

# Guideline:

# Potassium intake for adults and children

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<sup>&</sup>lt;sup>1</sup> This publication is a World Health Organization (WHO) guideline. A WHO guideline is any document, whatever its title, containing WHO recommendations about health interventions, whether they be clinical, public health or policy interventions. A recommendation provides information about what policy-makers, health-care providers or patients should do. It implies a choice between different interventions that have an impact on health and that have ramifications for the use of resources. All publications containing WHO recommendations are approved by the WHO Guidelines Review Committee.

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# **Abbreviations and acronyms**

AUB American University of Beirut

CDC Centers for Disease Control and Prevention

CI confidence interval

FAO Food and Agriculture Organization of the United Nations

FSANZ Food Standards Australia New Zealand

GRADE Grading of Recommendations Assessment,

Development and Evaluation

HDL high-density lipoprotein

IAEA International Atomic Energy Agency
KFDA Korea Food and Drug Administration

KHIDI Korea Health Industry Development Institute

LDL low-density lipoprotein

MD mean difference

NCD noncommunicable disease

NUGAG Nutrition Guidance Expert Advisory Group

NZFSA New Zealand Food Safety Academy

PICO population, intervention, control and outcomes

RCT randomized-controlled trial

RR risk ratio

UN United Nations

UNU United Nations University
USA United States of America

WASH World Action on Salt and Health

WHO World Health Organization

# **Symbols**

> greater than

< less than

≥ equal to or greater than

≤ equal to or less than

# **Executive summary**

# **Background**

Noncommunicable diseases (NCDs) are the main contributor to mortality and morbidity globally (1, 2), and interventions to reduce the burden of NCDs are valuable. Low potassium intake has been associated with a number of NCDs, including hypertension, cardiovascular disease, chronic kidney stone formation and low bone-mineral density. An increased potassium intake may reduce blood pressure, decrease risk of cardiovascular disease, have beneficial effects on bone-mineral density, and mitigate the negative consequences of high sodium consumption (3-5).

The World Health Organization (WHO) currently does not have a recommendation for potassium intake. However, interest in potassium intake and its potential use in public health is growing, due to the increasing burden of NCDs, and the need for well-understood, cost-effective and feasible interventions to combat NCDs. Therefore, Member States and the Codex Committee on Nutrition and Food for Special Dietary Uses requested WHO to develop a guideline on potassium intake for adults and children, to inform the development of public health nutrition programmes and policies aimed at reducing the risk of NCDs.

# **Objective**

The objective of this guideline is to provide recommendations on the consumption of potassium to reduce NCDs in adults and children. The recommendations given here can be used by those developing programmes and policies to assess current potassium intake levels relative to a benchmark. If necessary, the recommendations can also be used to develop measures to increase potassium intake, through public health interventions such as food and product labelling, consumer education, and the establishment of food-based dietary guidelines.

# Methods

WHO developed the present evidence-informed guideline using the procedures outlined in the WHO Handbook for guideline development (6). The steps in this process included:

- identification of priority questions and outcomes;
- retrieval of the evidence;
- assessment and synthesis of the evidence;
- formulation of recommendations;
- identification of research gaps;
- planning for dissemination, implementation, impact evaluation and updating of the guideline.

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (7) was followed to prepare evidence profiles related to preselected topics, based on up-to-date systematic reviews of the scientific literature. An international, multidisciplinary group of experts participated in three WHO technical consultations. The first was held in Geneva, Switzerland on 14–18 March 2011; the second in Seoul, the Republic of Korea on 29 November to 2 December 2011; and the third in Geneva, Switzerland on 27–30 March 2012. At these meetings, the group of experts reviewed and discussed the evidence, drafted recommendations, and reached consensus on the strength of each recommendation. In determining the strength of the recommendations, they took into consideration the desirable and undesirable effects of the recommendation, the quality of the available evidence, values and preferences related to the recommendation in different settings, and the cost of options available to public health officials and programme managers in different settings. All guideline group members completed a declaration of interests form before each meeting. An External Expert and Stakeholder Panel was involved throughout the process.

# The evidence

Increased potassium intake reduced systolic and diastolic blood pressure in adults. Across a wide range of baseline intakes, increasing potassium intake was beneficial in terms of blood pressure. The largest reduction in blood pressure was detected when the potassium intake was increased to 90–120 mmol/day, although potassium increases reaching other levels of intake also reduced blood pressure. Increased potassium intake had no significant adverse effect on blood lipids, catecholamine levels or renal function in adults. In children, increased potassium intake reduced systolic blood pressure by a small, non-significant amount. Higher potassium intake was associated with a reduced risk of incident stroke. There was no significant association between potassium intake and incident cardiovascular disease or coronary heart disease. However, the strong positive relationship between blood pressure and cardiovascular disease, and between blood pressure and coronary heart disease, provides indirect evidence that increasing potassium intake can improve these outcomes through a beneficial effect on blood pressure. Based on the entire body of evidence, WHO generated the following recommendations for potassium intake in adults and children.

# Recommendations

- WHO recommends an increase in potassium intake from food to reduce blood pressure and risk of cardiovascular disease, stroke and coronary heart disease in adults (*strong recommendation*<sup>1</sup>). WHO suggests a potassium intake of at least 90 mmol/day (3510 mg/day) for adults (*conditional recommendation*<sup>2</sup>).
- WHO suggests an increase in potassium intake from food to control<sup>3</sup> blood pressure in children (conditional recommendation). The recommended potassium intake of at least 90 mmol/day should be adjusted downward for children, based on the energy requirements of children relative to those of adults.

<sup>&</sup>lt;sup>1</sup>A strong recommendation is one for which the guideline development group is confident that the desirable effects of adherence outweigh the undesirable effects.

<sup>&</sup>lt;sup>2</sup> 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.

<sup>&</sup>lt;sup>3</sup> "Control" for this recommendation refers to the prevention of a deleterious rise in blood pressure with age.

These recommendations complement the WHO guideline on sodium intake. They should be used in conjunction with that and other nutrient guidelines and recommendations, to guide development of public health nutrition programmes and policies. Addressing the optimal ratio of intake of sodium to potassium was outside the scope of this guideline; however, if an individual consumes sodium at the levels recommended in the WHO guideline on sodium intake, and potassium as recommended in the current guideline, the ratio of sodium to potassium would be approximately one to one, which is considered beneficial for health (8). However, most populations around the world consume less than the recommended levels of potassium (9, 10), and consume a ratio of sodium to potassium of two to one or more (11). The successful implementation of these recommendations would have an important public health impact through reductions in morbidity and mortality, improvement in the quality of life for millions of people, and substantial reductions in health-care costs (2, 12, 13).

# Introduction

# **Scope and purpose**

The objective of this guideline is to provide recommendations on the consumption of potassium for adults and children. It is important to establish nutrient guidelines so that nutrition interventions can be developed in a logical, systematic, and scientific manner taking into account the best available evidence. The recommendations in this guideline can be used by programme and policy planners to assess current potassium intake levels relative to a benchmark and develop measures to increase potassium intake, where necessary, through public health interventions including, but not limited to, food and product labelling, consumer education, and the establishment of Food-Based Dietary Guidelines (FBDG). This guideline does not provide guidance on specific food intake because such dietary guidelines should be based on the overall dietary goals, which take into consideration all required nutrients. It should be used in conjunction with the guideline on sodium intake and other nutrient guidelines to guide public health nutrition programme and policy development.

This guideline provides a global, evidence-informed recommendation on potassium intake for:

- adults (≥16 years of age) for the reduction of blood pressure and risk of cardiovascular disease, stroke and coronary heart disease;
- children (2–15 years of age) for the control of blood pressure.

It does not provide recommendations for individuals with impaired urinary potassium excretion from a medical condition or drug therapy.

The guideline will help Member States and their partners to make informed decisions on appropriate nutrition actions to reduce noncommunicable diseases (NCDs). It is intended for a wide audience, including policy-makers and their expert advisers, and technical and programme staff in organizations involved in the design, implementation and scaling-up of nutrition actions for public health.

This document presents the key recommendations and a summary of the supporting evidence. Further details of the evidence base are provided in Annex 1 and other documents listed in the references.

# **Background**

NCDs are the leading cause of death globally, killing more people each year than all other causes combined (14). The major NCDs currently account for approximately 60% of all deaths and 43% of disease burden globally, and these levels are expected to continue to rise (2, 15). In 2008, 29 million NCD-related deaths (almost 80%) occurred in low and middle-income countries. In those countries, 29% of NCD-related deaths were in people under 60 years of age; in contrast, in high-income countries, only 13% of the NCD-related deaths were premature. In 2005, cardiovascular disease alone accounted for 30% of all deaths; the equivalent of infectious disease, nutritional deficiency, and maternal and perinatal conditions combined (2).

Hypertension is considered a major risk factor for cardiovascular diseases, particularly coronary heart disease and stroke. Suboptimal systolic blood pressure (>115 mmHg) is estimated to contribute to 49% of all coronary heart disease and 62% of all stroke (12). Thus, the burden of morbidity and mortality from hypertension and related NCDs is currently one of the most urgent public health problems globally. Although NCDs disproportionately affect adults, they and their risk factors are now being detected more frequently in paediatric populations. Diet-related NCDs are chronic, and take years or decades to manifest; delaying the onset of these diseases could improve lives and result in substantial cost savings (13). Blood pressure during childhood has a significant association with blood pressure during adulthood, meaning that children with increased blood pressure are at high risk for hypertension and its related morbidities as adults (16). Additionally, elevated blood pressure in childhood contributes to cardiovascular disease pathology during childhood itself (17). Thus, addressing during childhood the problem of elevated blood pressure and other risk factors for NCDs that could manifest later in life is crucial to combat NCDs.

