Risks of Longer Term Proton Pump Inhibitor Exposure in 228,752 Older Adults

Dr Jane Masoli
NIHR Clinical Doctoral Research Fellow & Geriatrics Registrar
CONFLICT OF INTEREST DISCLOSURE

I have no potential conflict of interest to report
Background: PPIs

• Commonly used, highly effective
• Much improved treatment and control of
  – peptic ulcers
  – GORD
  – NSAID-associated gastropathy
European examples: time trends of antisecretory drug consumption

A. Lanas, We Are Using Too Many PPIs, and We Need to Stop: A European Perspective, Am J Gastroenterol, 10 May 2016
Potential risks

• Potentially inappropriate prescribing
• Adverse outcomes of long term use poorly understood
• Costly:
  – 30% reduction in PPIs =£35 million 1 year saving
Aim

• To estimate the risk of specific adverse outcomes in older adults exposed to PPIs for \( \geq 1 \) year

• Outcomes of interest:
  – Fragility fractures
  – Pneumonia
  – Cardiovascular disease
Methods

• Data source: Clinical Practice Research Datalink
  – Primary care and hospital linked data (>2 million 60+)
• Retrospective cohort analysis of cases and matched controls
• Known confounding: standard methods
  – propensity scoring
  – regression adjustment with up to 78 covariates
• Unknown confounding
  – Prior event rate ratio (PERR)
• 4 year follow-up
Methods: PERR

• Uses the ratio between the HR of event in exposed and unexposed prior to the intervention to adjust incident rate ratios

• Assumes unknown confounding to be equal pre-and post-exposure
Results: Fragility Fractures

- n=86,469 cases (PPIs >1year) and 86,469 controls
Results: Pneumonia

- n= 75,050 cases (PPIs >1 year) and 75,050 controls
Results: Pneumonia

<table>
<thead>
<tr>
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<th>Pre-treatment period</th>
<th>Treatment period</th>
<th>Net estimate</th>
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<tr>
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<td>Full sample n=150,100</td>
<td>PERR-adjusted</td>
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<tr>
<td>HR (95% CI)</td>
<td>1.67 (1.37 to 2.02)</td>
<td>3.03 (2.60 to 3.53)</td>
<td>1.82 (1.27 to 2.54)</td>
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Results: Cardiovascular MI

- n= 114,376 cases (PPIs >1 year) and 114,376 controls
Results: Cardiovascular MI

- n = 114,376 cases (PPIs >1 year) and 114,376 controls
Results: Cardiovascular Stroke

• n= 114,376 cases (PPIs >1 year) and 114,376 controls
Results: Cardiovascular Stroke
Conclusions

• Longer term PPI exposure may lead to increased risk of excess fragility fracture, pneumonia and MI in some older adults

• Consider the appropriateness of each PPI prescription
Thanks

• NIHR
• Jan Zirk-Sadowski
• Alessandro Ble
• Professor David Melzer
  & the clinical epidemiology team