Scientific Advisory Committee on Nutrition

Consultation on the SACN draft report Saturated Fats and Health Report

Comments Form

Organisation:	X-PERT Health
Name of commentator and contact details:	Dr Sean Wheatley, PhD; Dr Trudi Deakin, PhD; Matthew Whitaker; Nina Evans; Paul Hollinrake

- **Please do not PDF the form.**
- **Please do not amend the formatting of this form.**
- **Please do not embed attachments into this form.**
- **Please list any references in full that you wish the committee to consider.**

Please email this form to: sacnsatfat@phe.gov.uk [You if you do not receive a receipt for your submission please email sacn@phe.gov.uk]

Closing date: 5pm 3 July 2018

General comments	Comments Please insert each new comment in a new row
Outcomes considered	The partitioning of evidence assessment by individual conditions is informative, but a consideration of total mortality has been precluded by this method. This is the most important outcome.
Consideration of null findings	The weighting given to null findings or areas where there is no or insufficient evidence appears to be significantly less than that given to findings of association or effect. When the strength and consistency between studies for most findings, particularly in relation to events or mortality, are often questionable this should perhaps not be the case. The only section for which there is consistent evidence is for blood lipids (as summarised in Table 9.1), but these findings do not translate to meaningful and consistent outcomes (as summarised in Table 8.1). Even within the blood lipids section elements of this consistency suggest a positive impact on health markers when saturated fat intake is increase, for example an increase in HDL cholesterol. It is also notable how the blood lipid outcomes imply an improvement when swapping saturated fat for carbohydrate, yet the cardiovascular outcomes suggested either no difference or the reverse. This helps to highlight the limitations of focusing on risk markers. For all other considered health outcomes there is little to no evidence to support a detrimental impact of saturated fat on health; as summarised in tables 10.1 (blood pressure), 11.1 (Type 2 diabetes and glycaemic control), 12.1 (anthropometrics), 13.1 (cancers) and 14.1 (cognitive outcomes). This does not appear to have been fully taken into account in the final recommendations.

Comments by paragraph	Comments Please insert each new comment in a new row
2.1	The decision to only include systematic reviews, meta-analyses and pooled analyses precludes the inclusion of any studies published after the literature searches of the most recent review articles were completed. Although we appreciate the difficulty of weighting any individual studies identified that fit into this category against review articles it is important to consider as much evidence as possible. An example of a study which may have provided useful information but was published more recently would be: Mente, A., et al. (2017). Association of dietary nutrients with blood lipids and blood pressure in 18 countries: a cross-sectional analysis from the PURE study. *Lancet Diabetes Endocrinol*.
2.6	The addition of papers outside of the systematic selection framework of the review could potentially provide a source of bias, and it is not immediately apparent which papers were included via this method. The addition of three papers after the call for evidence closing date by an “interested party” is particularly concerning on this front. The details of which papers and who the “interested party” were should be made clear in order to reduce any concerns over bias.

