



# **POTASSIUM-BASED SODIUM REPLACERS: ASSESSMENT OF THE HEALTH BENEFITS AND RISKS OF USING POTASSIUM-BASED SODIUM REPLACERS IN FOODS IN THE UK**

**A Joint Statement from the Scientific Advisory Committee on Nutrition and the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment**

## Executive Summary

### Background

In 2013, the Scientific Advisory Committee on Nutrition (SACN) was asked by the Department of Health to provide advice on the potential benefits and risks of reducing the sodium content of foods through the use of potassium-based sodium replacers. The use of potassium-based sodium replacers was not specifically recommended as part of the sodium (salt) reduction strategy because there were concerns that an increase in potassium consumption could be hazardous to some individuals, for example, those with undiagnosed kidney disease. It was also considered more appropriate for consumers' palates to become used to less salty tastes. However, industry is interested in using potassium-based sodium replacers in circumstances where sodium reduction alone would be difficult or impossible, for example where the sodium compound has a culinary function or has flavouring properties. The food industry therefore requested the use of potassium-based sodium replacers be reconsidered as a means of helping them comply with the government's sodium reduction targets.

The present report provides integrated advice based on independent position statements published by SACN and the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) that provide assessments of the benefits and risks, respectively, of increasing potassium intakes in foods.

### Approach

The Benefit-Risk Analysis for Foods (BRAFO)<sup>1</sup> methodology developed as part of the BRAFO project (Hoekstra et al., 2012), a tiered approach for the assessment of the health risks and benefits associated with foods, was used to evaluate the available evidence on the effects of increasing the potassium content and decreasing the sodium content of some foods in the UK population through the use of potassium-based sodium replacers. The BRAFO approach starts with a pre-assessment and problem formulation stage to establish the scope of the assessment and requires two scenarios, the reference and an alternative, to be defined. The SACN/COT working group defined the two scenarios as follows:

*Reference scenario:* UK general population with current sodium and potassium intakes.

*Alternative scenario:* UK general population with reduced sodium and increased potassium intakes resulting from the substitution of 15 to 25%<sup>2</sup> of sodium by potassium (sodium salts replaced by potassium chloride, potassium carbonate or potassium bicarbonate).

### Assessment

Initial analysis indicated that moving from the reference to the alternative scenario could result in both health benefits and risks to the general population, therefore, a comparison of

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<sup>1</sup> The BRAFO (Benefit-Risk Analysis for Foods) project was funded within the Sixth Framework programme of the European Commission to develop a framework that allowed for the quantitative comparison of human health benefits and risks in relation to foods and food compounds.

<sup>2</sup> 25% in all relevant foods except for bread, where sodium replacement would be at a maximum of 15%. For more information on the modelling see (SACN/COT, 2017), available [here](#).

the magnitude and extent of the totality of benefits and risks was necessary. The information available was such that a Tier 2 assessment was possible, involving the qualitative evaluation of the overall balance of beneficial and adverse effects. The benefits and risks of reducing dietary sodium were also included in the assessment, since replacing sodium in foods with potassium salts would result in a decrease in sodium intake. Potential beneficial effects of reducing sodium in foods through the use of potassium-based sodium replacers include reduced blood pressure and stroke. Potential risks include an increase in fatal and life threatening hyperkalaemia in individuals with previously undiagnosed chronic renal impairment. The assessment indicated that moving from the reference to the alternative scenario would result in an overall benefit to the general population of the UK.

### **Conclusion**

Overall, at a population level, the potential benefits of using potassium-based sodium replacers to help reduce sodium in foods outweigh the potential risks. The beneficial effects at an individual level are likely to be small in size but will impact a large proportion of the population.

### **Recommendations for government**

The government should consider encouraging food companies to explore the use of potassium-based sodium replacers to help reduce sodium levels in foods.

Risk managers should consider how to monitor the level of substitution of potassium for sodium in foods and the types of foods in which substitution is used.

If the age structure of the UK population, the percentage of people with chronic kidney disease (currently approximately 1% of the UK population), or potassium intakes become materially different from those assumed for the modelling performed for this benefit-risk assessment, the government should reassess the balance between benefits and risks.

# Assessing the health benefits and risks of using potassium-based sodium replacers in foods in the UK

## Introduction

1. Common or table salt is made up of sodium and chloride. High salt intakes are associated with increased blood pressure which is a major risk factor for cardiovascular disease (CVD). In 2003, following a detailed review of the evidence, the Scientific Advisory Committee on Nutrition (SACN) concluded that a reduction in the average population salt intake would proportionally lower population average blood pressure levels and that this would confer significant public health benefits by contributing to a decrease in the burden of CVD. SACN recommended a reduction in the salt intake of adults in the UK to 6g/day (and proportionally lower amounts for children)<sup>3</sup>.
2. SACN advised that a reduction in salt intake of the UK population to meet the recommended targets would be best achieved using a population-based approach through the adoption of a healthy balanced diet, low in salt and saturated and total fat, and rich in fruit, vegetables, and complex carbohydrates. The Committee also recognised that a reduction in the salt content of processed food and drinks would be necessary.
3. Although potassium salts had been used as replacements for their sodium equivalents, the use of salt replacers was not considered at that time. Food manufacturers were encouraged to reduce salt levels by using less salt in their products so that consumers' palates could become used to lower salt levels across all foodstuffs. In addition there were concerns that increasing potassium intakes could result in adverse effects on individuals with compromised kidney function.
4. In 2013, SACN was asked by the Department of Health (DH) to provide advice on the potential health benefits and risks of reducing the salt content of foods through the use of potassium-based sodium replacers. The request followed representations from the food industry, to help food companies comply with the government's salt reduction targets. In 2014, as part of the Public Health Responsibility Deal, the government set specific salt targets to be met by the food industry by the end of 2017<sup>4</sup>. These were republished as [Public Health England targets in 2017](#).
5. In response to this request, SACN asked the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) to assess the risks of using potassium-based sodium replacers.
6. SACN and COT have each published independent position statements that provide detailed assessments of the benefits and risks, respectively, of increasing potassium intake at a population level as a result of the potential introduction of potassium-based sodium replacers<sup>5,6</sup>.

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<sup>3</sup>[SACN Salt and Health Report](#) (2004)

<sup>4</sup>[Responsibility Deal Food Network – New salt targets: F9 Salt Reduction 2017 pledge & F10 Out of Home Salt reduction pledge](#).

<sup>5</sup> The SACN position statement "potassium-based sodium replacers: assessment of the benefits of increased potassium intake to health" is available [here](#).

7. However, as the SACN and COT position statements address separate perspectives, the purpose of the current document is to provide integrated advice to government based on an assessment of the balance of the totality of benefits and risks of increased potassium intake and concomitant reduced sodium intakes for the UK population.

### **Approach**

8. A Working Group (WG) of SACN and COT members was convened to undertake a formal benefit-risk assessment of the effects of increasing the potassium content and decreasing the sodium content of some foods in the UK population through the use of potassium-based sodium replacers. The Benefit-Risk Assessment of Foods methodology developed as part of the BRAFO project (Hoekstra et al., 2012), a tiered approach for the assessment of risk and benefits associated with foods, was used to help evaluate the evidence<sup>1</sup>.
9. The aim of the benefit-risk assessment was to answer the following question: what is the overall balance of health benefits and risks for the UK population of using potassium based sodium replacers in commonly consumed foods in the UK?
10. Additional background information and a more detailed narrative on the evidence referenced in this document are available in the separate [SACN](#) and [COT](#) position statements (see paragraph 6).

### **Pre-assessment and problem formulation**

11. Increasing potassium intakes through supplements, diet, or both, and decreasing dietary sodium intakes, have been associated with a number of positive health effects. These could apply to the whole population or specific “at-risk” population groups.
12. The potential benefits are:
  - Increase in potassium intakes leading to:*
    - Increased population potassium adequacy
    - Reduced systolic and diastolic blood pressure
    - Reduced risk of stroke
    - Improved bone health
  - Reduction in sodium intakes leading to:*
    - Reduced population sodium intakes
    - Reduced systolic and diastolic blood pressure
    - Reduced risk of stroke
    - Reduction in urinary calcium excretion and improved bone health
13. Increasing potassium intakes may also have potential risks, which could apply to the whole population or specific “at-risk” population groups.

