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Dietary Reference Values for potassium

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)

Abstract

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) derives Dietary Reference Values (DRVs) for potassium. The Panel decided to set DRVs on the basis of the relationships between potassium intake and blood pressure and stroke. The Panel considered that randomised controlled studies and an observational cohort study carried out in a European adult population provide evidence that a potassium intake of 3,500 mg (90 mmol)/day has beneficial effects on blood pressure in adults. Furthermore, there is consistent evidence from observational cohort studies that potassium intakes below 3,500 mg/day are associated with a higher risk of stroke. Available data could not be used to determine the average requirement of potassium but could be used as a basis for deriving an adequate intake (AI). A potassium intake of 3,500 mg/day was considered adequate for the adult population and an AI of 3,500 mg/day for adult men and women was proposed. For infants and children, the AIs were extrapolated from the AI for adults by isometric scaling and including a growth factor. An AI of 750 mg (19 mmol)/day was set for infants aged 7-11 months. For children, AIs from 800 mg (20 mmol)/day (1 to 3 years old) to 3,500 mg/day (15 to 17 years old) were set. Considering that the daily accretion rate of potassium in fetal and maternal tissues can be met by the adaptive changes which maintain potassium homeostasis during pregnancy, the AI set for adults applies to pregnant women. For lactating women, the amount of potassium needed to compensate for the losses of potassium through breast milk was estimated and an AI of 4,000 mg (102 mmol)/day was proposed.

Keywords: potassium, 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 (NDA) was asked to deliver a Scientific Opinion on Dietary Reference Values (DRVs) for the European population, including potassium.

Potassium is an essential mineral in the human diet. It is the predominant osmotically active element inside cells. It plays a major role in the distribution of fluids inside and outside cells, assists in the regulation of the acid-base balance, and contributes to establishing a membrane potential which supports electrical activity in nerve fibres and muscle cells. Also, potassium has a role in cell metabolism, participating in energy transduction, hormone secretion and the regulation of protein and glycogen synthesis.

Potassium is present in all natural foods, including starchy roots or tubers and vegetables, fruits, whole grains, dairy products and coffee. Based on the data from 13 dietary surveys in nine countries of the European Union, average potassium intakes ranged between 821 and 1,535 mg (21 and 39 mmol)/day in infants (< 1 year), between 1,516 and 2,005 mg (39 and 51 mmol)/day in children aged 1 to < 3 years, between 1,668 and 2,750 mg (43 and 70 mmol)/day in children aged 3 to < 10 years, between 2,093 and 3,712 mg (54 and 95 mmol)/day in children aged 10 to < 18 years, and between 2,463 and 3,991 mg (63 and 102 mmol)/day in adults (≥ 18 years).

Potassium deficiency, presenting as hypokalaemia, is defined as a serum potassium concentration lower than 3.5 mmol/L and may be caused by increased potassium losses (e.g. via diarrhoea, vomiting or excessive renal losses) or intracellular shift of potassium (e.g. during alkalosis). Hypokalaemia resulting from insufficient dietary intake is rare and may be associated with severe hypocaloric diets or occur during recovery from malnutrition.

About 90% of dietary potassium is absorbed, mainly in the small intestine. Body potassium content is regulated by the balance between dietary intake and renal excretion. Urine is the major route of potassium excretion, while the remaining part is eliminated in the faeces and, to a lesser extent, in sweat. Most of body potassium is located in muscle, with lower amounts present in bone, liver, skin and red blood cells.

Urinary potassium excretion, based on 24-hour urine collection, is regarded as a reliable biomarker of dietary intake in adults on a population basis. Because of tight homeostatic mechanisms, plasma potassium concentrations and total body potassium content are only minimally affected by variations in dietary potassium intake. The Panel therefore considered that there is no suitable biomarker of potassium status which can be used for setting DRVs for potassium in the general population.

The level of potassium intake has been reported to be associated with several health outcomes, particularly cardiovascular endpoints. Overall, the Panel considered that randomised controlled studies and an observational cohort study carried out in a European adult population provide evidence that a potassium intake of 3,500 mg (90 mmol)/day has beneficial effects on blood pressure in adults. Furthermore, there is consistent evidence from observational cohort studies that potassium intakes below 3,500 mg (90 mmol)/day are associated with a higher risk of stroke. The estimates of the association between potassium intake and coronary heart disease are unclear and inconsistent. Evidence in relation to diabetes mellitus type 2, kidney stones and bone health were also reviewed but the available data could not be used to derive DRVs for potassium.

The Panel decided to set DRVs for potassium on the basis of the relationship between potassium intake and blood pressure and stroke. Currently, available data cannot be used to determine the average requirement of potassium but can be used as a basis for deriving an adequate intake (AI). A potassium intake of 3,500 mg (90 mmol)/day can be considered adequate for the adult population and an AI of 3,500 mg (90 mmol)/day for adult men and women is proposed.

No data are available on which to base an average potassium requirement for infants and children. The Panel derived AIs extrapolated from the AI for adults, taking into account differences in reference body weight (isometric scaling) and including a growth factor to take into account requirements for growth. The AIs set for infants aged 7-11 months is 750 mg (19 mmol)/day. For children, AIs range from 800 mg (20 mmol)/day (1 to 3 years old) to 3,500 mg (90 mmol)/day (15 to 17 years old).

The Panel considered that the requirement for the daily accretion rate of potassium in fetal and maternal tissues can be met by the adaptive changes which maintain potassium homeostasis during pregnancy. The AI for pregnant women is set at 3,500 mg (90 mmol)/day, the same as for non-pregnant women.

Considering evidence which indicates that total body potassium content decreases in lactating women, a conservative approach was taken and the amount of potassium needed to compensate for the losses of potassium through breast milk was added to the AI for adult. Thus, an AI of 4,000 mg (102 mmol)/day is proposed for 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.[1] The report provided Reference Intakes for energy, certain macronutrients and micronutrients, but it did not include certain substances of physiological importance, for example dietary fibre.

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

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

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

TERMS OF REFERENCE AS PROVIDED BY THE EUROPEAN COMMISSION

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

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

- Carbohydrates, including sugars;
- Fats, including saturated fatty acids, polyunsaturated fatty acids and monounsaturated fatty acids, *trans* fatty acids;

[1] Scientific Committee for Food, 1993. Nutrient and energy intakes for the European Community. Reports of the Scientific Committee for Food, 31st series. Food – Science and Technique, European Commission, Luxembourg, 248 pp.

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

- 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) adopted an opinion on nutrient and energy intakes for the European Community. For potassium, the SCF proposed a Population Reference Intake (PRI) of 3,100 mg (80 mmol)/day for adults, including pregnancy and lactation, and a Lowest Threshold Intake of 1,600 mg (40 mmol)/day, which was accepted as the intake needed to avoid low plasma potassium concentrations (SCF, 1993).

2. Definition/category

2.1. Chemistry

Potassium (K) is an abundant and highly reactive alkali metal which makes up 2.4 mass % of the earth's crust. It has an atomic mass of 39.1 Da. Potassium is present in only one oxidation state (+ 1). It is a powerful reducing agent that is easily oxidised. Because of its high reactivity, potassium is not found free in nature but only as salts. Potassium compounds have good water solubility.

Naturally occurring potassium is composed of three isotopes, namely the stable isotopes ^{39}K (natural abundance 93.3%) and ^{41}K (6.7%), and the radioactive isotope ^{40}K (0.01%), which has a very long half-life (1.251×10^9 years). The latter is responsible for most of the naturally occurring radioactivity in the body (Kee et al., 2010; Crook, 2012).

2.2. Function of potassium

2.2.1. Biochemical functions

Potassium is an essential mineral in the human diet. Potassium is the predominant osmotically active element inside cells. Together with sodium and chloride, which are characteristic of the extracellular fluid, potassium contributes to osmolarity and plays a major role in the distribution of fluids inside and outside cells. In addition, potassium participates in the regulation of the acid-base balance. Differences in potassium and sodium concentrations across cell membranes are maintained by the specific permeability of membranes to each of these ions and by Na^+/K^+-ATPase activity, which pumps sodium out of and potassium into the cells (Bailey et al., 2014; Gumz et al., 2015). The enzyme Na^+/K^+-ATPase plays an important role in the strict homeostatic control of plasma potassium concentrations. As a result, the intracellular potassium concentration is about 30 times higher than that of plasma and interstitial fluid. This concentration gradient (largely responsible for driving the membrane potential) is important for the transmission of electrical activity in nerve fibres and muscle cells. Small changes in the ratio of extracellular to intracellular potassium concentration have large effects on neural transmission, muscle contraction, and vascular tone (Bailey et al., 2014; Gumz et al., 2015). Potassium transport across the membranes of the endothelial and vascular smooth muscle cells has important effects on their contractile state, which can, in turn, influence endothelial function, blood flow and blood pressure (Haddy et al., 2006). The concentration of potassium in cells of the collecting duct system of the kidney is important for the excretion of sodium. Maintenance of the trans-membrane gradient is the key element for electrolytes and fluid homeostasis, a critical factor in blood pressure regulation (Bailey et al., 2014; Gumz et al., 2015).

Passive transport of potassium occurs via intracellular and paracellular pathways. The intracellular transport mechanism involves potassium channels. Channels have "gates" which open or close in response to specific stimuli, such as voltage, ATP, ionic calcium concentration, hormones and neurotransmitters. Various stimuli sometimes act together on a channel. Potassium channels exhibit great diversity, and different types of potassium channels have been implicated in functions such as salivary secretion, bile and gastric acid secretion, protein digestion and absorption, insulin secretion, carbohydrate digestion and absorption, and taste transduction. There are four main groups of potassium channels: voltage-gated (Kv) channels; calcium-activated (KCa) channels, covering big conductance (BK), intermediate conductance (IK), and small conductance (SK) channels; inwardly

rectifying (Kir) channels, and two-pore domain (K2P) channels (Heitzmann and Warth, 2008; Horn et al., 2014).

Potassium has a role in cell metabolism, participating in energy transduction, hormone secretion and the regulation of protein and glycogen synthesis. Potassium is a cofactor for a number of enzymes including glycerol dehydrogenase, mitochondrial pyruvate carboxylase, pyruvate kinase, L-threonine dehydratase, ATPases and aminoacyl transferase (Page and Di Cera, 2006; Toraya et al., 2010).

2.2.2. Health consequences of deficiency and excess

2.2.2.1. Deficiency

Potassium deficiency, presenting as hypokalaemia, is defined as a serum potassium concentration lower than 3.5 mmol/L (Pepin and Shields, 2012). In general, deficiency may be caused by increased potassium losses via diarrhoea, vomiting, burns, or excessive renal losses (owing, for example, to renal tubular acidosis, high secretion of mineralocorticoids, some diuretics) leading to low total body potassium (Crop et al., 2007; Rodenburg et al., 2014). Hypokalaemia can also occur when total body potassium is normal in case of an intracellular shift of potassium (Rastegar, 1990). The most important causes of an intracellular shift include alkalosis, insulin excess, catecholamine excess, and familial periodic paralysis (i.e, a genetic disease related to malfunction in the ion channels in skeletal muscle cell membranes) (Gumz et al., 2015). Hypokalaemia resulting from insufficient dietary intake is rare and may be associated with severe hypocaloric diets or occur during recovery from malnutrition.

Hypokalaemia is generally associated with increased morbidity and mortality, especially from cardiac arrhythmias or sudden cardiac death. When serum potassium concentration is < 3 mmol/L, the prevalence of malignant ventricular arrhythmia has been observed to increase two-fold in patients on diuretic treatment (Byatt et al., 1990). The risk of atrial fibrillation is higher in hypokalaemic subjects compared to the general population (Krijthe et al., 2013). Other adverse consequences of hypokalaemia include polyuria, muscle weakness, decreased peristalsis possibly leading to intestinal ileus, mental depression and respiratory paralysis in severe cases (Rodenburg et al., 2014).

2.2.2.2. Excess

Hyperkalaemia is commonly defined as a serum potassium concentration greater than approximately 5.5 mmol/L in adults (Pepin and Shields, 2012; Michel et al., 2015). Hyperkalaemia is often asymptomatic and diagnosed because of conduction abnormalities on the electrocardiogram (Lehnhardt and Kemper, 2011). Clinical manifestations of mild to moderate hyperkalaemia are usually non-specific and may include generalised weakness, paralysis, nausea, vomiting, and diarrhoea (Pepin and Shields, 2012). Severe hyperkalaemia may lead to life-threatening cardiac arrhythmias (Paice et al., 1983; Lehnhardt and Kemper, 2011).

Hyperkalaemia is rare in the general population. The majority of cases occur from impaired renal function (Lehnhardt and Kemper, 2011; Crook, 2012). Non-renal causes include inappropriately high intakes of oral potassium supplements or parenteral potassium administration and a potassium shift from cells (for instance in the case of metabolic acidosis, hypoxia, severe tissue damage). Hyperkalaemia following excessive potassium dietary intake is rare due to effective homeostatis mediated by increased cellular uptake of potassium from the bloodstream by various organs and increased urinary excretion (Lehnhardt and Kemper, 2011).

No Tolerable Upper Intake Level (UL) has been set for potassium by EFSA due to insufficient data (EFSA NDA Panel, 2005). The Panel considered that the risk of adverse effects from potassium intake from food sources (up to 5,000–6,000 mg (129–154 mmol)/day in adults) is low for the general healthy population. It also stated that long-term intakes of about 3,000 mg (77 mmol) potassium/day as potassium chloride supplements, in addition to intake from food, have been shown not to have adverse effects in healthy adults. However, a few case studies have reported that supplemental potassium in doses of 5,000–7,000 mg (128–179 mmol)/day can cause adverse effects on heart

function in apparently healthy adults. Gastrointestinal symptoms have been observed in healthy subjects taking potassium supplements with potassium doses ranging from about 1,000 to 5,000 mg (26 to 128 mmol)/day (Perazella and Mahnensmith, 1997; EFSA NDA Panel, 2005; Cicero and Borghi, 2013).

2.3. Physiology and metabolism

2.3.1. Intestinal absorption

About 90% of dietary potassium is absorbed, mainly in the small intestine, mostly through passive mechanisms in response to electrochemical gradients (Agarwal et al., 1994; Bailey et al., 2014).

In the proximal small intestine, water absorption provides a driving force for the movement of potassium across the intestinal mucosa. In the ileum, the trans-epithelial electrical potential difference strongly influences its movement. It has been hypothesised that potassium may also be actively absorbed in the small intestine due to the presence of an H^+/K^+-ATPase in the apical membrane (Heitzmann and Warth, 2008). In surface cells of the distal colon, potassium is excreted through apical potassium channels in exchange for sodium which is reabsorbed through epithelial sodium channels. Potassium may also be reabsorbed in the colon through the action of luminal H^+/K^+-ATPases (colonic type), which can be of importance during potassium deprivation (Meneton et al., 1998).

2.3.2. Transport in blood

In healthy individuals, serum potassium concentrations range between 3.5 and 5.5 mmol/L, whereas plasma concentrations are lower by about 0.3–0.4 mmol/L. This difference is due to a release of potassium during clot formation (Nijsten et al., 1991; Sevastos et al., 2008). Homeostatic mechanisms act to maintain blood potassium concentration within a narrow range, even in the presence of wide variations in dietary potassium intake (Giebisch, 1998, 2004; Palmer, 2014; Gumz et al., 2015) (Section 2.3.3).

In plasma, most potassium is present as free ions and 10–20% is bound to proteins (Ifudu et al., 1992).

2.3.3. Distribution to tissues

Around 98% of systemic potassium is within the cells, making potassium the major intracellular cation. Most of body potassium is located in muscle (70%), with lower amounts present in bone, liver, skin and red blood cells (Weiner et al., 2010). Most of the body potassium (about 85%) is rapidly exchangeable (half time of less than 7 hours), while exchanges with red blood cells and brain pools are slower (Jasani and Edmonds, 1971).

Intra- and extracellular concentrations of potassium are maintained within narrow limits. After a meal, potassium is absorbed and rapidly enters the extracellular fluid. The subsequent rise in plasma potassium concentration is quickly attenuated by cellular uptake (Giebisch, 1998; Palmer, 2014). Na^+/K^+-ATPase is responsible for the active transport of potassium into the cells and for the maintenance of the extra- and intracellular sodium and potassium concentrations against electrochemical gradients. This ATPase is found in the cytoplasmic membrane of virtually all cells (McDonough and Nguyen, 2012). Potassium is also actively transported into some gastrointestinal cells and renal tubules by H^+/K^+-ATPase (Sections 2.3.1 and 2.3.5.1). Various Na^+-K^+-Cl^- cotransporters, which carry Na^+, K^+ and Cl^- into the cell and are driven by the force of ion gradients, have been identified in salivary glands, the gastrointestinal tract, and renal tubules (Sections 2.3.1 and 2.3.5.1). The K^+-Cl^- cotransporter plays an important role for erythrocytes to maintain a specific shape and mediates potassium efflux (Lote, 2007).

Potassium transfer between the extra- and intracellular milieus is influenced by a variety of endogenous and exogenous factors (Gumz et al., 2015). Cellular potassium uptake by muscle, liver, bone and red blood cells is promoted by the increase in plasma potassium concentration, by insulin, epinephrine and aldosterone, by metabolic alkalosis, and by drugs activating β-2 adrenergic receptors.

Conversely, a decrease in plasma potassium concentration, metabolic acidosis, hyperosmolarity of the extracellular fluid, and α-antagonist drugs induce potassium transport from cells to the extracellular fluid. Hyperkalaemia stimulates the secretion of insulin, aldosterone, and epinephrine, while hypokalaemia has the opposite effect (Giebisch, 2004; Grossman et al., 2013).

The mechanisms of feto–placental potassium transfer have not been fully elucidated. Animal studies indicate that potassium is actively transported across the placenta and that the developing fetus is efficient in maintaining constant potassium concentration in plasma (Atkinson et al., 2006; Lorenz, 2012). Fetal potassium content was observed to be maintained in case of maternal potassium restriction (Lorenz, 2012). In a cross-sectional study on 344 healthy pregnant women, potassium concentrations in both fetal and maternal plasma did not differ with gestational age (15 to 38 weeks of gestation), at 3.5–3.6 mmol/L in the fetuses and 3.3–3.6 mmol/L in the mothers (Moniz et al., 1985).

