DRAFT SCIENTIFIC OPINION

Scientific Opinion on Dietary Reference Values for magnesium[1]

EFSA Panel on Dietetic Products, Nutrition and Allergies (EFSA NDA Panel)[2,3]

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ABSTRACT

Following a request from the European Commission, the Panel on Dietetic Products, Nutrition and Allergies (NDA) derived Dietary Reference Values (DRVs) for magnesium. The Panel considers that Average Requirements (ARs) and Population Reference Intakes (PRIs) for magnesium cannot be derived for adults, infants and children, and therefore defines Adequate Intakes (AIs), based on observed intakes in healthy populations in the EU. This approach considers the range of average intakes of magnesium estimated by EFSA from dietary surveys in children and adults in nine EU countries. For adults, an AI for magnesium is set at 350 mg/day for men and 300 mg/day for women. For children aged 1 to < 3 years, an AI for magnesium is set at 160 mg/day for both sexes. For children aged 3 to < 10 years, an AI for magnesium is set at 230 mg/day for both sexes. For children aged 10 to < 18 years, an AI for magnesium is set at 300 mg/day for boys and 250 mg/day for girls. For infants aged 7–11 months, an AI for magnesium of 80 mg/day is derived by extrapolating upwards from the estimated magnesium intake in exclusively breast-fed infants aged 0–6 months and by considering observed average intakes in the few surveys for which data were available. For pregnant and lactating women, the Panel considers that there is no evidence for an increased need for magnesium, and the same AI is set as for non-pregnant, non-lactating women.

KEY WORDS

magnesium, balance, observed intake, Adequate 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 (EFSA NDA Panel) was asked to deliver a scientific opinion on Dietary Reference Values for the European population, including magnesium.

Magnesium is an alkaline earth metal. It occurs as the free cation Mg^{2+} in aqueous solutions or as the mineral part of a large variety of compounds, including chlorides, carbonates and hydroxides. Magnesium is a cofactor of more than 300 enzymatic reactions, acting either on the enzyme itself as a structural or catalytic component or on the substrate, especially for reactions involving ATP, which make magnesium essential in the intermediary metabolism for the synthesis of carbohydrates, lipids, nucleic acids and proteins as well as for specific actions in various organs in the neuromuscular or cardiovascular system.

Magnesium deficiency can cause hypocalcaemia and hypokalaemia, leading to neurological or cardiac symptoms when it is associated with marked hypomagnesaemia. Due to the widespread involvement of magnesium in numerous physiological functions and the metabolic interactions between magnesium and other minerals, it is difficult to relate magnesium deficiency to specific symptoms.

Magnesium absorption takes place in the distal intestine, mainly as the ionised form. Percentage absorption is generally considered to be 40–50 %, but figures from 10 to 70 % have also been reported. Magnesium absorption can be inhibited by phytic acid and phosphate and enhanced by the fermentation of soluble dietary fibre, though the physiological relevance of these interactions at adequate intakes remains to be established.

The majority of the body magnesium content is stored in bone (about 60 %) and muscle (about 25 %). A small amount is present in the serum, mainly as the free cation. Most cells are able to actively and rapidly buffer magnesium loss or accumulation through the involvement of specific magnesium transporters. The kidney plays a major role in magnesium homeostasis and maintenance of serum concentration. Urinary magnesium excretion is increased by high natriuresis, osmotic load, and metabolic acidosis, and reduced by metabolic alkalosis, parathyroid hormone, and, possibly, calcitonin. A large part of the magnesium content of faeces stems from unabsorbed magnesium. Endogenous magnesium is lost through bile, pancreatic and intestinal juices and intestinal cells, and part of this can be reabsorbed. Magnesium losses through sweat are modest and very variable depending on the techniques used for sweat collection, and losses through menstruation are negligible.

There is some evidence that urinary magnesium concentration reflects magnesium intake. Urinary, faecal, serum and erythrocyte magnesium concentrations have been used for the assessment of magnesium status, with serum magnesium concentration being the most frequently used marker. However, the Panel considers that the usefulness of serum magnesium concentration as a marker of intake or status is questionable and that there are at present no appropriate biomarkers for magnesium status that can be used for deriving DRVs for magnesium.

The Panel notes that a recent pooled analysis of balance studies in adults suggests that zero magnesium balance may occur at a magnesium intake of 165 mg/day. The Panel also notes that results of some large-scale and long-term prospective observational studies point to an inverse relationship between magnesium intake and risk of diabetes mellitus type 2, mostly at higher magnesium intakes.

Foods rich in magnesium are nuts, whole grains and grain products, fish and seafood, several vegetables, legumes, berries, banana, and some coffee and cocoa beverage preparations. The magnesium content of tap/bottled water can make a significant contribution to intake. On the basis of data from 13 dietary surveys in nine EU countries, dietary intake of magnesium was estimated by

EFSA using food consumption data from the EFSA Comprehensive European Food Consumption Database and composition data from the EFSA Food Composition Database.

For both sexes combined, average magnesium intake ranged from 72 to 120 mg/day (25–45 mg/MJ, 9.2–12.7 mg/kg body weight per day) in infants (< 1 year of age), from 153 to 188 mg/day (35–45 mg/MJ, 12.7–15.8 mg/kg body weight per day) in children aged 1 to < 3 years, from 184 to 281 mg/day (28–43 mg/MJ, 7.6–13.0 mg/kg body weight per day) in children aged 3 to < 10 years, from 213 to 384 mg/day (28–44 mg/MJ, 4.2–7.7 mg/kg body weight per day) in children aged 10 to < 18 years, and from 232 to 439 mg/day (31–51 mg/MJ, 3.4–5.3 mg/kg body weight per day) in adults (≥ 18 years). Main food groups contributing to magnesium intake were grains and grain-based products, milk and milk products and coffee, cocoa, tea and infusions.

Considering all evidence available, i.e. from balance studies and prospective observational studies, the Panel decided to set an Adequate Intake (AI) based on observed intakes in several EU countries. For adults of all ages, the Panel proposed to set AIs according to sex. Considering the distribution of observed average intakes (males 264–439 mg/day; females 232–357 mg/day), the Panel proposed for all adult men above 18 years an AI of 350 mg/day, and for all adult women an AI of 300 mg/day, after rounding.

The Panel also decided to set an AI for infants aged 7–11 months and children based on observed intakes in several EU countries. For infants aged 7–11 months, an AI in line with the proposal of SCF (1993) of 80 mg/day was set. This value represents, after rounding, the midpoint (78 mg/day) of the range between 35 mg/day (magnesium intake estimated by extrapolation using isometric scaling from intakes in breast-fed infants aged 0–6 months) and 120 mg/day (highest value of the range of observed mean intakes in the EU countries for which data are available). For children aged 1 to < 10 years, considering the absence of a strong basis for a distinct value according to sex and the distribution of observed mean intakes, AIs were set at the midpoint of average intakes (160 mg/day for boys and girls aged 1 to < 3 years, and 230 mg/day for boys and girls aged 3 to < 10 years). For children aged 10 to < 18 years, considering the rather large differences in magnesium intakes between boys and girls, the Panel proposed to set AIs according to sex, and to select the midpoints of average intakes as AIs, i.e. 300 mg/day for boys, and 250 mg/day for girls.

Considering that pregnancy induces only a small increase in magnesium requirement, which is likely covered by adaptive phyiological mechanisms, the Panel considers that the AI for non-pregnant women also applies to pregnant women. For lactating women, considering that 25 mg/day are secreted with breast milk during the first six months of exclusive breastfeeding and the possibility of adaptation of magnesium metabolism, both at the level of absorption and elimination, the Panel considers that the AI for non-pregnant women also applies to lactating women.

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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.[4] 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 (Department of National Health and Welfare) recommendations differ from the reference intakes in the SCF (1993) report. Although there is considerable consensus between these newly derived (Department of National Health and Welfare) 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 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 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,[5] 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 EFSA is asked to provide advice on energy, macronutrients and dietary fibre. Specifically advice is requested on the following dietary components:

- Carbohydrates, including sugars;

[4] 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.

[5] 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.

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

Following on from the first part of the task, 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, 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, 1993) adopted an opinion on the nutrient and energy intakes for the European Community. For magnesium, the SCF did not set a Population Reference Intake (PRI) but an Acceptable Range of Intakes for adults, including pregnant and lactating women. For children, approximate PRIs were defined on the basis of body weight.

2. Definition/category

2.1. Chemistry

Magnesium (atomic number 12, atomic mass 24.30 Da) is an alkaline earth metal belonging to the third group of elements in the periodic table; it is the eigth most abundant element in the earth crust and the eleventh in the human body. Like calcium, its usual oxidation state is +2 and, due to its strong reactivity, it does not occur in the native metallic state, but rather as the free cation Mg^{2+} in aqueous solution or as the mineral part of a large variety of compounds, including chlorides, carbonates and hydroxides. It can react with nitrogen, phosphorous, sulphur and halides; however, its bond to protein or other biological molecules tends to be weaker than that of calcium (Saris et al., 2000). There are three natural stable isotopes, i.e. ^{24}Mg (natural abundance 79 %), ^{25}Mg (10 %) and ^{26}Mg (11 %).

2.2. Function of magnesium

2.2.1. Biochemical functions

Magnesium is a cofactor of more than 300 enzymatic reactions, acting either on the substrate (especially for reactions involving ATP, where its binding to the nucleotide induces an adequate conformation and helps to weaken the terminal O–P bond of ATP, thereby facilitating the transfer of phosphate (Sanders et al., 1999; Rude and Gruber, 2004) or on the enzyme itself as a structural or catalytic component. Since ATP utilisation is involved in many metabolic pathways, magnesium is essential in the intermediary metabolism for the synthesis of carbohydrates, lipids, nucleic acids and proteins as well as for specific actions in various organs such as the neuromuscular or cardiovascular system. Magnesium can interfere with calcium at the membrane level or bind to membrane phospholipids, thus modulating membrane permeability and electrical characteristics. Magnesium has an impact on bone health through its participation to the structure of hydroxyapatite crystals in bone.

2.2.2. Health consequences of deficiency and excess

2.2.2.1. Deficiency

Magnesium deficiency can be induced by many different causes, including renal and gastrointestinal dysfunctions; magnesium deficiency can cause hypocalcaemia and hypokalaemia, leading to neurological or cardiac symptoms when it is associated with marked hypomagnesaemia (< 0.5 mmol/L). Due to the widespread involvement of magnesium in numerous physiological functions and the metabolic interactions between magnesium and other minerals, it is difficult to relate magnesium deficiency to specific symptoms such as neuromuscular irritability, muscle tremors and cramps, fasciculation, wasting and weakness, restless leg syndrome, fibromyalgia, i.e. conditions where the use of magnesium supplementation has led to inconsistent results (Brown et al., 2012).

2.2.2.2. Excess

A Tolerable Upper Intake Level (UL) was determined by the SCF (2001) based on studies in which mild diarrhoea occurred after ingestion of magnesium supplements and in which information on magnesium intake from foods and beverages was not available. A No Observed Adverse Effect Level (NOAEL) of 250 mg/day was derived and, using an uncertainty factor of 1, a UL of 250 mg/day was established for adults, including pregnant and lactating women, and children from 4 years onwards. Due to lack of data, a UL could not be established for children aged 1–3 years. The UL was established for readily dissociable magnesium salts (e.g., chloride, sulphate, aspartate, lactate) and compounds like magnesium oxide in nutritional supplements, water, or added to foods and beverages, but does not include magnesium normally present in foods and beverages.

2.3. Physiology and metabolism

2.3.1. Intestinal absorption

Magnesium absorption takes place in the distal intestine, mainly in ionised form through a paracellular process via tight junctions and is driven by electrochemical gradients and solvent drag. Saturable transcellular absorption seems to be significant only at low dietary intakes. At usual intakes, magnesium absorption is only loosely regulated; percentage absorption is generally considered to be 40–50 %, but figures from 10 to 70 % have also been reported. The fractional absorption of magnesium decreases with magnesium intake, which makes the comparison between studies difficult (Sabatier et al., 2003b). Magnesium absorption can be inhibited by phytic acid and phosphate and enhanced by the fermentation of soluble dietary fibre, though the physiological relevance of these interactions at adequate intakes remains to be established.

2.3.2. Transport in blood

Approximately 0.3 % of body magnesium is in the serum, as a free cation which is the bioactive form (about 54 %), a protein-bound form (about 33 %, mainly to albumin (75 %)) and as anion complexes (about 13 %) (Elin, 1987). Magnesium concentrations in blood cells are higher than in the serum: eight times in reticulocytes, three times in red blood cells.

2.3.3. Distribution to tissues

Magnesium is approximately equally distributed in bone and soft tissues, less than 1 % being present in blood compartments. Cellular magnesium concentrations are constantly high, in the range of 17–20 mmol/L (Swaminathan, 2003), despite rapid movements across cell membranes through multiple carriers and channels. Intracellular concentrations have been observed to decrease linearly with increasing age, without parallel changes in plasma magnesium concentration (Barbagallo et al., 2000; Barbagallo et al., 2009).

The most important transport systems to tissues appears to be the transient receptor potential melastatin 7 (TRPM7), associated with cell proliferation or apoptosis; TRPM7, which is also permeable to calcium, is negatively regulated by intracellular magnesium and magnesium-nucleotide complexes (Romani, 2011; Park et al., 2014). TRPM6, functioning with TRPM7 or independently, is specifically expressed in the colon and distal renal tubule, where it plays a role in the reabsorption of magnesium (Woudenberg-Vrenken et al., 2009; Romani, 2011). Some other non-specific transporters are also involved in magnesium transfer, such as claudins, Mag T1, SLC41, ACDP, NIPA and Huntingtin across cell membranes, Mrs2 across mitochondrial membranes and MMgt across Golgi membranes (Romani, 2011). As shown in *in vitro* studies, through the action of magnesium transporters enabling large magnesium fluxes, most cells are able to actively and rapidly buffer magnesium loss or accumulation (Romani, 2011). In the whole body, compartmental analysis using

stable isotopes showed the existence of at least two major extraplasma compartments: the first compartment represents 80 % of the rapidly exchangeable pool with an exchange rate of 48 mg/hour; the second pool has a faster exchange rate of 179 mg/hour, the sum of these rapidly exchangeable compartments amounting to around 25 % of the magnesium body pool (Sabatier et al., 2003a).

2.3.4. Storage

Total body magnesium content in a healthy adult is around 20–28 g (Rude, 2014). Of this, about 60 % is in bone (Musso, 2009), either strongly bound to apatite where it is difficult to mobilise or loosely adsorbed at the surface of mineral crystals, where it can be easily mobilised in response to variation in dietary supply (Laires et al., 2004). About 25 % of body magnesium is in muscle where mitochondria are considered to be the intracellular storage site (Kubota et al., 2005; Wolf and Trapani, 2008).

2.3.5. Elimination

2.3.5.1. Urine

The kidney plays a major role in magnesium homeostasis and maintenance of serum concentrations. Around 80 % of serum magnesium is ultrafiltrable through the glomerulus, but only around 3 % of the filtered fraction appears in the urine, due to an efficient reabsorption taking place mainly (60–70 %) in the thick ascending loop of Henle. This transport is being directly related to sodium chloride reabsorption and the positive luminal voltage in this segment. The main stimuli that increase urinary magnesium excretion are high natriuresis, osmotic load, and metabolic acidosis; those that reduce it are metabolic alkalosis, parathyroid hormone, and, possibly, calcitonin (Musso, 2009). The remaining part of the reabsorption takes place in the distal convoluted tubule via an active transcellular mechanism that finally controls the amount excreted in the urine (Dai et al., 2001).

2.3.5.2. Faeces

A large part of the magnesium content of faeces stems from unabsorbed magnesium (Lakshmanan et al. (1984). The endogenous routes of elimination of absorbed magnesium through the digestive tract are bile, pancreatic and intestinal juices, and intestinal cells; part of these endogenous losses can be reabsorbed (Swaminathan, 2003). Using stable isotopes, endogenous faecal excretion has been determined to be 49 ± 11 mg/day in six healthy men aged 26–41 years (Sabatier et al., 2003a), around 15 mg/day (0.1–0.9 mg/kg body weight per day) in 9- to 14 year-old boys and girls (Abrams et al., 1997), or ranging from 4.7 to 21.7 mg/day in five girls aged 12–14 years, without influence of calcium intake (Sojka et al., 1997). Basal losses at zero intake deduced from a compilation of balance studies in adults (Hunt and Johnson (2006); see Section 5.2.1) are around 20 mg/day (around 0.31 mg/kg body weight per day).