Potassium is an essential nutrient needed for maintenance of total body fluid volume, acid and electrolyte balance, and normal cell function (18). Normally, most ingested potassium is excreted via the urine. Under conditions of extreme heat and intense physical activity that result in a high sweat production, potassium losses in sweat are increased and appreciable. However, acclimation occurs rapidly, and potassium losses via sweat are reduced quickly. Thus, most individuals can replace needed potassium through food consumption without the need for supplements or specially formulated products (19-21). Potassium is commonly found in a variety of unrefined foods, especially fruits and vegetables. Food processing reduces the amount of potassium in many food products, and a diet high in processed foods and low in fresh fruits and vegetables is often lacking in potassium (22). Data from around the world suggest that the population average potassium consumption in many countries is below 70-80mmol/day, the value recommended by the 2002 Joint World Health Organization/Food and Agriculture Organization of the United Nations (WHO/FAO) Expert Consultation (8). Few countries report an average consumption of 90 mmol/ day, which is recommended in countries such as Belgium, Mexico, Spain and the United Kingdom of Great Britain and Northern Ireland (23-26). No countries report an average population consumption of 120 mmol/day, which is recommended in countries such as Bulgaria, Canada, the Republic of Korea and the United States of America (USA) (9, 10, 27-29). Women consistently have lower levels of potassium intake than men, but both groups commonly consume a level that is below current recommendations.

Reduced potassium consumption has been associated with hypertension and cardiovascular diseases, and appropriate consumption levels could be protective against these conditions (8). A recent meta-analysis including 11 cohort studies reported an inverse association between potassium intake and risk of stroke (30). Additionally, two meta-analyses of trials comparing increased potassium to lower potassium intake found that increased potassium intake lowers blood pressure (4, 31). These results were further supported by a systematic review without a meta-analysis, which concluded that increased potassium intake results in decreased blood pressure in adults (3). Thus, a public health intervention aimed at increasing potassium intake from food could be a cost-effective strategy to reduce the burden of NCD morbidity and mortality. Moreover, increasing potassium consumption from food in the population is safe; in individuals without renal impairment caused by medical conditions or drug therapy, the body is able to efficiently adapt and excrete excess potassium via the urine when consumption

exceeds needs (18, 32, 33). Intervention trials including potassium consumption as high as 400 mmol/day from food for several weeks and 115 mmol/day for up to a year have not reported any adverse effects (32, 33). There have been some isolated reports of acute toxicity from extremely high potassium intake in supplement form (34), but no reports of toxicity of potassium from consumption in food.

The function of potassium in the body is closely related to that of sodium (18, 35). As sodium consumption rises, increased consumption of potassium may be even more beneficial because, in addition to other benefits, it can mitigate the negative effects of elevated sodium consumption on blood pressure (4). Some studies have reported that the ratio of the two nutrients is an important factor in cardiovascular disease and mortality (36, 37). Additionally, there is evidence from randomized controlled trials (RCTs) that a combination of increased potassium and decreased sodium intake can be effective in reducing blood pressure, cardiovascular mortality and medical expenses (38, 39).

# **Justification**

Much of the human and social impact caused each year by NCD-related morbidity and mortality could be averted through interventions that are well understood, cost effective and feasible (14). As explained above, there is no evidence of adverse effects from increased potassium intake from foods in individuals with unimpaired potassium excretion, and increased potassium intake has been associated with reduced blood pressure and cardiovascular disease outcomes in cohort and intervention trials. Hence, intervening to increase dietary potassium consumption could make a positive change to blood pressure and cardiovascular outcomes. Most populations around the world consume sodium at levels far exceeding physiological needs and current recommendations (40); therefore, public health interventions to combat NCDs and their risk factors should be informed by guidance on potassium consumption, combined with reduced sodium consumption. Although the evidence for the safety of potassium intake from food is not disputed, there are some inconsistencies in the literature about the potential beneficial effect of increased potassium on blood pressure and cardiovascular outcomes. One meta-analysis of studies of individuals with hypertension reported no significant effect of increased potassium intake on blood pressure (41). Therefore, a systematic evaluation of all available epidemiological evidence to inform the generation of this guideline was warranted.

Considering this background, the 32nd Session of the Codex Committee on Nutrition and Food for Special Dietary Uses (held in Santiago, the Republic of Chile on 1–5 November 2010) made a special request to WHO to consider establishing a guideline for daily potassium intake for adults and children. Member States also requested WHO to develop a guideline on potassium intake to inform public policy. Therefore, the WHO Department of Nutrition for Health and Development, in collaboration with other departments of WHO Headquarters and regional offices, developed the following guideline on potassium consumption for adults and children.

# **Guideline development process**

This guideline was developed in accordance with the WHO evidence-informed guideline development procedures outlined in the WHO Handbook for guideline development (6).

# **Advisory groups**

Development of this guideline was undertaken by the WHO Department of Nutrition for Health and Development, in partnership with the Department of Research Policy and Cooperation<sup>1</sup>, and members of the WHO Secretariat (Annex 3). The work was guided by the WHO Steering Committee for Nutrition Guideline Development (Annex 4), which also provided overall supervision of the guideline development process. The WHO Secretariat and the Steering Committee included representatives from all departments of WHO with an interest in the provision of scientific advice on nutrition. Two additional groups were formed: an advisory guideline group and an external expert and stakeholder panel, as outlined below.

# Advisory guideline group

The WHO Nutrition Guidance Expert Advisory Group (NUGAG) Subgroup on Diet and Health was convened to support the development of this guideline (Annex 5). This group included experts who had previously participated in various WHO expert advisory panels, and others identified through open calls for specialists. In forming this group, WHO took into consideration the need for a balanced gender mix, expertise from multiple disciplinary areas and representation from all WHO regions. Efforts were made to include subject-matter experts; statistical, systematic review, programme evaluation and Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodologists; and representatives of potential stakeholder groups (e.g. programme managers and other professionals involved in the health-care process). There were no representatives of commercial organizations, because such individuals are prohibited from being members of any WHO guideline group. External resource persons (including subject matter experts, and systematic review and GRADE methodologists) were invited to the NUGAG meetings as observers to provide technical input. These individuals did not participate in the decision-making processes. NUGAG's role was to advise WHO on the choice of outcomes important for decision-making and on the interpretation of the evidence.

# Panel

The External Expert and Stakeholder Panel was formed during the planning stages of guideline development. The panel was consulted on the scope of the guideline, and on the specific research questions to be addressed and outcomes to be investigated in the systematic reviews of the literature. The panel was later asked to review and provide feedback on the completed draft guideline (Annex 6). During the consultations on both the scoping of the guideline and the draft guideline documents, there was an open call

<sup>&</sup>lt;sup>1</sup> The Department of Research Policy and Cooperation has since been reorganized and the nutrition guideline development work is being carried out in close collaboration with the Department of Knowledge Management and Sharing.

for all interested parties to join the External Expert and Stakeholder Panel. The panel comprises individuals who responded to direct solicitation for contribution based on their known expertise and interest in the subject matter, or to the WHO open call for public comment executed through the electronic mailing lists of the WHO Department of Nutrition for Health and Development and that of the Codex Alimentarius Commissioin, and through the posting of the call for public comment on the WHO and United Nations (UN) Standing Committee of Nutrition websites.

# Scoping of the guideline, evidence appraisal and decision-making

WHO developed an initial set of questions to be addressed in the guideline. These draft questions were based on the needs of Member States and international partners for policy and programme guidance. They were also influenced by the request of the Codex Committee of Nutrition and Foods for Special Dietary Uses. The population, intervention, control and outcomes (PICO) format was used in generating the questions (Annex 7). The PICO questions were first discussed and reviewed by the WHO Secretariat and the WHO Steering Committee for Nutrition Guideline Development, and were then made available for public comment from 1 to 28 February 2011. Feedback was received from 16 individuals or organizational stakeholders, and the questions were adapted accordingly.

The draft set of PICO questions was presented to the NUGAG Subgroup on Diet and Health during its meeting on 14–18 March 2011. During that meeting, the guideline topic was introduced and the scope of the guideline to be generated was finalized. The PICO questions were discussed, and outcomes and populations were ranked in importance by NUGAG members. The prioritization of the PICO questions defined the scope of the evidence to be used in informing the guideline development. Subsequent to the meeting, WHO reviewed the scientific literature and conducted new systematic reviews and meta-analyses to address the PICO questions. WHO was supported in the execution of these reviews by external experts with subject-matter expertise, and expertise in systematic reviews and the GRADE methodology.

A follow-up meeting of the NUGAG Subgroup on Diet and Health was held from 29 November to 2 December 2011. WHO presented the systematic reviews of evidence, and a draft recommendation that had been prepared before the meeting. This draft recommendation included:

- a summary of the evidence from the systematic reviews;
- draft GRADE evidence profiles assessing the quality of the body of evidence;
- potential research gaps, concerns and opportunities for feasible implementation of the recommendations in diverse cultural contexts;
- appropriate references.

The NUGAG Subgroup on Diet and Health discussed the evidence and the GRADE assessment of the quality of evidence, and advised WHO on the interpretation of

the results. The subgroup also discussed the draft recommendation and, through consensus, reached an agreement on that recommendation.

The systematic reviews and the GRADE evidence profiles for each of the critical outcomes were used as the evidence base for drafting the guideline. Classification of the strength of each recommendation included consideration of the desirable and undesirable effects of the recommendation, the overall quality of the evidence, values and preferences related to the recommendation in different settings, and the cost of options available to public health authorities in implementing the recommendation in different settings (Annex 8). The classification was discussed among the NUGAG members, invited external resource persons and the members of the WHO Secretariat present at the meeting. The final wording of the recommendations and determination of their strength were based on the consensus of members of the WHO Secretariat present and the NUGAG members only. There were no strong disagreements among the NUGAG members.

From 1 to 29 February 2012, a draft of this guideline was made available for public comment. Participants in the External Expert and Stakeholder Panel were consulted, and other interested parties were invited to comment, as outlined above. More than 165 comments were received from 30 individuals and representatives of stakeholder groups. WHO reviewed the comments and made appropriate updates to the guideline. The guideline was then presented for finalization to the NUGAG Subgroup on Diet and Health at their meeting on 27–30 March 2012. The finalized guideline was submitted for clearance by WHO before publication.

# Management of conflicts of interest

According to the rules in the WHO <u>Basic documents</u> (42), all experts participating in WHO meetings must declare any interest relevant to the meeting before participating. The declaration of interest forms for all guideline group members were reviewed by WHO when finalizing the composition of the NUGAG Subgroup on Diet and Health. All NUGAG members, external experts and other special invitees participating in each of the NUGAG meetings submitted a declaration of interests form, together with their curriculum vitae. In addition, each participant verbally declared interests at the beginning of each meeting. The procedures for management of interests strictly followed the WHO <u>Guidelines</u> for declaration of interests for WHO experts (43). The potential interests declared by members of the NUGAG Subgroup on Diet and Health and external expert and resource persons are summarized in Annex 9.