2.3.4. Storage

The total body content of potassium is about 40–55 mmol/kg bw (Rastegar, 1990; Agarwal et al., 1994; Crook, 2012; Bailey et al., 2014), which corresponds to 3–4 moles (110–150 g) for a 70 kg adult. Similar potassium body contents (expressed per kg bw) have been reported in infants and children (Fomon et al., 1982; Butte et al., 2000).

Based on 462 US children (232 boys and 230 girls) aged 3–18 years, no differences in total body potassium were observed for boys and girls between 12 and 30 kg of weight and 100 and 135 cm of height (about 10 years of age) (Flynn et al., 1972). Above these values, girls had less potassium per centimetre of height and per kilogram of weight than boys. In a sample of 116 US children (66 boys and 50 girls, aged 5–17 years), males had larger skeletal muscle (SM) and total body potassium (TBK) compared to females, while the SM:TBK ratio did not differ between both sexes (Wang et al., 2007). SM:TBK was positively correlated with age, weight and height ($r = 0.62$, $r = 0.63$, $r = 0.86$, respectively; all $p < 0.001$). The Panel notes that total body potassium accumulation during growth appears to reflect patterns of skeletal muscle gain.

2.3.5. Losses

Body potassium content is regulated by the balance between dietary intake and renal excretion. In addition to urinary excretion, small quantities of potassium are excreted in the faeces and through the skin.

2.3.5.1. Urine

The kidney is the main route of potassium excretion. Studies in humans reported average urinary excretion of potassium between 77 and 92% of total dietary intake (Mickelsen et al., 1977; Pietinen, 1982; Holbrook et al., 1984; Tasevska et al., 2006; Yoshida et al., 2012). Urinary excretion of potassium varies with dietary intake. According to results published by the Intersalt Cooperative Research Group in late 1980s (Intersalt Cooperative Research Group, 1988), a typical range observed with a mixed Western diet was 46–77 mmol/day.

Potassium is freely filtered by the glomerulus. In healthy adults, the rate of potassium filtration by the glomerular capillaries is 756 mmol/day, considering a glomerular filtration rate of 180 L/day multiplied by a plasma potassium concentration of 4.2 mmol/L (Guyton and Hall, 2006).

The renal tubules are capable of reabsorbing and secreting potassium in response to various stimuli (Rodenburg et al., 2014). The human kidney efficiently excretes potassium in response to high dietary intakes, but is less capable of sparing potassium when dietary intake is low (Kee et al., 2010).

The majority of filtered potassium is reabsorbed in the proximal tubule and loop of Henle, so that less than 10% of the filtered load reaches the distal nephron. In the proximal tubule, potassium absorption is primarily passive and proportional to sodium and water. Potassium reabsorption in the thick ascending limb of Henle occurs through both transcellular and paracellular pathways. The transcellular

component is mediated by the Na^+-K^+-$2Cl^-$ cotransporter located on the apical membrane. Potassium secretion begins in the early distal convoluted tubule and progressively increases along the distal nephron into the cortical collecting duct, where active reabsorption of sodium is accompanied by excretion of potassium into the lumen (Palmer, 2014). Most urinary potassium can be accounted for by electrogenic potassium secretion mediated by principal cells in the initial collecting duct and the cortical collecting duct (Gumz et al., 2015). An electroneutral potassium and chloride cotransport mechanism is also present on the apical surface of the distal nephron epithelium. Potassium can be reabsorbed in the collecting duct, in situations of potassium depletion. This process is mediated by upregulation of the apically located H^+/K^+-ATPase on alpha-intercalated cells (Sansom and Welling, 2007; Palmer, 2014; Gumz et al., 2015).

The major factors regulating potassium excretion include dietary potassium, distal nephron flow rate and sodium delivery, mineralocorticoids (including aldosterone), and acid-base balance (Palmer, 2014; Gumz et al., 2015). Renal potassium excretion has also a circadian rhythm independent of food intake (Gumz et al., 2015). The circadian rhythm, which originates from the brain, is transmitted to circadian clocks in the tubule cells responsible for variations in potassium excretion. As a result, potassium excretion is enhanced during the daylight phase and reduced during the night time phase (Gumz et al., 2015).

During pregnancy, potassium excretion is held constant through adaptive mechanisms of renal tubular potassium reabsorption, which adjust to the increased filtered potassium load and the increased retention of sodium mediated by aldosterone (Ehrlich and Lindheimer, 1972; Brown et al., 1986; Cheung and Lafayette, 2013). Progesterone, through its antikaliuretic effect, has been proposed to contribute to maintain potassium homeostasis in pregnant women (Lindheimer et al., 1987; Elabida et al., 2011).

2.3.5.2. Faeces

Potassium concentration in faeces is highly variable (ranging from 20 to 200 mmol/L). Distal ileum and the colon can actively secrete potassium (Sorensen et al., 2010) (Section 2.3.1). Net absorption only takes place when large gradients of concentration between the colon and the blood are present (Devroede and Phillips, 1969).

Faecal potassium excretion is about 10–25 mmol/day, constituting 10–20% of total potassium elimination from the body (Holbrook et al., 1984; Agarwal et al., 1994; Tasevska et al., 2006). Faecal potassium excretion increases with fibre intake (Cummings et al., 1976; Tasevska et al., 2006). Potassium losses in faeces may considerably increase in pathological situations, especially in cases of diarrhoea (Sandle and Hunter, 2010; West and von Saint Andre-von Arnim, 2014) or renal insufficiency (Sandle et al., 1986).

In a study on four adult men in which dietary potassium intake was severely restricted (less than 39 mg (1 mmol)/day) for 2 to 7 days, faecal potassium loss decreased and was 2.5 to 7.6 mmol/day at the end of the depletion period (Squires and Huth, 1959). This presumably represents obligatory potassium losses related to digestive secretions (salivary, gastric, biliary, and pancreatic), cell desquamation, and mucus secretion (Agarwal et al., 1994; Sorensen et al., 2010).

2.3.5.3. Dermal losses

The concentration of potassium in sweat is relatively low; typical values range from 3 to 7 mmol/L (Costill, 1977; Montain et al., 2007; Penney, 2008; Baker et al., 2009; Kilding et al., 2009; Maughan et al., 2009). In various studies, the concentration of potassium in sweat was not or only minimally affected by physical exercise (Montain et al., 2007), heat stress (Malhotra et al., 1976) or dietary sodium intake or ethnicity (Palacios et al., 2010), including conditions of dietary potassium restriction (Malhotra et al., 1981; Costill et al., 1982). Sweat potassium concentration stays relatively constant,

regardless of sweat rate, level of acclimatisation, or an individual's sodium concentration in the sweat (Weschler, 2008).

When sweat losses are several litres a day, as under heat or physical exercise stress conditions, potassium sweat losses may be up to 10–25 mmol/day (Consolazio et al., 1963; Malhotra et al., 1976; Malhotra et al., 1981).

The Panel considers that potassium losses through sweat at moderate physical activity performed around thermoneutrality are likely to be in the range of 2–3.5 mmol/day, assuming a daily sweat volume of around 0.5 L/day (Shirreffs and Maughan, 2005; Subudhi et al., 2005).

2.3.5.4. Breast milk

There is a decline in breast milk potassium concentration over the first weeks of lactation, with a high concentration in colostrum followed by a decrease (Atkinson et al., 1995). In longitudinal studies, potassium concentration in breast milk, once mature, was nearly constant (Nagra, 1989; Allen et al., 1991; Wack et al., 1997). Potassium concentration in breast milk shows diurnal variations, reciprocal to sodium concentration (Keenan et al., 1982b; Keenan et al., 1983).

Atkinson et al. (1995) collected data on the potassium content in breast milk from nine studies conducted in the USA, Canada and the UK. Mean potassium concentrations across studies were between 682 and 725 mg/L (17.4 and 18.5 mmol/L) at day 3 (colostrum), 569 and 659 mg/L (14.5 and 16.8 mmol/L) at day 14 (transitional milk), 464 and 600 mg/L (11.9 and 15.3 mmol/L), 405 and 542 mg/L (10.3 and 13.9 mmol/L) and 366 and 495 mg/L (9.4 and 12.7 mmol/L) at day 30, 90 and 180 of lactation (mature milk), respectively.

Appendix A reports data on potassium concentration in breast milk from additional studies which involved mothers of term infants in Western populations. Mean/median potassium concentrations are between 461 and 594 mg/L (11.8 and 15.2 mmol/L) from six studies which analysed mature breast milk (Keenan et al., 1982b; Parr et al., 1991; Holt, 1993; Wack et al., 1997; Fly et al., 1998; Witczak and Jarnuszewska, 2011) and 450 and 633 mg/L (11.5 and 16.2 mmol/L) in two studies which used mixed samples (collected between 1 and 8 weeks post partum) (Bauer and Gerss, 2011; Bjorklund et al., 2012).

Based on available data, the Panel considers an approximate midpoint of potassium concentration in mature breast milk of women from Western countries of 500 mg (12.8 mmol)/L. Based on a mean milk transfer of 0.8 L/day (Butte et al., 2002; FAO/WHO/UNU, 2004; EFSA NDA Panel, 2009) during the first six months of lactation in exclusively breastfeeding women, the Panel estimates the maternal loss of potassium through breast milk to be 400 mg (10.2 mmol)/day.

2.3.6. Interaction with other nutrients

2.3.6.1. Sodium

The metabolisms of potassium and sodium are strongly interrelated, principally due to the Na^+/K^+-ATPase. Sodium/potassium interactions are important at the cellular level (Adrogue and Madias, 2014). The renal regulation of sodium homeostasis is closely related to that of potassium (Section 2.3.5.1). However, sodium intake does not influence potassium excretion except at high sodium intakes (≥ 4,830 mg (210 mmol)/day) (Kirkendall et al., 1976; Luft et al., 1982). In the Dietary Approaches to Stop Hypertension (DASH) study, at sodium intakes of 1,500 mg (65 mmol), 2,400 mg (104 mmol), and 3,200 mg (140 mmol) per day for four weeks each, urinary potassium excretion did not exceed intake (1,600 ± 500 mg/day) and was similar at each sodium level (Sacks et al., 2001).

Salt sensitivity, defined as either the reduction in blood pressure in response to a lower sodium chloride intake or the rise in blood pressure in response to sodium loading (IOM, 2005), is a condition frequently observed in African Americans and is also associated with genetic or physiological factors

(Weinberger, 1996; Strazzullo et al., 2000). Dietary potassium intake modulates the variation of blood pressure levels due to salt-sensitivity in normotensive (Luft et al., 1979; Morris et al., 1999; Wilson et al., 1999), as well as in hypertensive individuals (Krishna et al., 1989; Coruzzi et al., 2001).

There is also evidence that the effect of potassium intake on blood pressure may be higher in individuals with high sodium chloride intake compared to those with low sodium chloride intake and that the sodium-to-potassium intakes ratio may also influence this relationship (Section 5.6.1.1).

The Panel notes the interaction of potassium and sodium in relation to their metabolisms and health effects, particularly under conditions of sodium load or in salt-sensitive individuals. The Panel considers that available data are insufficient, however, to derive DRVs for potassium depending on the level of dietary sodium intake.

2.3.6.2. Interactions with other minerals and vitamins

Calcium

Potassium depletion enhances urinary loss of calcium. In a study of six male and two female adults who underwent five days of potassium deprivation, increases in both fasting and 24-hour urinary calcium excretion were observed; levels returned to normal within five days after termination of potassium deprivation (Lemann et al., 1991).

In contrast, potassium supplementation may decrease urinary calcium excretion. Ten male and female adults aged 21–41 years on a controlled diet containing on average 3,323 ± 235 mg (85 ± 6 mmol) potassium/day, 866 ± 36 mg (21.6 ± 0.9 mmol) calcium/day and 3,795 ± 322 mg (165 ± 14 mmol) sodium/day, were supplemented with 90 mmol/day of potassium bicarbonate or potassium chloride (3,510 mg potassium) for four days. Potassium bicarbonate, but not potassium chloride, reduced fasting and 24-hour urinary calcium excretion (Lemann et al., 1991). In a meta-analysis, Lambert et al. (2015) found that supplementation with alkaline potassium salts (14 trials, potassium supplemental daily doses 1,170–7,020 mg (30–180 mmol)) reduced calcium excretion compared to a placebo; in studies which compared alkaline potassium salts with potassium chloride, a higher effect of the alkaline salt on calcium excretion was observed. The Panel notes that most studies used alkaline potassium salts and the independent effect of potassium as compared to alkali administration on calcium excretion is unclear.

Phosphorus and vitamin D

Administration of potassium salts may alter renal tubular phosphate transport and renal synthesis of $1,25(OH)_2$-vitamin D and may increase serum phosphorus concentration (Lemann et al., 1991). Sebastian et al. (1990) studied the effect of potassium supplementation (6,084 mg (156 mmol)/day as potassium bicarbonate and potassium chloride for eight days each) in six healthy males (25–40 years) on a fixed diet (3,220 mg (140 mmol) sodium, 2,024 mg (52 mmol) potassium, 361 mg (9 mmol) calcium, 836 mg (27 mmol) phosphorus per 70 kg bw). Both potassium forms caused an increase in serum phosphorus and a decrease in $1,25(OH)_2$-vitamin D compared to a control period in which no supplement was administrated.

The Panel considers that interactions between potassium and other minerals and vitamins, in the context of a mixed European diet, are not relevant for setting DRVs for potassium.

2.4. Biomarkers

2.4.1. Biomarkers of intake

In healthy people, a large proportion (about 90%) of dietary potassium intake is absorbed (Section 2.3.1). Urine is the major route of potassium excretion, while the remaining part is eliminated in the faeces and, to a lesser extent, in sweat (Section 2.3.5). Recovery rates of dietary potassium in the urine between 77 and 92% have been reported (Mickelsen et al., 1977; Pietinen, 1982; Holbrook et al.,

1984; Tasevska et al., 2006; Yoshida et al., 2012). In the study by Holbrook et al. (1984), duplicate samples of meals and beverages and all urine from 12 men and 16 women were collected daily for four 1-week periods and the potassium content was analysed to estimate the dietary intake and urinary excretion of potassium. Mean (± SEM) urinary potassium excretion was 77 ± 1.7% of potassium intake. Tasevska et al. (2006) conducted a controlled feeding study in which seven men and six women were hosted in a metabolic suite for 30 days. All urine and dietary duplicates were collected for potassium analysis. On average (± SD), 77 ± 6.7% of analysed potassium intake was excreted in the urine. High correlations between 24-hour urinary potassium excretion and potassium dietary intake were found in both studies (r = 0.82 and 0.89, respectively). Some studies have indicated a lower urinary excretion of potassium in black as compared to white individuals, although it is unclear whether it reflects differences in potassium intakes or other factors (Voors et al., 1983; Barlow et al., 1986; Langford et al., 1991; Wong et al., 2003; Aviv et al., 2004; Turban et al., 2013). Conversion factors of 1.25 (Freedman et al., 2004; Freedman et al., 2015) or 1.3 (Murakami et al., 2007; WHO, 2012d, 2012c; Aburto et al., 2013) have been proposed to estimate daily dietary potassium intake from 24-hour urinary potassium excretion. The Panel notes that the percentage of dietary intake recovered in the urine, although quite consistent in different studies, shows a significant inter-individual variability, probably in part due to inaccuracies in dietary assessment, errors in urine collections and/or other environmental or genetic factors.

Several equations have been proposed to estimate 24-hour urinary potassium excretion from a single morning fasting urine sample (Kawasaki et al., 1993) or random spot urine sample (Tanaka et al., 2002). Using data from 1,083 individuals (35–70 years) who provided both single fasting morning and 24-hour urinary samples, Mente et al. (2014) reported interclass correlation coefficients between formula-based and measured 24-hour potassium excretion of 0.55 (95% CI = 0.31–0.69) for the Kawasaki formula and 0.36 (95% CI = 0.07–0.60) for the Tanaka formula. Both methods were found to underestimate actual potassium excretion. In contrast, in another validation study where 24-hour and random spot urine samples were collected from 147 women (19–26 years), Hooft van Huysduynen et al. (2014) found that the Tanaka formula overestimated actual 24-hour urinary potassium excretion. No validation study used chemical analysis of dietary duplicates. The Panel notes that approaches based on spot urine samples may be of some value in population studies but they require cautious interpretation due to the risk of both over- or under-estimation of potassium excretion. The Panel notes that they provide imprecise estimates at individual level.

Measures of 24-hour potassium excretion in urine have been used for validating dietary questionnaires. Based on data from five validation studies, Freedman et al. (2015) reported average correlation coefficients of 0.37 with food frequency questionnaires (FFQs) and of 0.47 with a single 24-hour recall.

A few studies have examined urinary potassium excretion in children (Knuiman et al., 1988; Zwiauer et al., 1991; Kristbjornsdottir et al., 2012), and reported values between 1.3–1.8 mmol/kg bw per day. However, in the absence of data for dietary potassium intakes (analysed or calculated) in these studies, the reliability of urinary potassium excretion as a biomarker of dietary intake in children can not be assessed.

The Panel considers that urinary potassium excretion, based on 24-hour collection, is a reliable biomarker of dietary intake in adults on a population basis. However, the Panel notes that a single 24-hour urinary collection can not accurately assess an individual's usual intake. For converting 24-hour urinary potassium excretion values into potassium daily intakes (Section 5.6.1), the Panel selected a factor of 1.30, based on the ratio of potassium dietary intake to urinary excretion reported in two studies which used chemical analysis of the diet and 24-hour urinary collection (Holbrook et al., 1984; Tasevska et al., 2006). This corresponds to the factor applied by other authors (Murakami et al., 2007; WHO, 2012d, 2012c; Aburto et al., 2013).

2.4.2. Biomarkers of status

In healthy individuals, homeostatic mechanisms act to maintain plasma potassium concentrations within a narrow range (Section 2.3). Changes in extracellular potassium concentration as the result of changes in external potassium equilibrium (i.e. balance between potassium intake and output) usually occur slowly and are buffered by homeostatic changes in internal potassium equilibrium (i.e. shifts between the extra- and intracellular fluids) (Lorenz, 2012). As a result, plasma potassium concentration is a late indicator of changes in potassium balance. In addition, low plasma potassium concentrations can coexist with both normal or low total body potassium (Section 2.2.2.1). Thus, in most instances, serum potassium concentration does not accurately reflect total body potassium content.

