Author's response to reviews

Title: Deriving Utility Scores for Co-Morbid Conditions: A Test of the Multiplicative Model for Combining Individual Condition Scores

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Author's response to reviews: see over
Reply to Begg

Discretionary Revisions

1) We chose the word “purify” because it seemed to best represent the idea behind our procedure. We are making the assumption that the resulting HUI3 score is the health-related quality of life associated purely with a given reported condition (or set of conditions). Lacking a better alternative, we feel it best to retain the term “purify.” The term “adjust” seems somewhat vague and overused.

2) A comma has been inserted after reference [5] on page 4.

Reply to Iburg

Major Compulsory Revisions

2) We don’t think that there is a ceiling effect operating in the survey. There are responses with no loss of health on the HUI3 (i.e., scores of 1.0); and conversely, there are responses with scores less than 0 (i.e., indicating health states worse than death). Further, the HUI3 scores used as the ultimate unit of analysis for evaluating the co-morbidity rule are averages across persons reporting specific chronic conditions (or no chronic conditions). There might be a selection bias given that the CCHS surveys only the household population, which may be healthier than the institutional population (i.e., more severe conditions or combinations of conditions may be found in institutions). This potential limitation is already noted in the discussion, and it is suggested that future research might examine institutional populations. We do not have information on non-respondents to the CCHS, but the bootstrap weights used to obtain more efficient variance estimates are adjusted for non-response.

3) The reason for “purifying” the HUI3 scores is to avoid double counting the effects of conditions in the co-morbidity rule. Taking observed and purified HUI3 scores from Table 1, consider the following example:

Migraine headaches:       HUI3 = 0.90
Chronic Fatigue Syndrome  HUI3 = 0.81

If we assume that part of each of these scores is due to other (unspecified/unreported) background conditions with HUI3 = 0.94 then we have:

Migraine headaches:       HUI3 = 0.90 = 0.94 * 0.97
Chronic Fatigue Syndrome  HUI3 = 0.81 = 0.94 * 0.87

Therefore, in a straightforward multiplicative model we would obtain

Migraine & ChronicFS     HUI = 0.90 * 0.81 = (0.94 * 0.97) * (0.94 * 0.87) = 0.73
and we see that we are doubling the effect of the background conditions.

Thus, we think it is preferable to use a model that operates on a score that is “purely” associated with the conditions:

\[
\text{Migraine & ChronicFS} \quad \text{HUI} = 0.97 \times 0.87 = 0.84 \\
\text{Migraine & ChronicFS & Background Conditions} \quad \text{HUI} = 0.97 \times 0.87 \times 0.94 = 0.79
\]

Regarding the age-sex standardization procedure, our goal was to provide a single, overall co-morbidity rule (i.e., across all condition combinations). Providing one global rule is in line with our major objective in the paper, which was essentially to test the appropriateness of the multiplicative model (for condition weights) commonly used by the WHO to adjust burden of disease estimates. In our study, given that the age-sex distribution varied according to the conditions reported, we needed to age-standardize in order to compare the HUI3 scores for different conditions. This is a commonly used technique in this type of research study, and on page 9 we now reference a study [24] on the HRQoL impact of various chronic conditions, in which HUI3 scores were standardized using the Canadian population as a reference (1996 in this case).

4) Our intention here was to develop a general rule for combining the utilities associated two or more conditions, in the context of estimating summary measures of population health (SMPH). In this spirit, we have grouped all persons that reported no chronic conditions to get an average impact of this group as a whole – the goal was not to find the “healthiest” sub-group among those reporting no chronic conditions. We feel that cutting the population of those reporting no chronic conditions too finely would not respect the SMPH context of the study, and it would be very difficult to know which sub-population was actually the “right” one. For the group reporting having one or more chronic conditions, these are the only criteria we are using to include their HUI3 scores in the development of the co-morbidity rule, so it seemed most appropriate to base the purification on the population reporting no chronic conditions, without invoking additional criteria.

5) When introducing the synergy coefficient \( s \), we were not attempting to argue that there would necessarily be a synergistic effect on HRQoL of having two or more conditions. The synergy coefficient is just a way to gauge the appropriateness of the multiplicative rule. For instance, if \( s \) had been estimated to be 0.5, we would have concluded that the multiplicative rule was a poor rule (i.e., that there is considerable additional interaction between conditions that the multiplicative model is failing to account for); however, \( s \) was estimated to be 0.99 which indicates that the straightforward multiplicative rule is appropriate for this dataset, under the stated assumptions and limitations. If we did not actually estimate \( s \) through linear regression, and rather just looked at a sum of the squared differences between the observed utilities and those produced by the multiplicative model, it would have been more problematic and subjective to evaluate the appropriateness of the model. The \( s \) coefficient provides a convenient and efficient way of determining how well the multiplicative model represents the joint HRQoL impact of
having two or more conditions. However, we recognize that in the current version of the paper, introducing $s$ immediately as a way of capturing additional interaction among conditions may have been confusing, as it might have suggested that we hypothesized an interaction among conditions. Rather, we did not know precisely what to expect and so we let the data inform us about the degree of interaction and the appropriateness of the multiplicative model, via the $s$ coefficient. In the revised version of the paper, we have adjusted the relevant text slightly in an attempt to better convey the purpose of $s$, and do not mention the term interaction until the end of page 7.

Further, we reexamined the following portion of the Discussion and conclusions section (page 12-13): “it was found that a straightforward multiplicative model best suited the average utilities for 278 pairs of co-morbid conditions; a synergy coefficient $s$, added to capture any additional interaction between conditions, optimized model fit at a value of .99, thus reinforcing the fit of the straightforward multiplicative model.”

We also recognize that this statement could imply that we hypothesized or expected an interaction. Thus the wording has been modified to better convey the purpose of $s$ and the meaning of the findings:

“Specifically, a synergy coefficient $s$, added to the straightforward multiplicative model in order to allow best fit to the data, optimized model fit at a value of .99. This result shows that the utility linked to co-morbidity is adequately explained via simple multiplication of the utilities for the individual conditions; in other words, there appears to be no synergistic effect of having two or more conditions.”

6) The Mathers et al. (2006) paper does use an innovative way to adjust for dependent co-morbidity in the calculation of HALE. However, the authors do indicate (second-last paragraph of their Discussion and conclusions section) that the basic multiplicative assumption for the disability weights themselves is still being used here, and that it seems reasonable in the absence of research examining the best ways to combine disability weights. The purpose of our paper was to examine the tenability of the multiplicative model for the disability weights themselves, so we invoked this comment by Mathers et al. simply to emphasize that no research has empirically tested the appropriateness of the multiplicative model. Performing the actual co-morbidity adjustments to the SMPH (e.g., HALE) are not a component of this paper so we did not comment further on this aspect of the Mathers et al. article.

7) Two new references [29,30] have been added on page 15 supporting the comment that the prevalence of self-reported conditions may be under-estimated (as compared to the prevalence of clinician-reported conditions).

**Minor Essential Revisions**

8) The page numbering has been corrected.
9) All material has been included describing the age-sex standardization calculations, and is found in Appendix A.

**Discretionary Revisions**

10) The author list has been restructured.