2.3.5.3. Skin and sweat

Reported sweat magnesium concentrations are very variable, from 3 to 60 mg/L depending on the environment, with a hot and humid environment associated with the highest losses (Nielsen and Lukaski, 2006). After 24-hour exposure to 37°C, sweat losses amounted to 25 % of the total daily magnesium loss (Consolazio et al., 1963). Acclimatisation may reduce sweat magnesium concentration by around 40 % (Chinevere et al., 2008), though this finding may have been due to technical issues rather than an adaptive physiological process (Ely et al., 2013). In 7- to 9-year-old boys involved in sedentary activities in a metabolic unit, magnesium total body sweat loss was very variable but also very low, from 115 to 300 µg/day, representing only 0.05 to 0.13 % of the intake (range 172–300 mg/day). Daily loss through sweat was measured to be around 2 mg/day (0.6 % of the total output) in six men (McDonald and Margen, 1979). Costa et al. (1969) measured during exercise

a sweat magnesium concentration of around 15 µg/g. During work in a hot environment (27°C), Beller et al. (1975) determined the magnesium concentration of sweat to range from 1.6 to 5.5 mg/L. With a different technique collecting the totality of sweat, Shirreffs and Maughan (1997) measured a concentration of 12.2 ± 12.2 mg/L during four repeated trials in five healthy young men and women. Montain et al. (2007) determined a sweat magnesium concentration of 1.3 ± 0.6 mg/L in seven heat-acclimated subjects (6 males, 1 female) completing several hours of treadmill exercise at 27°C. In six healthy women aged 27 ± 4 years, a whole body magnesium loss of 35 ± 13 mg/day was measured; in this experiment, a patch technique has been shown to overestimate magnesium sweat loss by 3.6 times (Palacios et al., 2003). Whole body sweat magnesium concentration was 14.5 ± 4.8 mg/L for eight athletes, the patch technique overestimating this value by 48 % (Baker et al., 2011).

Hunt and Johnson (2006) reported on whole-body surface losses of magnesium in 11 young men. Subjects wore cotton suits for 48 hours after which time their skin was rinsed with deionised water. Whole-body surface losses of 4.1 mg/day were measured and considered to be negligible.

The Panel notes that very different figures have been reported for magnesium sweat losses, which can be at least partially explained by different techniques for sweat collection; the highest values are reported after intense exercise and/or in a hot environment. At moderate physical activity performed around thermoneutrality, the Panel considers that magnesium losses through sweat are likely modest, in the range of 1–5 mg/day, on the basis of a daily sweat volume of around 0.5 L/day (Shirreffs and Maughan, 2005; Subudhi et al., 2005).

2.3.5.4. Menses

Hunt and Schofield (1969) measured menstrual magnesium losses in five women (20–40 years of age); for the whole menstrual period, these varied from 2 ± 1 mg to 7 ± 5 mg in different experimental settings. On a daily basis, this loss appears to be marginal. Hunt and Johnson (2006) reported on menstrual magnesium losses amounting to 2.3 mg/day, with a range of 0.3–6.5 mg/day, though the source of these data is unclear. Considering a magnesium concentration in whole blood of around 35–40 mg/L in healthy women in the control group (Abdulsahib, 2011) and the volume of blood loss (median 18–30 mL per menstrual period (Hallberg et al., 1966; Harvey et al., 2005)), a median magnesium loss of around 0.7–1.2 mg/menstrual period can be calculated.

The Panel considers that magnesium losses through menstruation in women are negligible.

2.3.5.5. Breast milk

Two comprehensive literature searches were performed on breast milk magnesium concentrations (periods January 1990 to October 2011 (Brown et al., 2012) and October 2010 to January 2014 (LASER Analytica, 2014). These searches identified 16 studies on magnesium concentration in breast milk of mothers of term infants, one of which was a review (Dorea, 2000). Studies not yet considered in the review by Dorea (2000) are listed in Appendix A.

The studies report cross-sectional sample data from 1–365 days of lactation. Mean magnesium concentration from all breast milk studies ranged between 23 and 35 mg/L, in line with the conclusion of the review by Dorea (2000) where a median value of 31 mg/L from a range of 15 to 64 mg/L is provided. Dorea (2000) reported that 75 % of reported mean magnesium concentrations in breast milk were below 35 mg/L. Variation is likely due to different analytical techniques employed within studies and due to differences in dietary patterns between countries (Parr et al., 1991).

For the studies listed in Appendix A, there was no clear correlation between stage of lactation and breast milk magnesium concentration. Hunt et al. (2005) found that there was a relatively wide variation between subjects at a given stage of lactation.

Dengel et al. (1994) provided a controlled diet (218 mg/day) to six lactating, six non-lactating and seven never-pregnant women; from measurement of magnesium concentration in breast milk (33.3 ± 0.2 mg/L) and estimation of infant's intake by test weighing it was concluded that 25.2 ± 1.5 mg/day of magnesium was provided to the infant via breast milk.

The Panel considers that the magnesium concentration of mature human milk is 31 mg/L. Based on a mean milk transfer of 0.8 L/day (Butte et al., 2002; FAO/WHO/UNU, 2004; EFSA NDA Panel, 2009) and a concentration of magnesium in mature breast milk of 31 mg/L, a secretion of 25 mg/day of magnesium in breast milk is estimated during the first six months of lactation.

2.3.6. Interaction with other nutrients

On the basis of physiology, metabolism and biochemistry, many interactions of magnesium with other minerals, vitamins or substances present in foods can be suspected, some of which have already been mentioned; most of these interactions have been the subject of a very limited number of studies, frequently with a high risk of bias (Brown et al., 2012). Balance studies performed either in children or in adults did not detect an interaction between magnesium and calcium balances (Greger et al., 1978; Spencer et al., 1994; Andon et al., 1996; Abrams et al., 1997; Milne and Nielsen, 2000; Klevay and Milne, 2002). However, in two studies calcium balance was significantly more positive under conditions of negative magnesium balance (magnesium intake 118 mg/day) than with a positive magnesium balance (magnesium intake 318 mg/day) (Nielsen, 2004; Nielsen et al., 2007). Sodium intake might have some influence on magnesium absorption and balance (Nishimuta et al., 2006). Intake of 53 mg zinc/day during 90 days can decrease magnesium balance (Nielsen and Milne, 2004). There are some studies indicating a relationship with protein intake, possibly through increased apparent absorption. For example, in boys aged 13–14 years, Schwartz et al. (1973) showed that zero magnesium balance was obtained with an intake of 4.6 mg/kg body weight per day for a high-protein diet (265 mg nitrogen/kg body weight per day, i.e. 1.65 g protein/kg body weight per day) and with an intake of 7.6 mg/kg body weight per day for a low-protein diet (123 mg nitrogen/kg body weight per day, i.e. 0.77 g protein/kg body weight per day[6]) (see Appendix H). The balance study of Wisker et al. (1991) showed that % faecal magnesium excretion and balances differed significantly between low-fibre and high-fibre diets containing adequate amounts of protein; there is no clear effect in the study of Kelsay and Prather (1983) of diets low and high in fibre and oxalic acid.

Manganese shares physical properties that enable it to be interchangeable with magnesium in enzymatic phosphate transfer reactions and it has been used as a probe to study the role of magnesium in these processes, particularly in energy metabolism. The relevance of this inter-relationship to human dietary requirements is uncertain, but it is noteworthy that pigs fed 25 % of the recommended intake of magnesium had an increased incidence of cardiac changes and sudden death (Miller et al., 2000).

The Panel considers that data on interactions between magnesium and other minerals, protein or fibre are limited and cannot be used for setting DRVs for magnesium.

2.4. Biomarkers

For the assessment of magnesium status, the concentrations of magnesium in urine, faeces, serum and erythrocytes have been measured. Witkowski et al. (2011) assessed methods for determining magnesium status in humans and undertook meta-analyses. This systematic review included a total of 27 studies (randomised controlled trials, controlled trials, depletion–repletion or depletion–only studies). However, conclusions about the responsiveness of the identified relevant biomarkers and

[6] The PRI for protein for boys aged 13 years is 0.9 g/kg body weight per day and it is 0.89 g/kg body weight per day for boys aged 14 years (EFSA NDA Panel, 2012).

type, dose, or length of supplementation were not possible and there was a high degree of heterogeneity between studies.

2.4.1. Serum/plasma magnesium concentration

The sensitivity of serum/plasma magnesium concentration to magnesium intake is low. Combining data from 18 supplementation arms (daily doses of 197 mg to 23 mg/kg body weight for 3–52 weeks) and four depletion/repletion or depletion-only studies with 322 participants, Witkowski et al. (2011) showed a significant response of serum/plasma magnesium concentration to magnesium intake for all studies. However, the depletion/repletion or depletion-only studies did not reveal changes in serum/plasma magnesium concentration in response to changes in magnesium intake. Others have noted a lack of association between magnesium intake via self-selected diets and plasma magnesium concentration (Lakshmanan et al., 1984). In the study of Misialek et al. (2013), when stratifying for serum magnesium concentration and relating this to magnesium intake, the quintiles of serum magnesium concentration correspond to very similar average magnesium intakes, i.e. from 247 to 257 mg/day, whereas the quintiles of dietary intake range from less than 180 mg/day to more than 320 mg/day.

Serum magnesium concentration remains within a narrow range. Based on data from the US National Health and Nutrition Examination Survey I (5^{th} and 95^{th} percentiles, Lowenstein and Stanton (1986), it has been suggested that values below 0.75 mmol/L may indicate magnesium deficiency and values above 0.96 mmol/L may indicate excessive intakes; however, it has also been suggested that a serum magnesium concentration within this range cannot totally rule out the possibility of magnesium deficiency (Arnaud, 2008). Serum magnesium concentration remains constant with increasing age (Barbagallo et al., 2009).

Thus, despite serum/plasma magnesium concentration being the most frequently used biomarker for magnesium, the Panel considers that the usefulness of serum/plasma magnesium concentration as a marker of intake or status is questionable.

Theoretically, ionised magnesium in plasma, serum or blood would be a better marker of functional magnesium. However, the information is limited and the few studies available did not indicate that ionised magnesium changes in response to changes in magnesium intake (Durlach et al., 2002; Witkowski et al., 2011).

2.4.2. Red blood cell magnesium concentration

Erythrocytes contain a high concentration of magnesium (2.3 ± 0.24 mmol/L of packed cells; ionised magnesium 0.2 ± 0.2 mmol/L of cell water (Millart et al., 1995)), which is required for ATP utilisation and some other metabolic functions. The relationship between magnesium intake and red blood cell magnesium concentration has been described as weak (Lakshmanan et al., 1984). Several weeks of low magnesium intake are needed for decreasing red blood cell magnesium concentration, so that this marker may reflect medium-term magnesium status.

Compared to red blood cell magnesium concentration, magnesium concentration in platelets or lymphocytes may better reflect muscle and tissue concentrations (Arnaud, 2008). However, Witkowski et al. (2011) point out the paucity of available information in humans.

2.4.3. Urinary magnesium excretion

Magnesium intake (duplicate diet analysis of self-selected diets) and urinary magnesium concentration has been found to be correlated (r = 0.45) (Lakshmanan et al., 1984). According to Witkowski et al. (2011), the combination of data from 15 supplementation arms (with doses between

200 mg magnesium given once and 23 mg/kg body weight per day given for 52 weeks) and three depletion/repletion or depletion-only studies including 363 subjects revealed a significant response of urinary magnesium excretion to a change in magnesium intake, though there was considerable heterogeneity between studies. The authors stressed that the low number of studies with few subjects per study precludes conclusions to be drawn about potential relations between biomarker responsiveness and type, dose, or length of supplementation. Moreover, magnesium intake from diet alone is not reported in all supplementation studies.

2.4.4. Other potential biomarkers

The magnesium loading test has been proposed as a marker of magnesium status: when 24-hour urinary excretion of magnesium after a magnesium load is decreased, this is interpreted as an indicator of magnesium deficiency; however, there is no standardised protocol (Arnaud, 2008) and no consensus on the usefulness of the test (Elin, 2011; Günther, 2011). Similarly, hair and nail magnesium concentrations are difficult to interpret since the relationship to intake, deficiency or excess is still unclear (Arnaud, 2008).

Tissue magnesium concentrations (e.g. muscle) require invasive techniques and have not been frequently measured in human studies; non-invasive techniques such as neutron activation measuring magnesium in hand bones still require validation in clinical studies (Aslam et al., 2008).

Though magnesium is the cofactor of many enzymes, no functional biomarker has been identified to date; however, fasting C-peptide and plasma insulin concentrations have been proposed as possible markers following a study using a dose of supplemental magnesium above the UL (Chacko et al., 2011). The Panel notes the lack of specificity of these parameters for magnesium status.

2.4.5. Conclusions on biomarkers of intake and status

Reviews on biomarkers of magnesium intake or status generally conclude that all the proposed markers have limitations (Elin, 1987, 1991; Franz, 2004; Arnaud, 2008; Witkowski et al., 2011). The Panel considers that there are at present no appropriate biomarkers for magnesium status. The Panel also considers that the suitability of urinary magnesium excretion as a marker of intake requires confirmation in well-designed studies.

2.5. Effects of genotype

From twin studies, heritability of magnesium control appears to be limited (only 27 % of the variance may be genetically determined) (Hunter et al., 2002) and the underlying genetic control system might be complex (Henrotte et al., 1990). Several genetic disorders of magnesium homeostasis have been characterised in a limited number of affected individuals (Weber et al., 2001; Schlingmann et al., 2004). Genome-wide association studies have identified several loci that influence serum magnesium concentrations (Meyer et al., 2010). Some common genetic variants of TRPM6 and seven genes have been associated with a higher risk for diabetes mellitus type 2 in case of magnesium intake below 250 mg/day (Song et al., 2009), but this has not been confirmed in a large scale study combining the data from 15 prospective cohorts (Hruby et al., 2013). The Panel considers that there is currently no basis for taking into account the information on genotypes for the setting of DRVs for magnesium.

3. Dietary sources and intake data

3.1. Dietary sources

Foods rich in magnesium are nuts, whole grains and grain products, fish and seafood, several vegetables, legumes, berries, banana, and some coffee and cocoa beverage preparations. The magnesium content of tap/bottled water can make a significant contribution to intake.

Magnesium as magnesium acetate, magnesium carbonate, magnesium chloride, magnesium salts of citric acid, magnesium gluconate, magnesium glycerophosphate, magnesium salts of orthophosphoric acid, magnesium lactate, magnesium hydroxide, magnesium oxide, magnesium potassium citrate and magnesium sulphate may be added to both foods[7] and food supplements,[8] whereas magnesium L-ascorbate, magnesium bisglycinate, magnesium L-lysinate, magnesium malate, magnesium L-pidolate, magnesium pyruvate, magnesium succinate, magnesium taurate, magnesium acetyl taurate may be added to food supplements only.[6] The magnesium content of infant and follow-on formulae[9] and the maximum magnesium content of processed cereal-based foods and baby foods for infants and young children[10] is regulated.

3.2. Dietary intake

Dietary intake of magnesium was estimated by EFSA using the EFSA Comprehensive European Food Consumption Database (EFSA, 2011a) and the EFSA Food Composition Database, classified according to the food classification and description system FoodEx2 (EFSA, 2011b). Food consumption data from 13 dietary surveys from nine EU countries (Finland, France, Germany, Ireland, Italy, Latvia, the Netherlands, Sweden and the UK) were used. The data covered all age groups from infants to adults (Appendix B).

Nutrient composition data for magnesium were derived from the EFSA Nutrient Composition Database (Roe et al., 2013). Food composition information from Finland, France, Germany, Italy, the Netherlands, Sweden and the UK was used to calculate magnesium intake in these countries, assuming that the best intake estimate would be obtained when both the consumption data and the composition data are from the same country. For magnesium 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. EFSA intake estimates are based on consumption of foods, either fortified or not (i.e. without dietary supplements). The amount of borrowed magnesium values in these datasets varied between 14 % and 91 %. Magnesium concentration was directly available for 2 795 food terms of the food consumption data used in this assessment at least in one of the included food composition databases, and was missing for all included countries for 673 consumed food items, to which either a value from another food (in case the food with missing value was consumed frequently or in high quantities or belonged to a food group with a high magnesium concentration), or a zero value (otherwise), was attributed.

After consistency checks and replacement of missing values for magnesium in the EFSA Food Composition Database, magnesium intake was calculated in mg/day and mg/MJ, for males (Appendix C) and females (Appendix D). Magnesium intake was also calculated in mg/kg body weight per day. For this, the intakes were divided by the body weight of the person, if provided to EFSA. Magnesium

[7] Regulation 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.

[8] 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.

[9] 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.