# **Summary of evidence**

# **Evidence base**

This guideline is based on a review of the epidemiologic literature, including three new systematic reviews conducted by WHO (44-46) to summarize the evidence regarding potassium intake and health outcomes. Specific health outcomes considered were:

- in adults blood pressure, all-cause mortality, cardiovascular disease, stroke, coronary heart disease, renal function, blood lipids, catecholamine levels and other potential adverse effects;
- in children blood pressure, blood lipids, catecholamine levels and other potential adverse effects.

The specific research questions guiding these systematic reviews were:

- What is the effect of increased potassium intake compared with lower potassium intake on health outcomes in adults and children?
- Compared with lower potassium intake, what is the effect on health outcomes in adults and children of increased potassium intake to:
  - less than approximately 90 mmol/day;
  - approximately 90–120 mmol/day;
  - approximately 120–155 mmol/day;
  - more than approximately 155 mmol/day?

Evidence was considered conclusive of either a benefit or a harm from increased potassium intake if the point estimate suggested a benefit or harm and the 95%CI did not overlap a threshold of relevance. That is to say, if the real value were the high or the low 95%CI and that value was still of clinical relevance, the evidence was considered conclusive. If the point estimate were near the null value and the 95%CI did not overlap a threshold of relevance (e.g. if the real value were the high or the low 95%CI value and that value was not of clinical relevance) the evidence was considered conclusive of no effect. In such cases, the point estimates were considered precise.

Conversely, evidence was considered inconclusive if the point estimate suggested a benefit or a harm but the 95%CI crossed a threshold of relevance (e.g. if the real value were the high or the low 95%CI value and that value was not of clinical relevance). In such cases, the point estimates were considered imprecise.

# **Adults**

# Blood pressure in adults

WHO conducted a systematic review to explore the relationship between potassium and blood pressure in adults. The review identified 22 RCTs that met the inclusion criteria (44). Of these RCTs, 17 were conducted in individuals with hypertension (defined as a blood pressure ≥140/90 mmHg (47)), three in individuals without hypertension, and two in populations of individuals with and without hypertension. Two studies were conducted only in women, and the other 20 in populations of men and women. Studies were conducted in all regions of the world and all measured 24-hour urinary potassium excretion. WHO estimated potassium intake levels from 24-hour urinary potassium excretion using the conversion factor of 1.3 (48).

The lower potassium intake level varied among studies and ranged from 45 to 100 mmol/day, with a median value of 73 mmol/day. The increased potassium intake ranged from 70 to 247 mmol/day, with a median value of 127 mmol/day. There was a median difference in increased potassium relative to lower potassium of 57 mmol/day (74%).

The meta-analysis of 21 studies with 21 comparisons found that increased potassium resulted in a decrease in resting systolic blood pressure of 3.49 mmHg (95% confidence interval [CI]: 1.82, 5.15) (quality of evidence high¹) and a decrease in resting diastolic blood pressure of 3.02 mmHg (95%CI: 1.17, 4.86) (quality of evidence high). The meta-analysis of four studies with four comparisons reporting ambulatory blood pressure found that increased potassium intake decreased ambulatory systolic blood pressure by 3.04 mmHg (95%CI: 0.66, 5.42) (quality of evidence moderate), and ambulatory diastolic blood pressure by 1.24 mmHg (95%CI: -0.66, 3.13) (quality of evidence moderate). The findings demonstrate that across a wide range of baseline intakes, increasing potassium intake is beneficial in terms of blood pressure and they concur with three earlier systematic reviews and meta-analyses (3, 4, 31), but not with a fourth (41).

The results suggest that the greatest impact on blood pressure was achieved when the increased potassium intake was approximately 90–120mmol/day (44). The meta-analysis of five studies (with five comparisons) that achieved an increased potassium intake of 90–120mmol/day demonstrated a reduction in systolic blood pressure of 7.16 mmHg (95%Cl: 1.91, 12.41) (quality of evidence high), and a reduction in diastolic blood pressure of 4.01 mmHg (95%Cl: –0.42, 8.44) (quality of evidence moderate). Only one study with one comparison, in which the increased potassium intake was 90–120 mmol/day, reported ambulatory systolic and diastolic blood pressure; increased potassium intake resulted in a non-significant decrease of 1.80 mmHg (95%Cl: -2.42, 7.02) in ambulatory systolic blood pressure and 1.40mmHg (95%Cl: -2.34, 5.14) in ambulatory diastolic blood pressure (quality of evidence moderate).

All-cause mortality, cardiovascular disease, stroke, and coronary heart disease in adults

WHO conducted a systematic review on the relationship between potassium consumption and cardiovascular disease, stroke, coronary heart disease and all-cause mortality (45). The review updated and reanalysed data from the recent systematic review of D'Elia and colleagues (30). Only one study that met the inclusion criteria reported all-cause mortality. The results of this study were inconclusive (risk ratio [RR] 1.08²; 95%Cl: 0.91, 1.29) (quality of evidence very low). Twelve prospective cohort studies with more than 127,000 participants measured potassium intake through urinary potassium excretion, dietary records or some combination of these methods, and compared the incidence of cardiovascular disease, stroke or coronary heart disease between the lowest and highest potassium-consuming groups. Populations had wide ranges of potassium intake: some consumed approximately 35 mmol/day in the lowest group and 65 mmol/day or more in the lowest group and 110–150 mmol/day in the

<sup>&</sup>lt;sup>1</sup> Based on the grades of evidence set by the GRADE Working Group: **high quality**, we are very confident that the true effect lies close to that of the estimate of the effect; *moderate quality*, we have moderate confidence in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; **low quality**, our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect; **very low quality**, we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of the effect.

<sup>&</sup>lt;sup>2</sup> In the analysis of data from cohort studies, RR <1 indicates decreased risk with increased potassium intake.

highest group. The follow-up period ranged from 2 to 19 years. Studies were conducted in Asia, Europe and the USA, and one study used data from individuals in 40 different countries. Two studies were conducted exclusively in individuals without hypertension, two were specifically in a heterogeneous group of individuals both with and without hypertension, and the remaining studies did not specify the blood pressure status of the study population.

The meta-analysis of four studies with four comparisons with cardiovascular disease as an outcome was inconclusive regarding the association between potassium and cardiovascular disease (RR 0.88; 95%Cl: 0.70, 1.11) (quality of evidence very low). The meta-analysis of nine studies with 10 comparisons with stroke as an outcome was supportive of a reduction in risk of stroke with increased potassium (RR 0.79; 95%Cl: 0.68, 0.93) (quality of evidence low). The meta-analysis of four studies with four comparisons between a potassium intake of  $\geq$ 90 mmol/day and <90 mmol/day demonstrated a reduction in stroke associated with consuming  $\geq$ 90 mmol/day (RR 0.70; 95%Cl: 0.56, 0.88) (quality of evidence low). The outcome of the meta-analysis of three studies with three comparisons reporting coronary heart disease as the outcome was inconclusive (RR 0.97; 95%Cl: 0.77, 1.24) (quality of evidence very low).

There is a well-established relationship between increasing blood pressure and increasing risk of cardiovascular diseases, particularly coronary heart disease and stroke (12, 49). Blood pressure is thus considered a reliable biomarker for estimating risk of cardiovascular disease (50, 51). Recognizing the limitations of any biomarker, it was nonetheless determined that blood pressure could be a suitable proxy indicator for risk of cardiovascular disease, stroke, and coronary heart disease. Therefore, in addition to the direct evidence from observational cohort studies on the relationship between potassium intake and cardiovascular disease, stroke, and coronary heart disease, the data from RCTs on the effect of increased potassium consumption on blood pressure (44) were used as part of the evidence base for considering the effect of increased potassium intake on these outcomes.

# Potential adverse effects in adults

Potential adverse effects from increased potassium intake included changes in blood lipids (e.g. increased total cholesterol, low-density lipoprotein [LDL] cholesterol and triglyceride; decreased high-density lipoprotein [HDL] cholesterol); changes in renal function; increases in catecholamine levels; and any other adverse effects or minor side-effects (i.e. dizziness, headache, muscle pain) reported by study authors. The decrease in blood volume caused by increased potassium activates the sympathetic nervous system, resulting in the release of adrenaline and noradrenaline. Decreased blood volume may also be responsible for changes in blood lipid concentrations. The effect of 4 or more weeks of increased potassium consumption on these outcomes was addressed in the systematic review of the literature that considered the effect of potassium on blood pressure (44). The meta-analysis of three trials reporting total cholesterol concentration showed that increased potassium intake relative to lower potassium intake resulted in a non-significant decrease of 0.12mmol/L (95%Cl: -0.33, 0.09) in total cholesterol (quality of evidence high). Only one study in the literature reported LDL concentration, and the results indicated a non-significant decrease in LDL of 0.10 mmol/L (95%Cl: -0.18, 0.38) (quality of evidence high). Although the data were limited, the meta-analysis of two studies with two comparisons reporting HDL and triglyceride concentrations also showed non-significant decreases in those indicators with increased potassium consumption (HDL 0.01 mmol/L; 95%Cl: –0.1, 0.13; triglyceride 0.11 mmol/L; 95%Cl: –0.26, 0.48) (quality of evidence high). The meta-analysis of three trials showed that increased potassium intake relative to lower potassium intake resulted in a non-significant decrease of 4.32 pg/mL (95%Cl: –15.13, 23.78)in plasma noradrenaline (and 3.94 pg/mL (95%Cl: –1.34, 9.22) plasma adrenaline ( (quality of evidence high). No studies that met the inclusion criteria reported urinary catecholamine levels. As an indicator of renal function, three studies quantified serum creatinine concentration. The meta-analysis of these studies suggested that increased potassium intake had no effect on renal function with a non-significant increase of 4.86 µmol/L (95%Cl: –3.87, 13.59) in these samples of individuals with apparently normal renal function (quality of evidence high). Although the evidence was limited, the data from RCTs were conclusive of no adverse effect of increased potassium intake in terms of blood lipids, catecholamine levels or renal function.

No minor side-effects as a result of increased potassium intake were reported in any of the RCTs. Though these studies were all of relatively short duration, the absence of any complaints of adverse effects with increased potassium intake is consistent with the literature (32, 33). The body is able to efficiently adapt and excrete excess potassium via the urine when consumption exceeds needs (18, 32, 33), and there have been no reports of toxicity of potassium from consumption in food (34).

