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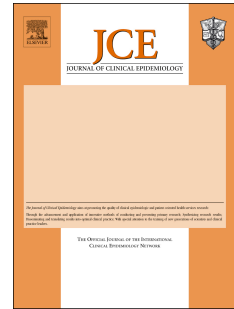
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**Node-making processes in network meta-analysis of non-pharmacological interventions should
be well planned and reported**

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We read with interest the paper of James and colleagues [1]. We agree there is a lack of guidance for generating nodes for network meta-analyses (NMAs) of non-pharmacological interventions, and the proposed elements are useful. Based on our experience of conducting NMAs of wound care devices [2, 3], we offer the following new considerations.

The authors have focussed on approaches to lumping or splitting as covered by the PRISMA extension for NMAs [4]. We consider it useful to discuss four possible approaches: (1) a broad lumping approach that groups similar interventions at a broad level and is useful to estimate effects of intervention groups, (2) a clinically-meaningful-element approach that groups interventions with similar components together, taking account of clinically important variables, (3) a component lumping-and-dismantling approach informed by meta-regression to investigate effects attributed to different components [5, 6], and (4) a class-effect model approach that lumps similar interventions together as a class, but assumes effect variations between these interventions; using modelling to estimate effects of specific interventions [7]. The choice of node-making method can drastically alter the network and subsequent results both between and within NMAs; therefore pre-specification of methods is essential and should be based on NMA objectives.

Support surfaces for pressure ulcer prevention, the focus of our recent NMA [2], can be grouped in several ways e.g. by their construction materials or their mechanism of action (reactive or active surfaces) [8]. Had we wanted to compare all reactive surfaces with all active surfaces we would have used approach (1). However, our objective was to investigate the effects of different *types* of reactive surface, so we used approach (2): drawing on important clinical classifications relating to materials and other features. This approach was both clinically relevant and allowed a more expansive network: comparisons of interventions within the same node in approach (1) (and thus excluded) remained in the NMA in approach (2), so increasing power.

In our NMA of dressings for pressure ulcers [3] the main analysis used approach (2) based on widely used clinical classifications. However, we also conducted a sensitivity analysis using approach (1) to lump dressing groups more broadly. This reduced the numbers of included studies (39 to 22) and participants (2127 to 959). Additionally, the network became unbalanced, increasing the risk of biased estimates of rank probabilities [9]; therefore, we questioned the validity of excluding a high proportion of participants. This emphasises the importance of considering the effect of lumping on exclusion of studies from the NMA [4].

We agree with James and colleagues [1] that limited description of non-pharmacological interventions in publications [10] can affect subsequent node-making. We recommend using additional sources of information to support node-making judgements [11] and that NMAs should report the sources of information (e.g., manufacturers' and/or product websites).

We believe that the formation of nodes should be undertaken independently by two reviewers, following a pre-planned node-making process, and that NMA reports should include a description of the methods used (e.g., dual process) to avoid arbitrary node-making.

ACCEPTED MANUSCRIPT

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Suggested amendments to memory Box 1: Elements proposed to consider for the node-making process in network meta-analyses (NMAs) assessing non-pharmacological treatments

Planning the node-making process might include:

1. Criteria for eligibility of the primary studies
2. Pre-specified inclusion criteria for each node

Reporting the node-making process might include:

1. *A pre-specification of lumping and/or splitting approach to node-making on the basis of the objectives of the NMA and sensitivity analyses proposed to examine alternative approaches (new consideration)*
2. *A description of sources of information for describing eligible interventions (new consideration)*
3. A description of each intervention assessed in primary studies included in the NMA
4. Explanation of the node's inclusion criteria (e.g., expert consensus, previous classification, *international standards* or conceptual frameworks)
5. If the content of nodes differs from that in other NMAs assessing the same clinical question, this point must be discussed
6. *A description of the methods used (e.g., dual process) to avoid arbitrary node-making (new consideration)*
7. Justification for secondarily lumping or splitting nodes
8. *Discussion of the effect of lumping on exclusion of studies from the NMA (new consideration)*