

**Consultation on the draft report:**

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

**Comments Form**

<b>Organisation</b>	HEART UK
<b>Name of commentator and contact details</b>	Lynne Garton, Dietetic Adviser

- Please do not PDF the form.
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- Please list any references in full that you wish the committee to consider.
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- Closing date: 9:30am 30 April 2020

General comments	Comments
	Please insert each new comment in a new row
<i>Overall feedback</i>	HEART UK welcomes the opportunity to comment on this report. The comments mainly relate to the findings on lipids as a secondary outcome of low carbohydrate diets in Type 2 Diabetes (T2D).
<i>General format</i>	It would be useful to have the overall conclusions, recommendations and research recommendations at the beginning of the report, comparable to the report on Saturated Fat
<i>Why was only RCT data considered given the limitation of these for nutritional recommendations</i>	<p>Although the report is comprehensive, we are disappointed that it 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 the clinical outcomes such as micro and macrovascular complications of T2D, CVD, mortality and long-term safety.</p> <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 cardiovascular mortality. The Atherosclerosis Risk in Communities Study found a U-shaped association between carbohydrate intake (% energy) and all-cause mortality, with the 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 mortality and an 8% increased risk of cancer death in associations with low carbohydrate dietary pattern (comparing between extreme quartiles, adjusted for BMI).</p> <p>We believe 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><b>References</b></p> <ul style="list-style-type: none"> <li>• Lagiou, P, Sandin, S, Weiderpass, E et al. (2007) Low carbohydrate-high protein diet and mortality in a cohort of Swedish women. J Intern Med 261, 366–374</li> </ul>

	<ul style="list-style-type: none"> <li>• Trichopoulou, A, Psaltopoulou, T, Orfanos, P et al. (2007) Low-carbohydrate-high-protein diet and long-term survival in a general population cohort. Eur J Clin Nutr 61, 575–581</li> <li>• Fung, TT, van Dam, RM, Hankinson, SE et al. (2010) Low-carbohydrate diets and all-cause and cause-specific mortality: two cohort studies. Ann Intern Med 153, 289–298</li> <li>• Sjogren, P, Becker, W, Warensjo, E et al. (2010) Mediterranean and carbohydrate-restricted diets and mortality among elderly men: a cohort study in Sweden. Am J Clin Nutr 92, 967–974.</li> <li>• Nilsson, LM, Winkvist, A, Eliasson, M et al. (2012) Low-carbohydrate, high-protein score and mortality in a northern Swedish population-based cohort. Eur J Clin Nutr 66, 694–700.</li> <li>• Noto, H, Goto, A, Tsujimoto, T et al. (2013) Low-carbohydrate diets and all-cause mortality: a systematic review and meta-analysis of observational studies. PLoS One 8, e55030.</li> <li>• Seidelmann, SB, Claggett, B, Cheng, S et al. (2018) Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. Lancet Public Health 3, e419–e428.</li> <li>• Dehghan, M, Mente, A, Zhang, X 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. Lancet 390, 2050–2062.</li> </ul>
<p><i>Why were studies comparing dietary patterns not included?</i></p>	<p>As described in the previous comment, in order to get a complete picture of the impact of low carbohydrate diets in T2D, we believe the totality of evidence needs to be assessed which includes studies examining dietary patterns.</p> <p>Recent network meta-analyses compared the impact of different dietary approaches in clinical trials on glycaemic control (primary outcome was HbA1c; n = 56; 4937 participants) and blood lipids (n = 52; 5360 participants) in patients with T2D. The meta-analyses examining blood lipids found that moderate-carbohydrate and vegan/vegetarian diets were more effective at reducing LDL-C 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-C. The Mediterranean and low-carbohydrate diets significantly reduced TG levels compared with low-fat and control diets.</p> <p>We believe this context should be included in the report.</p> <p><b>References:</b></p> <ul style="list-style-type: none"> <li>• Schwingshackl, L., Chaimani, A., Hoffmann, G., Schwedhelm, C., and Boeing, H. A network meta-analysis on the comparative efficacy of different dietary approaches on glycaemic control in patients with type 2 diabetes mellitus. Eur J Epidemiol. 2018; 33: 157–170</li> <li>• Neuenschwander, M., Hoffmann, G., Schwingshackl, L., and Schlesinger, S. Impact of different dietary approaches on blood lipid control in patients with type 2 diabetes mellitus: a systematic review and network meta-analysis. Eur J Epidemiol. 2019; : 1–16</li> </ul>

