Point-wise averaging approach in dose-response meta-analysis of aggregated data

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Conclusions

- A point-wise averaging approach can properly address differential dose-response curves and exposure distribution, and limit the impact of extrapolation.
- Results can be presented graphically for a grid of exposure values.
- Differences with a two-stage approach may depend upon exposure distributions and strategies used in the dose-response analysis.
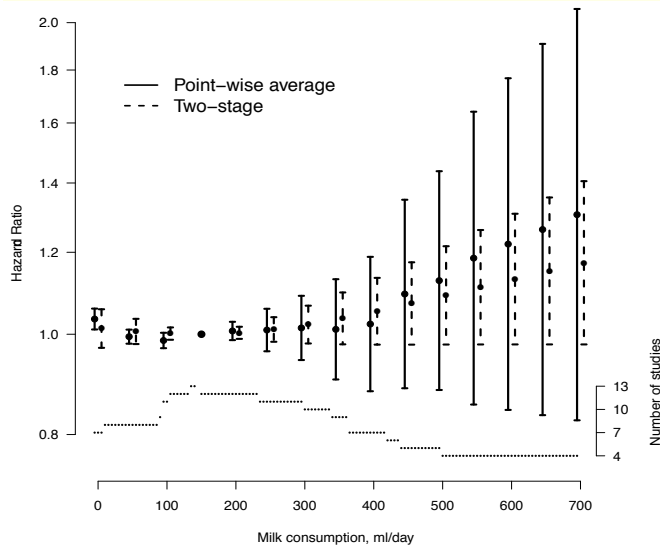

Figure 2. Comparison between point-wise averaging and two-stage approaches in a meta-analysis between milk and all-cause mortality. The step function at the bottom represents the number of studies contributing in the point-wise analysis. The predicted hazard ratios are presented on the log scale with 150 ml/day serving as referent.

Introduction

General limitations of a two-stage dose-response meta-analysis includes selection of a common curve for all the studies and discarding information about study-specific exposure distribution in pooling dose-response coefficients. As a consequence, some study-specific dose-response analyses may have a poor fit, and pooled estimates may be affected by extrapolation.

Aims

To propose a point-wise averaging approach for dose-response meta-analysis of aggregated data to take into account differential curves and exposure distributions.

Point-wise averaging approaches

It consists of the following steps:

1. Estimating study-specific dose-response curves;
2. Predicting study-specific effects (e.g. RRs, HRs) for a grid of exposure values;
3. Combining study-specific effects by meta-analysis.

Main advantages:

1. Study-specific analyses may differ (e.g. type of fractional polynomial, knots location);
2. Predictions may be limited to the observed study-specific exposure range, reducing the impact of extrapolation (Figure 1).
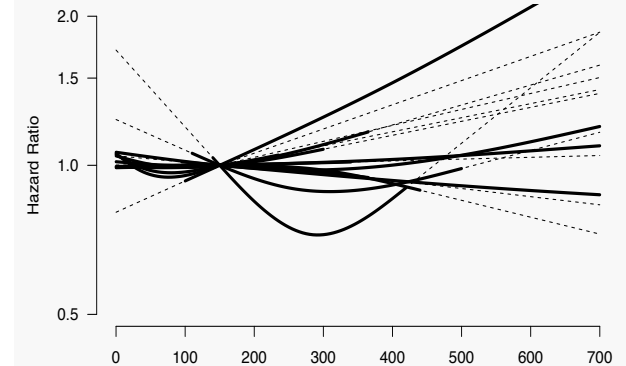

Figure 1. Study-specific dose-response curves on the association between milk and all-cause mortality. Dashed lines correspond to extrapolation. The predicted hazard ratios are presented on the log scale with 150 ml/day serving as referent.

Results

We re-analyzed a published dose-response meta-analysis on milk and all-cause mortality.

- The point-wise approach facilitated the individual dose-response analysis (different knots location).
- Study-specific predicted HRs were limited to the observed exposure range.
- As compared to a two-stage approach, similar results were obtained for intermediate exposure levels. Differences increased after 400 ml/day of milk consumption.
- The narrower confidence intervals for the two-stage approach may be explained by the effect of extrapolation (Figure 2).

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