Association between risk of c*lostridium difficile* infection and duration of proton pump inhibitor or H2-receptor antagonist use in hospitalized patients

Running title: Hospital acquired *Clostridium difficile* infection

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Supplemental data

Supplemental Table 1. Number of incident cases of *Clostridium difficile* infection by calendar year.

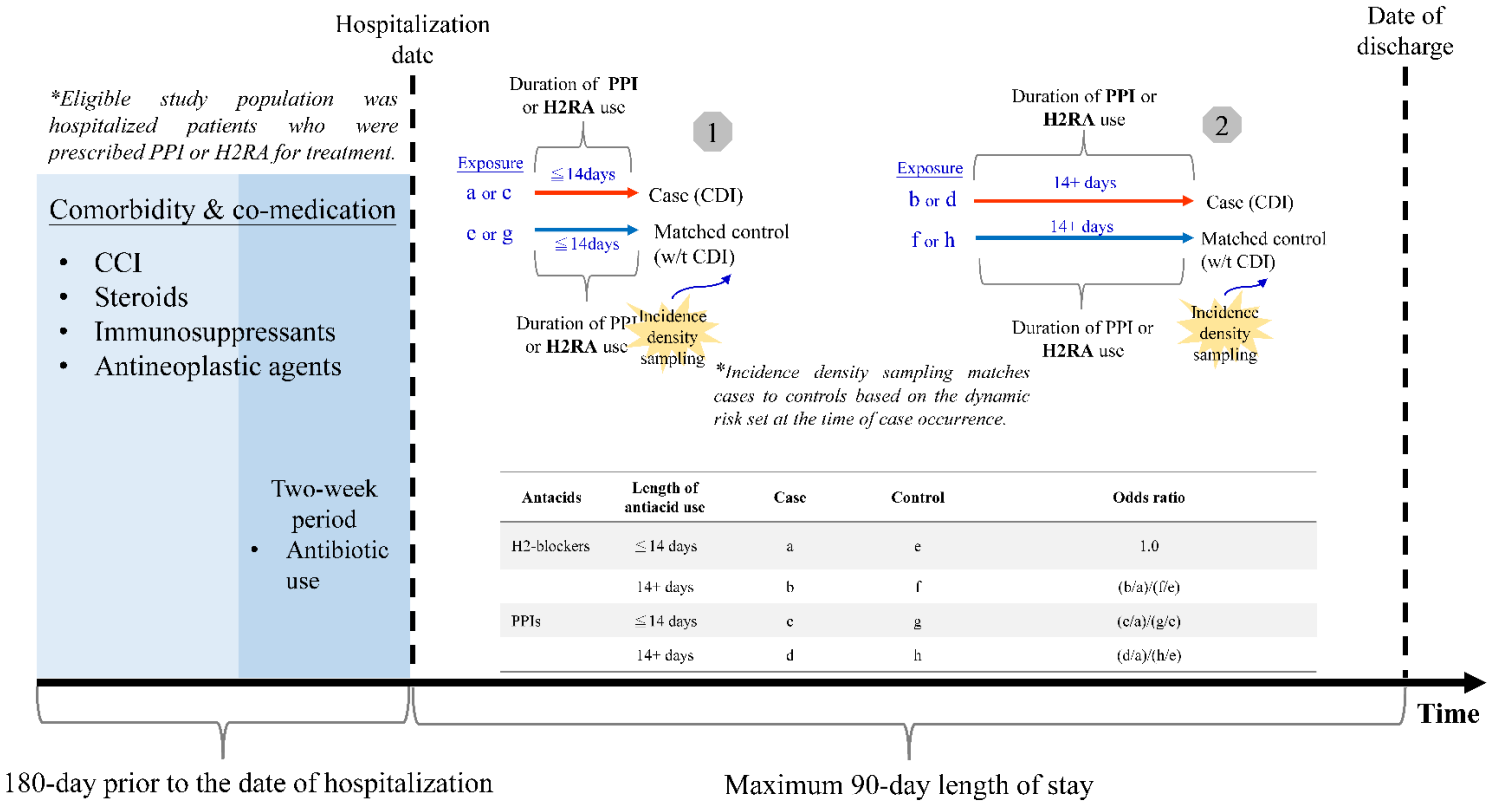
Year	Number of CDI cases
2012	1,113
2013	1024
2014	923
2015	922
2016	1,004
2017	1,014
2018	933

Supplemental Table 2. An example of a matrix for estimating odds ratios in a nested case-control study.

Antacids	Length of antiacid use	**Case**	**Control**	**Odds ratio**
H2-blockers	≦14 days	a	e	1.0
	14+ days	b	f	[b/a]/[f/e]
PPIs	≦14 days	c	g	[c/a]/[g/e]
	14+ days	d	h	[d/a]/[h/e]

Case and control represent outcome. Antacid and duration of antacid use represent exposure. We selected the control group with H2 blockers and ≦14 days as the reference group. Therefore, the unadjusted odds ratios of H2-blocker use and duration of antacid use over 14 days are [b/a]/[f/e]. The unadjusted odds ratios of PPIs use and duration of antiacid use less 14 days are [c/a]/[g/e]. The unadjusted odds ratios of PPIs use and duration of antiacid use over 14 days are [d/a]/[h/e].

Supplemental Figure 1. A framework of study design in this study.



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PPIs	≦14 days	c	g	(c/a)/(g/c)
	14+ days	d	h	(d/a)/(h/e)

Nested case-control study. The source population (eligible population) was our study cohort of hospitalized patients who were prescribed a PPI or H2RA for treatment. We then followed these patients, and if a patient had CDI during the PPI or H2RA exposure period, it was considered a case. Patients with CDI in this study were considered to be those who received oral metronidazole, fidaxomicin, or vancomycin for treatment at least seven days. If a patient becomes a case, we would randomly select a patient who did not have CDI at that time from the source population and matched by age, sex, and calendar year of entry into the cohort according to incidence density sampling as a control until the end of follow-up during the PPI or H2RA exposure period. The final case and control groups were matched to a case on a 1:1 basis for age, sex, and calendar year of cohort entry. Duration of PPI or H2RA use was based on PPI or H2RA exposure days in an as-treated design. PPI or H2RA exposure days began on the date of the first prescription and were censored at the date of discontinuation, switching, death, occurrence of CDI, hospital discharge, or the end of the study period after the first prescription, whichever occurred first. Discontinuation was defined as patients who stopped receiving PPIs or H2RAs within 7 days after the date of the last prescription.