



## Consultation on the SACN draft report Saturated Fats and Health Report

### Comments Form

<b>Organisation:</b>	Self employed
<b>Name of commentator and contact details:</b>	Dr Zoe Harcombe, & George Henderson (Auckland University of Technology)

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General comments	Comments
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Comments by paragraph	Comments
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Section 8	This section only includes comments on clauses that led to claims of evidence in Table 8.1 (p94).
8.2	<p>This paragraph contains a number of errors:</p> <p>1) One of the four Harcombe <i>et al</i> papers has been omitted (PCSs at the time the guidelines were set) (1).</p> <p>2) Schwingshackl &amp; Hoffman (2014) has been omitted (2).</p> <p>3) Hamley (2017) has been omitted (3). (This was published during the committee deliberations and should also have been included – it can be now at draft report stage.)</p> <p>4) Schwab <i>et al</i> (2014)(4) reported findings from Hooper <i>et al</i> (5) and Jakobsen <i>et al</i> (6), rather than doing any meta-analysis of their own and so should be deleted.</p> <p>5) Van Horn <i>et al</i> (2008)(7) is about assumed risk factors, not disease, and so should not appear in this section. Additionally, as with Schwab <i>et al</i> (2014)(4), Van Horn <i>et al</i> (2008)(7) reported passages from other articles, rather than doing any meta-analysis of their own and so should not be included.</p> <p>6) For the purposes of meta-analysis, Micha &amp; Mozaffarian (2010)(8) is a duplication of Mozaffarian <i>et al</i> 2010(9) and should be deleted.</p> <p>7) This paragraph reported: "The Hooper <i>et al.</i> (2015) review included virtually all randomised controlled trials (RCTs) included in other studies." This is correct. This paragraph should clarify the differences between Hooper and other studies, not just the similarities: Hooper <i>et al</i> (10) was the only meta-analysis to include four small studies for which CVD data were not published or peer reviewed (See 8.6).</p>
8.3-8.7 & 8.12	<b>Saturated fat intake and CVD: Table 8.1 claimed “Adequate evidence for reduced saturated fat intake on reduced CVD events” from RCTs (Nothing claimed from PCSs).</b>
8.3	This paragraph omitted Schwingshackl & Hoffman (2014)(2). This examined evidence for all-cause mortality, CVD mortality, CVD events and MIs for both reduced fat intake and modified fat intake with a systematic review and meta-analysis of RCTs. This study found "The present systematic review provides no evidence (moderate quality evidence) for the beneficial effects of reduced/modified fat diets in the secondary prevention of coronary heart disease. Recommending higher intakes of polyunsaturated fatty acids in replacement of saturated fatty acids was not associated with risk reduction."

