

Report on the Abstract “*Use of proton pump inhibitors and risk of osteoporosis-related fractures*”

[1] The topic of the study I chose is how proton-pump inhibitors (PPI's), a medication frequently prescribed for people experiencing acid reflux, may cause or worsen osteoporosis. The reason I'm interested in this topic is because my father, who was a healthy, athletic man well into his 80's, took this medication for many years and developed osteoporosis so severe that his spine fractured multiple times. This severely affected the quality of his life in his last years, and illustrates how important it is that we all personally investigate the medications we are prescribed rather than relying on physicians to do this for us.

[2] The researchers were investigating the duration of exposure to PPI's and osteoporosis-related fractures. Their findings were that taking PPI's for 6 or fewer years was not associated with increased risk of fractures; however, in patients who took PPI's for more than 7 years there was an increased risk of fractures.

[3] The researchers matched 15,792 cases of osteoporosis-related fractures with 47,289 controls. I'm assuming that within each of these groups, they further divided them into PPI and no-PPI groups. The researchers, listed in the abstract, collected data indirectly by using administrative claims to identify patients with a fracture of the hip, vertebra or wrist between April 1996 and March 2004. Since the authors of the study were from Canada (Manitoba), presumably the data came from Canadian patients though the abstract does not directly mention that.

[4] The treatment variable was use of proton pump inhibitors. The outcome was whether or not a patient had an osteoporosis-related bone fracture. The study was strictly observational; the subjects were not randomly assigned to the PPI vs. no-PPI groups. There was a comparison group (mentioned above, in paragraph 3). Because the sample of subject wasn't randomly selected, the results cannot be extended with confidence to the general population. The study was observational so we also can't conclude that there is a cause-and-effect relationship between PPI's and fractures; however, since it is a very large study and the researchers controlled for confounders, we can be very suspicious that there is, in fact, a causal relationship. The researchers controlled for the

confounders of age, sex, and comorbidities. A possible confounder the researchers didn't mention is that there could be a genetic link that affects a person's predisposition toward having gut issues (hence their use of PPI's) and also having osteoporosis.

[5] The statistical analysis performed was in computing an "odds ratio" for relative risk of bone fracture in people who take PPI's. Exposure of 7 or more years was associated with increased risk of an osteoporosis-related fracture (adjusted OR 1.92, 95% confidence interval [CI] 1.16–3.18, $p = 0.011$). What this means is that people taking PPI's for more than 7 years are 1.92 times more likely to have a fracture as compared to those who don't take PPI's. The confidence interval means that the OR could be between 1.16 and 3.18 but any OR over 1 is an indicator that the PPI's are associated with increased risk of osteoporosis. This was a statistically significant result, due to the small P-value ($p = .011 < .05$). The P-value means that there was a 1.1% chance that the association the data shows between taking PPI's and having an increased risk of fracture was only due to sampling variability, not because there was an actual association. There was an even higher risk of just hip fractures (OR = 4.52) with stronger evidence, as indicated by the P-value ($p = .002$).

[6] From this study, I learned that taking PPI's as a short term solution to stomach issues doesn't increase the risk of osteoporosis but that someone like my father, who had risk factors for osteoporosis (his mother developed osteoporosis at a relatively young age) should never have been prescribed PPI's as an ongoing treatment for 15+ years.

Words/phrases I wasn't sure about and had to look up or make assumptions about:

- (1) "administrative claims": I'm guessing these are claims for reimbursement from the Canadian health program (like our insurance companies in the U.S.).
- (2) "comorbidities": A Google search gave this definition: "When two disorders or illnesses occur in the same person, simultaneously or sequentially, they are described as comorbid. Comorbidity also implies interactions between the illnesses that affect the course and prognosis of both."
Source: <https://www.drugabuse.gov/publications/research-reports/comorbidity-addiction-other-mental-illnesses/what-comorbidity>
- (3) "odds ratio (OR)": A Google search gave this definition: The OR represents the **odds** that an outcome will occur given a particular exposure, compared to the **odds** of the outcome occurring in the absence of that exposure.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2938757/>

Abstract: <http://www.cmaj.ca/content/179/4/319.short>; accessed on March 11, 2017

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Use of proton pump inhibitors and risk of osteoporosis-related fractures

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Abstract

Background: The use of proton pump inhibitors has been associated with an increased risk of hip fracture. We sought to further explore the relation between duration of exposure to proton pump inhibitors and osteoporosis-related fractures.

Methods: We used **administrative claims** data to identify patients with a fracture of the hip, vertebra or wrist between April 1996 and March 2004. Cases were each matched with 3 controls based on age, sex and **comorbidities**. We calculated adjusted **odds ratios (OR)** for the risk of hip

fracture and all osteoporosis-related fractures for durations of proton pump inhibitor exposure ranging from 1 or more years to more than 7 years.

Results: We matched 15,792 cases of osteoporosis-related fractures with 47,289 controls. We did not detect a significant association between the overall risk of an osteoporotic fracture and the use of proton pump inhibitors for durations of 6 years or less. However, exposure of 7 or more years was associated with increased risk of an osteoporosis-related fracture (adjusted OR 1.92, 95% confidence interval [CI] 1.16–3.18, $p = 0.011$). We also found an increased risk of hip fracture after 5 or more years of exposure (adjusted OR 1.62, 95% CI 1.02–2.58, $p = 0.04$), with even higher risk after 7 or more years exposure (adjusted OR 4.55, 95% CI 1.68–12.29, $p = 0.002$).

Interpretation: Use of proton pump inhibitors for 7 or more years is associated with a significantly increased risk of an osteoporosis-related fracture. There is an increased risk of hip fracture after 5 or more years exposure. Further study is required to determine the clinical importance of this finding and to determine the value of osteoprotective medications for patients with long-term use of proton pump inhibitors.