

Protocol for the systematic literature search.

- Broad question 1: Is the antihyperglycaemic effect of DPP-4 inhibitors sustained over time?
- Specific question 1: Did trials assess glycaemic durability with DPP-4 inhibitors? The answer to this specific point was sought by searching trials that had glycaemic durability with DPP-4 inhibitors as main or secondary outcome.
- Specific question 2: in the absence of the durability outcome, which is the best way to assess durability of glycaemic control with DPP-4 inhibitors? The answer to this specific question was sought by searching trials with long follow up (at least 76 weeks) and serial measurements of haemoglobin A1c during the trial.
- Specific question 3: How can the antihyperglycaemic effect of DPP-4 inhibitor be quantified in function of time? The answer to this specific question was sought by using the difference between decrease of HbA1c from baseline at the end of follow-up (76-104 weeks) versus A1C decrease at intermediate assessments (24-52 weeks) during DPP-4 inhibitor administration as an index of glycaemic durability. The difference between final and intermediate HbA1c assessment was the primary endpoint.

The review followed the outlines of PICO (study characteristics):

1. Population: the population to be included in the review consisted of subjects with type 2 diabetes at baseline
2. Exposure: different DPP-4 inhibitors (sitagliptin, vildagliptin, saxagliptin, linagliptin, alogliptin).
3. Comparisons: HbA1c decrease at the end of follow up (second year of treatment) versus HbA1c decrease at an intermediate point (first year of treatment).
4. Outcomes: the difference between final and intermediate HbA1c assessment was the primary endpoint.

Published articles were considered eligible for this review: randomized controlled trials