	As explained in 8.2, Schwab <i>et al</i> (2014)(4) and Van Horn <i>et al</i> (2008)(7) were included and should not have been.
8.4	As explained in 8.2, Van Horn <i>et al</i> (2008)(7) should be deleted. Schwingshackl & Hoffman (2014)(2) should be included.
8.6	<p>This paragraph should have noted the limitations of the Hooper <i>et al</i> (10) report (not least as it is almost entirely relied upon for the case against saturated fat). (11):</p> <p>- SACN should have questioned why the Hooper <i>et al</i> review found something that the other meta-analyses didn't. The Hooper <i>et al</i> finding included 4 small studies (646 people in total), not included in any other meta-analysis, which were primarily studies of: diabetes(12); skin cancer(13); hypercholesterolemia(14); and glucose intolerance(15), but for which unpublished, non-peer-reviewed CVD event information was obtained by Hooper <i>et al</i> in personal correspondence.</p> <p>Houtsmuller (12) was the most striking outlier in Hooper <i>et al</i>'s meta-analysis for CVD events. This paper claimed "One group of patients was put on a diet (I), consisting of carbohydrates 50 cal%, saturated fats 35 cal% and proteins 15 cal%." This is nutritionally impossible. All foods that contain fat contain all three fats. There is no food comprising 100% saturated fat. No diet can equate total fat to saturated fat with no intake of unsaturated fat. Such data are not robust and should not have been included by Hooper <i>et al</i>. As every other researcher has shown, when only the dietary trials that had CVD/CHD as measured outcomes and peer reviewed data, are included, there are no findings to report.</p> <p>Additionally, when a sensitivity test was undertaken on the RCTs that actually significantly reduced SFA intake (as opposed to having the aim of reducing SFA intake), the CVD events finding (for &gt;52,000 participants) reduced from 17% to 9% and was no longer statistically significant (Hooper <i>et al</i> 2015 Table 8, p121)(10).</p> <p>Even had the one Hooper <i>et al</i> finding (among seven other non-findings) retained significance following the sensitivity test (and it didn't), any finding would still have lacked generalisability. The Hooper <i>et al</i> review (10) did not include a single study of healthy people of both genders and thus any findings would have lacked generalisability and could not be extrapolated to populations.</p>
8.7	<p>This paragraph should be deleted. Van Horn <i>et al</i> (7) is about assumed risk factors, not disease/events. Additionally, the statement "a systematic review of 83 primary studies and 19 review articles concluded that low intake of saturated fats (&lt;7% of total energy) resulted in reduced risk of CVD" is disingenuous.</p> <p>i) As above, this was related to assumed risk factors and not CVD events (which is the focus of this section) and ii) 82 studies and 19 review articles did not conclude that low intake of saturated fats (&lt;7% of total energy) resulted in reduced risk of CVD. Van Horn <i>et al</i> (7) referenced one paper that claimed reducing SFA to &lt;7% energy and dietary cholesterol of &lt;200 mg/day reduced LDL. Three RCTs were similarly reported as having lowered LDL with a &lt;7% SFA and &lt;200mg/day cholesterol diet.</p>

8.12	This paragraph should be amended to report that there is adequate evidence of no effect for reduced saturated fat intake on CVD events (2, 10).
8.13-8.17	<b>Substitution of saturated fats with polyunsaturated fats and CVD: Table 8.1 claimed “Adequate evidence for substitution of saturated fats with polyunsaturated fats on reduced CVD events” from RCTs.</b>
8.13	<p>This paragraph omitted Schwingshackl &amp; Hoffman (2014).(2) This examined evidence for all-cause mortality, CVD mortality, CVD events and MIs for both reduced fat intake and modified fat intake with a systematic review and meta-analysis of RCTs. This study found "The present systematic review provides no evidence (moderate quality evidence) for the beneficial effects of reduced/modified fat diets in the secondary prevention of coronary heart disease. Recommending higher intakes of polyunsaturated fatty acids in replacement of saturated fatty acids was not associated with risk reduction."</p> <p>This paragraph should delete Schwab <i>et al</i> (2014)(4) (See 8.16).</p> <p>This paragraph should delete Van Horn <i>et al</i> (2008)(7) (See 8.17).</p>
8.14	This paragraph claimed that there was a 27% lower risk of CVD events – "p<0.05" – with SFA replaced by PUFA. The original Hooper <i>et al</i> paper (Table 9. p121) reported the P value as 0.14, which makes the finding non-significant.
8.15	<p>This paragraph should clarify that Ramsden <i>et al</i> (2013)(16) contributed nothing to the claim for replacing SFA with PUFA and the impact on CVD events. Ramsden <i>et al</i> (2013) focused on CVD mortality. The word "events" did not appear in the Ramsden paper or appendix.</p> <p>This paragraph was also <i>not</i> reflective of the conclusions of Ramsden <i>et al</i>'s paper. Ramsden <i>et al</i>'s conclusion was: "In this cohort, substituting dietary linoleic acid [a PUFA] in place of saturated fats <b>increased</b> the rates of death from all causes, coronary heart disease, and cardiovascular disease" [my emphasis].</p>
8.16	<p>This paragraph claimed that "Schwab <i>et al</i> (2014) (4)...reported on the effect of saturated fat substitution with unsaturated fats (PUFA or MUFA) on CVD events. The authors reported a 14% reduction in RR of CVD events (RR 0.86, 95% CI 0.77 to 0.96; p=0.07; I<sup>2</sup> = 50%; 24 RCTs; 65,508 participants, 4586 CVD events."</p> <p>This is not correct. Schwab <i>et al</i> reported "A SR [A Systematic Review – my emphasis] concluded that there is moderate evidence that substitution of unsaturated fatty acids (MUFA or PUFA) for SFA can reduce CVD events by 14% (reference 67)." Reference 67 in their paper was for the Hooper <i>et al</i> 2011 review.(5) Schwab <i>et al</i> did not conduct an SR or meta-analysis of their own; they merely referenced another.</p> <p>Similarly, this paragraph in the SACN report continued "There was no effect of saturated fat change on CVD mortality (RR 0.94, 95% CI 0.85 to 1.04; p=0.23; I<sup>2</sup> =0%; 16 RCTs; 65,978 participants, 1407 CVD deaths)." All of this is from the Hooper <i>et al</i> 2011 review (which has been superseded by the 2015 review) and not from any work undertaken by</p>