# **Children**

Blood pressure in children

WHO conducted a systematic review of the effect of increased potassium intake on blood pressure, blood lipids, catecholamine levels and other potential adverse effects in children (46). Only four studies in children reporting on blood pressure met the inclusion criteria for the review, and none of these reported on blood lipids, catecholamine levels or other adverse effects. Three of the four studies were controlled trials conducted in the USA. They included a total of 326 boys and girls averaging 13 years of age. The potassium intake values in the lower groups averaged 57 mmol/day, compared with 95 mmol/day in the increased potassium groups. The fourth study was an observational cohort study conducted in the Netherlands; it included children aged 5-17 years of age at baseline and followed them for 7 years. The meta-analysis of the three controlled trials with five comparisons showed that increased potassium intake affected a nonsignificant decrease of 0.25 mmHg (95%CI: -0.49, 1.05) in systolic blood pressure and 0.92 mmHg (95%CI: -0.16, 2.00) in diastolic blood pressure(quality of evidence low). The results of the observational cohort study in children were consistent with a beneficial effect of increased potassium on blood pressure over time. In that study, potassium intake was inversely related to the rate of increase in blood pressure over a 7-year period (52).

There were few high-quality RCTs testing the effect of increased potassium intake on blood pressure and potential adverse effects in children. Hence, in generating the guideline for children, the data from the systematic review conducted in adults (44) were used as part of the evidence base for estimating the effect of increased potassium on health outcomes in children. Renal function is fully developed in early childhood; thus, it was considered acceptable to use information from adults to infer the effect of potassium intake on blood pressure in children. The evidence from studies conducted in adults was downgraded from high to moderate in quality because of indirectness (i.e. the use of a proxy population for the target population).

# Final considerations of the evidence

WHO attempted to discern differences in the effect of increased potassium on outcomes according to type of intervention (i.e. supplements, fortification or food), type of potassium supplement (i.e. potassium citrate, potassium chloride or other) and gender. In the systematic review and meta-analysis of RCTs in adults reporting blood pressure as an outcome (44), the subgroup analysis of 19 studies using potassium supplements showed a decrease in systolic blood pressure of 3.31 mmHg (95%CI: 1.55, 5.07) (quality of evidence high), and the subgroup analysis of three studies using dietary changes showed a decrease in systolic blood pressure of 4.19 mmHg (95%CI: 1.92, 6.46) (quality of evidence high). The results suggest that an increase in potassium intake from either supplement or food has a beneficial effect on blood pressure.

In assessing the results of supplementation studies, it was possible to isolate the effect of potassium because it was the only variable manipulated between increased potassium and usual or lower potassium groups. The consistency in results from studies with increased potassium through dietary change supports the health benefit of potassium specifically, and not the conjugate anion found in the supplements used in the supplementation studies. Additionally, all cohort studies compared groups consuming different levels of potassium from foods (44). The cohort studies suggested a positive effect of increased potassium on stroke, further strengthening the conclusion that specifically increasing potassium has beneficial effects on health. No studies that met the inclusion criteria looked specifically at potassium fortification of food, mainly because such studies also manipulated sodium levels. One study used potassium citrate, one used potassium bicarbonate and one used a combination of potassium citrate and bicarbonate, whereas all other supplementation studies used potassium chloride; thus, it was not possible to compare different supplement types. Twenty of the 22 RCTs and nine of the 12 cohort studies were in mixed populations of men and women. Although differences by gender could not be compared, the overall positive effect of increased potassium found in these studies supports a beneficial effect in both men and women.

Addressing the optimal ratio of sodium to potassium was outside the scope of this guideline; however, we undertook subgroup analysis of the RCTs to explore whether different levels of sodium intake influence the effect of potassium on blood pressure. Only one study had a mean sodium intake level of <2 g/day, and it found a non-significant decrease of 2.00 mmHg (95%CI: -7.70, 11.70) on systolic blood pressure with increased potassium intake (quality of evidence moderate), but conclusions should not be drawn from such limited evidence. In the 15 studies with a mean sodium intake of 2-4 g/day, increased potassium intake decreased systolic blood pressure by 1.97 mmHg (95%CI: 0.52, 3.41) (quality of evidence high). In the five studies with a mean sodium intake of >4 g/day, increased potassium intake decreased systolic blood pressure by 6.91 mmHg (95%CI: 2.29, 11.53) (quality of evidence high). Although the difference in the effect estimates was not statistically significant, the results suggest that potassium may be more effective in reducing blood pressure at higher sodium consumption levels, which is consistent with previous findings (4). There was still a significant benefit of increased potassium intake on blood pressure when populations consumed 2-4 g/day of sodium; hence, with most populations around the world consuming more than 2-4 g/day of sodium (40), increased potassium intake should benefit most countries.

The RCTs were also grouped by baseline potassium intake. In the two studies in which baseline intake was <50mmol/day, increased potassium intake decreased systolic blood pressure by 3.89 mmHg (95%Cl: 0.74, 7.03). In the 14 studies with a baseline potassium intake of 50-80mmol/day, increased potassium intake decreased systolic blood pressure by 3.39mmHg (95%Cl: 1.26, 5.51) and diastolic blood pressure by 1.53 mmHg (95%Cl: 0.25, 2.80). In the five studies with a baseline potassium intake of >80mmol/day, increased potassium intake decreased systolic blood pressure by 4.11 mmHg (95%Cl: 1.97, 6.26) and diastolic blood pressure by 3.38 mmHg (95%Cl: 2.02, 4.74). Thus, increased potassium intake had a beneficial effect on blood pressure regardless of baseline potassium intake.

The RCTs were grouped by blood pressure status at baseline. In the three studies conducted exclusively in individuals with normal blood pressure, increased potassium intake resulted in a non-significant increase in systolic blood pressure of 0.09 mmHg (95%CI: -0.95,0.77) (quality of evidence moderate). In the 16 studies conducted in individuals with hypertension, increased potassium intake decreased systolic blood pressure by 5.32 mmHg (95%CI: 3.43, 7.20 (quality of evidence high). Although it appears that potassium may only reduce blood pressure in individuals with hypertension, the studies in individuals without hypertension were of relatively short duration, and the effect over time on the prevention of elevated blood pressure is not known. Given the high prevalence of hypertension in adult populations globally (2), the relatively low potassium intake in most populations (9, 10, 53), and the clear benefit of increased potassium intake in individuals with high blood pressure, increasing potassium intake is likely to be broadly beneficial to populations around the world.

Finally, the modest reduction in systolic blood pressure (3.49 mmHg) and in diastolic blood pressure (3.02 mmHg) would have important public health benefits. Elevated blood pressure is the leading risk factor for mortality, accounting for almost 13% of death globally (2). In the USA, a relatively small decrease of 2 mmHg in diastolic blood pressure in the population could result in an estimated 17% decrease in the prevalence of hypertension, 6% decrease in risk of coronary heart disease, and 15% decrease in risk of stroke; it could also prevent an estimated 67,000 coronary heart disease events and 34,000 stroke events every year (54). In the United Kingdom, researchers estimate that a 5 mmHg reduction in systolic blood pressure could reduce the prevalence of hypertension by 50% (55). Additionally, the relationship between blood pressure and risk of vascular mortality is positive, strong and linear down to a systolic blood pressure of 115 mmHg, below which there is no evidence (49). Thus, almost all reduction in blood pressure is beneficial for health, and modest population-wide reductions in blood pressure result in important reductions in mortality, substantial health benefits and meaningful savings in health-care costs (2, 12, 13).

# **Recommendations and remarks**

# Recommendations

- WHO recommends an increase in potassium intake from food for reduction of blood pressure and risk of cardiovascular disease, stroke and coronary heart disease in adults (*strong recommendation*<sup>1</sup>). WHO suggests a potassium intake of at least 90 mmol/day (3510 mg/day) for adults (*conditional recommendation*<sup>2</sup>).
- WHO suggests an increase in potassium intake from food to control<sup>3</sup> blood pressure in children (*conditional recommendation*). The recommended potassium intake of at least 90 mmol/day should be adjusted downward for children, based on the energy requirements of children relative to those of adults.

# **Remarks**

- For this recommendation, "adults" includes all individuals ≥16 years of age.
- For this recommendation, "children" includes all individuals 2–15 years of age.
- The recommendation for children does not address the recommended period of exclusive breastfeeding (0–6 months) or the period of complementary feeding with continued breastfeeding (6–24 months).
- These recommendations apply to all individuals, with or without hypertension (including pregnant and lactating women) except for those with impaired urinary potassium excretion.
- These recommendations do not address the optimal ratio of sodium to potassium; however, if this guideline and the WHO guideline on sodium consumption are achieved, the molar ratio of sodium to potassium would be approximately one to one. To maintain this molar ratio at higher levels of sodium consumption, the recommended level of intake of ≥90 mmol/day potassium should be increased.
- These recommendations complement the WHO guideline on sodium consumption and should not be interpreted to replace or supersede that guideline. Public health interventions should aim to increase potassium intake through foods (Annex 2), and to simultaneously reduce sodium intake.

<sup>&</sup>lt;sup>1</sup> A strong recommendation is one for which the guideline development group is confident that the desirable effects of adherence outweigh the undesirable effects. The recommendation can be either in favour of or against an intervention. Implications of a strong recommendation are as follows: for patients, most people in their situation would desire the recommended course of action, only a small proportion would not; for clinicians, most patients should receive the recommended course of action, and adherence to this recommendation is a reasonable measure of good-quality care; for policy-makers, the recommendation can be adopted as a policy in most situations.

<sup>&</sup>lt;sup>2</sup> 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. The reason for not being confident could be the absence of high-quality evidence; the presence of imprecise estimates of benefit or harm; uncertainty or variation on how certain individuals will value the outcome; small benefits; and benefits that are not worth the costs (including the costs of implementing the recommendation). Implications of a conditional recommendation are as follows: for patients, most people in their situation would want the recommended course of action, but many would not; for clinicians, patients may need help to make a decision in relation to the recommendation that is consistent with their own values; for policy-makers, there is a need for debate and involvement of stakeholders in deciding whether to adopt the recommendation as policy.

 $<sup>^{3}</sup>$  "Control" for this recommendation refers to the prevention of a deleterious rise in blood pressure with age.

