Background: Multiple risk scores claim to predict the probability of post-operative pancreatic fistula (POPF) after pancreatoduodenectomy. A systematic review and meta-analysis assessed randomised controlled trials (RCTs) evaluating interventions to reduce All-POPF or clinically relevant (CR)-POPF after PD. A post-hoc analysis of negative RCTs assessed whether these had appropriate levels of statistical power.

Aim: To evaluate interventions to reduce postoperative pancreatic fistula (POPF) following pancreatectoduodenectomy (PD) with level 1 data.

Methods: A systematic review and meta-analysis assessed randomised controlled trials (RCTs) evaluating interventions to reduce All-POPF or clinically relevant (CR)-POPF after PD. A post-hoc analysis of negative RCTs assessed whether these had appropriate levels of statistical power.

Results: Among 22 interventions (n = 7,512 patients, 55 studies), 12 were assessed by multiple studies, and subject to meta-analysis. Of these, external pancreatic duct drainage was the only intervention found to be associated with significantly reduced rates of CR- and all-POPF. In addition, Ulinastatin was associated with significantly reduced rates of CR-POPF, whilst invagination (vs duct to mucosa) pancreaticojejunostomy was associated with significantly reduced rates of all-POPF. Review of negative RCTs found the majority to be underpowered, with post-hoc power calculations indicating that interventions would need to reduce the POPF rate to ≤1% in order to achieve 80% power in 16/34 (All-POPF) and 19/25 (CR-POPF) studies, respectively.

Conclusions: Meta-analysis supports a role for several interventions to reduce POPF after PD, although data is often inconsistent and/or based on small trials. Systematic review identifies other interventions which may benefit from further study. However, underpowered trials appear to be a fundamental problem, inherently more so with CR-POPF. Larger trials, or new directions for research are required to further understanding in this field.