[10] 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, 6.12.2006, p. 16.

intake calculations were performed only on subjects with at least two reporting days. Food consumption data of infants (aged 1–11 months in the Italian survey, 4–11 months in the UK survey and 6 or 6–11 months in the Finnish or German survey, respectively), either formula-fed or breast-fed, were provided by four studies. The consumption of human milk was taken into account if the amount of human milk consumed (Italian survey and UK survey) or the number of breast milk consumption events (German survey) were reported. In case of the Italian survey, the data provider had estimated the human milk consumption prior to submitting the data to EFSA based on the number of eating occasions using standard portions per eating occasion. In the Finnish DIPP study only the information "breast fed infants" was available, but without any indication about the number of breast milk consumption events or the amount of breast milk consumed per event. For the German VELS study, the total amount of breast milk was calculated based on the observations by Paul et al. (1988) on breast milk consumption during one eating occasion at different ages, i.e. the amounts of breast milk consumed on one eating occasion was set to 135 g/eating occasion for infants between 6 and 7 months of age and to 100 g/eating occasion for infants between 8 and 12 months of age, as in the original report by Kersting and Clausen (2003). Food consumption data in children were provided by ten studies, and data on adults by eight studies, including one on pregnant girls and women. EFSA estimates are based on consumption of foods, either fortified or not (i.e. without dietary supplements).

For both sexes combined, average magnesium intake ranged from 72 to 120 mg/day (25–45 mg/MJ, 9.2–12.7 mg/kg body weight per day) in infants (< 1 year of age), from 153 to 188 mg/day (35–45 mg/MJ, 12.7–15.8 mg/kg body weight per day) in children aged 1 to < 3 years, from 184 to 281 mg/day (28–43 mg/MJ, 7.6–13.0 mg/kg body weight per day) in children aged 3 to < 10 years, from 213 to 384 mg/day (28–44 mg/MJ, 4.2–7.7 mg/kg body weight per day) in children aged 10 to < 18 years, and from 232 to 439 mg/day (31–51 mg/MJ, 3.4–5.3 mg/kg body weight per day) in adults of both sexes (≥ 18 years). Average daily intake (but not energy-adjusted intake) was in most cases slightly higher in males (see Appendix C) compared to females (see Appendix D), mainly due to larger quantities of food consumed per day.

Main food groups contributing to magnesium intake were grains and grain-based products (up to 20–40 % in all groups except infants), milk and milk products (up to about 10–30 % of the total magnesium intake in children and less in older age classes) and coffee, cocoa, tea and infusions (up to about 20 % in adults) (see Appendices D and E). Differences in main contributors to magnesium intake between males and females were small.

EFSA's magnesium intake estimates in mg/day were compared with published intake values from the same survey and dataset and the same age class, using the German EsKiMo and VELS surveys in children (Kersting and Clausen, 2003; Mensink et al., 2007), the DIPP study in Finnish children (Kyttälä et al., 2008; Kyttala et al., 2010), the study in Finnish adolescents (Hoppu et al., 2010), the French national INCA2 survey (Afssa 2009), the Irish NANS (IUNA, 2011), the FINDIET 2012 Survey (Helldán et al., 2013), the Italian INRAN-SCAI Survey (Sette et al., 2011), the Dutch National Dietary Survey (van Rossum et al., 2011), the Swedish national survey Riksmaten (Amcoff et al., 2012), the UK NDNS (Bates et al., 2012) and the DNSIYC-2011 Study in UK infants and toddlers (Lennox et al., 2013). EFSA's intake estimates for the various surveys as compared to published values are shown in Table 1. Values below 100 % indicate that EFSA's intake estimates are lower than published values and vice versa.

Table 1: EFSA's average daily magnesium intake estimates, expressed as percentages of the intakes reported in the literature

Country	% of published intake (% range over different age classes in a specific survey)
Finland	93–110 % (DIPP, for ages ≥ 1 year), 105–106 % (Finnish adolescents), 94–97 % (FINDIET 2012)
France	96–109 % (INCA2)
Germany	82–86 % (VELS infants), 100–108 % (VELS children), 94–99 % (EsKiMo)
Ireland	111–120 % (NANS)
Italy	91 % (INRAN-SCAI, infants and young children), 104–108 % (children aged 3 to < 18 years), 117–121 % (adults)
NL	96–98 % (Dutch National Dietary Survey)
Sweden	113–119 % (Riksmaten)
UK	120–123 % (DNSIYC-2011), 108–118 % (NDNS–Rolling Programme, Years 1–3, for ages ≥ 3 years)

Comparisons had inherent limitations in case of the UK survey with published intake values from the first two years of the survey and EFSA data from the UK covering the first three years. In the survey in Finnish children aged 10–18 years, published values were for two consecutive days of dietary recall, while EFSA data comprised two 48-hour dietary recalls. Likewise, comparisons were not optimal for the EsKiMo study and the DIPP study, because the published intake values included supplement consumption, while the EFSA estimates are based on food consumption only. However, according to these publications (Mensink et al., 2007; Kyttala et al., 2010), magnesium supplements were not among the major contributors to magnesium intake in these age classes. A comparison could not be undertaken for the Latvian survey or the infants in the DIPP study, as no matching publication was available. The EFSA estimates differed up to about 10 % from the published values in Finland, France, Germany, and the Netherlands. For infants in the German VELS study the intakes were underestimates of 14–18 %. This is most probably due to differences in the composition data used for the intake estimations, because the quantification of breast milk consumption was done similarly both in the VELS study and in this assessment (Paul et al., 1988; Kersting and Clausen, 2003). The estimated Irish intakes showed to be higher by 11–20 % compared to published estimates, which may partly be due to the fact that data provided on composite dishes were almost completely disaggregated to ingredient level, thereby not capturing possible magnesium losses due to processing. EFSA intake estimates were also higher compared to published magnesium estimates for Sweden and the UK, which may partly be related to the high number of composite foods in these datasets, for which the national magnesium values for composite foods may have been more accurate compared to values of the somewhat limited list of composite foods in the FoodEx2 classification system.

Uncertainties in the estimates of all countries may be caused by inaccuracies in mapping food consumption data according to the FoodEx2 classification, in analysing or estimating magnesium composition for the food composition table, due to the use of borrowed magnesium values from other countries in the food composition database, and by replacing missing magnesium values by values of similar foods or food groups in the magnesium intake estimation process. These uncertainties may, in principle, cause both too high and too low estimates of magnesium intake. It is not possible to conclude which of these intake estimates would be closer to the actual magnesium intake.

4. Overview of Dietary Reference Values and recommendations

4.1. Adults

The German-speaking countries (D-A-CH, 2015) derived RIs based on results of balance studies (Jones et al., 1967; Marxhall et al., 1976; Lakshmanan et al., 1984; Wisker et al., 1991; IOM, 1997)

and urinary magnesium excretion before and after magnesium loading in older adults (Gullestad et al., 1994).

Previously, the Nordic countries had set Recommended Intakes (RIs) of 350 mg/day for men and 280 mg/day for women. For this, evidence from a balance study had been considered showing that a magnesium intake of 3.4 mg/kg body weight per day resulted in neutral magnesium balance in almost all subjects (Jones et al., 1967). For the Nordic Nutrition Recommendations (NNR) 2012, it was considered that the new evidence including a pooled analysis of 27 balance studies pointing to neutral magnesium balances at lower intakes (Hunt and Johnson, 2006) than these RIs does not indicate that the values should be changed (Nordic Council of Ministers, 2014).

The World Health Organization/Food and Agriculture Organization of the United Nations (WHO/FAO, 2004) highlighted the uncertainties in previously used approaches to derive magnesium requirements. It was also stated that previous estimates by other authorities may have been overestimates. Based on magnesium intake on a body weight basis considered by similar committees in the US, the EU and the UK to maintain zero magnesium balance and considering especially balance studies enabling the development of an equilibrium (Hunt and Schofield, 1969; Marxhall et al., 1976; Mahalko et al., 1983; Andon et al., 1996) Recommended Nutrient Intakes were proposed which were denoted as provisional. WHO/FAO (2004) assumed that older adults have a lower requirement "as requirements for growth diminish", but that at the same time absorption efficiency likely decreases as well.

On the basis of data from balance studies (Lakshmanan et al., 1984; Spencer et al., 1994), Afssa (2001) determined an Average Requirement (AR) for adults of 350 mg/day or 5 mg/kg body weight per day. By applying a coefficient of variation (CV) of 10 %, a PRI of 6 mg/kg body weight per day was set.

On the basis of balance studies conducted in men (Greger and Baier, 1983; Lakshmanan et al., 1984; Schwartz et al., 1986) and women (Lakshmanan et al., 1984; Wisker et al., 1991), IOM (1997) derived EARs of 330 mg/day for men and 255 mg/day for women aged 19 to 30 years. Applying a CV of 10 % to these EARs resulted in Recommended Dietary Allowances (RDAs) of 400 and 310 mg/day for men and women, respectively. For men aged 31–50 years, balance studies of Kelsay et al. (1979); Kelsay and Prather (1983); Mahalko et al. (1983); Lakshmanan et al. (1984); Spencer et al. (1994) were considered. As there were more instances of negative balance in the intake range of 300–350 mg/day for subjects in this age range, the EAR was set at a slightly higher amount, i.e. at 350 mg/day. For men aged 51–70 years, the aforementioned balance studies plus one in men with a mean age of 53 ± 5 years were considered (Schwartz et al., 1984) and the same EAR of 350 mg/day was derived. For women aged 31–50 years and 51–70 years, the EAR was raised to 265 mg/day based on the study by Lakshmanan et al. (1984) and considering the slight increase for men of these age ranges compared to younger men. RDAs of 420 and 320 mg/day were derived for men and women aged 31–70 years, respectively. For adults above 70 years, results from balance studies were not available and results from magnesium tolerance tests and red blood cell magnesium concentrations were considered. Given the uncertainty of these markers as indicators of magnesium requirement and the lack of balance studies for older adults, it was decided to retain the EAR and the RDA for adults aged 31–70 years also for this age group.

The SCF (1993) noted that results of balance studies are difficult to interpret due to methodological limitations in some, a long time to achieve equilibrium and the potential for physiological adaptations to low magnesium intakes (Marxhall et al., 1976; Seelig, 1982; Schwartz et al., 1984). It was stated that some balance data (Jones et al., 1967; Health and Welfare Canada Scientific Review Committee, 1990) suggest that a magnesium intake of 3.4 mg/kg body weight per day may be associated with zero balance, but a PRI was not set. Instead, an Acceptable Range of Intakes of 150–500 mg/day was proposed based on observed intakes (in the US and the UK).

The Netherlands Food and Nutrition Council (1992) considered on the basis of balance studies (Jones et al., 1967; Schwartz et al., 1978; Kelsay et al., 1979; van Dokkum et al., 1983; Schwartz et al., 1984) that no negative balances occur at magnesium intakes of 250–350 mg/day. Assuming that magnesium requirement is related to body weight, an Adequate Range of Intake of 300–350 mg/day for men and of 250–300 mg/day for women was derived.

The UK COMA (DH, 1991) considered balance studies to set DRVs (Jones et al., 1967; Marxhall et al., 1976; Seelig, 1982). Based on one study (Jones et al., 1967) showing that a magnesium intake of 3.4 mg/kg body weight per day is adequate for maintaining zero balance an EAR was derived by multiplication with reference body weights. Using a CV of 10 % for men and 17.5 % for women, Reference Nutrient Intakes (RNI) were set for men and women of all ages (Table 2).

Table 2: Overview of Dietary Reference Values for magnesium for adults

	D-A-CH (2015)	NCM (2014)	WHO/FAO (2004)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992)	DH (1991)
Age (years)	19–< 25	≥ 18	19–65	≥ 20	19–30	≥ 18	≥ 19	≥ 19
PRI								
Men (mg/day)	400	350	260	420	400	150–500 (a)	300–350 (a)	300
Women (mg/day)	310	280	220	360	310	150–500 (a)	250–300 (a)	270
Age (years)	≥ 25		> 65		≥ 31			
PRI								
Men (mg/day)	350		224		420			
Women (mg/day)	300		190		320			

NCM, Nordic Council of Ministers; NL, Netherlands Food and Nutrition Council
(a): Acceptable/Adequate Range of Intakes

4.2. Infants and children

The German-speaking countries (D-A-CH, 2015) assumed that there is a magnesium retention of 3 mg/kg body weight per day during growth which should be covered by an intake of 6 mg/kg body weight per day (IOM, 1997). RIs were derived on the basis of this value and taking into account reference body weights of the respective age groups.

For NNR 2012, the Nordic countries (Nordic Council of Ministers, 2014) maintained the RIs for children from 1996, which at that time had been taken over from SCF (1993).

WHO/FAO (2004) stated that results of magnesium balance studies and other studies possibly useful for assessing magnesium requirements should be interpreted in the light of protein and energy intakes of subjects studied. It was also stated that previously derived magnesium requirements by other authorities may have been overestimates. Based on magnesium intake on a body weight basis considered by similar committees in the US, the EU and the UK to maintain zero magnesium balance and considering especially balance studies enabling the development of an equilibrium (Hunt and Schofield, 1969; Marxhall et al., 1976; Mahalko et al., 1983; Andon et al., 1996) Recommended Nutrient Intakes were proposed which were denoted as provisional. Results of a study on nutritional rehabilitation of children suffering from protein-energy malnutrition and receiving or not magnesium supplements (Nichols et al., 1978) was considered to support the value derived for young children.

Afssa (2001) set an AI of 75 mg/day for infants from 6–12 months on the basis of magnesium intake from breast milk and solid food (Lonnerdal, 1995). Afssa (2001) noted that studies using isotopes indicate an AR of 5 mg/kg body weight per day for children (Abrams et al., 1997) which increases to 5.3 mg/kg per day in older children, due to an increase in growth velocity. The PRI of 6 mg/kg body weight per day derived for adults was also applied to children up to 12 years. For children aged 13–18 years, an additional intake of 25 mg/day was advised to cover needs related to the increased rate of growth.

IOM (1997) set an Adequate Intake (AI) of 75 mg/day for infants aged 7–12 months considering an average magnesium concentration in breast milk of 34 mg/L (Dewey et al., 1984; Allen et al., 1991), a mean breast milk intake of 0.6 L/day (Heinig et al., 1993) and a mean magnesium intake from solid foods of 55 mg/day as observed in formula-fed infants aged 9–12 months (Specker et al., 1997). For children from 1–18 years, EARs were set on the basis of magnesium balance studies. These were available for children aged 10–15 years (Schwartz et al., 1973; Greger et al., 1978; Greger et al., 1979; Andon et al., 1996; Abrams et al., 1997; Sojka et al., 1997) and 7–9 years (Schofield and Morrell, 1960). A magnesium intake of 5 mg/kg body weight per day appeared to have met the requirement of some but not all children in these studies. Using this value and reference body weights, EARs for younger children were extrapolated and were 65, 110 and 200 mg/day for children aged 1–3, 4–8 and 9–13 years, respectively. For children aged 14–18 years, average requirements were assumed to be greater per kg body weight and the EAR was estimated to be 5.3 mg/kg body weight per day. Using reference body weights, EARs of 340 and 300 mg/day were derived for boys and girls, respectively. In the absence of information about the variance in requirements, a CV of 10 % was applied to all EAR values to derive the RDAs (Table 3).

The SCF (1993) derived "quasi-PRIs" on the basis of body weights and assuming that requirements range from 7 mg/kg body weight per day (denoted slightly higher than the intake from breast milk) at 6–11 months to 4.2 mg/kg body weight per day (denoted slightly higher than the figure of 3.4 mg/kg body weight per day likely adequate in adults) at 15–17 years. An extra 30 % was added to allow for individual variations in growth. The SCF (1993) stressed the uncertainty around these values (Table 3).

The Netherlands Food and Nutrition Council (1992) extrapolated Adequate Ranges of Intake for children from those for adults on the basis of body weight. For breast-fed infants a daily magnesium intake of 25–35 mg was estimated (Wacker and Parisi, 1968; Neville et al., 1984), and the Adequate Range of Intake for infants aged 6–12 months was set at 35–60 mg/day.

The UK COMA (DH, 1991) derived an EAR of 6 mg/kg body weight per day for infants aged 4–6 months on the basis of magnesium intake via breast milk reported to contain 28 mg/L (range 26–30 mg/L, DHSS (1980). For children from 6 months to 18 years, the EAR was assumed to be 4.5 mg/kg body weight per day, which was interpolated between the value for infants aged 4–6 months and the EAR on a body weight basis for adults (see Section 4.1). EARs were derived using reference body weights and RNIs were set using CVs between 10 % and 16.5 % for the various age groups.

