



# **Lower carbohydrate diets for adults with type 2 diabetes**

## **Responses to public consultation on draft report**

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## Consultation procedure

The draft report on lower carbohydrate diets for adults with type 2 diabetes (T2D) was published for an eight-week [consultation](#) period from 5 March to 30 April 2020. Interested parties were invited to submit comments relating to the scientific content of the draft report and to alert the Joint Working Group on Lower Carbohydrates Diets for Adults with Type 2 Diabetes (WG) to any evidence that it may have missed.

Twenty-six responses were received from a variety of interested parties.

All the consultation comments were very carefully considered by the WG and by SACN and a response was agreed. Where consultation comments were similar, responses were standardised in order to ensure consistency.

Responses were not made to comments relating to risk management issues because these were outside the scope of this report.

References to chapters, paragraphs and page numbers refer to those in the draft report which went out for public [consultation](#).

In this document, respondents' consultation comments were reformatted to improve accessibility, by removing use of italics.

All correspondents are thanked for their comments; their input was much appreciated.

## Respondents

Comments were received from the following organisations and individuals:

1. British Association for Nutrition and Lifestyle Medicine (BANT)
2. British Nutrition Foundation (BNF)
3. Diabetes Specialist Group of British Dietetic Association (DSG-BDA)
4. Dr Donal Collins, GP
5. Prof Zbys Fedorowicz (Veritas Health Sciences Consultancy)
6. Elizabeth Gay
7. Dr Ronald Goldenberg, endocrinologist (LMC Diabetes & Endocrinology, Canada)
8. Dr Zoe Harcombe
9. Keith Hulme
10. HEART UK
11. Dr Shireen Kassam (plant-based health professional)
12. Kleijnen Systematic Reviews Ltd (Shelley de Kock)
13. Dr Elizabeth Morris and Professor Paul Aveyard (Nuffield Dept of Primary Care Health Sciences, University of Oxford)
14. Netherlands Health Council (Ivonne Sluijs and Janette de Goede)
15. Dr Gemma Newman (GP)
16. Obesity Group of the British Diabetic Association (OG-BDA)
17. Shivani Parikh
18. Dr Magda Robinson (Weight Medics)
19. Royal College of Physicians
20. David Sinon
21. South Asian Health Foundation
22. Dr Simon Tobin (GP)
23. Viva! Health
24. Justine Wadge
25. X-PERT Health
26. Tricia Williams (retired Senior Statistician, Government Statistical Service)

**Table 1: General comments on draft report**

Organisation/ Individual	Comments	SACN reply
BANT	<p><u>Report and general terms of reference and omissions</u></p> <ol style="list-style-type: none"> <li>1) The WG terms of reference do not align with the general SACN terms of reference. Omissions relate to vulnerable groups and risks/benefits of nutrients/food components for adults with T2D and background to T2D.</li> <li>2) The pathologies of T2D, treatment goals and markers and clinical outcomes should be aligned in paragraphs 3 and 4 and reflect the terms of reference in 1.4.</li> </ol>	<ol style="list-style-type: none"> <li>1) Terms of reference vary according to issue under consideration. They are agreed at outset by the WG and SACN.</li> <li>2) Unclear which paragraphs (3 and 4) are being referred to here. Also unclear how markers and clinical outcomes of T2D do not align with terms of reference.</li> </ol>
BNF	<p><u>Terms of reference and considerations of the outcomes of the report in practice:</u> The issue of low carbohydrate diets for weight loss, particularly for people with T2D, is one of great scientific and popular debate. As such, it is of great value to have a report from an authoritative body on this topic, in particular with it being developed by a joint working group including representation from Diabetes UK, the BDA [British Dietetic Association], RCP [Royal College of Physicians] and RCGP [Royal College of General Practitioners].</p> <p>With the majority of UK adults being overweight or obese and given the strong association between obesity and T2D, there is an urgent need to support people to lose weight and maintain healthier body weights. It is well established that weight loss can have a significant impact on glycaemic control in T2D as well as reducing the risk of comorbidities, and that, if enough weight is lost, the condition can effectively be put into remission. As such, providing consistent, evidence-based, practical advice on effective weight loss strategies is of paramount importance both for public health and reducing the economic impact of obesity and related comorbidities, including T2D. BNF’s mission is to communicate evidence-based nutrition science and would expect to refer to SACN’s final</p>	<p>These points relate to risk management and will be considered by PHE and Diabetes UK following publication of final report.</p>

Organisation/ Individual	Comments	SACN reply
	<p>report when delivering practical advice for health professionals, media and other stakeholders, as well as general info for people with T2D and those trying to lose weight. As such, our comments relate to how the findings of the final report can be communicated in a way that is helpful and supports public health.</p> <p>We understand that SACN's role in the development of this report is to assess the scientific evidence as directed by the terms of reference. However, there are a number of issues that need consideration in order to be able to provide advice to improve public health. The report itself as it stands may be of limited value unless supported by further public health guidance from PHE to address the widespread confusion about the efficacy of low carbohydrate diets for people with T2D and to support those with the condition who are trying to improve their health.</p> <p>The National Lipid Association (US) has published a <a href="#">scientific statement</a> (Kirkpatrick et al. 2020), reviewing current evidence and clinical recommendations on effects of low- and very-low-carbohydrate diets for management of body weight and other cardiometabolic risk factors. It concluded that there was no evidence that low carbohydrate diets were superior to other weight loss diets and that results for many CVD outcomes were mixed but that there might be advantages in relation to appetite control, reduced triglycerides and reduction in use of diabetes medications over 12-24 months. In looking at outcomes of systematic reviews on dietary approaches to weight loss, the authors noted that there were substantial inter-individual variations in the responses to each of the diet conditions with some achieving above average weight loss. The authors suggested that personal preference in the macronutrient composition of the diet was important and should be a consideration when offering dietary advice.</p> <p><u>Percentage of carbohydrate in the diets of studies included:</u> As highlighted in the draft report, there were a number of limitations in the evidence and the carbohydrate contents of the diets considered as 'lower carbohydrate' in the analysis varied widely from the very</p>	<p>Kirkpatrick et al (2020) is a narrative review of evidence from systematic reviews and meta-analyses on the effects of low and very-low-carbohydrate diets on body weight, lipoprotein lipids, glycaemic control, and other cardiometabolic risk factors. It includes a mixture of studies in adults with overweight and/or obesity and/or T2D or prediabetes.</p>

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	<p>low carbohydrate ‘ketogenic’ diets, typically less than 10% total energy (TE) from carbohydrate, to diets comprising up to 45% TE from carbohydrate. The report highlights that the majority of studies considered were in the range of 26-45% TE from carbohydrate. Thus, a variety of diets included as ‘lower carbohydrate’ represent huge differences in potential dietary patterns and nutrient composition (including fibre content) and, consequently, potential health effects of these diets. At under 10% TE from carbohydrate, the carbohydrate-containing foods that could be included would be very restricted, whereas at 45% this would not be the case; data from the most recent NDNS [National Diet and Nutrition Survey] indicate that the average proportion of carbohydrate in the diets of adults (19-64y) is 45.7% and so our current average diet is close to qualifying as ‘lower carbohydrate’ by this definition.</p> <p>To give clear advice, it is important to understand effects of different proportions of carbohydrate in diets and also substitution effects when carbohydrate is replaced by another macronutrient. A recent systematic review and meta-analysis by <a href="#">Fechner et al. (2020)</a> may be of interest. Low carbohydrate diets were divided into 3 groups; moderate-low (&lt;45-40% TE), low (&lt;40-30% TE) and very low (&lt;30-3% TE) and their effects on weight loss and other cardiometabolic risk markers were investigated. They also collected data on what carbohydrates had been replaced by and the fibre content of diets was taken into account. This allowed a comparison of the effects of different levels of carbohydrate restriction. For example, weight loss was similar across the diet groups but decreases in triacylglycerol were more pronounced as proportion of carbohydrates in the diets decreased. On the other hand, very low carbohydrate diets appeared to increase LDL cholesterol, especially where reduction in carbohydrate resulted in an increase in energy from saturated fatty acids, as well as a decreased fibre intake which often accompanies carbohydrate reduction (%E from fat/saturated fat was very high in some studies). Fechner et al. concluded that health effects of low carbohydrate diets are likely to be mediated by</p>	<p>Meta-analyses in Fechner et al (2020) included mixture of studies in healthy individuals, those with overweight/obesity and those with T2D. Results were not reported separately for adults with T2D. Outcomes were not reported by study duration (varied between 5 days and 24 months)</p>

Organisation/ Individual	Comments	SACN reply
	<p>what substitutes for carbohydrates, rather than carbohydrate restriction per se, and suggested this should be a focus of further research.</p> <p><u>Diet and carbohydrate quality</u>: While consideration of quality of carbohydrate and overall dietary quality were not part of the terms of reference, they are of vital importance to more fully understand effects of different dietary sources of carbohydrate (e.g. refined vs wholegrain) and provide practical advice for people considering a low carbohydrate diet. According to the NDNS, the UK population is close to meeting the current recommendation of 50% TE from carbohydrates. However, intakes of free sugars are higher than recommended and intakes of dietary fibre much lower. In terms of food choices from the starchy foods group, refined versions of these foods, such as white bread, pasta and rice, predominate in the UK diet. Thus, communication of the importance of carbohydrate quality in the diet is a particular challenge in relation to how the final conclusions of this report are used in subsequent public health advice.</p> <p>The <a href="#">Linear programming analysis</a> performed in development of the Eatwell Guide showed that intakes of wholegrains would have to significantly increase in order to meet current nutrient recommendations. Thus, existing advice on healthy diets is not translating into healthy dietary patterns within the population and so simply suggesting that people with T2D follow existing healthy eating advice for the population as is currently the case may not support improvements in public health unless ways are found to improve adoption of the advice. Those looking for advice on healthy eating are potentially subject to often poor and conflicting advice through traditional and social media and this represents a particular challenge in terms of how the conclusions of the final version of this report are communicated to attempt to tackle this. In the systematic review and meta-analysis by <a href="#">Fechner et al.</a> (2020) the authors noted that low carbohydrate diets with lower fibre contents were associated with increased LDL cholesterol and that blood glucose was higher on low carbohydrate diets with lower fibre intakes compared to moderate carbohydrate</p>	<p>Research recommendation noted.</p> <p>The point about carbohydrate quality is acknowledged as a limitation of the evidence base (paragraph 6.73).</p>



Organisation/ Individual	Comments	SACN reply
	<p>diets with higher fibre intakes. Thus, the fibre content of diets, whatever the proportion of carbohydrates, is an important consideration.</p> <p><a href="#">Churuangsuk et al.</a> (2020) reviewed evidence for low and reduced carbohydrate diets in managing and preventing T2D. They reported that low carbohydrate diets can be a valid weight loss treatment up to 1-2 years, although not superior to other weight loss approaches under controlled conditions. They caution about potential negative effects on health, including micronutrient deficiencies, raised LDL cholesterol and the potential for negative effects on the gut microbiome if the dietary pattern followed while restricting carbohydrates is unbalanced, but suggest that these effects can be avoided if prudent food choices are made within the diet.</p> <p><u>References</u></p> <p>Churuangsuk C, Lean MEJ &amp; Combet E. (2020) Low and reduced carbohydrate diets: challenges and opportunities for type 2 diabetes management and prevention. Proceedings of the Nutrition Society. <a href="https://doi.org/10.1017/S0029665120000105">https://doi.org/10.1017/S0029665120000105</a></p> <p>Fechner et al. The Effects of Different Degrees of Carbohydrate Restriction and Carbohydrate Replacement on Cardiometabolic Risk Markers in Humans-A Systematic Review and Meta-Analysis. <i>Nutrients</i>. 2020; 12(4), 991</p> <p>Ge et al. (2020). Comparison of dietary macronutrient patterns of 14 popular named dietary programmes for weight and cardiovascular risk factor reduction in adults: systematic review and network meta-analysis of randomised trials. <i>BMJ</i>. 2020; 369 doi: <a href="https://doi.org/10.1136/bmj.m696">https://doi.org/10.1136/bmj.m696</a></p> <p>Kirkpatrick et al. Review of Current Evidence and Clinical Recommendations on the Effects of Low-Carbohydrate and Very-Low-Carbohydrate (including Ketogenic) Diets for the Management of Body Weight and other Cardiometabolic Risk Factors. <i>A Scientific</i></p>	<p>Churuangsuk et al (2020) is a systematic review of systematic reviews. It is not restricted to individuals with T2D.</p>

Organisation/ Individual	Comments	SACN reply
	<p>Statement from the National Lipid Association. Journal of Clinical Lipidology 2019; <b>13</b> 689-711</p> <p>Scarborough et al. Eatwell Guide: modelling the dietary and cost implications of incorporating new sugar and fibre guidelines. BMJ Open 2016;6:e013182. doi:10.1136/bmjopen-201601318</p>	
D Collins	<p>The strategy of low-fat diets to control the obesity epidemic over the last 40 years clearly is not working. Please come up with a different strategy. Not sure it matters which diet you pick as long as it is not the one that has not worked. Look forward to your recommendations but hope you will allow patient choice, shared decision making, be part of guidelines.</p>	<p>Relates to risk management. For consideration by PHE and Diabetes UK following publication of final report.</p>
DSG-BDA	<ol style="list-style-type: none"> <li>1) Inter-relationship between carbohydrate intake and overall energy intake as well as relationship between weight loss and change in glycaemic control were not fully considered, as it is not possible to easily distinguish the effects of each variable on the other.</li> <li>2) NICE [National Institute for Health and Care Excellence], in their recent call for comments for the planned review of the management of T2D, stated that lifestyle aspects were not being reviewed. As a group we put out a statement about low carbohydrate diets but were informed there is not enough data. To allow the consideration of lower carbohydrate diets there appears to be at least a case for it to be supported as an option.</li> <li>3) This report adds little to the BDA [British Dietetic Association] statement on low carbohydrate diets (<a href="https://www.bda.uk.com/resource/low-carbohydrate-diets-for-the-management-of-type-2-diabetes-in-adults.html">https://www.bda.uk.com/resource/low-carbohydrate-diets-for-the-management-of-type-2-diabetes-in-adults.html</a>) and Diabetes UK Nutritional Guidelines</li> </ol>	<ol style="list-style-type: none"> <li>1) Detailed consideration of relationship between carbohydrate intake and overall energy intake or between weight loss and change in glycaemic control were outside remit of report.</li> <li>2) Relates to NICE guidance and is outside remit of report.</li> <li>3) Purpose of report was to assess the scientific evidence not to consider support options for people living with T2D.</li> </ol>

Organisation/ Individual	Comments	SACN reply
	<p>(<a href="https://diabetes-resources-production.s3.eu-west-1.amazonaws.com/resources-s3/2018-03/1373_Nutrition%20guidelines_0.pdf">https://diabetes-resources-production.s3.eu-west-1.amazonaws.com/resources-s3/2018-03/1373_Nutrition%20guidelines_0.pdf</a>) both published in 2018 and in fact offer more support to people living with diabetes and those who support their care.</p>	
Prof Z Fedorowicz	<p>My colleagues and co-authors, Dr van Zuuren, Professor Pijl and Prof Kuijpers, on the van Zuuren et al (2018) systematic review which was included in the report are delighted to see the clear and concise summary of our systematic review.</p>	<p>Comments noted and welcomed.</p>
E Gay	<p>Refers to book by Dr J Le Fanu, Too Many Pills. In chapter 5, on diabetes, Le Fanu reveals catalogue of catastrophic errors, from totally reversing dietary advice of low carbohydrate/high fat diet so successfully used before, to lowering the bar which indicated a person was diabetic. In Dr Unwin’s experience, ‘a low carbohydrate diet resulted in substantial weight loss in all patients and brought about normalisation of blood glucose. 7 patients were able to come off medication.’ However, the new dietary recommendation was that those with diabetes should be encouraged to ‘include starchy carbohydrate foods (bread, pasta, potatoes, noodles, rice, cereals) at each meal. Not surprisingly, they struggled to lose weight and lower their levels of blood sugar. This, Le Fanu believes, ‘accounts for 4-fold increase in T2D over past 25 years...an iatrogenic catastrophe of epic proportions.’</p>	<p>It was agreed to amend paragraphs relating to evidence from clinical practice studies, to summarise the direction of the evidence from these studies and to expand the explanation of why they were not included for consideration in the report.</p>
Dr R Goldenberg	<p>The document did not discuss low carbohydrate diets in the context of sodium-glucoseco-transporter-2 inhibitors (SGLT2i) treatment for T2D. There are multiple case reports where a low carbohydrate or ketogenic diet has been a trigger for SGLT2i associated diabetic ketoacidosis. After reviewing such data, perhaps it would be wise to suggest great caution or even avoidance of low carbohydrate diets in patients treated with SGLT2i. This is an overlooked issue in clinical practice, and with the rising use of both low carbohydrate diets and SGLT2i in clinical practice, a very important issue that perhaps should be discussed in</p>	<p>A detailed consideration of SGLT2i treatment was outside the scope of report.</p>

Organisation/ Individual	Comments	SACN reply
	the document.	
Dr Z Harcombe	<p>There are five fundamental flaws with this review:</p> <ol style="list-style-type: none"> <li>1. Conflicts of interest</li> <li>2. Not addressing what the review set out to address</li> <li>3. The decision to not study low carbohydrate diets</li> <li>4. The absence of common sense</li> <li>5. If only the same bar had been set for introduction of low fat high carbohydrate guidelines</li> </ol> <p>This review should be stopped until they have been addressed. Otherwise this draft report risks becoming the official position on T2D and low carbohydrate diets and that would be a travesty. The review requires:</p> <ol style="list-style-type: none"> <li>1) An independent panel with no conflicts of interest.</li> <li>2) Examination of the actual diets gaining attention, as the review claimed it set out to address.</li> <li>3) Genuine study of very low carbohydrate diets (low carbohydrate diets as an upper limit).</li> <li>4) Some common sense.</li> <li>5) Some humility and acknowledgement of how low the bar was set to get us into a public health crisis of obesity and T2D and how high the bar has been set to get us out of this. And then an acceptance of the Feinman et al position: The seriousness of diabetes requires that we evaluate all of the evidence that is available. The 12 points are sufficiently compelling that we feel that the burden of proof rests with those who are opposed.</li> </ol> <p><u>In relation to Flaw 1</u> (conflicts of interest): panel membership (p5)</p> <p>There are conflicts of interest among panel members</p>	

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	<p>a) Food and pharmaceutical organisations - 1 of the co-chairs and 2 other panel members have conflicts of interest with the International Life Sciences Institute (ILSI). Their members are a who's who of the fake food industry/manufacturers of processed carbohydrates including Coca-Cola, General Mills, Hershey, Kellogg's, PepsiCo, Red Bull and many more. (<a href="https://ilsina.org/about-us/membership/">https://ilsina.org/about-us/membership/</a>)</p> <p>One of the co-chairs also has conflicts with the BNF – another body representing the fake food industry/manufacturers of processed carbohydrates. BNF members include British sugar, Coca-Cola, Cargill, General Mills, Kellogg, Mars, McDonalds, Nestle, Pepsi, Tate &amp; Lyle sugar and many more.</p> <p>Other panel conflicts include Unilever, Mars, American Association of Cereal Chemistry International, Nestle, World Sugar Research Organization (more carbohydrate conflicts) and Amgen, Bayer, and Lilly (pharmaceuticals to counter the effect of carbohydrates).</p> <p>b) SACN carbohydrate review - One of the co-chairs and another panel member were on the SACN review “Carbohydrates and health” (2015). This concluded “It is recommended that the dietary reference value for total carbohydrate should be maintained at an average population intake of approximately 50% of total dietary energy.”</p> <p>An example of the bias that this leads to is captured in para 5.42, below Table 5.1 which defines low carbohydrate diets which states “According to the above categories of carbohydrate intake, government recommendations on carbohydrate intake for the general population (50% of TE) would be classified as high.” Yes – that’s the point. This is not the panel to overturn its own guidelines.</p> <p>c) Diabetes UK - Half the panel are employed by, research for, or have other conflicts with Diabetes UK. The official dietary advice from Diabetes UK is still low fat/high carbohydrate dominated. Diabetes UK published a position statement on low-carbohydrate diets in May 2017 (<a href="https://www.diabetes.org.uk/resources-s3/2017-09/low-carb-diets-position-">https://www.diabetes.org.uk/resources-s3/2017-09/low-carb-diets-position-</a></p>	<p>The register of interests for SACN members and members of SACN working group members is available here: <a href="https://www.gov.uk/government/groups/scientific-advisory-committee-on-nutrition#register-of-interests">https://www.gov.uk/government/groups/scientific-advisory-committee-on-nutrition#register-of-interests</a></p> <p>Declarations of interests are also published in the SACN annual report, available here <a href="https://www.gov.uk/government/collections/sacn-reports-and-position-statements#annual-reports">https://www.gov.uk/government/collections/sacn-reports-and-position-statements#annual-reports</a></p> <p>SACN’s methodology is set out to establish clarity.</p> <p>SACN and the WG includes a wide range of membership representing different perspectives in the systematic approach to assessing the evidence and reflecting not just academic concerns but, through its non-academic membership, concerns of the wider public.</p>

Organisation/ Individual	Comments	SACN reply
	<p><a href="#">statement-May-2017.pdf</a>) that can be summarised as begrudgingly supporting low-carbohydrate diets in the short term only; issuing cautions about safety; and thinking that lowering blood glucose is an issue rather than a highly desirable outcome.</p> <p><u>In relation to flaw 3</u> (the decision to not study low carbohydrate diets)</p> <p>The draft report shows that it knows what low and very low carbohydrate diets are (table 5.1) and yet has then chosen to ignore them.</p> <p>It is worth noting that the very low-calorie DiRECT diet was a low-carbohydrate diet. It provided 825-853 kcal/day, of which 59% was carbohydrate, thus providing 122-126g/day of carbohydrate. That's low carbohydrate (Table 5.1). DiRECT was thus low carbohydrate and very low calorie and yet no concerns about its safety were issued in the draft report.</p> <p>Para 6.2 informs us that just 4 systematic reviews with meta-analyses were used to provide the entire evidence in the SACN draft report. Normally systematic reviews with meta-analyses would provide the best evidence available but the goal of this review was ostensibly to review the growing interest in (very) low carbohydrate diets and this evidence is gathering at the current time – to ignore all of this is to render the draft review pointless.</p> <p>Earlier evidence was also ignored in the draft report (2008). Para 3.13 states “Currently, there is no cure for T2D but data from dietary weight management programmes and bariatric surgery confirm that weight loss can result in remission (Diabetes UK, 2018b).”</p> <p>In 2008, Dr E Westman et al published “The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes.”<sup>i</sup> The latter was a RCT which randomised people to either a ketogenic (&lt;20g/d carbohydrate) or a reduced calorie diet (500 cal deficit). The ketogenic diet achieved significantly better results for HbA1c, body weight, and reduction/elimination in diabetes medications. This provided evidence, as far back as 2008, that a genuinely low carbohydrate diet can put T2D into remission.</p>	<p>The report explains that the definition of a low carbohydrate diet varied across studies. Comparisons were therefore between lower and higher intakes.</p> <p>The DiRECT trial intervention was a very low energy diet. As explained in paragraphs 5.43 and 5.44, carbohydrate intake in very low energy diets might be relatively low in terms of grams/day, but relatively high in terms of % total energy intake. In this context, a 59% energy contribution from carbohydrates would be considered high.</p> <p>The objective of the review was to assess if there were differences between lower and higher carbohydrate diets on markers and clinical outcomes of T2D.</p> <p>The RCT by Westman et al (2008) was included in 3 out of the 4 prioritised SRs with MAs.</p>

