	Tolerable Upper Intake Level
UNU	United Nations University
UPLCP-MS/MS	ultra performance liquid chromatography tandem mass spectrometry
USDA	United States Department of Agriculture
VERA	Verbundstudie Ernährungserhebung und Risikofaktoren Analytik
WHO	World Health Organization

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