Table 3: Overview of Dietary Reference Values for magnesium for children

	D-A-CH (2015)	NCM (2014)	WHO/FAO (2004)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992)	DH (1991)
Age (months)	4–<12	6–11	7–12	7–12	7–12	6–11	6–12	7–9
PRI (mg/day)	60	80	54 [(b)]	75	75 [(a)]	80 [(b)]	35–60 [(c)]	75
Age (years)								10–12
PRI (mg/day)								80
Age (years)	1–<4	1–<2	1–3	1–3	1–3	1–3	1–4	1–3
PRI (mg/day)	80	85	60 [(b)]	80	80	85 [(b)]	60–70 [(c)]	85
Age (years)	4–<7	2–5	4–6	4–6	4–8	4–6	4–7	4–6
PRI (mg/day)	120	120	76 [(b)]	130	130	120 [(b)]	90–100 [(c)]	120
Age (years)	7–<10	6–9	7–9	7–9		7–10	7–10	7–10
PRI (mg/day)	170	200	100 [(b)]	200		200 [(b)]	120–140 [(c)]	200
Age (years)	10–<13	10–13	10–18	10–12	9–13	11–14	10–13	11–14
PRI (mg/day)				280				
Boys	230	280	230 [(b)]		240	280 [(b)]	150–175 [(c)]	280
Girls	250	280	220 [(b)]		240	280 [(b)]	155–185 [(c)]	280
Age (years)	13–<15			13–15			13–16	
PRI (mg/day)								
Boys	310			410			220–255 [(c)]	
Girls	310			370			210–250 [(c)]	
Age (years)	15–<19	14–17		16–19	14–18	15–17	16–19	15–18
PRI (mg/day)								
Boys	400	350		410	410	300 [(b)]	275–325 [(c)]	300
Girls	350	280		370	360	300 [(b)]	225–275 [(c)]	300

NCM, Nordic Council of Ministers; NL, Netherlands Food and Nutrition Council
(a): AI
(b): The uncertainty accompanying these values was expressed.
(c): Adequate Range of Intake

4.3. Pregnancy and lactation

The German-speaking countries (D-A-CH, 2015) stated that the fetus accumulates daily 5–7.5 mg of magnesium during the third trimester. It was, however, assumed that the Recommended Intake for (young) non-pregnant women covers the requirement arising from this. During lactation, considering a mean magnesium concentration of breast milk of 31 mg/L and a milk secretion of 0.75 L/day a daily magnesium loss of 24 mg via breast milk was assumed. Taking into account absorption efficiency, an additional magnesium intake of 80–90 mg/day was estimated to compensate for this loss.

For NNR 2012 it was considered that the RI for non-pregnant and non-lactating women is sufficient to also cover the needs during pregnancy and lactation (Nordic Council of Ministers, 2014).

WHO/FAO (2004) considered that the fetus accumulates 8 mg and fetal adnexa accumulate 5 mg of magnesium during the whole pregnancy. Taking into account absorption efficiency a total requirement of 26 mg over the whole pregnancy was calculated which was assumed to be met by adaptation. Thus, the Recommended Intake for pregnant women was the same as for non-pregnant women. During lactation, a daily magnesium loss of 25–28 mg via breast milk was assumed. An additional magnesium intake of 50–55 mg/day was estimated to cover this loss.

Afssa (2001) acknowledged that the requirement during pregnancy increases particularly during the third semester, due to to the transfer of magnesium to the fetus. Due to the absence of compensatory mechanisms for this increased requirement, an additional intake of 40 mg/day was advised during pregnancy. For lactating women, an increase in intake of 30 mg/day was recommended, despite a decrease in urinary magnesium excretion and an increase in bone resorption that may contribute to meeting the increased magnesium requirement during lactation.

IOM (1997) considered that inconsistent findings on the effects of magnesium supplementation on pregnancy outcome make it difficult to determine whether magnesium intakes greater than those

recommended for non-pregnant women are beneficial. It was noted that there are no data indicating that magnesium is conserved during pregnancy or intestinal absorption is increased. Thus, a factorial approach was used considering the gain in weight associated with pregnancy (increase in lean body mass of 6–9 kg with a midpoint of 7.5 kg (IOM, 1990), a magnesium concentration of lean body mass of 470 mg/kg (Widdowson and Dickerson, 1964) and an absorption efficiency of 40 % (Abrams et al., 1997)). A value of 33 mg/day was calculated and the additional requirement set to 35 mg/day. For lactation, IOM (1997) considered that consistent evidence does not exist to support an increased requirement for dietary magnesium during lactation. It was stated that decreased urinary excretion of magnesium and increased bone resorption during lactation may provide the necessary magnesium for milk production. Therefore, the EAR and RDA were estimated to be the same as for non-lactating women of similar age and body weight.

The SCF (1993) stated that the Acceptable Range of Intakes for adults (i.e. 150–500 mg/day) also applies to pregnant and lactating women.

The Netherlands Food and Nutrition Council (1992) stated that balance studies in pregnant women have shown that a daily magnesium intake of 400 mg is not always sufficient to maintain balance and that the increased requirement for magnesium is likely greatest during the third trimester. An Adequate Range of Intake of 300–350 mg/day was set. For lactating women an Adequate Range of Intake of 300–400 mg/day was derived.

The UK COMA (DH, 1991) considered that the fetus accumulates about 8 mg/day of magnesium and that there is a requirement of 10 mg/day for the accumulation of placenta and other tissues (Ziegler et al., 1976; Widdowson, 1980). However, it was considered that physiological adaptation during pregnancy and release from maternal stores ensures an adequate supply, and no additional intake was set. For lactating women, taking into account a magnesium concentration in breast milk of 28 mg/L (DHSS, 1980), assuming a magnesium secretion of 25 mg/day via milk and an absorption efficiency of 50 %, an additional intake of 50 mg/day was derived (Table 4).

Table 4: Overview of Dietary Reference Values for magnesium for pregnant and lactating women

	D-A-CH (2015)	NCM (2014)	WHO/FAO (2004)	Afssa (2001)	IOM (1997)	SCF (1993)	NL (1992)	DH (1991)
Pregnancy: additional intake (mg/day)	0	0	0	40	40	0	0–100	0
PRI (mg/day)	350 [(a)]/310 [(b)]	280	220	400	400 [(a)] 350 [(d)] 360 [(e)]	150–500 [(f)]	300–350 [(g)]	270
Lactation: additional intake (mg/day)	40 [(a)]/80 [(b)]	0	50	30	0	0	0-150	50
PRI (mg/day)	390	280	270	390	360 [(a)] 310 [(d)] 320 [(e)]	150–500 [(d)]	300–400 [(g)]	320

NCM, Nordic Council of Ministers; NL, Netherlands Food and Nutrition Council
(a): < 19 years
(b): ≥ 19 years
(c): Women in the 3rd trimester
(d): 19–30 years
(e): 31–50 years
(f): Acceptable Range of Intakes
(g): Adequate Range of Intake

5. Criteria (endpoints) on which to base Dietary Reference Values

5.1. Biomarkers as indicators of magnesium requirement

As stated in Section 2.4, the Panel considers that there is no adequate biomarker of magnesium intake or status that can be used for assessing magnesium requirement and for setting DRVs for magnesium.

5.2. Balance studies on magnesium

Balance studies are based on the assumption that a healthy subject on an adequate diet maintains an equilibrium or a null balance between nutrient intakes and nutrient losses: at this null balance, the intake matches the requirement determined by the given physiological state of the individual. When intakes exceed losses (positive balance), there is nutrient accretion that may be attributable to growth or to weight gain, anabolism or repletion of stores; when losses exceed intakes (negative balance), nutrient stores are progressively depleted resulting, in the long term, in clinical symptoms of deficiency. When performed at different levels of intake, balance studies enable the quantification of basal or obligatory losses by regression to zero. In addition to numerous methodological concerns about accuracy and precision in the determination of intakes and losses (Baer et al., 1999), the validity of balance studies for addressing requirements has been questioned: they might possibly reflect only adaptive changes before a new steady state is reached (Young, 1986), or they might reflect only the conditions for maintenance of nutrient stores in the context of a given diet and, consequently, the relevance of the pool size for health still needs to be established for each nutrient (Mertz, 1987).

5.2.1. Balance studies in adults

Many studies have been performed to assess magnesium balance (Jones et al., 1967; Hunt and Schofield, 1969; Marxhall et al., 1976; Schwartz et al., 1978; Kelsay et al., 1979; Seelig, 1982; Kelsay and Prather, 1983; Mahalko et al., 1983; van Dokkum et al., 1983; Lakshmanan et al., 1984; Schwartz et al., 1984; Schwartz et al., 1986; Wisker et al., 1991; Spencer et al., 1994). Considering the balance studies in adults, which have an *a priori* sufficient adaptation period (see Appendix G), the Panel notes that many of these were conducted to assess interactions of some nutrients on magnesium absorption and balance, and that the diversity of background diets makes comparisons of the results of these balance studies difficult. The number of subjects included in the studies is generally small. Contrary to studies in children, most of the studies in adults did not express the results in relation to body weight. For most of the studies, the variability of intakes is limited (in the range 200–400 mg/day, with the exception of the study of Spencer et al. (1994)). For the only study reporting on individual values (Jones et al., 1967), the same approach as used by Hunt and Johnson (2006) (see next paragraph) resulted in a requirement of 219 mg/day or 4 mg/kg body weight per day. Recent studies in Japanese subjects reported zero balance for a magnesium intake of 4.1 mg/kg body weight per day (Nishimuta et al., 2006) and 4.18 mg/kg body weight per day (Nishimuta et al., 2012); the latter study was a compilation of 13 balance studies performed between 1986 and 2007 on a total of 131 female subjects that concluded that the balances determined in this group were very close to the usual dietary intake; however, in the calculations, the adjustment to zero of the median values of several included studies where balances were positive hampers the interpretation of this result; moreover, adaptation periods were very short (2–4 days). In the study by Nielsen and Milne (2004) in postmenopausal women, positive balances (1–26 mg/day) were observed for a magnesium intake between 310 and 334 mg/day.

Hunt and Johnson (2006) compiled the results of 27 balance studies conducted in a metabolic unit under well-controlled conditions. None of these studies had been considered by the other committees because the results of these studies for magnesium were not published, as magnesium was not the primary objective of these studies. The 27 studies were carried out between 1976 and 2000 on 243 apparently healthy subjects (150 women and 93 men, mean age 51 and 28 years, respectively), after

877 excluding subjects who had insufficient (below the US EAR) or excessive (above the 99th percentile)
878 intakes of possibly interacting nutrients (calcium, copper, iron, phosphorus, or zinc). The last 6–14
879 days of each equilibrating dietary period of at least 28 days were considered for the calculation of
880 balances (difference between intakes and losses through faeces and urine), which resulted in 664
881 available data points. A total of 18 studies did not use magnesium supplements; three studies used
882 supplements in order to meet the US RDA (supplement providing 57, 114 or 171 mg/day); the other
883 studies provided a fixed daily magnesium amount (around 200 mg/day in six studies) and one study
884 provided 50 mg/day of supplemental magnesium; magnesium gluconate was the supplemental form in
885 all the studies using supplements except for one which used citrate dibasic magnesium salt. There was
886 no indication that magnesium gluconate was absorbed differently as compared to magnesium from
887 foods. Null balance was achieved at a magnesium intake of 165 mg/day [95 % prediction interval:
888 113, 237 mg/day; $Y = 19.8 + 0.880\ M$, where Y refers to magnesium output and M refers to
889 magnesium intakes], corresponding to 2.36 mg/kg body weight per day (95 % prediction interval:
890 1.58, 3.38 mg/kg body weight per day; $Y = 0.306 + 0.870\ M$), or 0.075 mg/kcal per day (95 %
891 prediction interval: 0.05, 0.11 mg/kcal per day; $Y = 0.011 + 0.857\ M$). Magnesium balance does not
892 seem to be affected by age (subjects ranging in age from 20 to 80 years were included in the studies)
893 and sex, suggesting that magnesium absorption does not change with age. From the characteristics of
894 the statistical models, the authors concluded on a strong homeostatic control of magnesium
895 metabolism within the wide range of intakes observed in the studies (84–589 mg/day), especially with
896 intakes below the null balance of 165 mg/day, with no suggestion of modifications of fractional
897 magnesium absorption within this range.

898 Shils and Rude (1996) considered that magnesium balance studies were the most suitable basis for
899 setting reference values for magnesium, as far as careful consideration is given to the quality of the
900 methodology used in the studies. Overall, the results of studies summarised in Appendix G are
901 inconsistent, and they therefore cannot be used to define the requirement of magnesium. On the other
902 hand, considering the number of subjects of both sexes and the number of individual balance data, the
903 large age range, the wide range of magnesium intake reported in the studies compiled, the
904 comparability of experimental settings between the studies, especially the expression of results in
905 relation to individual body weights, and the statistical analysis of the pooled data, the Panel considers
906 that the balance studies compiled by Hunt and Johnson (2006) provides a stronger weight of evidence
907 for adults than any of the other individual balance studies listed in Appendix G.

908 **5.2.2. Balance studies and other indicators of requirement in children**

909 There are some balance studies in children aged 7–9 years (Schofield and Morrell, 1960) and children
910 aged 10–15 years (Schwartz et al., 1973; Greger et al., 1978; Greger et al., 1979; Andon et al., 1996;
911 Abrams et al., 1997; Sojka et al., 1997) (see Appendix H). The Panel notes that most of these studies
912 have limitations (small number of subjects, adaptation period short or absent), are heterogeneous with
913 respect to their primary objective (e.g. influence of another nutrient on magnesium balance) and
914 background diet. The Panel notes that these studies have been used for setting DRVs for children
915 (Section 4.2). The Panel also notes that requirements which may be derived from these balance
916 studies with limitations are lower than average observed magnesium intakes in children (Section 3.2).

917 Magnesium accretion in bone is considered to be around 2.7 mg/day in infants aged 4–12 months and
918 3.1 and 4.2 mg/day in girls and boys, respectively, throughout childhood, with a peak rate of
919 8.4 mg/day in adolescence (Prentice and Bates, 1994). The Panel considers that this accretion rate
920 constitutes only a small amount and does not need to be considered in setting DRVs for magnesium.

921 Very few studies have investigated magnesium intake or status in relation to health outcomes in
922 children (Huerta et al., 2005; Bo et al., 2007), and the Panel is unaware of studies in healthy children.
923 The Panel considers that the available data on magnesium intake and health consequences in children
924 cannot be used for setting DRVs for magnesium for children.

5.3. Indicators of magnesium requirement in pregnancy

Magnesium transfer to the fetus across the placenta occurs separately from that of calcium, through the paracellular route and is driven by an electrochemical gradient; the existence of an active transport mechanism has still to be confirmed (Nandakumaran et al., 2002). The fetus accumulates magnesium, with a total content of around 0.6–0.8 g magnesium in mature fetuses weighing 3–4 kg, the percentage of magnesium in fetal fat-free mass being constant for fetuses weighing more than 2 kg, at around 0.26 mg/kg (Widdowson and Spray, 1951; Lentner, 1981). The placental magnesium content is low (around 36 mg, Challier et al. (1988)). The accretion of all these amounts would represent a daily net transfer of around 2–3 mg. According to Ziegler et al. (1976), accretion varies from 1.8 mg/day at week 24–25 to 7.5 mg/day at week 36–37 and thereafter decreases to 5 mg/day at week 39–40; this averages to a daily accretion of 4.7 mg/day from week 24 to week 40.

Magnesium sulphate is promoted as an efficient treatment of pre-eclampsia and eclampsia (WHO, 2011), but the usefulness of magnesium supplementation during pregnancy for decreasing the risk of this adverse event is controversial, due to the lack of good quality data (Makrides et al., 2014): this review did not show an influence of magnesium supplementation on infant or maternal outcomes when they were studied as primary outcomes.

A balance study in free-living subjects performed in the three trimesters of pregnancy in 10 women showed that a mean magnesium intake of 269 ± 55 mg/day led to a negative balance of 40 ± 50 mg (Ashe et al., 1979); according to Husain and Sibley (1993), this negative balance could be due to an unusually low value for the fractional absorption of magnesium, since faecal excretion represented around 80 % of the intake; other limitations of the study are the small number of subjects, the use of self-selected diets, the absence of information on pre-pregnancy intake, whereas a strength is the determination of 4–6 seven-day balances for each woman (two per trimester); the authors acknowledged that the important within- and between-subject variability might have obscured physiological adaptations.

The Panel concludes that infant or maternal clinical outcomes during pregnancy cannot be used to assess magnesium requirements during this phase. On the other hand, the available evidence indicates that there is only a small additional requirement during pregnancy that may be met by adaptive metabolic changes.

5.4. Indicators of magesnium requirement in lactation

According to Dorea (2000), concentrations of magnesium reported for breast milk vary over a wide range (15–64 mg/L), with a median value of 31 mg/L and 75 % of reported mean concentrations being below 35 mg/L (see Section 2.3.5.5). Dengel et al. (1994) compared six lactating and six post partum non-lactating women (75 ± 5 and 61 ± 5 days post partum, respectively) with seven never-pregnant women who received a constant diet providing 218 mg magnesium/day for 20 days. After an equilibration period of five days, urine and faeces were collected for the next 15 days. Comparing lactating to never-pregnant women, the authors observed that the export in milk of around 25 mg/day was compensated for by a reduction of 33 mg/day in urinary magnesium excretion. The Panel considers that there are adaptative mechanisms so that there may be no need to compensate for the amount of magnesium secreted in breast milk during lactation.