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	<p>The Feinman et al paper should have been used in the draft report for all of its evidence – not merely for the definitions of low carbohydrate diets. As the abstract summarises: “Here we present 12 points of evidence supporting the use of low-carbohydrate diets as the first approach to treating type 2 diabetes and as the most effective adjunct to pharmacology in type 1. They represent the best-documented, least controversial results. The insistence on long-term random-controlled trials as the only kind of data that will be accepted is without precedent in science. <b>The seriousness of diabetes requires that we evaluate all of the evidence that is available. The 12 points are sufficiently compelling that we feel that the burden of proof rests with those who are opposed.</b>”.</p> <p><u>References</u>  Feinman et al. Dietary Carbohydrate restriction as the first approach in diabetes management. Critical review and evidence base. Nutrition (Burbank, Los Angeles County, Calif) 2014.  Westman et al. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. Nutrition &amp; metabolism 2008.</p>	<p>The WG was not ‘opposed’. The evidence was assessed as set out in the terms of reference. Outcomes and methodological criteria were prespecified for objectivity and clarity. The selection criteria specified prospective cohort studies and RCTs for consideration. The reasons for consideration of this type of evidence is explained in the text.</p>
HEART UK	<ol style="list-style-type: none"> <li>1) General format: It would be useful to have overall conclusions, recommendations and research recommendations at the beginning of the report.</li> <li>2) Disappointed that the report has limited itself to looking only at RCT evidence. There are well documented issues that arise when dietary recommendations are based solely on this type of research. RCT evidence, whilst helpful in developing nutritional guidelines, is more appropriate to assessing the suitability and effectiveness of medication, where blind randomisation is possible. These studies do not have long enough follow-up to study clinical outcomes such as micro and macrovascular complications of T2D, CVD, mortality and long-term safety.</li> </ol>	<ol style="list-style-type: none"> <li>1) Overall conclusions and recommendations to be included in the summary at beginning of the final report.</li> <li>2) Inclusion criteria also specified systematic reviews of prospective cohort studies but none were identified.</li> </ol> <p>SACN’s remit was to consider the evidence in adults living with T2D. Much of the</p>

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	<p>While not specific to T2D, several prospective cohort studies and their meta-analyses show consistent findings that the low carbohydrate dietary pattern was associated with an increased risk of all-cause mortality and CVD mortality. The Atherosclerosis Risk in Communities Study found U-shaped association between carbohydrate intake (% energy) and all-cause mortality, with lowest mortality risk at 50–55% energy carbohydrate. The authors also conducted the meta-analysis for carbohydrate and mortality. Compared to a carbohydrate intake of about 50% energy, low carbohydrate intake (&lt;40 % energy) was associated with a 20% increased risk of all-cause mortality, and high carbohydrate intake (&gt;70 % energy) was also associated with a 23% increased risk of all-cause mortality. Another population-based cohort study also showed a 22% increased risk of all-cause mortality, a 13% increased risk of ASCVD [atherosclerotic cardiovascular] mortality and an 8% increased risk of cancer death in associations with low carbohydrate dietary pattern (comparing between extreme quartiles, adjusted for BMI [Body Mass Index]. This context should be included in the report and further cohort studies on those consuming low (&lt;26%) and very low (&lt;10%) carbohydrate diets should be conducted.</p> <p>3) <u>Why were studies comparing dietary patterns not included?</u> In order to get a complete picture of the impact of low carbohydrate diets in T2D, the totality of evidence needs to be assessed which includes studies examining dietary patterns. Recent network meta-analyses compared the impact of different dietary approaches in clinical trials on glycaemic control (primary outcome was HbA1c) and blood lipids in patients with T2D. The meta-analyses examining blood lipids found that moderate-carbohydrate and vegan/vegetarian diets were more effective at reducing LDL cholesterol compared with the control diet, and low-carbohydrate, high-protein, and low-fat dietary patterns. The Mediterranean diet was the only dietary pattern that increased HDL cholesterol. The</p>	<p>longitudinal evidence is in general populations.</p> <p>3) The remit of the review was to compare lower with higher carbohydrate diets on markers and outcomes of T2D. Consideration of other types of diets were outside remit. However, these comments will be considered in formulating recommendations and research recommendations.</p> <p>4) Noted for consideration.</p> <p>5) Noted and will be considered in formulating recommendations and research recommendations.</p> <p>6) These points will be considered by PHE and Diabetes UK following publication of final report.</p> <p>7) Comments welcomed.</p>



Organisation/ Individual	Comments	SACN reply
	<p>Mediterranean and low-carbohydrate diets significantly reduced triacylglycerol levels compared with low-fat and control diets. This context should be included in the report.</p> <p>4) <u>Overall findings on lipids</u>: Based on the inclusion criteria, the finding that there was no difference in LDL cholesterol is in contrast to other studies examining low carbohydrate diets with low fat diets. In these studies, low carbohydrate diets increased LDL cholesterol to a greater extent compared to low fat diets over 6 to 24 months intervention. The previously described meta-analysis also showed that mortality increased by 18% when replacing carbohydrate with animal-sourced fat and protein and decreased by 18% when replacing carbohydrate with plant-sourced fat and protein. Higher protein intake, particularly from plant proteins tends to lower LDL cholesterol relative to protein from animal sources.</p> <p>Due to the heterogeneity of the diets included in this report, the lack of information on carbohydrate quality and the wide overlap of fat and saturated fat in both low and high carbohydrate groups, it is not possible to draw conclusions on the impact of diet on lipids.</p> <p>It is well documented that the substitute nutrient and/ or food for carbohydrates will impact lipids. However, the impact on lipid profile is clearly difficult to assess in this analysis given the potential confounding effects of variations in calorie substitution strategies.</p> <p>The National Lipid Association Nutrition and Lifestyle Task Force also recently reviewed current evidence examining low carbohydrate diets for management of body weight and other cardiometabolic risk factors. They explained the conflicting results of the studies examining the effect of low carbohydrate and very low carbohydrate diets on blood lipids and lipoprotein levels in adults with overweight or obesity, with and without T2D, may be due to variations in carbohydrate and fat quantity and quality of</p>	

Organisation/ Individual	Comments	SACN reply
	<p>the diet interventions in the RCTs, and/or differences in adherence to the prescribed diets over the course of the study periods. They added that the lack of significant difference in LDL cholesterol between the diet groups in RCTs involving adults with T2D may be attributed to similar saturated fat content between diets, saturated fat intake not increasing from baseline in the diet groups, or carbohydrate being replaced with unsaturated fatty acids in the low-carbohydrate diets. They concluded that the available data suggest that controlling saturated fat intake is crucial to prevent significant increases in LDL cholesterol and for achieving improved cardiovascular health with low carbohydrate diets.</p> <p>We strongly believe these observations need to be included in the report to provide overall context and to be in line with other expert bodies.</p> <p>5) <u>Recommendations from other lipid expert committees to be considered</u>: In the recent European Society of Cardiology and European Atherosclerosis Society guidelines on dyslipidaemia the reduction of saturated fat intake and its substitution with unsaturated fat, as well as the replacement of a major proportion of refined starchy foods and simple sugars with fibre-rich foods like fruits, vegetables, and wholegrains is recommended for dyslipidaemias in T2D.</p> <p>The recommendation for low carbohydrate diets by the National Lipid Association Nutrition and Lifestyle Task Force is that carbohydrate is replaced by unsaturated fatty acids rather than saturated fat.</p> <p>6) Providing guidance to the media on reporting food stories – so consumers are not misled. This would be helpful to give a lead to the press and food industry. In the current climate confusion rains, fuelled by the distortion often caused by the media in their eagerness to have an interesting slant on health issues. Frequently news stories are driven by food companies with their own agendas. These stories, together with</p>	

Organisation/ Individual	Comments	SACN reply
	<p>their research, are reported as if they are factual (without reference to the totality of research which often suggests otherwise) and the reader is led to believe they represent a definite change in policy rather than a preliminary finding that requires scientific scrutiny and/or more detailed studies.</p> <p>7) HEART UK welcomes publication of this new report and commends the panel for their diligence in assessing the research, within the confines of the brief.</p> <p><u>References</u> relating to point 2</p> <p>Lagiou et al. (2007) Low carbohydrate-high protein diet and mortality in a cohort of Swedish women. <i>J Intern Med</i> 261, 366–374</p> <p>Trichopoulou et al. (2007) Low-carbohydrate-high-protein diet and long-term survival in a general population cohort. <i>Eur J Clin Nutr</i> 61, 575–581</p> <p>Fung et al. (2010) Low-carbohydrate diets and all-cause and cause-specific mortality: two cohort studies. <i>Ann Intern Med</i> 153, 289–298</p> <p>Sjogren et al. (2010) Mediterranean and carbohydrate-restricted diets and mortality among elderly men: a cohort study in Sweden. <i>Am J Clin Nutr</i> 92, 967–974.</p> <p>Nilsson et al. (2012) Low-carbohydrate, high-protein score and mortality in a northern Swedish population-based cohort. <i>Eur J Clin Nutr</i> 66, 694–700.</p> <p>Noto et al. (2013) Low-carbohydrate diets and all-cause mortality: a systematic review and meta-analysis of observational studies. <i>PLoS One</i> 8, e55030.</p> <p>Seidelmann et al. (2018) Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. <i>Lancet Public Health</i> 3, e419–e428.</p> <p>Dehghan et al. (2017) Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. <i>Lancet</i> 390, 2050–2062.</p>	

Organisation/ Individual	Comments	SACN reply
	<p>relating to point 3</p> <p>Schwingshackl et al. A network meta-analysis on the comparative efficacy of different dietary approaches on glycaemic control in patients with type 2 diabetes mellitus. <i>Eur J Epidemiol.</i> 2018; 33: 157–170</p> <p>Neuenschwander et al. Impact of different dietary approaches on blood lipid control in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. <i>Eur J Epidemiol.</i> 2019; 1–16</p> <p>relating to point 4</p> <p>Mansoor et al Effects of low-carbohydrate diets v. low-fat diets on body weight and cardiovascular risk factors: a meta-analysis of randomised controlled trials. <i>Br J Nutr.</i> 2016 Feb 14;115(3):466-79.</p> <p>Sackner-Bernstein et al Dietary Intervention for Overweight and Obese Adults: Comparison of Low-Carbohydrate and Low-Fat Diets. A Meta-Analysis. <i>PLoS One.</i> 2015 Oct 20;10(10):e0139817.</p> <p>Bueno et al Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials. <i>Br J Nutr.</i> 2013 Oct;110(7):1178-87.</p> <p>Hession et al. Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. <i>Obes Rev</i> 2009. 10, 36–50.</p> <p>Nordmann et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. <i>Arch Intern Med</i> 2006. 166, 285–293.</p> <p>Hu et al. Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. <i>Am J Epidemiol</i> 2012, 176 (Suppl. 7)</p> <p>Mensink RP. Effects of Saturated Fatty Acids on Serum Lipids and Lipoproteins: A Systematic Review and Regression Analysis. Geneva: World Health Organization; 2016:1–72</p>	

Organisation/ Individual	Comments	SACN reply
	<p>Seidelmann et al. (2018) Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. Lancet Public Health 3, e419–e428.</p> <p>relating to point 5</p> <p>Mach et al. ESC Scientific Document Group, 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Heart Journal, Volume 41, Issue 1, 1 January 2020, Pages 111–188</p>	
K Hulme	<p>Three key comments.</p> <ol style="list-style-type: none"> <li>1) The eligibility criteria used to select evidence means the question asked by PHE remains only partially answered. Some high quality evidence has been excluded, despite being compelling. It should be taken into account.</li> <li>2) Findings relating to reduced medications with lower carbohydrates have been downplayed. These findings are strengthened by the excluded evidence.</li> <li>3) SACN risk exposure to criticism and undermining of their credibility by taking such a narrow view of the evidence.</li> </ol> <p><u>Eligibility criteria used to include and exclude various types of evidence</u></p> <p>As a direct consequence of the criteria some strong evidence on the impact of a very low carbohydrate diet on T2D has been excluded. This is a significant exclusion and has affected the integrity of the SACN findings. The included studies were limited to systematic reviews, meta-analyses and pooled analyses of RCTs and prospective cohort studies. Whilst these studies may be considered the strongest type of evidence, this obviously depends on the availability of high quality well controlled studies clearly focussed on common objectives. Meta-analysis can surely only add value rather than dilute findings if the studies included are strictly homogeneous. In the current study these strengths have been substantially undermined by the limitations identified by SACN. These include</p>	<ol style="list-style-type: none"> <li>1) The search strategy was agreed at the outset and is in accordance with SACN’s approach to evaluating the evidence according to a hierarchy based on study design. The reasons for excluding evidence from clinical practice are explained in paragraphs 5.9-5.10 and it was agreed to include further details of these studies and an expanded explanation of why they were not included for consideration in the report.</li> <li>2) it was agreed to grade the evidence for change in medication use.</li> <li>3) see point 1 above.</li> </ol>

Organisation/ Individual	Comments	SACN reply
	<ul style="list-style-type: none"> <li>• Significant heterogeneity in the definition and level of carbohydrate considered</li> <li>• Poor control of dietary adherence and maintenance</li> <li>• Inconsistent assessment and reporting of medication adjustment and its effect on one of the primary outcomes, HbA1c</li> <li>• An assessed high risk of bias.</li> </ul> <p>These limitations mean the outcome assessment could only be described in terms of ‘lower vs higher carbohydrate diets’. The approach taken of grouping all forms of low carbohydrate diets into a single “lower” category is flawed. It has failed to address the type of diets that PHE referred to as “gaining attention and increasingly being promoted.” These are predominantly low or very low carbohydrate diets. The included studies were unable to satisfactorily differentiate between effects of the different carbohydrate levels. As a consequence the brief from PHE remains only partially answered by the present SACN study. In view of the recognised deficiencies in the eligible studies, consideration could and should have been taken of other evidence, some of which is compelling despite not satisfying the inclusion criteria. An example is the ongoing clinical trial conducted by Virta Health specifically addressing treatment of T2D. The protocol features very low carbohydrate diets combined with ongoing medical support and advice. This clinical trial has so far published peer reviewed papers covering results from 10 weeks, 12 months and 2 years, including an assessment of effect on CVD risk factors. (refs 1-4). The results of the excluded study are spectacular compared with expectation from standard care for T2D. Results show:</p> <ul style="list-style-type: none"> <li>• Substantial reductions or complete elimination of diabetes medication</li> <li>• Substantial improvement in HbA1c - often to non diabetic levels</li> <li>• Sustained weight losses</li> <li>• Improvements in CVD risk factors</li> </ul>	

Organisation/ Individual	Comments	SACN reply
	<p>The Virta Health study and others specifically addressing low or very low carbohydrate diets and their corresponding impact on T2D and CVD risk factors provide important strong evidence and should be reconsidered for inclusion. Inclusion would demonstrate that SACN has taken reasonable account of a broader evidence base and more fully responded to the PHE brief.</p> <p>Virta Health studies have been explicitly excluded. The stated rationale for exclusion (see para 5.9, referring to one of the Virta Health papers) is based on several “key limitations” specifically: lack of randomisation; lack of a comparator arm; and self-selection. These ‘limitations’ are not significant when compared to those identified by SACN for the included studies. Randomisation is clearly important when it can be difficult to account for potential confounding factors. However, when the outcomes are so compelling compared with expectation from usual standard of care where the expectation can be deduced from the National Diabetes Audit (ref 5) which has zero targets or measurement for medication reduction or normalisation of HbA1c but checks whether the NICE care processes are met. The only measure of diabetes control target is an HbA1c level of &lt;58 mmol/mol, compared with a non-diabetic level of &lt;48 mmol/mol. This is surely an effective ‘comparator arm’ for the Virta Health study and negates the need for randomisation.</p> <p>With regards to self-selection, this adds to the likelihood of protocol adherence, which has proved to be a limitation of the included studies. In addition, randomisation would deny some patients the benefits that are well established with the clinicians involved. Indeed it could be argued that randomisation would be unethical.</p> <p><u>Downplaying of the reduced medications</u></p> <p>Reducing (or de-prescribing) medication is clearly a highly desirable outcome and the data reported in the included studies, although limited, is highly supportive of low carbohydrates and should be highlighted rather than downplayed.</p>	

Organisation/ Individual	Comments	SACN reply
	<ul style="list-style-type: none"> <li>• The Huntriss (2018) paper includes the quote ‘From all 14 papers that included participants on diabetes medication at trial start and reported changes in diabetes medication, there was a unanimous report of the superior effect of medication reduction in the LCIA (low carbohydrate intervention arm) in comparison to the control group, with 9 out of 11 studies that discussed statistical significance of the difference between groups, finding a statistically significant reduction in diabetes medication in the LCIA.’</li> <li>• This finding is reinforced in the Virta Health papers which quantifies the dramatic reductions in diabetes medication with the low carbohydrate diet. In fact part of the protocol is to reduce medication very early to limit potential hypoglycaemic events.</li> <li>• Evidence for this outcome was not graded in the SACN report because a meta-analysis was not performed (para 7.44) although it was mentioned in para 7.45.</li> <li>• In the summary table (table 7.2) the comment was ‘no evidence’ with no mention of the qualitative benefit with low carbohydrate.</li> </ul> <p>This is an important outcome and should not be ‘disregarded’ or downplayed due to lack of quantification in the studies considered. Further evidence is provided in the excluded studies. Arguably reduction in medication should have been a primary outcome, more important than weight loss per se.</p> <p>SACN risk exposure to criticism and an undermining of their credibility by taking such a narrow view of the evidence. Failure to include a broader evidence base, taking account of much available clinical and other evidence has resulted in a paucity of good quality data and enabled rather weak conclusions to be drawn. These tend to support the status quo, reinforcing previous SACN reports and could be considered to be suggestive of bias on the authors behalf.</p> <ul style="list-style-type: none"> <li>• Long standing guidelines from PHE and Diabetes UK encourage high (50%) levels of carbohydrates for the general population including those with T2D.</li> </ul>	



Organisation/ Individual	Comments	SACN reply
	<ul style="list-style-type: none"> <li>• New and good evidence has emerged which challenge these long established guidelines and provide support for low or very low carbohydrate diets for those with T2D</li> <li>• By choice of eligibility criteria these studies have been excluded and assessment limited to heterogeneous studies with admitted serious limitations</li> <li>• Other bodies around the world (including the NHS have begun to include a low carbohydrate diet as one option for the care of T2D as described in para 3</li> <li>• As new data have become available since the SACN literature search it may be appropriate to reconsider both this new data and the breadth of evidence considered.</li> <li>• There is a swelling tide amongst clinicians that substantially reducing carbohydrates is an effective treatment for T2D especially since the evidence against dietary fat is proving to be less than convincing.</li> <li>• The discussion in paras 2 and 3 of the SACN report clearly show that with T2D there is the inability to manage blood glucose, high levels of which are caused by dietary carbohydrates.</li> </ul> <p>By ignoring the broader evidence base, SACN risk criticism of bias in their assessment which may be seen as an attempt to maintain their previous conclusions on carbohydrates</p> <p><u>References</u></p> <ol style="list-style-type: none"> <li>1. McKenzie et al 2017A Novel Intervention Including Individualized Nutritional Recommendations Reduces Hemoglobin A1c Level, Medication Use, and Weight in Type 2 Diabetes. <a href="https://diabetes.jmir.org/2017/1/e5/">https://diabetes.jmir.org/2017/1/e5/</a></li> <li>2. Hallberg et al 2018 Effectiveness and Safety of a Novel Care Model for the Management of Type 2 Diabetes at 1 Year: An Open-Label, Non-Randomized, Controlled Study. <a href="https://doi.org/10.1007/s13300-018-0373-9">https://doi.org/10.1007/s13300-018-0373-9</a>.</li> <li>3. Athinarayanin et al 2019. Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-randomized Clinical Trial. <a href="https://doi.org/10.3389/fendo.2019.00348">https://doi.org/10.3389/fendo.2019.00348</a></li> </ol>	

Organisation/ Individual	Comments	SACN reply
	<p>4. Bhanpuri et al 2018. Cardiovascular disease risk factor responses to a type 2 diabetes care model including nutritional ketosis induced by sustained carbohydrate restriction at 1 year: an open label, non-randomized, controlled study. <a href="https://cardiab.biomedcentral.com/articles/10.1186/s12933-018-0698-8">https://cardiab.biomedcentral.com/articles/10.1186/s12933-018-0698-8</a></p> <p>5. National Diabetes Audit, 2017-18. Report 1: Care Processes and Treatment Targets. England and Wales 13th June 2019. <a href="https://files.digital.nhs.uk/88/F1E544/National%20Diabetes%20Audit%202017-18%20Full%20Report%201%2C%20Care%20Processes%20and%20Treatment%20Targets.pdf">https://files.digital.nhs.uk/88/F1E544/National%20Diabetes%20Audit%202017-18%20Full%20Report%201%2C%20Care%20Processes%20and%20Treatment%20Targets.pdf</a></p>	
Dr S Kassam	<p>My concern is long term impact of low carb diets on health outcomes which I don't think have been emphasised enough. References listed in this document all demonstrate detrimental effects of long term health (all-cause mortality, death from CVD and cancer) in those eating low carbohydrate diets. This is especially true if carbohydrates are replaced by animal fat and protein which seems the practice for those advocating this diet pattern in the UK. Limiting whole grains, beans and some fruits from the diet will have adverse long term consequences. Higher fat diets also have an adverse effect on the gut microbiome and markers of inflammation and fail to reverse insulin resistance per se as shown in Kevin Hall's metabolic ward studies. The women's health initiative study showed benefits for those eating lower fat diets and increasing whole grains, fruits and vegetables and this included benefits for diabetes.</p> <p>Also concerned that low carbohydrate diets are being promoted as a means for preventing T2D, with replacement of carbohydrates with fat and protein often from animal sources. I accept that a lower carbohydrate diet can also emphasise plant proteins and fats but this is not the case for most people in the UK who continue to consume too much sat fat and not enough whole plant foods. A low carbohydrate diet does not prevent diabetes per se and</p>	<p>There is a lack of data from longer-term intervention studies. Consideration of primary observational evidence on long-term implications of low-carbohydrate diets was outside the scope of the review.</p> <p>Prevention of T2D was outside the scope of the review.</p>

Organisation/ Individual	Comments	SACN reply
	<p>most studies support predominately plant-based diets for prevention of diabetes and for maintaining weight loss. This could perhaps be emphasised more in the report.</p> <p><u>References</u>  Mazidi, M et al. (2019). Lower carbohydrate diets and all-cause and cause-specific mortality: a population-based cohort study and pooling of prospective studies. European Heart Journal, ehz174, <a href="https://doi.org/10.1093/eurheartj/ehz174">https://doi.org/10.1093/eurheartj/ehz174</a>  Prentice R, Aragaki A, Howard B et al. Low-Fat Dietary Pattern among Postmenopausal Women Influences Long-Term Cancer, Cardiovascular Disease, and Diabetes Outcomes, The Journal of Nutrition, Volume 149, Issue 9, September 2019, Pages 1565–1574, <a href="https://doi.org/10.1093/jn/nxz107">https://doi.org/10.1093/jn/nxz107</a>  Rosenbaum, M et al. (2019). Glucose and Lipid Homeostasis and Inflammation in Humans Following an Isocaloric Ketogenic Diet. Obesity 0, 1-11. doi:10.1002/oby.22468  Shan Z, Guo Y, Hu F et al. Association of Low-Carbohydrate and Low-Fat Diets with Mortality Among US Adults. JAMA Intern Med. Published online January 21, 2020. doi:10.1001/jamainternmed.2019.6980  Wan Y, et al. Gut 2019;0:1–13. doi:10.1136/gutjnl-2018-317609</p>	
Netherlands Health Council	<p>We would like to express our compliments for this work. The work was performed in a very structured and thorough manner and the report is clearly written.</p> <p>The following meta-analysis may be relevant to consider (published after September 2018): McArdle et al. Carbohydrate restriction for glycaemic control in Type 2 diabetes: a systematic review and meta-analysis. Diabet Med. 2019 Mar;36(3):335-348. <a href="https://www.ncbi.nlm.nih.gov/pubmed/30426553">https://www.ncbi.nlm.nih.gov/pubmed/30426553</a></p> <p>Below are some questions regarding the heterogeneity of the study diets.</p>	<p>The systematic review and meta-analysis by McArdle et al (2019) is included for consideration.</p> <p>1) The WG did not conduct any meta-analyses or sensitivity analyses. Grading of outcomes was based on results of meta-analyses in the 4 prioritised systematic reviews.</p>