- The recommended level of intake of ≥90 mmol/day is a conditional recommendation for adults because there is limited evidence regarding the precise level that will result in **maximum** health benefits. The recommendation is informed by moderate and high-quality evidence that consuming potassium at ≥90 mmol/day will provide a health benefit. However, the recommendation recognizes that the value may change if there are additional high-quality trials that determine the precise level of potassium intake that achieves the **most** favourable reduction in blood pressure and risk of cardiovascular disease, stroke and coronary heart disease, without a negative effect on other health outcomes such as blood lipids and catecholamine levels.
- The recommendation to increase potassium intake in children is conditional, because few studies in children have considered the effects of increased potassium on blood pressure, blood lipids, catecholamine levels, and other possible adverse effects. The recommendation is based on a limited amount of low-quality direct evidence from children, and moderate-quality indirect evidence from adults. Because renal function is fully developed early in childhood, an adult population is an appropriate proxy population for informing guidelines for children. This recommendation recognizes that there is a need for high-quality RCTs, to verify the effects of potassium intake on blood pressure and potential adverse effects in children. An adjustment in intake, based on energy requirement, is recommended because the relatively high energy intake on a per body-weight basis during periods of rapid growth implies a risk that the recommended level of potassium intake could be too low if adjustments to the adult recommended value are made on a per body-weight basis. Every country should determine the requirement of various age categories of the paediatric population relative to adults 20-50 years of age, to adjust the recommended minimum intake value of 90 mmol/day. If country-specific data are not available, data from another country with similar population demographics and dietary habits can be used to make this adjustment.
- These recommendations recognize that non-acclimated individuals engaged in intense physical activities (especially at high temperatures) for extended periods of time, resulting in the production of large volumes of sweat, should consume higher levels of potassium to replace potassium losses via sweat. For most individuals, sufficient potassium to replace such losses can be consumed through food, without the need for specially formulated food and beverage products.
- It is recommended that potassium be consumed through food. Because of the safety of consumption of increased potassium via food, no upper limit has been considered.

# **Translation and implementation**

This nutrient guideline on potassium can aid the logical, systematic, and scientific development of nutrition interventions taking into account the best available scientific evidence. This guideline should be used in conjunction with sodium and other nutrient guidelines to guide public health nutrition programmes and policies.

The recommendations in this guideline can be used by programme and policy planners to assess current potassium intake relative to a benchmark and develop measures to increase potassium intake, where necessary, through public health interventions including, but not limited to, food and product labelling and consumer education. Additionally, this guideline can be translated at the country-level into culturally and contextually specific FBDGs that take into account locally available food and dietary customs.

Though providing overall dietary guidance is outside the scope of this guideline because such dietary guidance should be based on overall dietary goals, which consider all required nutrients, it is recommended that potassium be consumed through food. It is also recognized that it is feasible to achieve this recommendation while respecting national dietary customs because potassium is found in a wide variety of foods (Annex 2). Additionally, because fresh fruits, vegetables and beans are high in potassium, an increased intake of potassium can be achieved without increasing caloric intake if these foods replace foods lower in potassium levels in the diet.

# Research gaps and future initiatives

# Implications for future research

- High-quality RCTs in children are needed that address the effects of increased potassium intake compared with lower potassium intake on blood pressure, and adverse effects such as changes in blood lipids and catecholamine levels.
- Further high-quality RCTs in adults are needed that assess the effects of increased potassium intake compared with lower potassium intake on cardiovascular disease, stroke and coronary heart disease.
- High-quality RCTs with multiple intervention arms designed to directly test the
  effect of multiple levels of potassium intake on health outcomes are warranted,
  to strengthen the evidence base for the precise target potassium intake value.
- High-quality trials with multiple intervention arms designed to test various forms of potassium compounds (i.e. potassium citrate, potassium bicarbonate and potassium chloride), in either supplement or fortification form, are warranted.

# Dissemination

The current guideline will be disseminated through:

- electronic media such as slide presentations;
- mailing lists of the WHO Department of Nutrition for Health and Development and the UN Standing Committee on Nutrition;
- the web site of the WHO Department of Nutrition for Health and Development.

A summary of this guideline will also be available in all six UN languages through the WHO Department of Nutrition for Health and Development's electronic Library of Evidence for Nutrition Actions. The library displays WHO guidelines related to nutrition, and complementary documents such as systematic reviews and other evidence informing the guidelines, biological and behavioural rationales for the effectiveness of a guideline, and other relevant resources produced by Member States and global partners.

# Updating the guideline

The recommendations in this guideline will be reviewed by the end of 2017. If new information is available by that date, a guideline review group will be convened to evaluate the new evidence and revise the recommendation. However, if a large amount of new evidence becomes available before that date, a guideline review group may be convened earlier. The Department of Nutrition for Health and Development at the WHO Headquarters in Geneva, together with partners in other departments within the WHO Secretariat, will be responsible for coordinating the updating of the guideline, following the formal WHO Handbook for guideline development (6) procedures. When the guideline is due for review, WHO will welcome suggestions for additional questions that could be addressed in the guideline.

# Annex 1 GRADE summary of findings tables

What is the effect of increased potassium intake relative to lower intake in adults (≥16 years of age)?

Outcomes	Effect (95 % CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
Cardiovascular disease ' (directly assessed; RR greater than 1 indicates increased risk with increased sodium intake)	<b>RR 0.88</b> (0.70 to 1.11)	29 067 (4 studies)	⊕⊝⊝⊝ very low	Data from cohort studies begin with a GRADE of low. Downgraded due to imprecision because 95%Cl crossed threshold of relevance of benefit or harm.
<b>Stroke</b> (directly assessed; RR less than 1 indicates decreased risk with increased potassium intake)	<b>RR 0.79</b> (0.68 to 0.93)	97 152 (9 studies)		Data from cohort studies begin with a GRADE of low.
<b>Coronary heart disease</b> (directly assessed; RR less than 1 indicates decreased risk with increased potassium intake)	<b>RR 0.97</b> (0.77 to 1.24)	31 162 (3 studies)	⊕⊝⊝⊝ very low	Data from cohort studies begin with a GRADE of low. Downgraded due to imprecision because 95%Cl crossed threshold of relevance of benefit or harm.
All cause mortality (directly assessed; RR less than 1 indicates decreased risk with increased potassium intake)	RR 1.08 (0.91, 1.29)	1 766 (1 study)	⊕⊝⊝⊝ very low	Only one study reported this outcome. Downgraded due to imprecision because 95%CI crossed threshold of relevance of benefit or harm.
Resting systolic blood pressure 2 (follow-up 1-36 months; units mmHg; better indicated by lower values)	MD 3.49 lower <sup>3</sup> (5.15 to 1.82 lower)	286 (5 studies)	⊕⊕⊕⊕ high	
<b>Total cholesterol</b> <sup>4</sup> (follow-up 1 - 2 months; units mmol/L; <b>MD 0.12 lower</b> better indicated by lower values) (0.33 lower to 0.09	MD 0.12 lower (0.33 lower to 0.09 higher)	208 (3 studies)	⊕⊕⊕⊕ high	Not downgraded due to imprecision because 95%Cl did not cross threshold of relevance of benefit or harm.
Plasma noradrenaline <sup>§</sup> (follow-up 1 - 2.5 months; units pg/ml; better indicated by lower values)	<b>MD 4.32 lower</b> (23.78 lower to 15.13 higher)	152 (3 studies)	⊕⊕⊕⊕ high	Not downgraded due to imprecision because 95%Cl did not cross threshold of relevance of benefit or harm.
Serum Creatinine (follow-up mean 1.5 months; units ng/mL filtrate; better indicated by lower values)	<b>MD 4.86 lower</b> (13.59 lower to 3.87 higher)	147 (3 studies)	⊕⊕⊕⊕ high	Not downgraded due to imprecision because 95%Cl did not cross threshold of relevance of benefit or harm.
Minor side effects (better indicated by lower values)				No studies reported this outcome

CI, Confidence interval; RR, Risk ratio; MD, Mean difference GRADE Working Group grades of evidence: **High quality:** We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We have moderate confidence in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different Low quality: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of the effect.

Composite cardiovascular disease as reported by original study authors. This variable included some or all of the following; fatal and non-fatal stroke, coronary heart disease, myocardial infarction, and/or congestive cardiac failure, or episode of coronary revascularization, bypass grafting, and/or angioplasty.

(MD 3.02 mmHg lower (4.86 to 1.17 lower)) (quality of evidence high); a meta-analysis of four RCTs with four comparisons reporting ambulatory systolic blood pressure is supportive of a benefit of increased potassium on blood pressure (MD 3.04 mmHg lower (5.42 to 0.66 lower)) (quality of evidence moderate); and a meta-analysis of four RCTs with four comparisons reporting ambulatory diastolic blood pressure is consistent with a Additional evidence from a meta-analysis of 21 randomized-controlled trials (RCTS) with 21 comparisons reporting resting diastolic blood pressure is supportive of a benefit of increased potassium on blood pressure benefit of increased potassium on blood pressure (MD 1.24 lower (3.13 lower to 0.66 higher))(quality of evidence moderate).

<sup>3</sup> A MD described as 10wer' signifies a reduction in the outcome in the increased potassium versus the lower potassium group.

Additional evidence on the relationship between potassium intake and blood lipids comes from a meta-analysis of two RCTs with two comparisons reporting high-density lipoprotein (HDL) cholesterol concentration glyceride concentration that is supportive of no effect of increased potassium on blood lipids (MD 0.11 mmol/L lower (0.48 lower to 0.26 higher)) (quality of evidence high). There was only one RCT in the literature that that is supportive of no effect of increased potassium in blood lipids (MD 0.01 mmol/L lower (0.13 lower to 0.11 higher) (quality of evidence high), and a meta-analysis of two RCTs with two comparisons reporting trireported low-density lipoprotein (LDL) cholesterol concentration and it was consistent with no effect of increased potassium on blood lipids (MD 0.10 mmol/L lower (0.38 lower to 0.18 higher).

. A meta-analysis of three RCTs with three comparisons reporting plasma adrenaline concentration is supportive of no effect of increased potassium on catecholamine levels (MD 3.94 pg/mL lower (9.22 lower to 1.34 higher)) (quality of evidence high). There were no studies identified that reported urinary catecholamine levels.