	<p>Schwab <i>et al.</i></p> <p>This paragraph should be deleted.</p>
8.17	<p>This paragraph claimed “A systematic review by Van Horn <i>et al.</i> (2008) reported a reduced risk of CVD when saturated fats were substituted with unsaturated fats including MUFA (&lt;20% of energy) and PUFA (&lt;10% of energy). However, it was unclear on which of the included RCTs this statement was based and no meta-analysis was performed.”</p> <p>The only reference to such data in the Van Horn <i>et al</i> paper is “The American Heart Association recommends a diet ... SFA and TFA should be replaced isocalorically with complex carbohydrates and/or UFA, including both MUFA (not to exceed 20% of energy) and PUFA (not to exceed 10% of energy).” (p292) As with 8.16, Van Horn <i>et al</i> have not done their own systematic review. SACN have reported Van Horn <i>et al</i>’s reporting of general advice. No RCTs have been studied by Van Horn <i>et al</i> (and this SACN paragraph is in the RCT/CVD event evidence section). There are a number of references to CVD events in the Van Horn <i>et al</i> paper (related to alcohol, exercise, vitamins, obesity, for example) but none relate to SFA/PUFA replacement.</p> <p>This paragraph should be deleted.</p>
8.18-8.19	<p><b>Substitution of saturated fats with polyunsaturated fats and CVD: Table 8.1 claimed “Limited evidence for substitution of saturated fats with polyunsaturated fats on reduced CVD mortality” from PCSs.</b></p>
8.18	<p>This paragraph claimed “Evidence from systematic reviews of PCS indicate a reduction in CVD mortality when saturated fats were substituted with PUFA (Schwab <i>et al.</i>, 2014; Van Horn <i>et al.</i>, 2008) or a combination of MUFA and PUFA (Schwab <i>et al.</i>, 2014), however there was no formal meta-analysis of these data which limits their quality.”</p> <p>Schwab <i>et al</i> (2014)(4) reported no evidence from systematic reviews of PCS for CVD mortality and substitution of saturated fats with PUFAs, or a combination of MUFA and PUFA.</p> <p>There are a number of references to CVD mortality in the Van Horn <i>et al</i> paper (related to alcohol, exercise, vitamins, obesity, for example) but none relate to SFA/PUFA replacement.</p> <p>This paragraph should be deleted.</p>
8.20 (Summary)	<p>This paragraph reiterated the claim that there was a 27% lower risk of CVD events. This was not a significant finding. The SACN report states: “These findings were consistent with the results of other systematic reviews of RCTs and the evidence was considered <i>adequate</i>.” This sentence needs to be deleted as per the comments on Ramsden <i>et al</i> (2013)(16), Schwab <i>et al</i>, 2014(4) and Van Horn <i>et al</i>, 2008(7), which left no other findings.</p> <p>The conclusion of this section should be:</p> <p>i) There is adequate evidence from two meta-analyses of RCTs (2, 10) that replacing SFA with PUFA has <i>no</i> effect on</p>