Organisation/ Individual	Comments	SACN reply
	<ol style="list-style-type: none"> <li>1) The RCT of Wolever et al (2008) reported prescribed carbohydrate intakes of 20 to 25% TE in the higher carbohydrate groups; this is much lower than in other RCTs. Have you considered the evidence excluding this RCT (e.g. sensitivity analysis)? Does this change the conclusions?</li> <li>2) The quality of the carbohydrates consumed may be of importance. In total, 15 of the 32 RCTs reported information on quality of carbohydrates prescribed. Are there subgroup analyses available of studies with comparable prescriptions on quality of carbohydrates, in order to additionally allow (preliminary) conclusions on the differential effects of lower carbohydrate diets versus quality of carbohydrates?</li> <li>3) The same holds for the quality of the comparator diet. This may be of importance as well. Although there was wide variety in comparator diets, are there subgroup analyses available of studies with comparable comparator diets?</li> </ol>	<ol style="list-style-type: none"> <li>2) Subgroup analyses by carbohydrate type or quality were not performed.</li> <li>3) Subgroup analyses by comparator diets were not performed.</li> </ol>
Dr G Newman	<p>I am a GP and have studied this area extensively. The 3 main dietary modalities for inducing disease reversal centre around caloric restriction (including intermittent fasting which is known to boost insulin sensitivity), HFLC (high fat low carbohydrate) diets or WFPB (whole foods plant based) diets. A dearth of data show that low carbohydrate approaches may be harmful to heart health and long term diabetes control, especially when compared to WFPB diets.</p> <p>WFPB diets have been shown to make development of diabetes far less likely and research suggests they can improve and reverse diagnosed diabetes. The American Association of Clinical Endocrinologists (AACE) (2018) guidelines suggest a plant-based diet as the preferred eating pattern for T2D patients. A study of &gt;2,300 Finnish men showed that vegetables and fruits may reduce T2D risk. Additionally, a study of &gt;70,000 female nurses aged 38-63y, who were free of CVD, cancer and diabetes, showed that consumption of green leafy vegetables and fruit was associated with a lower risk of diabetes over time. It</p>	<p>The remit of the review was to compare lower with higher carbohydrate diets on markers and outcomes of T2D. Consideration of other types of diets or T2D prevention were outside remit of report.</p>

Organisation/ Individual	Comments	SACN reply
	<p>also indicated that consumption of fruit juices may be associated with an increased risk among women.</p> <p>UK dietary guidelines on consumption of starchy vegetables and fruits has been conflicting in T2D management. To understand this, it is helpful to review the 3 main techniques commonly used to induce clinical remission of T2D. Along with other lifestyle factors, dietary approaches can include caloric restriction, limiting carbohydrate rich foods and adopting a WFPB approach.</p> <p>The DiRECT trial has had great results for people undertaking caloric restriction. Participants were given soups and meal replacement shakes and went on a very low calorie diet (VLCD): weight loss was 15kg or more in 24% of the intervention group but no weight loss in the control group. Remission was achieved in 68 (almost half) participants in the intervention group compared to 4% of control group. 9 serious adverse events were reported in the intervention group, with 2 events (biliary colic and abdominal pain) occurring in the same participant. Although this study suggests caloric restriction can be a highly effective strategy, VLCDs can be challenging to maintain longer term.</p> <p>Low carbohydrate high fat (LCHF) diets are also effective in achieving weight loss and diabetes improvements but a study using data from UK NDNS (2008-2016) showed that increased protein and fat consumption and reduced carbohydrate consumption correlated with increased diabetes rates. In those with T2D, LCHF diets resulted in worse control of the disease. Another study comparing dietary strategies for weight loss and health suggested that the quality rather than ratio of macronutrients remains key – people who ate healthy high or low carbohydrate diets (whole grains, non-starchy vegetables, whole fruits, nuts) had a lower risk of premature death than those who ate more low quality carbohydrates, animal protein and saturated fat. Metabolic ward studies have also shown that ketogenic approaches to weight loss results in loss of lean body mass and that 2 months of a tightly controlled ketogenic diet saw slowing of body fat loss compared to higher carbohydrate</p>	

Organisation/ Individual	Comments	SACN reply
	<p>diet. Also, a diet high in palmitic acid (from animal products and saturated fat) destroys pancreatic beta cells.</p> <p>Why have WFPB diets been recommended by the AACE Guidelines? Research suggests a diet rich in fruits and vegetables as well as other healthy carbohydrates can lead to significantly reduced intra-myocellular fat, higher insulin sensitivity, better blood glucose and insulin levels and improved beta-cell function. Even without weight loss, WFPB diets can improve damage from diabetic retinopathy and reduce insulin requirements dramatically in patients who have had T2D for <math>\geq 20</math> years and have required insulin. 1 study of around 20 men showed that half could come off insulin within days of change to a WFPB diet.</p> <p>The most effective weight loss and disease management diet strategy is the one the patient is willing to actually do. Being familiar with what works and is sustainable helps them to make a choice they can stick with.</p> <p><u>References</u></p> <p><u>Chiu et al.</u> Taiwanese Vegetarians and Omnivores: Dietary Composition, Prevalence of Diabetes and IFG, <u>PLoS One</u>. 2014; Feb 11 9(2): e88547.</p> <p>Vang et al. Meats, processed meats, obesity, weight gain and occurrence of diabetes among adults: findings from Adventist Health Studies. <u>Ann Nutr Metab</u>.</p> <p>Ye et al. Greater whole-grain intake is associated with lower risk of type 2 diabetes, cardiovascular disease, and weight gain. <u>J Nutr</u>. 2012;142:1304–13.</p> <p>Barnard et al. A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial. <u>Am J Clin Nutr</u>. 2009;89:1588s–1596s.</p> <p>Lim et al. Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. <u>Diabetologia</u>. 2011;54:2506–2514.</p>	

Organisation/ Individual	Comments	SACN reply
	<p>Barnard et al. Vegetarian and vegan diets in type 2 diabetes management. <i>Nutr Rev.</i> 2009;67:255–263.</p> <p>Lee et al. Effect of a brown rice based vegan diet and conventional diabetic diet on glycemic control of patients with type 2 diabetes: a 12-week randomized clinical trial. <i>PLoS One.</i> 2016;11:e0155918.</p> <p>Mursu et al. Intake of fruit, berries, and vegetables and risk of type 2 diabetes in Finnish men: the Kuopio Ischaemic Heart Disease Risk Factor Study–. <u><i>The American journal of clinical nutrition.</i></u> 2013 Nov 20;99(2):328-33.</p> <p>Bazzano et al. Intake of fruit, vegetables, and fruit juices and risk of diabetes in women. <u><i>Diabetes Care.</i></u> 2008 Apr 3.</p> <p>Lean et al. Primary care weight-management for type 2 diabetes: the cluster-randomised Diabetes Remission Clinical Trial (DiRECT) <i>Lancet.</i> 2018 Feb 10;391(10120):541-551.</p> <p>Churuangasuk et al. Lower Carbohydrate and Higher Fat Intakes are Associated with higher Haemoglobin A1c: findings from the UK National Diet and Nutrition Survey 2008-2011</p> <p>Fretts et al. Consumption of meat is associated with higher fasting glucose and insulin concentrations regardless of glucose and insulin genetic risk scores: a meta-analysis of 50,345 Caucasians. <i>Am J Clin Nutr.</i> 2015;102:1266–1278.</p> <p>Feskens EJ, Sluik D, van Woudenberg GJ. Meat consumption, diabetes, and its complications. <i>Curr Diab Rep.</i> 2013;13:298–306.</p> <p>Kim et al. A review of potential metabolic etiologies of the observed association between red meat consumption and development of type 2 diabetes mellitus. <i>Metabolism.</i> 2015;64:768–779.</p> <p>Shan et al Association of Low-Carbohydrate and Low-Fat Diets with Mortality Among US Adults <i>JAMA Intern Med.</i> Jan 21<sup>st</sup> 2020</p> <p>Hall et al. Energy expenditure and body composition changes after an isocaloric ketogenic diet in overweight and obese men. <i>Am J Clin Nutr.</i> 2016 Aug; 104(2): 324–333.</p>	

Organisation/ Individual	Comments	SACN reply
	<p>Goff et al. Veganism and its relationship with insulin resistance and intramyocellular lipid. Eur J Clin Nutr. 2005 Feb;59(2):291-8 (c)</p> <p>Gojda et al. Higher insulin sensitivity in vegans is not associated with higher mitochondrial density. Eur J Clin Nutr. 2013 Dec;67(12):1310-</p> <p>Oh et al. "Fatty Acid-Induced Lipotoxicity in Pancreatic Beta-Cells During Development of Type 2 Diabetes." Frontiers in endocrinology vol. 9 384. 16 Jul. 2018, doi:10.3389/fendo.2018.00384</p>	
S Parikh	<p>Consideration needed on whether replacement for carbohydrates is plant based or animal based along with other risks for an individual (such as heart disease) as a result of switch to a low carbohydrate diet and use of known long term effects of diet – even if they are not specific to diabetes as it is important that a diet being recommended is sustainable as otherwise, it could easily be misinterpreted. I would like to raise a number of concerns when considering changing guidelines using mainly short term analysis as impacts over long term are limited as the focus is only on those having T2D. If there are studies that suggest certain diets reduce the risk of developing T2D, then these shouldn't be ignored. Also I note that Diabetes.org.uk mentions: Research suggests that the best type of diet is one that you can maintain in the long term, so it's important to talk to your healthcare professional about what you think will work for you.</p> <p>As there is considerable evidence that a low carbohydrate diet is not healthy over the long term (some evidence included below), such a diet should not be promoted for the short term as it can't be maintained over the long term and if it is, this is shown to increase the risk of early deaths. Also, even if there are known to be short term benefits for diabetics, giving a message that a low carbohydrate diet could be beneficial is likely to contribute to the confusion that carbohydrates are bad and such a diet could then be advocated to say prevent diabetes and/or over the long term for those who have diabetes when studies</p>	<p>Consideration of different types of diets for individuals with T2D were outside remit of the report.</p> <p>The recommendations of the report will be considered by PHE and Diabetes UK in formulating public health advice.</p> <p>Consideration of observational data on long-term implications of low-carbohydrate diets was outside the scope of the report.</p>



Organisation/ Individual	Comments	SACN reply
	<p>suggest that it could have adverse impacts on mortality. My concern is that if government is sending out messages that low carbohydrate diets can be beneficial for diabetics over the short term (as it currently does), it legitimises the use of these diets not only for diabetics over the short term, but also for diabetics over the longer term and then for anyone who may want to prevent diabetes when there may be other diets which may be better for them. I understand that NHS already says this: There is evidence that low-carb diets are safe and effective in the short-term for most people with Type 2 diabetes. They help with weight-loss, diabetes control and reducing risk of complications. However, as NHS then doesn't specify the duration of the short term and any known adverse impacts of continuing such a diet over the long term and whether there are any benefits for those who don't have T2D, this can lead to people generally trying this diet and over the long term believing it to be a healthy diet in line with NHS guidelines. There are companies that are offering such a diet creating to this confusion with the Low Carb Program (as promoted by Diabetes Digital Media Ltd) and also Second Nature (as promoted by Our Path Ltd). Both programs focus on low carbohydrate diets only and as their apps are available on NHS Apps library, it legitimises their use for purposes for which NHS does not recommend the diet. Numerous recent studies also consider long term impact of low carbohydrate diets which are not specific to diabetes which suggest that the outcomes are impacted on whether plant-based or animal-based sources are considered. So, when formulating advice, it is not just an issue of whether fat can replace carbohydrates but the sources of the replacement can have a significant impact on the outcome. Although such studies don't meet the criteria, as they don't focus on outcomes for diabetic patients, I believe given other long term studies don't exist, these shouldn't be ignored. I'm also including studies that show increased CVD risk from high saturated fat intake as such knowledge shouldn't be ignored as it doesn't make sense to consider impact on diabetes in isolation if an individual is likely</p>	

Organisation/ Individual	Comments	SACN reply
	<p>to have increased risk of other diseases that could increase mortality risk over the long term.</p> <p><u>References</u></p> <p>Seidelmann et al. Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. <i>Lancet Public Health</i> 2018; 3: e419–28</p> <p>Ley et al. Contribution of the Nurses’ Health Studies to Uncovering Risk Factors for Type 2 Diabetes: Diet, Lifestyle, Biomarkers, and Genetics</p> <p>Adeva-Andany et al. Dietary habits contribute to define the risk of type 2 diabetes in humans. <i>Clin Nutr ESPEN</i>. 2019 Dec;34:8-17. doi: 10.1016/j.clnesp.2019.08.002. Epub 2019 Aug 30.</p> <p>Adeva-Andany et al. Effect of diet composition on insulin sensitivity in humans. <i>Clin Nutr ESPEN</i>. 2019 Oct;33:29-38. doi: 10.1016/j.clnesp.2019.05.014. Epub 2019 Jun 6.</p> <p>McMacken and Shah. A plant-based diet for the prevention and treatment of type 2 diabetes. <i>J Geriatr Cardiol</i>. 2017 May; 14(5): 342–354.</p> <p>Olfert et al. Vegetarian Diets and the Risk of Diabetes. 2018; 18(11): 101. Published online 2018 Sep 18. PMID: 30229314</p> <p>Meat and fish intake and type 2 diabetes: dose-response meta-analysis of prospective cohort studies. <i>Diabetes Metab</i>. 2020 Apr 14. pii: S1262-3636(20)30055-0. doi: 10.1016/j.diabet.2020.03.004.</p> <p>Dietary Protein Consumption and the Risk of Type 2 Diabetes: A Dose-Response Meta-Analysis of Prospective Studies. <i>Nutrients</i>. 2019 Nov 15;11(11). pii: E2783. doi: 10.3390/nu11112783.</p> <p>Food groups and risk of type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. <i>Eur J Epidemiol</i>. 2017; 32(5): 363–375.</p>	

Organisation/ Individual	Comments	SACN reply
	<p>Li et al. Saturated Fats Compared With Unsaturated Fats and Sources of Carbohydrates in Relation to Risk of Coronary Heart Disease: A Prospective Cohort Study. <i>J Am Coll Cardiol.</i> 2015 Oct 6;66(14):1538-1548. doi: 10.1016/j.jacc.2015.07.055.</p> <p>Can dietary viscous fiber affect body weight independently of an energy-restrictive diet? A systematic review and meta-analysis of randomized controlled trials. <i>AJCN</i>, Volume 111, Issue 2, February 2020, Pages 471–485</p> <p>Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality—a systematic review and dose-response meta-analysis of prospective studies. <i>International Journal of Epidemiology</i>, Volume 46, Issue 3, June 2017, p1029–1056,</p> <p>Dong et al. Association of Specific Dietary Fats With Total and Cause-Specific Mortality</p> <p>Barnard et al. Vegetarian and vegan diets in type 2 diabetes management</p> <p>Trapp and Barnard. Usefulness of vegetarian and vegan diets for treating type 2 diabetes.</p> <p>Carbohydrate and Fiber Recommendations for Individuals with Diabetes: A Quantitative Assessment and Meta-Analysis of the Evidence</p> <p>Association of Animal and Plant Protein Intake With All-Cause and Cause-Specific Mortality in a Japanese Cohort. <i>JAMA Intern Med.</i> 2019 Nov 1;179(11):1509-1518. doi: 10.1001/jamainternmed.2019.2806.</p> <p>Pan et al. Changes in red meat consumption and subsequent risk of type 2 diabetes mellitus: three cohorts of US men and women.</p> <p>Zong et al. Whole Grain Intake and Mortality From All Causes, Cardiovascular Disease, and Cancer. A Meta-Analysis of Prospective Cohort Studies Originally published 14 Jun 2016.</p> <p>Zeiber et al. High red and processed meat consumption is associated with non-alcoholic fatty liver disease and insulin resistance.</p> <p>Potential health hazards of eating red meat. <i>J Intern Med.</i> 2017;281(2):106-122. doi: 10.1111/joim.12543. Epub 2016 Sep 6.</p>	

Organisation/ Individual	Comments	SACN reply
	<p>A Plant-Based Dietary Intervention Improves Beta-Cell Function and Insulin Resistance in Overweight Adults: A 16-Week Randomized Clinical Trial</p> <p>Intake of individual saturated fatty acids and risk of coronary heart disease in US men and women: two prospective longitudinal cohort studies</p> <p>Ketoacidosis associated with low-carbohydrate diet in a non-diabetic lactating woman: a case report.</p> <p>Barnard et al. A Low-Fat Vegan Diet Improves Glycemic Control and Cardiovascular Risk Factors in a Randomized Clinical Trial in Individuals With Type 2 Diabetes.</p> <p>Barnard et al. A low-fat vegan diet and a conventional diabetes diet in the treatment of type 2 diabetes: a randomized, controlled, 74-wk clinical trial.</p> <p>Yokoyama et al. Vegetarian diets and glycemic control in diabetes: a systematic review and meta-analysis. Cardiovasc Diagn Ther. 2014 Oct; 4(5): 373–382. PMID: 25414824.</p> <p>Papamichou et al. Dietary patterns and management of type 2 diabetes: A systematic review of randomised clinical trials.</p>	
RCP	<p>The RCP is grateful for the opportunity to respond to the above consultation. We have liaised with our JSC for Endocrinology and Diabetes and the Association of British Clinical Diabetologists and would be happy to endorse the report.</p>	<p>Comments noted and welcomed.</p>
D Sinon	<p>5 years ago I was diagnosed with T2D and referred to a plant-based dietician. I have been on a plant-based diet for 25 years. 12 months into the dietician’s advice, upon my yearly blood glucose tests, I was told I was heading for a stroke, LDL way too high and blood pressure (BP) too high. I was shocked as I was following the supposedly healthy lifestyle confirmed by the dietician. I bluntly refused metformin, statins and BP tablets.</p>	<p>Evidence from individual experiences or case studies did not meet the inclusion criteria of the review.</p> <p>The reasons for excluding evidence from clinical practice are explained in paragraphs 5.9-5.10 and it was agreed to include further</p>

Organisation/ Individual	Comments	SACN reply
	<p>Since I was on Twitter and following a few doctors, including Dr D Unwin and Dr A Malhotra, I was ready to trial their dietary method which is similar to that of Dr G Fettke here in Australia. I started the low carbohydrate, high fat (LCHF) lifestyle and within a few weeks, my blood glucose dropped from 8.5 to 6.2. I continued with the LCHF for 3 months then went back to the doctor for tests - he was impressed with the improvements. Blood glucose was 5.5 and stable, no heart ailments, cholesterol and BP normalised. He wanted to know what I did I and I told him I did exactly what has been claimed as bad and unhealthy.</p> <p>I've cut back on eating too much carbohydrates, no sugary or pre-packed edibles, edibles with preservatives or additives, cooking oil other than cold press coconut oil, grass fed ghee and pure butter. I started eating more grass fed meat, free range bacon, free range eggs and minimal cruciferous veggies, avocado and minimal home grown fruits without pesticides. I'm 64 years old, medications free, full of energy, strength and enjoying life without ailments. Please, if you care for your own people, dig deep into these lifestyles: LCHF, KETO and Carnivore. There are growing numbers of medical practitioners online with authentic proofs.</p>	<p>details of these studies and an expanded explanation of why they were not included for consideration in the report.</p>
<p>South Asian Health Foundation</p>	<p>It is well recognised that people of Black, Asian and Minority Ethnicity (BAME) are more likely to have T2D; a cohort study of 1.9 million individuals in England from the CALIBER programme (CARDiovascular disease research using LInked Bespoke studies and Electronic health Records), found that people with T2D were about twice as likely to be of either Black or South Asian origin compared to those without diabetes.<sup>1</sup> In addition, the Southall and Brent Revisited (SABRE) cohort study showed a significantly higher prevalence of known diabetes in Indian Asian men (13%) compared to European men (3%).<sup>2</sup></p> <p>As commented in point 7.61, much of the data from studies available is limited to White populations and therefore does not take into consideration BAME populations who are at higher risk of T2D and metabolic syndrome. As documented, it is unclear if the effects</p>	<p>Agreed to include information about increased risk of T2D in minority ethnic population groups under section 'background on T2D'</p> <p>Agreed to include when formulating research recommendations.</p>

Organisation/ Individual	Comments	SACN reply
	<p>reported in these low carbohydrate diets with White participants apply to South Asians in whom the ideal BMI is lower than for their White counterparts (BMI 18-23 kg/m<sup>2</sup> compared with 20-25 kg/m<sup>2</sup> retrospectively). Hence this will be an important future research consideration.</p> <p>To achieve these lower ideal BMI targets, we propose that South Asians should not only have a lower carbohydrate content, but higher protein intake in their diets. The South Asian diet typically is high in carbohydrate calories and low in protein content. Protein as a macronutrient has the greatest positive effect on satiety; low-fat, energy-restricted diets of varying protein content (15 or 30% energy) promoted healthful weight loss, but diet satisfaction was greater in those consuming the high-protein diet.<sup>3</sup> In point 7.30, the RCTs did not show any difference in effect in between lower and higher carbohydrate diets in reducing body weight in the longer term. We note that the lower carbohydrate diets did vary in protein content (16-27%) in the included studies, however other studies have suggested that higher protein diets do aid satiety and therefore improve adherence to these diets and support weight loss.<sup>3,4</sup> We therefore believe it is important to consider that any lower calorie diet needs to have the higher protein content to increase satiety and weight loss; and certainly, this should be considered and encouraged in the BAME populations. This additionally lends itself to future research prospects.</p> <p><u>References</u></p> <ol style="list-style-type: none"> <li>1. Shah et al. Type 2 diabetes and incidence of cardiovascular diseases: a cohort study in 1.9 million people. <i>Lancet Diabetes Endocrinol.</i> 2015 Feb 1;3(2):105-13.</li> <li>2. Tillin et al. Southall And Brent REvisited: Cohort profile of SABRE, a UK population-based comparison of cardiovascular disease and diabetes in people of European, Indian Asian and African Caribbean origins. <i>Int J Epidemiol.</i> 2010 Nov 2;41(1):33-42.</li> <li>3. Johnston et al. High-protein, low fat diets are effective for weight loss and favourably alter biomarkers in healthy adults. <i>Journal of Nutrition.</i> 2004;134:586–591.</li> </ol>	<p>Consideration of protein intakes in people living with T2D was outside the remit of the report.</p>