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Outcomes	Effect (95 % CI)	Number of participants (studies)	Quality of the evidence (GRADE)	Comments
Cardiovascular disease <sup>1</sup> (directly assessed; RR greater than 1 indicates decreased risk with increased potassium intake)	RR 0.84 (0.61, 1.15)	2 809 (2 studies)	⊕⊝⊝⊝ very low	Data from cohort studies begin with a GRADE of low. Downgraded due to imprecision because 95%Cl crossed threshold of relevance of benefit or harm.
<b>Stroke</b> (directly assessed; RR less than 1 indicates decreased risk with increased potassium intake)	<b>RR 0.70</b> (0.56 to 0.88)	54 796 (4 studies)	⊕⊕⊖⊝ low	Data from cohort studies begin with a GRADE of low.
Coronary heart disease (directly assessed; RR less than 1 indicates decreased risk with increased potassium intake)				There were no studies with coronary heart disease as an outcome which addressed this question.
All cause mortality (directly assessed; RR less than 1 indicates decreased risk with increased potassium intake)				There were no studies with coronary heart disease as an outcome which addressed this question.
Resting systolic blood pressure <sup>2</sup> (follow-up 1-36 months; units mmHg; better indicated by lower values)	MD 7.16 lower <sup>3</sup> (12.41 to 1.91 lower)	286 (5 studies)	⊕⊕⊕⊕ high	
Total cholesterol				There were no studies with total cholesterol as an outcome which addressed this question.
Plasma noradrenaline				There were no studies with total cholesterol as an outcome which addressed this question.
Serum Creatinine				There were no studies with total cholesterol as an outcome which addressed this question.
Minor side effects				There were no studies with total cholesterol as an outcome which addressed this question.

CI, Confidence interval; RR, Risk ratio; MD, Mean difference.

GRADE Working Group grades of evidence:

**High quality:** We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We have moderate confidence in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Very low quality: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of the effect.

Low quality: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.

For details on studies included in the reviews, see references (44, 45)

Composite cardiovascular disease as reported by original study authors. This variable included some or all of the following: fatal and non-fatal stroke, coronary heart disease, myocardial infarction, and/or congestive cardiac failure, or episode of coronary revascularization, bypass grafting, and/or angioplasty.

s Additional evidence comes from a meta-analysis of 5 randomized-controlled trials with 5 comparisons reporting resting diastolic blood pressure is consistent with a benefit of increased potassium to 90 mmol/day on blood pressure (MD 4.01 mmHg lower (8.44 lower to 0.42 higher)) (quality of evidence moderate). There was 1 randomized-controlled trial with 1 comparison which reported ambulatory systolic and diastolic blood pressure. The results were inconclusive (ambulatory systolic blood pressure MD 1.80 lower (7.02 lower to 2.42 higher); ambulatory diastolic blood pressure MD 1.40 lower (5.14 lower to 2.34 higher)).

<sup>&</sup>lt;sup>3</sup> A MD described as 'lower' signifies a reduction in the outcome in the increased potassium versus the lower potassium group

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Outcomes	Effect (95 % CI)	Number of participants (studies)	Number of participants Quality of the evidence (studies)	Comments
Resting systolic blood pressure ¹ (assessed directly in children; follow-up 0.75-1 month; units mmHg; better indicated by lower values)	<b>MD 0.28 lower</b> <sup>2</sup> (1.05 lower to 0.49 higher)	236 (3 studies)		1 of 3 studies was not randomized. Downgraded for high risk of bias and imprecision.
Resting systolic blood pressure3 (assessed in adults; follow-up 1-36 months; units mmHg; better indicated by lower values)	MD 3.49 lower (5.15 to 1.82 lower)	1 892 (21 studies)	⊕⊕⊕⊝ moderate	Downgraded for indirectness
<b>Total cholesterol</b> (assessed directly in children)				No studies in children reported on this outcome.
Total cholesterol <sup>3</sup> (assessed in adults; follow-up 1 - 2 months; units mmol/L; better indicated by lower values)	<b>MD 0.12 lower</b> (0.33 lower to 0.09 higher)	208 (3 studies)	⊕⊕⊕⊝ moderate	Downgraded for indirectness. Not downgraded due to imprecision because 95%CI did not cross threshold of relevance of benefit or harm.
Plasma noradrenaline (assessed directly in children)				No studies in children reported on this outcome.
Plasma noradrenaline <sup>3</sup> (assessed in adults; follow-up 1 - 2.5 months; units pg/mL; better indicated by lower values)	<b>MD 4.32 lower</b> (23.78 lower to 15.13 higher)	152 (3 studies)	⊕⊕⊕⊝ moderate	Downgraded for indirectness. Not downgraded due to imprecision because 95%CI did not cross threshold of relevance of benefit or harm.
Minor side effects (assessed directly in children)				No studies in children reported on this outcome.
Minor side effects (assessed directly in children)				No studies in children reported on this outcome.

Cl, Confidence interval; RR, Risk ratio; MD, Mean difference.

GRADE Working Group grades of evidence:

High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate quality: We have moderate confidence in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low quality: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.

Very low quality: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of the effect.

' One cohort observational study in children is consistent with a beneficial effect of increased potassium on blood pressure over time.

² A MD described as lower signifies a reduction in the outcome in the increased potassium versus the lower potassium group

<sup>3</sup> Data from adults used as a proxy for children.

For details on studies included in the reviews, see references (46)

# Annex 2 Examples of foods that contain potassium, and their approximate potassium content

The table below provides examples of foods from around the world that contain potassium, and gives the approximate average potassium content of those examples from various food composition databases.

Food group	Approximate potassium content, (mg/100g fresh weight)	Examples
Beans and peas	1300	Cowpeas, pigeon peas, lima beans, African yam beans
Nuts	600	Hazelnuts, walnuts, cashew nuts, brazil nuts
Green vegetables	550	Spinach, cabbage, parsley
Root vegetables	200	Carrots, onions, beetroot
Other vegetables	300	Tomatoes, cucumbers, pumpkins
Fruits	300	Bananas, papayas, dates

Note: The information in this table is based on approximate calculations of the average potassium content from an example of foods within each food group from food composition databases from around the globe. The potassium content varies within the food groups. Thus, the information provided can be used only for approximate comparisons of various food groups, and should not be used to estimate daily intake.

Sources: (56-61)

# **Annex 3** WHO Secretariat

# **WHO** Headquarters

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Scientist

Nutrition Policy and Scientific Advice Unit Department of Nutrition for Health and Development

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**Guidelines Review Committee Secretariat** 

# **Dr Regina Kulier**

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# **Dr Margaret Harris**

**Guidelines Review Committee Secretariat** 

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# Dr Joao Breda

Scientist

WHO Regional Office for Europe Copenhagen, Denmark

# Dr Ayoub Al-Jawaldeh

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# **Dr Tommaso Cavalli-Sforza**

Regional Adviser

Nutrition

WHO Regional Office for the Western Pacific Manila, the Philippines

# Annex 4 Members of the WHO Steering Committee for Nutrition Guideline Development 2010 - 2011

# **WHO Headquarters**

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Director, Nutrition for Health and Development Department

# Dr Tikki Pang (Pangestu)

Director, Research Policy and Cooperation

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Scientist, Newborn and Child Health and Development

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Acting Director, Chronic Diseases and Health Promotion

Alternate:

# **Dr Godfrey Xuereb**

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Technical Officer, Ethics, Equity, Trade and Human Rights

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Director, Global Malaria Programme *Alternate*:

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Associate Director, Global Malaria Programme

# **Dr Aafje Rietveld**

Medical Officer, Global Malaria Programme

# Dr Willem Van Lerberghe

Director, Health Policy, Development and Services

# **Dr Gottfried Otto Hirnschall**

Director, HIV/AIDS

Alternate:

# Mr Craig Michael McClure

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### Dr Jean-Marie Okwo-Bele

Director, Immunization, Vaccines and Biologicals

# **Dr Michael Mbizvo**

Director, Reproductive Health and Research

# **Dr Mario Raviglione**

Director, Stop Tuberculosis *Alternate:* 

# **Dr Knut Lonnroth**

Medical Officer, Stop Tuberculosis

# **Dr Daniel Eduardo Lopez Acuna**

Director, Strategy, Policy and Resource Management

# Dr Nevio Zagaria

Acting Director, Emergency Response & Recovery Operations

# International Agency for Research on Cancer

# **Dr Isabelle Romieu**

Director, Nutrition Department

# **Annex 5**

# Members of the NUGAG Subgroup on Diet and Health and external resource persons 2010 - 2011

# Members of the NUGAG Subgroup on Diet and Health

(Note: the areas of expertise of each guideline group member are given in italics)

# **Professor Pascal Bovet**

University Institute of Social and Preventive Medicine, Lausanne University Hospital Switzerland and Ministry of Health Seychelles Programme manager, noncommunicable diseases

### **Professor Michael Clarke**

School of Nursing and Midwifery Trinity College, Ireland and United Kingdom Cochrane Centre United Kingdom Methods, systematic review

### **Professor John H Cummings**

Centre for Oncology and Molecular Medicine Division of Medical Sciences University of Dundee United Kingdom Carbohydrates, dietary fibre

# **Professor Ibrahim Elmadfa**

Institution of Nutritional Sciences

University of Vienna Austria Human nutrition, nutrient requirements, fats and fatty acids, dietary diversity

# **Professor Nahla Hwalla**

Faculty of Agricultural and Food Sciences American University of Beirut Lebanon Dietetics, nutrition, food-based dietary auidelines, diet and health

# **Associate Professor Rachel Huxley**

Division of Epidemiology & Community Health University of Minnesota USA Epidemiology, physiology, biostatistics, meta-analysis, obesity

# Professor Shiriki Kumanyika

Center for Clinical Epidemiology & Biostatistics University of Pennsylvania School of Medicine USA Human nutrition, epidemiology, obesity,

# **Professor Mary L'Abbe**

salt/sodium

Department of Nutritional Sciences
Faculty of Medicine
University of Toronto
Canada
Nutrition science, trans-fatty acids, risk
assessment and risk management,
diet and health

# **Professor Duo Li**

Department of Food Science and Nutrition Zhejiang University China Nutritional epidemiology, fats and fatty acids

# **Professor Jim Mann**

Department of Medical and Surgical Sciences University of Otago New Zealand Carbohydrates, sugars, diabetes, fats and fatty acids

### **Professor Carlos Monteiro**

Department of Nutrition, School of Public Health University of Sao Paulo Brazil Human nutrition, epidemiology, double-burden of malnutrition

# **Professor Dariush Mozaffarian**

Harvard School of Public Health Harvard University USA Cardiology, epidemiology, diet and health