	<p>CVD events.</p> <p>ii) There is no evidence from systematic reviews or meta-analyses of PCSs to draw any conclusion about the impact of substitution of saturated fats with polyunsaturated fats on CVD mortality.</p>
	<p>I have ignored all sections related to MUFAs, carbohydrates and protein as no claims were made against saturated fat. Table 8.1 claimed that there was limited evidence that substituting saturated fats with MUFAs would increase CHD events and that there was adequate evidence that substituting saturated fats with carbohydrates would increase CHD events. I have not addressed these claims.</p>
<b>8.31-8.38</b>	<p><b>Saturated fat intake and CHD: Table 8.1 claimed “Moderate evidence for reduced saturated fat intake on reduced CHD events” from RCTs.</b></p>
8.31	<p>8.31 Contains a number of errors:</p> <ol style="list-style-type: none"> <li>1) A Harcombe <i>et al</i> paper has been omitted.(1) This should be included in the list of systematic reviews without meta-analysis.</li> <li>2) The SACN report reference “Harcombe 2016a”(17) is incorrectly reported as a systematic review without meta-analysis. It is a systematic review <i>with</i> meta-analysis.</li> <li>3) Seven, not six, papers evaluated the results from PCS. There are two Harcombe <i>et al</i> papers published for cohort evidence (1, 17).</li> </ol> <p>NB for convenience – the three Harcombe <i>et al</i> papers referenced as 2016a, 2016b and 2015 in the SACN report are (with the references in this document in brackets):</p> <p>Harcombe Z, Baker JS, Cooper SM, Davies B, Sculthorpe N, DiNicolantonio JJ &amp; Grace F (2015) 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 2, e000196.(18)</p> <p>Harcombe Z, Baker JS &amp; Davies B (2016a) Evidence from prospective cohort studies does not support current dietary fat guidelines: a systematic review and meta-analysis. British Journal of Sports Medicine.(17)</p> <p>Harcombe Z, Baker JS, DiNicolantonio JJ, Grace F &amp; Davies B (2016b) Evidence from randomised controlled trials does not support current dietary fat guidelines: a systematic review and meta-analysis. Open Heart 3.(19)</p>
8.33	<p>This paragraph should report for Harcombe <i>et al</i> (2015)(18) that “the included papers deliberately only examined papers published before 1983 to examine the evidence base for the dietary guidelines at the time they were introduced. This, the only paper to examine this question for RCTs, found no evidence for the guidelines introduced.”</p> <p>It is important to document the fact that there was no evidence to support the introduction of the dietary fat guidelines at the time they were introduced. Any evidence being sought is retrospective.</p>

