Reviewer's report

Title: Implementing monitoring triggers and matching of triggered and control sites in the TEMPER study: A description and evaluation of a triggered monitoring management system

Version: 0 Date: 25 Nov 2018

Reviewer: Susan Wagland

Reviewer's report:

The manuscript supports the published TEMPER study results in Stenning et al (2018); specifically, on the logic decisions behind the matching of perceived higher-risk to lower-risk sites for matched pair monitoring visits in TEMPER. I was impressed by many features of the bespoke risk-based monitoring MS and its flexibility, e.g.: the variation in the way triggers could be set and fired; cumulative triggers that fire if a condition is met more than once; allowing thresholds to change; the addition of manual triggers; the integration of the report generation with the regular meeting to select sites for monitoring visits.

The method for selection of matched sites was very interesting. The authors chose also to match similar sites using time since opening and number of participants. Logarithmic plotting to reduce the importance of difference in time since opening when sites had been open longer was appropriate. As the matching algorithm is a critical part of the site pairing, and therefore the findings from TEMPER, I have commented on it in detail.

It should be acknowledged where data is reported here that is published in the 2018 TEMPER results (authors stated this in their covering letter):

The matching algorithm is in Stenning et al, 2018 as an Appendix
Some of Table 2.

Essential revisions and points for consideration

1. Line 25: please state how many sites participated in the three trials and what proportion of the sites were visited.

2. Lines 28-30: for clarity, it should be stated that the TEMPER-MS is an IT management system and not a process or paper-based system.

3. Lines 37-40 summarise the requirements of the management system (MS). It is not stated why a bespoke system was required, or whether a search was made for an existing MS,
either commercially available or within another trials unit, that would meet all or some of these requirements. Possibly, while many RBM systems exist, none would support the functionality of matching triggered to non-triggered sites in this way. Clarifying this point would support the rationale behind developing a bespoke system, which must have required considerable funding and resources.

4. The use of the penalty p (a constant to weight poorer performing sites in order to select a non-triggered match) is unclear, since the unweighted scores "two candidate sites A (site score = 0) and B (site score = 2)" are already different. Lines 161-164 do not explain the way p was chosen sufficiently well to remove any suggestion of bias, particularly as the statistician used a subjective judgement in this process. However, it is clear that once chosen, p was applied consistently.

5. Lines 145-149: please state whether this calculation used the actual time since first opening or the natural logarithm.

6. As each untriggered site was visited as one of a matched pair, and could (if each site was visited no more than once) be removed from the list of sites still available to visit, did the reducing number of available sites for matching cause any problem with subsequent matching? How closely matched were the matched pairs, by the end of the study?

7. Line 183 - 189: It is not stated how many sites were included in the three trials, therefore these appear to the reader to be large numbers (Figure 4 also). It is not stated whether triggers were only evaluated when a trigger meeting was due (every 3-6 months). Without this information it is hard to see the significance of comparing the number of evaluations to the number of firings, and the reason for including Figure 4.

Discretionary revisions and questions

1. Line 166-169: It is not clear why the algorithm was not sufficient for the allocation of sites to matched pairs; i.e. why there had to be a process of choosing (although explained in Stenning et al, 2018 and examples are given); the implication from the wording is that bias in site selection may have been introduced here.

2. Line 187 may be misleadingly worded, as not every trigger fired, according to Figure 4.

3. In the Discussion, "Evaluation of triggers" is fair. The MS was able to isolate the contribution of each trigger for prognostic analysis. Traffic light assessments are
potentially a useful refinement and are used in the presentation of data from commercial RBM IT systems.

4. Line 304-312: Some of this functionality may be available already in a commercial system.

5. Please check the pages cited in Reference 1.

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