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<sup>6</sup> The COT statement “potassium-based replacements for sodium chloride and sodium-based additives” is available [here](#).

14. The potential risks are:
- Increase in potassium intakes leading to:*
- Hyperkalaemia (high serum potassium concentration)<sup>7</sup> and associated adverse cardiac effects, arrhythmias and death.
- Decrease in sodium intakes leading to:*
- Increased hyponatraemia (low serum sodium concentration)<sup>8</sup> associated morbidities and deaths.
15. The evidence for the potential beneficial effects is primarily derived from: (a) systematic reviews and meta-analyses of randomised controlled trials (RCTs) (for the effect on blood pressure); (b) systematic reviews and meta-analyses of prospective cohort studies (for the association with stroke); and (c) systematic reviews and meta-analyses of RCTs and metabolic studies (for the effect on bone health).
16. No studies were identified that specifically assessed the effect of potassium-based sodium replacers in foods on any health outcome. Evidence was based on meta-analyses of RCTs that, in most cases, considered the effect of potassium supplements on blood pressure and bone health. Reviews that only included RCTs that increased potassium intakes through dietary sources (for example, fruit and vegetables) were excluded.
17. The supplements used in the studies considered below contained potassium bicarbonate, potassium chloride, or potassium citrate. No RCTs were identified for CVD and therefore meta-analyses of prospective cohort studies that assessed dietary potassium intake through different dietary assessment methods were considered. These dietary assessment methods have well documented limitations in relation to their ability to accurately assess dietary intakes. Prospective cohort studies have a number of weaknesses which include differential loss to follow-up and residual confounding. Only some studies included in the reviews controlled for either sodium intake or any other nutrients (for example, calcium and magnesium) found in food sources of potassium. However, in the absence of RCTs, cohort studies are considered stronger evidence than other study designs. Finally, in the dietary surveys potassium intake was measured through self-reported 4-day food diaries and not urinary potassium excretion, which is considered to provide a more accurate assessment of potassium intake. It is unclear whether the effects of potassium-based sodium replacers in foods would be the same as those of potassium supplements or potassium from dietary sources.
18. Evidence for the potential risks is derived from clinical observations and experience, clinical audits and case reports. It is well established that individuals with reduced renal function have reduced potassium excretion and a greater risk of increased serum potassium levels. Renal function is reduced in older adults and individuals suffering from conditions such as diabetes. Use of certain medications may increase the risk of hyperkalaemia. Clinical audits have been conducted to assess the extent of hyperkalaemia, with published case reports describing adverse events following exposure to specific medications or dietary components. Whilst the majority would be

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<sup>7</sup> Blood potassium concentration > 5.5 mmol/L.

<sup>8</sup> Blood sodium concentration < 135 mmol/L.

under medical supervision, there are a significant number of individuals in the population with undiagnosed chronic kidney disease (CKD). Similarly, hyponatremia has been described clinically and observational studies suggest that it is associated with increased morbidity.

### **Reference and alternative scenarios**

19. The reference and alternative scenarios were defined as follows:
  - *Reference scenario*: UK general population with current sodium and potassium intakes.
  - *Alternative scenario*: UK general population with reduced sodium and increased potassium intakes resulting from the substitution of 15 to 25%<sup>9</sup> sodium by potassium (sodium salts replaced by potassium chloride, potassium carbonate, potassium bicarbonate)<sup>10</sup>.

### **BRAFO Tier 1 level (characterisation & screening)**

20. A number of benefits and risks were identified with changes from the reference scenario to the alternative scenario. These health consequences are described below and summarised in Annex 1 (Table 1), in terms of the quality of the evidence, the magnitude of the effect and the affected population.
21. The Tier 1 analysis indicated that moving from the reference to the alternative scenario could result in both benefits and risks to the general population therefore a comparison of the magnitude and extent of the totality of benefits and risks was necessary. The nature of the available information was such that a Tier 2 assessment was possible, involving the qualitative evaluation of the overall balance of beneficial and adverse effects. The benefits and risks of reducing dietary sodium were also included in the assessment, since replacing sodium in foods with potassium salts would result in a decrease in sodium intakes.

### **Positive health effect identification and characterisation**

22. Additional background information and a more detailed narrative on the evidence for the potential benefits of increasing potassium intakes at a population level, as a result of the potential introduction of potassium-based sodium replacers is available in the individual [SACN position statement](#).

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<sup>9</sup> 25% in all relevant foods except for bread, where sodium replacement would be at a maximum of 15%. For more information on the modelling see paper [SACN COT/Potassium/16/04](#)

<sup>10</sup> (SACN/COT, 2017)

## Increase in potassium intakes

### *Potassium intakes of the population*

23. Table 1 shows mean population intakes of potassium in both the reference and alternative scenarios as modelled by the Food Standards Agency<sup>11</sup>.

**Table 1: Potassium intakes mmol/day (mg/day) for UK population – reference scenario compared with alternative scenario**

Age group (years)	Reference nutrient intake	Population mean intake	
		Reference scenario <sup>2</sup>	Alternative scenario <sup>3</sup>
1.5 to 3	20 (800)80	46 (1800)	54 (2113)
4 to 10	28-50 (1100-2000) <sup>1</sup>	56 (2187)	68 (2655)
11 to 18	80-90 (3100-3500) <sup>1</sup>	61 (2384)	76 (2978)
19 to 49	90 (3500)	71 (2764)	86 (3373)
50 to 64	90 (3500)	77 (3005)	91 (3554)
65 to 74	90 (3500)	77 (3004)	91 (3564)
75+	90 (3500)	68 (2666)	80 (3143)

<sup>1</sup> Reference nutrient intakes for potassium are 28 mmol/day (1100 mg/day) (4-6y), 50 mmol/day (2000 mg/day) (7-10y), 80 mmol/day (3100 mg/day) (11-14y), 90 mmol/day (3500 mg/day) (15-18y).

<sup>2</sup> Reference scenario: UK general population with current sodium and potassium intakes. Source: NDNS rolling programme Years 1-4 (2008/09–2011/12) (Bates et al., 2014).

<sup>3</sup> Alternative scenario: UK general population with reduced sodium and increased potassium intakes resulting from the substitution of 15-25% sodium by potassium (SACN/COT, 2017).

1 mmol = 39.1 mg potassium.

24. Dietary Reference Values (DRVs) for potassium were set by the Committee on Medical Aspects of Food Policy (COMA) in 1991 (COMA, 1991). The Reference Nutrient Intake (RNI) represents the amount (intake) of a nutrient that is likely to meet the needs of 97.5% of people in the population. If the average intake of the population is at the RNI, then the risk of deficiency in the population is judged to be very small. However, if the average intake is less than 90% of the RNI there is concern of inadequacy for some individuals. The adequacy of vitamin or mineral intake of the population is also expressed as the proportion of individuals with intakes below the lower reference nutrient intake (LRNI). The LRNI represents a level of intake considered likely to meet the needs of only 2.5% of the population.
25. The figures in Table 1 indicate that the use of potassium-based salts to reduce the sodium content of commonly consumed foods would result in an increase in potassium intake at a population level.
26. The same modelling estimated that in the alternative scenario (reduced sodium and increased potassium intakes) there would be a substantial reduction in the number of adults with potassium intakes below the LRNI: from 19% to 7% in 19-49 year-olds; from 9% to 5% in 50-64 year-olds; from 11% to 4% in 65-74 year-olds; and from 17% to 5% in 75 year-olds and over.
27. The modelling also estimated that mean potassium intakes would increase from 80 mmol/day (3130 mg/day (89% RNI) and 81 mmol/day (3150 mg/day) (90% RNI) for

<sup>11</sup> For more information on the modelling see paper [SACN COT/Potassium/16/04](#)



men aged 19-64 and 65+ years to 97 mmol/day (3800 mg/day) (109% RNI) and 96 mmol/day (3760 mg/day) (107% RNI), respectively. For women in the same age groups, the changes would be from 65 mmol/day (2550 mg/day) (73% RNI) and 68 mmol/day (2640 mg/day) (75% RNI) to 78 mmol/day (3050 mg/day) (87% RNI) and 79 mmol/day (3080 mg/day) (88% RNI), respectively (see Annex 2 for LRNI and RNI for different age groups).