8.38	<p>This paragraph rightly reported that Hooper <i>et al</i> (2015) (10) reported <i>no</i> effect of reduced saturated fat intakes on CHD events.</p> <p>The paragraph then wrongly tried to claim that a fixed effects model would have given a significant result. A fixed effects model cannot be used given the heterogeneity of dietary fat trials. The I<sup>2</sup> of 66% confirms this. Hooper <i>et al</i> calculated the fixed effects model as a sensitivity test, not as a finding that SACN can opt for in preference to the random effects (correct) conclusion. At no time has Hooper <i>et al</i> made a claim for a significant finding for CHD events.</p> <p>This paragraph confirms the confirmation bias of the SACN panel.</p>
8.39-8.47	<p><b>Saturated fat intake and CHD: Table 8.1 claimed “Moderate evidence for reduced saturated fat intake on reduced CHD mortality” “Moderate evidence for reduced saturated fat intake on reduced CHD events” both from PCSs.</b></p>
8.39	<p>A Harcombe <i>et al</i> paper is missing(1).</p>
8.40	<p>This paragraph confirmed de Souza <i>et al</i> (20) – the most recent systematic review - "...reported no association between the highest and lowest intakes of saturated fats and CHD mortality" AND "Furthermore no association was reported between the intake of saturated fats and total CHD."</p> <p>The reason for restating the conclusion of de Souza <i>et al</i> (20) will become clear.</p>
8.41	<p>This paragraph confirmed Chowdhury <i>et al</i> (21) – the most comprehensive systematic review and meta-analysis – found “No association was found with CHD outcomes when comparing the top tertile of saturated fat intakes with the bottom tertile.” This was the conclusion reported by Chowdhury. This finding came from Random Effects methodology, which is the correct methodology that every researcher in this field has used. It is the only acceptable methodology to use given the heterogeneity of the dietary trials that have been undertaken since 1965.</p> <p>Again, this paragraph tries to present results from a Fixed Effects methodology, when the correct Random effects methodology has been presented by Chowdhury <i>et al</i>. This paragraph confirms the confirmation bias of the SACN panel.</p> <p>The reason for restating the conclusion of Chowdhury <i>et al</i> (21) will become clear</p>
8.42	<p>This paragraph confirmed Siri-Tarino <i>et al</i> (22) – "No association was found between upper and lower quartiles of saturated fats intake and CHD."</p> <p>The reason for restating the conclusion of Siri-Tarino <i>et al</i> (22) will become clear.</p>
8.43	<p>This paragraph confirmed Skeaff &amp; Miller (23) – "There was no association with CHD mortality at 5 to 16 years follow-</p>



	<p>up ... or CHD events at 5 to 20 years follow-up..." AND</p> <p>"Analysis of 5% total energy increments in saturated fats also showed no association for either CHD mortality... or CHD events."</p> <p>The reason for restating the conclusion of Skeaff &amp; Miller (23) will become clear.</p>
8.44	<p>This paragraph is referring to the wrong Harcombe <i>et al</i> paper and it has reported the wrong conclusion. This should read: Harcombe <i>et al</i> (1) included data from 6 PCS, all published before 1982 (for the reason stated in 8.33), involving 31,445 participants and 360 CHD deaths with a mean follow-up of 6.2 to 7.5 years. The data were not conducive to meta-analysis. It was reported that one of the six studies found an association between CHD deaths and intakes of saturated fats across countries; none found a relationship between CHD deaths and saturated dietary fat in the same population."</p> <p>The reason for restating the conclusion of Harcombe <i>et al</i> (1) will become clear.</p>
8.44B New para needed	<p>Harcombe <i>et al</i> (17) concluded: "Across 7 studies, involving 89,801 participants (94% male), there were 2,024 deaths from CHD during the mean follow-up of 11.9 ± 5.6 years. The death rate from CHD was 2.25%. Eight data sets were suitable for inclusion in meta-analysis; all excluded participants with previous heart disease. Risk ratios (RR) from meta-analysis were not statistically significant for CHD deaths and total or saturated fat consumption. The risk ratio (RR) from meta-analysis for total fat intake and CHD deaths was 1.04 (95% CI 0.98 to 1.10). The RR from meta-analysis for saturated fat intake and CHD deaths was 1.08 (95% CI 0.94 to 1.25)."</p> <p>The reason for stating the conclusion of Harcombe <i>et al</i> (17) will become clear.</p>
8.45	<p>This paragraph confirmed Mente <i>et al</i> (24) – "when the highest intakes of saturated fats were compared with the lowest, no association between saturated fats and coronary outcomes were identified."</p> <p>The reason for restating the conclusion of Mente <i>et al</i> (24) will become clear.</p>
8.46 (Summary RCTs)	<p>As per 8.38, this paragraph reported "Hooper <i>et al</i> (2015)(10) also found no effect on CHD events when using a random-effects model." This was the correct reporting of the correct conclusion from Hooper <i>et al</i>. However, the SACN committee again tried to use fixed effects methodology and sensitivity tests undertaken by Hooper <i>et al</i> to claim a different conclusion, one that was not made by the original researchers. At no time has Hooper <i>et al</i> made a claim for a significant finding for CHD events.</p> <p>This paragraph confirms the confirmation bias of the SACN panel.</p> <p>This paragraph should be amended to reflect the correct conclusion: that there is adequate evidence of no effect of saturated fat intake on CHD events (Hooper <i>et al</i> (2015)(10)).</p>

