**SP32 Checks of statistical aspects of BMJ paper by Abramson et al.  BMJ 2013; 347:f6123.**

Carol Coupland, Associate Professor and Reader in Medical Statistics, Division of Primary Care, University of Nottingham.

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I have focussed on checking the statistics and numbers in the paper, rather than issues of interpretation or wider aspects of the literature selected.

| | Statistical issue | Rating | Comments |
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| 1 | *Second paragraph of Abramson paper.*<br><br>Are values quoted correctly for % of men and women with ≥ 20% risk using QRisk2? | A<br>(except for one small discrepancy) | Using the numbers in reference 6, Table 7 the values in the Abramson paper are correct if rounded up to the nearest percentage point, expect the value for men in their 60s should be 46% rather than 48%.<br>Is reference 5 correct here? |
| 2 | *First paragraph in the section 'Why did Cochrane change its advice?'*<br><br>Is it correct that inclusion of 3 additional clinical trials in the Cochrane review did not substantially alter the previously documented effect of statin therapy? | A | The relative risks for the outcomes assessed are very similar in the 2011 and 2013 Cochrane reviews. |
| 3 | *Second paragraph in the section 'Why did Cochrane change its advice?'*<br><br>Is average five year risk of 2.6% quoted correctly? | A | This value is given in the Discussion section of the CTT Lancet paper. It is the mean 5-year risk for major coronary events. I was unable to find it in the Results section or tables of the CTT paper though. |
| 4 | *Second paragraph in the section 'Why did Cochrane change its advice?'*<br><br>Are other numerical values from the CTT Lancet 2012 paper quoted correctly (i.e. 9.1%, 20%, 11/1000)? | A | The CTT authors reported a rate ratio of 0.91 (0.88 to 0.93) for all cause-mortality per 1.0 mmol/L reduction in LDL cholesterol with statin therapy (Webfigure 8). This would be a 9% reduction in all-cause mortality (Abramson quotes 9.1%).<br><br>They also reported a rate ratio of 0.79 (0.77 to 0.81) for major vascular events per 1.0 mmol/L reduction in LDL cholesterol with statin therapy (Figure 1) – i.e. around a 20% reduction as stated by Abramson. These are in patients across all levels of risk.<br>The CTT authors reported that these reductions seemed similar in each risk category, though they did also state that there were "too few deaths among the lower risk participants to allow reliable assessment of the effects of statin therapy (appendix p |

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| | | | 13)". The CTT authors did calculate that in low risk patients statins prevented 11 major vascular events per 1000 people treated for five years for each 1.0 mmol/L reduction in LDL cholesterol. This statement is given in the Abstract, the panel and the Discussion of the CTT paper, though it is not entirely clear how this value was obtained since it is not presented in their Results section. |
| 5 | *Table 1 of Abramson paper.*<br><br>Are calculations in Table 1 correct? | B | Using numbers from Figure 3 in the CTT paper I get the same values as Abramson gives in Table 1, other than some very small differences likely to be due to rounding. Figure 3 however included all vascular and non-vascular deaths but did not include some additional deaths of unknown cause. Webfigure 8 includes all deaths. Repeating the calculations in Abramson Table 1 using Webfigure 8 values gives:<br>RR= 0.96 (95% CI 0.80 to 1.16) in <5%<br>RR= 0.90 (95% CI 0.81 to 1.10) in ≥5%, <10%<br>RR= 0.92 (95% CI 0.84 to 1.01) in <10%.<br>It should be noted that these calculations compare event rates overall for statin treatment versus control rather than per 1.0 mmol/L reduction as per the meta-analysis results in the Lancet paper. They are in all patients with and without vascular disease at baseline. Also they do not account for the individual trials as in a meta-analysis approach, which could change these values somewhat.<br><br>Applying similar calculations to Figure 1 – major coronary events to compare the methods of analysis I get:<br>RR= 0.58 (95% CI 0.40 to 0.83) in <5%<br>RR= 0.63 (95% CI 0.54 to 0.74) in ≥5%, <10%<br>These are similar to those in the Figure per 1.0mmol/L reduction, but with rather narrower confidence intervals. |
| 6 | *Third paragraph in the section 'Examining the data'*<br><br>Are calculations and numbers relating to exclusion of coronary revascularisation procedures correct? | B | The numerical value given of 35% as a percentage of total major vascular events is correct (derived from numbers in CTT paper web figure 5), and applying this value to the 11/1000 does gives a value of 7.15/1000 which does equate to an NNT of 140 over 5 years. |

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| | | | The exact figure for the reduction the rate of in "hard" events however is difficult to obtain from the numbers in the CTT paper since there is some overlap between different outcome events in web figure 5 (i.e. some of the patients with coronary revascularisation have also had a major coronary event or stroke). I calculate that as a minimum 23% of events will be coronary revascularisation alone (assuming no overlap between major coronary events and stroke), and assuming the same rate ratio applies to "hard" events as to "major vascular" events, then this gives a reduction in the rate of "hard" events of 8.5/1000 patients treated over 5 years and an NNT of 118 over 5 years. The actual values will lie somewhere between these.<br><br>I'm not sure where the value of 0.6% comes in the CTT paper but this equates to an NNT of 167. There is a value of 6/1000 in Figure 5 in the CTT paper, although I think this includes coronary revascularisation. |
| 7 | *Section 'Myopathy'*<br><br>Are numbers in this section quoted/calculated correctly? | A | The excess risk of myopathy quoted in the CTT paper is 0.5 per 1000 over 5 years, which does equate to an NNH of 2000. This comes from the Discussion section of the CTT paper, referring to another paper.<br><br>Reference 13 of Abramson's paper did report an adjusted odds ratio of 1.50 for any musculoskeletal pain. I'm not sure where the excess risk value of 53/1000 for muscle pain comes from but it does equate to an NNH of 19 over 5 years.<br><br>The numbers from reference 14 in Abramson's paper are quoted correctly, it is not stated in reference 14 what period of time the NNH apply to.<br><br>The numbers are quoted correctly from reference 15. |
| 8 | *Section 'Diabetes'*<br><br>Are numbers in section on diabetes risks quoted/calculated correctly? | A | The numerical values are quoted correctly from the CTT paper (absolute excess of 0.1% per year equates to 5 per 1000 over 5 years). This comes from the Discussion section of the CTT paper, referring to another paper. |

| | | | The numerical values quoted from reference 16 in Abramson's paper are calculated correctly using results from Table 4 in the paper – my calculations give an excess of 10.5 new diagnoses of diabetes per 1000 women taking statins over 1.9 years and 27.6 over 5 years. This is more than 5 times the value given in the CTT discussion section (5 per 1000 over 5 years), though that was for men and women combined.<br><br>The value (48%) was quoted correctly from reference 17. |
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| 9 | *Second paragraph in the section 'Limitations of research data'*<br><br>Are numbers in paragraph on possible mechanisms quoted correctly (ref 23)? | - | I don't have access to the full text of this article. |
| 10 | *Fourth paragraph in the section 'Limitations of research data'*<br><br>Are numbers in last paragraph in this section quoted/calculated correctly? | B | Reference 24 doesn't relate to clinical trials but to an observational study of patients with diabetes in the community.<br><br>Values are quoted correctly from reference 25 which is a review article quoting other papers. |
| 11 | *Final box*<br><br>Check numbers in final box match those in the paper. | B | The numbers match the values in the text of the paper. I am not sure where the justification for the statement that there is no reduction in risk of serious illness comes from though. |

Rating A= definitely justified, B=uncertain C=incorrect