### ***Change in blood pressure***

#### ***Adults***

28. Five meta-analyses of RCTs were identified that investigated the effect of increased potassium intake on blood pressure; 4 included participants with and without hypertension (Binia et al., 2015; Geleijnse et al., 2003; Whelton et al., 1997; Aburto et al., 2013a) and 1 was in participants with hypertension (Dickinson et al., 2006). With the exception of the Cochrane meta-analysis by Dickinson et al. (2006), all reported a significant reduction in both systolic blood pressure (SBP) and diastolic blood pressure (DBP) in participants with or without hypertension; the average potassium supplementation dose in the studies was 64 mmol/day (2500 mg/day). Only 1 meta-analysis reported a significant reduction in SBP in participants without hypertension (Whelton et al., 1997); no significant effect on DBP was seen in participants without hypertension or this outcome was not reported or assessed. No adverse effect of potassium supplementation on blood pressure was reported in participants with or without hypertension.

#### ***Children***

29. Few studies have investigated the relationship between increased potassium intake and blood pressure in children. A meta-analysis of 2 RCTs and 1 non-randomised controlled trial (Aburto et al., 2013a) reported no significant effect of potassium supplements on SBP (0.28 mm Hg; 95% CI -0.49 to 1.05; p=0.47) or on DBP (0.92 mm Hg; 95% CI -0.16, 2.00; p value not reported). These findings, and those of a prospective cohort study also discussed in the review, were based on limited data and the authors considered the evidence to be at high risk of bias.

### ***Incidence of stroke***

30. Three meta-analyses of prospective cohort studies were identified, which investigated the association between potassium intake and risk of stroke (D'Elia et al., 2011; Larsson et al., 2011; Aburto et al., 2013a). All reported a significantly lower risk of stroke with higher potassium intake. Aburto et al. (2013a) and D'Elia et al. (2011) reported a 24% and 21% lower stroke risk, respectively. Larsson et al. (2011) reported an 11% lower risk of stroke for every 26 mmol/day (1000 mg/day) higher potassium intake. Both D'Elia et al. (2011) and Aburto et al. (2013a) reported no significant association between potassium intake and cardiovascular disease (CVD) or coronary heart disease (CHD). However, prospective studies have a number of limitations (see paragraph 17) which should be considered in their interpretation.

### ***Bone health***

31. A meta-analysis by Lambert et al. (2015), which included 14 RCTs and metabolic studies, examined the effects of potassium bicarbonate and potassium citrate on

markers of bone resorption. Both potassium salt supplements significantly reduced the excretion of the bone resorption marker, urinary cross-linked N-telopeptide of type 1 collagen (NTX). However, since studies using potassium chloride have reported either a small or no effect on markers of bone health (Frassetto et al., 2000; He et al., 2010), it is unclear whether the effect reported by Lambert et al. (2015) was due to potassium or the conjugate anion. Importantly, evidence from this meta-analysis cannot be used to specifically predict a beneficial effect on bone density or fracture risk.

***Change in prevalence of hypokalaemia (not included in benefit-risk table)***

32. There is very limited evidence on the prevalence of hypokalaemia (low serum potassium concentration)<sup>12</sup> in the general population. Figures in individual studies range from 1% in healthy adults (Weiner & Wingo, 1997) to 2.7% in an elderly community-based population (Liamis et al., 2013). No evidence was identified to suggest that hypokalaemia is caused by low potassium intakes. Most cases of hypokalaemia are observed in populations with a predisposing disease or occur as a consequence of therapeutic interventions such as diuretics (Weiner & Wingo, 1997) and are therefore in people under medical supervision. Although no evidence was identified to support the hypothesis that increasing the potassium intakes of the general population would significantly benefit people with hypokalaemia, no adverse effect would be anticipated on this or in the general population in moving from the reference to the alternative scenario.

**Decrease in sodium intake**

***Sodium intakes of the UK population***

33. Table 2 below shows mean population intake of sodium in both the reference and alternative scenarios as modelled by the FSA.

**Table 2: Sodium intakes mmol/day (mg/day) for UK population – reference scenario compared with alternative scenario**

Age group (years)	Reference nutrient intake for sodium	Population mean	
		Reference scenario <sup>2</sup>	Alternative scenario <sup>3</sup>
1.5 to 3	26 (500)	53 (1221)	44 (1002)
4 to 10	30-50 (700-1200) <sup>1</sup>	74 (1703)	60 (1376)
11 to 18	70 (1600)	90 (2068)	72 (1652)
19 to 49	70 (1600)	95 (2182)	76 (1756)
50 to 64	70 (1600)	88 (2016)	71 (1631)
65 to 74	70 (1600)	87 (1999)	70 (1620)
75+	70 (1600)	77 (1775)	63 (1442)

<sup>1</sup> The reference nutrient intake for sodium is 30mmol/day (700 mg/day (4-6y) and 50 mmol/day (1200mg/day) (7-10y).

<sup>2</sup> Source: NDNS rolling programme Years 1-4 (2008/09–2011/12) (Bates et al., 2014).

<sup>3</sup> Source: FSA modelling (SACN/COT, 2017).

1 mmol = 23 mg sodium

<sup>12</sup> Usually defined as serum potassium < 3.5 mmol/L.

34. The figures indicate that the use of potassium-based sodium replacers to reduce the sodium content of commonly consumed foods would result in a reduction in sodium intakes at a population level.
35. If achieved, these reductions in intake would make a significant contribution to achieving salt reduction targets at a population level. For more information on the modelling see SACN/COT (2017).

### ***Change in blood pressure***

#### *Adults*

36. There is evidence from RCTs on the effect of reduced sodium intake on blood pressure. In a meta-analysis undertaken to inform the World Health Organisation's (WHO) guidance on sodium intake, Aburto et al. (2013b) reported a significant reduction in resting SBP by 3.39 mm Hg (95% CI 2.46, 4.31) and resting DBP by 1.54 mm Hg (95% CI 0.98, 2.11) based on data from 36 RCTs. A meta-analysis by He et al. (2013), which included data from 34 RCTs, reported similar reductions (SBP: 4.18 mm Hg; 95% CI 3.18, 5.18; DBP: 2.06 mm Hg; 95% CI 1.45, 2.67). In both reviews, the reductions in SBP and DBP were greater in participants with hypertension than in participants with normal blood pressure. The authors did not mention whether they took account of potential increases in potassium.
37. A Cochrane meta-analysis (Graudal et al., 2011) reported a similar beneficial effect of reduced sodium on blood pressure in White, Black and Asian populations. However, this meta-analysis included a large number of short-term trials that involved very large changes in sodium intake, which do not reflect the changes that would be expected in the general population.

#### *Children*

38. Meta-analyses by Aburto et al. (2013b) reported that reducing sodium intake significantly reduced resting SBP by 0.84 and DBP by 0.87 mm Hg in children. The meta-analysis for SBP was based on 6 RCTs and 3 non-randomised controlled trials, with 8 of these trials included in the meta-analysis for DBP. The authors considered the evidence to be at high risk of bias.

### ***Incidence of stroke***

39. Two authors (Strazzullo et al., 2009; Aburto et al., 2013b) reported a significantly higher risk of stroke incidence with higher sodium intake from meta-analyses of cohort studies (RR: 1.23, 95% CI 1.06 to 1.43; RR: 1.24, 95% CI 1.08 to 1.43 respectively).

### ***Cardiovascular disease incidence and mortality (not included in benefit-risk table)***

40. Although Aburto et al. (2013b) reported that higher sodium intake was associated with a significantly higher risk of CHD mortality (RR: 1.32; 95% CI 1.13 to 1.53), no significant association was reported for CVD incidence, CVD mortality, CHD incidence or all-cause mortality. Similarly, Strazzullo et al. (2009) reported no significant association between sodium intake and CVD incidence.