Organisation/ Individual	Comments	SACN reply
	<p>4. Hill &amp; Blundell. Macronutrients and satiety: the effects of a high-protein or high-carbohydrate meal on subjective motivation to eat and food preferences Nutrition and Behaviour. 1986;3(2):133-144.</p>	
<p>Dr S Tobin</p>	<p>I have been Lead GP for diabetes at my surgery for 25 years and care for 545 people with diabetes. For the first 18 years of my clinical practice I recommended the Eatwell Plate to my patients with diabetes. Very few made significant improvements in their glycaemic control; most showed a worsening in control over a period of years. For the last 7 years I have recommended low carbohydrate diets as an option and have found astonishing success with substantial improvements in all markers of metabolic health. My practice now has a cohort of over 200 people with T2D who are using low carbohydrate diets to manage their condition.</p> <p>In my experience, low carbohydrate diets outperform every other intervention in T2D by some distance. Together with colleagues I have published my results in the peer reviewed International Journal for Environmental Research and Public Health (see below). In summary, the results show that carbohydrate restriction in T2D delivers:</p> <ul style="list-style-type: none"> <li>• HbA1c: An average drop of about 15 mmol/mol</li> <li>• BP: an average drop of 11/6mmHg</li> <li>• Mean weight reduction of 9.5Kg</li> <li>• Total cholesterol: an average drop of 0.8mmol</li> <li>• HDL: 8% increase</li> <li>• Triglycerides: 32% decrease</li> </ul> <p>There is the potential to make big savings to drug budgets. We were able to discontinue many medications for both diabetes and hypertension. As a consequence, my practice makes annual drug budget savings of about £43,000.</p>	<p>Evidence from clinical practice did not meet the inclusion criteria of the review</p> <p>The reasons for excluding evidence from clinical practice are explained in paragraphs 5.9 to 5.10.</p> <p>It was agreed to amend these paragraphs to summarise the direction of the evidence from these studies and to expand the explanation of why they were not included for consideration in the report.</p>

Organisation/ Individual	Comments	SACN reply
	<p>I have also become aware that low carbohydrate diets are sustainable over long periods. Many of my patients have benefits continuing after 2 years. Low carbohydrate diets have revolutionised my management of people with T2D. The impact on all important metabolic markers of health is considerable. I have no doubt that low carbohydrate diets are the future of managing T2D – they work!</p> <p><u>Reference:</u> Unwin et al. Substantial and Sustained Improvements in Blood Pressure, Weight and Lipid Profiles from a Carbohydrate Restricted Diet: An Observational Study of Insulin Resistant Patients in Primary Care. <i>Int. J. Environ. Res. Public Health</i> <b>2019</b>, 16(15), 2680; <a href="https://doi.org/10.3390/ijerph16152680">https://doi.org/10.3390/ijerph16152680</a></p>	
Viva! Health	<p><u>Focus</u> - Focussing on carbohydrates as a uniform category would be misleading because whilst simple carbohydrates are not ideal and excessive consumption is detrimental to our health and poses a problem for diabetics, complex carbohydrates promote good health and can help in the management of T2D.</p> <p>Complex carbohydrates - Plant-based diets, centred around complex carbohydrates, protein and essential unsaturated fats have been shown to be extremely helpful in diabetes management. As McMacken and Shah (2017) state: “Evidence from observational and interventional studies demonstrates the benefits of plant-based diets in treating type 2 diabetes and reducing key diabetes-related macrovascular and microvascular complications. Optimal macronutrient ratios for preventing and treating type 2 diabetes are controversial; the focus should instead be on eating patterns and actual foods. However, the evidence does suggest that the type and source of carbohydrate (unrefined versus refined), fats (monounsaturated and polyunsaturated versus saturated and trans), and protein (plant versus animal) play a major role in the prevention and management of type 2 diabetes. Multiple potential mechanisms underlie the benefits of a plant-based diet in ameliorating insulin resistance, including promotion of a healthy body weight, increases in</p>	<p>The WG’s remit was to compare lower with higher carbohydrate diet on T2D outcomes. Consideration of other types of diets for management of T2D was outside the remit of the report.</p> <p>Few of the primary RCTs considered carbohydrate type. This issue to be included as a recommendation for future research.</p>



Organisation/ Individual	Comments	SACN reply
	<p>fiber and phytonutrients, food-microbiome interactions, and decreases in saturated fat, advanced glycation end-products, nitrosamines, and heme iron.”</p> <p><u>HbA1c</u> - Yokoyama et al. (2014) analysed 6 RCTs, 5 of them assessed effects of a vegan diet and 1 examined effects of a lacto-ovo-vegetarian diet. Their analysis showed that these plant-based diets resulted in a statistically significant reduction in HbA1c (–0.39 percentage points) compared with control diets. In one of the studies, the reduction in HbA1c was up to -0.9 percentage points (Kahleova et al., 2011). According to an analysis by Salas-Salvadó et al. (2019), the effect of plant-based diets on HbA1c was on average –0.41 percentage points. These authors concluded that: “The beneficial effects of these dietary patterns may be explained by mechanisms specifically related to the increased intake of fiber, PUFAs, MUFAs, and antioxidant and anti-inflammatory micronutrients, and the reduced intake of SFAs, heme iron, sodium, nitrites, and nitrates. In conclusion, the overall evidence suggests that patients with T2D will benefit from adopting dietary patterns emphasizing the consumption of plant foods. The components of these dietary patterns might confer benefits on glycemia by counterbalancing the detrimental effect of animal foods.”</p> <p><u>Dietary guidelines</u> - A recent review and meta-analysis of RCTs undertaken to update the European Association for the Study of Diabetes (EASD) clinical practice guidelines for nutrition therapy (Viguiliouk et al., 2019) came to the same conclusions. Results showed that plant-based diets based on wholefoods significantly improve glycaemic control in people with T2D, lower the risk of diabetes-associated health complications and should therefore be included in diabetes management guidelines.</p> <p><u>High carbohydrate diets</u> - A recent study examined a fully plant-based diet emphasising brown rice, pulses, fruit and vegetables (and therefore rich in complex carbohydrates) and its effects on patients with T2D. After 12 weeks, the participants’ HbA1c fell by 0.5-0.9% – significantly more than in the control group – demonstrating that limiting all carbohydrates should not be the focus of diabetes dietary management (Lee et al., 2016).</p>	

Organisation/ Individual	Comments	SACN reply
	<p><u>Food focus rather than nutrient focus</u> - Harvard University scientists support this approach (Ley et al., 2014): “The quality of dietary fats and carbohydrates consumed is more crucial than is the quantity of these macronutrients. Diets rich in wholegrains, fruits, vegetables, legumes, and nuts; moderate in alcohol consumption; and lower in refined grains, red or processed meats, and sugar-sweetened beverages have been shown to reduce the risk of diabetes and improve glycaemic control and blood lipids in patients with diabetes.”</p> <p><u>Dangers of low-carbohydrate diets</u> - Low carbohydrate diets may produce promising results in the short-term but if followed for long periods of time, they have a whole range of unpleasant adverse effects such as constipation, headaches, kidney fatigue, bad breath, increased cholesterol levels, increased risk of heart disease, cancer and even premature death (Bilsborough &amp; Crowe, 2003; Fung et al., 2010; Banach, 2018; Farhadnejad et al., 2019; Mazidi et al., 2019). Furthermore, low carbohydrate diets don’t improve glycaemic control in T2D sufferers more than plant-based diets – in fact, they appear less effective - and they don’t improve any of the health parameters linked to diabetes complications, such as blood cholesterol and blood pressure (Huntriss et al., 2018).</p> <p><u>Summary</u></p> <ul style="list-style-type: none"> <li>• Lower-carbohydrate diets do not necessarily improve glycaemic control in people with T2D.</li> <li>• The emphasis in diabetes nutrition management should be on promoting consumption of complex carbohydrates and limiting simple carbohydrates, rather than limiting carbohydrates in general.</li> <li>• Focusing on the source of nutrients – foods – may bring about better results than focusing on single nutrients.</li> </ul>	

Organisation/ Individual	Comments	SACN reply
	<ul style="list-style-type: none"> <li>Plant-based diets centred around wholefoods and complex carbohydrates have been shown to significantly improve glycaemic control in diabetes sufferers, as well as their cardiovascular and kidney health.</li> </ul> <p><u>References</u></p> <p>Banach M. 2018. Low-carbohydrate diets and all-cause and cause-specific mortality: a population-based cohort study and pooling prospective studies. European Society of Cardiology – study presented at ESC Congress 2018.</p> <p>Bilsborough SA, Crowe TC. 2003. Low-carbohydrate diets: what are the potential short- and long-term health implications? Asia Pacific Journal of Clinical Nutrition. 12 (4) 396-404.</p> <p>Farhadnejad et al. Low-Carbohydrate High-Protein Diet is Associated With Increased Risk of Incident Chronic Kidney Diseases Among Tehranian Adults. Journal of Renal Nutrition. 2019; 29 (4) 343-349.</p> <p>Fung et al. Low-carbohydrate Diets and All-Cause and Cause-Specific Mortality: Two Cohort Studies. Annals of Internal Medicine. 2019; 153(5): 289-98.</p> <p>Huntriss et al. The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: a systematic review and meta-analysis of randomised controlled trials. EJCN. 2018; 72 (3): 311-325.</p> <p>Kahleova et al. Vegetarian diet improves insulin resistance and oxidative stress markers more than conventional diet in subjects with Type 2 diabetes. Diabetes Medicine. 2011; 28 (5): 549-559.</p> <p>Lee et al. Effect of a Brown Rice Based Vegan Diet and Conventional Diabetic Diet on Glycemic Control of Patients with Type 2 Diabetes: A 12-Week Randomized Clinical Trial. PLoS One. 2016; 11 (6): e0155918.</p> <p>Ley et al. Prevention and management of type 2 diabetes: dietary components and nutritional strategies. Lancet. 2014; 383 (9933): 1999-2007.</p>	

Organisation/ Individual	Comments	SACN reply
	<p>McMacken M, Shah S. 2017. A plant-based diet for the prevention and treatment of type 2 diabetes. <i>Journal of Geriatric Cardiology</i>. 14 (5): 342–354.</p> <p>Mazidi et al. Lower carbohydrate diets and all-cause and cause-specific mortality: a population-based cohort study and pooling of prospective studies. <i>European Heart Journal</i>. 2019; 40 (34) 2870-2879.</p> <p>Salas-Salvadó et al. Dietary Patterns Emphasizing the Consumption of Plant Foods in the Management of Type 2 Diabetes: A Narrative Review. <i>Advances in Nutrition</i>. 2019; 10 (Suppl_4): S320-S331.</p> <p>Viguiliouk et al. Effect of vegetarian dietary patterns on cardiometabolic risk factors in diabetes: A systematic review and meta-analysis of randomized controlled trials. <i>Clinical Nutrition</i>. 2019; 38 (3): 1133-1145.</p> <p>Yokoyama et al. Vegetarian diets and glycemic control in diabetes: a systematic review and meta-analysis. <i>Cardiovascular Diagnosis and Therapy</i>. 2014; 4 (5): 373-382.</p>	
J Wadge	<p>I have been on a low carbohydrate diet for my T2D. In 6 months my sugars dropped from 74 to 46, my retinopathy had improved and physical symptoms of vomiting every day went away. Sometimes it is a struggle to follow – mainly at lunch times as food choices on the go are difficult to find and the way carbohydrates are laid out on nutritional labelling makes it difficult to know what counts as carbohydrates. I would like to see this as a recognised diet as when travel and state on airlines that I am diabetic, fed the usual bland wild rice, fruit, reduced fat items which is not good for diabetics on a low carbohydrate diet so education for dieticians would be very helpful.</p>	<p>Evidence from individual experiences did not meet the inclusion criteria of the review. The reasons for excluding this type of evidence are explained in paragraphs 5.9 to 5.10. It was agreed to amend these paragraphs to summarise the direction of the evidence from these studies and to expand the explanation of why they were not included for consideration in the report.</p>

Organisation/ Individual	Comments	SACN reply
X-pert Health	<ol style="list-style-type: none"> <li>1) <u>Secretariat qualifications/experience</u> - As members of the secretariat performed crucial parts of the data extraction and report preparation it would be beneficial to the reader to have an understanding of their profession and relevant qualifications.</li> <li>2) <u>Carbohydrate intake</u> - Report repeatedly refers to “achieved” carbohydrate intake, but this should be changed to “reported” carbohydrate intake to acknowledge limitations in measuring this.</li> <li>3) <u>Unnecessarily limited in scope</u> - The decision to restrict review to systematic reviews including meta-analyses of RCTs immediately made an important body of literature assessing lower carbohydrate diets in more ecologically valid settings unavailable for consideration. This literature could have helped to answer some of the questions that the identified systematic reviews were unable to, including around adherence and impact of true low carbohydrate diets. Future SACN reports should perhaps consider a consultation phase on the scoping of questions and setting of inclusion/exclusion criteria to reduce issues of this nature.</li> <li>4) <u>Redundant data extraction</u> - The value of much the content extracted and summarised in paragraphs 5.28 to 5.33 and associated annexes is questionable, as the data inclusion was narrowed further (significantly) before the evidence was graded and considered. The reasons used to justify this would have been apparent before data extraction occurred, and the presentation of this information does not add any value. Further, the info extracted from RCTs included in the identified reviews is never included in any meaningful analysis and is not considered in the grading of evidence – so the value of this exercise is unclear.</li> <li>5) <u>Failure to account for limitations</u> - A number of important limitations were identified but does not appear to have been any attempt to consider them in grading of evidence. Having extracted information for all of the RCTs included in the meta-analyses it would</li> </ol>	<ol style="list-style-type: none"> <li>1) All members of the secretariat have expertise in nutrition science and nutritional epidemiology.</li> <li>2) Agreed to change to ‘reported’ carbohydrate intake.</li> <li>3) The reasons for excluding evidence from more ‘ecologically valid settings’ is explained in paragraphs 5.9 to 5.10. It was agreed to amend these paragraphs to summarise the direction of the evidence from these studies and to expand the explanation of why they were not included for consideration in the report. SACN has now agreed to include public consultations on the scope of reviews and this was done for the most recent nutritional and maternal health review.</li> <li>4) Disagree. Data were extracted from the primary RCTs because the WG considered these details would be important for informing its assessment.</li> <li>5) Limitations were considered in assessing the quality of the evidence. The grading was based on results of the meta-analyses in the 4 prioritised systematic reviews.</li> </ol>

Organisation/ Individual	Comments	SACN reply
	<p>have been possible to consider the studies which were less limited in relation to some of the key issues. For example, the review could have assessed the outcomes only in studies that had a reported carbohydrate intake in line with the definitions for low carbohydrate diets (Table 5.1). Tables 6.2 and 6.3, and Figure 6.1, make it clear that the majority of the research does not validly compare diets based on carbohydrate intake (even ignoring the failure of many to be classified as low carbohydrate, there is an overlap in carbohydrate intake between the “lower” and “higher” groups in many); thus additional analyses of this nature would have been highly valuable. The number of limitations provides further support to calls to include non-RCT evidence in the review, as these were (somewhat ironically) omitted due to their perceived limitations</p> <p>6) <u>No analyses favoured higher carbohydrate</u> - It is not acknowledged that none of the analyses from the prioritised systematic reviews, which the grading of evidence was based solely on, favoured the higher carbohydrate group (i.e. ALL analyses either favoured lower carbohydrate diets or found no difference). This is very important, and suggests that lower carbohydrate diets are at least as effective as higher carbohydrate diets</p> <p>7) <u>Classifications of “Inconsistent evidence” should include qualification</u> - For a number of outcomes the evidence is graded as inconsistent. Although this is true to an extent, in all analyses where this is the case the outcomes reported either favoured lower carbohydrate or found no difference between diets (i.e. no analyses favoured higher carbohydrate diets). “Inconsistent” incorrectly implies, or at the very least could easily be inferred to mean, that this inconsistency is across all possible outcomes. This is not true, and this should be reflected</p> <p>8) <u>Absence of harm not fully acknowledged</u> - Lower carbohydrate diets are often criticised in relation to changes in lipoprotein markers, including total cholesterol (though validity of using this as a marker of health in isolation is debatable) and LDL cholesterol (where</p>	<p>6) Only significant findings were considered to be relevant.</p> <p>7) The criteria for the evidence grade of ‘inconsistent’ were provided in Table 5.3.</p> <p>8) The draft report acknowledges that there was no difference in adverse events between lower and higher carbohydrates diets in the short-term.</p> <p>9) It was agreed to grade the evidence on change in medication use. Evidence on adverse events was not graded.</p> <p>10) Amendments to the section on adverse events were agreed.</p>

Organisation/ Individual	Comments	SACN reply
	<p>there is again meaningful debate to be had around the relative importance of LDL-cholesterol compared to number of LDL particles). Ignoring these nuances, in this review there were no differences between diets for these variables suggesting this common criticism of lower carbohydrate diets is not supported by the evidence. The importance of this in the context of current beliefs should be acknowledged explicitly</p> <p>9) <u>Failure to fully consider medication changes</u> - Despite highlighting its importance (paragraph 6.77) this issue has not been fully considered. Changes in the other outcomes are not considered in context of medication changes (an omission that will affect consideration of HbA1c changes in particular), 3 of the 4 prioritised systematic reviews are not included in consideration of medication changes despite reporting on them (relevant findings are summarised in table A12.2 but not considered otherwise – findings are consistently in favour of lower carbohydrate diets), and the WG decline to provide a grading for this outcome due to the absence of a relevant meta-analysis despite the grading criteria (Table 5.3) allowing for evidence to be graded based on findings of primary studies (a decision that is particularly questionable given decision to grade the evidence for adverse events based on less, and less consistent, evidence). The findings across all reviews and RCTs are consistently in favour of lower carbohydrate diets, demonstrating that they regularly lead to a reduced requirement for anti-hyperglycaemic medications. A failure to consider this in the recommendations, which is what will occur if a grading is not provided for this outcome, will mean a key component of their possible benefits is not considered. As a result, their efficacy will be underestimated</p> <p>10) <u>The adverse events section is highly biased and largely invalid</u> - As per the specific comments laid out below (paragraphs 6.200 to 6.211), a number of statements in this section are not supported by the available evidence, utilise evidence in a non-systematic and non-transparent way, and include caveats regarding long-term effects of</p>	

Organisation/ Individual	Comments	SACN reply
	<p>lower carbohydrate diets that are equally true of other ways of eating but are seldom (if ever) used to qualify other diets. Further, the only study used to suggest a potentially greater rate of adverse events in lower carbohydrate diets (which is used to grade the evidence, despite the working group deciding not to grade evidence for medication changes where data from 6 shorter-term and 8 longer-term RCTs were available) is not a valid study in the context of considering the effects of lower carbohydrate diets (the lower carbohydrate diet was also a very low energy diet using protein shakes in the initial phases), and should be omitted from the review entirely.</p>	



**Table 2: Specific comments on chapter 1. Introduction** (pages 9-10)

Paragraph	Organisation/ Individual	Comments	SACN reply
1.1	Dr Z Harcombe	<p><u>In relation to Flaw 2</u> (not addressing what the review set out to address)</p> <p>Para 1.1 stated: “The purpose of this report is to review the evidence on lower carbohydrate diets compared to current UK government advice for adults with type 2 diabetes (T2D). It was initiated in 2017, in response to a request from Public Health England (PHE), in recognition that such diets are gaining attention and increasingly being promoted.”</p> <p>I am not aware of anyone promoting lower carbohydrate diets for T2D. I am aware of a number of academic and medical doctors, in the UK and US especially, researching, publishing academic papers about, and promoting very low carbohydrate diets (and low carbohydrate diets as an upper, not lower, limit) – definitions in Table 5.1.</p>	<p>As clearly explained in the report (paragraph 5.39), the term ‘lower’ was used because the definition of ‘low’ carbohydrate varied across studies.</p> <p>Agreed to include explanation in chapter 1 of why the term ‘lower’ was used.</p>
1.5	X-pert Health	<p>In the context of the current review, this should clarify that none of the studies included in the 2015 SACN report included individuals with T2D.</p>	<p>Agreed to clarify.</p>

**Table 3: Specific comments on chapter 2. Background on carbohydrates** (pages 11-14)

Paragraph	Organisation/ Individual	Comments	SACN reply
2.9	BANT	Processed starches (calorific maltodextrins) should be flagged as having high GI ranking. <u>Reference:</u> Hofman et al. Nutrition, Health, and Regulatory Aspects of Digestible Maltodextrins. Crit Rev Food Sci Nutr. 2016;56(12):2091–2100. doi:10.1080/10408398.2014.940415	Paragraph 2.9 explains terminology used to describe carbohydrates. Information about GI is provided later in this chapter.
2.9	X-pert Health	Structure of second sentence somewhat difficult to follow.	Agreed to reconsider sentence for clarification.
2.11 2.14	BANT	Fructose insufficiently characterised particularly in relation to liver steatosis. See point on para 3.14 below.	Detailed consideration of fructose and of liver steatosis was outside remit of report.
2.13	D Collins	Should be noted that body makes glucose via gluconeogenesis by the liver - so it is available from another source other than food.	Detailed consideration of glucose metabolism was outside remit of report.
2.13	X-pert Health	Second sentence requires qualification, i.e. the glucose requirement for these purposes is small and this glucose does not necessarily have to come from dietary carbohydrate.	As above.
2.14	X-pert Health	First sentence should be more specific about how glucose is “under control” of insulin, there should be a comma after “insulin”, and it should be reflected that circulating insulin can increase before glucose is absorbed.	As above.

Paragraph	Organisation/ Individual	Comments	SACN reply
2.17	D Collins	Is glycaemic index (GI) a reasonable measure - brown bread is higher than table sugar. Fructose is low GI score but is a significant toxin in excess to our liver and insulin resistance. Should we measure insulin response to certain types of food?	A detailed consideration of GI and insulin response was outside remit of report.
2.17	X-pert Health	Cut point for high GI classification should be provided, as it is for low GI.	Agreed to include.
2.18	X-pert Health	This paragraph conflates food quality and glycaemic index, but the two are not necessarily synonymous	Agreed to amend paragraph.

**Table 4: Specific comments on chapter 3. Background on type 2 diabetes** (pages 15-19)

Paragraph	Organisation/ Individual	Comments	SACN reply
n/a	Dr M Robinson	Not enough emphasis on mechanisms of insulin resistance. I have written extensively on low-carbohydrate diets and effect on physiology. This includes mechanisms of sat fat-mediated inflammation and insulin resistance. Evidence collated into a 257 page book: <u>Reference</u> : Eat Carbohydrates: Get Thin and Healthy. The Medical Consequences of Low-Carbohydrate, High-Protein Diets. It can be purchased from lulu.com or read for free online: <a href="http://issu.com/drmagdarobinson/docs/eat_carbohydrates_get_thin_and_healthy_,_dr_magd">issu.com/drmagdarobinson/docs/eat_carbohydrates_get_thin_and_healthy_,_dr_magd</a>	This chapter provides background information on T2D. A comprehensive discussion of the pathophysiology of T2D was outside the remit of report.
3.1	D Collins	Should be recognized that for most T2Ds a hyperinsulaemic state exists. So not just low or inefficient, in fact there is a lot of it around.	As above.
3.1 3.7 3.8	Dr Z Harcombe	<u>Relating to flaw 4</u> (the absence of common sense) Section 2 “classification of carbohydrates” informs us that: i) glucose is one of the three main monosaccharides; ii) glucose is present in fruit and milk (glucose is present in all three disaccharides); iii) starch is “a polysaccharide of glucose monomers.” This section confirms that every food that contains carbohydrate contains glucose. Para 3.1 states “Diabetes is a condition in which the body does not produce sufficient insulin to regulate blood glucose levels and the insulin produced does not work effectively. This leads to elevated blood glucose concentrations which causes damage to blood vessels and nerves.” Para 3.7 states “Diagnosis of T2D is on the basis of elevated blood glucose concentrations...”	The WG’s remit was to compare lower with higher carbohydrate diet on T2D outcomes, including markers of glycaemic control.

