

One Episode of Acute Pancreatitis is Just the Beginning: the Incidence of Recurrent Acute and Chronic Pancreatitis. A Systematic Review and Meta-analysis

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Introduction: Acute pancreatitis (AP) has a high incidence, and patients can develop recurrent acute pancreatitis (RAP) and chronic pancreatitis (CP) after AP.

Aim: We aimed to estimate the pooled incidence rates (IR), cumulative incidences, and RAP and CP proportions after AP.

Methods: Our protocol was registered on PROSPERO (CRD42021283252). The systematic search was conducted in three (Medline, Embase, Cochrane) databases on October 25th, 2022. Articles reporting the proportion of RAP or CP in patients after the first and multiple episodes of AP were eligible. The random effects model was used to calculate the pooled IR with 95% confidence intervals (CI). The I² value assessed heterogeneity. The risk of bias assessment was conducted with the Joanna Briggs Institute Critical Appraisal Tool.

Results: We included 106 articles in the quantitative synthesis and 26 in the IRs calculations (**Figure 1.**). Our results showed that the IR of RAP in adult patients after AP was 5.5 per 100 person-years (CI: 4.1 to 7.3; I²=93%), while in children, it was 3.7 per 100 person-years (CI: 2.8 to 5.0; I²=0%) (**Figure 2.**). We also found that the IR of CP after AP was 1.4 per 100 person-years (CI: 0.9 to 2; I²=75%), while after RAP, it increased to 4.3 per 100 person-years (CI: 3.1 to 6.0, I²=76%) (**Figure 3.**). All the other results can be seen in **Table 1**. The risk of bias was moderate in the majority of the included studies.