Whole body counting of ^{40}K has been proposed for the determination of total body potassium content (Tyson et al., 1970) and has been used for the assessment of body composition (Forbes, 1987; Dittmar and Reber, 2004; Murphy et al., 2014). This method permits a reliable estimate of total body potassium (Forbes, 1987; Hansen and Allen, 1996). Like plasma potassium concentration, total body potassium content is only minimally affected by variations in dietary potassium intake. Total body potassium depletion is usually caused by excessive potassium losses (through urine, diarrhoea or vomiting) associated with certain health conditions or medicines (Section 2.2.2.1).

The Panel considers that there is no biomarker of potassium status which can be used for setting DRVs for potassium in the general population.

2.5. Effects of genotypes

Genetic mechanisms may contribute to the blood pressure response to dietary potassium intake (Section 5.6.1.1). In particular, different chromosome regions (Kelly et al., 2010), or genetic variants (Zhao et al., 2010; He et al., 2011; Liu et al., 2013) were found to be associated with the individual variability of the blood pressure response to oral potassium intake ("potassium sensitivity").

The Panel considers that, although genetic factors may affect the individual blood pressure response to dietary potassium intake, no genotypes have yet been identified that would require consideration with regard to the derivation of DRVs for potassium in the general population.

3. Dietary sources and intake data

3.1. Dietary sources

Potassium is present in all natural foods, including starchy roots or tubers and vegetables, fruits, whole grains, dairy products and coffee. Substantial potassium losses may occur during food processing. Drinking water and many food additives also contain potassium, however it is unlikely that they represent major sources.

Potassium as potassium-L-ascorbate, magnesium potassium citrate, potassium iodide, potassium iodate, potassium bicarbonate, potassium carbonate, potassium chloride, potassium citrate, potassium gluconate, potassium glycerophosphate, potassium lactate, potassium hydroxide, potassium salts of orthophosphoric acid, potassium fluoride may be added to both foods[3] and food supplements,[4] whereas potassium sulphate, potassium L-pidolate, potassium malate and potassium molybdate may only be used in the manufacture of food supplements.[7] The potassium content of infant and follow-on

[3] 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.

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

formulae[5] and processed cereal-based foods and baby foods for infants and young children[6] is regulated.

3.2. Dietary intake

EFSA estimated dietary intakes of potassium from food consumption data available through the EFSA Comprehensive Food Consumption Database (EFSA, 2011b), classified according to the food classification and description system FoodEx2 (EFSA, 2011a). Data from 13 dietary surveys in nine countries of the European Union (EU) were used. The countries included were Finland, France, Germany, Ireland, Italy, Latvia, Netherlands, Sweden and the UK. The data covered all age groups from infants to adults (Appendix B).

Nutrient composition data for potassium 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 were used to calculate potassium intakes 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 nutrient intake estimates of Ireland and Latvia, food composition data from the UK and Germany, respectively, were used, because no specific composition data from these countries were available. The amount of borrowed potassium values in the seven composition databases used varied between 15% (Germany) and 84% (Sweden); in all the countries except Germany the percentage of borrowed values was higher than 55% of the total. Estimates were based on the consumption of food, including salt substitutes where available, but not dietary supplements.

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

Average potassium intakes across countries ranged between 821 and 1,535 mg/day (279–546 mg/MJ) in infants (< 1 year, four surveys), between 1,516 and 2,005 mg/day (356–495 mg/MJ) in children aged 1 to < 3 years (five surveys), between 1,668 and 2,750 mg/day (284–473 mg/MJ) in children aged 3 to < 10 years (seven surveys), between 2,093 and 3,712 mg/day (280–464 mg/MJ) in children aged 10 to < 18 years (seven surveys), and between 2,463 and 3,991 mg/day (338–497 mg/MJ) in adults (≥ 18 years, eight surveys). Average daily intakes were in most cases slightly higher in males (Appendix C) compared to females (Appendix D), mainly due to larger quantities of food consumed per day.

The main food groups contributing to potassium intakes were starchy roots or tubers and products thereof, sugar plants, grains and grain-based products, milk and dairy products, and vegetables and vegetable products (Appendices E and F). In the youngest population, food products for young population (infants), and milk and dairy products (toddlers and other children) were the most important contributors. In infants, in some surveys, the average contribution of food products for young population represented more than 50% of the total intake of potassium. The impact of milk and

[5] Commission Directive 2006/141/EC of 22 December 2006 on infant formulae and follow-on formulae and amending Directive 1999/21/EC, OJ L 401, 30.12.2006, p.1.

[6] 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.

dairy products on the intake of potassium in this age class was also quite important, with average contributions up to 22% of the total.

EFSA intake estimates were compared with published intake estimates from the same national surveys and age ranges (Appendix G). The differences between EFSA estimates and those published were always below 10%, except for male adolescents in the German EsKiMo study where the EFSA estimates were 12% higher than the published ones. Published data on potassium intake were also available from the UK diet and nutrition survey of infants and young children (DNSIYC) 2011 survey but comparisons with the EFSA estimates were difficult as they were reported by ethnic groups and socio-economic classes. Overall, EFSA average estimates for infants (1,370–1,535 mg/day) and toddlers (1,688–1,794 mg/day) were slightly higher than those reported (1,024–1,161 mg/day for infants, 1,433–1,633 mg/day in toddlers) in that survey. Several sources of uncertainties may contribute to the differences between EFSA estimates and those published, including inaccuracies in mapping food consumption data according to FoodEx2 classification, analytical errors or errors in estimating potassium, which may cause both too high and too low estimates of potassium intake. As the intake calculations rely heavily on estimates of both food composition and food consumption, it is not possible to conclude which of these intake estimates would be closer to the actual potassium intakes of the respective population groups.

4. Overview of Dietary Reference Values and recommendations

4.1. Adults

The Nordic countries (Nordic Council of Ministers, 2004, 2014) based their recommendations on the favourable effect of potassium on blood pressure (Intersalt Cooperative Research Group, 1988; Jula et al., 1990; Appel et al., 1997; Geleijnse et al., 1997; Whelton et al., 1997; Sacks et al., 1998; Gu et al., 2001; Sacks et al., 2001; Geleijnse et al., 2003; Naismith and Braschi, 2003; Dickinson et al., 2006; van Bommel and Cleophas, 2012). The recommended intakes for potassium were set at 3,500 mg (90 mmol)/day for men and 3,100 mg (80 mmol)/day for women. It was noted that potassium intakes "somewhat over and above these values might have further beneficial effects". A lower limit of 1,600 mg (40 mmol)/day was proposed.

WHO conducted a systematic review to explore the relationship between potassium and blood pressure in adults (WHO, 2012c), which served as the basis for setting a strong recommendation[7] for an increase in potassium intake from food for reduction of blood pressure and risk of cardiovascular disease, stroke, and coronary heart disease in adults, and for suggesting a conditional recommendation[8] for an intake of 3,510 mg (90 mmol)/day for adults (WHO, 2012a).

The German-speaking countries (D-A-CH, 2015) considered that observed intakes of adults between 2,000–3,000 mg (50–75 mmol)/day from common diets in Central Europe are sufficient under normal conditions. An amount of 2,000 mg (50 mmol)/day was designated an estimated value for a minimal intake.

The US Institute of Medicine (IOM, 2005) set an Adequate Intake (AI) of 4,700 mg (120 mmol)/day based on data on the amount of potassium found to eliminate severe salt sensitivity in African American men (Morris et al., 1999) and considering the decreased risk of kidney stones observed in a three-year intervention trial (Barcelo et al., 1993) and three epidemiological studies (Curhan et al., 1993; Curhan et al., 1997; Hirvonen et al., 1999). Data from studies in non-hypertensive individuals were considered supportive of this level of intake as a means to lower blood pressure. Epidemiological studies also suggested that higher levels of potassium intake from foods were associated with decreased bone loss, mainly when potassium is associated with bicarbonate precursors (New et al., 1997; Tucker et al., 1999; New et al., 2000; Jones et al., 2001; Macdonald et al., 2004; New et al.,

[7] A strong recommendation is one for which the guideline development group is confident that the desirable effects outweigh the undesirable effects.

[8] A conditional recommendation is one for which the guideline development group concludes that the desirable effects of adherence probably outweigh the undesirable effects, but the group is not confident about the trade-off.

2004). For older adults, although less energy is consumed, there is an increased risk of elevated blood pressure; therefore the value was not adjusted.

Afssa (2001) considered that the usual potassium intakes of 2,000–6,000 mg (50–150 mmol)/day by the general population (Burgess et al., 1999) exceeds the estimated minimum requirement of 390–585 mg (10–15 mmol)/day. No DRV was derived.

The SCF (1993) suggested a Lowest Threshold Intake of 1,600 mg (40 mmol)/day, to avoid low plasma concentrations and loss of total body potassium (Sebastian et al., 1971). An Average Requirement (AR) was not set. Using evidence from studies investigating the relationship between potassium intake and blood pressure (Matlou et al., 1986; Rose, 1986; Intersalt Cooperative Research Group, 1988; Krishna et al., 1989), the PRI was set at 3,100 mg (80 mmol)/day.

The UK DH (1991) estimated the requirements based on a factorial approach considering daily potassium losses. The Reference Nutrient Intake (RNI) for adults was set at 3,500 mg (90 mmol)/day. It set a Lower Reference Nutrient Intake (LRNI) of 2,000 mg (50 mmol)/day. No AR was derived.

An overview of DRVs for potassium for adults is given in Table 1.

Table 1: Overview of Dietary Reference Values for potassium for adults

	D-A-CH (2015)[(b)]	NCM (2014)[(a)]	WHO (2012a)[(c)]	IOM (2005)[(d)]	Afssa (2001)[(d)]	SCF (1993)[(a)]	DH (1991)[(a)]
Age (years)	≥ 19	≥ 18	≥ 16	≥ 19	≥ 20	≥ 18	≥ 19
DRV							
Men (mg/day)	2,000	3,500	≥ 3,510	4,700	-	3,100	3,500
Women (mg/day)	2,000	3,100	≥ 3,510	4,700	-	3,100	3,500

Afssa, Agence française de sécurité sanitaire des aliments; D–A–CH, Deutschland–Austria–Confoederatio Helvetica; DH, Department of Health; DRV, dietary reference value; IOM, US Institute of Medicine of the National Academy of Sciences; NCM, Nordic Council of Ministers; SCF, Scientific Committee for Food; WHO, World Health Organization.
(a): Population Reference Intake
(b): Adequate minimal intake
(c): Suggested intake
(d): Adequate Intake

4.2. Infants and children

For children and adolescents, the Nordic countries (Nordic Council of Ministers, 2014) extrapolated recommendations from adult values based on differences in body weight and needs for growth. PRIs of 1,800 mg (46 mmol)/day and 2,000 mg (51 mmol)/day were set for children aged 2–5 years and 6–9 years, respectively. For boys and girls aged 10–13 years, the PRI are 3,300 mg (84 mmol)/day and 2,900 mg (74 mmol)/day, respectively.

WHO (2012a) suggested an increase in potassium intake from food to control[9] blood pressure in children based on an observational study (Geleijnse et al., 1990) and a systematic review in adults (WHO, 2012c). Based on the energy requirements of children relative to those of adults, a conditional recommendation for potassium intake of at least 3,510 mg (90 mmol/day) was set.

The German-speaking countries (D-A-CH, 2015) estimated potassium needs to maintain electrolyte homeostasis and for growth of cellular mass. It was considered that infants during the first four months of life, because of their rapid growth, need 35 mg (0.9 mmol)/day for the development of cellular mass. Boys and girls up to 12 years need 16–20 mg (0.4–0.5 mmol)/day. For the period of accelerated growth in puberty, 35 mg (0.9 mmol)/day is required (Fomon, 1993). The requirement for the maintenance of homeostasis was estimated on the basis of total energy intake which, in turn, should be proportional to cell mass and, thus, the body's total potassium content.

[9] "Control" for this recommendation refers to the prevention of a deleterious rise in blood pressure with age.

730 For infants, IOM (2005) proposed an AI that reflects the calculated mean potassium intake of infants
731 principally fed breast milk, or a combination of breast milk and complementary foods. For age 0–
732 6 months, a mean potassium intake of 390 mg (10 mmol)/day was estimated based on an average
733 breast milk intake of 0.78 L/day (Keenan et al., 1982b; Butte et al., 1984; Chandra, 1984; Neville et
734 al., 1988) and an average breast milk potassium concentration of 500 mg/L (Gross et al., 1980;
735 Picciano et al., 1981; Keenan et al., 1982b; Lemons et al., 1982; Dewey and Lönnerdal, 1983). For age
736 6–12 months, the average potassium intakes were estimated at 300 mg (8 mmol)/day from breast milk
737 considering an average intake of milk of 0.6 L/day (Heinig et al., 1993) and 440 mg (11 mmol)/day
738 from complementary foods. After rounding, the AI was set at 700 mg (18 mmol)/day for this age
739 group. Due to a lack of evidence in children, the AI for age 1–18 years was extrapolated from the AI
740 for adults based on energy intake (IOM, 2000). This was a conservative choice because of concern that
741 adjustment based on weight might lead to a relatively low and potentially inadequate value; it was
742 considered that greater intake of potassium could also mitigate the effects of high sodium intake
743 associated to the high energy intake relative to weight observed in children.

744 As for adults, Afssa (2001) considered that the usual potassium intakes of children cover the minimum
745 requirement and did not set a DRV.

746 The SCF (1993) and UK DH (1991) concluded that there is a lack of evidence on basal potassium
747 losses in children. The two committees considered urinary excretion of 27–90 mg/kg bw per day (0.7–
748 2.3 mmol/kg bw per day) and an amount needed for growth and lean tissue synthesis of 2,000 mg/kg
749 bw. With these and other factors to allow for faecal losses and for integumental losses, PRIs for
750 children were estimated factorially.

751 An overview of DRVs for potassium for infants and children is given in Table 2.

752

753 **Table 2:** Overview of Dietary Reference Values for potassium for infants and children

	D-A-CH (2015)[a]	NCM (2014)[b]	IOM (2005)[c]	SCF (1993)[b]	DH (1991)[b]
Age (months)	4–< 12	6–11	7–12	6–11	4–6
DRV (mg/day)	650	1,100	700	800	850
Age (months)		12–23			7–12
DRV (mg/day)		1,400			700
Age (years)	1–< 4	2–5	1–3	1–3	1–3
DRV (mg/day)	1,000	1,800	3,000	800	800
Age (years)	4–< 7	6–9	4–8	4–6	4–6
DRV (mg/day)	1,400	2,000	3,800	1,100	1,100
Age (years)	7–< 10	10–13	9–13	7–10	7–10
DRV					
Boys (mg/day)	1,600	3,300	4,500	2,000	2,000
Girls (mg/day)	1,600	2,900	4,500	2,000	2,000
Age (years)	10–< 13	14–17	14–18	11–14	15–18
DRV					
Boys (mg/day)	1,700	3,500	4,700	3,100	3,500
Girls (mg/day)	1,700	3,100	4,700	3,100	3,500
Age (years)	13–< 15			15–17	
DRV (mg/day)	1,900			3,100	
Age (years)	15–< 19				
DRV (mg/day)	2,000				

754 D–A–CH, Deutschland–Austria–Confoederatio Helvetica; DH, Department of Health; DRV, dietary reference value; IOM,
755 US Institute of Medicine of the National Academy of Sciences; NCM, Nordic Council of Ministers; SCF, Scientific
756 Committee for Food.
757 (a): Adequate minimum intake
758 (b): Population Reference Intake
759 (c): Adequate Intake

760 ### 4.3. Pregnancy and lactation

761 The Nordic and the German-speaking countries as well as the SCF considered that pregnancy and
762 lactation do not impose an additional potassium requirement (SCF, 1993; Nordic Council of Ministers,
763 2014; D-A-CH, 2015).

764 The IOM (2005) concluded that potassium accretion during pregnancy is very small and that data are
765 not sufficient to suggest a different requirement for potassium during pregnancy. Therefore, the AI
766 was the same as for non-pregnant women. An AI of 5,100 mg (130 mmol)/day was set for lactation,
767 considering an additional need of around 400 mg (10 mmol)/day of potassium. This was based on an
768 average potassium concentration of breast milk of 500 mg/L (Gross et al., 1980; Picciano et al., 1981;
769 Keenan et al., 1982b; Lemons et al., 1982; Dewey and Lönnerdal, 1983) and an average milk
770 production of approximately 0.78 L/day (Keenan et al., 1982b; Butte et al., 1984; Chandra, 1984;
771 Neville et al., 1988), during the first six months of lactation. In the absence of information to the
772 contrary, it was assumed that the efficiency of conversion of dietary potassium to milk produced is
773 100%.

774 The UK DH (1991) assumed that the RNI value would apply for all women in their
775 reproductive years.

776 Afssa (2001) and WHO (2012a) gave no specific recommendations for pregnant and lactating women.

An overview of DRVs for potassium for pregnant and lactating women is given in Table 3.

Table 3: Overview of Dietary Reference Values for potassium for pregnant and lactating women

	IOM (2005)
Age (years)	14–50
AI	
Pregnancy (mg/day)	4,700
Lactation (mg/day)	5,100

AI, Adequate Intake; IOM, US Institute of Medicine of the National Academy of Sciences.

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

5.1. Biomarkers as indicators of potassium requirement

Plasma potassium concentration and measures of total body potassium cannot be used for setting DRVs for potassium (Section 2.4.2).

The Panel considers that there are no biomarkers of potassium status that can be used for deriving DRVs for potassium in the general population.

5.2. Balance studies

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. 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 and exchangeable body pools in the context of a given diet, and the relevance for health of the size of the pools still needs to be established for each nutrient (Mertz, 1987).