41. A meta-analysis by Graudal et al. (2014), based on data from 23 cohort studies and 2 follow-up studies of RCTs, reported that risks of CVD events were lower in participants with usual sodium versus those with very low sodium intake (HR: 0.90; 95% CI 0.82 to 0.99) and higher in participants with high sodium intake versus those with usual sodium intake (HR 1.12; 95% CI 1.02 to 1.24). Low sodium intake was defined as mean sodium intake of < 115 mmol/day Na (6.7 g NaCl); usual sodium intake as mean sodium intake of 115-215 mmol/day (6.7-12.6 g NaCl); and high sodium intake as > 215 mmol/d (12.6 g NaCl).
42. A Cochrane review of RCTs investigated the effect of reduced dietary salt for the prevention of CVD (Adler et al., 2014). The authors reported a significant effect of reduced salt intake on CVD events when 6 trials were pooled (RR: 0.77; 95% CI 0.63 to 0.95). However, it was noted that these findings were driven by the results of 1 trial and that the pooled analyses were insufficiently powered.

### ***Combined effect of increased potassium and decreased sodium on blood pressure***

43. A number of reviews have hypothesised that the combined effect of increasing potassium and reducing sodium on blood pressure reduction may be greater than the effect of a change in either cation alone. A systematic review by Perez & Chang (2014) identified 17 trials that investigated the sodium-to-potassium ratio in participants with or without hypertension. Of the 10 trials that used supplements rather than food-based interventions to alter potassium and/or sodium intake, 7 compared the effect of combined changes in potassium and sodium against either a reduction in sodium or an increase in potassium alone. Three of these trials reported a greater reduction in SBP and/or DBP with a combination of reduced sodium and increased potassium intake compared with an increase in potassium intake or decrease in sodium intake only; 4 studies reported no significant difference in the effect. No adverse effects of increasing the ratio of potassium to sodium were reported.
44. A meta-analysis by Binia et al. (2015) investigated the relationship between the sodium-to-potassium ratio and blood pressure through meta-regression analysis. The authors reported that a decreased sodium-to-potassium ratio was associated with blood pressure reduction, with every unit of reduction of sodium/potassium associated with a decrease of SBP of 2.1 mm Hg (95% CI 0.1 to 4.1; p=0.035).

## **Hazard identification and characterization**

### **Increased potassium intake**

#### ***Hyperkalaemia and changes in electrocardiogram***

45. In healthy individuals, serum potassium concentration is not related to dietary intakes. The body is able to accommodate a high intake of potassium without any substantial change in plasma or serum concentration by coordinated alterations to renal and extra-renal handling (EFSA, 2005). Serum potassium is maintained within a narrow concentration range of 3.5 to 5 mmol/L, ensuring an appropriate voltage difference across cell membranes. As serum potassium concentration increases, gradual changes

occur to the electrocardiogram (ECG) trace as cardiac excitability is decreased. The changes in the ECG that occur are well established (Schaefer & Wolford, 2005). The earliest manifestations occur at > 6.5 mmol/L in the form of tented or peaked T waves, manifested as a flattening of the P wave, lengthening of the PR interval and disappearance of the P wave. Ultimately, this can progress until ventricular asystole or fibrillation. Hyperkalaemia and the physiological changes that accompany it are classified so that serum potassium concentrations of 5.5 to 6.5 mmol/L are considered minimal elevations, 6.6 to 8 mmol/L moderate and > 8 mmol/L, severe. The physiological changes do not correlate exactly with serum potassium concentrations and a sudden increase in serum potassium may be more hazardous than a long-term high serum potassium concentration (Paice et al., 1983; Indermitte et al., 2007).

46. As well as the heart, hyperkalaemia affects the neuromuscular and gastrointestinal systems. Patients may present with malaise, gastrointestinal symptoms or generalised weakness.
47. The vast majority of cases of hyperkalaemia occur when potassium excretion is impaired by a medical condition such as chronic kidney disease (CKD), diabetes mellitus, or the use of certain medications in those with some degree of underlying renal dysfunction. Dietary salt substitutes, potassium supplements, treatment with potassium penicillin and consumption of potassium-softened water could potentially induce hyperkalaemia in pre-disposed individuals (Schaefer & Wolford, 2005).
48. Whilst the majority of individuals with medical conditions such as CKD or diabetes mellitus or those taking certain medications would be under medical supervision, there are estimated to be a significant number of individuals in the UK population with CKD who have not been diagnosed (approximately 157,000 individuals)<sup>13</sup>. Since the prevalence of CKD increases with age, it is expected to increase in the coming years due to the demographic increase in the proportion of older people in the UK population.
49. Not all individuals with CKD need to restrict their potassium intake. This is unlikely to be necessary until renal function is less than 40% of normal (WHO, 2009). This will largely be individuals with stage 4 or 5 CKD, approximately 1% of the population (NICE, 2013) or around 542,000 individuals aged > 16 years in the UK (including both diagnosed and undiagnosed individuals).
50. In a clinical audit conducted to inform COT discussions, it was reported that serum potassium concentration was elevated (> 5.3 mmol/L) in 219 of 17,110 (1.28%) admissions in a UK hospital, of whom, 160 (73%) had serum potassium concentration higher than 5.3 but lower than 6.0 mmol/L. Analysis of a subset of 37 of the 59 patients with serum potassium concentrations > 6.0 mmol/L suggested that many of the individuals were undergoing treatment for renal disease or were taking medication that was known to increase the risk of hyperkalaemia. Fourteen of these cases (38%) had a diverse range of morbidities but would not necessarily have been identified as requiring advice to avoid high intakes of potassium.
51. A number of observational studies have been conducted to estimate the prevalence of hyperkalaemia in different populations. Fleet et al. (2012) reported that 2.6% of

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<sup>13</sup> Estimated using NICE (2013) and PHE (2014)

individuals presenting at a US Emergency Department had serum potassium concentrations of > 5.5 mmol/L, while 3.5% of the patients admitted to hospital had potassium concentrations > 5.5 mmol/L. Hawkins (2003) reported that 1.5% of potassium analyses performed at a Singapore hospital laboratory servicing both hospital and community patients, revealed serum potassium concentrations > 6.0 mmol/L. Serum potassium concentrations > 5.8 mmol/L were reported in 0.84% of tests conducted in a US medical centre, in an ambulatory setting (Moore et al., 2006). Serum potassium was elevated (> 5.5 mmol/L) in 13.7% of inpatients and outpatients from a population of US veterans (Einhorn et al., 2009). Paice et al. (1983) reported that 1.4% of 29,063 patients admitted to a UK teaching hospital had significant hyperkalaemia (> 6.0 mmol/L on a single occasion) and mortality was higher in this group compared to controls. Of the 406 hyperkalaemic patients, 244, 93 and 69 had serum potassium concentrations of 6-6.4, 6.5-6.9 and  $\geq 7.0$  mmol/L respectively. Whilst these are not inconsistent with the results of the hospital audit reported above, none of the studies was designed to assess the extent of undiagnosed hyperkalaemia in the general population. In a community study, mild hyperkalaemia was reported in up to 0.7% of 5179 individuals from the Rotterdam cohort but severe hyperkalaemia (> 6.0 mmol/L) was not observed (Liamis et al., 2013).

52. There are only limited data linking serum potassium concentration to ECG changes in a defined population sample. In a group of 11 inpatients with a mean  $\pm$  SD age of  $70 \pm 8.8$  years, mean serum potassium concentration  $\pm$  SD was  $6.7 \pm 0.8$  mmol/L (Charytan & Goldfarb, 2000). Among these 11 patients, 5 had minimal hyperkalaemia (mean  $\pm$  SD serum potassium  $6.0 \pm 0.3$  mmol/L), another 5 had moderate hyperkalaemia (mean  $\pm$  SD serum potassium  $7.0 \pm 0.4$  mmol/L) and 1 had severe hyperkalaemia with a serum potassium concentration of 8.4 mmol/L. Changes to ECG were seen in 1/5 (20%) of the minimal hyperkalaemia group, 3/5 (60%) of the moderate hyperkalaemia group and in the individual with severe hyperkalaemia.