2.12	Last bullet point of “Interpretation of results and their analysis” section states that “the results of sub-group and sensitivity analyses” will be included when assessing systematic review, meta-analyses and pooled analyses. It is clear this was not always the case, notably in relation to the CVD event reduction analysis in Hooper et al. 2015 where sensitivity analyses impacted upon the outcome (see comments pertaining to paragraph 8.6).
2.13	States that an effect/association would be deemed statistically significant using the $p<0.05$ criterion. The use of statistical significance using the highly arbitrary p-value cut-point of 0.05 is outdated and not an appropriate means to appraise evidence, particularly that which is being used to inform national guidelines. But equally as concerning, if we ignore the limitations of this and judge the appraisal of evidence within the SACN review based on the methods stated, this criterion appears to have been ignored on more than one occasion (e.g. paragraphs 8.16 and 8.51) allowing the inclusion of evidence that didn’t achieve this threshold without any qualification.
2.14	The assertions made in this paragraph are to an extent debatable. It is standard practice to use a random-effects model when dealing with studies of the nature of those in this review due to the high between-study heterogeneity. Indeed most reviews included this study used random-effects models as their primary analyses, reflecting this. Some of the conclusions of the SACN review over rely on the interpretation of meta-analyses using fixed effects models (e.g. paragraphs 8.38 and 8.41), even where the corresponding random effects models produced non-significant results, which is of some concern.
2.18	One of the listed limitations is an acknowledgement that “individual saturated fatty acids exert distinct effect on lipid metabolism and therefore have a differential impact on health”. This is a key limitation as the length of the saturated fatty acid chain may have an important influence. Short chain saturated fatty acids have been suggested to be beneficial for the gut microbiome (Bugaut (1987). *Comparative Biochemistry*, 86(3):439-72) whilst medium chain fatty acids are metabolised rapidly in the liver and have been shown to be associated with less body weight gain and smaller fat depots (St-Onge and Jones (2002) *The Journal of Nutrition*, 132(3), 329-32). Longer-chain saturated fatty acids (20:0, arachidic acid; 22:0, behenic acid; 23:0, tricosanoic acid; and 24:0, lignoceric acid) have been shown to have an inverse association with Type 2 diabetes, for example, perhaps due to having a distinct metabolic pathway to other fatty acids (Forouhi et al. (2014). *The Lancet Diabetes & Endocrinology*, 2(10), 810-8). As well as the length of the chain there is also evidence for a differential effect of odd and even saturated fatty acid chains. An inverse association was observed between odd chain saturated fatty acids (15:0, pentadecanoic acid; and 17:0, heptadecanoic acid: both associated with exogenous dairy consumption) and Type 2 diabetes in the EPIC-InterAct case-cohort study (Forouhi et al. (2014)). This is opposed to the positive association seen with even chain saturated fatty acids (14:0, myristic acid; 16:0, palmitic acid; and 18:0, stearic acid). It should be noted however that these associations were for plasma rather than dietary saturated fatty acids. The underlying cause of increased circulating even chain saturated fatty acids in the blood has been shown to be increased de novo lipogenesis in the liver, thus this association may better reflect the impact of dietary carbohydrate intake than exogenous saturated fat consumption (Forouhi et al. (2014), Postic and Girard. (2008). *Diabetes Metab*, 34, 643-648). Despite the importance of considering the differential impacts of different saturated fatty acids, it is asserted by SACN that “Consideration of individual saturated fatty acids was outside the scope of this review”. Based on the stated terms of reference and inclusion criteria we do not believe that some assessment of the differential impact of saturated fatty acids from different foods sources was precluded, and believe that some consideration of this is vital.

	For example any review considering the impact of normal versus low fat dairy products, or high milk and dairy versus low(er) milk and dairy consumption, would provide an indication of the impact of the saturated fatty acids content of the normal fat dairy products (indeed the search strategy included the term “dairy”, and so it is likely that such studies would have been identified using the applied method). An example of a potentially eligible study would be: Alexander *et al*. (2016). Dairy Consumption and CVD: a Systematic Review and Meta-Analysis. *British Journal of Nutrition,* 115, 737-750. A meta-analysis of 31 independent prospective cohort studies. This review found there was not a statistically significant association between total dairy and cardiovascular disease or coronary heart disease; with an inverse association observed between total dairy and stroke. Appraisal of this information could potentially be applied, depending on the outcomes, to provide caveats to any recommended restrictions. Without some form of assessment of these differential effects the impact of saturated fat on, or relationship of saturated fat consumption with, health cannot be validly assessed. The review in its current form is therefore largely redundant. The SACN framework for the evaluation of evidence (point 26b) states that when reviewing evidence it will be considered “if there is confidence that the observed effects are not due to confounding”. Due to the heterogeneity between foods that contain different saturated fat, and the number of different types of saturated fat in these foods, the outcomes of this review cannot be concluded with confidence to be free of the impact of possible confounding.
7.8	Acknowledges that the “ratio of total cholesterol:HDL cholesterol has subsequently become more widely used in clinical practice and is the primary lipid parameter in the QRISK2 assessment to predict CVD risk”, yet there was no evidence that reducing saturated fat intake had an impact on this marker (see table 9.1 and paragraph 9.80). This null finding should perhaps have been given greater weighting when this marker is regularly used in preference to other risk markers included in the review.
7.9	In the context of the review it could be inferred the CVD reduction statistics are implying a positive impact of guidance to reduce saturated fat, and of the evidence that there has been a reduction in saturated fat intake. There is no evidence of a causal relationship however and it would perhaps be prudent to acknowledge this, and that other factors- such as reduction in smoking and trans fats in the diet, as well as improvements in acute care (e.g. emergency stenting and use and availability of defibrillators)- will likely have played an important role.
8.6	A 17% reduction in CVD events with a reduction in saturated fat is reported (Hooper et al, 2015), but this fails to consider limitations with this particular analysis. The I^2 value was 65%, thus sensitivity analyses were required. When only studies within which the intervention group significantly reduced their saturated fat intake were included (the same studies that are presented in figure A2.2 of the SACN report) the relative risk dropped to indicate a 9% reduction in events, but importantly the finding was no longer statistically significant (RR = 0.91, 95%CI 0.79 to 1.04; see table 8, page 137 of Hooper et al. 2015). The validity of including the other studies in the main analysis of Hooper et al. 2015 where there was no evidence of a reduction in saturated fat intake in the intervention groups can be questioned regardless. The SACN methods state in paragraph 2.12 that sensitivity analyses will be considered when appraising evidence from meta-analyses, but that does not seem to have been the case here.