<p><i>Secondary Outcomes – lipids chosen to represent CVD risk</i></p>	<p>As well as serum LDL-C, HDL-C, total cholesterol, triacylglycerols and total cholesterol: HDL-C ratio, why were non-HDL-C and apolipoprotein B (apoB) not chosen? These are now well-recognised lipoproteins associated with CVD risk. In fact, the European Society of Cardiology and European Atherosclerosis Society, recommend that because of the potential inaccuracy of LDL-C 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><b>References:</b></p> <ul style="list-style-type: none"> <li>Furtado JD, Yamamoto R, Melchior JT, Andraski AB, Gamez-Guerrero M, Mulcahy P, He Z, Cai T, Davidson WS, Sacks FM. Distinct proteomic signatures in 16 HDL (high-density lipoprotein) subspecies. <i>Arterioscler Thromb Vasc Biol.</i> 2018; 38:2827–2842</li> </ul>
<p><i>Overall findings on lipids</i></p>	<p>Based on the inclusion criteria, the findings that there was no difference in LDL-C 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. Furthermore, 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-C 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 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 the current evidence examining low carbohydrate diets for the management of body weight and other cardiometabolic risk factors in order to provide clinical recommendations for practitioners. 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 the diet interventions in the RCTs, and/or differences in adherence to the prescribed diets over the course of the study periods.</p>

	<p>They added that the lack of significant difference in LDL-C 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 <u>the available data suggest that controlling saturated fat intake is crucial to prevent significant increases in LDL-C and for achieving improved cardiovascular health with low carbohydrate diets.</u></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><b>References:</b></p> <ul style="list-style-type: none"> <li>• Mansoor N, 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. Br J Nutr. 2016 Feb 14;115(3):466-79.</li> <li>• Sackner-Bernstein J, et al Dietary Intervention for Overweight and Obese Adults: Comparison of Low-Carbohydrate and Low-Fat Diets. A Meta-Analysis. PLoS One. 2015 Oct 20;10(10):e0139817.</li> <li>• Bueno NB, et al Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials. Br J Nutr. 2013 Oct;110(7):1178-87.</li> <li>• Hession, M, 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. Obes Rev 2009. 10, 36–50.</li> <li>• Nordmann, AJ, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. Arch Intern Med 2006. 166, 285–293.</li> <li>• Hu, T, et al. Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. Am J Epidemiol 2012, 176 (Suppl. 7)</li> <li>• 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</li> <li>• Seidelmann, SB, Claggett, B, Cheng, S et al. (2018) Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. Lancet Public Health 3, e419–e428.</li> </ul>
<p><i>Recommendations from other lipid expert committees to be considered</i></p>	<p>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><b>References:</b></p> <ul style="list-style-type: none"> <li>François Mach, Colin Baigent, Alberico L Catapano, Konstantinos C Koskinas, Manuela Casula, Lina Badimon, M John Chapman, Guy G De Backer, Victoria Delgado, Brian A Ference, Ian M Graham, Alison Halliday, Ulf Landmesser, Borislava Mihaylova, Terje R Pedersen, Gabriele Riccardi, Dimitrios J Richter, Marc S Sabatine, Marja-Riitta Taskinen, Lale Tokgozoglu, Olov Wiklund, 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</li> </ul>
<i>Additional point to be included in the general limitations in the evidence base - Dietary approach and assessment section</i>	An additional point needs to be included 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.
<i>Primary Outcomes section</i>	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.
<i>Conclusions – risk of bias</i>	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.
<i>Providing guidance to the media on reporting food stories – so that consumers are not misled</i>	This would be helpful in order to give a lead to the press and food industry. In the current climate confusion reigns, fuelled by the distortion often caused by the media (either innocently or deliberately) in their eagerness to have an interesting slant on health issues. Frequently news stories are driven by food companies with their own agenda's. These stories, together with 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 further more detailed studies.
<i>The full report</i>	Despite the comments above, HEART UK does welcome the publication of this new report, and commends the panel for their diligence in assessing the research, within the confines of the brief

Please add extra rows as needed

Comments by paragraph	Comments
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6.206	<p><i>‘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’.</i></p> <p>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.</p>
6.207	<p><i>‘In the primary RCTs, total and saturated fat intakes were above government recommendations in the lower carbohydrate diets. This is a potential concern since long-term higher consumption of saturated fats increases CVD risk (SACN, 2019). However, in the evidence considered, increased concentrations of surrogate markers of CVD risk (serum total cholesterol, triacylglycerol and LDL cholesterol) were not observed over the study duration periods’.</i></p> <p>We feel this is a misleading statement:-</p> <ul style="list-style-type: none"> <li>• As there was considerable overlap of total fat 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.</li> <li>• The second 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.</li> </ul>
6.208	<p>Additional paper to consider on nutritional deficiencies</p> <p><b>References</b> Elidottir, AS, Halldorsson, TI, Gunnarsdottir, I et al. (2016) Dietary intake and cardiovascular risk factors in Icelanders following voluntarily a low carbohydrate diet. PLoS One 11, e0156655</p>
7.53	It would be useful to have another bullet point stating there was an overlap in intakes between the high and low carbohydrate diets

7.54	This sentence is confusing in light of the previous statement in the report... <i>'Comparisons were, therefore, mainly between the impact of lower and higher carbohydrate diets'</i> . Should this read mainly between lower and moderate carbohydrate diets?
7.55	It would be clearer, when referring to 'lower' and 'higher' carbohydrate diets if ranges of carbohydrate intakes were provided in brackets
7.58	Further context is required when discussing the relationship between low carbohydrate diets on lipids. As well as medication and weight loss, the 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.
7.64	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.

Please add extra rows as needed