### **Decreased sodium intake**

#### ***Change in prevalence of hyponatraemia***

53. Hyponatraemia is the most common electrolyte disorder, occurring in around 5% of hospital admissions and increasing to 20 to 30% depending on age, medical condition and drug treatment (Whelton, 2016; Liamis et al., 2013).
54. Hyponatraemia can result in a number of largely neurological symptoms and may be associated with an increased risk of CVD and, particularly, mortality. However, it is uncertain whether it is always secondary to other conditions or whether it can occur as a result of restricting intake of foods containing sodium. Miller et al. (1995) reported that low sodium tube-feeding exacerbated hyponatraemia in a nursing home population, while Dahl (1958) stated that excessive restriction of dietary sodium could result in hyponatraemia, but it is unclear what evidence the latter statement was based on. Sodium balance is also affected by water/fluid balance. For example, hyponatremia may occur due to high water/fluid intake rather than reduced sodium intake, for example when sodium is lost via fluid loss but the sodium is replaced by fluids with a lower sodium concentration.

55. In conclusion, there are insufficient data to suggest that hyponatraemia should be included in the benefit-risk assessment for the UK population.

### **BRAFO Benefit-Risk Assessment**

56. The Tier 1 analysis indicated that moving from the reference to the alternative scenario, i.e. moving from the current sodium and potassium intakes of the UK general population to reduced sodium and increased potassium intakes as a result of substituting 15 to 25% of sodium with potassium, was likely to provide some health benefits. However, from a risk perspective, some uncertainties still remained and a Tier 2 assessment was therefore undertaken (see Annex 1).

### **Limitations**

57. The magnitude of the effects are likely to be lower than stated in Annex 1, Table 1 as the proposed substitution levels would not necessarily be implemented in full by all companies in each food category. However, as the reduced effects would apply to both the benefits and the risks, the overall balance would not be altered.
58. There is uncertainty around i) whether the health effects included in this assessment would occur at the substitution levels identified in the alternative scenario because the evidence comes from studies where larger dietary changes have been used; ii) the accuracy of the estimates of reduced blood pressure and stroke cases in moving from the reference to the alternative scenario.
59. No evidence was identified that specifically assessed the effect of potassium-based sodium replacers in foods on any health outcome; evidence was based on RCTs that used potassium supplements (or in some cases increased intakes of dietary sources of potassium) or prospective cohort studies that assessed dietary potassium intake through different dietary assessment methods.
60. The balance between the benefits and risks is applicable to the current size and structure of the UK population. If any influencing factors were to change significantly, including the age structure, the percentage of people with CKD, and the dietary intakes of the population due to behavioural and food composition changes, the balance between the benefits and risks would need to be reassessed.

## **Conclusion and recommendations for government**

### **Conclusion**

61. Potential beneficial effects of reducing sodium in foods through the use of potassium-based sodium replacers include reduced blood pressure and reduced stroke incidence. Potential risks include an increase in hyperkalaemia in individuals with previously undiagnosed chronic renal impairment.
62. Overall, at a population level, the potential benefits of using potassium-based sodium replacers to help reduce sodium in foods outweigh the potential risks. Moving from the reference to the alternative scenario, i.e. moving from the current sodium and potassium intakes of the UK general population to reduced sodium and increased

potassium intakes as a result of substituting 15-25% of sodium with potassium<sup>14</sup>, would result in an overall benefit to the general population of the UK. These beneficial effects at an individual level are likely to be small in size but would impact a large proportion of the population.

### **Recommendations for government**

63. The government should consider encouraging food companies to explore the use of potassium-based sodium replacers to help reduce sodium levels in foods, up to the levels of substitution and in the foods considered in the modelling performed for this benefit-risk assessment.
64. Risk managers should consider how to monitor the level of substitution of potassium for sodium in foods and the types of foods in which substitution is used. If these become materially different from those assumed for the modelling performed for this benefit-risk assessment, the government should reassess the balance between benefits and risks.
65. If the age structure of the UK population, or the percentage of people with CKD (currently approximately 1% of the UK population), or potassium intakes become materially different from those assumed for the modelling performed for this benefit-risk assessment, the government should reassess the balance between benefits and risks.

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<sup>14</sup> Achieved by replacing sodium salts by potassium chloride, potassium carbonate or potassium bicarbonate.



# Annex 1

## BRAFO Benefit-Risk Assessment

### Tier 1

1. The Tier 1 analysis indicated that moving from the reference to the alternative scenario, i.e. moving from the current sodium and potassium intakes of the UK general population to reduced sodium and increased potassium intakes as a result of substituting 15 to 25% of sodium with potassium, was likely to provide some health benefits. However, from a risk perspective, some uncertainties still remained and a Tier 2 assessment was therefore undertaken.

### Tier 2

#### *Benefit assessment*

2. Although there were insufficient data to accurately calculate the effect severity for each health outcome in the current assessment, available data have been used to estimate the possible reduction in i) blood pressure (in mm Hg) and ii) stroke incidence that might occur when moving from the reference to the alternative scenario.

#### *Increased potassium intake*

#### *Blood pressure reduction*

3. The meta-analyses included in table 1 of this Annex, on the effect of increased potassium intake on blood pressure, reported a reduction of between 3.5 and 6.8 mm Hg in SBP and between 2.5 and 4.6 mm Hg in DBP in participants with hypertension. This effect was observed at an average supplementation dosage of 64 mmol (2,500 mg) of potassium across the different meta-analyses. As this dosage was about 4.5 times higher than the estimated increase in potassium intake in the alternative scenario (14 mmol (550 mg)), the estimated effect on blood pressure would be less (reduced to a decrease of 0.8 to 1.5 mm Hg for SBP and 0.6 to 1.0 mm Hg for DBP, assuming proportionality).

#### *Incidence of stroke*

4. The number of strokes in the UK per annum has been estimated at 152,000 (Stroke Association, 2015). Three meta-analyses have reported a significantly lower risk of stroke with higher potassium intake (Larsson et al., 2011; Aburto et al., 2013a; D'Elia et al., 2011). Insufficient data were provided in the meta-analysis by Aburto et al. (2013a) to model the reduction in stroke cases that might be expected in the alternative scenario. Using the meta-analysis by D'Elia et al. (2011), which reported a 21% lower incidence of stroke at 42 mmol (1,640 mg) per day higher potassium intake, a reduction in the number of strokes by 10,700 is estimated at the potassium intake levels in the alternative scenario (approximately 14 mmol (550 mg)), assuming a proportional decrease. Using the meta-analysis by Larsson et al. (2011), which reported a 11% lower risk of stroke for every increased 26mmol/day (1000 mg/day) of

potassium, a reduction in the number of strokes by 9,200 is estimated, assuming proportionality (Annex 4).

#### *Decreased sodium intake*

##### *Blood pressure reduction*

5. The meta-analyses included in table 1 of this Annex, investigating the effect of reduced sodium intake on blood pressure, reported a reduction of between 4.1 and 5.4 mm Hg in SBP and between 2.3 and 2.8 mm Hg in DBP in participants with hypertension. Insufficient data were provided in the meta-analysis by Aburto et al. (2013b) to model the reduction that could be expected with a move from the reference to the alternative scenario. We therefore used the He et al. (2013) meta-analysis which reported a reduction in SBP and DBP of 5.4 and 2.8 mm Hg and of 2.4 and 1.0 mm Hg in participants with hypertension and without respectively, with a mean daily reduction in urinary sodium excretion in the intervention group of 75 mmol (1,730 mg). As this level of sodium reduction was about 4.5 times higher than estimated in the alternative scenario (75 v 17 mmol (1,730 v 400 mg)), the estimated effect on blood pressure would be considerably less (reduced to 1.2 and 0.6 for SBP and DBP in participants with hypertension and 0.5 to 0.2 for SBP and DBP in participants without hypertension), assuming proportionality.