8.47 (Summary PCSs)	<p>The conclusions from paragraphs 8.40-8.45 inclusive have been reiterated in this document to show that NONE of: de Souza <i>et al</i> (20); Chowdhury <i>et al</i> (21); Siri-Tarino <i>et al</i> (22); Skeaff &amp; Miller (23); Harcombe <i>et al</i> (1); Harcombe <i>et al</i> (17); OR Mente <i>et al</i> (24) found an association between saturated fat intake and CHD mortality or CHD outcomes. The conclusion of this section should have been a categorical statement “The Committee found adequate evidence of no effect.”</p> <p>Instead, this paragraph reported one fixed effects test from just one of these studies (Chowdhury <i>et al</i> (21)) and ignored all other evidence: “The committee, on balance, therefore considered these data to be <i>moderate</i> evidence” for reduced saturated fat intake on CHD mortality and CHD events.</p> <p>This paragraph is an extraordinary example of the confirmation bias of the SACN panel. An independent panel could not have concluded as this paragraph did from the conclusions presented in paragraphs 8.40-8.45 inclusive.</p>
<b>8.48-8.54</b>	<p><b>Substitution of saturated fats with polyunsaturated fats and CHD: Table 8.1 claimed “Limited evidence for substitution of saturated fats with polyunsaturated fats on reduced CHD events” from RCTs.</b></p>
8.48	<p>“Five systematic reviews analysed the results from RCTs (Ramsden <i>et al.</i>, 2016(25); Hooper <i>et al.</i>, 2015(10); Micha &amp; Mozaffarian, 2010(8); Mozaffarian <i>et al.</i>, 2010(9); Skeaff &amp; Miller, 2009(23)” is not correct. Micha &amp; Mozaffaria 2010 merely reported the finding of Mozaffarian <i>et al.</i>, 2010, which was in print at the time, so this was duplication and should be removed.</p> <p>8.48 Hamley’s paper “The effect of replacing saturated fat with mostly n-6 polyunsaturated fat on coronary heart disease: a meta-analysis of randomised controlled trials” (3) was published during the committee deliberations and should have been included.</p> <p>This specifically addressed the confounding variables in diet heart trials and sought to focus on the results from trials that most accurately tested the effect of replacing SFA with mostly n-6 PUFA. This found “When pooling results from only the adequately controlled trials there was no effect for major <i>CHD events</i> (<math>RR = 1.06</math>, <math>CI = 0.86–1.31</math>), <i>total CHD events</i> (<math>RR = 1.02</math>, <math>CI = 0.84–1.23</math>), <i>CHD mortality</i> (<math>RR = 1.13</math>, <math>CI = 0.91–1.40</math>) and <i>total mortality</i> (<math>RR = 1.07</math>, <math>CI = 0.90–1.26</math>). Whereas, the pooled results from all trials, including the inadequately controlled trials, suggested that replacing SFA with mostly n-6 PUFA would significantly reduce the risk of total CHD events (<math>RR = 0.80</math>, <math>CI = 0.65–0.98</math>, <math>P = 0.03</math>), but not major CHD events (<math>RR = 0.87</math>, <math>CI = 0.70–1.07</math>), CHD mortality (<math>RR = 0.90</math>, <math>CI = 0.70–1.17</math>) and total mortality (<math>RR = 1.00</math>, <math>CI = 0.90–1.10</math>).”</p>
8.49	<p>As 8.48 – the duplicated reference to the finding in Mozaffarian <i>et al</i>, 2010 needs to be removed i.e. Micha &amp; Mozaffarian, 2010 needs to be removed for the review of evidence from RCTs.</p>
8.50	<p>Hooper <i>et al</i> (2015)(10) has been wrongly and disingenuously reported. The claim that “there was a 24% reduction in CHD events (<math>RR\ 0.76</math>, 95% <math>CI\ 0.57\ to\ 1.00</math>; &gt;3000 participants, 737 events)” is misleading. This is not statistically significant, as it includes the line of no effect. Hooper <i>et al</i> have never made such a claim for CHD events.</p>