In the study by Holbrook et al. (1984) in the USA, 28 free-living adults, 12 men and 16 women (20–53 years), consumed self-selected diets and maintained a daily dietary record for one year. During four 7-day periods, one in each season of the year, duplicate samples of meals and beverages and all urine and faeces for the same period were collected and analysed for potassium content by atomic absorption spectrometry. Mean (± SEM) analysed intake of potassium was 3,300 ± 100 mg (84 ± 2 mmol)/day for men and 2,400 ± 600 mg (61 ± 15 mmol)/day for women (mean analysed intakes for the study group ranged from 2,600 to 2,900 mg (66 to 74 mmol)/day among the four balance periods). Mean (± SEM) intake calculated from the dietary records was 2,900 ± 100 mg (74 ± 2 mmol)/day for men and 2,100 ± 100 mg (54 ± 2 mmol)/day for women. The correlation between urinary excretion and dietary intake of potassium was significant (r = 0.92). Mean (± SEM) apparent absorption of potassium was 84.5 ± 0.6% and did not change significantly over the range of intakes. Mean (± SEM) balance calculated from the analysed potassium intake was positive, + 280 ± 50 mg/day. For the four study periods, mean balances were + 250 mg/day in spring, + 400 mg/day in summer, + 210 mg/day in autumn and + 280 mg/day in winter, respectively (significant difference between summer and autumn). The Panel notes that other losses of potassium, including dermal losses (skin and sweat), were not measured, and these might explain the more positive balance observed in the summer compared with the autumn.

Sriboonlue et al. (1999) undertook a 10-day balance study in 15 Thai men aged 25–50 years (mean (± SD) body weight 63 ± 9 kg) in two areas (no adaptation period). Subjects were given a fixed diet. Foods were weighed both before and after meals for each subject. Aliquots of foods consumed were taken for potassium analysis. Potassium in urine and faeces were measured daily in all subjects, however, potassium lost in sweat was analysed only in one subject. The rural group (n = 10) had a mean (± SD) potassium intake of 1,731 ± 138 mg (44 ± 4 mmol)/day and the urban group (n = 5) had a mean intake of 1,839 ± 145 mg (47 ± 4 mmol)/day (not significantly different). Urinary and faecal excretions of potassium were 721 ± 129 and 148 ± 25 mg/day in the rural group and 919 ± 186 and 164 ± 21 mg/day in the urban group, resulting in potassium balances of + 860 ± 140 in the rural group and + 756 ± 222 mg/day in the urban group, respectively. Regression of potassium balance vs intake indicated that rural and urban subjects needed potassium intakes of 832 and 884 mg (21 and 23 mmol)/day to stay in balance. For the one participant in whom sweat potassium was measured, mean balance over the ten days was + 847 ± 373 mg/day and + 396 ± 344 mg/day without and with subtraction of sweat potassium excretion. The authors reported high ambient temperatures during the study period (mean (± SD): 30.9 ± 1.7°C at 12.00 a.m. and 35.2 ± 2.0°C at 3.00 p.m.) and substantial sweat losses (mean (± SD): 1,927 ± 420 ml/day for the rural subjects and 1,759 ± 408 ml/day for the urban subjects, roughly estimated by subtracting the 24-hour urine volume from the daily water intake). The Panel notes the lack of an adaptation period, the small number of subjects, the fact that the study was conducted in a Thai population, under particular environmental conditions, and the largely positive balance estimates. These may partly be explained by the lack of consideration of potentially substantial potassium losses in sweat (Section 2.3.5.3). Consequently, the Panel considers that these data cannot be used to estimate the potassium requirement of European people.

Eleven potassium balance studies were conducted in Japan between 1984 and 2000, which involved 109 volunteers (23 males, 86 females; 18–28 years) (Kodama et al., 2005). The duration of the study periods ranged from 5 to 12 days, with 2 to 4 days adaptation period. The diet of subjects was controlled and duplicate diet samples were taken. Faeces and urine were collected throughout the experiment. In six studies (n = 49), arm sweat was collected during exercise on a bicycle ergometer. Total sweat loss of potassium during exercise throughout the balance period was divided by days of the balance period and expressed as sweat loss in mg/kg bw per day. The potassium content of the diet, faeces, urine and sweat were measured by atomic absorption spectrometry. The mean dietary intakes of potassium ranged between 1,830 and 3,610 mg (47 and 92 mmol)/day across studies. From the regression equation describing the relationship between potassium intake and balance of all individuals, the mean (95% CI) intake of potassium when potassium balance was null was 39 (37–42) mg/kg bw per day. The Panel notes the short adaptation periods of the studies and the fact that they were conducted in Japanese populations, and hence considers that this result cannot be used to estimate the potassium requirement of European people.

Nishimuta et al. (2012) applied a similar approach to data from 13 balance studies conducted on young Japanese women (n = 131, 18–26 years). As the median of the potassium balance distribution was found to be positive, the authors adjusted the individual data to set the median value to zero, under the assumption that the positive balance was due to the fact that some pathways of potassium losses had not been assessed, as regulatory mechanisms would successfully maintain the balance at zero. The Panel notes that this adjustment hampers the interpretation of this study.

Potassium balance studies have been found to underestimate potassium losses as compared with repeated assays of body potassium content by the ^{40}K counting method (Isaksson and Sjogren, 1963; Forbes et al., 1981; Forbes, 1983). Several sources of error in the estimation of potassium balances were proposed, including skin losses, other routes for losses (e.g. shaving, nail clipping), systematic errors (systematic overestimation of intake and underestimation of output), and lack of appropriate adaptation time.

The Panel notes that the relatively few available potassium balance studies are heterogeneous with regard to the populations examined, the presence and duration of equilibration periods and the duration of balance periods. The Panel notes the many limitations of these studies and considers that

the data derived from the available balance studies cannot be used for setting DRVs for potassium for adults.

5.3. Indicators of requirement in children

No balance studies on potassium on children have been identified.

During growth, total body potassium accumulation appears to reflect patterns of skeletal muscle gain (Section 2.3.4). Butte et al. (2000) reported mean (± SD) total potassium body content of 6.0 ± 0.9 g and 21.5 ± 2.7 g in girls and of 6.4 ± 0.7 g and 22.9 ± 2.1 g in boys, at age 6 months and 2 years, respectively (n = 76 children, mainly Caucasian). This corresponds to an increase in potassium body content of about 16 g over 18 months. Based on a sample of 292 Caucasian children aged 5–18 years, Ellis et al. (2000) found mean total body potassium content from 36.9 ± 4.8 g to 100.0 ± 41.8 g in girls aged 5–7 years and 17–19 years, respectively. In boys, the mean content was 41.9 ± 6.4 g and 152.4 ± 20.7 g at age 5–7 years and 17–19 years, respectively. This represents a total accretion of potassium of 64 g in girls and 111 g in boys over a period of 12 years. From these data, the net daily accretion of potassium in new tissues is estimated to range between ca. 10 and 50 mg/day depending on children's age and sex. The Panel notes that net daily accretion of potassium in new tissues only partly reflects children's potassium requirement.

The Panel considers that there are no data relating to potassium requirement which can be used for deriving DRVs for potassium for children.

5.4. Indicators of potassium requirement in pregnancy

Plasma potassium concentration has been observed to decrease during pregnancy by 0.2–0.4 mmol/L (Brown et al., 1986; Lindheimer et al., 1987). Despite increased filtered potassium load in the kidney and mineralocorticoid activity, healthy pregnant women do not typically develop hypokalaemia. Renal reabsorption of potassium accompanies the physiological changes which occur during pregnancy and urinary potassium excretion is held constant (Section 2.3.5.1).

Several studies have measured total body potassium in pregnant women using whole body counting. From a cohort of 40 women in the UK followed as of 12–22 weeks of pregnancy, Godfrey and Wadsworth (1970) estimated an accumulation of 307 mmol (12 g) potassium during pregnancy after correcting for possible analytical underestimation due to the changes in mass and body shape. In a longitudinal study of 22 pregnant Swedish women, total body potassium content was of 2,397 ± 327 mmol (93.5 ± 12.7 g), 2,224 ± 298 mmol (86.7 ± 11.6 g), 2,290 ± 330 mmol (89.3 ± 13.0 g), 2,507 ± 307 mmol (97.8 ± 12.0 g) before pregnancy and at 16–18, 30 and 36 weeks of pregnancy, respectively (Forsum et al., 1988). A total accretion of 283 mmol (around 11 g) potassium between weeks 16–18 and week 36 can be estimated from this study. In 34 US women with a normal BMI, Butte et al. (2003) reported total body potassium of 2,610 ± 328 mmol (101.8 ± 12.8 g), 2,543 ± 343 mmol (99.2 ± 13.4 g), 2,602 ± 338 mmol (101.5 ± 13.2 g) and 2,777 ± 382 mmol (108.3 ± 14.9 g) before pregnancy and at 9, 22 and 36 weeks of gestation, respectively. This would represent a total potassium accretion of 234 mmol (around 9 g) potassium between week 9 and week 36 of pregnancy. Both studies indicate that most potassium accretion occurs during the last trimester of pregnancy. During this period, a daily accretion in the order of 3 mmol (120 mg) potassium can be estimated from these data.

A total content of potassium in mature fetuses and full-term neonates between about 100 mmol (4 g) (Ellis et al., 1993) and 150 mmol (6 g) has been reported (Widdowson and Spray, 1951; Widdowson, 1980). Ziegler et al. (1976) and Widdowson (1980) estimated potassium accretion in the fetus based on data from chemical analyses of human fetuses (n = 22 and 38, respectively) and daily increments of weight gain. Daily potassium accretion rate was found to increase progressively over the course of pregnancy. Ziegler et al. (1976) found accretion rates from 0.5 mmol/day at 24–25 weeks to 1.5 mmol/day at 36–37 weeks. Widdowson (1980) reported values from 0.1 mmol/day at weeks 12–16 to 1.4 mmol/day at weeks 36–40 of pregnancy. Placental potassium content around 240 mmol/kg dry

weight has been reported (Challier et al., 1988). Considering a mean placenta dry weight of 92 g at term (Hohler et al., 1972), this would correspond to a net transfer of potassium to placental tissues of 22 mmol (858 mg) over the whole pregnancy.

The Panel considers that the requirement for the daily accretion rate of potassium in fetal and maternal tissues can be met by the adaptive changes which maintain potassium homeostasis during pregnancy.

5.5. Indicators of potassium requirement in lactation

Data on body potassium content changes during lactation are very limited. In a sample of 40 lactating and 36 non-lactating women in the USA, significantly greater losses in total body potassium content, measured by whole body counting, were found in lactating women than non-lactating women between 0.5 and 3 months postpartum (Butte and Hopkinson, 1998). The Panel notes that this indicates that total body potassium content decreases in lactating women; however, no quantitative data on the extent of potassium body losses in lactating vs non-lactating women are available from the paper.

Based on available data, the Panel estimates a loss of potassium of 400 mg (10 mmol)/day through breast milk during lactation (Section 2.3.5.4).

5.6. Potassium intake and health consequences

The level of potassium intake has been reported to be associated with several health outcomes. Most studies focused on its relation with cardiovascular endpoints and, in particular, blood pressure and stroke. Several other outcomes, such as bone health and kidney stones and metabolic disease, have also been investigated.

5.6.1. Cardiovascular disease-related outcomes

A large number of observational and intervention studies have addressed the relationship between the dietary intake of potassium and risk of cardiovascular disease in adults, focusing on blood pressure and hypertension, as well as the risk of stroke, ischaemic heart disease, and arrhythmia. This section summarises evidence mainly from meta-analyses of randomized controlled trials (RCTs) and prospective observational studies on the relationship between potassium intake and cardiovascular disease-related outcomes, particularly blood pressure, stroke and coronary heart disease. Where studies measured 24-hour urinary potassium excretion as a marker of potassium intake, the Panel applied a factor of 1.3 to estimate the corresponding daily potassium intake (Section 2.4.1).

5.6.1.1. Blood pressure

There is a direct relationship between blood pressure and risk of cardiovascular disease in the general population. The Panel notes that blood pressure is a continuum and studies conducted in people classified as hypertensive may inform the relationship between potassium intake and blood pressure in the general population. The Panel also notes that raised blood pressure affects a large proportion of the adult European population. According to WHO estimates, prevalence of raised blood pressure (defined as systolic and/or diastolic blood pressure equal to or above 140/90 mmHg) in adults aged ≥ 25 years is 44.5% in males and 37.1% in females in the European region (WHO, 2010). The Panel examined the data relating potassium intake to blood pressure when expressed as a continuous variable from intervention studies conducted in normotensive and/or hypertensive people. The Panel also reviewed the evidence, from observational studies, for an association between potassium intake and the risk of developing hypertension. The Panel notes that different criteria may have been used for defining "hypertension" across studies; the Panel uses the term as defined by the authors when describing the individual studies.

Data in adults

(a) Evidence from randomised controlled trials

Several meta-analyses of RCTs have been conducted on the effect of potassium intake on blood pressure. These include a Cochrane review (Dickinson et al., 2006), a meta-analysis commissioned by WHO (Aburto et al., 2013) as a basis for its guideline on potassium intake (WHO, 2012a), an update of the latter by the Food Standards Australia New Zealand (FSANZ, 2014), and a more recent meta-analysis by Binia et al. (2015). These meta-analyses differ with respect to their inclusion criteria. The review by Dickinson et al. (2006) was limited to RCTs carried out in hypertensive subjects, with at least 8 weeks of potassium intervention and with no other intervention than manipulation of the potassium intake. Aburto et al. (2013), FSANZ (2014) and Binia et al. (2015) included RCTs in both normotensive and hypertensive subjects, with a minimum period of potassium intervention of 4 weeks, and which reported 24-hour urinary potassium at the end of the intervention as a marker of potassium intake. Aburto et al. (2013) and FSANZ (2014) included studies in hypertensive subjects with or without blood pressure-lowering medication, while Binia et al. (2015) restricted the included studies to those performed on hypertensive subjects without medication. For the three latter meta-analyses, studies manipulating other dietary factors in addition to potassium intake (such as changes in sodium intake) were eligible.

In the meta-analysis by Dickinson et al. (2006) in hypertensive subjects, five RCTs (n = 425) met the inclusion criteria. Four studies used potassium supplements (between 1,872 mg (48 mmol) and 4,680 mg (120 mmol) per day; background intake levels were not reported), while in one study participants were advised to increase their dietary intake of potassium (>100 mmol/day). Potassium supplementation compared to control resulted in an overall reduction in systolic blood pressure (SBP) of −11.2 mmHg (95% CI = −25.2–2.7; I^2 = 98%) and in diastolic blood pressure (DBP) of −5.0 mmHg (95% CI = −12.5–2.4; I^2 = 99%). Sensitivity analysis restricted to the two high quality trials found overall reductions in SBP of −7.1 mmHg (95% CI = −19.9–5.7; I^2 = 87%) and in DBP of −5.5 mmHg (95% CI= −14.5–3.5; I^2 = 87%). The Panel notes that all studies included involved hypertensive subjects without blood pressure-lowering treatment. Despite the high heterogeneity, the Panel notes that the point estimates obtained in both the overall analysis and with the high-quality studies suggest a blood pressure-lowering effect of potassium supplementation. The Panel also notes that no additional studies which meet the inclusion criteria of this meta-analysis have been published to date.

The meta-analysis by Aburto et al. (2013) included 21 RCTs (n = 1,892), of which 16 studies were conducted in treated and untreated hypertensive subjects, three studies in normotensive subjects and two studies in mixed populations. In the overall analysis, increased potassium intake, through supplementation or dietary advice, reduced SBP by −3.49 mmHg (95% CI = −5.15–−1.82; I^2 = 65%) and DBP by −1.96 mmHg (95% CI = −3.06–−0.86; I^2 = 55%) compared with the controls. When restricting the assessment to the three studies in normotensive adults, no effect of potassium supplementation on blood pressure was found. When only the studies in treated and untreated hypertensive subjects were considered, an increased potassium intake reduced SBP (−5.32 mmHg; 95% CI = −7.20–−3.43; I^2 = 21%)) and DBP (−3.10 mmHg; 95% CI = −4.53– −1.66; I^2 = 24%)). Effects of potassium intake on blood pressure levels were also found in sub-group analyses according to the use of blood pressure-lowering treatment (hypertensive subjects without treatment: SBP change: −3.63 mmHg; 95% CI = −5.69–−1.57; I^2 = 72%; and DBP change: −1.37 mmHg; 95% CI = −2.50–−0.23; I^2 = 51%); pharmacologically-treated hypertensive subjects: SBP change: −5.85 mmHg; 95% CI = −10.61–−1.08; I^2 = 34%) and DBP change: −3.80 mmHg; 95% CI = −8.25–0.66; I^2 = 66%)).

Aburto et al. (2013) conducted subgroup analyses where studies were classified according to the 'achieved' potassium intake in the intervention groups (estimated by multiplying urinary potassium following potassium supplementation by a factor of 1.30), the duration of the intervention, or the population average sodium intake at baseline.

The 'achieved' potassium intake in the intervention group was below 3,500 mg (90 mmol)/day in two studies, between 3,500 and 4,700 mg (90 and 120 mmol)/day in five studies, between 4,700 and 6,000 mg (120 and 155 mmol)/day in 11 studies and ≥ 6,000 mg (155 mmol)/day in four studies. The largest reduction in SBP and DBP was found in the subgroup characterised by an 'achieved' potassium intake of 3,500–4,700 mg (90–120 mmol)/day. The SBP and DBP changes were −7.16 mmHg (95% CI = −12.41–−1.91; I^2 = 71%) and −4.01 mmHg (95 % CI = −8.44–0.42; I^2 = 75%), respectively. A reduction in blood pressure was already apparent in the subgroup of studies with a potassium intake below 3,500 mg (90 mmol)/day. The Panel notes that all studies were included in this subgroup analysis (i.e. studies in normotensive, hypertensive and mixed populations). No separate subgroup analyses were carried out which included only studies in normotensive or hypertensive people.

No effect of duration of intervention (< 2 months, 2–4 months and > 4 months) was found.

A larger blood pressure-lowering effect of potassium was observed in the subgroup of studies with the highest baseline sodium intakes (> 4 g/day) compared to the subgroups of studies with lower sodium intakes (< 2 g/day and 2–4 g/day).

FSANZ (2014) revised the meta-analysis of Aburto et al. (2013) and included one newly-published study (Matthesen et al., 2012). The latter had found no effect of supplementation with 3,900 mg (100 mmol) potassium/day for 28 days on either 24-hour or central blood pressure in 21 Danish normotensive subjects, whose background potassium intake was around 3,800 mg (99 mmol)/day based on urinary potassium excretion. The revision and the update had a limited impact on the overall effect estimates and FSANZ concluded that the results of the analysis from Aburto et al. (2013) remained valid.