##### *Incidence of stroke*

6. The estimated number of strokes per annum in the UK is 152,000 (Stroke Association, 2015). Insufficient data were provided in the meta-analysis by Aburto et al. (2013b) to model the reduction in the number of strokes that might be expected from the levels of sodium reduction in the alternative scenario. We therefore used data from the Strazzullo et al. (2009) meta-analysis, which reported a 6% higher risk of stroke for every 50 mmol/day (1,150 mg) higher sodium intake. As this dosage was about three times higher than expected in the alternative scenario (50 mmol v 17 mmol (1,150 mg v 400 mg)), a reduction in the number of strokes by 3,200 is estimated at the decreased sodium intake levels in the alternative scenario, assuming proportionality.

#### **Summary**

7. The potential benefits, although generally modest in terms of individual risk reduction, are meaningful in relation to medical conditions or chronic diseases that affect a large number of individuals in the UK population. Consequently, even the small effects that could be expected when moving from the reference (*UK general population with current sodium and potassium intakes*) to the alternative scenario (*UK general population with reduced sodium and increased potassium intakes resulting from the substitution of 15 to 25% sodium by potassium (sodium salts replaced by potassium chloride, potassium carbonate or potassium bicarbonate)*) could have a large impact on public health.

#### **Risk assessment**

8. Whilst the vast majority of individuals would not be adversely affected by increased potassium intakes, there are some sub-groups of the UK population who are vulnerable to developing hyperkalaemia. These are people with medical conditions

such as chronic kidney disease (CKD) or diabetes or who are taking certain medications. Whilst the majority would be under medical supervision, there are a significant number of individuals with CKD who are not diagnosed. It has been estimated that in the UK population, 3.2 million individuals >16y would be expected to have CKD stage 3 to 5, of whom, 929,000 (29%) would be undiagnosed<sup>15</sup>.

9. Not all individuals with CKD stage 3 to 5 would need to restrict their potassium intake. This is unlikely to be necessary until renal function is less than 40% of normal (WHO, 2009). This will largely be individuals with stage 4 or 5 CKD, approximately 1% of the population (NICE, 2013), or 542,000 UK individuals >16y. If 29% of this population were undiagnosed, this would be approximately 157,000 individuals.
10. The prevalence of CKD increases with age, so that while 1.9% of people aged <64 years have CKD stage 3-5, this rises to 13.5% in people aged 65-74 years and 32.7% in people aged >75 years (PHE, 2014).
11. In a clinical audit conducted to inform COT discussions (COT, 2017) it was reported that serum potassium was elevated (> 5.3 mmol/L) in 219 of 17,110 (1.28%) of hospital admissions. Of these 219 individuals, 160 (73%) had potassium levels of 5.3 to 6.0 mmol/L. A subset of 37 of the remaining 59 cases where serum potassium was >6.0 mmol/L was then considered in more detail. Of these, 7 (19%) were on renal replacement therapy, a further 12 (32%) were under regular out-patient follow-up in the renal department because of known kidney disease, and an additional 4 (11%) were taking prescribed medicines that increase the risk of hyperkalaemia. The remaining 14 (38%) had diverse morbidity, but would not necessarily have been identified as requiring advice to avoid high intakes of potassium. The COT did a crude scaling of these figures, to indicate what could occur at a national level<sup>16</sup>. From this it can be estimated that around 19,000 cases might present to hospital with life-threatening hyperkalaemia per year, with 960 being fatal. In addition, approximately 7,000 cases would occur in people who could not reasonably be warned in advance to avoid high consumption of potassium and thus would be vulnerable to increased potassium intake. It was noted that there were major uncertainties associated with this analysis. In particular, the catchment population studied may not have been nationally representative, and the estimates, especially for mortality, are liable to random sampling error. In addition, the age range is another source of uncertainty since younger people are likely to be less vulnerable, and hence this value is likely to be an over-estimate as it is based on the whole population. Nevertheless, COT considered that this gave a rough indication of the frequency of serious problems from hyperkalaemia.
12. A prevalence of 1.28% is consistent with other observational studies which have estimated the prevalence of hyperkalaemia in different populations of hospital patients to be 0.8 to 13.7% depending on the population and the criteria used to define hyperkalaemia. In a community study, mild hyperkalaemia was reported in up to 0.7% of 5179 individuals from the Rotterdam cohort, but severe hyperkalaemia (> 6.0 mmol/L) was not observed (Liamis et al., 2013).

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<sup>15</sup> The estimates made in this and the following paragraph are set out in full in the COT statement available [here](#).

<sup>16</sup> This scaling calculation is set out in detail in the COT statement available [here](#).

13. Although elevated serum potassium is known to result in changes to ECG, there are few studies where this has been examined in more detail. The study reported by (Charytan & Goldfarb, 2000) (see paragraph 52 of report) suggests that these serum levels could be associated with observed changes to ECG.
14. If population potassium intakes increase, then the prevalence of hyperkalaemia may also increase because of the increased exposure in individuals with undiagnosed CKD. In the absence of empirical data on the distribution of tolerable intakes among people with unrecognised vulnerability to higher dietary potassium, as an illustrative calculation, it might be assumed that the increase in the proportion exceeding their individual tolerance would be comparable to the increase in individuals exceeding the RNI of 90 mmol/day (3500 mg/day). This would increase from 19 to 43%, i.e. approximately 2.2-fold (COT, 2017; SACN/COT, 2017). This would imply that maximal potassium-based sodium replacement could add to the number of cases of life-threatening hyperkalaemia presenting to hospital by 2.2 fold, this would be approximately 8500 additional cases, leading to an estimated total of 15,500 (COT, 2017)<sup>17</sup>.

### **Summary**

15. The majority of people would not be affected by an increase in potassium intake. However, there are individuals prone to hyperkalaemia who are potentially at risk of adverse effects; in particular, individuals with undiagnosed CKD who would, if diagnosed, be restricting their potassium intakes, to prevent potassium accumulating. Mild hyperkalaemia may be of low concern, but increasing serum potassium levels can affect the functioning of the heart, with adverse effects ranging from observable changes in ECG to life threatening severe ventricular dysrhythmias. The effects increase in severity depending on the level of serum potassium, but the speed of potassium increase is also important with chronic high potassium being less harmful than rapidly rising potassium.
16. The potential size of this vulnerable group in the UK is difficult to define accurately. The number of individuals with undiagnosed CKD stages 4 and 5 may be estimated to be approximately 157,000 at the present time. The number of these individuals who might go on to experience severe cardiac effects is uncertain. Results from a clinical audit, conducted on behalf of COT, were extrapolated as a way of estimating this, suggested that, with no change to current diet, approximately 7000 cases of life-threatening hyperkalaemia might occur in the UK every year in individuals who might not be reasonably warned in advance to restrict their potassium intake. It is estimated that this could increase approximately 2.2 fold or by an additional 8500 cases at maximal levels of potassium-based sodium replacement as per the alternative scenario.

### **Grading of Evidence**

17. The evidence in the benefit risk assessment was not graded for the following reasons:
  - *For the benefit assessment*, although a number of relevant meta-analyses were identified, evidence was from studies that investigated the effects of potassium

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<sup>17</sup> This calculation is set out in the COT statement available [here](#).

supplements and not potassium-based sodium replacers in manufactured food. Additionally, although there was some evidence that specific health effects could occur, there was no evidence that these effects would occur at the substitution levels modelled in the alternative scenario. There was also uncertainty around the accuracy of the numbers related to blood pressure and stroke incidence modelled for the Tier 2 assessment.

- *For the risk assessment*, RCTs and systematic reviews were lacking and the data were limited to a number of clinical surveys, audits and observational studies of various designs.

### **Tier 2 outcome**

18. The Tier 2 assessment indicates that the potential beneficial effects of using potassium-based sodium replacers to help reduce sodium in foods outweigh the potential risks. Moving from the reference to the alternative scenario, i.e. moving from the current sodium and potassium intakes of the UK general population to reduced sodium and increased potassium intakes as a result of substituting 15-25% of sodium with potassium<sup>18</sup>, would result in an overall benefit to the general population of the UK. These beneficial effects at an individual level are likely to be small in size but will impact a large proportion of the population.
19. Since the Tier 2 assessment indicates that the potential benefits outweigh the potential risks and since adequate data for quantitative estimates of potential benefits and risks are currently unavailable, this benefit-risk assessment was stopped at Tier 2.