# **Professor Srinath Reddy**

Public Health Foundation of India India Cardiovascular diseases, obesity, noncommunicable diseases

# **Professor Murray Skeaff**

University of Otago New Zealand Fats and fatty acids, biomarkers, diet and health, human nutrition

# Professor H.H. (Esté) Vorster

Faculty of Health Sciences North-West University South Africa Nutrition physiology, public health nutrition, food-based dietary quidelines

# **External resource persons**

# **Professor Francesco Cappuccio**

University of Warwick Warwick Medical School United Kingdom

# **Professor Paul Elliott**

MRC-HPA Centre for Environment and Health and Department of Epidemiology and Biostatistics School of Public Health Imperial College London United Kingdom

# **Dr Caroline Lee Hooper**

School of Medicine, Health Policy and Practice University of East Anglia United Kingdom

# **Dr Sarah Kelly**

Institute for Ageing and Health School of Dental Sciences University of Newcastle United Kingdom

# **Dr Cho-il Kim**

Department of Food and Nutrition Industry Korea Health Industry Development Institute The Republic of Korea

# **Dr Joerg Meerpohl**

German Cochrane Centre Institute of Medical Biometry and Medical Informatics University Medical Center Freiburg Germany

# **Professor Paula Moynihan**

Institute for Ageing and Health School of Dental Sciences University of Newcastle United Kingdom

# **Annex 6** External Expert and Stakeholder Panel

# Members commenting on priority questions (February 2011)

Comments received from	Affiliation
Eduard Baladia (on behalf of Maria Manera, Julio Basulto and Eduard Baladia)	Spanish Association of Dietitians & Nutritonists, Spain
Gerda Feunekes	Unilever, the Netherlands
Suzanne Harris	International Life Sciences Institute, USA (with offices around the world)
Mark Huffman	Northwestern University Feinberg School of Medicine, USA
Siobhan Jennings	Health Service Executive, Ireland
Erika Ketterer	Heart and Stroke Foundation, South Africa
Anatoliy Khudaiberganov	Ministry of Health, Uzbekistan
Branka Legetic (on behalf of the Pan American Health Organization Expert Group on Salt Reduction)	Pan American Health Organization Expert Group on Salt Reduction, Americas
Graham MacGregor	Consensus Action on Salt and Health, United Kingdom
Bruce Neal	The George Institute for Global Health, Australia
Aileen Robertson	Metropolitan University College Copenhagen, Denmark
Barbara Schneeman	U.S. Food and Drug Administration; U.S. Delegate to the Codex Committee on Nutrition and Foods for Special Dietary Uses and the Codex Committee on Food Labelling, USA
Hans Verhagen	National Institute for Public Health and the Environment (RIVM), the Netherlands
Jacqueline Webster	The George Institute for Global Health, Australia

# Members commenting on the draft guidelines (February 2012)

Comments received from	Affiliation	
Nebal Aboul Ella	National Nutrition Institute, Egypt	
Michael Alderman	The Albert Einstein College of Medicine, USA	
Leila Alouane	National Institute of Nutrition and Food Technology, Tunisia	
Salmeh Bahmanpour	Shiraz University of Medical Sciences, Iran (Islamic Republic of)	
Amber Bastian	Health Promotion Board, Singapore	
Wulf Becker	National Food Agency, Sweden	
Lucie Bohac	Network for Sustained Elimination of Iodine Deficiency, Canada	
Norm Campbell	University of Calgary, Canada	
Jalila el Ati	National Institute of Nutrition and Food Technology, Tunisia	
Sheila Fleischhacker	Institute of Food Technologists, USA	
Gihan Fouad	National Nutrition Institute, Egypt	
Isabel Gaertner	German Federation for Food Law and Food Science, Germany	
Mark Huffman	Northwestern University Department of Preventive Medicine, USA	
Antti Jula	National Institute for Health and Welfare, Finland	
Chor San Khoo	ILSI North America, USA	
Marzia Lazzerini	WHO Collaborating Center for Maternal and Child Health, IRCCS Burlo Trieste, Italy	
Sandrine Lauret	EuSalt (European Salt Producers' Association), Belgium	
Graham MacGregor	Wolfson Institute, Queen Mary University of London, United Kingdom	

Comments received from	Affiliation	
Kathryn McMurry	National Heart, Lung, and Blood Institute, United States of America	
Viola Michael	Non Communicable Disease Section, Disease Control Division, Ministry Of Health, Malaysia	
Gulsen Saleh	National Nutrition Institute, Egypt	
Rusidah Selamat BT	Nutrition Division, Ministry of Health, Malaysia	
Letty Shiu	Health Promotion Board, Singapore	
Pasquale Strazzullo	Department of Clinical and Experimental Medicine, University of Naples Medical School, Italy	
Eman Sultan	National Nutrition Institute, Egypt	
Alison Tedstone	Department of Health, England, United Kingdom	
Ljiljana Trajkovic Pavlovic	Institute of Public Health of Vojvodina / School of Medicine University of Novi Sad, Republic of Serbia	
Jacqueline Webster	The George Institute for Global Health, Australia	
Clare Whitton	Health Promotion Board, Singapore	
Sahar Zaghloul	National Nutrition Institute, Egypt	

#### Annex 7 Priority questions in the format of population, intervention, control and outcomes (PICO)

## **Adults**

What is the effect of increased potassium compared with lower intake on health outcomes? What is the optimal level of potassium intake for maximum benefit?

Adults (≥16 years of age) with or without hypertension, or a population **Population** 

> of adults (some with and some without hypertension) not acutely ill and not requiring potassium management (with or without type 2 diabetes,

previous cardiovascular disease, previous cancer, etc)

Intervention Intervention: increased potassium via advice, specific foods, supplements (or exposure)

or whole diet provided and unconfounded by other dietary, weight,

lifestyle or pharmaceutical interventions.

Exposure: single baseline or repeated potassium intake measurement by

dietary intake assessment or urinary potassium excretion

Control Diet with a potassium level lower than in the intervention (may be usual

intake or specific potassium intake) via advice or no advice or specific

foods or supplements or whole diet provided.

Specific Increased potassium intake (any level) versus lower potassium

comparisons (usual potassium intake)

> Increased potassium intake to at least 90mmol/day versus lower intake. Increased potassium intake to at least 120mmol/day versus lower intake. Increased potassium intake to at least 155mmol/day versus lower intake.

cardiovascular disease, stroke, coronary heart disease, renal function, adverse effects (blood lipids, catecholamine levels and any other adverse

Blood pressure (systolic and/or diastolic), all-cause mortality,

events reported by study authors)

Settings All countries

**Outcomes** 

## Children

What is the effect of increased potassium intake compared with lower intake on blood pressure and potential adverse effects?

**Population** Children or adolescents (2–15 years inclusive), not acutely ill and not

requiring potassium management (with or without type 2 diabetes,

previous cardiovascular disease, previous cancer, etc.)

Intervention (or exposure)

Intervention: increased potassium via advice, specific foods, supplements or whole diet provided and unconfounded by other dietary, weight,

lifestyle or pharmaceutical interventions.

Exposure: single baseline or repeated potassium intake measurement by

dietary intake assessment or urinary potassium excretion

**Control** Diet with a potassium level lower than in the intervention (may be usual

intake or specific potassium intake) via advice or no advice or specific

foods or supplements or whole diet provided.

Specific

comparisons

Increased potassium intake (any level) versus lower potassium

(usual potassium intake)

Increased potassium intake to at least 90mmol/day versus lower intake. Increased potassium intake to at least 120mmol/day versus lower intake. Increased potassium intake to at least 155mmol/day versus lower intake.

Outcomes Blood pressure (systolic and/or diastolic), adverse effects (blood lipids,

catecholamine levels and any other adverse events reported by study

authors)

**Settings** All countries

# Annex 8 Summary of considerations for determining the strength of the recommendations

# Quality of evidence:

- High-quality evidence that increasing potassium is beneficial for blood pressure with no indication of adverse effects in adults.
- Because of the well-established relationship between blood pressure and cardiovascular disease outcomes, the evidence of an effect of potassium on blood pressure was also considered moderate-quality indirect evidence for cardiovascular disease, stroke and coronary heart disease.
- The limited amount of direct evidence regarding cardiovascular disease and coronary heart disease shows no harm or benefit from increased potassium intake.
- Low-quality direct evidence suggests a benefit of increased potassium intake on reducing risk of stroke.
- Moderate-quality evidence for blood pressure with no indication of adverse effects in children.
- High and moderate-quality evidence that increasing potassium intake to at least 90 mmol potassium/day in adults is beneficial; however, high quality RCTs testing varying levels of potassium intake to maximize health benefits are lacking, and additional research may clarify the precise optimal target level of intake.

# Values and preferences:

- NCDs are the main contributor to mortality globally, and interventions to reduce the burden of NCDs are valuable.
- NCDs affect countries in all regions and all income levels, meaning that interventions to reduce the burden of NCDs are valuable in all contexts.

# Trade-off between benefits and harm:

- High-quality evidence of benefit of increasing potassium intake to decrease blood pressure in adults.
- Blood pressure is a good proxy indicator for risk of cardiovascular disease, stroke and coronary heart disease outcomes. Although inconclusive, there was evidence from the meta-analyses of cohort studies measuring cardiovascular disease or coronary heart disease that a benefit of increased potassium was possible. The cohort data supported the beneficial effect of increased potassium on stroke.
- Moderate-quality (indirect) evidence of benefit of increasing potassium intake in children on blood pressure.
- High-quality evidence of no harm on blood lipids, catecholamine levels, or renal function with increased potassium intake in adults.
- No evidence of harm in children.
- No risk of toxicity with consumption through food.

# Costs and feasibility:

- Individuals can feasibly reach these intake goals through the consumption of a reasonable amount of fresh fruits and vegetables, beans, dairy and other potassium-containing foods.
- Implementation of this intervention requires consumer education, public health communications and nutrition communication.
- Reduction of NCDs is highly cost beneficial.
- These recommendations can be incorporated into existing public health nutrition education campaigns and other existing nutrition programs at the global, regional, national and subnational level.

## **Annex 9** Management of conflict of interest

### **NUGAG** members

Professor John Cummings, Professor Shiriki Kumanyika and Professor Este Vorster declared that they received support from the local organizers of the third meeting of the Subgroup on Diet and Health; that is, the Korean Food and Drug Administration (KFDA)/Korea Health Industry Development Institute (KHIDI).