5.5. Magnesium intake and health consequences

A comprehensive literature search covering the period from 1990 to October 2011 was performed as preparatory work for this opinion (Brown et al., 2012), focusing on original studies reporting on quantitative relationships between intake and status, status and health or intake and health. Overall, the preparatory report concluded that high quality data for health outcomes on which to derive DRVs

for magnesium are limited. The literature search was continuously updated until endorsement of this draft opinion.

The analysis presented in this section is restricted to the conditions relevant for the general population, where a sufficient body of evidence exists and quantitative data on magnesium intake are available (studies only reporting on serum magnesium are not considered in this section). Many other clinical conditions have been studied in relation to magnesium intake/status that consider the therapeutic potential of magnesium (such as in migraine headaches, neuromuscular issues such as restless leg syndrome, or clinical depression) or its potential role on the basis of mechanistic considerations, such as for the immune system (Wu and Veillette, 2011).

5.5.1. Cardiovascular disease-related outcomes

5.5.1.1. Blood pressure

Previous systematic reviews and meta-analyses on studies investigating the effect of magnesium supplementation on systolic (SBP) and diastolic blood pressure (DBP) have shown inconclusive results. Several of these reviews included hypertensive subjects, and information on dietary magnesium intake was not generally available (Burgess et al., 1999; Jee et al., 2002; Dickinson et al., 2006; Kass et al., 2012). From the compilation of a set of 30 observational studies (mainly cross-sectional), Mizushima et al. (1998) concluded that there may be an inverse relationship between magnesium intake and SBP and DBP, though quantitative analysis was not possible due to heterogeneity and various methodological limitations. In a recent cross-over study lasting eight weeks, with a four-week wash-out period inbetween, supplementation of magnesium (368 mg/day) to 14 healthy normotensive young men did not affect their SBP or DBP (Cosaro et al., 2014).

5.5.1.2. Cardiovascular events

The meta-analysis by Qu et al. (2013b) included 13 prospective cohort studies reporting on dietary magnesium (477 680 participants and over 14 900 cardiovascular events) and showed a significant inverse association between magnesium intake and risk of cardiovascular disease (CVD) events comprising stroke, coronary heart disease and CVD death (relative risk (RR) = 0.85, 95 % CI 0.78–0.92, I^2 = 39 %, comparing the highest and the lowest category of magnesium intake). Dose–response analyses showed evidence of a non-linear association, with the greatest reduction occurring for a magnesium intake between 150 and 400 mg/day, though it is unclear whether supplement use was always considered.

The meta-analysis by Del Gobbo et al. (2013) included nine prospective studies providing estimates of dietary magnesium, mostly from validated food frequency questionnaires (FFQ), with a median intake across studies of 289 mg/day, and incident CVD (including 7 889 CVD events, 4 319 events of ischaemic heart disease, and 1 158 fatal ischaemic heart disease events). Only two of nine studies described the use of magnesium supplements, and seven of the nine studies were also considered by Qu et al. (2013b). Using 200 mg/day-increments in dietary magnesium, dietary intake was not associated with total CVD. The authors found a significant non-linear association with fatal ischaemic heart disease; in comparison with lower intakes, a 27 % lower risk of fatal ischaemic heart disease was observed up to a magnesium intake of about 250 mg/day (RR = 0.73, 95 % CI 0.62–0.86).

Combining six prospective cohort studies (including four already included in the meta-analyses of Qu et al. (2013b) and Del Gobbo et al. (2013)), the meta-analysis by Xu et al. (2013) did not find a significant association between magnesium intake and total CVD mortality; however, a subgroup analysis suggested an inverse association in women, leading the authors to conclude that sex might be one of the major sources of heterogeneity between studies. This meta-analysis included only studies

providing adjusted risk estimates, but also included two studies focusing on magnesium intake from water (and using this intake for comparisons).

The Panel notes the discrepancies between these meta-analyses, suggesting that inclusion of non-adjusted results might confound the association of magnesium intake and CVD events.

In the Nurses' Health Study, the relationship between dietary magnesium (including from supplements) and risk of coronary heart disease after a median follow-up of 28 years was investigated (Chiuve et al., 2013). After controlling for classical coronary heart disease risk factors, higher magnesium intake was not associated with overall coronary heart disease risk; however, the authors observed a lower risk of fatal coronary heart disease (RR 0.61, 95 % CI 0.45–0.84) comparing the highest quintile (dietary intake > 342 mg/day) with the lowest quintile (< 246 mg/day). A cross-sectional study in 2 695 men and women of the Framingham cohort showed an inverse association of total (i.e. dietary and supplemental) magnesium intake with calcification of the coronary artery, each 50 mg/day-increment in magnesium intake resulting in 22 % less calcification ($p < 0.001$), whereas total magnesium intake was not associated with calcification of the abdominal aorta (Hruby et al., 2014).

5.5.1.3. Stroke

Nie et al. (2013) performed a meta-analysis on the relationship between magnesium intake and stroke, including eight prospective cohort studies (8 367 strokes in 304 551 participants). The weighted average magnesium intake was 306 mg/day (range 228–471 mg/day). There was an inverse association between magnesium intake and incidence of total stroke (RR = 0.89, 95 % CI 0.82–0.97, $I^2 = 0$ %); the dose–response analysis showed a small borderline significant inverse association between magnesium intake per 100 mg/day-increment and total stroke risk (RR = 0.98, 95 % CI 0.95–1.00, $I^2 = 33$ %), whereas subgroup analysis showed a significantly lower risk of ischaemic stroke when comparing highest intake to lowest intake (RR = 0.88, 95 % CI 0.80–0.98, p for heterogeneity = 0.509). These results are similar to those of Larsson et al. (2012), whose meta-analysis included seven prospective studies (6 477 strokes among 241 378 participants; only one out of seven studies showed a significant reduction in stroke incidence) also included in the meta-analysis by Nie et al. (2013). For every 100 mg/day-increment in magnesium intake the risk of total stroke slightly decreased (RR = 0.92, 95 % CI 0.88–0.99, $I^2 = 0$ %). An inverse association between magnesium intake and stroke risk was also observed in the Dutch cohorts (n = 36 094, 631 strokes) of the European Prospective Investigation into Cancer and Nutrition study (Sluijs et al., 2014). Total magnesium intake (i.e. from diet and supplements) for the lowest and the highest quartile was ≤ 285 mg/day and ≥ 398 mg/day, respectively. Per 100 mg/day-increment in total magnesium intake, stroke risk decreased by 22 % (hazard ratio = 0.78, 95 % CI 0.65–0.93).

5.5.1.4. Arrhythmia

Although magnesium has been suggested for the therapy of arrhythmia, few studies have investigated the relationship of magnesium intake and heart rhythm changes in apparently healthy populations. Nielsen et al. (2007) submitted 14 healthy postmenopausal women to a magnesium depletion diet providing 100 mg/8.4 MJ (2 000 kcal); the depletion period was planned to have a duration of 78 days; five women developed heart rhythm alterations which required magnesium repletion earlier than planned (after 42–64 days instead of after 78 days). This study suggests that a magnesium intake of 100 mg/8.4 MJ (2 000 kcal) may be inadequate. In white and African American men and women in the prospective Atherosclerosis Risk in Communities study, no association was observed between dietary magnesium intake and risk of atrial fibrillation (Misialek et al., 2013).

5.5.1.5. Conclusions on cardiovascular disease-related outcomes

The Panel notes that the association between magnesium intake and CVD-related outcomes may be confounded by dietary fibre intake and other dietary factors. For example, in the meta-analysis of 19 studies by Qu et al. (2013b), only four of the included studies have adjusted for dietary fibre and only three for potassium intake. Del Gobbo et al. (2013) reported that about half of the studies included in their meta-analysis were adjusted for both sociodemographic and lifestyle variables including age, sex, ethnicity, body mass index, waist circumference, smoking, alcohol consumption, and physical activity. Therefore, for all these studies, it is difficult to unravel the effect of magnesium *per se* from the effect of foods rich in magnesium or of the total diets associated with consumption of these foods.

The Panel considers that data on magnesium intake and CVD-related outcomes cannot be used for setting DRVs for magnesium.

5.5.2. Metabolic syndrome

Some studies have investigated the relationship between magnesium intake and risk of metabolic syndrome. Combining eight cross-sectional and two prospective cohort studies (30 092 participants, eight studies with healthy subjects and two studies including patients with diabetes mellitus type 2 and recipients of living-donor kidney transplant), Ju et al. (2014) showed that every 150 mg/day-increment in magnesium intake was inversely associated with risk of metabolic syndrome (pooled RR = 0.88, 95 % CI 0.84–0.93, I^2 = 36 %). The meta-analysis of Dibaba et al. (2014) on six cross-sectional studies (24 473 individuals and 6 311 cases of metabolic syndrome), of which all but one were also included in the meta-analysis of Ju et al. (2014), also concluded on an inverse association of magnesium intake and risk of metabolic syndrome.

The Panel considers that data on magnesium intake and metabolic syndrome cannot be used for setting DRVs for magnesium.

5.5.3. Diabetes mellitus type 2

In the meta-analysis of Larsson and Wolk (2007) of seven prospective cohort studies (10 912 incident cases and 286 668 participants) the relative risk of diabetes mellitus type 2 for a 100 mg/day-increase in magnesium intake was 0.85 (95 % CI 0.79–0.92). In the dose–response analysis, studies were combined reporting associations between diabetes risk and magnesium intake (assessed continuously or categorically).

The meta-analysis by Dong et al. (2011) with 13 prospective cohort studies (24 516 incident cases for 536 318 participants, including the studies analysed by Larsson and Wolk (2007)) found a RR of 0.86 (95 % CI 0.82–0.89) for each 100 mg/day-increment in magnesium intake. In this meta-analysis, the relative risk was not significantly modified when considering only the studies where adjustments were made for dietary fibre intake. In addition, the observed inverse association remained in a subgroup analysis among studies of individuals with an average BMI $\geq$ 25 kg × m^{-2}, but no association was observed among those with a BMI < 25 kg × m^{-2}. This finding suggests that the evidence for an inverse association may not be consistent and may rather concern overweight/obese individuals than normal weight individuals which are the target population for DRVs. However, in the very large cohorts of the NHS and HPFS (included in the meta-analysis), no significant interaction was observed between magnesium intake and BMI and the risk reduction remained significant in stratified analysis by BMI ($\leq$ 27 and > 27 kg × m^{-2}) (Lopez-Ridaura et al., 2004). The Panel notes that the association between magnesium intake and diabetes mellitus type 2 may be confounded by dietary fibre intake and other dietary factors and that several observational studies did not adjust for this.

Details on magnesium intake and risk estimates for the individual prospective studies included in these meta-analyses are summarised in Appendix I.

In the most recent study (Weng et al., 2012), not included in the aforementioned meta-analysis, 1 604 Taiwanese adults were followed up for a period of 4.6 years and a significant trend for a decreased risk of diabetes mellitus type 2 incidence was observed when the lowest quintile of magnesium intake (median intake 212 mg/day) was compared to the highest (median intake 405 mg/day).

Supplementation studies in subjects with diabetes mellitus type 1 or type 2 or overweight individuals with insulin resistance show inconsistent results with respect to improvement of insulin sensitivity and glycaemic control (Sales and Pedrosa Lde, 2006; Martini et al., 2010; Volpe, 2013).

The Panel considers that there is evidence for an inverse association of magnesium intake and risk of diabetes mellitus type 2. The Panel notes that there is insufficient evidence for a dose–response relationship between magnesium intake and type 2 diabetes risk and considers that data on magnesium intake and diabetes mellitus type 2 cannot be used for setting DRVs for magnesium.

5.5.4. Cancer

In the report by WCRF/AICR (2007), magnesium was not considered as such, but some subsequent studies point to a possible association between magnesium intake and colorectal cancer risk.

The meta-analysis of Chen et al. (2012) included eight prospective studies with 338 979 participants and 8 000 colorectal cancer cases. The summary RR for the highest versus lowest category of magnesium intake for colorectal cancer was 0.89 (95 % CI 0.79–1.00, I^2 = 0 %). In dose–response analyses, every 50 mg/day-increment in magnesium intake was associated with a 5 % reduced risk of colorectal cancer (RR = 0.95, 95 % CI 0.89–1.00, I^2 = 49 %). Similar results were obtained in the meta-analysis of Qu et al. (2013a) of seven prospective cohort studies (333 510 participants and 7 435 cases), all of which were also considered by Chen et al. (2012). Qu et al. (2013a) observed a non-linear dose–response relationship between dietary magnesium and risk of colorectal cancer (RR for every 100 mg/day-increment in magnesium intake = 0.82, 95 % CI 0.64–1.00, I^2 = 63 %), with the greatest reduction of risk for an intake between 200 and 270 mg/day, but little evidence of a further reduction with higher intake.

The Panel considers that the available information on the relationship between dietary magnesium and colorectal cancer risk is insufficient to provide a basis for setting DRVs for magnesium.

5.5.5. Bone health-related outcomes

Magnesium has an impact on bone health through its participation to the structure of hydroxyapatite crystals in bone. Some studies of different design (cross-sectional and prospective observational studies, intervention studies using magnesium supplementation) reported on various associations of magnesium intake with bone mineral density (BMD) or bone mineral content (BMC) (Tucker et al., 1999; Ryder et al., 2005; Carpenter et al., 2006; Farrell et al., 2009). Carpenter et al. (2006) enrolled 8–14 year-old girls with a dietary magnesium intake below 220 mg/day; supplementation with 300 mg/day for one year significantly improved serum magnesium concentration and BMC of the hip by about 3 %, but not of the lumbar spine, compared to placebo. There was no difference in BMD between the treatment and placebo groups. In the prospective cohort study with 73 684 postmenopausal women enrolled in the Women's Health Initiative Observational Study (Orchard et al., 2014), baseline hip BMD was 3 % higher ($p < 0.001$) and whole-body BMD was 2 % higher ($p < 0.001$) in women who consumed > 422.5 mg magnesium/day compared to < 206.5 mg/day. However, the incidence and relative risk of hip and total fractures did not differ across quintiles of magnesium intake. In contrast, risk of lower-arm or wrist fractures increased significantly with higher magnesium

intake. As the women with the highest magnesium intake were also more physically active and at increased risk of falls, the authors concluded that the association of magnesium intake and fractures may possibly be related to more physical activity and falls.

In their literature search, Brown et al. (2012) retrieved two studies which reported on the influence of magnesium on markers of bone formation and bone resorption, one of which was an uncontrolled study (Fatemi et al. (1991)). Doyle et al. (1999) conducted a randomised cross-over study in 26 young women, which compared a usual dietary magnesium intake (about 275 mg/day) for four weeks with a usual dietary intake supplemented with about 250 mg magnesium/day for four weeks. There were no significant differences in biomarkers of bone formation and resorption between the two study periods.

The Panel notes that although the role of magnesium in bone structure and physiology is well established, there are few quantitative data for using this relationship for setting DRVs for magnesium.

6. Data on which to base Dietary Reference Values

The Panel considers that there is no adequate biomarker of magnesium intake or status that can be used for assessing magnesium requirement and for setting DRVs for magnesium (see Section 5.1).

6.1. Adults

The Panel notes that a recent pooled analysis of well-controlled balance studies in adults suggests that zero magnesium balance may occur at a magnesium intake of 165 mg/day [95 % prediction interval based on a linear mixed-effect model: 113, 237 mg/day] (Section 5.2.1). The Panel, bearing in mind that balance studies might also reflect adaptive changes before a new steady state is reached, evaluated the evidence from balance studies in combination with the findings of large-scale and long-term prospective observational studies. Several of these point to an inverse relationship between magnesium intake and risk of diabetes mellitus type 2, at daily intakes ranging between 244 and 773 mg/day (medians of highest quintiles), compared to daily intakes ranging between 115 and 230 mg/day (medians of lowest quintiles). The Panel notes, however, that there is insufficient evidence for a dose–response relationship between magnesium intake and risk of diabetes mellitus type 2 in the general healthy population and that the evidence cannot be used to identify a certain magnesium intake level above which risk of diabetes mellitus type 2 is not further reduced.