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<sup>18</sup> Achieved by replacing sodium salts by potassium chloride, potassium carbonate or potassium bicarbonate.

**Table 1: Potassium-based sodium replacers – benefit-risk assessment for a change from the reference scenario<sup>19</sup> to the alternative scenario<sup>20</sup> for Tiers 1 and 2**

Health effect	Change	Quality of evidence	Magnitude of effect (at population level)	Population affected	Health impact	References to the quality of evidence	Number of individuals <sup>21</sup>
<b>BENEFITS</b>							
<b>Increased potassium intake</b>							
Change in blood pressure	Reduction in SBP and DBP	Not possible to grade <sup>22</sup>	Major (Reduction of 0.8 to 1.0 mm Hg for SBP and 0.6 to 1.0 mm Hg for DBP)  0 to minor  0	Adult population – hypertensives.  Adult population – normotensives.  Children.	Beneficial	(Whelton et al., 1997; Geleijnse et al., 2003; Dickinson et al., 2006; Aburto et al., 2013a; Binia et al., 2015)  (Aburto et al., 2013a)	16 m adults in the UK are estimated to have high blood pressure <sup>23</sup> .

<sup>19</sup> Reference scenario: UK general population with current sodium and potassium intakes.

<sup>20</sup> Alternative scenario: UK general population with reduced sodium and increased potassium intakes resulting from the substitution of 15-25% sodium by potassium.

<sup>21</sup> This column estimates the size of the potential population affected rather than a study population. For potassium, the column includes estimates of the number of individuals potentially affected by either strokes or by an increase in hyperkalaemia.

<sup>22</sup> See paragraph 17 of this Annex for explanation.

<sup>23</sup> Based on data from [BHF](#).

Health effect	Change	Quality of evidence	Magnitude of effect (at population level)	Population affected	Health impact	References to the quality of evidence	Number of individuals <sup>21</sup>
Incidence of stroke	Decrease in stroke incidence	Not possible to grade	Major (Lower number of strokes estimated at 9,200 – 10,700 per annum)	Adult population.	Beneficial	(Aburto et al., 2013a; D'Elia et al., 2011; Larsson et al., 2011)	152,000 stroke victims annually in UK. (Association, 2015)
Bone health	Reduction in bone resorption	Not possible to grade	0 – potassium chloride  Low – other potassium salts	Adult population at risk of osteoporosis/ fractures.	Beneficial	(Frassetto et al., 2000; He et al., 2010)  Lambert et al. (2015)	UK population at risk of osteoporosis: <i>Men</i> ≥50 y: 10.1 m <i>Women</i> ≥50 y: 11.5 m (Svedbom et al., 2013).  Hip fracture incidence (≥50y, per 100,000 person years): <i>Men</i> : 186.0 <i>Women</i> : 523.5 (Svedbom et al., 2013).

Health effect	Change	Quality of evidence	Magnitude of effect (at population level)	Population affected	Health impact	References to the quality of evidence	Number of individuals <sup>21</sup>
Population potassium intake	Decreased percentage of population below the RNI and improved population mean intake relative to the RNI	Not possible to grade	<p>Major (Change in estimated weighted proportion of adults below the LRNI:  19-49y: 18.6% to 7.2%  50-64y: 8.8% to 4.5%  65-74y: 11.0% to 3.6%  75+y: 16.6% to 4.7%</p> <p>Change in mean intake:  <u>Men:</u>  19-64y: 89% to 109% RNI  65+ y: 90% to 107% RNI  <u>Women:</u>  19-64y: 73% to 87% RNI  65+ y: 75% to 88% RNI</p>	Adult population, particularly those with low dietary potassium intakes.	Beneficial	<p>FSA modelling using NDNS data<sup>24</sup></p> <p>FSA modelling using NDNS data<sup>12</sup></p>	<p>Change in estimated number of adults with K intakes below the LRNI:  19-49y: 5 m to 1.9 m  50-65y: 1 m to 0.5 m<sup>25</sup>.</p> <p>Number of adults with increased potassium intake<sup>26</sup>:  <i>Men</i>  19-49y: 13.4 m  50-65y: 5.6 m  <i>Women</i>  19-49y: 13.3 m  50-65y: 5.7 m</p>

<sup>24</sup> See paper Joint Working Group on potassium. Potassium salt replacers in vulnerable groups - modelling potential potassium intakes by UK population. SACN/COT/potassium/16/04 Update January 2017.

<sup>25</sup> Calculated using [figures from Office for National Statistics](#). Mid 2008, 2009, 2010 and 2011 Population Estimates. [Online]; and NDNS data years 1-4 (Bates et al., 2014). See Annex 3 for calculations.

<sup>26</sup> Calculated using [figures from Office for National Statistics](#). Mid 2008, 2009, 2010 and 2011 Population Estimates. [Online]



Health effect	Change	Quality of evidence	Magnitude of effect (at population level)	Population affected	Health impact	References to the quality of evidence	Number of individuals <sup>21</sup>
<b>Reduced sodium intake</b>							
Change in blood pressure	Reduction in systolic and diastolic blood pressure	Not possible to grade	Major (Reduction of 1.2 mm Hg for SBP and 0.63 mm Hg for DBP)	Adult population - with hypertension.	Beneficial	(Aburto et al., 2013b; He et al., 2013)	16 m adults in the UK are estimated to have high blood pressure <sup>27</sup> .
			Major (Reduction of 0.5 mm Hg for SBP and 0.2 mm Hg for DBP)	Adult population – without hypertension.			
			0 to minor	Children			
Incidence of stroke	Decrease in stroke incidence	Not possible to grade	Major (Lower number of strokes estimated at 3,000 per annum)	Adult population.	Beneficial	(Aburto et al., 2013b; Strazzullo et al., 2009)	152,000 victims annually in UK (Stroke Association, 2015).

<sup>27</sup> <https://www.bhf.org.uk/research/what-we-research/high-blood-pressure>

Health effect	Change	Quality of evidence	Magnitude of effect (at population level)	Population affected	Health impact	References to the quality of evidence	Number of individuals <sup>21</sup>
Population sodium intake	Reduction in sodium chloride intake towards the target of 6 g/day	Not possible to grade	Major (Reduction of 0.8 g to 1.1 g sodium chloride/day)	General adult population, especially people with high blood pressure.	Beneficial	FSA modelling using NDNS data <sup>28</sup>	38 m adults in the UK population aged 19-64y.
<b>Sodium and Potassium Combined</b>							
Change in blood pressure	Reduction in systolic and diastolic blood pressure	Not possible to grade	0 to minor (or greater)	Adult population without hypertension.	Beneficial	(Binia et al., 2015; Perez & Chang, 2014)	16 m people in the UK are estimated to have high blood pressure <sup>11</sup> .
<b>RISKS</b>							
<b>Increased potassium intake<sup>29</sup></b>							
Changes in electrocardiogram	Increased serum potassium (> 6.5 mmol/L)	Not possible to grade	Minor to moderate	People with undiagnosed CKD, stages 3-5.	Adverse	(Schaefer & Wolford, 2005)	750,000 <sup>30</sup> undiagnosed CKD 3-5; 157,180 undiagnosed CKD 4-5 <sup>31</sup> .

<sup>28</sup> See paper SACN COT/Potassium/16/4; p29 Table 1. The potential salt intake reduction was estimated by converting sodium intakes to salt (NaCl) intakes, assuming all the sodium is from NaCl. Figures not published.

<sup>29</sup> Increased potassium intake would not be expected to affect individuals in the absence of a risk factor such as CKD or the use of certain medication.

<sup>30</sup> PHE (2014)

<sup>31</sup> Estimated using NICE (2013) and PHE (2014).