8.12 (and 15.16)	Hooper et al. (2015) is the only meta-analysis used demonstrating a reduction in CVD events, and this finding no longer holds when appropriate sensitivity analyses are used. It is therefore not justified to assert that there is adequate evidence that reducing saturated fat intake will reduce CVD events.
8.14	This paragraph again quotes Hooper et al. (2015), asserting there was a 27% lower risk of CVD events when saturated fat was replaced by PUFA. There are a number of limitations with this conclusion however: This meta-analysis did not truly assess the substitution of nutrients. Rather than considering which nutrient was the main replacement for saturated fat they included any studies where intake of the nutrient in question was significantly increased in the intervention group compared to the control group. This method does not warrant for changes in any other nutrients, which would influence the observed outcomes. For example it is possible that where there was an increase in PUFA - qualifying a study for this analysis as long as it was statistically significant - there could also have been an increase, potentially with a greater magnitude, of MUFA/protein/carbohydrate which could have a confounding effect. These analyses, used as a proxy indication of the effect of substitution of nutrients, were carried out as sensitivity analyses rather than primary assessments. For the PUFA analysis the I^2 value was 69%, which would make sensitivity analyses required. As this was already a sensitivity analysis however no further assessment was carried out, and so the confidence that can be had in this finding is somewhat limited. There were also no forest plots presented to allow additional appraisal of this outcome. (N.B. these points are not a criticism of the paper, as it would not be practical to perform sensitivity analyses to follow up on all outcomes of already performed sensitivity analyses. It is however a limitation with applying this evidence that shouldn't be overlooked) Based on the summary of included papers on pages 61 to 109 of Hooper et al (2015) it appears that there were only three studies that had a higher intake of PUFA as a percentage of energy in the intervention group versus the control group AND which reported CVD events (DART 1989, Stars 1992 and the Veterans Admin study 1696). The SACN summary reports there were seven studies included in this sensitivity analysis. These studies had a combined total of 2929 participants, not >3000 as Hooper et al reported or 3895 as SACN reported.
8.16	Regarding the statement: "The authors reported a 14% reduction in RR of CVD events (RR 0.86, 95% CI 0.77 to 0.96; p=0.07; I^2 =50%; 24 RCTs; 65,508 participants, 4586 CVD events)." SACN methods state they will be using $p<0.05$ as marker of statistical significance, but the reported finding from Schwab et al (2014) does not achieve this, and so should not be used as evidence of effect based on SACNs own defined criteria. At the very least the statement should be qualified somehow. Perhaps more importantly, the 14% reduction reported by SACN was NOT a finding of Schwab et al, but rather is from Hooper et al (2012; accessible from the Cochrane Database of Systematic Reviews, 5, CD002137). If Hooper et al 2012 was not identified and included in its own right, and was not subjected to appropriate considerations regarding its strengths and limitations, this finding should not be included. For avoidance of doubt, this finding in Hooper et al was

