10th MEETING

Carbohydrates Working Group

28th January 2011, Room LG11, Wellington House
135-155 Waterloo Road, London, SE1 8UG

FINAL MINUTES

Chair:	Professor Ian Macdonald
SACN Members:	Professor Annie Anderson
	Dr David Mela
	Professor Ian Young
	Professor Julie Lovegrove
	Professor Angus Walls
	Professor Ian Johnson
Other attendees:	Dr Victoria Burley (University of Leeds) (agenda item 3 only)
	Dr Darren Greenwood (Statistician, University of Leeds) (agenda item 3 only)
	Dr Charlotte Evans (University of Leeds) (agenda item 3 only)
	Ms Alison Eastwood (CRD York)
	Dr Peter Sanderson (by phone agenda item 5 only)
Observer:	Dr Alison Tedstone

Secretariat: Dr Elaine Stone
Mrs Vicki Pyne
Ms Emma Peacock
Mr Andrew James (Statistician) (agenda item 3 only)

Agenda item 1 – Chair's introduction and welcome

1. The Chair welcomed members to the 10th meeting of the SACN Carbohydrates Working Group.

2. Apologies were received from Professor Tim Key, Mrs Christine Gratus and Dr Mark Beattie.

3. The Chair asked members for any changes in their declarations of interest. Professor Angus Walls informed the Working Group that he is providing consultancy to Chlorhexidine Technology Inc.

Agenda item 2 – Minutes of the 9th meeting (SACN/Carbohydrates/10/mins/04)

4. Members were invited to comment on the minutes of the 9th meeting of the Carbohydrates Working Group.

5. The Chair discussed the comments circulated by Professor Tim Key prior to the meeting.

6. Paragraph 53 requires rewording because it infers that more weight should be given to smaller studies. However, while some small studies are of high quality, others will also be of poor quality and maybe more affected by publication bias due to reporting of positive results. Therefore, it was suggested that the sentence is amended to, "Members noted that the random effects model had been used. This may give greater weight to smaller studies".

7. The Working Group agreed with the above revision.

8. Paragraph 69, “A member raised the point that alcohol was not usually considered as an important risk factor for cardiovascular disease and by excluding studies that had not adjusted for alcohol intake a number of studies would be excluded.” Alcohol is a risk factor for cardiovascular disease (CVD) in observational studies, therefore the sentence needs amending to reflect this. The preference would be to consider studies that have adjusted for alcohol unless it is considered to be of minor relevance in the population.

9. Professor Ian Young agreed that alcohol is a risk factor for CVD, but it is not as strong a risk as other factors, such as smoking and age. For example, the INTERHEART study showed that alcohol was the least important of the nine risk factors identified, which together explained 95% of the risk. Therefore why should studies, which fail to correct for alcohol consumption, be excluded, whilst including those that fail to correct for other risk factors such as BMI or vegetable and fruit intake, which may be more important.

10. The Chair informed members that he had a prior discussion with Professors Tim Key and Ian Young about the issues raised and they had agreed that CVD studies that did not adjust for alcohol intake should still be included in the review.

11. It was agreed that paragraph 69 should be amended to the following: "A member raised the point that there were a number of other risk factors for CVD more important than alcohol. By excluding studies that had not adjusted for alcohol intake a number of studies would be excluded. It was questionable if studies which had failed to correct for alcohol consumption should be excluded while including studies which had failed to adjust for more important risk factors such as BMI."

12. A member raised the point that as well as risk factors, consideration should be given to what factors confound the relationship between carbohydrate and CVD.

13. Members agreed that CVD studies should adjust for age and smoking in order to be included in the review.

14. Paragraph 83, the last sentence, “The obesity section should be submitted to the Secretariat by 7th January”, should be a matters arising. Members were informed that the progress of the cardiometabolic review would be discussed after matters arising.

15. A member raised concern about the term sugar sweetened beverage, as it implies that the beverage has been sweetened by adding sugar, which is not the case for fruit juices. It was agreed that the term beverages containing sugars would be used instead.

16. Paragraph 19, typo- World Health Organisation (WHO), should be "Organization"

17. A member stated that milk had been excluded from the search terms in the review. Members agreed that sugars in milk would be covered under the carbohydrates search terms but that there should be an explanation in the text as to why milk *per se* was not included. A member asked whether milkshakes would be picked up under sugar sweetened beverages. It was agreed that Peter Sanderson would check that these are picked up in the searches.

