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Abstract (oral session)

**Association between acid-suppression therapy and Clostridium difficile infection: a systematic review and meta-analysis**

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Objective: Emerging epidemiological evidence suggests that acid-suppression therapy use may increase the risk of Clostridium Difficile infection (CDI). We sought to systematically review the association between acid-suppression use and the risk of CDI. Methods: Two authors independently searched Ovid MEDLINE, EMBASE, ISI Web of Science, and Scopus from inception through August 2010. We performed random-effect meta-analyses for all studies together, separately for Proton Pump Inhibitors (PPIs) and H2-receptor antagonists (H2). case-control studies and cohort studies. Results: We identified 30 eligible studies (21 case-control and 9 cohort studies) with corresponding 52 effect estimates. All included studies were of very good quality. In a random effect meta-analysis, acid-suppression use was associated with a higher risk of CDI: odds ratio (OR)=1.58, 95% CI (1.38, 1.80), I<sup>2</sup>=82.6% (Figure). The pooled proportion of CDI cases that were exposed to antibiotics was 0.70, 95% CI (0.64, 0.75). The influence of a range of a-priori selected study-level and aggregated individual-level parameters on the observed pooled estimate was investigated by means of meta-regressions. We observed that Canadian studies had lower effect estimates than studies performed in other countries. Comparison of different country-specific study characteristics including the quality of studies showed that CDI cases in Canadian studies had higher exposure to antibiotics vs. non-Canadian studies (mean percentage: 90.0% (±5.5%) vs. 72.0% (±5.1%), p=0.024). Contour-enhanced funnel plot showed evidence of publication bias. A novel regression based method was used to adjust for publication bias and resulted in an adjusted average OR of 1.38 (95% CI, 1.21 – 1.58). Sensitivity analyses using the rule-out approach revealed that an unmeasured confounder has to be severely imbalanced between the acid-suppression users and non users (OR=10) or has to increase the risk of CDI by at least 2-fold to account for this association. Conclusions: This rigorously conducted systematic review and meta-analysis strongly suggests that acid-suppression use is associated with a higher risk of CDI, independent of antibiotic use. Our results were robust across different subgroups and to different assumptions of publication bias and residual confounding. Our findings have global implications both on the inappropriate use of acid-suppression therapy and its high associated costs and on the increasing incidence of CDI.