The meta-analysis by Binia et al. (2015) included 14 RCTs. Most of the studies had a potassium intervention of 2,340–2,535 mg/day (60–65 mmol/day), three had a potassium intervention of 1,560 mg/day (40 mmol/day) or less and one study had a potassium intervention at least 4,680 mg (120 mmol/day). The 24-hour urinary potassium excretion increased to between 55 mmol (2,145 mg) and 200 mmol (7,800 mg) in the intervention groups. Results of overall analysis yielded an effect of potassium intervention on SBP of −4.7 mmHg (95% CI = −7.0–−2.4; I^2 = 79%) and on DBP of −3.5 mmHg (95% CI = −5.7–1.3; I^2 = 93%). When limiting the analysis to untreated hypertensive subjects (10 trials), larger reductions in SBP and DBP were observed. Total daily urinary potassium excretion between 2,300 and 3,900 mg (60 and 100 mmol)/day, corresponding to potassium intakes from 2,900 to 4,900 mg (75 to 125 mmol), was associated with the highest blood pressure reduction; no dose–response effect was identified. The Panel notes that subgroup analyses according to normotensive vs. hypertensive status were not carried out. The Panel notes that results from two of the trials (Chalmers et al. (1986) and He et al. (2010)) were partially considered in the analysis and that two eligible trials (Grobbee et al., 1987; Matthesen et al., 2012) were not included.

One additional RCT has become available since these meta-analyses were published. This involved 37 untreated (pre)hypertensive men and women (baseline SBP: 130–159 mmHg) given a potassium supplement of 2,800 mg/day together with a controlled background diet (sodium: 2400 mg/day; potassium: 2,300 mg/day) for four weeks (Gijsbers et al., 2015). 24-hour ambulatory blood pressure was reduced in the intervention group compared to the control group (mean difference SBP −3.9 mmHg (95% CI = −6.9–−0.9); DBP −1.6 mmHg (95% CI = −3.2–−0.1)). Office SBP (−3.0 mmHg, 95% CI = −6.7–0.6) but not DBP (−0.3 mmHg, 95% CI = −2.1–1.6) was reduced in the intervention group compared with the controls.

The Panel considers that there is evidence from RCTs for a beneficial effect of potassium intake on blood pressure in subjects classified as hypertensive (with or without medication), but not in subjects classified as normotensive. The Panel further notes that in the analysis from Aburto et al. (2013), which combined studies in hypertensive and normotensive subjects, the largest reduction in SBP and

DBP was found in the subgroup characterised by an 'achieved' potassium intake of 3,500–4,700 mg (90–120 mmol)/day, compared with lower and higher amounts.

(b) Evidence from observational cohort studies

Two longitudinal observational studies assessed the association between urinary potassium excretion and incidence of hypertension.

A study conducted in Taiwan included 1,520 middle-aged and older subjects who were free from hypertension at baseline (Chien et al., 2008). Participants were asked to collect their overnight urine and sleep time was recorded in order to estimate 24-hour urinary excretion of potassium. Incident hypertension cases were diagnosed according to office blood pressure measurements and medication history. During a median of 7.93 years of follow-up (interquartile range (IQR) 4.07–9.04 years), 669 cases of incident hypertension were documented. No association was found between potassium excretion and risk of hypertension in a multivariate model. The Panel, however, notes the methodological limitation of using an overnight urine collection to estimate daily potassium excretion.

Risk of hypertension was studied in 5,511 normotensive subjects of Caucasian origin from the Netherlands, aged 28 to 75 years (Kieneker et al., 2014). This population was part of the Prevention of Renal and Vascular End-Stage Disease (PREVEND) study, which recruited a cohort of 8,592 individuals in 1997–1998, oversampling subjects with albuminuria (Kieneker et al., 2016). Potassium excretion was measured in two 24-hour urine specimens at baseline (1997–1998) and midway during follow-up (2001–2003). Baseline median potassium excretion was 70 mmol/24 hours (IQR 57–85 mmol/24 hours), which corresponds to a dietary potassium intake of approximately 3,500 mg (91 mmol)/day. The within-subject correlations for potassium excretion between the paired 24-hour urine collections at the first and second examinations were $r = 0.59$ ($p < 0.0001$; $n = 5,489$) and $r = 0.64$ ($p < 0.0001$; $n = 4,410$), respectively. The within-subject correlation between the averaged potassium excretions of the first and the second examinations (separated by a median of 4.3 years; IQR 4.0–4.8 years) was $r = 0.49$ ($p < 0.0001$; $n = 4,429$). Incident hypertension cases were diagnosed according to office blood pressure measurements and medication history. During a median follow-up of 7.6 years (IQR 5.0–9.3 years), 1,172 subjects developed hypertension. The lowest sex-specific tertile of potassium excretion (men: < 68 mmol/24 hours; women: < 58 mmol/24 hours) had an increased risk of hypertension after multivariable adjustment (hazard ratio (HR) = 1.20; 95% CI = 1.05–1.37), compared with the upper 2 tertiles combined ($P_{\text{nonlinearity}} = 0.008$). A multivariable-adjusted spline curve indicated a nonlinear inverse association of urinary potassium excretion with risk of hypertension. A higher risk of hypertension was found with potassium excretion levels lower than 70 mmol/24 hours, corresponding to a potassium intake of 3,500 mg (90 mmol)/day.

Three prospective cohort studies in adults have investigated the association between potassium intake, estimated through dietary assessment, and subsequent blood pressure levels and/or hypertension incidence.

Ford and Cooper (1991) analysed data from the US National Health and Nutrition Examination Survey (NHANES) Epidemiologic Follow-up study (1971–1984). Dietary intake of potassium at baseline was estimated through a 24-hour recall dietary questionnaire (mean = 2,145 mg/day). The average SBP and DBP data from two readings taken at the follow-up examination (mean follow-up 10 years) were used to determine hypertensive status in a total of 5,411 white and black men and women free from hypertension at baseline, and with complete dietary data available for analysis. Dietary potassium intake at baseline was not associated with the incidence of hypertension (1,438 cases) in multivariate analysis, when adjusting for age and energy intake. The Panel notes the methodological limitation of a single 24-hour dietary recall in assessing usual potassium intake of individuals.

A large prospective study involved 30,681 predominantly white US male health professionals, 40–75 years old, without diagnosed hypertension at baseline (Ascherio et al., 1992). Potassium intake at baseline was measured by a semi-quantitative FFQ (validated with 2 weeks of dietary records;

correlation for potassium = 0.65). The lowest category of potassium intake was < 2,400 mg (61 mmol)/day and the highest category of potassium intake was ≥ 3,600 mg (92 mmol)/day. In this cohort, 1,248 men self-reported a diagnosis of hypertension during the 4 years of follow-up. No associations were observed between potassium intake and blood pressure levels at baseline and at the end of follow-up, or blood pressure changes during the follow-up, when calcium, magnesium and dietary fibre were considered in the model, except for DBP level at baseline. No association was found in multivariate analysis between potassium intake and risk of hypertension, after adjustment for potential dietary confounders (calcium, magnesium and dietary fibre) in addition to age, BMI and alcohol intake.

Another large prospective study involved 41,541 predominantly white US female nurses, aged 38 to 63 years, without hypertension at baseline (Ascherio et al., 1996) updating a previous report in the same cohort (Witteman et al., 1989). Potassium intake at baseline was measured through a semi-quantitative FFQ (validated from 2 weeks of dietary records; correlation for potassium = 0.61). The lowest of five categories of potassium intake was < 2,000 mg (51 mmol)/day and the highest potassium intake category was ≥ 3,200 mg (82 mmol)/day. A total of 2,526 women reported to have had a diagnosis of hypertension during the 4 years of follow-up. Using a multivariate analysis, no association was found between potassium intake and the risk of hypertension, across the various categories of daily potassium intake (< 2,000 , 2,000–2,390, 2,400–2,790, 2,800–3,190, ≥ 3,200 mg), adjusting for calcium, magnesium and dietary fibre intake in addition to age, BMI and alcohol consumption. Among women who did not report being diagnosed with hypertension, no associations were observed between potassium intake and subsequent (after 2 or 4-years follow-up) self-reported blood pressure levels, when calcium, magnesium and dietary fibre were considered in a multivariate regression model.

The Panel is aware of the inherent limitations in observational studies in relation to exposure misclassification (particularly for studies based on dietary questionnaires) or unmeasured confounding. Overall, the Panel notes that the study by Kieneker et al. (2014), which used a multiple assessment of 24-hour urinary potassium excretion and which was carried out in a European population, provides evidence for an inverse association between potassium intake and risk of hypertension. In this study, an increased risk of hypertension was observed in the lowest tertile of potassium excretion (men: < 68 mmol/24 hours; women: < 58 mmol/24 hours). A spline regression analysis indicated a higher risk of hypertension with urinary potassium excretion lower than 70 mmol/24 hours, corresponding to a potassium intake of 3,500 mg (90 mmol)/day.

Data in children

The relationship between potassium intake and blood pressure levels has also been studied in children.

WHO (2012b) carried out a meta-analysis of three intervention studies conducted in children. It included a RCT in African-American boys and girls aged 13–15 years without hypertension (Wilson et al., 1996), a RCT in individuals averaging 13 years of age and whose blood pressure was > 109 mmHg for boys and > 108 mmHg for girls (Sinaiko et al., 1993) and one non-randomised trial in normotensive boys and girls aged 11–14 years (Miller et al., 1987). The interventions consisted of three weeks with a high potassium (80 mmol/day; n = 20) vs usual diet (n = 20) (Wilson et al., 1996), three years with potassium supplementation (1 mmol/kg bw per day; n = 71) vs placebo (n = 69) (Sinaiko et al., 1993), and four weeks with potassium supplementation (36.2 ± 12.8 mmol/day for girls and 45.0 ± 17.4 mmol/day for boys; n = 38) (Miller et al., 1987), respectively. Children were characterised by background dietary potassium intakes in the order of 2,000 mg (51 mmol)/day (Wilson et al., 1996), 2,800 mg (72 mmol)/day (Sinaiko et al., 1993) and 1,900 mg (49 mmol)/day (Miller et al., 1987), as estimated through urinary potassium excretion. When pooling the estimates, there was no effect of potassium supplementation on blood pressure levels (−0.28 mmHg (95% CI =−1.05–0.49) for resting SBP and −0.92 mmHg (−2.00–0.20) for resting DBP).

In another case-cross-over RCT in 24 normotensive blacks and whites (aged 14.1 ± 1.6 and 15.4 ± 2.1 years, respectively), who received 40 mmol/day potassium supplement or a placebo for

seven days and then the alternate treatment, no effect of the potassium supplementation was found on blood pressure levels (Pratt et al., 1997).

Three observational cohort studies on potassium intake and subsequent blood pressure levels have been carried out in children.

The first study by Geleijnse et al. (1990) assessed urinary potassium excretion in 233 Dutch children (mean (± SD) age: 13.2 (± 2.7) years; range 5–17 years), who were followed for an average of seven years. Average potassium excretion during the follow-up was determined on the basis of six or more annual overnight urine samples. During the study period, age showed no independent association with estimated potassium intake. Office blood pressure (average of two readings) was assessed yearly. The subjects in the upper urinary potassium tertile (≥ 47.8 mmol/day), compared with those in the lowest tertile (≤ 37.7 mmol/day), had a lower increase in SBP during an average follow-up of 7 years (1.4 vs 2.4 mmHg, p = 0.007), while no association was found for DBP.

Brion et al. (2008) investigated the association between potassium intake in infancy (1-day diary at 4 months and three-day diary at 8 months of age, including breastfeeding) and office blood pressure (average of two readings) at 7 years in children of the Avon Longitudinal Study of Parents and Children. In age- and sex-adjusted models, higher potassium intake at 4 months of age (n = 533) was associated with higher SBP at follow-up (mean difference per 1 SD potassium = 0.89 mmHg; 95% CI = 0.09–1.69, p = 0.03). No association was found with potassium intake at 8 months (n = 710; mean difference = 0.12 mmHg/SD; 95% CI = −0.59–0.83; p = 0.7).

Buendia et al. (2015) assessed the association between potassium intake and blood pressure in a US cohort study including 2,185 black and white girls initially aged 9 to 10 years and who were followed up for 10 years. Potassium intake was estimated through 3-day diet records in 8 of the 10 study years and blood pressure as the average of two readings taken every year. Potassium intake was inversely associated with the magnitude of blood pressure change throughout adolescence (p < 0.001 for SBP and DBP) and at the end of follow-up (p = 0.02 for SDP and p = 0.05 for DBP). In the multivariate analysis adjusting for the largest number of potential confounders and using the potassium residuals method, there was an inverse association of potassium intake with SBP in black and with DBP in white subjects, with lower blood pressure values in the highest daily potassium intake category (≥ 2,400 mg (61 mmol)/day).

The Panel notes that two prospective observational studies suggest that a "higher" potassium intake is associated with a reduction in the age-related increase in blood pressure. A limited number of intervention studies with total potassium intake between 1,700 and 5,100 mg (43 and 130 mmol)/day, and lasting one week to three years were carried out in children with baseline potassium intakes between 1,900 and 2,800 mg (49–72 mmol)/day. These studies did not show an effect of potassium supplementation on blood pressure levels. The Panel notes the small sample size of these studies and considers that available evidence is limited and cannot be used for the setting of DRVs for potassium for children.

Factors affecting the relationship between potassium intake and blood pressure

(a) Sodium intake

In their meta-analysis, Aburto et al. (2013) conducted subgroup analyses according to levels of sodium intake, as assessed through baseline urinary sodium excretion (Section 5.6.1.1). The largest blood pressure-lowering effect of potassium was associated with the highest category of sodium intake (greater than 4 g/day) compared to the lower categories (< 2 g/day and 2–4 g/day). The summary estimates for SBP changes in the respective categories were −6.91 mmHg (95% CI = −11.53–−2.29), −1.97 mmHg (95% CI = −3.41–−0.52) and −2.00 mmHg (95% CI = −11.70–7.70), while summary estimates for DBP changes were −2.87 mmHg (95% CI = −6.96–1.22), −1.96 mmHg (95% CI = −3.16–−0.76) and 0.00 mmHg (95% CI = −6.12–6.12). When the meta-analysis was restricted to

studies on individuals with hypertension, the systolic blood pressure was further reduced in those studies where the baseline sodium intake was 2–4 g/day (−4.07 mmHg; 95% CI = −5.76–−2.37).

The Panel notes that these data indicate that the blood pressure-lowering effect of potassium is observed in subjects consuming 2–4 g/day of sodium and is greater in subjects consuming more than 4 g/day of sodium, compared with lower levels of sodium intake.

(b) Sodium-to-potassium intake ratio

Attention has also been paid to the possibility that the sodium-to-potassium intake ratio, rather than potassium and sodium intakes independently, may be related to hypertension or generally blood pressure outcomes (Perez and Chang, 2014), or that such ratio may independently influence blood pressure besides potassium (or sodium) intake itself (Binia et al., 2015).

In a systematic review by Perez and Chang (2014), evidence from RCTs carried out in hypertensive subjects suggests that the sodium-to-potassium ratio is more strongly associated with blood pressure outcomes than either sodium or potassium alone (supported by 7 out of 13 studies). All studies except one included in this meta-analysis estimated the sodium-to-potassium intake ratio based 24-hour urinary excretion collections. The methodological quality of studies which provided support for a greater hypotensive effect of low sodium combined with high potassium intakes compared to low sodium or high potassium alone (seven studies including four large RCTs that followed subjects for at least four weeks) was generally stronger than that characterizing the studies that found no effect (three studies, with small study sizes or which used dietary intervention as ancillary treatment). RCTs in normotensive subjects were scarce. A number of observational studies (1 prospective cohort and 23 cross-sectional studies) were also included in the review. The prospective cohort and the majority of the cross-sectional studies reported that the sodium-to-potassium ratio was more strongly associated with hypertension and/or systolic and diastolic blood pressure levels than either sodium or potassium alone. In two prospective cohort studies not included in this systematic review, no association was found between the sodium-to-potassium excretion ratio and the risk of incident hypertension after multivariate adjustment (Chien et al., 2008; Kieneker et al., 2014).

In their meta-regression analyses of 11 RCTs which assessed the effect of potassium intake on blood pressure levels in normotensive (1 study) and hypertensive subjects (10 studies), Binia et al. (2015) found that the addition of the sodium-to-potassium excretion ratio in the model better explained the effect of potassium supplementation in reducing SBP.

(c) Ethnic and genetic factors

Ethnic factors have been associated with differential blood pressure response to potassium in a few observational studies (Liu et al., 2001; Stamler et al., 2013; Bartley et al., 2014), while evidence from intervention studies is limited (Whelton et al., 1995).

A few studies have investigated the potential ability of some SNPs to modify the blood pressure response to modifications in potassium intake (generally associated with dietary sodium manipulations). In Chinese populations, some SNPs have been found to modify such relation, including common genetic variants of the adiponectin gene (Chu et al., 2016), of nuclear receptor subfamily 3, group C, member 2, angiotensin II type 1 receptor, hydroxysteroid (11-beta) dehydrogenase 1, and hydroxysteroid (11-beta) dehydrogenase 2 genes (He et al., 2011), and endothelin 1 (Montasser et al., 2010). A cross-sectional report from the large EPIC-Norfolk study has shown that the association between urinary sodium-to-potassium ratio and blood pressure was modified by the SNP rs17238540 in the HMGCR gene (Freitas et al., 2009). The Panel notes that the clinical significance and the size of the effects of possible interactions between genetic characteristics and blood pressure response to potassium intake are not well defined. Data in European and Western populations are limited.

(d) Conclusion

The Panel notes that most data available to date come from studies conducted in adult populations.

The Panel considers that the potential modification of the effect of potassium intake on blood pressure levels by sodium intake, sodium-to-potassium intake ratio, salt sensitivity, ethnic and genetic factors needs to be further investigated and available evidence cannot be used for the setting of DRVs for potassium.