Considering all evidence available, the Panel decided to set Adequate Intakes (AIs) based on observed intakes in several EU countries. The range of average intakes for nine European countries is 317–439 mg/day (midpoint 378 mg/day) for men and 254–357 mg/day (midpoint 306 mg/day) for women aged 18 to < 65 years (see Appendix C and D). For older adults (65 to < 75 years), the ranges are 312–407 mg/day (midpoint 360 mg/day) for men and 241–343 mg/day (midpoint 292 mg/day) for women. For adults above 75 years, the ranges are 264–388 mg/day (midpoint 326 mg/day) for men and 232–347 mg/day (midpoint 290 mg/day) for women. The Panel notes that midpoints of ranges for intake estimates in these age and sex groups are in good agreement with medians, for the respective sex and age groups, of the average intakes estimated per survey.

The Panel notes that there is at present insufficient evidence for considering different DRVs according to age in adults and decided to merge the ranges for all men above 18 years (observed mean magnesium intakes of 264–439 mg/day), for which the midpoint is 352 mg/day. Similarly, for women, the merged range for all women above 18 years is 232–357 mg/day, with a midpoint at 295 mg/day. The median of average intakes of women of all ages is 298 mg/day, and the median of average intakes of men of all ages is 341 mg/day.

Considering the rather large differences in magnesium intakes between men and women, the Panel proposes to set AIs according to sex. For men, considering the distribution of the observed average intakes, the Panel proposes an AI of 350 mg/day. For women, on the same basis and after rounding, the Panel proposes an AI of 300 mg/day.

The Panel considers that these AIs apply to all adults, including older adults.

6.2. Infants aged 7–11 months

The Panel notes that in breast-fed infants aged 0–6 months, magnesium intake is estimated to be around 25 mg/day (Section 2.3.5.5). Using isometric scaling as the most conservative extrapolation method, which is justified by bone magnesium accretion, to extrapolate to the magnesium intake of infants aged 7–11 months results in an estimated magnesium intake of 35 mg/day in older infants. This is calculated using the below formula and rounding to the nearest unit. Averages of the median weight-for-age of male and female infants aged three months (6.1 kg) and nine months (8.6 kg) according to the WHO Growth Standards (WHO Multicentre Growth Reference Study Group, 2006) are used for the calculation.

Magnesium intake of infants aged 7–11 months = Magnesium intake of infants aged 0–6 months × (weight of infants aged 9 months/weight infants aged 3 months).

SCF (1993) proposed a guidance value of 80 mg/day on the basis of intakes considered appropriate for the majority of infants aged 6 to < 12 months, amounting to 3.5–7 mg/kg body weight per day, in line with the results of balance studies in older children.

The Panel notes that mean observed intakes in four EU countries for which data are available are in the range 72–120 mg/day (Appendix C and D). These estimates include the consumption of food products for the young population and thus of foods fortified with magnesium according to current EU regulations (see Section 3.1).

Therefore, a potential range for DRVs for magnesium would be between 35 and 120 mg/day (midpoint 78 mg/day). In the absence of other evidence and in line with the proposal by SCF (1993), the Panel decided to set an AI for infants aged 7–11 months of 80 mg/day.

6.3. Children

In the absence of well-controlled balance studies in children and on other evidence that may be used for deriving a requirement for magnesium in children, the Panel decided to set AIs based on observed intakes in EU countries.

In young children (1 to < 3 years), mean observed magnesium intake from five surveys in four EU countries ranges from 162–188 mg/day (midpoint 175 mg/day) in boys and from 153–174 mg/day (midpoint 164 mg/day) in girls (Appendix C and D). For boys and girls aged 1 to < 3 years, considering the absence of a strong basis for a distinct value according to sex and the distribution of the observed mean intakes, the Panel selects the midpoint of average intakes and sets an AI of 160 mg/day for boys and girls.

In children aged 3 to < 10 years, mean observed magnesium intake from seven surveys in six EU countries ranges from 202–281 mg/day (midpoint 242 mg/day) in boys and from 184–259 mg/day (midpoint 222 mg/day) in girls (Appendix C and D). For boys and girls aged 3 to < 10 years, on the same basis as for young children, considering the distribution of the observed mean intakes, the Panel selects the midpoint of average intakes and sets an AI of 230 mg/day for boys and girls.

In children aged 10 to < 18 years, mean observed magnesium intake from seven surveys in seven EU countries ranges from 257–344 mg/day (midpoint 301 mg/day) in boys and from 213–384 mg/day (midpoint 299 mg/day) in girls (Appendix C and D). However, the Panel notes that the data provided for Latvia include pregnant girls below 18 years of age and that intakes are rather high compared to other datasets; excluding Latvia provides a more narrow range of intakes of 213–292 mg/day (midpoint 253 mg/day). Considering the rather large differences in magnesium intakes between boys and girls aged 10 to <18 years, the Panel proposes to set AIs according to sex. For boys aged 10 to < 18 years, considering the distribution of the observed average intakes, the Panel selects the midpoint of average intakes and sets an AI of 300 mg/day. For girls aged 10 to < 18 years, considering the distribution of the observed average intakes, the Panel selects the midpoint of average intakes in non-pregnant girls and sets an AI of 250 mg/day.

6.4. Pregnancy

Considering that pregnancy induces only a small increase in magnesium requirement (see Section 5.4), which is likely covered by adaptive phyiological mechanisms, the Panel considers that the AI for non-pregnant women also applies to pregnant women.

6.5. Lactation

About 25 mg/day are secreted with exclusive breastfeeding during the first six months after birth (see Section 2.3.5.5).

The Panel notes the possibility of adaptive processes in magnesium metabolism, both at the level of absorption and elimination (see Section 2), and considers that an additional dietary intake may not be needed during the lactation period. The study by Dengel et al. (1994) (see Section 2.3.5.5) supports this approach.

The Panel concludes that the AI for non-pregnant women also applies to lactating women.

CONCLUSIONS

The Panel concludes that Average Requirements (ARs) and Population Reference Intakes (PRIs) for magnesium cannot be derived for adults, infants and children, and proposes Adequate Intakes (AIs) based on observed intakes. For children and adults, this approach considers the range of average magnesium intakes estimated from dietary surveys in nine EU countries. For infants aged 7–11 months, the Panel proposes AIs after consideration of observed intakes, estimated intakes in fully breast-fed infants and upward extrapolation by isometric scaling. The AI set for pregnant and lactating women is the same as for non-pregnant, non-lactating women.

Table 5: Summary of Adequate Intakes for magnesium

Age	Adequate Intake (mg/day)	
	Males	Females
7–11 months	80	80
1– < 3 years	160	160
3– < 10 years	230	230
10– < 18 years	300	250
≥ 18 years [(a)]	350	300

(a): Including pregnancy and lactation

RECOMMENDATIONS FOR RESEARCH

The Panel recommends that research is needed to characterise systematically:

- the functional and homeostatic responses to a range of exposures to magnesium with a view to identifying and validating markers of marginally adequate and excessive intakes of magnesium and of chronic and acute magnesium status. Such work might include for example: investigating the value of urinary excretion of magnesium, the magnesium tolerance test, and the content of magnesium in blood cells and platelets;
- the nature of possible pathogenic bases for the association of low magnesium status with impaired substrate (carbohydrate and lipid) metabolism, and sequelae of the metabolic syndrome including diabetes mellitus.

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APPENDICES

Appendix A. Magnesium concentration in human milk of mothers of term infants

Reference	Number of women (number of samples)	Country	Stage of lactation	Magnesium concentration (mg/L)		
				Mean ± SD	Median	Range
Bauer and Gerss (2011)	10	Germany	1–8 weeks	31.6 ± 4.86		
Bjorklund et al. (2012)	60	Sweden	14–21 days	28 ± 4.8	28	21–43
Bocca et al. (2000)	60 (60)	Italy	Not reported	23.0 ± 0.51		
Doybak et al. (1999)	35	Turkey	1–4 months (28–123 days)	1st month: 28 ± 7 4th month: 31 ± 8		
Friel et al. (1999)	19 (136) (17) (16) (16) (15) (15) (15) (15) (15) (12)	Canada	2 or 3 days–3 months	 week 1: 30.41 ± 4.74 week 2: 26.69 ± 3.98 week 3: 26.25 ± 4.40 week 4: 26.73 ± 4.71 week 5: 28.33 ± 5.59 week 6: 29.20 ± 5.02 week 7: 31.47 ± 5.76 week 8: 33.20 ± 5.24 week 12: 34.58 ± 6.02		26–35
Hunt et al. (2005)	45	USA	> 10 days–4 months	Month 1: 28.6 ± 2.2 Month 4: 33.0 ± 2.2		
Rakicioglu et al. (2006)	21	Turkey	2–5 months	During Ramadan (second week): 29 ± 5 2 weeks after the end of Ramadan: 33 ± 5		
Sievers et al. (2000)	14 infants	Germany	Infant age median 3.6 weeks (range 2.6–4.7)		28.6	21.2–44

Reference	Number of women (number of samples)	Country	Stage of lactation	Magnesium concentration (mg/L)		
				Mean ± SD	Median	Range
Vitolo et al. (2004)	90	Brazil	30–90 days	Low socio-economic adolescents (n = 31): 25.8 ± 4.4 Low socio-economic women (n = 30): 28.2 ± 5.6 High socio-economic women (n = 29): 27.0 ± 5.6		
Witczak and Jarnuszewska (2011)	(9)	Poland	5–6 months	40		
Yamawaki et al. (2005)	(1170) Summer: (577) Winter: (593)	Japan	1–365 days	Mean total: 27 ± 9 By season: Summer : 26 ± 9 Winter: 27 ± 9 By stage of lactation: Day 1–5: 32 ± 5 Day 6–10: 30 ± 9 Day 11–20: 29 ± 6 Day 21–89: 25 ± 7 Day 90–180: 27 ± 11 Day 181–365: 33 ± 7		

This table considers studies not yet considered in the review by Dorea (2000).

Appendix B. Dietary surveys in the EFSA Comprehensive European Food Consumption database included in the nutrient intake calculation and number of subjects in the different age classes

Country	Dietary survey	Year	Method	Days	Age (years)	Number of subjects						
						< 1 y	1 to < 3 y	3 to < 10 y	10 to < 18 y	18 to < 65 y	65 to < 75 y	≥ 75 y
Finland/1	DIPP	2000–2010	Dietary record	3	< 1–6	499	500	750				
Finland/2	NWSSP	2007–2008	48-hour dietary recall [(a)]	2x2 [(a)]	13–15				306			
Finland/3	FINDIET2012	2012	48-hour dietary recall [(a)]	2 [(a)]	25–74					1 295	413	
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	159	347	299				
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_PREGNANTWOMEN 2011	2011	24-hour dietary recall	2	15–45				12 [(b)]	991 [(c)]		
Netherlands	DNFCS	2007–2010	24-hour dietary recall	2	7–69			447	1 142	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 (1–3 years)	2008–2011	Dietary record	4	1–94		185	651	666	1 266	166	139

y, years; DIPP, type 1 Diabetes Prediction and Prevention survey; DNSIYC, Diet and nutrition survey of infants and young children; DNFCS, Dutch National Food Consumption Survey; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale de Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia; FC_PREGNANTWOMEN, food consumption of pregnant women in Latvia; 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 comprises two consecutive days.

(b): 5^{th} or 95^{th} percentile of intake calculated from less 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}, 95^{th} percentile estimates will not be presented in the intake results.

(c): One subject was excluded from the dataset due to only one 24-hour dietary recall day being available, i.e. final n = 990.

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

1859 **Appendix C. Magnesium intake in males in different surveys according to age classes and country**

Age	Country	Survey	Intake expressed in mg/day					Intake expressed in mg/MJ				
			n [a]	Average	Median	P5	P95	n [a]	Average	Median	P5	P95
< 1 year	Finland	DIPP_2001_2009	247	76.2 [b]	80.0 [b]	[b]	[b]	245	42.2 [b]	37.8 [b]	[b]	[b]
	Germany	VELS	84	110.7	102.8	60.0	172.7	84	34.2	33.8	21.3	48.3
	Italy	INRAN_SCAI_2005_06	9	75.8	56.0	[c]	[c]	9	24.8	24.1	[c]	[c]
	United Kingdom	DNSIYC_2011	699	120.1	117.0	62.7	186.3	699	35.1	34.7	22.2	47.8
1 to < 3 years	Finland	DIPP_2001_2009	245	161.5	160.3	90.6	236.4	245	44.5	44.1	29.0	58.5
	Germany	VELS	174	169.4	166.5	106.7	249.8	174	36.4	35.6	25.7	47.9
	Italy	INRAN_SCAI_2005_06	20	173.1	170.2	[c]	[c]	20	35.1	35.9	[c]	[c]
	United Kingdom	DNSIYC_2011	663	167.6	164.2	96.8	247.4	663	40.0	39.3	28.2	53.1
	United Kingdom	NDNS-RollingProgrammeYears1-3	107	187.9	182.3	129.1	268.0	107	38.6	37.4	29.0	53.8
3 to < 10 years	Finland	DIPP_2001_2009	381	244.5	240.8	169.4	332.2	381	41.8	41.6	31.6	52.7
	France	INCA2	239	214.7	205.2	117.7	329.4	239	34.3	32.9	24.7	47.7
	Germany	EsKiMo	426	280.5	271.6	181.3	397.5	426	36.7	36.2	26.7	48.7
	Germany	VELS	146	201.5	190.4	124.7	307.2	146	35.8	35.4	26.3	48.1
	Italy	INRAN_SCAI_2005_06	94	249.4	238.2	160.9	365.7	94	34.4	31.6	24.3	48.5
	Netherlands	VCPBasis_AVL2007_2009	231	247.7	240.7	151.3	370.8	231	28.9	28.9	18.8	41.1
	United Kingdom	NDNS-RollingProgrammeYears1-3	326	224.9	217.8	138.6	325.6	326	35.8	34.8	25.8	48.6
10 to < 18 years	Finland	NWSSP07_08	136	343.8	327.3	201.4	500.8	136	42.8	42.9	28.2	58.5
	France	INCA2	449	256.7	248.4	151.5	399.0	449	32.6	31.5	24.4	43.7
	Germany	EsKiMo	197	292.4	281.8	179.5	439.2	197	36.1	35.5	26.1	48.7
	Italy	INRAN_SCAI_2005_06	108	309.4	298.3	188.8	461.0	108	32.1	30.3	23.0	43.7
	Netherlands	VCPBasis_AVL2007_2009	566	298.4	283.6	167.9	473.3	566	28.0	27.4	17.5	40.2
	United Kingdom	NDNS-RollingProgrammeYears1-3	340	258.5	253.0	152.7	404.6	340	31.7	30.7	22.5	44.9
18 to < 65 years	Finland	FINDIET2012	585	401.7	391.4	226.5	602.0	585	43.9	43.2	30.9	59.7
	France	INCA2	936	316.6	305.4	175.9	486.5	936	36.4	35.1	25.3	51.1
	Ireland	NANS_2012	634	367.3	355.8	192.6	576.5	634	36.7	36.0	24.5	52.3
	Italy	INRAN_SCAI_2005_06	1068	356.8	347.0	213.9	529.2	1068	39.9	38.0	27.3	58.6
	Netherlands	VCPBasis_AVL2007_2009	1023	387.8	371.5	217.6	597.3	1023	34.9	33.5	22.0	50.9
	Sweden	Riksmaten 2010	623	439.1	424.9	211.0	703.6	623	44.9	43.1	30.2	65.0
	United Kingdom	NDNS-RollingProgrammeYears1-3	560	320.9	312.0	169.9	510.6	560	36.6	35.6	24.0	51.8

Age	Country	Survey	Intake expressed in mg/day					Intake expressed in mg/MJ				
			n [(a)]	Average	Median	P5	P95	n [(a)]	Average	Median	P5	P95
65 to < 75 years	Finland	FINDIET2012	210	360.1	350.6	202.3	544.0	210	44.6	44.2	30.1	61.5
	France	INCA2	111	312.0	309.2	175.2	465.0	111	36.2	35.4	26.7	47.5
	Ireland	NANS_2012	72	331.3	328.3	144.6	497.1	72	38.3	37.1	22.6	55.7
	Italy	INRAN_SCAI_2005_06	133	356.5	351.3	189.5	514.0	133	41.1	39.3	30.3	58.8
	Netherlands	VCPBasis_AVL2007_2009	91	341.7	336.0	214.3	488.0	91	37.8	37.0	25.8	53.1
	Sweden	Riksmaten 2010	127	406.9	378.5	230.8	639.8	127	47.5	44.7	36.5	67.0
	United Kingdom	NDNS-RollingProgrammeYears1-3	75	329.9	328.4	152.3	514.1	75	39.4	38.3	26.1	56.2
≥ 75 years	France	INCA2	40	284.8	278.8	(c)	(c)	40	37.0	35.4	(c)	(c)
	Ireland	NANS_2012	34	294.9	275.3	(c)	(c)	34	38.3	39.9	(c)	(c)
	Italy	INRAN_SCAI_2005_06	69	340.1	326.0	208.2	497.5	69	39.1	37.0	29.3	55.0
	Sweden	Riksmaten 2010	42	387.7	375.5	(c)	(c)	42	46.1	45.8	(c)	(c)
	United Kingdom	NDNS-RollingProgrammeYears1-3	56	264.3	241.1	(c)	(c)	56	36.7	36.9	(c)	(c)

y, years; DIPP, type 1 Diabetes Prediction and Prevention survey; DNSIYC, Diet and nutrition survey of infants and young children; DNFCS, Dutch National Food Consumption Survey; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale de Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia; FC_PREGNANTWOMEN, food consumption of pregnant women in Latvia; 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): Number of individuals in the population group.