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>Para 3.8 states “Elevated blood glucose concentrations over time can have serious long-term consequences such as heart attacks... and premature death.”</p> <p>If diabetes is a condition in which the body cannot regulate blood glucose levels and raised blood glucose levels are catastrophic, why would diabetics be advised to consume the majority of their diet in the form of carbohydrate – the only macronutrient to provide glucose?</p>	
3.5	BANT	<p>First sentence should be more precise and read “T2D accounts.... and occurs following <u>beta-cell dedifferentiation</u> which results in reduced insulin secretion and increased insulin resistance”. In addition to ADA 2019a, Cinti 2016 should be cited.</p> <p><u>Reference</u>: Cinti et al. Evidence of <math>\beta</math>-Cell Dedifferentiation in Human Type 2 Diabetes. J Clin Endocrinol Metab. 2016;101(3):1044–1054. doi:10.1210/jc.2015-2860</p>	A comprehensive discussion of the pathophysiology of T2D was outside the remit of the report.
3.5	X-pert Health	<p>This paragraph should reflect that the pattern of beta-cell insulin secretion is impaired (i.e. the first phase insulin response is reduced or lost) before the volume of insulin secretion is. Insulin levels are usually elevated in comparison to normoglycaemic individuals for multiple years before secretion begins to reduce.</p>	As above.
3.6	BANT	<p>Winkley et al (2013) also stated “in multi-ethnic inner-city populations, onset of type 2 diabetes occurred almost 10 years earlier in non-white populations than in white participants, predicating a prolonged morbidity.” This should be noted in the report.</p>	Point noted but agreed that this detail was not required additional to the point acknowledging differences by ethnicity (see point 15 above).

Paragraph	Organisation/ Individual	Comments	SACN reply
3.6	X-pert Health	Refers to T1D, despite paragraph 3.4 stating that this would not be considered further in the report.	Agreed to delete reference to T1D.
3.7	X-pert Health	Should reflect that T2D can also be classified based on the results of an OGTT [Oral Glucose Tolerance Test], or on the basis an individual is prescribed anti-hyperglycaemic medications.	Agreed that additional diagnostic criteria were not necessary.
3.11 3.8 4.4	BANT	Paragraph 3.11 should be deleted as it is not consistent with position taken in 4.4 that BP would not be included as a secondary outcome. Nor is it consistent with statements in 3.8 which also includes renal and eye diseases. PHE (2019) Public Health Outcomes Framework Indicator refers to preventable sight loss -diabetic eye disease (E12c). If 3.11 is maintained it should include treatment goals of improved renal function and liver steatosis (E06b PHE Public Health Indicator), which should also then be secondary outcomes in chapter 4.	Agreed to retain this paragraph.
3.13	D Collins	Surprised no mention from great work of Women’s Health Initiative <a href="https://www.whi.org/SitePages/WHI%20Home.aspx">https://www.whi.org/SitePages/WHI%20Home.aspx</a>	Noted but not considered directly relevant.
3.13	X-pert Health	This paragraph would be better placed in previous section (“Background on T2D”) as it is not overtly included in existing NICE criteria for management of T2D. It should perhaps also state that recent evidence has now made it clear that T2D need not be a progressive condition.  Evidence pertaining to the possibility of T2D remission following adoption of a very low carbohydrate diet should be included in this section. As it was deemed acceptable to include Sjostrom et al (2014), an analysis of data from a prospective matched cohort study, there does not appear to be any justification for excluding non-RCT evidence of	A comprehensive review of T2D remission was outside the remit of the report.

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>other forms; such as that provided by Athinarayanan et al (2014) which provided good evidence that carbohydrate restriction can lead to T2D remission.</p> <p><u>Reference:</u> Athinarayanan et al. Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-year Non-randomized Clinical Trial. <i>Frontiers in Endocrinology</i>. 2018;10:348.</p>	
3.14	BANT	<p>In underweight and normal weight T2D a reduction in energy intake cannot be recommended. This paragraph fails to spotlight specific nutrients/food components which increase risk of liver steatosis. The report fails to consider unique aspects of fructose metabolism in stimulating lipogenesis and inducing insulin resistance and how it alters the metabolism of glucose by driving more glucose through oxidation pathways.</p> <p><u>References</u>            Softic et al. Role of Dietary Fructose and Hepatic De Novo Lipogenesis in Fatty Liver Disease. <i>Dig Dis Sci</i>. 2016;61(5):1282–1293. doi:10.1007/s10620-016-4054-0            Varma et al. Fructose Alters Intermediary Metabolism of Glucose in Human Adipocytes and Diverts Glucose to Serine Oxidation in the One-Carbon Cycle Energy Producing Pathway. <i>Metabolites</i>. 2015;5(2):364–385. doi:10.3390/metabo5020364</p>	<p>Paragraph 3.14 states that energy reduction is recommended only to those living with overweight or obesity. Consideration of liver steatosis and fructose metabolism were outside the remit of the report.</p>
3.14-3.22	D Collins	<p>Dietary Management of T2D: there is a lot of concern about low carbohydrate diets being really detrimental from dietician organizations mostly - where is the evidence of harm from low carbohydrate foods or is there a carbohydrate deficiency syndrome? We should recognize one if it exists?</p>	<p>Adverse events are considered in chapter 6. Consideration of carbohydrate deficiency was outside the remit of the report.</p>
3.14	DSG-BDA	<p>Use of person focused language could be improved.</p>	<p>Agreed.</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
3.16	X-pert Health	<p>In 1st sentence, “health dietary pattern” should be in quotation marks to avoid any suggestion that other ways of eating may not be healthy.</p> <p>2nd sentence implies the SACN 2015 report made recommendations for people with T2D which is not the case.</p> <p>4th sentence should reflect that the NICE NG28 recommendations regarding individualised advice specifically allude to carbohydrate intake, and that in the NICE response to comments during the 2019 consultancy on this guidance it was stated that “NICE guideline NG28 already advises individualising recommendations for carbohydrate intake, and meal patterns, which could include low carbohydrate and low calorie diets”* to make it clear that the promotion and support of LCDs for people with T2D is not precluded by existing guidance, an important point for providing context for the current review</p> <p><a href="https://www.nice.org.uk/guidance/ng28/evidence/appendix-b2-stakeholder-consultation-comments-table-ng28-pdf-6837997937">https://www.nice.org.uk/guidance/ng28/evidence/appendix-b2-stakeholder-consultation-comments-table-ng28-pdf-6837997937</a></p>	<p>Healthy dietary pattern is used by NICE to describe its recommendation</p> <p>SACN carbohydrate report is aimed at the general population, including those with T2D. Agreed to clarify wording of this sentence.</p> <p>Not considered appropriate to include NICE response to comments received during consultation on its guidance.</p>
3.17	DSG-BDA	Is this referring to the correct SIGN, is it 2017 not the 2019 referred to?	Text refers to SIGN 2017 and not 2019.
3.17	Dr M Robinson	<p>Risks of very low carbohydrate diets (VLCHF/KDs) need to be fully elucidated. Paragraph states that intakes less than 50g/day are safe for up to 6 months. Evidence of increased risks in the short term. A comprehensive review of low carbohydrate diets by the National Lipid Association (Kirkpatrick et al, 2019) examines the risks. I quote directly from the review here:</p> <p>“With VLCHF/KDs, gastrointestinal complaints tend to be the most common adverse effects, including constipation, nausea, and abdominal pain, which are experienced in the first few weeks. Some individuals may experience symptoms described as the “keto flu”</p>	<p>Paragraph 3.17 reproduces SIGN guidance, which does not discuss risks associated with very-low-carbohydrate, high-fat ketogenic diets (VLCHF/KD).</p> <p>The majority of evidence from Kirkpatrick et al (2019) for adverse effects of these diets is</p>



Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>within 2 to 4 days of beginning a VLCHF/KD, which may occur as the body adapts to using ketone bodies for fuel, may last a few days to one week, and include lightheadedness, dizziness, fatigue, difficulty exercising, poor sleep, and constipation.<sup>1</sup> Other adverse effects that have been reported in individuals strictly following VLCHF/KDs include headache, skin rash, muscle cramps, weakness, diarrhea, dehydration, hypoglycemia, increased levels of blood uric acid, and vitamin/mineral deficiencies. Increased urination can lead to reduced levels of electrolytes, including sodium, magnesium, and potassium, and may be associated with symptoms of hypovolemia, as well as dizziness related to the need to reduce hypertension and/or hyperglycemia medications.”</p> <ul style="list-style-type: none"> <li>• Caution in patients with ASCVD, risk of atrial fibrillation, and a history of heart failure, kidney disease, and liver disease</li> <li>• Close medical supervision is essential for individuals with ASCVD, risk of atrial fibrillation, or the presence or history of heart failure, kidney disease, or liver disease who choose to follow a very-low-CHO diet or KD.</li> <li>• VLCHF/KDs are contraindicated in patients with a history of hypertriglyceridemia-associated acute pancreatitis, severe hypertriglyceridemia, or inherited causes of severe hypercholesterolemia.</li> <li>• Individuals with T2D should receive medical supervision and cardiometabolic monitoring while on very-low-CHO diets or KDs.</li> <li>• Low-CHO and very-low-CHO diets can lead to hypoglycemia or hypotension and may require adjustment in diabetes or hypertension medications.</li> <li>• Patients taking SGLT2 inhibitors should avoid very-low-CHO KDs because of an increased risk of SGLT2 inhibitor-associated ketoacidosis.</li> <li>• More frequent monitoring of vitamin K-dependent anticoagulation therapy may be required with very-low-CHO diets due to the potential change in vitamin K bioavailability and its effect on anticoagulation therapy.</li> </ul>	<p>based on studies in the general population and not people with T2D.</p> <p>Other detailed points discussed in this paper are outside remit of report.</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
		<ul style="list-style-type: none"> <li>Both low- and high-CHO intake has been associated with a higher risk of mortality in the general population; moderate-CHO intake has been associated with the lowest risk of mortality in the general population.”</li> </ul> <p><u>Reference</u> Kirkpatrick et al. Review of current evidence and clinical recommendations on the effects of low-carbohydrate and very-low-carbohydrate (including ketogenic) diets for the management of body weight and other cardiometabolic risk factors: A scientific statement from the National Lipid Association Nutrition and Lifestyle Task Force. J. Clin. Lipidol. 2019, S1933–S2874.</p>	
3.20	X-pert Health	<p>Important, relevant statements from the ADA [American Diabetes Association] guidance are omitted; for example it is asserted that “Reducing overall carbohydrate intake for individuals with diabetes has demonstrated the <b>most evidence</b> for improving glycaemia and may be applied in a variety of eating patterns that meet individual needs and preferences” (emphasis is ours) and “...from the current evidence, this eating pattern does not appear to increase overall cardiovascular risk...”, with the authors noting that this was the case even though most of the included trials did not restrict saturated fat. The inclusion of such statements is important to provide adequate context for the current review, as a non-specialist reader may not be aware of the increasing acceptance of such approaches internationally.</p>	<p>ADA guidance was updated in 2020. It was agreed to amend text to reflect the updated recommendations.</p>
3.20 & Table 3.1	Dr Z Harcombe	<p><u>Relating to Flaw 1</u> (conflicts of interest)</p> <p>Para 3.20 and Table 3.1 sets out the Diabetes UK position. Table 3.1 summarises the current position among peers of Diabetes UK and thus sets as a foundation the belief that carbohydrates should be 45-60% of intake, fat should be less than 35% and protein should be no more than 20%. With half the panel conflicted with Diabetes UK, this, again, is not the panel to overturn its own guidelines.</p>	<p>Diabetes UK does not make specific recommendations for macronutrients and this is explicit in both the text and Table 3.1</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>The draft SACN report is dated January 2020, so para 3.20 should have captured the US consensus report published in May 2019. This report examined low-carbohydrate diets (26-45% of total calories) as well as very low-carbohydrate diets (20-50g/day of carbohydrate). Both diets were reported to reduce HbA1c, deliver weight loss, lower blood pressure, and improve the lipid profile. The US consensus report did not caution that (very) low-carbohydrate diets were only safe and effective in the short term. The US consensus report did not use isolated papers to issue unnecessary safety concerns. The US consensus report contained 345 references. It went as far as to advise eating non-starchy vegetables.</p> <p><u>Reference:</u> Evert et al. Nutrition Therapy for Adults With Diabetes or Prediabetes: A Consensus Report. Diabetes Care 2019.  <a href="https://care.diabetesjournals.org/content/diacare/42/5/731.full.pdf">https://care.diabetesjournals.org/content/diacare/42/5/731.full.pdf</a>).</p>	<p>It was agreed to update the text to reflect the current ADA guidance published in Diabetes Care in 2020.</p>
Table 3.1	Dr E Morris & Prof P Aveyard	<p>Diabetes Australia row – Carbohydrate content – “low carbohydrate diets” should be followed by 2 asterisks ** (referring to definition of low carb diets) rather than 1 * (referring to NICE guideline).</p>	<p>To be corrected.</p>
Table 3.1	X-pert Health	<ol style="list-style-type: none"> <li>1) NICE are referred to as the “National Institute for Clinical Excellence”, this should read “National Institute for Health and Care Excellence”.</li> <li>2) The value provided for NICE guidance on carbohydrate intake should include the caveat that individualised carbohydrate intake is recommended.</li> <li>3) The information provided for SIGN [Scottish Intercollegiate Guidelines Network] and ADA guidance on carbohydrate intake should perhaps have accompanying statements, similar in nature to that provided for the Diabetes UK guidance.</li> </ol>	<ol style="list-style-type: none"> <li>1) To be corrected.</li> <li>2) This was included in a response to stakeholder comments and does not appear in the guidance proper.</li> <li>3) Agreed to retain current wording.</li> </ol>

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>4) The EASD [European Association for the Study of Diabetes] guidance provided is inconsistent with the position in their 2018 joint position statement with the ADA (Davies et al, 2018) which presumably supersedes the Mann et al (2004) reference used here.</p> <p>5) The footnote notation within the Diabetes Australia section appears to be incorrect.  <u>Reference</u> Davies et al. Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2018;41(12):2669-2701.</p>	<p>4) The reference provided is a consensus report. It does not address specific recommendations for nutrition from the EASD.</p> <p>5) To be corrected.</p>

**Table 5: Specific comments on chapter 4. Markers and clinical outcomes of type 2 diabetes** (pages 20-22)

Paragraph	Organisation/ Individual	Comments	SACN Reply
n/a	BANT	<p>Inconsistencies in markers, outcomes and goals</p> <ol style="list-style-type: none"> <li>1) WG Terms of reference are to consider “.markers and clinical outcomes of T2D including any potential adverse effects” but there is no narrative to justify omission of diabetic retinopathy, diabetic nephropathy and diabetic neuropathy which are prominent clinical outcomes of T2D as set out in the Background.</li> <li>2) Diagnosis of T2D is on basis of glycaemic markers. Body weight, which is neither a symptom or marker for T2D and is described in 3.5 as ‘associated with risk of developing T2D’, is set as a primary outcome. 3.10 states ultimate aim of treatment is to reduce and maintain HbA1C concentration at a value below cut-off for definition of T2D. A successful dietary intervention is described (4.13) as reduction in T2D symptoms (glycaemia, BP and blood lipids) and reduced need for diabetes medication.</li> <li>3) Background omits exposition as fat infiltration of pancreas and liver as causal to beta-cell insufficiency. Body weight as a primary outcome skews the review and analysis of evidence.</li> <li>4) Secondary outcomes (4.2) omit BP which does not align with para 4.13 as establishing successful dietary intervention. Secondary outcomes also omit liver steatosis which is an important factor and is in line with PHE (2019) E06b Public Health Outcomes Indicator (under 75 premature mortality from liver disease considered preventable).</li> </ol>	<ol style="list-style-type: none"> <li>1) An improvement in glycaemic control would have minor effects on these clinical outcomes over the time periods considered in the primary data. Evidence considering these outcomes is also lacking.</li> <li>2) Disagree. Body weight is a relevant marker for T2D since weight loss improves glycaemic control.</li> <li>3) The chapter provides background details. It is not intended to be a comprehensive review of the pathophysiology of T2D.</li> <li>4) Reasons for excluding BP as an outcome is explained in paragraph 4.3. Liver steatosis is not routinely considered in the clinical management of T2D and</li> </ol>

Paragraph	Organisation/ Individual	Comments	SACN Reply
			most studies did not assess this as an outcome.
n/a	Dr E Morris & Prof P Aveyard	<p><u>Primary outcomes:</u> Rationale for reporting BMI only at 12 months, but HbA1c from 3 months, is not clear. Report states “many short-term interventions are able to achieve weight loss but the maintenance of weight loss is challenging”; however the same could be argued for HbA1c (difficult to sustain improvement over time). Weight loss interventions that lead to short-term weight loss also lead to longer-term weight loss compared to control groups. Currently no evidence that any particular type of intervention, with different trajectories of weight loss, change the trajectory of weight regain. Additionally, there are recognised cardiometabolic and general health benefits seen with weight loss that persist even beyond the time of any potential weight regain. In this context, the decision to discount weight loss outcomes at &lt;12m in case they are not sustained does not seem clinically justified and examining the evidence of short- as well as longer-term effects would be valuable. As recognised in the results, sensitivity analyses within the meta-analyses (e.g. Sainsbury et al 2018) suggest that a significant proportion of the HbA1c improvements may be due to weight loss; and the conclusions again restate that it is difficult to separate the effect of weight change on the outcomes. It is therefore hard to interpret the reported HbA1c results (and other outcomes) for shorter-term studies (3-12m) without reporting the corresponding weight losses.</p>	It was agreed to include consideration of shorter-term ( $\geq 3$ to < 12 months) weight change as a secondary outcome.
4.1	BANT	Body weight cannot be supported as a primary or secondary outcome as it is not a clinical outcome of T2D. Body weight (or % weight gain/loss) is not a marker for T2D and not consistent with aim set out in 3.10. While weight loss may drive improvements in T2D for those who are obese, it is not reconcilable for	Disagree. Body weight is a relevant outcome for T2D since weight loss improves glycaemic control.

Paragraph	Organisation/ Individual	Comments	SACN Reply
		underweight (Asian Indians) or normal weight T2D patients. Nor is it compatible with the state of metabolically healthy obesity (normal glucose and lipid parameters and absence of hypertension).	
4.1	DSG-BDA	The need to use HbA1c is necessary as this is the best and most used outcome measure in these studies, often due to heterogeneity, change in medication use and achieving remission are not adequately reported or defined.	Noted and agreed.
4.1-4.2	OG-BDA	We support the choice of body weight and HbA1c as primary outcomes and fasting plasma glucose and blood lipids as secondary outcomes. Given that majority of those with T2D have overweight or obesity at the time of diagnosis, that HbA1c is a meaningful measure of glycaemic control and that poorly controlled diabetes is a risk factor for CVD (for which blood lipids are surrogate measures), these make sense.	Noted and agreed.
4.3	X-pert Health	<p>Disagree with rationale for omitting BP as a marker of interest. BP may be reduced through weight independent means, such as due to a reduced retention of sodium following a reduction in circulating insulin levels. Supporting this, there is evidence that low carbohydrate diets may be able to reduce BP in a manner that is at least partly independent of weight reduction (Unwin et al, 2019).</p> <p><u>Reference:</u> Unwin et al. Substantial and Sustained Improvements in Blood Pressure, Weight and Lipid Profiles from a Carbohydrate Restricted Diet: An Observational Study of Insulin Resistant Patients in Primary Care. International Journal of Environmental Research and Public Health. 2019;16(15):2680.</p>	The reasons for excluding BP as an outcome is explained in the report (paragraph 4.3).

Paragraph	Organisation/ Individual	Comments	SACN Reply
4.5	DSG-BDA	The challenge of excluding studies <12m is that this limits the data on intervention studies and there is a valid critique that current practice lacks data too. Although, by the nature of restricting carbohydrate and the likely increased energy deficit seen acutely in many studies this is possibly necessary.	It was agreed to include consideration of shorter-term ( $\geq 3$ to < 12 months) weight change as a secondary outcome.
4.5	OG-BDA	We support exclusion of studies with duration <12m for measurement of body weight. The maintenance of healthy body weight in the long-term is well documented as challenging so including shorter term studies could potentially over-estimate any effect of low carbohydrate diets on weight and health.	It was agreed to include consideration of shorter-term ( $\geq 3$ to < 12 months) weight change as a secondary outcome.
4.6	BNF	<p>1) The draft report does not consider results on body weight from studies under 12m duration in order to reflect longer-term maintenance of weight loss, whereas, for other outcomes, results from 3m are considered. Whilst it is certainly the ideal that weight loss should be maintained in the longer term in order to gain the most health benefit, the available evidence indicates that the efficacy of all weight loss diets, regardless of macronutrient composition declines after 12 months.</p> <p>2) For example, a <a href="#">recent systematic review</a> (Ge et al. 2020) looked at a variety of weight loss diets, including low carbohydrate and higher fat, higher carbohydrate and lower fat, as well as diets comprising macronutrients in more moderate proportions as per current UK healthy eating guidance. This study found that all of the diets resulted in modest weight loss and improved cardiovascular risk factors at 6m but these effects had largely disappeared by 12m. Thus, while there is insufficient evidence to suggest that low carbohydrate</p>	<p>1) It was agreed to include consideration of shorter-term (<math>\geq 3</math> to &lt; 12 months) weight change as a secondary outcome</p> <p>2) Noted.</p> <p>3) Noted. This is a matter for risk management. PHE will consider the report when it has been finalised and make public health recommendations regarding lower carbohydrate diets for individuals with T2D.</p>



Paragraph	Organisation/ Individual	Comments	SACN Reply
		<p>diets (however defined) are superior to other weight loss approaches in the longer term, evidence is also lacking that diets comprising around 50% energy from carbohydrate, such as those suggested by current UK dietary recommendations for the general population including people with T2D, would offer any better outcomes in terms of weight control.</p> <p>3) With the exception of very low carbohydrate diets, adverse effects have not been shown to be associated with lower carbohydrate diets in SACN’s draft report. We would agree that the available evidence doesn’t support a recommendation to use low carbohydrate diets over other dietary approaches. However, in relation to public health advice that follows on from the final version of this report, we would suggest that given the huge task the UK has in tackling obesity and T2D, it would be helpful to have some guidance for those who may choose to try a low carbohydrate approach in order to support them to do this in a balanced way. We know that adherence to weight loss diets is necessary for sustaining weight loss and the associated health benefits, and so considering the range of individual preferences for such approaches is important. This has been done by Diabetes UK in its <a href="#">low carbohydrate guidance and eating plan</a> and is reflected in its <a href="#">position statement on low carbohydrate diets</a>. We acknowledge that risk management is not the role of this report or of SACN but that it is for PHE to consider how the outcomes of the report feed into public health advice. To have such guidance from a Government source would be very helpful in encouraging consistency of messaging and supporting a balanced approach, for example to encourage the inclusion of wholegrains, pulses and a variety of fruit and vegetables if choosing a lower carbohydrate diet.</p>	

Paragraph	Organisation/ Individual	Comments	SACN Reply
4.6	D Collins	Only certain studies will be looked at - will you clearly demonstrate the funding of those studies you do look at so there is an equal spread of industry sponsored to governmental/altruistic funding. Transparency will be important.	Information on funding for the systematic reviews and meta-analyses is provided in Annex 4 (Table A4.1). Information on the primary trials included in the systematic reviews and meta-analyses is provided in Annex 5 (Table A5.1).
4.8	Netherlands Health Council	This paragraph defines the HbA1c cut-offs for the diagnosis of diabetes. However, the current work applies to people who have already been diagnosed with diabetes. It may be helpful to clarify that diabetes diagnoses are not an outcome of the current work but rather used as inclusion criterion.	Agreed to clarify that HbA1c is used both for diagnosis of T2D and as marker of glycaemic control in T2D management.
4.9	X-pert Health	Question word choice of “around”; “at least” may be preferable.	Agreed to retain existing wording.
4.10	Netherlands Health Council	Similar to comment re paragraph 4.8: it may be helpful to specify that glucose cut-offs are not used as outcome.	Agreed to clarify text to make distinction between glucose cut-offs for diagnosis and for management of T2D.
4.10	X-pert Health	Although we acknowledge that evidence would likely be limited, some consideration of blood glucose beyond fasting levels would be of benefit; for example, blood glucose variability or time in range. Even without the ability to fully	Agreed that blood glucose variability and change in time were potential markers of interest but were not

Paragraph	Organisation/ Individual	Comments	SACN Reply
		assess this the potential utility of such markers beyond single point measures should be acknowledged.	considered due to lack of evidence on these markers.
4.11	X-pert Health	<p>There does not appear to be any consideration of the possible effect of blood lipid lowering medications.</p> <p>This should reflect that the pattern and/or type/size of lipoproteins may be important, beyond a simple consideration of amounts.</p> <p>The 3rd sentence adds no value, it is essentially a repeat of the preceding 2 sentences.</p>	<p>Focus was on change in diabetes medication.</p> <p>Consideration of the pattern and/or type/size of lipoproteins was outside scope of review.</p> <p>Since most studies did not consider lipoproteins in such detail, data were not available for analysis.</p> <p>Agreed to retain 3<sup>rd</sup> sentence.</p>
4.12	D Collins	Are we measuring the right cholesterol- small dense lipoproteins/ Apob/ApoA ratios? Have we explained why Familial Hypercholesterolemia survivors into old age have in fact reduced all-cause mortality despite huge exposure over many years to this toxic compound. I understand Framingham has found similar with those aged over 60 years with raised LDLs doing better than those with low LDL? What is going on?	Outside the scope of review.
4.12	HEART UK	As well as serum LDL cholesterol, HDL cholesterol, total cholesterol, triacylglycerols and total cholesterol: HDL-C ratio, why were non-HDL cholesterol and apolipoprotein B (apoB) not chosen? These are now well-recognised lipoproteins associated with CVD risk. The European Society of Cardiology and European Atherosclerosis Society, recommend that because of the potential inaccuracy of LDL	Role of these lipoproteins on T2D risk was outside the scope of this review.

