SP31 Checks of statistical aspects of BMJ paper by Abramson et al. BMJ 2013; 347:F6123.

This was completed by Stephen Evans, LSHTM, 12th June 2014

{Template designed by Carol Coupland, University of Nottingham. June 8th 2014.}

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
1	*Second paragraph of Abramson paper.* Are values correctly quoted for % of men and women with ≥ 20% risk using QRisk2?	A	Not absolutely precise but not really misleading. F 2 & 16 are 1.94 & 15.3 M 9 & 48 are 8.3 & 45.8
2	*First paragraph in the section 'Why did Cochrane change its advice?'* 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	A paragraph at the end of the document gives a comment from the Cochrane Review in 2013 about this[i]. The changes in their estimates are trivial with additional trials[ii].
3	*Second paragraph in the section 'Why did Cochrane change its advice?'* Is average five year risk of 2.6% correctly quoted?	B	I did not see how this figure (risk of what?) was reached. The total mortality (vascular + non-vascular) I could only get as an average across all groups. Using data from Table 2 & Figure 3, I got the results below[iii]. Webtable 2 gives 2.8% as overall risk of MVE in <5% category & 7.4% in 5-10%.
4	*Second paragraph in the section 'Why did Cochrane change its advice?'* Are numerical values from the CTT Lancet 2012 paper correctly quoted (i.e. 2.6%, 9.1%, 20%, 11/1000)?	A	(RR 0.97) 3% {precise calculation may give 2.6%} (RR 0.89) 9.1% both from webfigure 8 p13 of Appendix (not p 14 as stated in text though 15th pade of .pdf!). The RR of -80 (20% reduction) is for all participants. Low risk is about 30% {Fig 2 of paper}. 11/1000 direct quote P 586.
5	*Table 1 of Abramson paper.* Are calculations in Table 1 correct?	B	There are alternative figures in the appendix: They give RRs of 0.97 & 0.89, but with wide CIs[iv] From what I can see what they said they did is correct but it may not be the best way of estimating effect on overall mortality.
6	*Third paragraph in the section 'Examining the data'* Are calculations and numbers relating to exclusion of coronary revascularisation procedures correct?	A/B	My calculation from webfigure 5 p10 is a total of 769/1857=41%. This is even larger than Abramson suggests, so the point is correct. Abramson uses RR=1 if NS
7	*Section 'Myopathy'* Are numbers in this section quoted/calculated correctly?	A/B B A	the CTT quote Armitage from 2007. not their data. This 2007 paper is extremely relevant. Other sources not checked This trial is very small but quote is correct. Note from Armitage that HPS actively checked for muscle problems & measured CPK. Liver effects noted.
8	*Section 'Diabetes'* Are numbers in section on diabetes risks	A	.5% over 5 years correct, based on ref 41/42/43. Higher rate at higher doses.

	quoted/calculated correctly?	A	Jupiter numbers correct, but emphasis on higher effect in women.
		A	WHI value is adjusted: 71% raw value!
9	*Second paragraph in the section 'Limitations of research data'* Are numbers in paragraph on possible mechanisms quoted correctly (ref 23)?	A	Bero review quoted correctly but not paired as far as I can tell.
		?	I can't access ref 23, but I see no major issue
10	*Fourth paragraph in the section 'Limitations of research data'* Are numbers in last paragraph in this section quoted/calculated correctly?	A	I do not have the full papers but from abstracts these seem correct
11	*Final box* Check numbers in final box match those in the paper.	A/C	The benefits are correct, the 20% ADR rate is not but this has been noted in the correction.
	Any other comments:		

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

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[i] "Our previous conclusion urging caution in the use of statins in people at low risk of cardiovascular events is no longer tenable in light of the CTT Collaboration findings. Several issues remain to be considered before widespread use of statins could be recommended in people at low risk (Ebrahim 2012; Smeeth 2012).

These include: i) the feasibility and desirability of having to treat the majority of people over the age of 50 with a statin; ii) the cost effectiveness of such a strategy using a conventional healthcare delivery system; iii) diversion of attention from achieving coverage in people at high risk of events; iv) use of alternative public health strategies to lower blood cholesterol; v) the views of patients on life-long drug therapy; and vi) limited evidence on less serious but nonetheless potentially important adverse effects and quality of life."

[ii] Total mortality

0.84 [0.73, 0.96] 2011
0.86 [0.79, 0.94] 2013

Total Number of CVD Events

0.74 [0.66, 0.85] 2011
0.75 [0.70, 0.81] 2013

[iii]

% deaths over ?5 years
0.7   <5%

2.3   ≥5% to <10%
8.0   ≥10% to <20%
12.3   ≥20% to <30%
19.2   ≥30%
7.6   Overall

[iv] Alternative estimates & CIs for all cause mortality, including unknown causes from appendix webfigure 8 per 1.0 mmol/L reduction in LDL. Deaths & numbers at risk (unknown?)

< 5%	232	?	244	?	0.97	(0.76 – 1.24)
≥ 5%,<10%	639	?	710	?	0.89	(0.77 – 1.03)