| **Author, Year** | **Purpose of Study** | **Databases Searched, Date of Last Search** | **Number of Studies** | **Types of Studies Included** |
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| **Intensive glucose control** | | | | |
| Buehler, 2013114 Good | Examine the effect of tight versus conventional glucose control in people with DM | Cochrane library, MEDLINE, EMBASE, ISI Web of Knowledge through May 2011 | 6 RCTs | Trials comparing tight versus conventional glucose control conducting in people age ≥18 years with DM and followup ≥1 year |
| Hemmingsen, 2012115 Good | Assess the effects of targeting intensive versus standard glycemic control in people with DM | Cochrane Library, MEDLINE, EMBASE, Science Citation Index Expanded, LILACS, CINAHL through December 2010 | 20 RCTs | Trials that prespecified different targets of glycemic control in adults with DM. |
| Coca, 2012116 Good | Compare the effects of intensive glucose control and standard glucose control on renal events in people with DM | MEDLINE, EMBASE, CCRCT through December 2010 | 7 RTCs | Trials comparing surrogate renal end points and clinical renal end points in patients with DM receiving intensive glucose control vs those receiving standard glucose control. |
| Hemmingsen, 2011117 | Assess the effect of intensive versus standard glycemic control on all-cause and CV mortality, non-fatal MI, microvascular complications and severe hypoglycemia | Cochrane Library, MEDLINE, EMBASE, Science Citation Expanded Index, LILACS, CINAHL through December 2010. Hand searches of reference lists, conference proceedings, pharmaceutical companies, FDA | 14 RCTs | Trials comparing targeted intensive glycemic control with standard glycemic control in patients with DM. Published and unpublished trials in all languages were included, irrespective of predefined outcomes. |
| Boussageon, 2011118 Good | To determine all-cause mortality and deaths from cardiovascular events related to intensive glucose lowering treatment in people with DM | MEDLINE, EMBASE, CDSR through July 2010 | 13 RCTs | Trials that assessed the effect of intensive glucose lowering treatment on CV and microvascular events |
| Castagno, 2011119 Good | To determine whether improved glycemic control reduces the risk of heart failure. | PubMed, CCRCT, metaRegister, pre-MEDLINE, and CINAHL through October 2010 | 8 RCTs | Trials comparing strategies of more versus less intensive glucose-lowering reporting HF events. |
| Wu, 2010120 Good | To evaluate the efficacy of intensive glucose control in the prevention of cardiovascular events when compared with standard glucose controls | MEDLINE, EMBASE, the Cochrane Library, and Science Citation Index through January 2009 | 6 RCTs | Trials comparing intensive glucose control strategies and standard glucose control strategies in populations with DM reporting all-cause and CV mortality and macrovascular events |
| Kelly, 2009121 Good | To summarize clinical benefits and harms of intensive versus standard glucose control for people with DM | MEDLINE database through April 2009 with no language restrictions. | 5 RCTs | Trials comparing intensive glucose control with standard glucose control with prespecified glucose targets, reporting CVD as the primary outcome and n>500 |
| Ma, 2009123 Good | To assess the relationship between major vascular events and intensive glycemic control | MEDLINE, EMBASE through December 2008, and the Cochrane Library, Issue 4, 2008 | 8 RCTs | Trials comparing intensive and standard glycemic control reporting vascular events, with target HbA1c levels |
| Mannucci, 2009124 Good | To assess of the effects of improvement of glycemic control on the incidence CVD | MEDLINE, EMBASE, and the Cochrane library through December 2008, restricted to randomized clinical trials, published in English | 5 RCTs | Trials reporting the between-group difference in mean HbA1c during the trial was at least 0.5%, planned duration of treatment of at least 3 years, CV outcomes. |
| Ray, 2009122 Good | To assess the effect of an intensive glucose-lowering regimen on mortality and CV outcomes | MEDLINE, the Cochrane Library, and EMBASE through January 2009 | 5 RCTs | Trials of intensive vs standard glucose lowering reporting CV events |
| **Intensive blood pressure control** | | | | |
| Bangalore, 2011125 | To evaluate target BP goals for patients with type 2 diabetes, impaired fasting glucose or glucose intolerance | PUBMED, EMBASE, Cochrane, through October 2010 | 13 RCTs | Trials with achieved SBP ≤140 mm Hg in both groups with at least 3 mm Hg difference between groups |
| Reboldi, 2011134 | To define the relation between the magnitude of BP reduction and the risk of stroke and MI in patients with diabetes | MEDLINE, EMBASE, Cochrane through March 2010 | 5 RCTs | Trials of more versus less intensive BP control, though criteria for inclusion not clearly defined |
| **Aspirin** | | | | |
| De Berardis, 2009132 | To assess the benefits and harms of low-dose aspiring in people with DM but without CVD | MEDLINE, Cochrane through November 2008 | 6 RCTs | Trials (blinded or open) of aspirin vs no aspirin reporting mortality, nonfatal MI or nonfatal stroke |
| Stavrakis, 2011133 | To assess the effect of low-dose aspirin for primary prevention of CV events in people with diabetes | MEDLINE, EMBASE through November 2009 | 7 RCTs | Trials (blinded or open) conducted in people with no prior CVD reporting mortality, MI or stroke |

| **Author, Year** | **Methods for Rating Methodological Quality of Primary Studies** | **Methods for Synthesizing Results of Primary Studies** | **Interventions** |
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| **Intensive glucose control** | | | |