8.51	Skeaff & Miller (2009)(23) has been wrongly and disingenuously reported. The SACN report claimed that high PUFA and lower saturated fats “reduced the risk for CHD events (RR 0.83, 95% CI 0.69 to 1.00; p=0.05; I <sup>2</sup> =44.2%; 8 RCTs; 4528 participants, 284 events...” This is not statistically significant, as it includes the line of no effect.
8.52	Mozaffarian <i>et al</i> (2010)(9) should be excluded for its study selection, as was explained in this peer reviewed critique paper (26). Mozaffarian <i>et al</i> (2010)(9) omitted two studies that cautioned about the potential harm/toxicity of PUFAs (27, 28) and it included the non-randomised, non-controlled Finnish Mental Hospital cross-over trial, which all other respectable researchers, including Cochrane, omitted (29).
8.54	The Micha & Mozaffarian 2010(8) article did <i>not</i> do a different meta-analysis. The finding quoted in 8.54 is from the abstract of Mozafarrian (2010)(9). The non robust study (Mozaffarian 2010) should not have been included, let alone duplicated.  This paragraph should be deleted.
<b>8.55-8.60</b>	<b>Substitution of saturated fats with polyunsaturated fats and CHD: Table 8.1 claimed “Adequate evidence for substitution of saturated fats with polyunsaturated fats on reduced CHD mortality” and “Adequate evidence for substitution of saturated fats with polyunsaturated fats on reduced CHD events” both from PCSs.</b>
8.55	Reference to Schwab should be deleted (2014)(4). As reported in paragraph 8.56, Schwab <i>et al.</i> (2014)(4) limited their analysis to a summary of the findings of Jakobsen <i>et al</i> (2009)(6) and thus this duplication is misleading.
8.56	As paragraph 8.55, this paragraph should be deleted.
8.57	This paragraph reported “Overall, a 5% lower energy intake from saturated fats and a concomitant higher energy intake from PUFA was significantly associated with a decrease in CHD deaths (HR 0.74, 95% CI 0.61 to 0.89; p-value not reported) and CHD events (HR 0.87, 95% CI 0.77 to 0.97; p-value not reported).”  The two p-values were reported by Jakobsen <i>et al</i> (2009)(6) as 0.40 and 0.70 respectively, which are not significant. This non-significance was confirmed by the fact that significance could not be reached for women or men for coronary events or for coronary deaths when reviewed separately (three out of four confidence intervals including 1.0 and all p values for between-study heterogeneity and for effect modification by sex being substantially higher than 0.05 – as high as 0.81 for example).
8.58	This paragraph reported “Farvid <i>et al.</i> (2014), in a systematic review with meta-analysis of 13 PCS with 310,602 participants, reported on the substitution of saturated fats with dietary linoleic acid (n-6 PUFA). Increasing percent of energy from linoleic acid (by 5%) instead of saturated fats was associated with a 13% lower risk of CHD deaths using a fixed-effect (Mantel-Haenszel) model (RR 0.87, 95% CI 0.82 to 0.94; p<0.05; I <sup>2</sup> =0.0; 10 PCS). This finding was

