

**Appendix 3: Ranges of frequency ratios for harms associated with proton pump inhibitors, and related references**

Harm	Frequency ratios (and confidence intervals)	Reference
Increased risk of fractures (overall)	RR- 1.14 (1.06, 1.24) – 1.29 (1.18, 1.41)	[1–4]
Increased risk of spine fracture	RR- 1.07(1.01,1.14) – 1.56 (1.31, 1.85)	[2–4]
Increased risk of hip fracture	RR- 1.16 (1.07, 1.27) – 1.30 (1.19, 1.43)	[2–6]
<i>Clostridium difficile</i> infections	RR- 0.9 (0.90,1.50) – 5.0 (1.3, 19.4)	[7–12]
<i>Clostridium difficile</i> -related diarrhoea	RR- 2.04 (1.93, 2.17) – 2.74 (1.85, 4.07)	[13,14]
<i>Campylobacter</i> infections	RR - 3.5 (1.1, 12.0) – 11.7 (2.5,54.0)	[12]
<i>Salmonella</i> infections	RR - 4.2 (2.2, 7.9) – 8.3 (4.3,15.9)	[12]
Community-acquired pneumonia	RR- 1.17 (1.11, 1.24) – 1.65 (1.25, 2.19)	[15–17]
Hospitalisation for community-acquired pneumonia	RR - 1.05 (0.89,1.25)	[17]
Gastric cancer	OR- 1.39 (1.19, 1.64)	[18]
Gastric atrophy	OR - 1.50 (0.59, 3.80)	[19]
Intestinal metaplasia	OR - 1.46 (0.43, 5.03)	[19]
Simple ECL hyperplasia	OR - 5.01 (1.54, 16.26)	[19]
Focal ECL hyperplasia	OR - 2.48 (0.44, 14.13) - 3.98 (1.31, 12.16)	[19,20]
Colorectal cancer	OR - 1.08 (0.96, 1.20)	[21]
Corporal chronic inflammation	OR - 1.30 (0.68, 2.48)	[20]
Increased risk of vascular events among patients taking clopidogrel	RR- 1.10 (0.75, 1.61) – 1.60 (1.07, 2.40)	[22–31]
Bacterial peritonitis	RR- 2.22 (1.28 – 3.83) – 3.15 (2.09, 4.74)	[32–35]
Small intestine bacterial overgrowth	RR- 2.82 (1.24, 4.21)	[36]

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