Health effect	Change	Quality of evidence	Magnitude of effect (at population level)	Population affected	Health impact	References to the quality of evidence	Number of individuals <sup>21</sup>
Severe ventricular dysrhythmias	Increase in fatalities due to severe ventricular dysrhythmias (8-10 mmol/L)	Not possible to grade	Minor	People with undiagnosed CKD, stages 3-5.	Adverse	(Schaefer & Wolford, 2005)	750,000 undiagnosed CKD 3-5 <sup>24</sup> ; 157,180 undiagnosed CKD 4-5 <sup>25</sup> .
Potentially life-threatening hyperkalaemia	Increased hyperkalaemia-associated fatalities	Not possible to grade	Not possible to quantify <sup>32</sup>	People with undiagnosed hyperkalaemia.	Adverse	COT statement (COT, 2017)	18,888 cases of life threatening hyperkalaemia, of which 960 would be fatal. Estimated 7146 cases from undiagnosed CKD; 363 potential fatalities (estimated for reference scenario) COT estimated an additional 8520 cases – an increase from 7,146 to 15,666 in undiagnosed population.

**Abbreviations:** CHD, coronary heart disease; DBP, diastolic blood pressure; DRV, dietary reference value; FSA, Food Standards Agency; K, potassium; KCitr, potassium citrate; KHCO<sub>3</sub>, potassium bicarbonate; LRNI, lower reference nutrient intake; m, million; Na, sodium; mm Hg, millimetres of mercury; NDNS, National Diet and Nutrition Survey; NTX, N-terminal telopeptide; RNI, reference nutrient intake; SBP, systolic blood pressure.

<sup>32</sup> The magnitude of effect cannot be quantified as there is no way of measuring the size of life threatening hyperkalaemia, just the number of individuals that could be affected. This contrasts with for example, blood pressure where measurements can be made and assessed as a population mean.

## Annex 2

### Dietary reference values for potassium (COMA, 1991)

Age	Lower Reference Nutrient Intake (LRNI) mmol/day (mg/day)	Reference Nutrient Intake (RNI) mmol/day (mg/day)
0-3 months	10 (400)	20 (800)
4-6 months	10 (400)	22 (850)
7-9 months	10 (400)	18 (700)
10-12 months	12 (450)	18 (700)
1-3 years	12 (450)	20 (800)
4-6 years	15 (600)	28 (1100)
7-10 years	24 (950)	50 (2000)
11-14 years	40 (1600)	80 (3100)
15-18 years	50 (2000)	90 (3500)
19-50 years	50 (2000)	90 (3500)
50+ years	50 (2000)	90 (3500)

1mmol = 39.1mg potassium

## Annex 3

### Calculations of changes in the number of people below the lower reference nutrient intake (LRNI) for potassium in the UK

Age Group Country	Male	Female	Total	Current % below LRNI	Current number of people below LRNI	% below LRNI with modelling	Number of people below LRNI with modelling	Decrease in number of people below LRNI
<b>19-49y</b>								
England	11,273,960	11,196,234	22,470,194					
Wales	600,163	607,908	1,208,072					
Scotland	1,093,243	1,125,085	2,218,328					
Northern Ireland	386,390	389,243	775,632					
<b>Total</b>	<b>13,353,756</b>	<b>13,318,470</b>	<b>26,672,225</b>	<b>18.6%</b>	<b>4,961,034</b>	<b>7.2%</b>	<b>1,920,400</b>	<b>3,040,634</b>
<b>50-64y</b>								
England	4,623,054	4,763,529	9,386,582					
Wales	286,306	297,469	583,775					
Scotland	491,828	518,602	1,010,430					
Northern Ireland	149,011	153,272	302,283					
<b>Total</b>	<b>5,550,198</b>	<b>5,732,872</b>	<b>11,283,070</b>	<b>8.8%</b>	<b>992,910</b>	<b>4.5%</b>	<b>507,738</b>	<b>485,172</b>

Source: Calculated using [figures from Office for National Statistics](#). Mid 2008, 2009, 2010 and 2011 Population Estimates. [Online] and NDNS data years 1 - 4 (Bates et al. 2014)

## Annex 4

### Modelling of effect of increased potassium and decreased sodium intakes on blood pressure and stroke cases when moving from the reference to the alternative scenario

#### 1. Reduction in blood pressure from increased potassium intake

Increased potassium intake when moving to alternative scenario: 14 mmol (550 mg)<sup>33</sup>

Average potassium supplementation dose in studies: 65 mmol (2,500 mg)

Proportion (alternative scenario/supplementation dose): 0.22

#### **Effect on population with hypertension**

Increased potassium intake when moving from reference to alternative scenario: 14 mmol (550 mg)

Average potassium supplementation dose in studies: 65 mmol (2,500 mg)

Proportion (alternative scenario/supplementation dose): 0.22

SBP reduction observed in meta-analyses: 3.5 to 6.8 mm Hg

SBP that might be observed when moving to the alternative scenario ( $3.5 \times 0.22$  to  $6.8 \times 0.22$ ) mm Hg = **0.8 to 1.5 mm Hg**

DBP reduction observed in meta-analyses: 2.5 to 4.6 mm Hg

DBP that might be observed when moving to the alternative scenario ( $2.5 \times 0.22$  to  $4.6 \times 0.22$ ) mm Hg = **0.6 to 1.0 mm Hg**

*Effect on population without hypertension not modelled as evidence is limited*

#### 2. Reduction in stroke cases from increased potassium intake

Number of annual strokes in the UK: 152,000

#### **D'Elia et al. (2011)**

Increased potassium intake when moving to alternative scenario: 14 mmol (550 mg)<sup>34</sup>

Dose at which risk reported in study: 42 mmol (1,640 mg)

Proportion (alternative scenario/supplementation dose): 0.34

Reduced risk observed in study = 21%

Reduced risk that might be observed when moving to alternative scenario:  $21\% \times 0.34 = 7\%$

Number of stroke cases that might be prevented when moving to alternative scenario: ( $7\% \times 152,000$ ) = **10,700**

#### **Larsson et al. (2011)**

Increased potassium intake when moving to alternative scenario: 14 mmol (550 mg)<sup>31</sup>

Dose at which risk reported in study: 26 mmol (1,000 mg)

Proportion (alternative scenario/supplementation dose): 0.55

<sup>33</sup> Alternative scenario: UK general population with reduced sodium and increased potassium intakes resulting from the substitution of 15-25% sodium by potassium.

<sup>34</sup> These are estimated figures taken from Tables 1 and 2; however they do not reflect the exact adult average figure.

Reduced risk observed in study = 11%

Reduced risk that might be observed when moving to alternative scenario:  $11\% * 0.55 = 6\%$

Number of stroke cases that might be prevented when moving to alternative scenario:  $(6\% * 152,000) = \mathbf{9,200}$

### **3. Reduction in blood pressure from reduced sodium intake**

Reduction in sodium intake when moving to alternative scenario: 17 mmol (400 mg)<sup>31</sup>

Average potassium supplementation dose in studies: 75 mmol (1730 mg)

Proportion (alternative scenario/supplementation dose): 0.23

#### **Effect of population with hypertension**

SBP reduction observed in meta-analyses: 5.4 mm Hg

SBP that might be observed when moving to the alternative scenario  $(5.4 * 0.23)$  mm Hg = **1.2 mm Hg**

DBP reduction observed in meta-analyses: 2.8 mm Hg

DBP that might be observed when moving to the alternative scenario  $(2.8 * 0.23)$  mm Hg = **0.6 mm Hg**

#### **Effect on population without hypertension**

SBP reduction observed in meta-analyses: 2.4 mm Hg

SBP that might be observed when moving to the alternative scenario  $(2.4 * 0.23)$  mm Hg = **0.5 mm Hg**

DBP reduction observed in meta-analyses: 1.0 mm Hg

DBP that might be observed when moving to the alternative scenario  $(1.0 * 0.23)$  mm Hg = **0.2 mm Hg**

### **4. Reduction in stroke cases from reduced sodium intake**

Number of annual strokes in UK: 152,000

#### **Strazzullo et al. (2009)**

Reduced sodium intake when moving to alternative scenario: 17 mmol (400 mg)<sup>31</sup>

Dose at which risk reported in study: 50 mmol (1150 mg)

Proportion (alternative scenario/supplementation dose): 0.35

Reduced risk observed in study = 6%

Reduced risk that might be observed when moving to alternative scenario:  $6\% * 0.35 = 2\%$

Number of stroke cases that might be prevented when moving to alternative scenario:  $(2\% * 152,000) = \mathbf{3,200}$

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