

Appendix 1: Methods

In consultation with an information scientist, we searched MEDLINE, EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials databases from their earliest date to September 2010. Non-English articles were translated. The following search terms were used: insulin, hypoglycemic agent, initiation, start, begin, and regimen. Appropriate wildcards were used in the search in order to account for plurals and variations in spelling. Additional articles were identified through reference lists or discussions with experts. The titles and abstracts of studies identified through the literature search were screened for eligibility by two independent reviewers. Papers that passed the initial screening process were retrieved, and the full text was reviewed by two individuals who assessed the study quality and completed data abstraction. The data were manually compared for accuracy, and disagreements were resolved by a third reviewer or by the senior author.

We conducted the meta-analysis in R version 2.12.0 using the contributed package metafor version 1.4-0.¹ For each outcome in studies involving an oral antihyperglycemic agent as a comparator, we performed a meta-regression analysis that considered drug type or insulin regimen as a moderator variable. If the moderator showed no meaningful association with the outcome, it was subsequently ignored and the pooled random-effects estimate of treatment effect was based on all studies. If a moderator effect was present, group-specific estimates were obtained. The random-effect estimates were obtained by Restricted Maximum Likelihood (REML) estimation. For studies that cross-compared insulin, a common comparison group was not possible. Therefore, a separate meta-analysis was completed for each study type.²

References

1. Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw* 2010;96(3):1-48.
2. R Development Core Team. *R. A language and environment for statistical computing*. Vienna, Austria: 2008.