Overall conclusion on potassium and blood pressure

The Panel considers that there is evidence from RCTs lasting from four weeks to three years for a beneficial effect of potassium intake on blood pressure in subjects classified as hypertensive (with or without medication), but not in subjects classified as normotensive. In the analysis from Aburto et al. (2013), which combined studies in hypertensive and normotensive people, the largest reduction in SBP and DBP was found in the subgroup characterised by an 'achieved' potassium intake of 3,500–4,700 mg (90–120 mmol)/day, compared with lower and higher amounts. The Panel notes that the only observational prospective cohort study which assessed potassium intake through potassium excretion based on multiple 24-hour urine collections and was carried out in a European adult population of normotensive people, with a follow-up of 7.6 years, reported an inverse association between potassium intake and hypertension incidence, with an increased risk observed for potassium intake below 3,500 mg (90 mmol)/day (Kieneker and al., 2014).

5.6.1.2. Stroke

A number of prospective cohort studies have investigated the association between potassium intake and risk of stroke and have been combined in several systematic reviews and meta-analyses. Appendix H features the four most recent meta-analyses (Larsson et al., 2011a; WHO, 2012d; Aburto et al., 2013; D'Elia et al., 2014; Adebamowo et al., 2015b), including an overview of the studies included and respective pooled estimates. Overall, 13 prospective cohort studies contributed to these meta-analyses (from 10 to 12 studies per meta-analysis), of which 8 were included in all of the four meta-analyses. Individual studies assessed potassium intake through dietary questionnaires (11 studies) or urinary potassium excretion (2 studies), investigated stroke incidence (11 studies) or stroke mortality (2 studies), had 4 to 19 years of follow-up, and were conducted in the USA (6 studies), Europe (4 studies), Asia (2 studies) or over several continents (1 study). Based on most adjusted study-specific RRs, pooled RRs between 0.76 (95% CI = 0.66–0.88) and 0.91 (95% CI = 0.88–0.94) were found when the highest category of potassium intake was compared to the lowest.

Larsson et al. (2011a) conducted a dose–response meta-analysis by using a restricted cubic spline analysis. Data from eight prospective cohort studies, which reported relative risks (RRs) and 95% CIs for at least three quantitative categories of potassium intake, were used in the model. The lowest value of 1,053 mg/day of potassium intake was used for the estimation of all relative risks. The analysis showed a linear decrease in the risk of total stroke with increasing potassium intake up to around 3,500 mg/day. Above this value, the inverse relationship is weakened and more uncertain (wide confidence interval).

In an analysis in which the risk ratios of the individual studies were stratified according to the level of potassium intake in the comparison groups (7 studies, 13 comparisons), Aburto et al. (2013) found that the risk of incident stroke was lowest when the intake was between 3,500 and 4,680 mg (90 and 120 mmol)/day (RR = 0.70; 95% CI = 0.56–0.88).

Additional prospective cohort studies have been published after these meta-analyses, including two studies which measured urinary potassium excretion as a surrogate for potassium intake (O'Donnell et al., 2014; Kieneker et al., 2016) and four studies which estimated potassium intake through validated FFQs (Seth et al., 2014; Sluijs et al., 2014; Adebamowo et al., 2015a; Adebamowo et al., 2015b).

O'Donnell et al. (2014) investigated the association between 24-hour potassium excretion as estimated from a single fasting morning urine specimen (the Kawasaki formula was used to extrapolate to 24-hour urinary excretion) and stroke incidence in the Prospective Urban Rural Epidemiology (PURE) cohort study (mean follow-up = 3.7 years). A total of 101,945 adults aged 35 to 70 years from 17 countries (mainly from China (> 40%) and only 2% from European population (Poland)) were involved. The study population included normotensive and hypertensive subjects, with and without treatment. Estimated 24-hour urinary excretion was 54 ± 15 mmol (mean ± SD), corresponding to an intake of 2,700 mg (70 mmol)/day. A total of 872 cases of stroke occurred. In the most adjusted multivariate analysis (no adjustment for blood pressure), the OR for the highest (>78 mmol/24 hours) vs. the lowest (< 38 mmol/24 hours) categories was 0.97 (95% CI = 0.72–1.31) and ORs for stroke did not show any linear trend across categories of potassium excretion. The Panel notes that the level of stratification used in this study does not allow the relationship for potassium excretions above 78 mmol, corresponding to intakes above 3,955 mg (100 mmol)/day to be explored. The Panel also notes the very small representation of European people, the relatively small number of cases and the use of a single fasting morning urine specimen to estimate daily potassium excretion which may result in exposure misclassification (Section 2.4.1).

Sluijs et al. (2014) examined the risk of stroke in 36,094 Dutch subjects enrolled in two cohorts (age range: 21–70 years). During a 12 year follow-up, 631 stroke cases occurred (360 ischemic stroke, 170 haemorrhagic stroke, 101 of unknown type). Mean (± SD) daily intake of potassium was 3,672 ± 903 mg (94 ± 23 mmol)/day. After adjustment for potential confounders (including dietary calcium; no adjustment for blood pressure), the RRs for stroke were 0.82 (95% CI = 0.65–1.03) for the 2nd quartile (3060–3587 mg/day), 1.01 (95% CI = 0.78–1.30) for the 3rd quartile (3,588–4,186 mg/day) and 0.95 (95% CI = 0.68–1.33) for the 4th quartile (≥ 4,187 mg (107 mmol)/day), compared with the 1st quartile (≤ 3,059 mg (78 mmol)/day). The Panel notes the use of FFQ to estimate potassium intake and that the level of potassium intake in this population was in the highest range among available studies.

Seth et al. (2014) investigated the risk of stroke in 90,137 US postmenopausal women (50–79 years) from the Women's Health Initiative (WHI) observational study. A total of 3,046 cases (2,190 ischemic stroke, 484 haemorrhagic stroke) were recorded during an average follow-up of 11 years. The average potassium intake was 2,611 mg (67 mmol)/day. In multivariate analyses (adjusted for hypertension status), lower incidence of all stroke (HR = 0.88; 95% CI = 0.79–0.98) and ischemic stroke (HR = 0.85; 95% CI = 0.75–0.96) were found when comparing the second quartile (⩾ 1,925.5–2,519.4 mg (49–65 mmol)/day) to the first quartile (<1,925.5 mg (< 49 mmol)/day) of potassium intake. These effects were limited to individuals not affected by hypertension at baseline (all stroke Q2 vs Q1: HR = 0.75; 95% CI = 0.64–0.89; ischemic stroke Q2 vs Q1: HR = 0.71; 95% CI = 0.58–0.86). Similar results were obtained when Q3 or Q4 were compared to Q1. There was no association with haemorrhagic stroke in this study. The Panel notes the use of FFQ to estimate potassium intake.

In a US cohort of 42,669 male health professionals (40–75 years at enrolment), 1,547 events were observed during 24 years of follow-up (Adebamowo et al., 2015a). In the fully adjusted model (including magnesium and calcium intakes and history of hypertension), the RR for the highest quintile (mean intake = 4,438 mg (113 mmol)/day) vs the lowest quintile (2,600 mg (66 mmol)/day) was 0.93 (95% CI = 0.75–1.15; p trend = 0.44). After stratifying for sources of potassium intake, the RR associated to potassium from diet alone was 1.01 (95% CI = 0.80–1.27; p trend = 0.96), while that associated with potassium from dietary supplements was 0.73 (95% CI = 0.53–0.99; p trend = 0.05). The Panel notes the use of FFQ to estimate potassium intake.

In two cohorts of US women (n = 86,149 in NHS I; n= 94,715 in NHS II; 25–55 years at enrolment) with 3,780 cases over the 30 years of total follow-up, the pooled RR for the highest quintile of total potassium intake (means Q5: NHS I, 3,590 mg (92 mmol)/day; NHS II, 3,261 mg (84 mmol)/day) vs the lowest (mean Q1: NHS I, 2,247 mg (58 mmol)/day; NHS II, 2,315 mg (59 mmol)/day) was 0.91 (95% CI = 0.78–1.06; p trend = 0.16) in the fully adjusted multivariate model (including magnesium and calcium intakes and history of hypertension) (Adebamowo et al., 2015b). The pooled RRs for

hemorrhagic stroke were 0.81 (95% CI = 0.56–1.16) and for ischaemic stroke 0.89 (95% CI = 0.72–1.11), respectively. Pooled RRs for all stroke were 1.00 (95% CI = 0.84–1.18; p trend = 0.76) when only potassium from dietary sources was considered. The Panel notes the use of FFQ to estimate potassium intake.

Kieneker et al. (2016) investigated the association between urinary potassium excretion and risk of stroke in a Dutch population within the PREVEND study (median follow-up: 10.5 years). The population included 7,795 subjects free of cardiovascular events at baseline (age range: 28–75 years), with oversampling of subjects with albuminuria. Potassium excretion was measured in two 24-hour urine samples both at the study start (1997–1998) and during the follow-up (2001–2003). For events occurring after 2003, the mean of the two baseline and two follow-up 24-hour urinary excretion was used in the analysis. Median baseline potassium excretion was 70 mmol/day (IQR 56–84 mmol/day), corresponding to a daily intake of 3,500 mg (2,184–3,549 mg). There was no association between potassium excretion and subsequent incidence of stroke (172 events; HR per each 26-mmol/24-hour increase in urinary potassium excretion = 1.13; 95% CI = 0.88–1.46), in the fully adjusted model (including 24-hour urinary sodium and magnesium excretion; no adjustment for blood pressure). Taking Q3 (64–76 mmol/24 hours) as the reference, HRs were 0.76 (95% CI = 0.49–1.18) for Q1 (< 50 mmol/24 hours), 0.82 (0.67, 1.72) for Q2, 1.07 (0.67, 1.72) for Q4, and 1.01 (95% CI = 0.59–1.73) for Q5 (> 90 mmol/24 hours). There was no evidence of effect modification by 24-hour sodium excretion, hypertensive status, gender and other factors, neither of effects of oversampling subjects with albuminuria as ascertained with sensitivity analysis. The Panel notes that the number of stroke cases in this study was low and the level of potassium intake in this population was in the highest range among available studies.

Evidence for a possible modifying effect of hypertensive status on the potassium–stroke relationship is unclear and inconsistent. In a Swedish cohort study the risk of stroke was inversely and strongly associated with baseline potassium intake in hypertensive women, while no association emerged in normotensive women (Larsson et al., 2011b). These findings contrast with those observed in the WHI observational study (Seth et al., 2014), where an inverse association with risk of stroke, and specifically of ischaemic stroke, was only apparent in women without hypertension.

Conclusion

The Panel is aware of the inherent limitations in observational studies in relation to exposure misclassification (particularly for studies based on dietary questionnaires) or unmeasured confounding. The Panel notes that there is evidence from available meta-analyses for an inverse relationship between potassium intake and risk of stroke. The dose–response analysis conducted by Larsson et al. (2011a) shows a linear decrease in the risk of total stroke with increasing potassium intake up to around 3,500 mg (90 mmol)/day. Above this value and taking into account the most recent cohort studies, the risk of stroke does not appear to decrease further.

5.6.1.3. Coronary heart disease and overall cardiovascular disease

Seven observational prospective studies have investigated the association between potassium intake and the risk of coronary heart disease or myocardial infarction (incidence or mortality). Five studies measured urinary potassium excretion as a surrogate for potassium intake (Tunstall-Pedoe et al., 1997; Geleijnse et al., 2007; O'Donnell et al., 2011; O'Donnell et al., 2014; Kieneker et al., 2016) and two studies estimated potassium intake through dietary questionnaires (Bazzano et al., 2001; Umesawa et al., 2008). When comparing the highest to the lowest categories of potassium intake or excretion, four studies reported inverse associations, two studies found positive associations, and one study found no association between potassium intake and the risk of coronary heart disease or myocardial infarction. There was substantial uncertainty associated with all risk estimates. The Panel considers that, overall, these studies provided unclear and inconsistent evidence for an association between potassium intake and coronary heart disease risk.

A number of cohort studies also investigated the relationship between potassium intake and "overall cardiovascular disease" (Geleijnse et al., 2007; Umesawa et al., 2008; Cook et al., 2009; O'Donnell et al., 2011; O'Donnell et al., 2014; Kieneker et al., 2016). A meta-analysis of the four studies published until 2013 yielded a summary RR of 0.88 (95% CI = 0.70–1.10; I^2 = 69%) (Aburto et al., 2013). However, the Panel notes that different definitions of "overall cardiovascular disease" were applied in these studies, covering heterogeneous endpoints (i.e., stroke and coronary disease were included in all cases, plus different additional cardiovascular outcomes), thus hampering comparisons between studies and data interpretation.

Therefore, the Panel concludes that the results of these studies do not yield additional evidence that could inform the setting of DRVs for potassium.

5.6.1.4. Conclusion on cardiovascular disease-related outcomes

The Panel notes the strengths and limitations of the evidence on the relationship between potassium intake and cardiovascular outcomes and considers that there is evidence that a potassium intake of 3,500 mg (90 mmol)/day has beneficial effects on blood pressure in adults. Furthermore, there is consistent evidence that potassium intake below 3,500 mg (90 mmol)/day is associated with a higher risk of stroke. Results on the association between potassium intake and coronary heart disease are unclear and inconsistent.

Overall, the Panel considers that the evidence on the relationship between potassium intake and blood pressure and stroke can be used for setting DRVs for potassium for adults.

5.6.2. Diabetes mellitus type 2

A few prospective cohort studies have investigated the association between potassium intake and risk of metabolic disease, in particular, diabetes mellitus type 2.

No association was found between baseline 24-hour urinary potassium excretion and risk of type 2 diabetes over 18 years follow-up in a cohort of 1,935 Finnish individuals aged 35–64 years (Hu et al., 2005).

Colditz et al. (1992) found an inverse association between dietary potassium intake (assessed with a semi-quantitative FFQ) and the risk of type 2 diabetes in a 6 year prospective cohort of non-obese registered nurses in the USA (RR in Q1 vs Q5, 0.62; X trend −2.65 (p = 0.008)). In two prospective studies carried out in the USA, no association was found between dietary potassium intake (assessed by FFQ) and risk of incident diabetes in a cohort of 1,475 adults aged 45–65 years (9 years follow-up) and in a cohort of 4,754 subjects aged ≥ 65 years (median follow-up of 12 years), after adjusting for potential confounders (Chatterjee et al., 2010; Chatterjee et al., 2015).

In another cohort of US adults aged 18–30 years, Chatterjee et al. (2012) considered 24-hour urinary potassium excretion as well as dietary potassium intake estimated through a quantitative FFQ. When using urinary potassium (n = 1,066), the risk of incident type 2 diabetes was higher in individuals in the lowest quintile of urinary potassium (< 35.3 mmol/24 hours) compared to individuals in the highest quintile (≥ 73.2 mmol/24 hours) (HR = 2.45; 95% CI = 1.08–5.59; p for trend = 0.04), after adjustment for potential confounders. No dose-response relationship emerged. When using dietary potassium intake (n = 4,754), African-Americans but not whites had a higher risk of developing type 2 diabetes in the lowest quintiles of dietary potassium intake compared with the highest quintile (≥ 1,614 mg/1,000 kcal per day); no dose-response relationship was evident.

The Panel considers that data from prospective studies investigating a relationship between urinary potassium excretion or dietary potassium intake and risk of type 2 diabetes are limited and conflicting. The Panel concludes that these data cannot be used to derive DRVs for potassium.

5.6.3. Bone health

A few intervention studies have assessed the effect of potassium supplementation on bone mineral density (BMD). In a RCT where 276 post-menopausal women received 2,164 mg (55.5 mmol) or 6,493 mg (166.5 mmol) potassium per day as potassium citrate or a placebo for two years (mean potassium intake at baseline: 3,200–3,500 mg/day across the groups), mean spine and hip BMD losses in the placebo group did not differ from those in the treatment groups (Macdonald et al., 2008). Frassetto et al. (2012) investigated a possible influence of salt sensitivity on bone response to potassium alkali supplements by retrospectively analysing a subset of data from the trial of (Macdonald et al., 2008) (70 out of 276 subjects) and a dataset from a previous trial on 196 postmenopausal women who received daily doses of 1,200, 2,300 or 3,500 mg (30, 60 or 90 mmol) potassium as potassium bicarbonate or a placebo for two years (Frassetto et al., 2005). No effect of dietary alkali treatment on BMD was found for either study subgroup, nor did adjustment for the possible calcium- or potassium-lowering effects on blood pressure alter these results. Jehle et al. (2013) conducted a RCT on 201 older healthy adults who received either 7,020 mg (180 mmol) potassium/day as potassium citrate or placebo, along with calcium (500 mg/day) and vitamin D_3 (10 µg/day), for two years. Mean (± SD) urinary potassium excretion at baseline was 74 ± 19 mmol/24 hours and 73 ± 22 mmol/day in the placebo and treatment groups, respectively. The net effect of potassium citrate administration was an increase in BMD at the lumbar spine (primary endpoint) by 1.7% (95% CI = 1.0–2.3). Positive effects of potassium citrate were also found for BMD at femoral neck, total hip and total body. Potassium citrate also had positive effects on volumetric BMD (measured by CT scanning) for both dominant and nondominant radius and tibia.

A number of studies investigated the effect of alkaline potassium salts on urinary calcium and acid excretion and markers of bone turnover. In a meta-analysis, Lambert et al. (2015) found that supplementation with alkaline potassium salts reduced calcium excretion and net acid excretion compared to a placebo. Alkaline potassium salts lowered the bone resorption marker NTX (urinary collagen type 1 cross-linked N-telopeptide), while no effect on markers of bone formation was observed. Most studies used supplemental daily potassium doses ≥ 2,300 mg (60 mmol). Notably, in studies which compared alkaline potassium salts with potassium chloride, a higher effect of the alkaline salt on net acid excretion, as well as calcium excretion, was observed.

In a subset of 4,000 individuals (age at baseline: 59.7 ± 9.6 years for men and 59.8 ± 9.5 years for women) from the EPIC–Norfolk cohort, no association was found between dietary intake of potassium, assessed by a 7-day food diary, and risk of hip, spine, and wrist fractures at follow-up stratified by sex and quintile of potassium dietary intake (1,502 fracture cases, mean follow-up 13.4 years) (Hayhoe et al., 2015).

The Panel notes the lack of evidence about an association between potassium intake and fracture risk and the limited and inconsistent evidence for an effect of potassium supplementation on BMD. The Panel also notes that most studies used alkaline potassium salts and cannot conclude on an independent effect of potassium on bone health.