Action: Peter Sanderson

18. Subject to the above changes, the minutes were agreed as an accurate record of the meeting.

Action: Secretariat

Matters arising (SACN/Carbohydrates/11/01)

19. The Chair introduced the matters arising.

Matters arising – Carbohydrates and oral health

20. Elaine Stone informed members that due to budget constraints the oral health review will not be commissioned externally, however, it had been agreed with the Chair that Peter Sanderson would undertake this work instead.

21. A member enquired whether Peter would have adequate support to conduct the oral health review. The Working Group was informed that Professor Angus Walls will provide input from an oral health perspective and Andrew James (DH statistics) will

provide statistical support.

Agenda item 3 – Carbohydrates and cardiometabolic health

22. Andrew James (AJ) explained to the Working Group the approach he had agreed with Darren Greenwood (DG) and Peter Sanderson (PS) for meta-analyses. In both reviews, a meta-analysis will be performed where there are three or more cohorts and the I^2 is $<75\%$. Random effects models will be used and heterogeneity investigated where there are ten or more cohorts. In studies where analyses have been performed by subgroup only, e.g. men and women or colon and rectal cancer, the groups will be combined before being entered into the random effects model so that one risk estimate is produced for the study population or outcome of interest.

23. Members highlighted that the summary measures used differ between the two reviews. For the colorectal health review, the highest vs. lowest quartiles approach was used, whereas the cardiometabolic health review used dose-response trends. This is because a large number of studies would be lost from the colorectal health review if the dose response trend was used, however this is the most powerful approach.

24. The Chair noted that the difference in the approach used would affect the conclusions that can be drawn.

25. The Chair noted that the rationale for choosing different methods would have to be explained in the report. However, the Working Group still faces the difficulty of not having similar quantitative results.

26. Members agreed to ask PS to perform the meta-analyses using dose-response trends so the Working Group can compare the results of the two approaches.

Action: Peter Sanderson

27. A member asked about the reliability of linearity in the dose-response trends. AJ informed the Group that the methods test for linearity and the results show a linear

relationship. If they are not linear then a dose-response trend is not performed.

28. The Leeds team have amended the structure of the report in light of comments made at the previous meeting. If members had any further comments, they should raise them during agenda item 3.

29. The Chair informed members that there was a three month delay in the cardiometabolic health review and the diabetes section presented at today's meeting is incomplete. It is anticipated that the Working Group should receive the further sections of the review in early April. The reason for the delay is because the Leeds team have found more literature than they originally envisaged.

Agenda item 4 – Carbohydrates and colorectal health

30. In the absence of Dr Mark Beattie, the Chair agreed to carry over the outstanding issues on the definition of functional constipation and the inclusion of treatment trials and studies from the developing world. Secretariat to add these to the matters arising for the April Meeting.

Action Secretariat

Agenda item 3- Draft carbohydrate and cardio-metabolic health review (SACN Carbohydrates/11/03) Diabetes Section.

31. The Chair welcomed Dr Victoria Burley (VB), Dr Darren Greenwood (DG) and Dr Charlotte Evans (CE) from the University of Leeds.

32. VB drew members' attention to revisions in the methods section, which have largely been removed from the main document to be placed in an appendix.

33. At the previous meeting, a member enquired how many of the potentially relevant studies that were originally excluded, were actually included in the review. On page 11, it is explained that of the 17 articles found to be potentially relevant, five of them were included in the review, four of which had been identified through hand searching.

Therefore, the Leeds team are confident that articles are not being missed.

34. A member enquired whether e-publications are being included in the review. VB confirmed that this was the case.

35. The team are currently writing the introductory paragraphs, which provide background on the outcomes and characteristics of the studies.

36. An example table of trial design on p18 was highlighted to members. It was noted that the length of follow up could be different from the duration of intervention. Ideally, measurements taken after the intervention should be captured.

37. VB asked members what should be recorded when it is not clear when the data was collected. For example in some RCTs only diet plans were administered. It was agreed that where there was uncertainty about whether the results were given immediately after the intervention period or not, it should be highlighted in the table and text.

38. VB agreed to go back and check the trials to see if the results are reported immediately after the intervention period or after follow up.