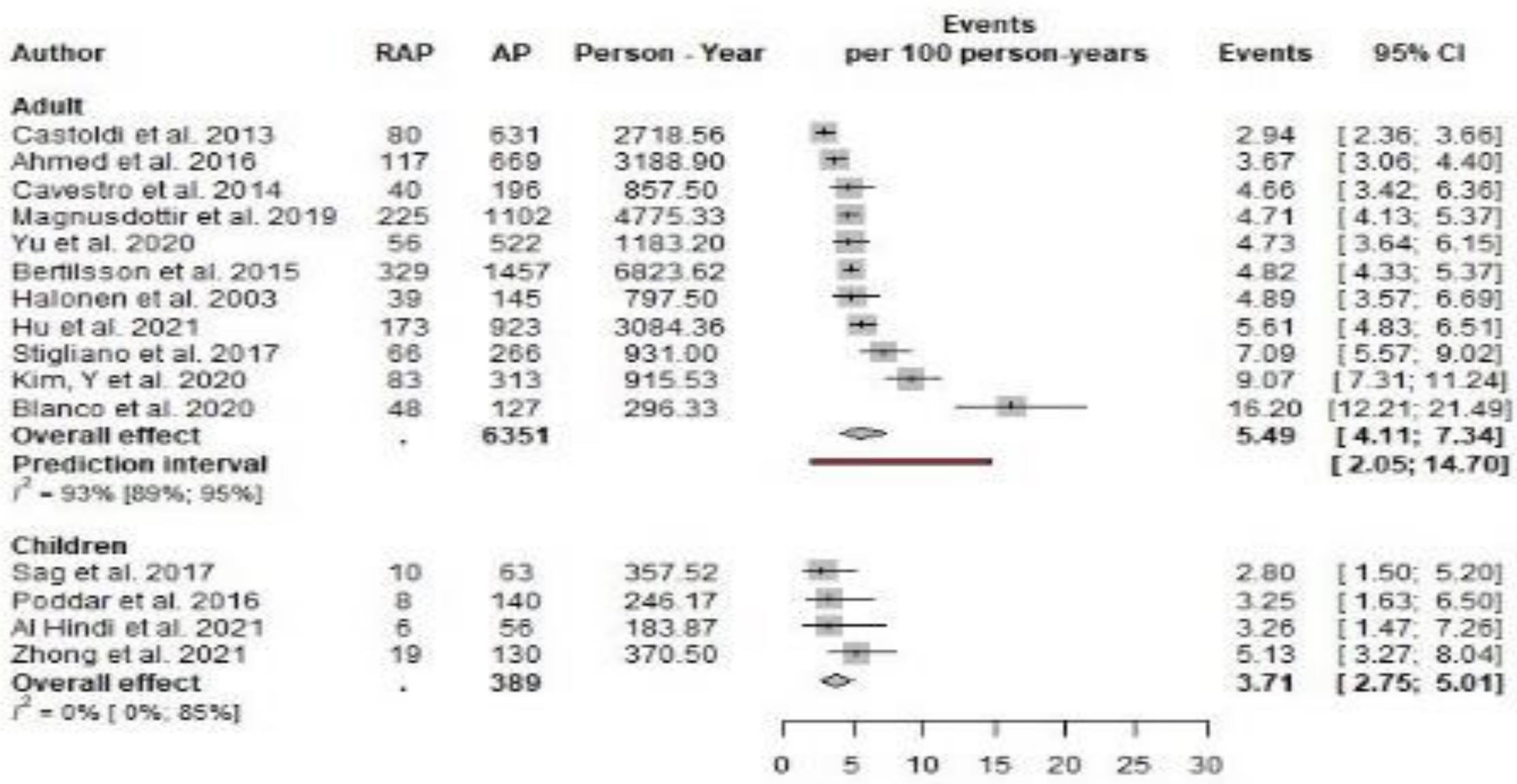


Figure 2. Forest plots showing the incidence rates of recurrent acute pancreatitis in adults and children; RAP, recurrent acute pancreatitis; AP, acute pancreatitis; CI, confidence interval; I², Higgins, and Thompson I² statistics;