	<p>similar using a random-effects model (RR 0.86, 95% CI 0.76 to 0.97). There was a 9% lower risk of CHD events using a fixed-effect model (RR 0.91, 95% CI 0.87 to 0.96; <math>p=0.012</math>; <math>I^2=55.9\%</math>; 8 PCS), which was non-significant using a random-effects model (RR 0.90, 95% CI 0.80 to 1.01)."</p> <p>As above, fixed effects methodology is not appropriate for studies with such heterogeneity (there are virtually no circumstances when a fixed effects model is appropriate). The reporting of the CHD events as non-significant using a random effects model is correct and thus this finding can be ignored.</p> <p>The reporting of the CHD deaths as significant using a random-effects model is incorrect. The sentence "This finding was similar using a random-effects model (RR 0.86, 95% CI 0.76 to 0.97)" is from P1572 of Farvid <i>et al</i> (30). The full extract is "Across 10 cohort studies that examined the association between LA and total CHD events (14 estimates), LA consumption was inversely associated with risk of total CHD events. The fixed effect summary of RR for comparing the highest with lowest category was 0.85 (95% CI, 0.78–0.92; Figure 2) with medium heterogeneity (<math>I^2=35.5\%</math>). This finding was similar using a random-effects model (RR, 0.86; 95% CI, 0.76–0.97)."</p> <p>A random effects finding from another part of the paper has thus been wrongly connected to the CHD deaths fixed effects model. No random effects result was presented alongside the fixed effect RR for CHD deaths and thus there is no significant random effects finding to be taken into consideration.</p> <p>Notwithstanding that Schwab (2014)(4) should not have been mentioned and neither Jakobsen <i>et al</i> (2009)(6) nor Farvid <i>et al</i> (2014) survived scrutiny, there are a number of factors that should be taken into consideration in this section:</p> <ol style="list-style-type: none"> <li>1) Jakobsen <i>et al</i> (2009)(6) and Farvid <i>et al</i> (2014) are mathematical modelling exercises. No PUFAs were swapped in for SFAs. The Hamley paper (3) is the important one, as this did test replacement of SFAs with PUFAs and it also addressed the issue of the quality of trials. It concluded: "When pooling results from only the adequately controlled trials there was no effect for major CHD events (<math>RR = 1.06</math>, <math>CI = 0.86–1.31</math>), total CHD events (<math>RR = 1.02</math>, <math>CI = 0.84–1.23</math>), CHD mortality (<math>RR = 1.13</math>, <math>CI = 0.91–1.40</math>) and total mortality (<math>RR = 1.07</math>, <math>CI = 0.90–1.26</math>)."</li> <li>2) There have been a number of PCSs since Jakobsen <i>et al</i> (2009)(6) and Farvid <i>et al</i> (2014) that would counter any findings had they been significant (31-33).</li> <li>3) There have been a number of studies warning about the potential harm from administration of polyunsaturated fats.(16, 25, 27, 28, 31, 34) Public health advice thus needs to be extremely cautious in this area.</li> </ol>
8.59	<p>The conclusion of this section should be – as reported – that there is adequate evidence of no effect for CHD mortality.</p> <p>The conclusion for CHD events should also be that there is adequate evidence from meta-analyses of RCTs (3, 10, 23) that replacing SFA with PUFAs has <i>no</i> effect on CHD events.</p>
8.60	<p>The conclusion of this section should be – there is adequate evidence of no effect for both CHD mortality and CHD events from meta-analyses of PCSs.</p>

Table 8.1	Needs to change to reflect all of the above.
15.16	There was <i>adequate</i> evidence from RCTs that reducing intake of saturated fats had no effect on CVD events.
15.19	There was <i>adequate</i> evidence from RCTs that substituting saturated fats with PUFA had no effect on CVD events.
15.20	There was no evidence from PCSs that substituting saturated fats with unsaturated fats was associated with a lower risk of CVD mortality. There was no evidence for CVD events.
15.26	There was <i>adequate</i> evidence from RCTs that reducing intake of saturated fats had no effect on CHD events.
15.27	There was <i>adequate</i> evidence from PCS that reducing intake of saturated fats had no effect on CHD mortality or CHD events.
15.29	There was adequate evidence from RCTs that replacing SFA with PUFAs had no effect on CHD events.
15.30	There was adequate evidence from PCSs that replacing SFA with PUFAs had no effect on both CHD mortality and CHD events.

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