Action: Victoria Burley

39. A member queried why an industry funded category was included in the trial bias table, as this information could be perceived as indicating that if a study is funded by industry it will automatically be biased in some way. Following further discussion, it was agreed that this information should be captured in the trial characteristics table under a 12th column.

Action: Victoria Burley

40. It was noted that in some of the columns there were missing values and it was recommended that if information is not reported it is better to state this, rather than to have blank entries.

41. A member asked what was meant by selective outcome reporting. VB informed members

that this is where in the methods the authors state they are going to perform certain measurements, but the findings are not reported.

42. VB asked members how they would like the introductory sections on outcomes written and whether this should be done by disease endpoints or risk markers.

43. The Chair recommended that the Leeds team look for good quality reviews to use as a basis for the introductory paragraphs and to write the sections according to disease endpoint.

Action: Victoria Burley

44. A member enquired whether studies had documented how diabetes has been defined. The Working Group was informed that quite often this was not defined, but where this was the case, it was done by self report, physician report or according to the WHO definition.

45. DG informed members that the meta-analyses have been revised in light of his discussions with AJ. For example where the I^2 statistic is >75%, meta-analysis has not been performed. However, the amendments have not been made in the draft presented to members.

46. VB tabled the summary plot for pooled estimates of cohort studies on type 2 diabetes. These are given per one standard deviation (SD) from UK intakes taken from the National Diet and Nutrition Survey (NDNS).

47. It was noted that in some instances the increments are greater than the mean intake, which implies skewing. For example, fibre in legumes the SD is three times higher than total intake. This is a problem where there is skewed data.

48. It was requested that VB contacts the Nutrition Surveys Team at DH to ask how total carbohydrate was calculated, as the figures provided in the plot do not add up to 70g/day.

Action: Victoria Burley

49. The Chair asked members if they are content with the standard units used. Members

confirmed that they were content with units used in the summary plot, however footnotes detailing the possible caveats should be included. For example, soluble fibre appears to reduce the risk of developing type 2 diabetes, but studies may have failed to adjust for other sources of fibre and would, therefore, bias the results.

50. For diabetes, if studies have not adjusted for age they should be excluded from the review. Smoking is less important as a confounder, but studies should definitely adjust for BMI in order for them to be included. This information should be added as a deviation to protocol. Members agreed that the Leeds team should check that all included diabetes studies have minimally adjusted for age and BMI.

Action: Leeds team

51. It was suggested that the results of all studies could be compared to those, which have adjusted for age and BMI. A member stated that it would be possible to produce a forest plot as a visual aid, but not to include a summary estimate, except when studies adjust for age and BMI. However, it needs to be consistent with the cardiovascular disease section.

52. It was noted that the forest plots of total sugars, glucose and fructose and type 2 diabetes will be omitted because the I^2 is >75%.

53. On page 53 it states that there is weak evidence for an elevated risk with increasing intakes in obese (but not non-obese) women in Colditz *et al*., 1992a. However, the table on page 58, shows that the relative risk was increased (non-significantly) in non-obese women. DG agreed to check the information presented.

Action: Darren Greenwood

54. A member highlighted that the inclusion of Wannamethee *et al.,* 2009 in the forest plots of fibre intake is problematic because it is a UK study and will, therefore be measuring NSP only. All the other studies are likely to be measuring AOAC fibre. It is important to highlight in the report the issues surrounding the measurement of fibre.

55. The issue of Wannamethee *et al.,* 2009 will affect the values provided in the summary plots, therefore this requires revisiting. The Working Group agreed that this study should

be removed from the forest plots, but should be highlighted in the text as the only study to measure NSP.

Action: Victoria Burley

56. It was highlighted to members that the units on the forest plot for cereal fibre have been changed from 10g/day to 4g/day. Meta-regression will be performed to investigate the high degree of heterogeneity between these studies.

57. A member questioned whether heterogeneity between cohort studies of legume and potato fibre was actually 0%. It was agreed that this will be checked.

Action: Darren Greenwood

58. It was noted that there is no text for potato fibre on p88.

59. The method used to measure fibre in Montonen et al., 2003 needs to be checked. If only NSP has been analysed, the study will have to be excluded from the meta-analysis, which will leave only two studies and, therefore, the forest plot on p91 will need to be omitted all together.