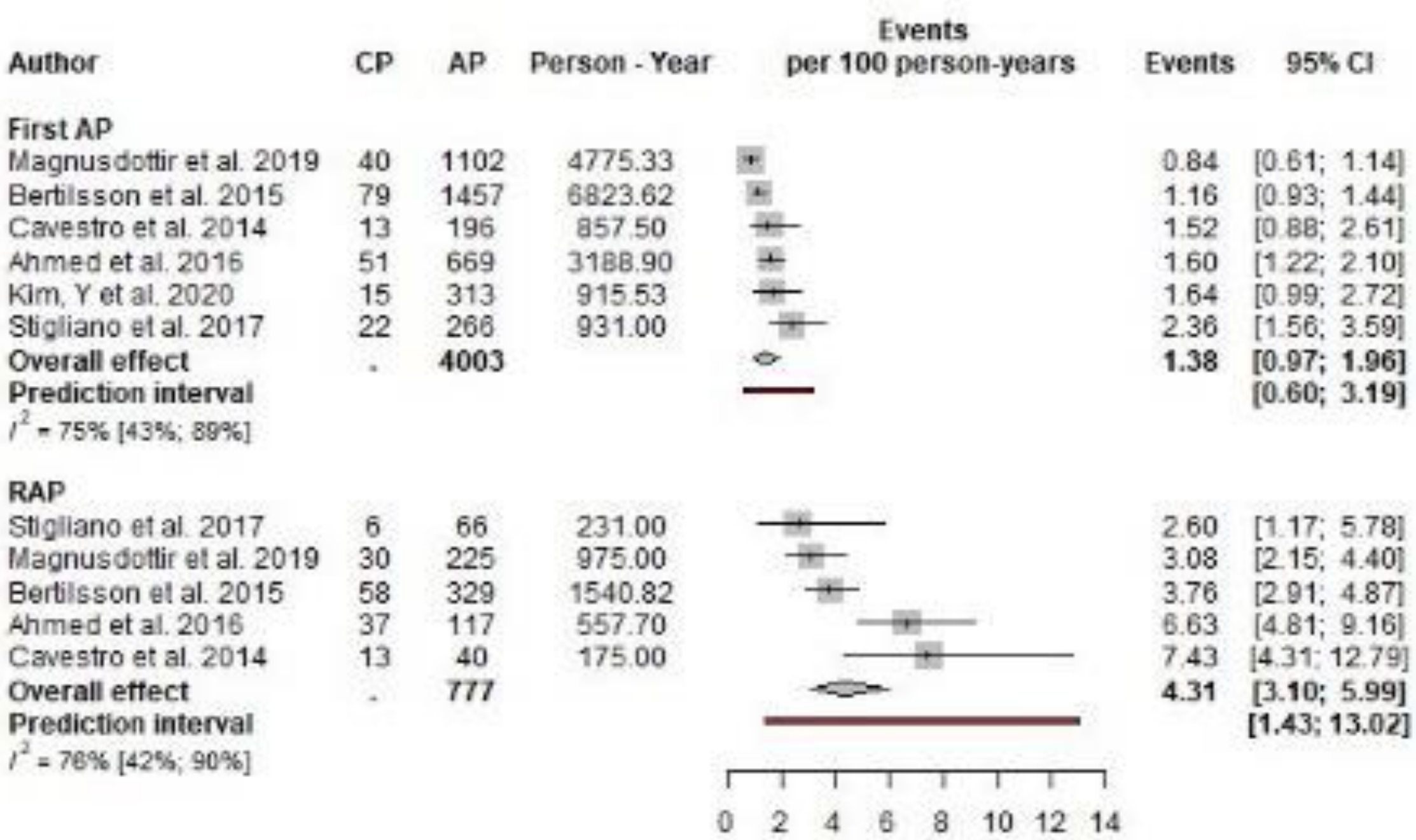


Figure 3. Forest plots showing the incidence rates of chronic pancreatitis after acute pancreatitis and recurrent acute pancreatitis; AP, acute pancreatitis; RAP, recurrent acute pancreatitis; CP, chronic pancreatitis; CI, confidence interval; I², Higgins, and Thompson I² statistics;

Conclusion: Our results showed that RAP affects many patients with AP. Compared to patients with the first AP episode, RAP leads to a threefold higher incidence rate for developing CP.