The Panel concludes that these data cannot be used to derive DRVs for potassium.

5.6.4. Kidney stones

In a prospective cohort study which involved 45,619 US men aged 40 to 75 years, potassium intake (assessed with FFQ) was inversely related to the risk of kidney stones after 14 years of follow-up (multivariate RR Q1 (< 2,914 mg (75 mmol)/day) vs Q5 (> 3,958 mg (101 mmol)/day) = 0.54; 95% CI = 0.42–0.68; p for trend < 0.001) (Taylor et al., 2004). In another cohort of 91,731 US women aged 34 to 59 years participating in the NHS I (12 years follow-up), the multivariate RR among women in the highest quintile (> 4,099 mg (105 mmol)/day) of potassium intake compared with those in the lowest quintile (< 2,407 mg (626 mmol)/day) was 0.65 (95 % CI = 0.51–0.84; p for trend < 0.001) (Curhan et al., 1997). In a cohort of 27,001 Finnish male smokers aged 50 to 69 years followed up for five years, no association was found between baseline potassium intake and the

incidence of kidney stones in the fully adjusted multivariate model (RR = 0.79; 95 % CI = 0.52–1.19; p for trend = 0.34) (Hirvonen et al., 1999). In that cohort, median potassium daily intakes in each quartile were 3,800 mg (97 mmol), 4,600 mg (118 mmol), 5,100 mg (131 mmol) and 5,800 mg (149 mmol), respectively.

The use of potassium citrate, as well as other citrate salts, has been investigated for the management of stone disease (Phillips et al., 2015). Because available RCTs used potassium in the form of alkaline salts, an independent effect of potassium on stone formation or stone growth cannot be ascertained. Potassium citrate is used in the treatment of hypocitraturia, which is one of the most common metabolic abnormalities associated with calcium kidney stone formation (Türk et al., 2015). Although the potassium moiety has been proposed to have an independent effect on urinary citrate excretion (Jaipakdee et al., 2004), RCTs found no effect of potassium chloride on urinary citrate excretion (Sakhaee et al., 1991; Tosukhowong et al., 2002; Jaipakdee et al., 2004; Maalouf et al., 2011). Similarly, no independent effect of potassium on urinary pH was found (Jaipakdee et al., 2004; Maalouf et al., 2011).

The Panel notes that there is some evidence for an association between low potassium intake and the increased risk of kidney stones from prospective cohort studies. However, an independent effect of potassium on kidney stones cannot be ascertained from available RCTs. Available RCTs using potassium chloride do not support an independent effect of potassium on urinary citrate excretion and pH.

The Panel concludes that these data cannot be used to derive DRVs for potassium.

6. Data on which to base Dietary Reference Values

The Panel decides to set DRVs for potassium on the basis of the relationships between potassium intake and blood pressure and stroke (Section 5.6.1).

6.1. Adults

There is evidence that a potassium intake of 3,500 mg (90 mmol)/day has a beneficial effect on blood pressure in adults. Furthermore, there is consistent evidence that potassium intakes below 3,500 mg (90 mmol)/day are associated with a higher risk of stroke. Currently, available data do not allow the determination of the distribution of individual requirements for potassium in relation to these endpoints. The Panel considers that available data cannot be used to determine the average requirement for potassium but can be used as a basis for deriving an adequate intake (AI).

The Panel considers that a potassium intake of 3,500 mg (90 mmol)/day can be considered adequate for the adult population. The Panel sets an AI of 3,500 mg (90 mmol)/day for adult men and women.

6.2. Infants and children

No data are available on which to base an average potassium requirement for infants and children. The Panel proposes AIs extrapolated from the AI for adults: considering the distribution of potassium in all the compartments of the body and the size of the rapidly exchangeable pool (Section 2.3.3), isometric scaling was used, taking into account differences in reference body weight (isometric scaling) and including a growth factor to take into account requirements for growth:

$AI_{child} = AI_{adult}$ (body weight of child / body weight of adult) (1 + growth factor).

The following growth factors have been applied: 0.57 for boys and girls aged 7 to 11 months, 0.25 for boys and girls aged one to three years, 0.06 for boys and girls aged four to six years, 0.13 for boys and girls aged 7–10 years, 0.11 for boys and 0.08 for girls aged 11–14 years, and 0.08 for boys and 0.03 for girls aged 15–17 years (EFSA NDA Panel, 2014).

During childhood, there are differences in potassium body accretion rates between boys and girls, which reflect their respective patterns of skeletal muscle gain (Sections 2.3.4 and 5.3). However, the Panel considers that these differences are negligible relative to the overall potassium requirement. The Panel decides to set AIs that apply to both boys and girls. The age categories proposed by the EFSA NDA Panel (2010) are applied (Table 4).

Table 4: Reference body weights and Adequate Intakes (AIs) of potassium for children

Age	Reference body weight (kg)[(a)]	AI (mg/day)[(b),(c)]
7–11 months	8.6	750
1–3 years	11.9	800
4–6 years	19.0	1,100
7–10 years	28.7	1,800
11–14 years	44.6	2,700
15–17 years	60.3	3,500

(a): Rounded mean of median weight-for-age of boys and girls aged 24 months, according to the WHO Growth Standard (WHO Multicentre Growth Reference Study Group, 2006), and aged 5, 8.5, 12.5 and 16 years, according to van Buuren et al. (2012).
(b): Adequate Intakes were derived from the unrounded AI for adults after adjustment on the basis of differences in reference body weight and application of a growth factor, then rounded to the closest 50.
(c): Equivalent to: 19 mmol/day for infants 7–11 months, 20 mmol/day for children aged 1–3 years, 28 mmol/day for children aged 4–6 years, 46 mmol/day for children aged 7–10 years, 69 mmol/day for children aged 11–14 years and 90 mmol/day for children aged 15–17 years.

6.3. Pregnancy

The Panel notes that there is a lack of data on potassium requirement in pregnancy, but considers that the requirement for the daily accretion rate of potassium in fetal and maternal tissues can be met by the adaptive changes which maintain potassium homeostasis during pregnancy (Section 5.4); thus, the AI for pregnant women is set at 3,500 mg (90 mmol)/day, the same as for non-pregnant women.

6.4. Lactation

An average amount of potassium secreted in breast milk of 400 mg (10 mmol)/day was estimated (Section 2.3.5.4). There are no data on adaptive changes in potassium metabolism during lactation, but some evidence indicates that total body potassium content decreases in lactating women (Section 5.5). Taking a conservative approach, the Panel proposes to increase the AI for lactating women in order to compensate for the losses of potassium through breast milk.

There is no specific information on potassium absorption efficiency in lactating women. Considering an absorption efficiency of 90 % from usual diets based on data in non-lactating subjects (Section 2.3.1), an additional potassium intake of 444 mg (11 mmol)/day was considered sufficient to replace these losses. Thus, an AI of 4,000 mg (102 mmol)/day is proposed for lactating women, after rounding up to the closest 100.

CONCLUSIONS

The Panel concludes that there is insufficient evidence to derive an AR and a PRI for potassium. Evidence on the relationships between potassium intake and blood pressure and risk of stroke are used to set an AI for adults (Table 5). It is considered unnecessary to give sex-specific values. The Panel proposes that the adult AI also applies to pregnant women. For lactating women, an increase in AI is proposed on the basis of the estimated loss of potassium secreted in breast milk. In infants over six months of age and in children, AIs are proposed based on extrapolation from the adult AI using isometric scaling and body weights of the age groups and application of a growth factor.

1570 **Table 5:** Summary of Dietary Reference Values for potassium

Age	AI[(a)] (mg/day)
7–11 months	750
1–3 years	800
4–6 years	1,100
7–10 years	1,800
11–14 years	2,700
15–17 years	3,500
≥ 18 years	3,500
Pregnancy	3,500
Lactation	4,000

1571 (a): Equivalent to: 19 mmol/day for infants 7–11 months, 20 mmol/day for children aged 1–3 years, 28 mmol/day for
1572 children aged 4–6 years, 46 mmol/day for children aged 7–10 years, 69 mmol/day for children aged 11–14 years,
1573 90 mmol/day for children aged 15–17 years, 90 mmol for adults, including pregnant women, and 102 mmol for lactating
1574 women.

1575 ## RECOMMENDATIONS FOR RESEARCH

1576 The Panel recommends improving the knowledge of potassium metabolism and homeostasis, and of
1577 its inter-relationship with the metabolism of sodium and chloride. This would, in turn, allow the
1578 identification of potential biomarkers for validation and use in population-based health studies.

1579 The Panel recommends further studies on the relationship between potassium intake and
1580 cardiovascular endpoints, in particular in relation to hypertension and stroke risk. Further investigation
1581 into the mechanisms involved in the protective role of potassium against these conditions is needed.

1582 The Panel recommends that the potential modification of the effect of potassium intake on blood
1583 pressure by sodium intake, sodium-to-potassium intake ratio, salt sensitivity, ethnic and genetic factors
1584 be further investigated.

1585 The Panel recommends further research on a potential 'independent' effect of potassium on bone
1586 health.

1587 The Panel also recommends generating evidence that can be used to assess the potassium requirements
1588 of infants and children.

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APPENDICES

Appendix A. Potassium concentration in breast milk from mothers of term infants in Western countries

Reference	Number of women (number of samples)	Country	Stage of lactation	Potassium concentration (mg/L)		Analytical method
				Mean ± SD	Median	
Bauer and Gerss (2011)	10	Germany	1–8 weeks	450 ± 74		Absorption spectrometry and colorimetry
Bjorklund et al. (2012)	60 (60)	Sweden	2–3 weeks	633 ± 40	636 (range:549–729)	ICP–MS
Fly et al. (1998)	14 (28)	USA	2–8 months	459 ± 24 (at rest) 445 ± 15 (after exercise)		ICP–AES
Holt (1993)	4 (28)	UK	5–16 weeks	594 ± 86		Flame photometry
Keenan et al. (1982a)	28 (40)	USA	3.5–6 weeks 8.5–18 weeks 20–32 weeks	592 ± 70 538 ± 50 519 ± 43		Flame photometry
Parr et al. (1991)	(71) (29)	Hungary Sweden	3 months		554 548	AAS
Wack et al. (1997)	30 (140)	USA	0–60 days 61–120 days 121–180 days 181–240 days 241–300 days 301–360 days >360 days	585 ± 124 490 ± 85 485 ± 66 473 ± 63 470 ± 72 445 ± 53 461 ± 89		ICP–AES
Witczak and Jarnuszewska (2011)	(9)	Poland	5–6 months	520		ICP–AES

Studies were identified by a comprehensive literature search for publications from October 2010 to January 2014 (LASER Analytica, 2014) and additional searches of the literature before these dates. If studies did not report whether infants were born at term or not it was presumed that infants were born at term.

AAS, atomic absorption spectroscopy; ICP–AES, inductively coupled plasma atomic emission spectroscopy; ICP–MS, inductively coupled plasma mass spectrometry.

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)	Year	Method	Days	Age (years)	Number of subjects						
						Infants < 1 year	Children 1– < 3 years	Children 3– < 10 years	Children 10– < 18 years	Adults 18– < 65 years	Adults 65– < 75 years	Adults ≥ 75 years
Finland/1	NWSSP	2007–2008	48–hour dietary recall[(a)]	2 × 2 [(a)]	13–15				306			
Finland/2	FINDIET2012	2012	48–hour dietary recall[(a)]	2 [(a)]	25–74					1,295	413	
Finland/3	DIPP	2000–2010	Dietary record	3	< 1–6	499	500	750				
France	INCA2	2006–2007	Dietary record	7	3–79			482	973	2,276	264	84
Germany/1	EsKiMo	2006	Dietary record	3	6–11			835	393			
Germany/2	VELS	2001–2002	Dietary record	6	< 1–4	158	348[(b)]	296[(b)]				
Ireland	NANS	2008–2010	Dietary record	4	18–90					1,274	149	77
Italy	INRAN–SCAI	2005–2006	Dietary record	3	< 1–98	16[(c)]	36[(c)]	193	247	2,313	290	228
Latvia	FC_PREGNANTWOMEN	2011	24–hour dietary recall	2	15–45				12[(c)]	991[(b)]		
Netherlands	DNFCS	2007–2010	24–hour dietary recall	2	7–69			447	1,142	2,057	173	
Sweden	Riksmaten	2010–2011	Dietary records (web)[(d)]	4	18–80					1,430	295	72
United Kingdom/1	DNSIYC	2011	Dietary record	4	0.3–1.5	1,369	1,314					
United Kingdom/2	NDNS Rolling Programme (Years 1–3)	2008–2011	Dietary record	4	1–94		185	651	666	1,266	166	139

DIPP, type 1 Diabetes Prediction and Prevention survey; DNFCS, Dutch National Food Consumption Survey; DNSIYC, Diet and Nutrition Survey of Infants and Young Children; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale des Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione – Studio sui Consumi Alimentari in Italia; 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): Four subjects from the VELS study (one toddler and 3 other children) and one subject from the Latvian study (one adult) were not considered in the assessment due to the fact that only one 24-hour dietary recall day was available.

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

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

Appendix C. Potassium intakes in males in different surveys according to age classes and country

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ				
			n[(a)]	Average	Median	P5	P95	n[(a)]	Average	Median	P5	P95
< 1 year[(b)]	Germany	VELS	84	1,408	1,404	914	1,882	84	439	447	300	554
	Finland	DIPP_2001_2009	247	873	914	160	1,533	245	496	450	295	916
	United Kingdom	DNSIYC_2011	699	1,535	1,531	916	2,174	699	453	463	307	569
	Italy	INRAN_SCAI_2005_06	9	821	782	(c)	(c)	9	279	250	(c)	(c)
1 to < 3 years	Germany	VELS	174	1,680	1,600	992	2,457	174	361	354	229	506
	Finland	DIPP_2001_2009	245	1,792	1,753	960	2,616	245	494	488	322	673
	United Kingdom	NDNS RollingProgramme years 1–3	107	2,005	1,985	1,300	3,301	107	411	408	301	521
	United Kingdom	DNSIYC_2011	663	1,794	1,777	1,115	2,595	663	431	430	314	563
	Italy	INRAN_SCAI_2005_06	20	1,974	1,853	(c)	(c)	20	417	400	(c)	(c)
3 to < 10 years	Germany	EsKiMo	426	2,499	2,493	1,596	3,554	426	330	326	221	445
	Germany	VELS	146	1,857	1,738	1,176	2,931	146	331	322	233	455
	Finland	DIPP_2001_2009	381	2,749	2,667	1,808	3,906	381	469	471	348	596
	France	INCA2	239	2,094	2,040	1,283	3,080	239	338	329	242	479
	United Kingdom	NDNS RollingProgramme years 1–3	326	2,234	2,210	1,408	3,156	326	356	352	255	464
	Italy	INRAN_SCAI_2005_06	94	2,538	2,512	1,537	3,880	94	348	332	231	482
	Netherlands	DNFCS 2007-2010	231	2,457	2,408	1,458	3,676	231	285	284	195	394
10 to < 18 years	Germany	EsKiMo	197	2,578	2,546	1,601	3,756	197	319	316	221	428
	Finland	NWSSP07_08	136	3,712	3,617	2,323	5,295	136	454	451	323	580
	France	INCA2	449	2,464	2,398	1,457	3,692	449	315	308	228	422
	United Kingdom	NDNS RollingProgramme years 1–3	340	2,597	2,535	1,551	3,959	340	322	316	222	439
	Italy	INRAN_SCAI_2005_06	108	3,144	3,087	1,846	4,719	108	326	311	229	463
	Netherlands	DNFCS 2007-2010	566	2,983	2,855	1,591	4,729	566	280	278	183	396
18 to < 65 years	Finland	FINDIET2012	585	3,991	3,856	2,298	6,059	585	439	428	288	606
	France	INCA2	936	2,964	2,901	1,583	4,481	936	341	334	237	468
	United Kingdom	NDNS RollingProgramme years 1–3	560	3,203	3,178	1,780	4,976	560	368	363	247	516
	Ireland	NANS_2012	634	3,827	3,770	2,107	5,658	634	385	376	267	516
	Italy	INRAN_SCAI_2005_06	1,068	3,043	2,963	1,809	4,631	1,068	339	327	228	480
	Netherlands	DNFCS 2007–2010	1,023	3,799	3,663	2,186	5,708	1,023	343	329	227	512
	Sweden	Riksmaten 2010	623	3,835	3,734	2,043	5,846	623	393	389	260	527

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ				
			n[(a)]	Average	Median	P5	P95	n[(a)]	Average	Median	P5	P95
65 to < 75 years	Finland	FINDIET2012	210	3,675	3,521	2,086	5,722	210	460	443	281	671
	France	INCA2	111	3,209	3,111	1,872	4,795	111	374	363	267	510
	United Kingdom	NDNS RollingProgramme years 1–3	75	3,391	3,344	1,543	4,970	75	410	410	272	565
	Ireland	NANS_2012	72	3,511	3,685	1,833	5,040	72	409	390	280	574
	Italy	INRAN_SCAI_2005_06	133	3,135	3,060	1,910	4,284	133	363	341	264	526
	Netherlands	DNFCS 2007–2010	91	3,529	3,548	2,043	5,014	91	390	376	276	564
	Sweden	Riksmaten 2010	127	3,819	3,768	2,152	5,984	127	444	437	345	600
≥ 75 years	France	INCA2	40	2,856	2,720	(c)	(c)	40	375	366	(c)	(c)
	United Kingdom	NDNS RollingProgramme years 1–3	56	2,884	2,803	(c)	(c)	56	404	407	(c)	(c)
	Ireland	NANS_2012	34	3,164	3,075	(c)	(c)	34	411	423	(c)	(c)
	Italy	INRAN_SCAI_2005_06	69	3,095	3,186	1,860	4,632	69	359	351	252	468
	Sweden	Riksmaten 2010	42	3,634	3,743	(c)	(c)	42	436	429	(c)	(c)

P5, 5th percentile; P95, 95th percentile; DIPP, type 1 Diabetes Prediction and Prevention survey; DNFCS, Dutch National Food Consumption Survey; DNSIYC, Diet and Nutrition Survey of Infants and Young Children; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale des Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione - Studio sui Consumi Alimentari in Italia; 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): The proportions of breast-fed infants were 58% in the Finnish survey, 40% in the German survey, 44% in the Italian survey and 21% in the UK survey. Most infants were partially breast-fed. For the Italian and German surveys, breast milk intake estimates were derived from the number of breastfeeding events recorded per day multiplied by standard breast milk amounts consumed on an eating occasion at different ages. For the UK survey, the amount of breast milk consumed was either directly quantified by the mother (expressed breast milk) or extrapolated from the duration of each breastfeeding event. As no information on the breastfeeding events was reported in the Finnish survey, breast milk intake was not taken into consideration in the intake estimates of Finnish infants.

