METHODS Data source We analyzed the Korean nationwide cohort database of the National Health Insurance Service (NHIS) from 2014 to 2020.Statistical analysis was performed on all data using SAS version 9.3 (SAS Institute Inc., Cary, NC, USA), and statistical significance was tested with a significance probability of 0.05 and a two-tailed test.Concomitant diseases such as chronic obstructive pulmonary disease (COPD), testicular dysfunction, hypothalamic dysfunction, hyperthyroidism, hyperparathyroidism, Cushing's syndrome, hyperprolactinemia, vitamin D deficiency, idiopathic hypercalciuria, diabetes, anorexia nervosa, systemic lupus erythematosus, hypertension, intestinal absorption disorder, inflammatory bowel disease, chronic kidney disease, and secondary amenorrhea were also identified.We also identified concomitant drugs that may affect osteoporotic fractures such as bisphosphonates, glucocorticoids, anticonvulsants, hormone replacement therapy, warfarin, heparin, antacids, selective serotonin reuptake inhibitors, benzodiazepines, and tricyclic antidepressants.This included patients with a diagnosis code of osteoporotic fracture (M80) and those with fracture codes for specific locations (thoracic vertebrae [S220–S221], lumbar vertebra [S320, S327], spine [M484, M485], proximal humerus [S422, S423], femur [S720, S721], and distal radius [S525, 526]), following treatment and diagnosis of osteoporosis (M81, M82) [15].Conditional logistic regression analysis was performed to determine the association between the use of anti-peptic agents and the incidence of osteoporotic fractures, and the results are presented as hazard ratio (HR) and 95% confidence interval (CI).Patients under the age of 50, those diagnosed with malignancy, acquired immunodeficiency syndrome, osteoporosis and fracture, and those prescribed anti-peptic agents within 1 year prior to the entry date were excluded.The MPAs included eupatilin, irsogladine, ecabet sodium, sodium alginate, misoprostol, rebamipide, teprenone, and troxipide.Categorical variables, such as sex, types of health insurance, presence of comorbidities, and presence of concomitant medications, are presented as frequencies and percentages, while continuous variables, such as age and CCI, are presented as mean and standard deviation.Logistic regression analysis was conducted for each factor to determine its statistical significance in predicting the risk of osteoporotic fractures.Drug exposure and covariates We confirmed the prescription and duration of PPI, H2RA, and MPA using the drug code (main ingredient code) in the NHIS claims database.Study population Patients who had been prescribed anti-peptic agents, such as PPI, H2RA, or MPA, for more than 2 days between 2014 and 2020 were selected from the NHIS database.Osteoporotic fractures were confirmed according to International Classification of Diseases 10th Revision (ICD-10) codes included in the medical claims data of the NHIS.The PPIs included rabeprazole, pantoprazole, S-pantoprazole, lansoprazole, dexlansoprazole, omeprazole, esomeprazole, and ilaprazole.The H2RAs included roxatidine, nizatidine, lafutidine, famotidine, cimetidine, and .ranitidine.All methods were performed in accordance with relevant guidelines and regulations