| Buehler, 2013114 Good | Assessment of allocation concealment, blinding of study participants, outcome assessors and investigators, intention to treat analysis and completeness of followup. | Random effects meta-analysis, included assessment of heterogeneity | A. Intensive glucose control (n=14,792)  B. Standard glucose control (n=12,862) |
| Hemmingsen, 2012115 Good | Assessment of sequence generation, allocation concealment, blinding or participants and study personnel, presence of incomplete outcome data, selective outcome reporting and other sources of bias. | Cochrane Handbook for Systematic Reviews methods; heterogeneity examined by meta-regression; Sensitivity analysis performed. | A. Intensive glucose control (n=16,106)   B. Standard glucose control (n=13,880) |
| Coca, 2012116 Good | Assessment of method of allocation and concealment; blinding of participants, staff, and outcome assessors; incomplete outcome data; selective outcome reporting; and other sources of bias. | Forest plots were created to determine pooled measures using random effects model, heterogeneity was assessed. | A. Intensive glucose control (n=13,644) B. Standard glucose control (n=12,383) |
| Hemmingsen, 2011117 | Assessment of sequence generation, allocation concealment and blinding. | Random and fixed effects models and heterogeneity assessed. Sensitivity analysis including trial sequential analysis. | A. Intensive glucose control (n=15 269)  B. Standard glucose control (n=13 345). |
| Boussageon, 2011118 Good | Assessment of sequence generation, allocation concealment and blinding. | Calculation of risk ratios and 99% CIs, meta-analysis using used fixed effects model or random effects model if heterogeneity was significant. Absolute risk reductions calculated using the range risk estimates for each outcome in the control group of the three most powerful and recent trials (ACCORD, ADVANCE, and VADT) over a five year period. Sensitivity analysis was carried out according to the Jadad score. | A. Intensive glucose control (n=18,315)  B. Standard glucose control (n= 16,218) |
| Castagno, 2011119 Good | Assessment method unclear though authors state included studies were quality assessed; dual review was undertaken | Odds ratios (ORs) and 95% CIs, were calculated; heterogeneity was assessed. Egger's linear regression test was used to ascertain potential funnel plot asymmetry. | A. Intensive glucose control (n=19,562) B. Standard glucose control (n=17,667) |
| Wu, 2010120 Good | Assessment of randomization, allocation and blinding. | Relative risk and 95% CI calculated and results pooled using a random effects model with sensitivity analyses. Publication bias was assessed. | A. Intensive glucose control (n=14,792)  B. Standard glucose control (n=13,273) |
| Kelly, 2009121 Good | Assessment of randomization, blinding, adjudication procedures for outcomes, loss to followup. | Relative risk and CIs calculated and pooled using fixed-effects and DerSimonian and Laird random effects models with assessment of heterogeneity. | A. Intensive glucose control (n=14,662) B. Standard glucose control (n=13,410) |
| Ma, 2009123 Good | Assessment of randomization, allocation concealment, blinding, loss to followup/withdrawals, and similarity of baseline characteristics | Relative ratio and 95% CIs were calculated. Results pooled using a fixed effects or, if significant heterogeneity was present, a random effects model. | A. Intensive glucose control (n=5,544) B. Standard glucose control (n=3,984) |
| Mannucci, 2009124 Good | Assessment using QUOROM methods | Expected and observed event rates reported. Heterogeneity was assessed. If present both random and a fixed-effects models used. Weighted mean differences in BMI at endpoint, and Mantel-Henzel Odds Ratio (MH-OR) with 95% CI for all categorical endpoints, were calculated. Meta-regression was performed. | A. Intensive glucose control (n=17,267 B. Standard glucose control (n=15,362) |
| Ray, 2009122 Good | Assessment method not reported | Meta-analysis using random effects model, heterogeneity was assessed. a sensitivity analysis, odds ratios from the main analysis were compared with corresponding rate ratios. All p-values are two-sided (p<0·05). | A. Intensive glucose control (n=17,267) B. Standard glucose control (n=15,773) |
| **Intensive blood pressure control** | | | |
| Bangalore, 2011125 | Cochrane Collaboration methods: sequence generation of allocation, allocation concealment, blinding of participants/personnel/outcomes assessors, incomplete outcome data, selective outcome reporting, and other sources of bias | Meta-regression analysis to evaluate SBP and outcomes. Sensitivity analyses used Bayesian random-effects model | A. Intensive BP lowering (achieved SBP ≤135 mm Hg; n=19,042) B. Standard BP lowering (achieved BP ≤140 mm Hg; n=18,694) |
| Reboldi, 2011134 | Cochrane Collaboration methods: sequence generation of allocation, allocation concealment, blinding of participants/personnel/outcomes assessors, incomplete outcome data, selective outcome reporting, and other sources of bias | Fixed-effect and random-effect meta-regression | A. Intensive BP lowering (no specific BP targets; n=4,093) B. Standard BP lowering (no specific BP targets; n=4,239) |
| **Aspirin** | | | |
| De Berardis, 2009132 | Assessment of allocation concealment, blinding, intention to treat and completeness of followup | Random effects meta-analysis, included assessment of heterogeneity | A. Aspirin (n=5,064) B. No aspirin (n=5,053) |
| Stavrakis, 2011133 | Assessment of method of randomization, blinding and withdrawals/dropouts | Random and fixed effects models using DerSimonian-Laird method; included assessment of heterogeneity | A. Aspirin (n=not reported) B. No aspirin (n=not reported) |

**Abbreviations:** CI = confidence interval; CV = cardiovascular; CVD = cardiovascular disease; DM = diabetes mellitus; RCT = randomized, controlled trial.