(b): Excluding the contribution from breast milk.

(c): 5^{th} or 95^{th} percentile intakes calculated from less 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 will not be presented in the intake results.

Appendix D. Magnesium intake in females in different surveys according to age classes and country

Age	Country	Survey	Intake expressed in mg/day					Intake expressed in mg/MJ				
			n [a]	Average	Median	P5	P95	n [a]	Average	Median	P5	P95
< 1 year	Finland	DIPP_2001_2009	252	71.7 [b]	72.8 [b]	[b]	[b]	251	45.1 [b]	42.5 [b]	[b]	[b]
	Germany	VELS	75	95.0	94.1	55.3	141.4	75	32.7	32.7	21.0	42.8
	Italy	INRAN_SCAI_2005_06	7	89.1	105.0	[c]	[c]	7	28.9	35.0	[c]	[c]
	United Kingdom	DNSIYC_2011	670	107.5	103.2	52.5	175.7	670	34.8	34.5	20.9	49.6
1 to < 3 years	Finland	DIPP_2001_2009	255	153.0	151.2	85.0	227.7	255	44.9	44.5	30.0	60.5
	Germany	VELS	174	154.5	149.4	93.1	234.0	174	36.2	34.9	26.2	50.9
	Italy	INRAN_SCAI_2005_06	16	166.0	167.5	[c]	[c]	16	35.3	34.3	[c]	[c]
	United Kingdom	DNSIYC_2011	651	156.3	151.6	87.0	241.5	651	39.6	39.1	26.7	54.0
	United Kingdom	NDNS-RollingProgrammeYears1-3	78	173.9	166.6	99.1	278.3	78	38.0	37.6	26.1	51.4
3 to < 10 years	Finland	DIPP_2001_2009	369	225.7	221.8	150.0	310.6	369	42.9	42.2	33.0	55.0
	France	INCA2	243	199.0	196.6	128.4	285.6	243	35.9	34.4	25.9	51.1
	Germany	EsKiMo	409	259.2	250.9	158.3	385.5	409	38.3	37.6	27.1	50.4
	Germany	VELS	147	184.2	178.1	114.4	268.9	147	35.7	34.7	25.3	48.8
	Italy	INRAN_SCAI_2005_06	99	238.0	233.8	157.5	352.7	99	33.1	31.6	25.3	50.5
	Netherlands	VCPBasis_AVL2007_2009	216	224.9	217.2	138.0	341.0	216	27.8	27.5	17.8	40.2
	United Kingdom	NDNS-RollingProgrammeYears1-3	325	217.6	211.1	128.0	328.0	325	36.3	35.1	26.2	50.6
10 to < 18 years	Finland	NWSSP07_08	170	291.8	284.7	166.2	443.4	170	44.4	44.2	30.8	59.6
	France	INCA2	524	213.1	207.2	122.1	321.3	524	33.8	32.6	24.4	47.6
	Germany	EsKiMo	196	278.1	274.9	171.9	395.2	196	37.3	36.9	27.2	48.3
	Italy	INRAN_SCAI_2005_06	139	260.9	250.6	161.1	397.2	139	32.9	31.8	23.0	51.3
	Latvia	FC_PREGNANTWOMEN_2011 [d]	12	384.2	393.8	[c]	[c]	12	39.0	40.3	[c]	[c]
	Netherlands	VCPBasis_AVL2007_2009	576	252.7	249.7	153.8	370.5	576	28.9	28.5	18.0	41.3
	United Kingdom	NDNS-RollingProgrammeYears1-3	326	214.7	207.2	119.1	327.9	326	31.9	30.4	21.6	46.6
18 to < 65 years	Finland	FINDIET2012	710	333.8	321.6	191.7	503.1	710	47.2	45.4	31.0	66.5
	France	INCA2	1340	253.8	244.7	141.4	403.0	1340	39.6	37.5	27.4	58.5
	Ireland	NANS_2012	640	276.0	264.0	149.6	427.6	640	37.6	36.8	24.4	53.7
	Italy	INRAN_SCAI_2005_06	1245	311.1	302.6	184.8	452.4	1245	43.5	40.9	28.2	67.6
	Latvia	FC_PREGNANTWOMEN_2011 [d]	990	352.6	337.9	226.2	531.9	990	41.6	40.1	29.6	59.7
	Netherlands	VCPBasis_AVL2007_2009	1034	302.4	289.7	174.0	468.6	1034	37.0	35.6	22.6	56.8
	Sweden	Riksmaten 2010	807	356.9	335.2	192.5	603.5	807	51.1	44.8	29.6	71.5
	United Kingdom	NDNS-RollingProgrammeYears1-3	706	257.7	252.2	133.1	405.7	706	39.1	37.4	24.7	57.6

Age	Country	Survey	Intake expressed in mg/day					Intake expressed in mg/MJ				
			n [(a)]	Average	Median	P5	P95	n [(a)]	Average	Median	P5	P95
65 to < 75 years	Finland	FINDIET2012	203	303.9	299.2	181.7	457.2	203	49.8	49.0	33.7	68.5
	France	INCA2	153	241.3	239.3	142.2	348.4	153	38.9	37.9	28.5	52.3
	Ireland	NANS_2012	77	296.8	287.4	162.1	444.5	77	43.8	43.1	27.3	60.1
	Italy	INRAN_SCAI_2005_06	157	298.2	292.7	181.1	433.9	157	44.1	41.6	30.4	65.2
	Netherlands	VCPBasis_AVL2007_2009	82	307.6	291.0	186.9	441.4	82	42.5	40.3	27.6	65.9
	Sweden	Riksmaten 2010	168	342.5	329.5	206.4	527.9	168	49.3	48.3	36.5	62.4
	United Kingdom	NDNS-RollingProgrammeYears1-3	91	263.4	253.7	141.2	401.2	91	43.9	41.7	28.2	73.8
≥ 75 years	France	INCA2	44	231.7	232.0	[(c)]	[(c)]	44	39.0	37.4	[(c)]	[(c)]
	Ireland	NANS_2012	43	279.9	288.1	[(c)]	[(c)]	43	44.6	41.7	[(c)]	[(c)]
	Italy	INRAN_SCAI_2005_06	159	282.1	274.2	183.8	422.9	159	42.9	40.1	29.6	68.5
	Sweden	Riksmaten 2010	30	346.5	333.5	[(c)]	[(c)]	30	51.2	47.4	[(c)]	[(c)]
	United Kingdom	NDNS-RollingProgrammeYears1-3	83	267.2	253.8	162.6	416.9	83	44.0	42.0	27.7	65.1

y, years; DIPP, type 1 Diabetes Prediction and Prevention survey; DNSIYC, Diet and nutrition survey of infants and young children; DNFCS, Dutch National Food Consumption Survey; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale de Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia; FC_PREGNANTWOMEN, food consumption of pregnant women in Latvia; 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): Number of individuals in the population group.

(b): Excluding the contribution from breast milk.

(c): 5^{th} or 95^{th} percentile intakes calculated from less 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 will not be presented in the intake results.

(d): Pregnant women only.

Appendix E. Minimum and maximum % contribution of different FoodEx2 level1 food groups to magnesium intake in males

Food groups	< 1 y	1 to < 3 y	3 to < 10 y	10 to < 18 y	18 to < 65 y	65 to < 75 y	≥ 75 y
Additives, flavours, baking and processing aids	< 0.1	< 0.1–0.1	0–0.2	0–0.3	0–0.1	0 [(a)]	0
Alcoholic beverages	< 0.1	< 0.1	< 0.1	< 0.1–1.7	3.7–10.5	3–8.5	2.8–6.8
Animal and vegetable fats and oils	< 0.1–0.3	< 0.1–0.4	0.1–0.6	0.1–0.6	0.1–0.5	0.1–0.5	0.1–0.5
Coffee, cocoa, tea and infusions	< 0.1–0.4	< 0.1–3.9	1.3–10.3	2–8.2	5.6–23.4	8–22.6	7.9–19.4
Composite dishes	0.1–3.5	0.3–5.9	0.1–5.9	0.3–8.6	0.5–8.3	0.6–7.6	0.4–7.6
Eggs and egg products	< 0.1–0.2	0.2–0.6	0.2–0.9	0.2–0.9	0.2–0.9	0.2–0.9	0.3–0.8
Fish, seafood, amphibians, reptiles and invertebrates	< 0.1–0.4	0.2–3.1	0.3–3.1	0.3–3	0.7–2.7	0.9–3.7	2.2–4.1
Food products for young population	20.6–46.1	2.6–11	0.2–0.7	< 0.1–0.1	< 0.1	-	-
Fruit and fruit products	3.4–14.3	8.9–10.2	3.8–6.8	2.7–4.9	2.6–5.2	3.9–7.6	4.8–7
Fruit and vegetable juices and nectars	0.3–1.7	0.8–3.9	2.1–5.7	1.9–5.3	0.7–3.3	0.3–2.6	0.5–2.1
Grains and grain-based products	4.6–19	24–29.9	22.8–39.5	26.5–40.8	21.8–33.6	21.2–36.9	21.5–39.9
Human milk	< 0.1–16.1	< 0.1–0.6	-	-	-	-	-
Legumes, nuts, oilseeds and spices	0.7–2.4	1.4–3.8	1.6–5.6	2–5.1	2.3–5.7	2.4–6.5	1.6–3.8
Meat and meat products	0.4–3.8	3.1–6.5	4.8–9.1	5.6–11.2	5.9–11	5.7–10.1	5–9.3
Milk and dairy products	8.5–15.5	21.5–27.6	14.7–30.1	11.2–25.3	7.4–15.1	6.7–14.4	9.3–12
Products for non-standard diets, food imitates and food supplements or fortifying agents	0.1–0.6	0–0.6	< 0.1–1	0.1–0.8	< 0.1–2.2	< 0.1–0.5	< 0.1–1.5
Seasoning, sauces and condiments	0.1–0.4	0.6–2.4	0.2–2.1	0.2–2.3	0.2–2.2	0.2–2.3	0.2–2.6
Starchy roots or tubers and products thereof, sugar plants	0.6–11.9	2.9–10.4	4.4–9.1	5.3–11	3.6–9.7	3.7–11.1	4.8–10.7
Sugar, confectionery and water-based sweet desserts	< 0.1–0.3	0.2–4.1	2.1–5.7	2.3–6	0.8–2.4	0.3–1.8	0.3–2.1
Vegetables and vegetable products	1.1–8.7	2.5–5.9	3–8.4	2.9–10.7	2.2–11.2	2.4–12.6	2.9–10.7
Water and water-based beverages	1.3–17.5	2.5–6.9	1.9–7	2.6–7.9	1.8–6.2	1.2–5.6	1.2–5.9

y, years

(a): '-' 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 % contribution of different FoodEx2 level1 food groups to magnesium intake in females

Food groups	< 1 y	1 to < 3 y	3 to < 10 y	10 to < 18 y	18 to < 65 y	65 to < 75 y	≥ 75 y
Additives, flavours, baking and processing aids	< 0.1	0–0.1	0–0.2	0–0.2	0–0.1	0 [(a)]	0
Alcoholic beverages	< 0.1	< 0.1	< 0.1	< 0.1–0.3	< 0.1–3.9	0.6–3.3	1.2–1.9
Animal and vegetable fats and oils	< 0.1–0.3	0.1–0.4	0.1–0.6	0.1–0.6	0.1–0.5	0.1–0.5	0.1–0.5
Coffee, cocoa, tea and infusions	< 0.1–0.4	0.1–5	0.4–11.2	2.7–8.2	5.3–23.4	11.5–22.1	9.9–22
Composite dishes	< 0.1–1.9	0.3–5.7	0.1–5.9	0.4–9	0.5–8.6	0.3–9.1	0.5–7.8
Eggs and egg products	< 0.1–0.2	0.2–0.6	0.3–1.3	0.1–1	0.3–0.8	0.3–0.8	0.3–0.9
Fish, seafood, amphibians, reptiles and invertebrates	0–0.4	0.1–3.5	0.2–2.5	0.3–4	0.7–2.8	0.8–3.7	1.7–3.4
Food products for young population	20.1–51.9	2.3–11.1	< 0.1–0.4	< 0.1–0.1	< 0.1	-	< 0.1
Fruit and fruit products	7.5–12.7	6.4–9.5	4.1–7.4	3.5–10.4	4.1–7.6	5.8–9.5	5.8–9.3
Fruit and vegetable juices and nectars	0.1–1.3	0.8–3.8	2.1–5.1	1.8–5.3	0.8–2.8	0.8–2.3	0.8–2.1
Grains and grain-based products	12.9–18.9	23.4–34	21.7–38.6	25.6–38.9	20.2–35.4	18.9–35.5	17–38.5
Human milk	< 0.1–6.8	< 0.1–0.5	-	-	-	-	-
Legumes, nuts, oilseeds and spices	0.6–3	1.3–4.1	1.9–4.7	2.2–4.5	2.5–6.5	2.5–5.1	2.2–4.9
Meat and meat products	0.7–3.2	3.1–5.3	4.3–9.5	5.3–10.1	5.3–9	4.4–8.8	4–8.4
Milk and dairy products	4.6–21.8	20.4–31.2	14.7–30.3	10.1–22	8.5–15.7	8.4–14.5	10.2–13.1
Products for non-standard diets, food imitates and food supplements or fortifying agents	< 0.1–0.4	< 0.1–0.6	0–1.3	< 0.1–1	0.1–3.8	0.2–0.9	< 0.1–1.8
Seasoning, sauces and condiments	0.2–0.5	0.2–0.8	0.4–2.1	0.1–2.4	0.2–2.4	0.2–3.1	0.3–2.9
Starchy roots or tubers and products thereof, sugar plants	2.4–11.5	4.8–9.1	4.9–9.8	5–11	3.5–9.9	4.2–8.3	4–7.6
Sugar, confectionery and water-based sweet desserts	< 0.1–1.2	0.2–3.7	2.1–6.2	2.6–6.1	0.8–7.6	0.4–2	0.4–2.3
Vegetables and vegetable products	3.3–9.4	2.2–6.6	3.3–8.5	3.4–11	3.4–12.1	3.3–13.1	3.9–12.7
Water and water-based beverages	1.5–10.8	2.5–7.7	1.9–7	1.6–7.9	1.3–7.5	1.7–7	1.7–7.5

y, years

(a): '-' 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.

