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Age-related decline of gastric secretion: facts and controversies

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ADMINISTRATIVE INFORMATION

Support - FCT/MCTES.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 June 2025 and was last updated on 18 June 2025.

INTRODUCTION

Review question / Objective Does gastric secretion reduce with aging? By addressing gaps in knowledge and suggesting future exploration, this review aims to contribute to (1) Assessing the influence of aging in gastric secretion, (2) Evaluating the importance in the gastric secretion of factors frequently associated with aging, and (3) Discussing the potential clinical impact of these findings.

Background Society is witnessing a remarkable increase in life expectancy, resulting in a greater ageing population worldwide. Healthcare providers require a basic understanding of essential ageing medicine to provide adequate healthcare to older patients. However, current knowledge about digestive changes in the older population is scarce, as most clinical trials exclude elderly patients.

Normal physiology of the stomach is required for digestion, absorption of nutrients and drugs, and protection against ingested pathogens, as the gut is the largest human surface of contact with environmental factors. Aging is associated with structural and functional decline in all organs and systems, including the digestive tract. Indeed, previous studies have documented several structural and functional changes in the gastrointestinal tract, as up to 80% of older individuals have morphological gastric changes. The stomach has an important secretory function: producing pepsinogen for primary protein digestion, hydrochloric acid in a protective role, and intrinsic factor (IF) for the uptake of cobalamin.

Rationale Despite a progressively ageing population, the influence of age on gastric secretion remains a matter of debate, with several studies from different research teams reporting conflicting results. Moreover, the impact of sex, smoking status, geography, metabolic, and clinical factors have not been clearly ascertained. Due to multimorbidity and the lack of deprescribing procedures, elderly patients are particularly prone to polypharmacy. Proton pump inhibitors (PPIs) are one of the most prescribed drugs for the treatment

of heartburn, gastroesophageal reflux disease, and peptic ulcer disease, as well as for concomitant treatment for Helicobacter pylori (H. pylori) infection. Furthermore, PPIs are very frequently prescribed as "gastric protection" for senior citizens under polypharmacy. However, data about a possible age-related decline in gastric secretion may show that PPIs and other antisecretory therapies can be pointless and inappropriate in these patients.

METHODS

Strategy of data synthesis A comprehensive search of four electronic databases (i.e., PubMed, Web of Science, Embase and Google Scholar) was conducted up to December 2024. Given the paucity of recent studies, no restrictions were applied regarding the publication date of the sources.

Eligibility criteria Articles must be published in English or another language with an accompanying English abstract. The sample under consideration must be composed of either animal models or human beings. The articles must address the possible impact of aging on gastric secretion. It was determined that articles lacking English abstracts or failing to meet the inclusion criteria were to be excluded from the study.

Source of evidence screening and selection The integration of keywords and subject headings was conducted following the thesaurus of each database, employing the following search strings: (Aging OR elder OR older OR geriatric) AND (1) (gastric secretion); OR (2) (hydrochloric acid OR gastric acid); OR (3) (intrinsic factor); OR (4) pepsin OR pepsinogen). A manual search for the reference lists of the final included studies was conducted to identify any additional relevant literature.

Data management In order to fulfil the requirements of the article selection task, a preliminary evaluation of the titles and abstracts was conducted to ascertain the extent to which there was consensus regarding their inclusion and/or exclusion under the predefined criteria. In instances where the title and abstract were either uninteresting or inconclusive, the entire document was read to mitigate any potential loss of valuable information that might have occurred during the study. The selection of articles for inclusion in the study was based on their relevance to the subject matter. A predefined table extracted the necessary data from each eligible study, listing the author's last name, publication year, study characterisation (animal studies or human studies), number of patients (younger and older groups, if applicable), outcomes in gastric secretion, and general comments that could influence generalisation.

Language restriction Articles must be published in English or another language with an accompanying English abstract.

Country(ies) involved Portugal.

Keywords Aging; Gastric secretion; Chronic atrophic gastritis; Helicobacter pylori; Precision medicine.

Contributions of each author

Author 1 - Francisco Vara-Luiz - Author 1: conceptualization, methodology, formal analysis, investigation, drafting the manuscript.
Author 2 - Ivo Mendes - Author 2: Methodology, investigation, drafting the manuscript.
Author 3 - Carolina Palma - Author 3: Methodology, investigation, drafting the manuscript.
Author 4 - Paulo Mascarenhas - Author 4: Methodology, investigation, reviewing the manuscript.
Author 5 - Marta Patita - Author 5: Methodology, investigation, reviewing the manuscript.
Author 6 - Gonçalo Nunes - Author 6: Methodology, investigation, reviewing the manuscript.
Author 7 - Jorge Fonseca - Author 6: Conceptualization, Methodology, investigation, reviewing the manuscript.