60. Only one study was identified for nutrient based dietary patterns, the Working Group members were asked whether they thought the amount of narrative was sufficient. The Chair highlighted that it is important not to over emphasise the results from just one study. A member raised the point that if it is a large, well conducted study, it would still be informative for the study to be documented. It was agreed that the current description of the findings is adequate.

61. The units for the forest plot of wholewheat bread have changed to relative risk per half serving/day (one slice of bread) as it better reflects UK consumption. Members agreed that a definition of a serving needs to be provided in the text.

62. A member enquired whether studies investigating breakfast cereals also adjusted for high fibre bread. From the table on p108, it does not appear as though this has been done and needs to be highlighted in the text.

63. The Leeds team were asked about how a serving of breakfast cereal is defined? VB informed members that in some studies this information had not been given, however where this has been provided information on servings will be included in the tables.

64. A summary estimate for potatoes has not been included in the pooled estimate forest plot of cohort studies. VB agreed to add this information.

Action: Victoria Burley

65. VB informed the Working Group that fruit juices have not been included under sugar sweetened beverages in the draft chapter on diabetes because the team are still checking the cohort studies and so this will need to be interpreted separately.

66. It was noted that a number of cohort studies investigating glycaemic index (GI) and the risk of type 2 diabetes have not adjusted for fibre.

67. The pooled estimate states there are 11 studies on glycaemic load (GL), whereas on p137 it states that 10 studies were included in the meta-analysis. This needs to be checked.

Action: Victoria Burley

68. Members were informed that due to differences in defining wholegrain, it is difficult to pull all the evidence together. It was noted that five of the studies were conducted in the US, so these could potentially be summarised together.

69. It is important to note that in relation to Feskens et al., 2005, impaired glucose tolerance is different from impaired fasting glucose and this should be captured in the text.

70. On page 165 it states that results from the longest follow up period were reported for trials using low carbohydrate/high fat diets vs. high carbohydrate/low fat diets, however findings from the end of the intervention period should be presented.

71. On page 166, check if the value given for Segal-Isaacson is mmol/l, as it appears as to be

in mg/dl.

Action: Charlotte Evans

72. Members suggested that the text should state if differences are significant or not.

73. On page 189, remove the column headed trial type from table 4.37.

74. On page 197, last paragraph should read "other soluble dietary fibres" rather than isolates.

75. A member queried what is meant by soluble isolates and saccharides on p198 and why are they classed as separate entities.

76. VB informed members these categories encompass different components and asked if it is useful to pool these studies under particular headings. It was agreed that if there is a way of categorising and defining the terms, studies can be pooled, but if not, studies should be presented as separate entities.

77. The forest plot should be amended on page 198 as Lehtimaki et al., 2005 have presented their findings as percentage change, rather than mmol/l.

78. The x-axis of the forest plot on p232 is difficult to understand, members suggested omitting the minus signs.

Action: Victoria Burley

79. CE informed members that in order to perform meta-analysis on the insulinaemia studies, the units had been standardised.

80. A member highlighted that because of the different methodologies to measure insulin levels, measurements in one study do not reflect the same measurements in another study. It is possible to standardise insulin units, but not across different populations. Therefore, it was agreed that the studies identified for this review could not be pooled.

81. The Chair questioned whether the units of μIU/L were correct for the data on fasting blood insulin on p242. If this is the case, the differences observed are small and not

physiologically relevant. The Chair agreed to look at a few of the studies to check the units.

Action: Chair

82. In light of the above concerns, the Working Group requested that the Leeds team only provide narrative on studies investigating insulinaemia, describing the limitations in the data and the direction of effect and whether findings are significant or not in original units. The issues around the assay methodology should also be highlighted

Action: Victoria Burley

83. Prof Young informed the Leeds team that standard units for glycated haemoglobin are about to be rolled out across the UK to mmol of Hb1Ac/ mol of Hb (mmol/mol), therefore the pooled estimate must be converted to these units. It was agreed that the conversion factor will be sent to the Leeds team.

Action: Ian Young

84. On page 335, first paragraph should read, "…the risk of an HbA1c level ≥ 6.3% was reduced by 11 percentage points…."

85. It was noted that Hb1Ac is more of a long term measure since the turn over of erythrocytes is 120 days. Therefore, it was requested that the results can only be pooled, if the intervention and follow up had lasted more than 12 weeks, to allow turnover of sufficient numbers of erythrocytes.