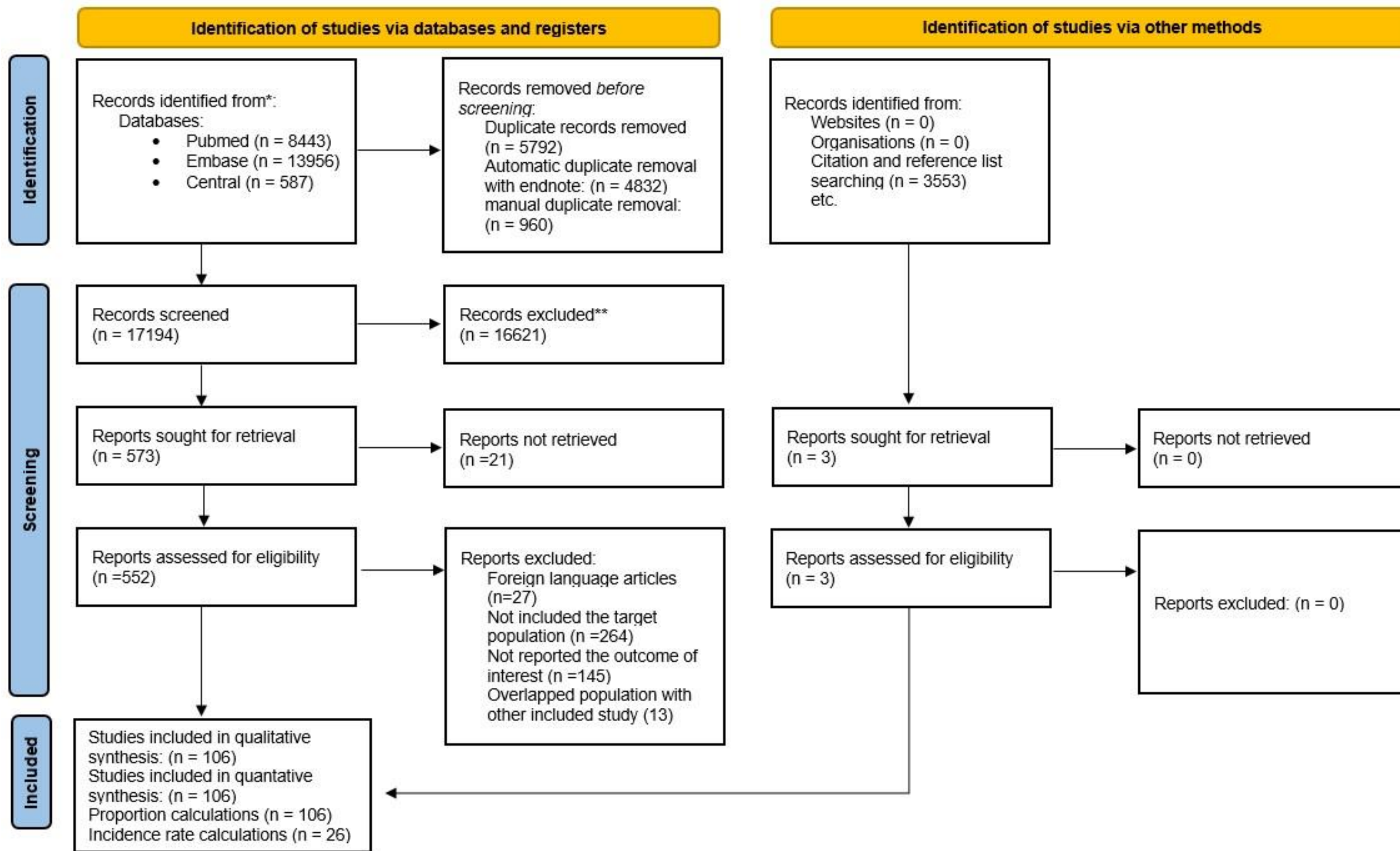


Figure 1. PRISMA FLOWCHART of the included studies in the meta-analysis; PRISMA, Preferred Reporting Items for Systematic Reviews, and Meta-Analyses

Table 1. Summary table with all results of the study

| Groups | Outcomes | Incidence rates (Events per 100 person-years) | Five - year Cumulative incidences | Proportions (recurrence rates and progression rates) | | |
|--|--------------|---|---|---|---|-----|
| | | | | Overall proportions (%) | Proportions (%) based on geographical region or etiology | |
| Adults with all etiologies of AP | RAP | 5.49 | 24% | 20% | Europe | 23% |
| | CP | 1.38 | 6.6% | 8% | - | - |
| | CP after RAP | 4.31 | 19.3% | 24% | Alcoholic | 22% |
| Children with all etiologies of AP | RAP | 3.71 | 16,9% | 20% | - | - |
| | CP | - | - | 7% | - | - |
| Based on the etiology and the severity of AP in Adults | | | | | | |
| HTG | RAP | 9.65 | 38.2% | 27% | - | - |
| Alcoholic | RAP | 6.62 | 28.1% | 24% | Europe | 30% |
| | CP | 2.66 | 12.4% | 18% | - | - |
| Idiopathic | RAP | 4.95 | 21.9% | 22% | Europe | 24% |
| | CP | 1.10 | 5.3% | 7% | - | - |
| Biliary | RAP | 3.03 | 14% | 8% | Europe | 7% |
| | CP | 0.33 | 1.6% | 2% | - | - |
| Drug-induced | RAP | - | - | 7% | - | - |
| Mild | RAP | 4.85 | 21.5% | 20% | - | - |
| Moderate | RAP | 7.56 | 31.4% | 21% | - | - |
| Severe | RAP | 4.90 | 21.7% | 13% | - | - |
| Based on the etiology and the severity of AP in Children | | | | | | |
| Idiopathic | RAP | - | - | 26% | - | - |
| Biliary | RAP | - | - | 14% | - | - |
| Mild | RAP | - | - | 16% | - | - |
| Moderate | RAP | - | - | 22% | - | - |
| Severe | RAP | - | - | 79% | - | - |

Abbreviations: AP, acute pancreatitis; RAP, recurrent acute pancreatitis; CP, chronic pancreatitis, HTG, hypertriglyceridemia. Each number or percentage in the incidence rate and proportions columns results from a meta-analysis/forest plot. The numbers in the cumulative incidence column were calculated from the incidence rate results. (Cumulative Incidence = $1 - e^{(-IR \times T)}$, where 'e' = 2.71828; e, Euler number; IR, incidence rate; T, 5 years)