

## Drugs to curb excess stomach acid may be linked to heightened risk of death

*May be time to restrict use of widely available proton pump inhibitors, say researchers*

Proton pump inhibitors (PPIs)—a widely available class of drug designed to curb excess stomach acid production—may be linked to a heightened risk of death, indicates research published in the online journal ***BMJ Open***.

Given how widely available these drugs are, and the accumulating evidence pointing to links with a range of potentially serious side effects, it may be time to restrict the indications for use and duration of treatment with PPIs, suggest the researchers.

Recent research has indicated a link between PPI use and a heightened risk of chronic kidney disease/kidney disease progression, dementia, *C difficile* infections, and bone fractures in people with brittle bone disease (osteoporosis).

Although far from conclusive, emerging evidence suggests that PPIs may boost the risk of tissue damage arising from normal cellular processes, known as oxidative stress, as well as the shortening of telomeres, which sit on the end of chromosomes and perform a role similar to the plastic tips on the end of shoelaces.

The researchers base their findings on national US data obtained from a network of integrated healthcare systems involving more than 6 million people whose health was tracked for an average of almost six years—until 2013 or death, whichever came first.

They carried out three comparative analyses: those taking PPIs with those taking another type of drug used to dampen down acid production called histamine H2 receptor antagonists or H2 blockers for short (349, 312 people); users and non-users of PPIs (3,288,092 people); and users of PPIs with people taking neither PPIs nor H2 blockers.

Compared with H2 blocker use, PPI use was associated with a 25% heightened risk of death from all causes, a risk that increased the longer PPIs were taken.

The other analyses revealed a similar level of risk between users and non-users of PPIs and between those taking PPIs and those taking no acid suppressant drugs.

The risk of death was also heightened among those who were taking PPIs despite having no appropriate medical indication for their use, such as ulcers, *H pylori* infection, Barrett's oesophagus (pre-cancerous changes to the food pipe) and gullet (oesophageal) cancer.

This is an observational study, so no firm conclusions can be drawn about cause and effect, added to which participants were mostly older white US veterans, possibly limiting the wider applicability of the findings. Nor were the researchers able to obtain information on the causes of death.

Although there is no obvious biological explanation for their findings, the researchers nevertheless suggest that the consistency of their results and the growing body of evidence linking PPI use with a range of side effects is "compelling."

They write: "Although our results should not deter prescription and use of PPIs where medically indicated, they may be used to encourage and promote pharmacovigilance [monitoring the side-effects of licensed drugs] and [they] emphasise the need to exercise judicious use of PPIs and limit use and duration of therapy to instances where there is a clear medical indication and where benefit outweighs potential risk."