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Reference	Number of subjects	Characteristics	Experimental period	Data collection for balance	Magnesium intake (mg/day unless otherwise indicated) mean ± standard error	Balance (mg/day), mean ± standard error	Comments
Andersson et al. (1983)	6 subjects, 1 woman 5 men	25–55 years	3 consecutive 24 day-periods, 12 days of adaptation	Last 12 days of each period, urine and faecal losses considered	A: 224 ± 29/236 ± 29 [a, b] B: 308 ± 19 [a] C: 404 ± 19 [a] duplicate diet analysis	-9.7 ± 26.7/-19.4 ± 19.4 [a, b] -34.0 ± 19.4/-26.7 ± 26.7 [a] -19.4 ± 24.3/-14.6 ± 12.2 [a]	Subjects housed in metabolic ward; periods differed by the type of bread providing 3.3 (A), 10.9 (B), or 18.7 g (C) of non-starch polysaccharides/day and about 2.1–2.3 mmol phytate/day, mean total fibre intake 16.1 (A), 23.7 (B), or 31.5 (C) g/day
Hunt and Johnson (2006)	150 women, 93 men	19–77 years 19–65 years, mostly white	At least 12 days of adaptation (median 31 days), at least 18 days including balance	6–12 days, urine and faecal losses considered	Dietary intake ≈ 80–600, additional supplemental intake of 50–171 in 4 studies, another 6 studies had 50 % of data points with supplemental intake, duplicate diet analysis	165 mg/day (null balance)	Pooled analysis of 27 studies (664 data points) carried out from 1976-2001 in a metabolic ward under strict supervision of subjects; studies with supplements used Mg gluconate in addition to the diet, except for one study that used Mg citrate dibasic
Kelsay and Prather (1983)	12 men	34–58 years, 61–97 kg	28 days	Last 14 days, urine and faecal losses considered	A: 300 ± 11/308 ± 10 [b] B: 375 ± 10/350 ± 7 [b] C: 346 ± 10/326 ± 10 [b], duplicate diet analysis	-20 ± 14/20 ± 14 [b] 28 ± 10/-10 ± 13 [b] 21 ± 5/18 ± 13 [b]	Subjects housed in metabolic ward during the week, but no supervision on weekends; diets were low fibre with spinach (A), higher fibre with spinach (B) and higher fibre without spinach (C); when pooling data for weeks 3 and 4, diet had no effect on Mg balance
Kelsay et al. (1979)	12 men	37–58 years	26 days, 21 days of adaptation	Last 7 days	356 ± 10 (low fibre diet) 322 ± 12 (high fibre diet), duplicate diet analysis	28 ± 17 (low fibre diet) -32 ± 10 (high fibre diet), $P < 0.01$	High fibre diet had ≈ 24 g/day from fruits and vegetables, low fibre diet had ≈ 5 g/day

Reference	Number of subjects	Characteristics	Experimental period	Data collection for balance	Magnesium intake (mg/day unless otherwise indicated) mean ± standard error	Balance (mg/day), mean ± standard error	Comments
Lakshmanan et al. (1984)	18 women, 16 men	20–53 years	1 year	1 week per season, 4 collection periods in total, urine and faecal losses considered	234 (women) 323 (men) 0.14 mg/kcal per day (both sexes), 4.3 mg/kg body weight per day (men) 4.15 mg/kg body weight per day (women), duplicate diet analysis	-25 mg/day (women) -32 mg/day (men)	Self-selected diets, free-living subjects Effect of magnesium, calcium, phosphorus, protein, and fibre intakes on urinary and faecal excretion and balance tested separately in men and women, with no consistent influence noted
Mahalko et al. (1983)	10 men	19–64 years, 76 ± 11 kg	28 days, 16 days of adaptation	Last 12 days, urine and faecal losses considered	229 ± 24 [(a)] 258 ± 24 [(a)] duplicate diet analysis	13 ± 30 (65 g protein/day) [(a)] 17 ± 36 (94 g protein/day) [(a)]	Subjects housed in metabolic ward; the study was done at USDA but not included in the meta-analysis of Hunt and Johnson (2006)
Nielsen and Milne (2004)	21 post-menopausal women in groups of 9 or 12	50–76 years 65.1 ± 9.5 kg	90 days, 12 days of adaptation	Last 36 days, urine and faecal losses considered	310 (low Cu, low Zn) 313 (low Cu, high Zn) 328 (high Cu, low Zn) 334 (high Cu, high Zn), 180 mg/day as supple-mental Mg gluconate, duplicate diet analysis	23.1 1.0 26.0 5.6	Subjects housed in metabolic ward, 4 diets combining high (3 mg) and low (1 mg) copper with high (53 mg) and low (3 mg) zinc intakes daily, high dietary zinc significantly decreased magnesium balance. the study was done at USDA but not included in the meta-analysis of Hunt and Johnson (2006)
Schwartz et al. (1984)	8 men	48–62 years, 55–94 kg	100–130 days, at least 22 days of adaptation	Collection of urine and faeces for 5-6 days after each test day and throughout study	331–447 mg/day, 50 mg/day as Mg oxide	All balances were positive (from 6 to 48 mg/day)	Subjects housed in metabolic ward, study focused on magnesium absorption from 4 freeze-dried leafy vegetables incorporated into muffins
Schwartz et al. (1978)	4 men	48–75 years, 67–83 kg	149 days, at least 35 days of adaptation	Days 66–76 and 109–119, urine and faecal losses considered	243–321, including 50 mg/day of supplemental Mg oxide	Individual balances from -44 to + 20 (4 positive or null, 4 negative), no statistics	Subjects housed in metabolic ward, objective of the study was magnesium absorption

Reference	Number of subjects	Characteristics	Experimental period	Data collection for balance	Magnesium intake (mg/day unless otherwise indicated) mean ± standard error	Balance (mg/day), mean ± standard error	Comments
Spencer et al. (1994)	5 men	38–75 years, osteoporosis or psychoneurosis, otherwise healthy	Unclear, but at least 28 days of adaptation	Unclear if more than 6 days, urine and faecal losses considered	240 ± 24 (normal Ca) 264 ± 26 (low Ca), duplicate diet analysis; periods with supplemental Mg not considered here	-26 ± 14 -23 ± 21	Subjects housed in metabolic ward
Wisker et al. (1991)	12 women	22–28 years	3 separate experiments each for 22 days with 14 days of adaptation	Last 6 days, urine and faecal losses considered	252 ± 9 245 ± 8 243 ± 9, duplicate diet analysis	7.3 ± 4.9 4.9 ± 2.4 -12 ± 4.9	Comparison of low fibre (22.5 g/day and 1.1 g protein/kg body weight per day), high fibre/high protein (38.6 g/day and 1.1 g protein/kg body weight per day) and high fibre/adequate protein (38.6 g/day and 0.8 g protein/kg body weight per day)
Schwartz et al. (1986)	7 men	22–32 years	1–3 weeks	7 day periods	657–719 Duplicate diet analysis	Balance close to zero, conclusions more on experimental requirements than on balances	The objective was to determine apparent magnesium absorption in the presence of bran.
van Dokkum et al. (1983)	10–12 men	23 ± 2 years, 67 ± 6 kg	16 days	20 days	312–389 Duplicate diet analysis	From 3 ± 15 to 16 ± 23 [(a)]	The objective was to determine the influence of fat and linoleic acid on absorption (no impact on magnesium balance); no negative balance with intakes of 300–400 mg/day
Nishimuta et al. (2006)	10 men, 80 women	18–28 years	Not reported	8–12 days	154–334 mg/day, 2.4–6.4 mg/kg body weight per day	Null balance at 4.1 mg/kg body weight per day (regression, $r^2 = 0.141$)	Sodium intake can influence magnesium absorption and balance

Studies not included in this table because of adaptation periods below 12 days: Slavin and Marlett (1980); Greger and Baier (1983); McDonald and Margen (1979) and because of short duration of adaptation and balance periods: Jones et al. (1967).
(a): mean value ± SD.
(b): values for 3rd/4th period of 6 or 7 days.

Appendix H. Balance studies in children

Reference	Number of subjects	Age (years)	Experimental period	Data collection for balance	Magnesium intake (mg/day unless otherwise specified), mean ± standard deviation	Balance (mg/day unless otherwise specified), mean ± standard deviation	Comments
Abrams et al. (1997)	12 boys	10.9 ± 1.1	10 days	Not reported	261 ± 40 (6.4 ± 1.2 mg/ kg per day) (range 194–321)	15.6 ± 36.8	11 out of 25 subjects were in negative balance
	13 girls	12.3 ± 1.6				-0.9 ± 41.2	
Andon et al. (1996)	13 girls	11.3 ± 0.5	14 days	Samples from the 2nd week used to calculate magnesium balance	Basal diet: 193 ± 39	19 ± 25	Magnesium balance study conducted 15 weeks after the start of supplementation trial. All balances positive if intake > 5 mg/kg per day. Calcium intake has no effect on magnesium balance
	13 girls	11.3 ± 0.7			Basal diet plus calcium supplement: 199 ± 45	22 ± 15	
Greger et al. (1978)	14 girls	12.5–14.5	30 days in total. 9 days equilibration, 21 days for experimental diets	Meal and urine samples on a daily basis, faecal samples each 6 days period. Excreta not collected during the first 3 days of adjustment period	Baseline: 196 ± 17	-5.0 ± 26.8	Magnesium concentration in the metabolic diet was insufficient for most of the girls to maintain positive balances
					$S_0Z_{13.4}$: 190 ± 26	-5.6 ± 16.5	
					$S_{30}Z_{7.4}$: 195 ± 29	-6.8 ± 10.4	
					$S_{30}Z_{13.4}$: 195 ± 29	-1.8 ± 2.2	
Schofield and Morrell (1960)	35 children	7–9	7 weeks	Not reported	From 135.6 ± 2.5 to 231.7 ± 12.7 in three different groups	All balances positive (from 10.4 ± 6.4 to 16.2 ± 8.6)	Low protein diets (17–20 g/day)

Reference	Number of subjects	Age (years)	Experimental period	Data collection for balance	Magnesium intake (mg/day unless otherwise specified), mean ± standard deviation	Balance (mg/day unless otherwise specified), mean ± standard deviation	Comments
Schwartz et al. (1973)	12 boys	13–14	30 days	10 days, 5 first days of each 15-day experimental period regarded as adjustment period and excreta not collected	LPLM: 4.3 ± 0.21[a] LPHM: 14.5 ± 0.61[a] HPLM: 4.1 ± 0.16[a] HPHM: 13.1 ± 0.5 (a)	-0.62 ± 0.07 (a) 0.88 ± 0.48 (a) 0.19 ± 0.08 (a) 1.25 ± 0.26 (a)	Diets with either low (43 g/day) or high (93 g/day) amount of protein or magnesium Magnesium retention was significantly increased by consumption of the high protein diet
Sojka et al. (1997)	5 girls	12–14	2 × 21 days with 5 week interval in-between	14 days	800 mg Ca: 305 ± 30 1 800 mg Ca: 286 ± 9	13 ± 35 (1/5 negative) -34 ± 48 (4/5 negative)	

Ca, calcium; S_0,$Z_{13.4}$, 13.4 mg zinc and no soy; S_{30},$Z_{13.4}$, 13.4 mg zinc and 30 % of meat replaced by soy; S_{30},$Z_{7.4}$, 7.4 mg zinc and 30 % of meat replaced by soy; LPLM, low protein and low magnesium diet; LPHM, Low protein and high magnesium diet; HPLM, high protein and low magnesium diet; HPHM, high protein high magnesium diet
(a): mg/kg

1905 **Appendix I. Characteristics of prospective cohort studies on magnesium intake and risk of type 2 diabetes (adapted from Dong et al. (2011))**

Reference	Number of subjects, place of study (number of cases)	Age (years)	Duration (years)	Median magnesium intake (highest vs. lowest, mg/day)	Adjusted RR unless otherwise specified (95 % CI)	Adjustment for potential confounders
Hodge et al. (2004)	34 641 adults Australia (365)	40–69	4	773 vs. 230 [(a)]	0.55 (0.32–0.97)	Age, BMI, sex, education, country of birth, family history, WHR, weight change, physical activity, and intakes of total energy and alcohol
Hopping et al. (2010)	75 512 adults, USA (8 587)	45–75	14	370 vs. 260 [(b)]	Men: 0.77 (0.70–0.85); women: 0.84 (0.76–0.93)	BMI, physical activity, education, ethnicity, and total energy intake
Kao et al. (1999)	11 896 adults, USA (1 106)	45–64	6	361 vs. 154 [(c)]	White: 1.08 (0.78–1.49); black: 0.98 (0.57–1.72)	Age, BMI, sex, education, family history, WHR, sports index, diuretic use, and intakes of alcohol, calcium, and potassium
Kim et al. (2010)	4 497 adults, USA (330)	18–30	20	403 vs. 200 [(d)]	0.53 (0.32–0.86)	Age, BMI, sex, ethnicity, study centre, education, smoking, physical activity, family history, systolic blood pressure, and intakes of total energy, alcohol, saturated fat, and crude fibre
Kirii et al. (2010)	17 592 adults, Japan (459)	40–65	5	303 vs. 158	0.64 (0.44–0.94)	Age, BMI, family history, smoking, hours of walking and sports participation, and intakes of total energy, alcohol, green tea, and coffee
Lopez-Ridaura et al. (2004)	42 872 men, USA (1 333)	40–75	11	457 vs. 270	0.72 (0.58–0.89)	Age, BMI, family history, hypertension, hypercholesterolemia, smoking, physical activity, and intakes of total energy, alcohol, glycaemic load, PUFA, TFA, processed meat, and cereal fibre
Lopez-Ridaura et al. (2004)	85 060 women, U.S. (4 085)	30–55	17	373 vs. 222	0.73 (0.65–0.82)	Age, BMI, family history, hypertension, hypercholesterolemia, smoking, physical activity, and intakes of total energy, alcohol, glycaemic load, PUFA, TFA, processed meat, and cereal fibre

Reference	Number of subjects, place of study (number of cases)	Age (years)	Duration (years)	Median magnesium intake (highest vs. lowest, mg/day)	Adjusted RR unless otherwise specified (95 % CI)	Adjustment for potential confounders
Meyer et al. (2000)	35 988, USA (1 141)	55–69	6	362 vs. 220	0.67 (0.55–0.82)	Age, BMI, education, smoking, WHR, physical activity, intakes of total energy, alcohol, whole grains, and cereal fibre
Nanri et al. (2010)	59 791 adults, Japan (1 114)	45–75	5	348 vs. 213	Men: 0.86 (0.63–1.16); women 0.92 (0.66–1.28)	Age, BMI, study area, smoking, family history, leisure time physical activity, hypertension, and intakes of total energy, alcohol, coffee, and calcium
Schulze et al. (2007)	25 067 adults, Germany (844)	35–65	7	377 vs. 268	0.99 (0.78–1.26)	Age, BMI, sex, education, sports activity, cycling, occupational activity, smoking, WC, and intakes of total energy, alcohol, carbohydrate, PUFA-to-SFA ratio, MUFA-to-SFA ratio, and cereal fibre
Song et al. (2004)	38 025 women, USA (918)	≥ 45	6	399 vs. 252	0.89 (0.71–1.10)	Age, BMI, family history, smoking, physical activity, and intakes of total energy and alcohol
van Dam et al. (2006)	41 186 women, USA (1 964)	21–69	6	244 vs. 115	0.65 (0.54–0.78)	Age, BMI, education, family history, smoking, physical activity, and intakes of total energy, alcohol, coffee, sugar-sweetened drinks, red meat, processed meat, and calcium
Villegas et al. (2009)	64 191 women, China (2 270)	40–70	6.9	318 vs. 214	0.80 (0.68–0.93)	Age, BMI, WHR, smoking, physical activity, income, education, occupation, hypertension, and intakes of total energy and alcohol
Weng et al. (2012)	1 604 adults, Taiwan (141)	38–63	4.6	406 vs. 212	2.61 (1.42–4.79) [(e)]	Age, sex, age-sex interaction, caloric intake, residential area, family history of diabetes, BMI, central obesity, education, smoking habits, current drinking habits, frequency of activity, hypertension, hypercholesterolaemia, hypertriglyceridaemia and low HDL-cholesterol

BMI, body mass index; CI, confidence interval; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; RR, relative risk; SFA, saturated fatty acid; TFA, trans fatty acid; WC, waist circumference; vs., versus; WHR, waist-to-hip ratio.
(a): The primary paper reports median magnesium intake (g/day) across glycaemic index quartiles.
(b): The primary paper reports median magnesium intake expressed as g/4 184 KJ/day.
(c): The primary paper reports mean magnesium intake expressed as mg/4.2 KJ.
(d): The primary paper reports median magnesium intake expressed as mg/1 000 kcal.
(e): Hazard ratio using the highest quintile as the reference category.

1913 **ABBREVIATIONS**

Afssa	Agence française de sécurité sanitaire des aliments
AI	Adequate Intake
AR	Average Requirement
BMI	body mass index
COMA	Committee on Medical Aspects of Food Policy
CVD	cardiovascular disease
Da	Dalton
D–A–CH	Deutschland–Austria–Confoederatio Helvetica
DH	UK Department of Health
DIPP	Type 1 Diabetes Prediction and Prevention survey
DNFCS	Dutch National Food Consumption Survey
DNSIYC	Diet and Nutrition Survey of Infants and Young Children
DRV	Dietary Reference Value
EAR	Estimated Average Requirement
EsKiMo	Ernährungsstudie als KIGGS-Modul
EU	European Union
FAO	Food and Agriculture Organization
INCA	Etude Individuelle Nationale des Consommations Alimentaires
INRAN-SCAI	Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia
IOM	U.S. Institute of Medicine of the National Academy of Sciences
LTI	Lower Threshold Intake
NANS	National Adult Nutrition Survey
NDNS	National Diet and Nutrition Survey
NNR	Nordic Nutrition Recommendations
NOAEL	No Observed Adverse Effect Level
NWSSP	Nutrition and Wellbeing of Secondary School Pupils

PRI	Population Reference Intake
RI	Recommended Intake
RDA	Recommended Dietary Allowance
RR	relative risk
SCF	Scientific Committee for Food
UL	Tolerable Upper Intake Level
UNU	United Nations University
VELS	Verzehrsstudie zur Ermittlung der Lebensmittelaufnahme von Säuglingen und Kleinkindern für die Abschätzung eines akuten Toxizitätsrisikos durch Rückstände von Pflanzenschutzmitteln
WHO	World Health Organization

1914