	from an analysis comparing fat modification or reduction with usual diet. It was not specific to saturated fat and should not be included in the SACN review. Further, this analysis had an I^2 value of 50%, making sensitivity analyses required by Cochrane standards. Sensitivity analyses removing studies where there were systematic differences other than fat intake produced results which were no longer significant (see page 207 in Hooper et al 2012).
8.17	The reference to Van Horn et al (2008) in this paragraph is inappropriate. The outcomes reported pertaining to substitution of saturated fat for PUFA appear to be in relation to a discussion within the Van Horn review (on page 292) about the current guidelines - rather than relating to any content communicating any actual analysis, study, review or meta-analysis. Within Van Horn et al (2008) it states that "Due to vast numbers of articles identified, additional inclusion and exclusion criteria were applied to each topic." Changing search criteria after commencement of a review is not good practice. A search of the website the reader is directed to within the review failed to locate any additional information regarding the search strategy applied, so the risk of bias associated with any amendments to the method could not be made. The inclusion of this review in section 8 is highly questionable anyway as the review predominantly discusses risk factors rather than disease outcomes, and largely reports sections from other reviews rather than contributing anything additional.
8.20 (and 15.19)	When limitations of the evidence presented in 8.14 and 8.16 are factored in it becomes highly questionable to conclude that there is adequate evidence that replacing saturated fat with PUFA results in a reduction in CVD events.
8.38	The only positive outcome demonstrated in this paragraph comes from a choice to use the fixed rather than random effects outcome from a meta-analysis. Despite this being within the scope of what is stated in the methods it is questionable whether an outcome derived from a debatable statistical approach is appropriate when it is being used as a primary driver of the overall conclusion of the section (rather than as an additional piece of research supporting an overall body of evidence).
8.41	This study by Chowdhury et al. (2014) provides the only positive association observed within this section, and that finding is only present in the fixed effects model (the random effects model produced a non-significant result). As mentioned elsewhere the decision to use fixed effects models is not without limitation and controversy. If there were other findings supporting this outcome then it would be understandable to consider this as part of a bigger body of evidence, but as outlined below this was not the case.
8.47 (and 15.27)	As stated above, the only positive association noted in this section is from using fixed over random effects in Chowdhury et al. None of de Souza et al, Siri-Tarino et al, Skeaff & Miller et al, Harcombe et al (either paper) or Mente et al found an association between saturated fat intake and CHD mortality or events. This consistency of null findings, compared to the limitations with the single positive association, would be better summarised as adequate evidence of no effect.
8.50	Hooper et al. (2015) was cited, with a 24% reduction in CHD events being reported. However, as the 95% confidence intervals included the value of no effect (95%CI 0.57 to 1.00) this finding was non-significant and should not have been

	included. I^2 for this particular analysis was also 71%, but as this was already a sensitivity analysis no further sensitivity analyses were performed to identify the source of this heterogeneity. As such this finding should be interpreted with caution. At the very least these limitations should be noted and considered within the SACN report.
8.51	The reported finding that CHD events were reduced was not-significant, as the 95% confidence intervals included the value of no effect. This is therefore not a robust finding supporting the conclusions drawn by SACN within this section. The discussion around serum cholesterol should not be included in this section.
8.52	The meta-analysis by Mozaffarian et al includes the Finnish Mental Hospital trial, which should not be included as it is not an RCT. Therefore the validity of including this paper can be questioned. This review also identified studies based on whether they increased n-6 PUFA intake, rather than whether they reduced saturated fat intake. There was no mention of saturated fat in the study's methods. It cannot be assumed that an increase in n-6 PUFA corresponds to a decrease in saturated fat (particularly not of an equivalent magnitude), or that any changes in health markers in a group who increases intake of n-6 PUFA saw these as a result of swapping saturated fat for n-6 PUFA.
8.54	The findings reported as being from Micha and Mozaffarian (2010) are simply a repeat of the meta-analysis outcome from Mozaffarian et al (2010). The prospective cohort study evidence in this review is largely reliant on Jakobsen et al (2009) too, thus this review does not provide any additional information to that already considered and should not be included.
8.57	The evidence from Jakobsen et al (2009) is overstated, failing to account for key limitations. This paper uses statistical modelling to estimate the effect of replacing saturated fat with other nutrients, rather than including any data where an actual substitution or dietary shift can be demonstrated to have occurred. Importantly, only baseline dietary information was available for the analyses in this review. This is an important limitation when this information is then used to predict longitudinal outcomes based on a change in diet, as there is no directly relevant information on dietary changes available to inform this type of assessment.
8.58	The only positive effect observed reported from Farvid et al (2014), is based on a decision to use the fixed effects model outcome from a meta-analysis. In the absence of other strong, supporting evidence this finding – and the appropriateness of including it - can be questioned.
8.59 (and 15.29)	Based on the limitations of the evidence presented in paragraphs 8.50, 8.51, 8.52 and 8.54 it is not justified to say there is evidence (even limited evidence) demonstrating that replacing saturated fat with PUFA is associated with a reduction in CHD events
8.60 (and 15.30)	The classification that there is adequate evidence that replacing saturated fat with PUFA is associated with reduced CHD mortality is not justified, particularly considering the limitations of the reviews used in paragraphs 8.57 and 8.58. Beyond the other limitations of this research much of the evidence from these reviews did not actually assess studies where a substitution of saturated fat for an alternative nutrient had been made, thus there is an overreliance on estimates from models.