It was considered that the declared interests did not constitute any conflict of interest for their roles as members of the NUGAG Subgroup on Diet and Health, nor did they represent any conflict of interest for the work being undertaken by the NUGAG Subgroup on Diet and Health.

Professor Ibrahim Elmadfa declared that he has received research grants from the Ministry of Health, Austria; the European Commission; the European Food Standard Agency; and Nutrisciencia, Switzerland. The grants were received by his university, and funds were mainly used for staff costs for those working in the research projects and fieldwork.

Further information obtained from Professor Elmadfa regarding Nutrisciencia indicated that it is a Liechtenstein for-profit foundation, registered with the Public Registry of the Principality of Liechtenstein under number FL-0002.251.294-8. The purpose of the foundation is to support research, education and science to universities in Germany. It also contributes to charitable and humanitarian organizations. No commercially operating companies are involved in the operation of the foundation, either directly or indirectly. The declared interests were not considered to constitute any conflict of interest for Professor Elmadfa's role as a member of the NUGAG Subgroup on Diet and Health, nor did they represent any conflict of interest for the work being undertaken by the NUGAG Subgroup on Diet and Health.

Professor Nahla Hwalla declared that she has received research support including grants, collaborations, sponsorships and other funding from WHO, the International Atomic Energy Agency (IAEA), the Lebanese National Council for Scientific Research, the UN University (UNU) and Nestle Middle East.

Further information obtained from Professor Hwalla regarding the declared grant received from Nestle Middle East indicated that the grant supports two types of projects at the American University of Beirut (AUB): intervention activities to promote healthy eating in schools, and research activities of three faculty members in the Faculty of Agriculture and Food Sciences, where Professor Hwalla, as the Dean of the Faculty, oversees the implementation of these activities. Professor Hwalla also indicated that there is an agreement between AUB and Nestle Middle East that all intellectual property (including technology, method, know-how or data rights) produced during the course of the projects will belong to AUB. Professor Hwalla's declared interests do not present any conflict of interest for the work of the NUGAG because the funds she received for her own research were from UN agencies (i.e. WHO, IAEA and UNU) and a governmental institution (i.e. the Lebanese National Council for Scientific Research). It was agreed that Professor Hwalla could participate in the March 2011 meeting as a member of the NUGAG Subgroup on Diet and Health, especially since:

- the interest is not personal;
- the amount received is not significant in view of the total budget of the faculty;
- funding is going to a programme that was already established before the Nestle contribution and that has governmental support. It was suggested that an appropriate disclosure statement be prepared to indicate her declared interest. Professor Hwalla participated in the March 2011 NUGAG meeting but was not able to attend the November 2011 meeting when the current guideline was developed.

Professor Mary L'Abbe declared that she received research grants from the Canadian Institutes of Health Research, to evaluate the impact of Canada's sodium reduction policy; the Public Health Agency of Canada, to prepare a report on public food procurement policies related to sodium; and the Beef Information Centre (a non-profit research foundation funded, but administered at arm's length, by the Canadian beef industry), to examine the iron bioavailability of the diets of Canadians. Professor L'Abbe also receives other funding for research in NCD prevention and health promotion. She also declared that she has spoken at the annual meeting of the Canadian Meat Council to explain Canada's Sodium Working Group report recommendations, and the process being used to develop Canada's sodium targets for foods. Her travel expenses were paid by the Canadian Meat Council, but no honorarium was received. Professor L'Abbe appeared as a witness to the Canadian Parliament's Standing Committee on Health, as Chair of Canada's Sodium Working Group, to advocate for action to reduce sodium in Canadian foods and to increase consumer awareness of sodium, and to support research in the sodium field.

The research grant received from the Beef Information Centre was for a study to examine the iron availability of the diets among the Canadian populations; this activity was not related to the area of recommendations being reviewed and updated by the NUGAG Subgroup on Diet and Health. Hence, it was suggested that the declared interest be reported in the process and the meeting report with details, but that no action be taken and Professor L'Abbe be accepted as a member of the NUGAG Subgroup on Diet and Health.

Professor Jim Mann declared that he is employed by a university that has an interest in nutrition as it relates to human health, and receives research grants from New Zealand governmental agencies. He also declared that, as an individual and as advisory committee member, he has provided expert advice relating to nutrition and human health to innumerable national and international bodies including WHO, FAO, the World Cancer Research Fund and the media.

The declared interests were not considered to constitute any conflict of interest for Professor Mann's role as a member of the NUGAG Subgroup on Diet and Health, nor did they represent any conflict of interest for the work being undertaken by that subgroup.

Professor Dariush Mozaffarian declared that he has received a significant number of research grants to study the effects of dietary factors on chronic diseases from the US National Institutes of Health; the Searle Scholar Award from the Searle Funds at the Chicago Community Trust; the Genes and Environment Initiative at the Harvard School of Public Health; the Gates Foundation/WHO Global Burden of Diseases, Injuries and Risk Factors Study; and GlaxoSmith Kline, Sigma-Tau and Pronova for an investigator-initiated, not-for-profit trial of fish oil to prevent post-surgical arrhythmia. He has also received modest honoraria and travel reimbursement for

speaking at scientific conferences and reviewing on topics related to diet and cardiovascular disease, including from the US Food and Drug Administration, International Life Sciences Institute, Aramark, Unilever, SPRIM, Nutrition Impact, WHO, UpToDate, and several universities and scientific organizations. He has no ownership, patents, stocks, advisory board membership or speaking board membership.

The trial of fish oil, for which Professor Mozaffarian received grants from GlaxoSmith Kline, Sigma-Tau and Pronova, is not related to the work of the NUGAG Subgroup on Diet and Health. Given Professor Mozaffarian's honoraria, travel reimbursement and speaking and reviewing engagements, it was agreed that the declared interest in the process be documented in the meeting report and that no action be taken. It was decided he could participate as member of the NUGAG and his participation in the quideline development meetings would be reviewed for each meeting topic in the future.

Professor Murray Skeaff declared various memberships as follows:

- Serving as a member of the Public Health Scientific Advisory Group and the chair of the Food and Nutrition Working Group of the New Zealand National Heart Foundation. These groups advise the Heart Foundation, a nongovernmental organization, about the scientific basis of its public health efforts to reduce the burden of heart disease in New Zealand. He is not an employee of the Heart Foundation and receives no remuneration for work related to the Advisory Group.
- Appointed in 2008 as a Scientific Fellow of Food Standards Australia New Zealand (FSANZ). "The FSANZ Fellows Program aims to establish a network of distinguished scientists and experts from key disciplines in areas relevant to food regulation. The network is intended to promote close collaborative relations between FSANZ staff, the Fellows, and their affiliated institutions to the benefit of all parties." No remuneration is given to Fellows.
- Serving as a member of the New Zealand Food Safety Academy (NZFSA). The NZFSA is a
  governmental department within the Ministry of Agriculture and Fisheries. From time to
  time, NZFSA seeks the advice of experts in areas where its staff do not have the required
  expertise or where it requires confirmation of the advice provided by its staff. NZFSA
  also establishes expert groups to seek more specific assistance in relation to particular
  issues, drawing experts from the members of the academy. A \$1000 honorarium is paid
  to Professor Skeaff's university each year.

The declared interests were not considered to constitute any conflict of interest for his role as a member of the NUGAG Subgroup on Diet and Health, nor did they represent any conflict of interest for the work being undertaken by that subgroup.

## **External experts and resource persons**

Professor Francesco Cappuccio declared that he provided expert testimony on salt and cardiovascular disease as part of the Guidance Development group of the National Institute of Health and Clinical Excellence of England in 2009. He is an unpaid member of Consensus Action on Salt and Health (2000–present), the World Action on Salt and Health (WASH) (2003–present), the National Heart Forum (2010–present), the Pan American Health Organization/WHO Salt Group (2009–2011), and the European Salt Action Group (2007–present).

Professor Paul Elliott declared that he is a member of WASH. He also declared that his university is currently receiving research funds for the INTERMAP study from the US National Institutes of Health, and that he received research support for a sodium intake study from the US Centers for Disease Control and Prevention (CDC) in 2010. He declared that he provided an expert opinion related to:

- population sodium intake to the US National Heart, Lung, and Blood Institute National Health and Nutrition Examination Survey Sodium Working Group, Bethesda, USA in January 2011;
- sodium intake measurement methods and efficacy for the Epidemiology & Surveillance Branch of CDC, USA during 2010–2011.

Dr Lee Hooper declared that she has received research funding from Barry Callebaut (to her university) to carry out a systematic review on the effects of chocolate and cocoa on markers of oxidative stress; the review was completed in August 2010. She has also received research funding from Soy Nutrition Institute (to her university) to carry out a systematic review on the effects of soy and isoflavones on hormonal status in women; the review was completed in July 2008.

Dr Sarah Kelly declared the support for her participation at the third meeting of the NUGAG Subgroup on Diet and Health from the local organizers of the third meeting of the Subgroup on Diet and Health; that is, the KFDA/KHIDI.

Dr Cho-il Kim declared that, in 2009, she provided an expert opinion to the KFDA when they were developing a guideline to identify "energy-dense and nutritient-poor" foods according to the Special Act on Food Safety Management for Children. Since 2009, the sale of such food has been prohibited within school premises and in designated stores in the vicinity of schools (referred to as the "Green Food Zone"). Since 2010, television advertisements for such food are prohibited between 5:00 pm and 7:00 pm every day. Dr Kim thought that this information was relevant because the regulations on energy-dense and nutrition-poor foods deal with the fat and sugar content of food, and the meeting of the NUGAG Subgroup on Diet and Health was also reviewing recommendations related to total fat and sugars.

Professor Paula Moynihan declared that she received a research grant (to her university) that included reviewing the intake of sugars in care homes as a small component of a large dietary study from the United Kingdom Food Standard Agency/Department of Health; the study was completed in January 2011. She also declared that her travel costs for the third meeting of the NUGAG Subgroup on Diet and Health were covered by research funds from her university. External experts and resource persons were involved in the discussions of the evidence, but did not vote at the NUGAG meetings at which the recommendations were formulated. The final wording and determination of the strength of the recommendations were based on the consensus of the NUGAG members only.

Members of the External Expert and Stakeholder Panel were also required to submit a signed declaration of interests form and a current curriculum vitae before commenting on the draft recommendations and guideline document.

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