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

Appendix D. Potassium intakes in females in different surveys according to age classes and country

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ				
			n[(a)]	Average	Median	P5	P95	n[(a)]	Average	Median	P5	P95
< 1 year[(b)]	Germany	VELS	75	1,252	1,276	857	1,679	75	434	437	287	562
	Finland	DIPP_2001_2009	253	826	833	176	1,543	251	546	474	303	972
	United Kingdom	DNSIYC_2011	670	1,370	1,360	741	2,058	670	449	457	266	583
	Italy	INRAN_SCAI_2005_06	7	1,175	1,304	(c)	(c)	7	397	390	(c)	(c)
1 to < 3 years	Germany	VELS	174	1,516	1,510	949	2,195	174	356	350	241	507
	Finland	DIPP_2001_2009	255	1,690	1,648	826	2,555	255	495	496	337	661
	United Kingdom	NDNS RollingProgramme years 1–3	78	1,752	1,741	1,090	2,502	78	390	396	267	498
	United Kingdom	DNSIYC_2011	651	1,688	1,683	1,016	2,416	651	429	426	302	554
	Italy	INRAN_SCAI_2005_06	16	1,789	1,710	(c)	(c)	16	383	375	(c)	(c)
3 to < 10 years	Germany	EsKiMo	409	2,324	2,251	1,419	3,489	409	343	339	240	461
	Germany	VELS	147	1,668	1,630	987	2,390	147	324	318	219	458
	Finland	DIPP_2001_2009	369	2,492	2,448	1,680	3,535	369	473	468	352	614
	France	INCA2	243	1,939	1,894	1,269	2,693	243	350	343	261	459
	United Kingdom	NDNS RollingProgramme years 1–3	325	2,126	2,105	1,314	3,074	325	358	351	259	467
	Italy	INRAN_SCAI_2005_06	99	2,417	2,349	1,274	3,389	99	336	333	245	482
	Netherlands	DNFCS 2007–2010	216	2,306	2,270	1,397	3,355	216	284	274	193	413
10 to < 18 years	Germany	EsKiMo	196	2,450	2,363	1,402	3,730	196	330	319	217	463
	Finland	NWSSP07_08	170	3,057	3,050	1,719	4,649	170	464	470	331	597
	France	INCA2	524	2,093	2,071	1,185	3,015	524	333	324	236	454
	United Kingdom	NDNS RollingProgramme years 1–3	326	2,202	2,157	1,268	3,365	326	329	320	225	477
	Italy	INRAN_SCAI_2005_06	139	2,685	2,523	1,588	4,150	139	339	330	214	484
	Latvia	FC_PREGNANTWOMEN_2011[(d)]	12	3,692	3,603	(c)	(c)	12	373	376	(c)	(c)
	Netherlands	DNFCS 2007–2010	576	2 579	2 528	1 473	3 920	576	294	284	185	432
18 to < 65 years	Finland	FINDIET2012	710	3,297	3,237	1,885	4,997	710	467	452	310	684
	France	INCA2	1,340	2,487	2,414	1,381	3,830	1,340	389	375	264	573
	United Kingdom	NDNS RollingProgramme years 1–3	706	2,673	2,645	1,481	3,994	706	408	395	265	598
	Ireland	NANS_2012	640	2,982	2,896	1,726	4,522	640	408	396	276	579
	Italy	INRAN_SCAI_2005_06	1,245	2,715	2,659	1,535	4,024	1,245	377	359	248	566
	Latvia	FC_PREGNANTWOMEN_2011[(d)]	990	3,452	3,384	2,165	5,048	990	412	402	264	603
	Netherlands	DNFCS 2007–2010	1,034	3,061	2,973	1,722	4,719	1,034	377	364	225	573
	Sweden	Riksmaten 2010	807	3,179	3,080	1,843	4,772	807	435	411	282	592
65 to < 75 years	Finland	FINDIET2012	203	3,031	2,962	1,935	4,494	203	497	483	334	683
	France	INCA2	153	2,562	2,503	1,485	3,752	153	413	403	281	563

Age class	Country	Survey	Intakes expressed in mg/day					Intakes expressed in mg/MJ				
			n[(a)]	Average	Median	P5	P95	n[(a)]	Average	Median	P5	P95
	United Kingdom	NDNS RollingProgramme years 1–3	91	2,781	2,698	1,708	4,016	91	465	436	314	679
	Ireland	NANS_2012	77	3,201	3,071	1,855	4,851	77	474	473	334	626
	Italy	INRAN_SCAI_2005_06	157	2,791	2,751	1,463	4,110	157	410	385	268	660
	Netherlands	DNFCS 2007–2010	82	3,050	2,895	1,804	4,369	82	428	407	268	604
	Sweden	Riksmaten 2010	168	3,262	3,160	2,001	4,595	168	470	463	360	597
≥ 75 years	France	INCA2	44	2,463	2,465	(c)	(c)	44	414	397	(c)	(c)
	United Kingdom	NDNS RollingProgramme years 1–3	83	2,731	2,750	1,692	3,512	83	459	454	319	635
	Ireland	NANS_2012	43	2,924	2,948	(c)	(c)	43	471	464	(c)	(c)
	Italy	INRAN_SCAI_2005_06	159	2,602	2,580	1,604	3,767	159	394	384	253	588
	Sweden	Riksmaten 2010	30	3,339	3,180	(c)	(c)	30	484	484	(c)	(c)

P5, 5th percentile; P95, 95th percentile; DIPP, type 1 Diabetes Prediction and Prevention survey; DNFCS, Dutch National Food Consumption Survey; DNSIYC, Diet and Nutrition Survey of Infants and Young Children; EsKiMo, Ernährungsstudie als KIGGS-Modul; FINDIET, the national dietary survey of Finland; INCA, étude Individuelle Nationale des Consommations Alimentaires; INRAN-SCAI, Istituto Nazionale di Ricerca per gli Alimenti e la Nutrizione - Studio sui Consumi Alimentari in Italia; 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): The proportions of breast-fed infants were 58% in the Finnish survey, 40% in the German survey, 44% in the Italian survey and 21% in the UK survey. Most infants were partially breast-fed. For the Italian and German surveys, breast milk intake estimates were derived from the number of breastfeeding events recorded per day multiplied by standard breast milk amounts consumed on an eating occasion at different ages. For the UK survey, the amount of breast milk consumed was either directly quantified by the mother (expressed breast milk) or extrapolated from the duration of each breastfeeding event. As no information on the breastfeeding events was reported in the Finnish survey, breast milk intake was not taken into consideration in the intake estimates of Finnish infants.

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

(d): Pregnant women only.

Appendix E. Minimum and maximum percentage contribution of different food groups (FoodEx2 level1) to potassium intakes in males

Food groups	Age (years)						
	< 1 year	1 to < 3 years	3 to < 10 years	10 to < 18 years	18 to < 65 years	65 to < 75 years	≥ 75 years
Additives, flavours, baking and processing aids	< 1	< 1	0	< 1–1	< 1	< 1	0
Alcoholic beverages	< 1	< 1	< 1	< 1–1	3–7	2–7	2–7
Animal and vegetable fats and oils	< 1	< 1	< 1	< 1	< 1	< 1	< 1
Coffee, cocoa, tea and infusions	< 1–2	< 1–5	1–8	2–6	5–13	5–14	4–12
Composite dishes	< 1–4	< 1–7	< 1–7	< 1–10	< 1–13	< 1–12	< 1–12
Eggs and egg products	< 1	< 1–1	< 1–1	< 1–1	< 1–1	< 1–1	< 1–1
Fish, seafood, amphibians, reptiles and invertebrates	< 1–1	< 1–4	< 1–4	< 1–4	1–4	2–5	2–5
Food products for young population	20–54	3–16	< 1–1	< 1	< 1	–	–
Fruit and fruit products	5–14	9–14	6–11	4–9	4–11	6–14	6–14
Fruit and vegetable juices and nectars	< 1–2	1–8	4–10	4–10	1–6	1–5	1–3
Grains and grain-based products	3–6	8–14	9–19	11–20	11–15	11–17	12–19
Human milk	< 1–26	< 1–1	–	–	–	–	–
Legumes, nuts, oilseeds and spices	< 1–2	1–3	1–4	1–4	1–4	1–4	1–3
Meat and meat products	< 1–4	4–8	6–13	8–16	9–15	8–13	7–12
Milk and dairy products	7–18	25–34	17–36	13–30	9–19	8–18	10–14
Products for non-standard diets, food imitates and food supplements or fortifying agents	< 1	0	< 1–1	< 1–1	< 1–2	< 1	< 1–1
Seasoning, sauces and condiments	< 1–1	< 1–1	< 1–2	< 1–2	< 1–3	< 1–1	< 1–1
Starchy roots or tubers and products thereof, sugar plants	1–21	6–19	10–18	12–21	9–19	9–18	12–19
Sugar, confectionery and water-based sweet desserts	< 1	< 1–1	1–4	1–4	< 1–1	< 1–1	< 1–1
Vegetables and vegetable products	1–15	5–10	7–16	7–19	5–24	5–24	6–22
Water and water-based beverages	< 1	< 1–1	< 1–2	< 1–2	< 1–4	< 1–2	< 1–2

"–" means that there was no consumption event of the food group for the age and sex group considered, whereas "0" means that there were some consumption events, but that the food group does not contribute to potassium intake in the age and sex group considered.

Appendix F. Minimum and maximum percentage contribution of different food groups (FoodEx2 level1) to potassium intakes in females

Food groups	Age (years)						
	< 1 year	1 to < 3 years	3 to < 10 years	10 to < 18 years	18 to < 65 years	65 to < 75 years	≥ 75 years
Additives, flavours, baking and processing aids	< 1	0	0	< 1–1	< 1	< 1	0
Alcoholic beverages	< 1	< 1	< 1	< 1	< 1–3	1–3	1–2
Animal and vegetable fats and oils	< 1	< 1	< 1	< 1	< 1	< 1	< 1
Coffee, cocoa, tea and infusions	< 1–15[(a)]	< 1–5	1–8	2–6	4–15	4–17	4–12
Composite dishes	< 1–2	< 1–7	< 1–7	< 1–10	< 1–14	< 1–12	< 1–14
Eggs and egg products	< 1	< 1–1	< 1–1	< 1–1	< 1–1	< 1–1	< 1–1
Fish, seafood, amphibians, reptiles and invertebrates	0	< 1–6	< 1–3	< 1–4	1–4	1–5	1–5
Food products for young population	19–57	3–16	< 1–1	< 1	< 1	–	< 1
Fruit and fruit products	8–12	9–14	7–12	6–15	7–13	9–16	9–17
Fruit and vegetable juices and nectars	< 1–2	1–7	3–10	3–10	2–6	1–4	2–4
Grains and grain-based products	4–6	9–14	9–18	12–19	12–23	10–16	10–18
Human milk	< 1–9	< 1–1	–	–	–	–	–
Legumes, nuts, oilseeds and spices	< 1–2	1–3	1–4	1–3	2–4	1–3	1–2
Meat and meat products	1–4	4–7	5–14	7–14	8–12	7–11	6–11
Milk and dairy products	4–22	23–38	17–37	11–27	10–20	10–18	12–16
Products for non-standard diets, food imitates and food supplements or fortifying agents	< 1	< 1	0–1	< 1–1	< 1–2	< 1–1	< 1–1
Seasoning, sauces and condiments	< 1–1	< 1–1	< 1–2	< 1–2	< 1–2	< 1–1	< 1–1
Starchy roots or tubers and products thereof, sugar plants	4–20	6–17	10–19	11–23	8–17	9–15	10–13
Sugar, confectionery and water-based sweet desserts	< 1–1	< 1–1	1–3	1–4	< 1–5	< 1–1	< 1–1
Vegetables and vegetable products	4–17	6–12	8–16	8–20	7–24	7–24	7–22
Water and water-based beverages	< 1–1	< 1–1	< 1–3	< 1–2	< 1–4	< 1–3	< 1–3

"–" means that there was no consumption event of the food group for the age and sex group considered, whereas "0" means that there were some consumption events, but that the food group does not contribute to potassium intake in the age and sex group considered.

(a): The value of 15% comes from the INRAN_SCAI_2005_06 survey (n girls < 1 year = 7) and originates from one subject who drank small amounts of tea on each of the three days of the survey.

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

Country	Survey (age range)	Reference	% of published intake[(a)]
Finland	NWSSP (13–15 years)	Hoppu et al. (2010)	102–103%
	FINDIET 2012 (25–74 years)	Helldán et al. (2013)	95–97%
France	INCA2 (3–17 years)	Afssa (2009)	92–102%
Germany	EsKiMo (6–11 years)	Mensink et al. (2007)	105–112%
	VELS (<1–4 years)	Kersting and Clausen (2003)	97–105%[(b)]
Ireland	NANS (18–90 years)	IUNA (2011)	101–107%
Italy	INRAN-SCAI (1 month–98 years)	Sette et al. (2011)	95–109%
Netherlands	DNFCS 2007_2010 (7–69 years)	van Rossum et al. (2011)	96–99%
UK	NDNS years 1–3 (3–94 years)	Bates et al. (2012)	97–107%

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

(a): Range over different age groups in a specific survey.

(b): For the VELS survey, the comparison refers to median values, as average potassium intake estimates were not available in the literature.

Appendix H. Meta-analyses of prospective cohort studies on potassium intake and risk of total stroke

Individual studies	Country	Larsson et al. (2011a)	Aburto et al. (2013) WHO (2012d)	D'Elia et al. (2014)	Adebamowo et al. (2015b)
Khaw and Barrett-Connor (1987)	**USA**	x	x	x	x
Ascherio et al. (1998)	**USA**	x	x	x	x
Iso et al. (1999)	**USA**	x	x	x	x
Bazzano et al. (2001)	**USA**	x	x	x	x
Green et al. (2002)	**USA**	x	x	x	x
Geleijnse et al. (2007)[(a)]	**Netherlands**	x	x	x	x
Larsson et al. (2008)	**Finland**	x	x	x	x
Umesawa et al. (2008)	**Japan**	x	x	x	x
Weng et al. (2008)	**Taiwan**	x	x	x	x
Larsson et al. (2011b)	**Sweden**	x	-	x	x
O'Donnell et al. (2011)[(a)]	**40 countries[(b)]**	-	x	x	-
Sluijs et al. (2014)	**Netherlands**	-	-	x	x
Adebamowo et al. (2015b)	**USA**	-	-	-	x
Number of studies included		10	10	12	12
Pooled RR (95% CI)[(c)]		0.89 (0.83–0.96) by 1000 mg increase of potassium intake (I^2 = 50.8%[(d)])	0.76 (0.66–0.88) for higher potassium intake compared to lower potassium intake (I^2 = 62%)	0.80 (0.72–0.90) for higher potassium intake compared to lower potassium intake (I^2 = 47%) 0.90 (0.84–0.96) by 1000 mg increase of potassium intake (I^2 = 47%)	0.91 (0.88–0.94) by 1000 mg increase of potassium intake (I^2 not reported)

CI, confidence interval; I^2, heterogeneity index; RR, relative risk.

(a): Potassium intake estimated on the basis of urinary potassium excretion

(b): Argentina, Australia, Austria, Belgium, Canada, China, Czech Republic, Denmark, Finland, France, Germany, Greece, Hong King, Hungary, Ireland, Italy, Malaysia, Mexico, Netherland, New Zealand, Norway, Philippines, Poland, Portugal, Russia, Singapore, Slovakia, South Africa, South Korea, Spain, Sweden, Switzerland, Taiwan, Thailand, Turkey, Ukraine, United Arab Emirates, United Kingdom, USA.

(c): Calculated from study-specific RRs adjusted for the most number of covariates.

(d): In a sensitivity analysis, Khaw and Barrett-Connor (1987) was found to account for the observed heterogeneity. When that study was omitted, the pooled RR was 0.91 (95% CI = 0.86–0.96) and between-study heterogeneity was I^2 = 20.7%.

ABBREVIATIONS

Afssa	Agence française de sécurité sanitaire des aliments
AI	Adequate Intake
AR	Average Requirement
ATP	adenosine triphosphate
BMD	bone mineral density
BMI	body mass index
bw	body weight
COMA	Committee on Medical Aspects of Food Policy
CI	confidence interval
D-A-CH	Deutschland-Austria-Confoederatio Helvetica
DBP	diastolic blood pressure
DH	Department of Health
DRV	Dietary Reference Value
EPIC	European Prospective Investigation into Cancer and Nutrition study
EsKiMo	Ernährungsstudie als KIGGS-Modul
FAO	Food and Agriculture Organization
FFQ	food frequency questionnaire
FINDIET	National dietary survey of Finland
FSANZ	Food Standards Australia New Zealand
HMGCR	3-hydroxy-3-methylglutaryl-CoA reductase
HR	hazard ratio
I^2	heterogeneity index
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	US Institute of Medicine of the National Academy of Sciences
IQR	interquartile range
LRNI	Lower Reference Nutrient Intake

NDNS	UK National Diet and Nutrient Survey
NHANES	US National Health and Nutrition Examination Survey
NHS	Nurses' Health Study
NNR	Nordic Nutrition Recommendations
NWSSP	Nutrition and Wellbeing of Secondary School Pupils
NTX	urinary collagen type 1 cross-linked N-telopeptide
PREVEND	Prevention of Renal and Vascular End-Stage Disease study
PRI	Population Reference Intake
PURE	Prospective Urban Rural Epidemiology study
RCT	randomised controlled trial
RNI	Recommended Nutrient Intake
RR	Relative risk
SBP	systolic blood pressure
SCF	Scientific Committee for Food
SD	standard deviation
SEM	standard error of the mean
SM	skeletal muscle
SNP	single nucleotide polymorphism
TBK	total body potassium
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
WHI	Women's Health Initiative study
WHO	World Health Organization