Paragraph	Organisation/ Individual	Comments	SACN Reply
		<p>cholesterol in dyslipidaemia among patients with Diabetes Mellitus or high triacylglycerols levels, measurement of both ApoB and non-HDL-C is recommended as part of routine lipid analysis for risk evaluation in patients with elevated plasma TGs.</p> <p>If they weren't included in the studies reviewed for this report this should be highlighted and an explanation provided on the most up to date views on the role of these lipoproteins in CVD risk in T2D.</p> <p><u>Reference:</u> Furtado et al. Distinct proteomic signatures in 16 HDL (high-density lipoprotein) subspecies. <i>Arterioscler Thromb Vasc Biol.</i> 2018; 38:2827–2842</p>	
4.12	X-pert Health	<p>It should be acknowledged here and/or in subsequent sections that the duration of fasting is a significant confounder when assessing changes in blood lipids.</p> <p>The inclusion of total cholesterol in isolation can be challenged, as this is not a marker that would be used clinically due to the differential effects of different components of it.</p>	<p>There was insufficient detail on fasting duration in the included studies to be considered independently.</p> <p>Total cholesterol was not considered in isolation. Other blood lipids were also considered.</p>
4.13	BANT	<p>Markers of a successful intervention need to be consistent – so BP should be excluded if not included as a secondary outcome.</p>	<p>Paragraph 4.13 describes indicators of a successful intervention, which includes a reduction in medication use for managing BP.</p>

Paragraph	Organisation/ Individual	Comments	SACN Reply
4.13	Netherlands Health Council	The meaning of the term 'diabetes-related symptoms' is not clear. It would be helpful if you could give a definition of this term. Does it, for instance, include long term complications such as myocardial infarction and chronic kidney disease?	It was agreed to delete 'diabetes-related symptoms'.
4.13 5.11	Netherlands Health Council	Related to point above: Did you also specifically search for long term hard clinical outcomes such as myocardial infarction and chronic kidney disease? If yes, which endpoints? If not, why not?	Given the relatively short-term nature of the primary studies in the evidence base, long-term hard clinical outcomes were not included in the search.
4.13	X-pert Health	<ol style="list-style-type: none"> <li>1) This section should be more specific regarding which symptoms were considered of interest.</li> <li>2) Agree with statement made in 2nd sentence, but this does not appear to have been fully considered subsequently (i.e. changes in health markers are considered independent of changes in medication, and the changes in medication are not considered fairly against the grading criteria set out in Table 5.3).</li> </ol>	<ol style="list-style-type: none"> <li>1) It was agreed to delete 'diabetes-related symptoms'.</li> <li>2) In the evidence considered, changes in outcomes were reported independently of changes in medication. It was agreed to grade the evidence on changes in medication.</li> </ol>

**Table 6: Specific comments on chapter 5. Methods** (pages 23-37)

Paragraph	Organisation/ Individual	Comments	SACN reply
n/a	Dr E Morris & Prof P Aveyard	<ol style="list-style-type: none"> <li>1) Report provides helpful overview of 4 main systematic reviews and meta-analyses. It follows a slightly unusual methodological process, which means that some studies which are in more than 1 systematic review are ‘double-counted’ and it is not clear why a new meta-analysis of studies identified in the reviews was not conducted. However, findings are fairly consistent with findings of individual reviews with our understanding of the literature. Since there are no subgroup analyses it is hard to know who these dietary interventions may work for, and how.</li> <li>2) It is important that the report appropriately focusses on “higher quality” evidence provided by systematic reviews and meta-analyses of RCTs, in order to address the stated aim to review the evidence on lower carbohydrate diets compared to current UK government advice (high carbohydrate diets) for adults with T2D. It broadly concludes an absence (or absence of evidence) of superiority at 1y, for the pre-specified outcomes. However, it is important to distinguish between question of superiority (is it the best approach) and effectiveness (does it work for some people); and the focus on comparative trial data risks overlooking effectiveness outcomes. This could be brought out more clearly in the report.</li> <li>3) Much of excluded observational literature (and within-group analyses reported in supplementary appendix) do demonstrate potential for clinically significant improvements in weight and HbA1c reduction (for example), suggesting some short-term effectiveness (though not superiority) of low-carbohydrate approaches for some patients. This is reflected in the reported UK and international dietary recommendations for T2D, many of which now include low carbohydrate diets as 1 option (that are “safe and effective in the short term”) to consider as part of an</li> </ol>	<ol style="list-style-type: none"> <li>1) Noted and agreed.</li> <li>2) Noted. Consideration of effectiveness outcomes was outside the scope of review.</li> <li>3) Agreed to consider this point when finalising conclusions of report.</li> <li>4) Noted. Agreed that the evidence did not allow comparisons to usual care.</li> </ol>

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>individualised approach. This more nuanced approach is not addressed in the conclusions of the report.</p> <p>4) Majority of studies compared 2 programmes in which people were advised and supported to consume (on average) a lower-energy diet without carbohydrate restriction, or a diet using carbohydrate restriction as an additional or alternative means to reduce energy intake. Few comparisons were made to true “usual care”, i.e. current UK government advice and how this is routinely delivered, or in “healthy” individuals with T2D. So while a lack of superiority of low-carbohydrate (or higher-carbohydrate) diets shows that either may be equally valid in context of a weight loss programme, the results of this report do not currently tell us whether healthy people with T2D, who are not explicitly aiming to lose weight, should be advised to lower their carbohydrate intake or not.</p>	
5.1-5.2	Dr Z Harcombe	<p><u>Relates to flaw 5</u> (if only same bar had been set for introduction of low fat high carbohydrate guidelines)</p> <p>5.1 informed us that only “evidence provided by systematic reviews with meta-analyses” will be considered and only from RCTs (5.2).</p> <p>6.206 stated “the implications of long-term restriction of carbohydrates in adults with T2D are currently unknown since there is a lack of data from longer-term studies.”</p> <p>The implications of long-term restriction of fat (and concomitant increase in carbohydrates) in all adults was unknown at the time of the introduction of precisely these dietary guidelines (1977 US/1983-84 UK).</p> <p>My PhD was an examination of the evidence base (using only systematic reviews and meta-analyses) for introduction of the low-fat (high-carbohydrate) guidelines. There was no evidence at the time these guidelines were introduced from systematic reviews and</p>	<p>Focus of this report was to compare lower versus higher carbohydrate intakes.</p> <p>SACN’s assessment of saturated fats and health is available here:</p> <p><a href="https://www.gov.uk/government/publications/saturated-fats-and-health-sacn-report">https://www.gov.uk/government/publications/saturated-fats-and-health-sacn-report</a></p>

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>meta-analyses of RCTs (1). (There was no evidence from cohort studies either (2)) There has been no more evidence from systematic reviews and meta-analyses of RCTs since (3) We had no idea of the implications of long-term restriction of fat (and concomitant abundance of carbohydrate) and yet we introduced these dietary guidelines anyway. It would appear that the bar to change the guidelines (back to where they were) is substantially higher than the zero-bar applied to their introduction.</p> <p><u>References</u></p> <p>Harcombe et al. Evidence from randomised controlled trials did not support the introduction of dietary fat guidelines in 1977 and 1983: a systematic review and meta-analysis. Open Heart 2015.</p> <p>Harcombe et al. Evidence from prospective cohort studies did not support the introduction of dietary fat guidelines in 1977 and 1983: a systematic review. Br J Sports Med 2016.</p> <p>Harcombe et al. Evidence from randomised controlled trials does not support current dietary fat guidelines: a systematic review and meta-analysis. Open Heart 2016.</p>	
5.1-5.2	X-pert Health	<p>Although the statement in 5.1 is not fundamentally incorrect we do not believe it is sufficient justification for limiting the scope of the review, in part because this limits the ability of the WG to assess any questions beyond those which are already subject to published systematic reviews and meta-analyses (which, for example, have not been able to assess evidence pertaining to T2D remission due to relative novelty of the field). Paragraph 5.2 confirms that criteria are in place to include and validly assess evidence of other forms, which would have provided an opportunity to assess clinically relevant questions in more detail using evidence from routine practice and non-RCT evidence. Despite their limitations, which can be accounted for when appraising the evidence,</p>	<p>Reasons for excluding evidence from clinical practice is explained in paragraphs 5.9 to 5.10. It was agreed to amend these paragraphs to summarise the direction of the evidence from these studies and to expand the explanation of why they were not included for consideration in the report.</p>



Paragraph	Organisation/ Individual	Comments	SACN reply
		alternative forms of evidence do have strengths in comparison to RCTs; such as being more ecologically valid.	
5.3	Netherlands Health Council	Report is based on evidence from systematic reviews with meta-analyses (para 5.1). In our view, this means that only systematic reviews accompanied with meta-analyses sufficed for this work, and thus no systematic reviews that were not accompanied with meta-analyses. Is this the case and was this a pre-defined inclusion criterion? We specifically ask this question since it is not explained that way in para 5.3.	Inclusion criteria did not specify that only systematic reviews accompanied by meta-analyses would be included in review.
5.4 & 5.7	X-pert Health	It is good practice when performing a systematic review to not place limits on language of publication and to include grey literature. The resources available for the current review should have made it possible to follow such practices	The literature search included peer-reviewed literature only.
5.7-5.8	D Collins	Exclusion criteria: I note primary care studies will be excluded. I understand from an academic point of view there are bias in place which means it is not RCTs. But this is excluding the voice of the patient. Could we be in danger of replicating the naval disaster surrounding vitamin C. 1600, Surgeon capt Lancaster demonstrated vitamin C cures scurvy. 1700, Lindt does first ever RCT in medicine demonstrating again that vitamin C cures scurvy (50% mortality on board ships). It is 1850 before Navy make this standard operating procedure across all ships- waiting for evidence from respected senior officers.	Studies conducted in primary care were not excluded (RCTs can be conducted in primary care settings).
5.8	Netherlands Health Council	Did you specifically search for systematic reviews/meta-analyses performed in the general population as well? These may include subgroup analyses in people with type 2 diabetes.	The literature search did not include systematic reviews and meta-analyses in the general population.

Paragraph	Organisation/ Individual	Comments	SACN reply
			<p>Only systematic reviews that included studies that recruited people with pre-diagnosed T2D (as defined in the primary RCTs) when they entered the study were considered (paragraph 5.5).</p> <p>Studies that also included individuals without T2D were included if data from individuals with T2D were reported separately.</p>
5.9	BANT	<p>The introduction (1.2) explains SACN does not normally make recommendations on clinical conditions. The SACN Framework (2020) is designed for population health. Adjustments should be made so that evidence from clinical practice studies is included. Clinicians must meet a patient-centred standard of care which is logical and reasonable, ref House of Lords 1997 Bolitho v City and Hackney Health Authority.</p> <p>Evidence cited at 5.9 should therefore be considered.</p> <p>Evidence from clinical practice studies should be included if the report is expected to be a guide for clinicians who must meet a patient-centred standard of care.</p>	<p>Reasons for excluding clinical practice studies are explained in paragraphs 5.9 to 5.10.</p> <p>It was agreed to amend these paragraphs to summarise the direction of the evidence from these studies and to expand the explanation of why they were not included for consideration in the report.</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
5.9-10	Dr Z Harcombe	<p><u>Relating to flaw 2</u> (not addressing what the review set out to address)</p> <p>Paras 5.9 and 5.10 are remarkable. - para 5.9 opens with: “A number of clinical studies (including Saslow et al (2017)...) and case reviews (Unwin &amp; Tobin, 2015) have assessed the effectiveness of lower carbohydrate diets on glycaemic control and other markers in adults with T2D.” Para 5.10 then states: “These studies were not considered in this report because of the number of limitations associated with this study type. They also did not meet the inclusion criteria for study selection.”</p> <p>These paragraphs effectively state, “we’ll set the inclusion criteria and then we’ll dismiss – in 2 paragraphs – all evidence from the genuinely low-carbohydrate doctors and academics.” There were more publications not even cited and dismissed. These are in my EndNotes, just as examples. There will be many more still if the panel were minded to look for them. Facing a crisis of the scale that T2D presents, you would think that any and all evidence would be welcomed with open arms. It would seem not.</p> <p><u>References</u></p> <p>Unwin D, Unwin J. Low carbohydrate diet to achieve weight loss and improve HbA1c in type 2 diabetes and pre-diabetes: experience from one general practice. Practical Diabetes 2014.</p> <p>Unwin DJ et al. A pilot study to explore the role of a low-carbohydrate intervention to improve GGT levels and HbA1c. Diabesity in Practice 2015.</p> <p>Saslow RL et al. Outcomes of a Digitally Delivered Low-Carbohydrate Type 2 Diabetes Self-Management Program: 1-Year Results of a Single-Arm Longitudinal Study. JMIR Diabetes. 2018.</p> <p>Unwin DJ et al. Substantial and Sustained Improvements in Blood Pressure, Weight and Lipid Profiles from a Carbohydrate Restricted Diet: An Observational Study of Insulin</p>	<p>Reasons for excluding clinical practice studies are explained in paragraphs 5.9 to 5.10.</p> <p>It was agreed to amend these paragraphs to summarise the direction of the evidence from these studies and to expand the explanation of why they were not included for consideration in the report.</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>Resistant Patients in Primary Care. International Journal of Environmental Research and Public Health. 2019.</p> <p>Saslow LR et al. A Randomized Pilot Trial of a Moderate Carbohydrate Diet Compared to a Very Low Carbohydrate Diet in Overweight or Obese Individuals with Type 2 Diabetes Mellitus or Prediabetes. PLoS One. 2014.</p> <p>Evert AB et al. Nutrition Therapy for Adults with Diabetes or Prediabetes: A Consensus Report. Diabetes Care. 2019.</p> <p>McKenzie LA et al. A Novel Intervention Including Individualized Nutritional Recommendations Reduces Hemoglobin A1c Level, Medication Use, and Weight in Type 2 Diabetes. JMIR Diabetes. 2017.</p>	
5.9	T Williams	Extremely disappointed that you chose to omit the extensive analysis available from primary care cases; as a statistician I do not agree with your reasoning for this. In doing so you have weakened the case for supporting low carbohydrate diets and omitted longer-term case studies that help to disprove the extremely weak evidence, mainly supposition, about adverse effects.	<p>Reasons for excluding clinical practice studies are explained in paragraphs 5.9 to 5.10.</p> <p>It was agreed to amend these paragraphs to summarise direction of the evidence from these studies and to expand explanation of why they were not included for consideration in the report.</p>
5.9-5.10	X-pert Health	1) As per our comments on paragraphs 5.1/5.2, we disagree with the decision to not include studies of this nature as they provide an important insight into the possible efficacy and effectiveness of low carbohydrate dietary approaches. When considered alongside meta-analyses of RCTs they provide value and help to address some of the	1) Reasons for excluding clinical practice studies are explained in paragraphs 5.9 to 5.10. It was agreed to amend these

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>gaps and limitations with the body of research that was included in the current review. Again, the SACN evidence grading criteria allows for consideration of such research – thus the decision to exclude it can be questioned.</p> <p>2) Future SACN reports should perhaps consider a consultation phase on the scoping of questions and the setting of inclusion/exclusion criteria to reduce issues of this nature, which are likely to be raised by a number of respondents during the consultation period.</p>	<p>paragraphs to summarise direction of the evidence from these studies and to expand the explanation of why they were not included for consideration.</p> <p>2) SACN has now agreed to include public consultations on the scope of future reviews and this was done for the most recent nutritional and maternal health review.</p>
5.10	T Williams	<p>I would hope that as a minimum your conclusions point to the weakness resulting from the restrictive inclusion criteria. The use of n=1 case studies may be inappropriate but exclusion of the extensive case studies analyses by Unwin, etc. is indefensible. Selecting the single case study while ignoring published research that included larger populations makes analyses appear biased. You have taken a much strict line on the positive evidence while including unevidenced or weakly evidenced negative lines.</p>	<p>Reasons for excluding clinical practice studies are explained in paragraphs 5.9 to 5.10. It was agreed to amend these paragraphs to summarise direction of the evidence from these studies and to expand the explanation of why they were not included for consideration</p>
5.14	Netherlands Health Council	<p>It is not clear which documents you refer to; the description is quite broad. Could you specify to certain categories and/or give examples?</p>	<p>Agreed to clarify text.</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
5.18-5.26 Fig 5.1	Netherlands Health Council	It is quite challenging to rebuild figure 5.1 based on text provided in paragraphs 5.18 to 5.25. It required additional calculations to come from the numbers provided in text to the numbers in the figure. We believe this is particularly due to the differences in order of presentation of numbers in text and figure. It would be helpful to get a more direct explanation of how the numbers in the figure were derived.	Agreed to clarify text.
5.24	X-pert Health	<ol style="list-style-type: none"> <li>1) As the McArdle SR and Saslow et al, 2017 were identified before end of the call for evidence the decision to omit them from the review appears to be unwarranted, and any consideration “post-consultation” raises some concerns as there will be no opportunity for stakeholders to provide feedback</li> <li>2) It should be acknowledged that although data from Tay et al, 2018 were included in the van Zuuren SR/MA the paper was not referenced in the main paper (it was only mentioned explicitly in the supplementary material), to avoid any confusion amongst individuals seeking to follow up on the evidence and references used within the SACN review.</li> </ol>	<ol style="list-style-type: none"> <li>1) McArdle et al (2019) was not identified before the end of call for evidence (7/3/18) but after the cut-off date for consideration of evidence (30/9/18). Findings from McArdle et al (2019) will be considered. Saslow et al (2017) is included in by McArdle et al (2019) and van Zuuren et al (2018).</li> <li>2) Tay et al (2018) (which reports outcomes at 2 years) was included in meta-analyses in van Zuuren et al (2018) but was wrongly referenced as Tay et al (2014) (which reports outcomes at 24 weeks).</li> </ol>

Paragraph	Organisation/ Individual	Comments	SACN reply
5.32	X-pert Health	<p>A large number of the publications (15 RCTs) referred to in paragraph 5.28 do not appear at all in Annex 6. It may be helpful to the reader to clarify what these other studies looked at, and/or to clarify the reason(s) for their omissions.</p>	<p>Paragraph 5.28 explains that there were 48 publications relating to 44 RCTs in 8 systematic reviews with meta-analyses that were eligible for inclusion. A summary of all 48 publications is included in Annex 5.</p> <p>Annex 6 shows the overlap in primary RCTs included in the meta-analyses of the 8 eligible systematic reviews, for each outcome. There are fewer RCTs here because not all RCTs were included in the meta-analyses.</p>
5.38	DSG-BDA	<p>Definitions do not come until p30. Terminology of what is meant by lower and higher needs to be clearer. Also state recommendations for defining carbohydrate intakes and how research and practice (including service evaluation) may be able to measure and report on carbohydrate intake in future.</p> <p>Including such definitions in the glossary would be helpful as would consideration whether percentage energy, amount or reduction from usual intake is important, especially considering the role of energy restriction and weight loss in influencing improvements in glycaemic control.</p>	<p>Agreed to check and amend text for clarity.</p> <p>Agreed to add definitions of 'lower' and 'higher' carbohydrate diets in glossary.</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
5.40	X-pert Health	Closed bracket missing from end of first sentence.	To be corrected.
5.47	Netherlands Health Council	Why were 2 evaluation frameworks used? How do these complement each other?	<p>SACN's Framework for the Evaluation of Evidence (SACN, 2012) was used as the basis for assessing the quality of the evidence.</p> <p>This was complemented with the use of AMSTAR 2 which is a tool specifically for assessment of systematic reviews.</p> <p>Use of both evaluation frameworks was considered to be appropriate.</p>
5.62	Netherlands Health Council	<p>Would be helpful to get more insight in how the risk of bias of the individual RCTs was taken into account in the grading of the evidence. This currently is not fully clear to us. To illustrate: In Table 5.3 it is explained that the identified publications should be of good quality in order to provide adequate evidence. The evidence for effects on body weight and HbA1c (in shorter term and at <math>\geq 24</math> months) were graded as adequate, whereas it was noted that the individual RCTs contributing to this evidence often have a high or unclear risk of bias. This seems not fully in line with the explanation in Table 5.3.</p>	<p>Grading of the evidence was based on the criteria outlined in Table 5.3.</p> <p>Paragraph 5.62 describes how risk of bias was taken into account when grading the evidence. Risk of bias also informed discussion and expert judgement made by WG</p>



Paragraph	Organisation/ Individual	Comments	SACN reply
			members in grading the evidence.
Table 5.3	Netherlands Health Council	<p>Questions regarding explanatory notes:</p> <ol style="list-style-type: none"> <li>1) When MAs convincingly show ‘no difference in effect’, could this also be considered adequate evidence of no effect? This is currently not included in the explanatory notes of the category ‘adequate’.</li> <li>2) What are the definitions of ‘good’, ‘moderate’ and ‘poor’ quality? What exactly are the ‘key factors’ referred to in this regard? It would be helpful if you could clarify and/or quantify the considerations regarding those key factors to separate good from moderate and poor quality?</li> <li>3) What is considered an ‘adequate size’? It would be helpful if you could address this.</li> </ol>	<p>1) Evidence of ‘no difference in effect’ between intervention groups could not be considered as evidence of ‘no effect’.</p> <p>2) &amp; 3) The approach is based on that used in previous SACN reports (see paragraph 5.58) and explained in table 5.3. Criteria outlined in this table informed discussions and qualitative expert judgements made by the WG members.</p> <p>These comments will be taken into account when SACN review the terminology used to describe the quality of the evidence and the grading criteria.</p>

**Table 7: Specific comments on chapter 6. Assessment of the evidence** (pages 38-73)

Paragraph	Organisation/ Individual	Comments	SACN reply
n/a	HEART UK	Primary outcomes section: When comparing outcomes between ‘lower’ and ‘higher’ carbohydrate intakes it would make it clearer if these intakes were quantified or classified. Currently it is unclear what amounts are being compared.	The terms ‘lower’ and ‘higher’ were used because definitions of ‘low’ and ‘high’ ‘carbohydrate intakes varied across studies. It was not possible to quantify them because of the variation.
6.1	DSG-BDA	Missing reference: McArdle et al (2019) <a href="https://onlinelibrary.wiley.com/doi/abs/10.1111/dme.13862">https://onlinelibrary.wiley.com/doi/abs/10.1111/dme.13862</a> sought to consider effect of the quantity of carbohydrate consumed and its effect on outcomes. Perhaps this should have been considered more clearly in the evidence review.	McArdle et al (2019) was not included in draft report because it was identified after the cut-off date for consideration of evidence (September 2018). The report explains that any evidence highlighted through consultation process or published after September 2018 will be considered by the committee (paragraph 5.16).
6.2	X-pert Health	Not a bad thing that Iqbal et al (2010) was omitted, as there were no statistically significant differences in macronutrient intake between the arms of the study at any time point (and carbohydrate intake was actually slightly higher in the low carb group at multiple time points). This should perhaps be stated to make it clear that this will not prejudice the outcomes in any way.	Noted.