8.66	See limitations of Jakobsen et al. (2009) outlined in comment on paragraph 8.57.
8.75	See limitations of Jakobsen et al. (2009) outlined in comment on paragraph 8.57.
8.102	States that “The effect may depend on the type of carbohydrate consumed” in relation to the observed outcomes when saturated fat was replaced by carbs. It could be interpreted that this assertion is to downplay the significance of findings related to replacing saturated fat with carbohydrates. It is entirely inconsistent to downplay these findings due to the lack of consideration of type whilst making sweeping statements about saturated fat without warranting for the food source or quality. The approach applied to consideration of carbs here should be applied to all nutrients, as the type and quality is likely more important in relation to their impact on health.
15.22	Although we make no comment regarding the specific conclusion in this point, the justification for classing the evidence as “Limited” is that “…the conclusion relied heavily on a study which did not explicitly test for the effect of substituting saturated fats with carbohydrate or protein.” At other points of the SACN review however evidence has been considered without qualification despite this same limitation being present. For example, this applies the use of evidence from Hooper et al (2015) in paragraph 8.14 and the application of several reviews included in the section summarised in paragraph 8.60. For both of these sections the evidence was ultimately classed as “adequate” despite these limitations.
16.5	States that new evidence published since 1994 “supports and strengthens” the original COMA conclusion that a reduction in saturated fat intake from current population levels would be beneficial. Within the summary tables however it is clear that for many of the outcomes there was no, limited or insufficient evidence. Even where the evidence was classified as moderate or adequate this is often based on expert opinion, much of which could be open to debate (for example when to use fixed- or random-effects models when interpreting meta-analyses). Further still, a number of these outcomes suggest improvements in health markers or outcomes in the higher saturated fat groups. Overall there are clearly uncertainties, and so to suggest the conclusion to reduce saturated fat has been strengthened is unjustified. Acknowledging this uncertainty is important in order to not give the impression the science is settled on the matter.
16.6	Figure 8.1 demonstrates broadly the success of studies in achieving a saturated fatty acid intake of <10% in their intervention arms, in line with the current recommendations. If this cut point were clearly supported more consistent positive outcomes would be expected. Thus, based on this and an appraisal of the other information presented and available, we would like to register our disagreement to the suggested maintenance of the guideline recommending the restriction of ALL saturated fats.
16.7	Existing dietary advice, as depicted by the Eatwell Guide, is more likely to lead to saturated fat being replace by carbohydrates than by mono- or poly-unsaturated fatty acids; with the guidance given being to choose unsaturated oils in small amounts with starchy carbohydrates forming the basis of meals. This guidance does not warrant effectively for the type and quality of carbohydrate, although there is no evidence presented within this review that would support any claim that the replacement of saturated fat with even high quality carbohydrates would result in an improvement in health. The evidence from the current review, as presented in table 8.1 for example, suggests that the

	replacement of saturated fat with carbohydrate is more likely to result in worse health outcomes than in an improvement.
17.1	These recommendations should include an increased consideration of the differential roles of different types of saturated fat and, in particular, the differential impact of different foods that contain saturated fat. Continued advice based around macronutrient content is not supported by the evidence base, and is therefore not appropriate.