86. On page 338, Schwab *et al*., 2006 needs to be checked to ascertain if measurements taken at 12 weeks represent post intervention or post follow up.

87. VB informed members that the studies on the metabolic syndrome do not report on the individual components and only present findings on the metabolic syndrome itself. Members advised that these studies should still be included and a narrative written. However, members noted that the metabolic syndrome would not represent the same condition either within the same study or across different studies due to the nature of how

the condition is identified.

88. The Chair asked the Leeds team about timelines and progress of the remaining sections of the cardiometabolic health review. VB informed members that they have revised the majority of the CVD section following comments from the previous meeting, progress has been made with makers of CVD and obesity.

89. VB requested guidance on what blood lipid outcomes to include, it was agreed that a list will be sent to Julie Lovegrove and Ian Young who will advise the Leeds team on this.

Action: Victoria Burley/ Julie Lovegrove/ Ian Young

90. The Working Group members were asked whether the trials on energy intake should be analysed and members confirmed that analysis should be conducted.

91. The Chair asked the Leeds team what would be realistic to deliver for the April meeting. VB informed members that draft sections on markers of inflammation (CVD) and obesity will be circulated in early April.

Action: Victoria Burley

Agenda item 5- Protocol for carbohydrates and oral health review (SACN/Carbohydrates/11/03)

92. Dr Peter Sanderson (PS) introduced the protocol for the carbohydrates and oral health review.

93. The Working Group members were informed that there are *in situ* studies where an enamel device is placed in the mouth and effects of diet can be measured over a short time period. The enamel can be marked with a reference point, which is very useful when measuring changes to the surface. These studies are generally accepted as predictors of risk and should be included in the review. Therefore, a time limit of duration should not be applied.

94. PS enquired whether studies using bovine enamel should be included, members confirmed that these studies should be captured because bovine enamel is similar to human enamel.

95. Dental erosion will not occur without acid, however a lot of acid containing drinks will also contain sugar such as soft drinks and fruit juice. Members agreed to include acid containing drinks. PS agreed to perform searches (erosion and acid containing drinks) and feedback results to Working Group.

Action: Peter Sanderson

96. Members agreed that chewing gums should be included as they are a form of confectionary, however mouth rinses and toothpaste should be excluded.

97. A member raised the issue of minimal adjustment and what confounders should be considered for a study to be included in the review.

98. The Working Group were informed that fluoridation is rare in the UK, so if a study has not adjusted for this factor it should still be included in the review.

99. Members agreed that studies must adjust for age, smoking and oral hygiene. If these factors are not considered in the analyses, the study will not be included in the review.

Action Peter Sanderson

100. Members considered the list of outcome measures and recommended that the following were added: quantitative laser fluorescence (QLF), Diagnodent® and electrical impedance measures.

101. The assessment of plaque and gingivitis should include qualitative as well as quantitative measures.

102. Dentine should be included with quantitative assessment of mineral loss.

103. Decayed, missing, filled figures at surface as an index in lower case (dmfs) needs to be added to the clinical assessments, as this is index is used for deciduous teeth whereas DMFS is an index of caries in permanent teeth.

104. Members considered the dietary carbohydrate exposure search terms in the protocol and noted that terms for smoothie and infant feeding were missing. It was suggested that terms for infant feeding, breastfeeding, bottle feeding and formula feeding are included. Study duration should be at least 6months and follow up to 2 years.

105. PS agreed to develop terms for infant feeding and circulate to members via email for agreement.

Action: Peter Sanderson

Agenda item 6- Future work programme

106. Members were informed that an updated draft of the colorectal health review will be circulated by email to members for comment at the end of February and the necessary revisions made prior to the meeting. Any conflicting comments will be briefly discussed at next meeting.

Action: Peter Sanderson and All Members

107. A member enquired whether 10% of studies excluded in the colorectal health review had been checked. It was agreed that the Secretariat will ask PS if this has been done. A quality assurance step by a second reviewer will also need to be included for the oral health review. The Secretariat will take this forward.

Action: Secretariat

Agenda item 7- AOB

108. The dates of next meetings are 27th April 2011 and 1st August 2011. The April meeting will focus on the obesity and markers of CVD risk sections of the

cardiometabolic health review and a progress report on the oral health review.

109. The Chair thanked members for their attendance and closed the meeting.