Paragraph	Organisation/ Individual	Comments	SACN reply
6.4	X-pert Health	Based on this, which would have been apparent from the outset, it can be questioned why it was ever decided to permit the inclusion of this study? This essentially constitutes a change in review protocol.	The RCT by Iqbal et al (2010) was included in 3 of the 8 eligible SRs with MAs. It was not included in the 4 prioritised SRs with MAs that informed the conclusions and grading of the outcomes. This is explained in paragraph 6.2.
6.6	X-pert Health	Should acknowledge that all 4 prioritised SRs [systematic reviews] considered medication changes, even if they were not stated as outcomes.	It was agreed to amend paragraph 6.6 to acknowledge that all 4 prioritised systematic reviews considered changes in medication use although only 1 considered medication change as an outcome.
Table 6.1	Dr Z Harcombe	<p><u>Relating to flaw 3</u> (the decision to not study low carbohydrate diets)</p> <p>Table 6.1 summarised the “carbohydrate intake comparisons” in the 4 studies forming the entire basis for the SACN draft report.</p> <p>Huntriss et al (2018) – “low carb diet must have achieved lower carbohydrate intake than the control group.” (That was it – just lower – no amount specified).</p> <p>Korsmo-Haugen et al (2018) – “Diet &lt;40% TE versus diet &gt;40% TE from carbohydrates.”</p> <p>Sainsbury et al (2018) – “Diet ≤45% TE versus diet &gt;45% TE from carbohydrates.”</p> <p>Van Zuuren et al (2018) – “Diet ≤40% TE from carbohydrates versus low fat diet (≤30% TE).”</p>	Paragraph 5.39 explains that carbohydrate comparisons in the report were between ‘lower’ and ‘higher’ carbohydrate intakes because definitions of a ‘low’ carbohydrate diets varied across studies.

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>LowER carbohydrate really does simply mean just lowER in carbohydrate than the other diet. Below 45% vs above 45% of carbohydrate intake. That's all it needs to mean. The entire review is nonsensical. This was reported as a limitation of the SACN review (para 6.62). It should have been reported as a fatal flaw.</p> <p>Notwithstanding that low carbohydrate diets were not studied, lowER carbohydrate diets performed better in the significant findings (HbA1c at 3 &amp; 6m; fasting plasma glucose, 3 to <math>\leq</math>12m; triacylglycerol, 3 to <math>\leq</math>12m):</p>	
6.28	X-pert Health	<p>Paragraph 6.2 states that there is only 1 RCT included in the initially identified reviews that was not included in the 4 prioritised reviews, but there were previously 48 studies listed and now there are only 32. The reasons for this should be clarified. Further, is there any value on focusing on these 32 RCTs instead of the 48 initially included? There does not appear to be any real justification for omitting the additional trials – though the RCTs do not appear to have been used in any meaningful way in subsequent analyses, despite this data extraction having been undertaken.</p>	<p>It was agreed to amend paragraphs 6.26 to 6.28 to clarify that there were 31 RCTs in the <u>meta-analyses</u> of the 4 prioritised systematic reviews. There were 48 publications (relating to 44 RCTs) in the 8 eligible systematic reviews but these were not all included in the meta-analyses of the 4 prioritised systematic reviews. It was agreed to check the text for clarity and to include a flow diagram of the process.</p>
6.35-6.37	X-pert Health	<p>Why is there not a summary of outcomes for this section comparable to that in the preceding “Loss to follow up” section? The information presented in this section is largely redundant without a comparison between groups, considering differences at baseline as well as any differences in the change in medication use during the</p>	<p>This was omitted by mistake. It was agreed to amend text to include this information.</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
		studies. This is a key outcome, thus the failure to appraise this evidence fully is a major omission	
6.36 6.38	Netherlands Health Council	In 6.36 it is stated that <b>3</b> RCTs included only newly diagnosed T2D individuals. In 6.38 it is stated that <b>2</b> RCTs reported study participants were newly diagnosed with T2D. This seems inconsistent.	It was agreed to check and amend text accordingly.
6.42	Netherlands Health Council	It is stated that few studies reported carbohydrate quality as part of the advice. Based on the explanation written in this paragraph, we count that 15 RCTs reported on carbohydrate quality, of which 9 reported to promoted low-GI foods. Is that correct? If yes, we do not fully agree that few RCTs reported on carbohydrate quality; it is almost half of the RCTs.	The RCTs mentioned in paragraph 6.42 advised on aspects of carbohydrate type rather than providing comprehensive advice. Agreed to amend text to improve clarity.
6.42 6.73 6.44-6.51	Netherlands Health Council	<ol style="list-style-type: none"> <li>1) What is the difference between carbohydrate type (p. 6.73) and quality (p. 6.42)?</li> <li>2) Given that type/quality of carbohydrates may be important drivers of the effects of lower carbohydrate diets, it would be helpful to get more detailed information about the quality and types of carbohydrates of the diets in the individual RCTs. More specifically, it would be relevant to know whether the prescriptions on type/quality of carbohydrates were given to both groups or only to the lower carbohydrate groups (paragraphs 6.42 and 6.73). Also, it would be helpful if carbohydrate quality/types could be quantified in the prescribed and achieved diets (p 6.44 to 6.51).</li> </ol>	<ol style="list-style-type: none"> <li>1) Noted that publications use both terms. Agreed to explain this in the text but to use the term 'type' rather than 'quality' in report.</li> <li>2) Details on carbohydrate type in the primary RCTs were limited as explained in paragraph 6.73. Information on the dietary approach taken by individual RCTs is provided in Annex 5 (Table A5.3).</li> </ol>

Paragraph	Organisation/ Individual	Comments	SACN reply
6.44-6.61	DSG-BDA	<p>Macronutrient &amp; energy intakes:</p> <p>Often there is inadequate consideration of low carbohydrate intakes in an isocaloric diet. As by its nature a carbohydrate reduced diet tends to be hypocaloric. This is an important consideration and the effect of low carbohydrate diets on glycaemic control and cardiovascular risk in weight stable individuals needs further consideration.</p> <p>The methodology used in development of the report was based upon systematic reviews of RCTs which by their nature compared a target amount of carbohydrate against another. The report rightly acknowledges that this was rarely achieved. It is a risk that levels of carbohydrate intake which are often poorly reported and measured in studies can mean that there is considerable overlap or at least a relatively small difference between groups with respect to carbohydrate intake.</p> <p>There needs to be a clearer definition of low and in this case lower carbohydrate. There is debate where a percentage energy is the most appropriate method or whether an absolute amount is preferable. More research is required to inform practice.</p> <p>The focus on lower carbohydrate, needs to consider the impact of overall dietary pattern and intake. This extends beyond energy intake to include nutrient and non-nutrient factors as well as the socio-economic influences of food intake and culture. Therefore recommendations should be framed in one which supports long term maintenance of behaviour change as the data suggests little difference beyond 12 months.</p> <p>The focus on low which has moved to lower, which is hard to define appears to ignore the level of reduction achieved in studies and it is plausible that the</p>	<p>Noted. These comments will be considered in formulating recommendations and research recommendations.</p> <p>Report notes that carbohydrate intakes are expressed in absolute amounts or as % of total energy intake and acknowledges that categories of carbohydrate intake can vary according to how they are expressed (see paragraph 5.43).</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
		reduction from previous intake could be as important as the intake achieved at the end of studies.	
6.44-6.61	OG-BDA	<p>Quantity of carbohydrate intake is clearly an issue in studies of this type since prescribed and achieved carbohydrate intakes in both short and longer term studies do not equate. Studies included in this review primarily compared moderate rather than low carbohydrate intakes with higher carbohydrate intakes, with considerable overlap between low, moderate and high intakes, and heterogeneity of quantities consumed within each category. This makes the effect of low carbohydrate diets hard to ascertain with any certainty.</p> <p>Lower carbohydrate diets resulted in higher intakes of protein and fat including total and saturated fat intakes. While considerable heterogeneity of intake was seen, poorly controlled diabetes is a risk factor for increased CVD risk (for which higher fat intakes are also a risk factor). The question of what carbohydrate is replaced with in low carbohydrate groups is of great importance.</p> <p>Despite this, no differences in either total serum cholesterol or serum LDL cholesterol between low and high intake groups were seen either in the short term (3 - &lt;12m; moderate and adequate evidence respectively) or longer term (<math>\geq</math>12m; adequate evidence). However lower serum triglyceride concentrations were lower in lower carbohydrate compared to higher intake groups in shorter term studies (3 - &lt;12m; adequate evidence), although no consistent effect was seen in studies <math>\geq</math>12m. Inconsistent effects were found for serum HDL levels in both short and longer term studies for lower compared with higher carbohydrate intakes.</p>	Noted and agreed.
6.44-6.61	X-pert Health	There is no consideration of diet quality. Although this may not have been possible in any meaningful way, this limitation should be acknowledged.	The limitations section notes that studies did not consider type of

Paragraph	Organisation/ Individual	Comments	SACN reply
			carbohydrate (paragraph 6.73), the potential impact of increasing proportions of other macronutrients to compensate for reduced carbohydrate intake and the wide variety of comparator diets.
6.46	X-pert Health	If carbohydrate intake was not reported for 5 of the RCTs they should perhaps have been omitted	The primary RCTs were not assessed separately. Since they were included in the meta-analyses of the 4 prioritised systematic reviews, it was not possible to omit them.
6.55-6.57 Table 6.2	X-pert Health	It would have been more informative to report the protein intake in absolute terms alongside the relative terms presented. The protein leverage hypothesis posits that individuals will continue to seek food until they have met their protein requirement (in absolute terms) and so differences in the relative proportion of protein in diets may help to explain any differences in total ad libitum energy consumption during a day (i.e. if the diet has a higher proportion of protein in it then the protein requirement for the day would be met earlier and with a lower total energy intake).	Detailed consideration of protein intakes was outside the scope of this report.
6.58-6.61 Table 6.2	X-pert Health	Consideration of energy intake should differentiate between where participants were provided with explicit targets and guidance compared to when they were instructed to consume food ad libitum. A number of studies provide specific targets to reduce energy intake to the higher carbohydrate arms whilst allowing the lower	Outside scope of report.



Paragraph	Organisation/ Individual	Comments	SACN reply
		carbohydrate arms to consume food ad libitum. This, and possible differences in hunger between people on each diet, are important factors that have not been considered.	
Table 6.3	X-pert Health	Regarding the ** footnote, it is unclear how this has been dealt with. As the lower range presented is 23 rather than 20 we assume the Wolever study has been omitted here, but as it was still included in the meta-analyses that have been considered in subsequent analyses there is no value to this. This possible limitation does not seem to have been acknowledged anywhere.	The study by Wolever et al (2008) was included in Table 6.3 because it was in 3 of the systematic reviews. It prescribed carbohydrate intakes between 20 to 25% TE (23% TE represents the average value).
6.62-6.81	Dr E Morris & Prof P Aveyard	<p>General limitations in the evidence base. Review appropriately highlights several important points:</p> <ul style="list-style-type: none"> <li>• Despite the large numbers of publications in the field, there remains limited robust evidence comparing objectively low- and high- carbohydrate diets for people with T2D. In large part due to variability in prescribed (and achieved) carbohydrate proportions (and absolute amounts consumed) in the studied diets. Most comparisons were between moderate- and high carbohydrate diets, with relatively little data on very-low and low-carbohydrate diets; this limited absolute difference in intake between groups may contribute to the limited differences in outcomes seen. Improved consistency of reporting in future studies and use of the now widely accepted criteria for very low- and low-carbohydrate diets, should be encouraged.</li> <li>• The confounding effects of medication changes are highlighted here. With inconsistent and very variable reporting of medication changes throughout the</li> </ul>	Noted. These points will be taken into consideration when formulating research recommendations.

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>studies, it is impossible to assess the impact of either the different diets, or potential reduction in medications, on glycaemic control.</p> <ul style="list-style-type: none"> <li>• There is a paucity of research in ethnic groups other than white populations; and in people with T2D but without overweight or obesity (who make up a small, but significant, proportion of people with T2D), limiting the application and generalisability of these conclusions in routine care settings.</li> </ul>	
6.65-6.68	HEART UK	<p>Include additional point to provide context. In addition to the heterogeneity of the diets, due to the lack of information on carbohydrate and fat quality, food sources of protein and the wide overlap of fat and saturated fat in both low and high carbohydrate groups, it is not possible to draw conclusions on the impact of diet on lipids.</p>	Noted. Will consider this point when finalising conclusions of report.
6.65-6.68	OG-BDA	<p>Many of the difficulties inherent in dietary studies are evident in this review. Differences between intakes prescribed and achieved, lack of clarity about what a low carbohydrate diet actually comprises and difficulties in comparing the effects of studies which had variable approaches and differing levels of dietary adherence were all issues. In addition, blinding to the diet group was not possible and intakes were self-reported with possible under-reporting as a consequence (whether any such under-reporting was systematic by type of diet is unclear).</p>	Noted and agreed.
6.66	X-pert Health	<p>Without evidencing this statement it is simply conjecture and is inappropriate. In an analysis we have previously undertaken (limited to RCTs with greater than 50 participants and that lasted for at least 3 months – in line with previous NICE criteria for evidence inclusion - and where the low carbohydrate group were consuming less than 130g/day or 26% total energy from carbohydrate) there was</p>	Agreed to amend as follows: The majority of primary RCTs were of dietary advice rather than feeding studies so adherence may have been challenging.

Paragraph	Organisation/ Individual	Comments	SACN reply
		little difference in adherence between groups; thus we do not feel this statement is supported by the available evidence.	
6.69-6.71	OG-BDA	Whether or not actual carbohydrate intakes achieved were actually low depended on how they were expressed i.e. whether they were expressed as quantities per day or as a % of energy intake. Where energy intakes were restricted a carbohydrate intake which appeared low (expressed in quantities consumed per day) was actually moderate (expressed as % energy intake) in some studies included. This makes the actual effect of carbohydrate restriction hard to ascertain.	Noted and agreed.
6.73	OG-BDA	From a nutritional and health perspective, the quality of carbohydrate consumed is of relevance particularly for those living with diabetes. However, most of the studies included did not consider quality, focusing solely on the quantity of carbohydrate consumed. From a metabolic perspective the type of carbohydrate consumed would be expected to impact upon metabolic indicators.	Noted and agreed.
6.75	X-pert Health	A large number of comparison groups provided guidance in line with current UK dietary guidance, thus it is questionable whether last sentence of this paragraph is justified. Further, as data were extracted for all the RCTs included in the systematic reviews/meta-analyses why were further analyses not performed to assess this issue if it was deemed the systematic reviews/ meta-analyses themselves were not able to answer this question (which was the purpose of the review).	Assessment was based on the published systematic reviews and meta-analyses.
6.77	Netherlands Health Council	"In relation to blood lipids, ... to lower lipids". Not immediately clear how this could confound the impact of lower carbohydrate diets. Could you explain this further?	Since statins are prescribed to lower LDL cholesterol it is not clear if any change is due to diet or cholesterol

Paragraph	Organisation/ Individual	Comments	SACN reply
			lowering medication. It was agreed to replace 'confounded' with 'affected'.
6.77	X-pert Health	Fully agree with this paragraph though do not believe that this is an issue that has been fairly and adequately considered subsequently.	Noted.
6.78	OG-BDA	The effect of lower carbohydrate intakes on body weight independent of calorie intake is hard to ascertain since similar energy intakes were achieved in both low and high carbohydrate groups; there is considerable overlap in energy intakes between them.	Noted and agreed.
6.78	X-pert Health	Debatable whether the reasons for any improvements matters, the key point is the efficacy and effectiveness of the intervention – not the mechanisms. We therefore question the inclusion of this as an issue.	Disagree. This was included because it was considered an important point.
6.79	X-pert Health	The issues presented in this paragraph are also true for higher carbohydrate arms of studies but are presented as a limitation that favours the lower carbohydrate arms. This is unfair and suggests a bias against low carbohydrate diets.	It was agreed to amend sentence to 'it could over-estimate the effects of the diets'.
6.81	OG-BDA	Generalisability of studies is an issue since the effects of dietary change may vary by ethnicity and weight status at study commencement.	Noted and agreed.
6.81	OG-BDA	People First language should be used in this paragraph.	Agreed.

Paragraph	Organisation/ Individual	Comments	SACN reply
6.81 7.29 7.61	X-pert Health	<p>Paragraph 6.29 states that in the 10 RCTs that reported ethnicity, the average number of white participants was 48.3% (range 14 to 75%). This is not consistent with the statement that the majority of participants were white.</p> <p>That the majority of participants were overweight or obese is not a limitation in a review regarding effects of an intervention for people with T2D as this is a fair representation of the population of people with T2D.</p>	It was agreed to check the wording of this paragraph.
6.85	X-pert Health	<p>Failure to consider within-group analyses can be questioned. The purpose of the review is not necessarily to demonstrate the superiority of one group over another. Where there are no differences between groups, within group differences are important as they provide a picture of whether the intervention is likely to result in health improvements. The only criteria for recommending any intervention should be a) non-inferiority compared to current care guidelines, and b) evidence of likely benefit being greater than possible harm. Within-group analyses provide valuable information when considering these questions.</p>	The purpose of the review was to compare between-group differences in change from baseline for each outcome.
6.90	X-pert Health	<ol style="list-style-type: none"> <li>1) The upper bound of the confidence intervals for the 3 months results should be “-0.23”, rather than a positive value.</li> <li>2) The subgroup analyses from this SR are relevant, with a meaningful difference being observed between the low (&lt;26% TE) and high carbohydrate diets that has not been reported (WMD = -2.47kg, 95%CI -3.33 to -1.60).</li> </ol>	<ol style="list-style-type: none"> <li>1) To be corrected.</li> <li>2) Agreed to check.</li> </ol>
6.109	X-pert Health	<p>We believe that the values for low compared to high carbohydrate diets should be reported as WMD -0.36%, 95%CI -0.62 to -0.09, <math>p = 0.008</math>, <math>I^2 = 0\%</math>, 5 RCTs (based on data presented in figure 1b).</p>	To be corrected.

Paragraph	Organisation/ Individual	Comments	SACN reply
6.1156.12 7-129 6.135 6.139	OG-BDA	The effects of length of study were evident. While in short term studies (3 - <12m) significantly greater weight loss (evidence not graded), reduced fasting plasma glucose (moderate evidence) and reduced HbA <sub>1c</sub> in lower carbohydrate compared with higher carbohydrate intakes (adequate evidence) were apparent, the same was not true of longer term studies (>12m). While no difference in weight between groups was observed (adequate evidence), inconsistent results were observed for HbA <sub>1c</sub> with some studies finding a greater reduction in lower carbohydrate groups and others not. Studies followed up to 24m found no difference in HbA <sub>1c</sub> between lower and higher carbohydrate groups (adequate evidence). There was insufficient evidence for fasting plasma glucose in longer term studies (≥12m). Weight is an important potential confounder for any metabolic differences observed between groups.	Noted.
6.130 7.32	X-pert Health	Based on the analysis in its current form, we disagree (to an extent) with the classification for the evidence for studies between 12 and 24m. Although the evidence is inconsistent all analyses either favoured lower carbohydrate or found no difference. "Inconsistent" incorrectly implies, or at the very least could easily be inferred to mean that this inconsistency is across all possible outcomes. This is not true, and this should be reflected.	The criteria for the evidence grade 'inconsistent' are provided in Table 5.3.
6.1316.15 2 6.177	X-pert Health	Results from the van Zuuren meta-analyses should be included for completeness, in a similar manner to how the weight loss results of less than 12m were (though unclear why the discussion of this meta-analysis is in a separate paragraph for the triglyceride and HDL cholesterol sections but not the fasting plasma glucose section?).	Results from meta-analyses at 24m were omitted because only 2 studies were included (see Table 5.3).  Discussion of this MA is in a separate paragraph for triglyceride and HDL

Paragraph	Organisation/ Individual	Comments	SACN reply
			cholesterol because there were 2 other MAs that considered these outcomes It is not in a separate paragraph for the plasma glucose section because only van Zuuren considered this outcome.
6.163 7.39	X-pert Health	Based on the analysis in its current form, we disagree (to an extent) with the classification for the evidence for studies of longer than 12m in duration. Although the evidence is inconsistent all analyses either favoured lower carbohydrate or found no difference. “Inconsistent” incorrectly implies, or at the very least could easily be inferred to mean, that this inconsistency is across all possible outcomes. This is not true and should be reflected.	The criteria for the evidence grade ‘inconsistent’ are provided in Table 5.3.
6.1887.41 7.42	X-pert Health	Based on the analysis in its current form, we disagree (to an extent) with the classification for the evidence. Although the evidence is inconsistent all analyses either favoured lower carbohydrate or found no difference. “Inconsistent” incorrectly implies, or at the very least could easily be inferred to mean, that this inconsistency is across all possible outcomes. This is not true, and this should be reflected.	The criteria for the evidence grade ‘inconsistent’ are provided in Table 5.3.
6.1936.19 4	X-pert Health	These sections should acknowledge that all of the non-significant findings still showed greater reductions in favour of lower carbohydrate diets, thus ALL studies with relevant data favoured the lower carbohydrate arm.	Only significant findings were considered to be relevant.

Paragraph	Organisation/ Individual	Comments	SACN reply
6.198 7.44	X-pert Health	<p>Strongly disagree with the decision to not grade the evidence for medication changes. The justification provided is the absence of a meta-analysis but the grading criteria (in Table 5.3) explicitly allows for a gradation without a requirement for one. Evidence can be graded as “adequate” if “... there is convincing evidence of a consistent significant effect/association in the primary studies considered.” This is clearly the case with this outcome, as even within the single review included for this outcome ALL of the RCTs found results that favoured lower carbohydrate diets (differences that were statistically significant in 5/6 short-term studies and 4/8 longer-term studies). All other priority reviews and a number of other systematic reviews that were not included as priority reviews, considered medication changes too and universally concluded that reductions were greater with lower carbohydrate diets.</p> <p>This is a highly important issue as the decision to grade this evidence defines whether or not it is included when making the final recommendations, and the absence of this evidence prejudices low carbohydrate diets and will result in their possible benefits being underestimated (particularly as the other outcomes have not been considered in the context of medication changes, an omission that will have significant implications for HbA1c changes in particular).</p>	It was agreed to grade the evidence for change in medication use.
Table 6.4	X-pert Health	As per previous comments, the “inconsistent” findings should be qualified (“inconsistent” incorrectly implies, or at the very least could easily be inferred to mean, that this inconsistency is across all possible outcomes – whereas all outcomes favoured lower carbohydrate diets or found no difference) and we strongly disagree with the decision to not grade the evidence for medication changes.	The criteria for the evidence grade ‘inconsistent’ are provided in Table 5.3.



Paragraph	Organisation/ Individual	Comments	SACN reply
6.200 6.203 6.204 6.206	Dr Z Harcombe	<u>Relating to flaw 1</u> (conflicts of interest) - Further example of bias shown in reporting of adverse events. 2 systematic reviews/meta-analyses did not report on adverse events. 1 reported that the most serious adverse event was in the higher carbohydrate diet (para 6.200). None of the 13 primary RCTs.. which reported on adverse events reported any serious adverse events related to the diet (para 6.204). This did not stop the draft report noting “All 4 SRs with MAs observed the potential of carbohydrate-restricted diets to detrimentally impact CVD risk markers.” (para 6.203). Furthermore, despite the 4 chosen studies and 13 primary RCTs providing no evidence of harm, SACN added their own comments in a section “Potential long-term concerns.” The 1st comment in this section (para 6.206) stated “implications of long-term restriction of carbohydrates in adults with T2D are currently unknown since there is a lack of data from longer-term studies.” (See Flaw 5). The review started off with confirmation bias and thus we can have no expectation of a genuinely independent outcome.	It was agreed to delete paragraph 6.203.
6.201	Netherlands Health Council	Did the hypoglycaemic episodes appear in participants on insulin therapy?	Yes – individuals who experienced hypoglycaemic episodes were either on oral hypoglycaemic medication or insulin therapy.
6.201	X-pert Health	It is not fair to include this statement when the authors have stated that they did not systematically assess the matter. Without assessing the primary research fully there is no way to know how the rates of adverse events compared between groups, and without a full assessment this information is invalid and potentially biased.	Agreed to add paragraph to note that the 4 systematic reviews did not systematically assess adverse events.

Paragraph	Organisation/ Individual	Comments	SACN reply
6.203	X-pert Health	This statement is completely unjustified and invalid, it is purely based on conjecture which was not borne out in the outcomes (including those reported in the current review, where NONE of the included analyses demonstrated an increase in any risk factors compared to the higher carbohydrate group). This statement again implies a bias against lower carbohydrate diets and it should be removed.	It was agreed to delete paragraph 6.203.
6.204	X-pert Health	This paragraph should clarify whether there was any difference in the reported rates of these minor adverse events between diets.	This is reported in paragraph 6.205.
6.205	X-pert Health	The study cited here (which is not actually included in the reference list) should not be included. The lower carbohydrate diet in this study was in fact a very low energy diet (which you have stated in paragraph 5.44 should not be confused with a lower carbohydrate diet) using protein shakes for the first 2 phases, and as such is not a fair representation of a lower carbohydrate diet and none of the reported adverse events can be causally linked to carbohydrate restriction. This paragraph should be deleted, and its use in this manner is concerning – particularly in the light of the fact it is the only occasion in this review where a single study is used to justify a point and is used for the only graded evidence statement in the review which is negative for lower carbohydrate diets.	It was agreed to include less detail on study by Goday et al (2016). Although evidence on adverse events was not graded, agreed that use of the words ‘limited evidence’ in paragraph 6.210 could give impression that it was. It was agreed to delete this paragraph.
6.206 -208 7.63	Dr M Robinson	Long term low-carbohydrate diets increase mortality. Several large cohort studies in N America and Europe report increased mortality with low carbohydrate intake (Mazidi et al, 2019; Lagiou et al, 2007; Li et al, 2014; Nilsson et al, 2012; Trichopoulou et al 2007; Noto et al, 2013).	Consideration of observational data on long-term implications of low-carbohydrate diets was outside the scope of the review. In addition, much of the longitudinal evidence is

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>Some studies have analysed the source of protein and reported that low carbohydrate intake is associated with increased mortality, but only if the carbohydrate is replaced with animal sources of protein and fat. If carbohydrate is replaced with plant-based sources there is a reduced mortality (Fung et al, 2010; Seidelmann et al, 2018).</p> <p><u>References:</u>  Mazidi et al. Lower carbohydrate diets and all-cause and cause-specific mortality: a population-based cohort study and pooling of prospective studies. <i>Eur Heart J.</i> 2019;40:2870–2879.  Lagiou et al. Low carbohydrate-high protein diet and mortality in a cohort of Swedish women. <i>J Intern Med</i> 2007; 261: 366–74.  Li et al. Low carbohydrate diet from plant or animal sources and mortality among myocardial infarction survivors. <i>J Am Heart Assoc</i> 2014;3:e001169.  Nilsson et al. Low-carbohydrate, high-protein score and mortality in a northern Swedish population-based cohort. <i>Eur J Clin Nutr</i> 2012; 66: 694–700.  Trichopoulou et al. Low-carbohydrate-high-protein diet and long-term survival in a general population cohort. <i>Eur J Clin Nutr</i> 2007; 61: 575–81.  Noto et al. Low-carbohydrate diets and all-cause mortality: a systematic review and meta-analysis of observational studies. <i>PLoS One</i> 2013; 8: e55030.  Fung et al. Low-carbohydrate diets and all-cause and cause-specific mortality: two cohort studies. <i>Ann Intern Med</i> 2010; 153: 289–98.  Seidelmann et al. Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. <i>Lancet Public Health.</i> 2018;3(9):e419–e428.  doi:10.1016/S2468-2667(18)30135-X</p>	<p>in general populations rather than on people living with T2D</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
6.206	HEART UK	As described in the general comments, there is observational data suggesting an association between low carbohydrate diets and long term outcomes. This should be included here.	As above.
6.206 6.211	X-pert Health	This statement should acknowledge that this is true for all dietary approaches, as there is an absence of high quality, long-term studies of any way of eating. It is unfair to expect lower carbohydrate diets to clear a higher barrier than other diets can, or to include caveats when discussing lower carbohydrate diets which are rarely, if ever, used for other diets.	Amendments to these paragraphs were agreed.
6.206-208	OG-BDA	Unclear from data presented, whether lower carbohydrate intakes are associated with adverse effects although many potential adverse effects have been identified. It does not appear that lower carbohydrate diets are specifically beneficial for those with T2D, albeit several limitations to the data have been identified. Only fasting plasma glucose, HbA <sub>1c</sub> and serum triglyceride were lower in the short term (3 - <12m) in lower intake compared with higher intake groups, however this was not shown in the longer term (≥12m). Whether these were due to weight differences or lower carbohydrate intakes per se is unclear since weight loss was a primary outcome for many of the primary studies included and is a potential confounder. Differences in body weight between lower and higher carbohydrate groups were not seen in longer term studies although they were reported in the shorter term studies (evidence not graded). On the other hand adverse effects from following a lower carbohydrate diet were also not shown, although following a very low carbohydrate intake (20-50g/day; <10% total energy) resulted in some adverse effects.	Amendments to these paragraphs were agreed.

Paragraph	Organisation/ Individual	Comments	SACN reply
6.207	HEART UK	<p>This is a misleading statement: As there was considerable overlap of total and saturated fat in both the higher and lower carbohydrate diets, total and saturated fat intakes were above government recommendations in both diets not just lower carbohydrate diets. At the upper end, both diets had total and saturated fat intakes greater than the government recommendations. At the lower end, both groups were below or within the recommendations. This, and the other dietary factors already alluded to make it impossible to draw conclusions on the impact of diet on lipids.</p> <p>The 2nd sentence implies that the dietary findings are related to the surrogate markers of CVD risk. This should be reworded, for the reasons above, but also earlier in the report it was highlighted that increasing the proportion of other macronutrients on markers and clinical outcomes was generally not considered. Furthermore, the impact of medication and weight could have also influenced these results.</p>	Agreed to consider the wording of this paragraph.
6.208	HEART UK	<p>Additional paper to consider on nutritional deficiencies.</p> <p><u>Reference</u>: Elidottir et al. (2016) Dietary intake and cardiovascular risk factors in Icelanders following voluntarily a low carbohydrate diet. PLoS One 11, e0156655</p>	Noted.
6.208 7.49	X-pert Health	<p>Reference used in paragraph 6.208 is inappropriate, as this review found no cases of nutrition deficiencies and didn't even look at fibre. The overall statement in both 6.208 and 7.49 is purely conjectural and without adequate evidence being presented it should not be included. If fibre intake was deemed to be an issue of concern, why was this data not extracted from the primary RCTs included in the identified systematic reviews and meta-analyses for analysis? Further, it is unclear</p>	Agreed to delete this paragraph.

Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>why it is deemed acceptable to introduce sources of evidence outside of those identified through the stated search and inclusion criteria for this purpose when other evidence sources that may favour lower carbohydrate diets have not been permitted. The decision made here again appears to be biased against lower carbohydrate diets.</p>	
6.210	X-pert Health	<p>This statement appears to be based on a single study. Beyond the fact the study used (Goday et al, 2016) should not have been included in the review anyway (see comment pertaining to paragraph 6.205), the criteria for grading evidence set out in Table 5.3 does not allow for a gradation above “Insufficient” when there are “&lt;3-4 eligible randomise control trials”.</p> <p>The decision to award this statement a grade when changes in medication were not graded (despite data being available from 6 shorter-term and 8 longer-term RCTs) appears inconsistent, and bias against lower carbohydrate diets (i.e. RCTs have been used to grade inconsistent evidence which is negative for lower carbohydrate diets but have not been used despite more, and more consistent, evidence when it favoured lower carbohydrate diets).</p>	<p>To note, evidence referred to in this paragraph was not graded but it was agreed to delete this paragraph.</p>

**Table 8: Specific comments on chapter 7. Overall summary and conclusions** (pages 74-83)

Paragraph	Organisation/ Individual	Comments	SACN reply
n/a	DSG-BDA	<p>There does not seem to be clear case based on the evidence to either recommend for or against the use of lower carbohydrate diets in the management of T2D. It is therefore logical that both should be supported depending on the individual's preferences, culture and other health needs (a point which is key to the BDA statement on low carbohydrate diets (<a href="https://www.bda.uk.com/resource/low-carbohydrate-diets-for-the-management-of-type-2-diabetes-in-adults.html">https://www.bda.uk.com/resource/low-carbohydrate-diets-for-the-management-of-type-2-diabetes-in-adults.html</a>) and the Diabetes UK Nutritional Guidelines (<a href="https://diabetes-resources-production.s3.eu-west-1.amazonaws.com/resources-s3/2018-03/1373_Nutrition%20guidelines_0.pdf">https://diabetes-resources-production.s3.eu-west-1.amazonaws.com/resources-s3/2018-03/1373_Nutrition%20guidelines_0.pdf</a>) both published in 2018). As supporting the person living with diabetes to manage their dietary intake in a sustainable way for them, although not specific to lower carbohydrate diets, systematic review evidence supports the important role of the dietitian in achieving this <a href="https://academic.oup.com/ajcn/article/106/6/1394/4823147">https://academic.oup.com/ajcn/article/106/6/1394/4823147</a></p> <p>The influence and potentially the importance of weight loss in improving glycaemic control and potentially inducing remission of T2D needs to be considered as a primary goal given the majority of individuals with T2D are overweight or obese. How a reducing carbohydrate intake as part of this needs to be part of future research and considered as a personal preference of the person living with diabetes.</p>	Noted. These comments will be considered when formulating recommendations and research recommendations.
n/a	HEART UK	A large majority of the studies included in the report either have a high risk of bias or bias is unclear. It would be useful to highlight this in the general conclusions as it reduces the confidence that can be placed on the findings.	Agreed.

Paragraph	Organisation/ Individual	Comments	SACN reply
n/a	OG-BDA	<p>Based on this evidence there does not appear to be a clear reason either to recommend lower carbohydrate diets for those with T2D or to advise against them. Where individuals wish to follow them, advice should focus on the quality of the carbohydrate being consumed to ensure that adequate intakes of fruit and vegetables are achieved and that complex carbohydrates are well represented at the expense of simple carbohydrates. Based on a tailored approach and starting with the individuals' current intake, intakes of simple sugars should be reduced as a starting point if necessary. This may not necessarily result in a low carbohydrate intake but will contribute to an improved overall dietary profile.</p> <p>The majority of those diagnosed with T2D have overweight or obesity and obesity is a recognised risk factor for T2D. Any dietary approach which helps people to manage their weight is likely to benefit their diabetes. Although lower carbohydrate diets have not been shown to be superior to higher carbohydrate diets for body weight in the longer term, they may be preferred by some individuals and in that case they should be supported to achieve a healthy overall intake while aiming for a healthy weight.</p> <p>Many of the studies included did not measure low carbohydrate intake compared to high intakes; but lower compared with higher intakes. The effects are hard to ascertain given the extent of the limitations identified in the studies. Future research should address the limitations identified in this report. There is a lack of clarity about the effect of truly low carbohydrate diets in those with diabetes on body weight and metabolic measures and research is needed to clarify this. It is not clear whether the participants included in this report had longstanding diagnoses of T2D or whether it had been recently diagnosed.</p>	Noted. These comments will be considered when formulating recommendations and research recommendations.
n/a	Dr E Morris & Prof P Aveyard	This report highlights the need to achieve consistency in definitions and reporting standards. Adopting consistent definitions of very low, low, moderate and high	Noted. These comments will be considered when



Paragraph	Organisation/ Individual	Comments	SACN reply
		<p>carbohydrate diets, such as those used in this report, and quantitative reporting of medication changes throughout studies, would enable more robust comparisons and conclusions to be drawn in future reviews and reports.</p> <p>The report highlights several significant gaps in the evidence. Further research into the effects, and effectiveness, of low-carbohydrate diets for people with T2D is needed in ethnic groups other than white populations, and in those populations in whom the effects of LCDs are relatively under-researched but the burden of T2D is high (e.g. South Asian population); and in people with T2D with a normal BMI (both in the context of weight loss and weight maintenance).</p> <p>Additionally, the existing studies, and this report, cannot answer the question of whether UK government advice for people with T2D should advise them to reduce their carbohydrate intake, outside the context of weight loss and weight loss programmes. There is an important evidence gap in understanding what the optimal diet for standard “healthy eating” with T2D should be.</p> <p>This report recognises that UK and international recommendations endorse an “individualised” approach to weight loss and dietary change for people with T2D, which may include low-carbohydrate diets (as being safe and effective in the short term). There is currently little evidence to inform how a person may be assessed or supported (particularly in routine care, where 90% of the management of T2D is conducted) to determine which dietary management strategy may be most appropriate, or effective. While an “individualised” approach and patient choice fits with the UK model of patient-centred care, it is important to understand whether this approach to dietary management improves patient outcomes, and how this could be operationalised in routine consultations.</p>	<p>formulating recommendations and research recommendations.</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
n/a	Netherlands Health Council	We missed information on population characteristics in the summary. The description of macronutrient intakes is rather extensive for a summary.	Agreed to include paragraph summarising population characteristics. Agreed to make section on macronutrient intakes less detailed.
7.3	BANT	This paragraph should include an explicit statement that practice-based evidence did not meet the inclusion criteria.	Agreed to amend text to include this information.
7.49	BANT	Is there any evidence for this statement? In this context vegetables includes both low and high starch so the statement is imprecise.	Agreed to remove this statement.
7.53	HEART UK	It would be useful to have another bullet point stating there was an overlap in intakes between the high and low carbohydrate diets.	Agreed to amend text as suggested.
7.53	X-pert Health	This statement is mainly true based on decision to restrict the analyses primarily to the 4 prioritised systematic reviews and meta-analyses. By using the identified RCTs it would have been possible to perform additional analyses, even if they were limited in scope and numbers, to address the initially posed questions more specifically. This statement does not full acknowledge that, when reported carbohydrate intake was considered, none of the 4 prioritised systematic reviews and meta-analyses considered low carbohydrate diets (the mean intake in the systematic review and meta-analysis with the lowest reported intake was 31%) and that all 4 of them had an	Agreed (see above) to amend text to include point about overlap in intakes between higher and lower carbohydrate diets.

Paragraph	Organisation/ Individual	Comments	SACN reply
		overlap in the reported carbohydrate intake between the lower and higher carbohydrate groups when the ranges reported were considered.	
7.54	HEART UK	This sentence is confusing in light of the previous statement in the report... 'Comparisons were, therefore, mainly between the impact of lower and higher carbohydrate diets'. Should this read mainly between lower and moderate carbohydrate diets?	No. The sentence is correct as it stands.
7.55	HEART UK	It would be clearer, when referring to 'lower' and 'higher' carbohydrate diets if ranges of carbohydrate intakes were provided in brackets.	It was agreed not to include the ranges in brackets.
7.55	X-pert Health	<p>The longer-term outcomes for HbA1c should be summarised more specifically, to acknowledge that a number of analyses favoured lower carbohydrate diets and thus they may be superior (and, again, that no analyses favoured higher carbohydrate diets).</p> <p>Again, use of the term "inconsistent" should be qualified to reflect that this was between favouring lower carbohydrate diets and there being no difference. Without this qualification it is implied there was inconsistency across all outcomes, but no analyses favoured higher carbohydrate diets.</p> <p>Disagree with wording around medication use. the available evidence (whether you limit this to the single systematic review that included it as a stated outcome, include all 4 prioritised systematic reviews, or include all identified systematic reviews and consider the RCTs independently) is clear and consistent in favour of lower carbohydrate diets</p>	<p>This paragraph summarises whether there were significant differences between diets for each outcome,</p> <p>The term inconsistent refers to the evidence grade (criteria defined in Table 5.3)</p> <p>Agreed to grade the evidence on changes in medication use.</p>

Paragraph	Organisation/ Individual	Comments	SACN reply
7.56	X-pert Health	<ol style="list-style-type: none"> <li>1) This paragraph should state clearly that none of the findings favoured higher carbohydrate diets.</li> <li>2) This paragraph should state that the evidence demonstrates that lower carbohydrate diets appear to be at least as effective as higher carbohydrate diets, if not more so, for management of T2D; and that there was no evidence of harm (either in terms of an increased risk of adverse events or due to an increase in CVD risk factors).</li> <li>3) The statement that the long-term effects are unclear should be qualified, as per our comment on paragraph 7.55 and on earlier sections.</li> <li>4) Disagree with the conclusion that there was no difference for HDL cholesterol, as all findings either favoured lower carbohydrate diets or showed no difference.</li> </ol>	<ol style="list-style-type: none"> <li>1) Agreed not to amend the current wording of this paragraph but to add a sentence regarding the evidence on change in medication use after grading.</li> <li>2) Agreed to consider when formulating recommendations.</li> <li>3) This is a summary paragraph. The previous paragraph (7.55) includes more detail.</li> <li>4) The conclusion for evidence on HDL cholesterol (in last sentence) needs to be amended from 'no difference' to 'inconsistent' in the shorter and longer term.</li> </ol>
7.57	X-pert Health	This statement is irrelevant and should be removed. The reason for any improvement is not important in the context of whether a lower carbohydrate diet can be a suitable option for people with T2D.	It was agreed to retain this paragraph.

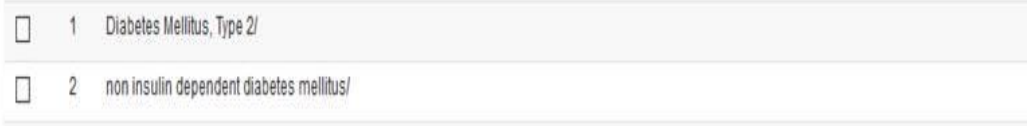
Paragraph	Organisation/ Individual	Comments	SACN reply
7.58	X-pert Health	This issue is not considered within the review so it is unusual that it appears here. Unless there is any evidence that use, or change in use, of these medications is different between diets then this point is not really relevant.	Agreed to delete this paragraph.
7.58	HEART UK	Further context required when discussing the relationship between low carbohydrate diets on lipids. As well as medication and weight loss, heterogeneity of the diets, the wide overlap of fat and saturated fat intake in both low and high carbohydrate groups, the lack of information on carbohydrate and fat quality and food sources of dietary protein, it is not possible to draw conclusions on the impact of diet on lipids.	See above.
7.60 7.63	X-pert Health	The statements made in paragraph 7.60 and last sentence of 7.63 are equally true of all diets. It is not appropriate to highlight this for low carbohydrate diets as if it is an issue that is specific to them, particularly when such qualifiers are seldom applied to other ways of eating.	Agreed to retain the existing wording in these paragraphs.
7.61	T Williams	There are case study analyses of T2D patients whose starting weight was within the normal range for BMI. Why is there no reference to these?	Case studies did not meet the inclusion criteria for the review.
7.64	BANT	If no trials included in the review provided information about the type of carbohydrate consumed, how can any conclusions be made by this WG at all?	The WG's assessment compared amounts of carbohydrates consumed (lower vs higher) rather than type of carbohydrate.

Paragraph	Organisation/ Individual	Comments	SACN reply
7.64	HEART UK	Limited RCTs on the effect of food choices/sources of protein and fat in replacing carbohydrate have been conducted. Evidence is also lacking over whether the main energy source during low carbohydrate diets should be fat or protein. Long-term, high-quality RCT of low carbohydrate diets with different food sources between animal and plants, aiming for hard clinical endpoints instead of weight loss are needed.	Noted for consideration when formulating research recommendations.

**Table 9: Comments relating to research recommendations**

Organisation/ Individual	Comments	SACN reply
BNF	<p>In order to support practical and consistent advice for people with T2D who have heard about low carbohydrate diets or may be considering following this approach we would suggest that the following should be included in the research recommendations of the report:</p> <ul style="list-style-type: none"> <li>• Further investigation of the health effects of different levels of carbohydrate restriction</li> <li>• Further investigation of potential adverse effects of low carbohydrate diets, including potential effects of higher protein intakes on kidney function.</li> <li>• Consideration of carbohydrate quality (including fibre) when looking at the health effects of diets with different levels of carbohydrate restriction.</li> <li>• Consideration of the health effects of the substitutions made when carbohydrate intake is restricted (micronutrient and macronutrient).</li> <li>• Investigation of the potential effects of lower carbohydrate diets on the gut microbiome.</li> </ul>	Noted for consideration when formulating research recommendations.

**Table 10: Comments relating to annexes**

Section	Organisation/ Individual	Comments	SACN reply
Annex 2 Table A2.1	Kleijnen Systematic Reviews	<p>Search strategy provided in Table A2.1. When you update the searches please consider using the correct Emtree term for diabetes type 2 which is <b>non insulin dependent diabetes mellitus/</b></p> <p>You have only included the MeSH subject heading which does not appear to work effectively in Embase. Please see a screenshot below showing the difference in numbers between using the term you have provided and the correct Emtree term</p>  <p>In addition, please also consider searching CENTRAL as part of The Cochrane Library as this may give additional references which are not on Medline or Embase.</p>	Noted for future reference.
Table A2.1	S Parikh	Details of literature search: This could have included vegetarian, vegan and plant based diets as these are generally high carbohydrate diets which are low in fat and some of them would have comparisons with conventional diets which are higher in fat intake which would allow for some comparisons.	Consideration of such diets were outside scope of review.



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