

## **INFLUENCE OF GLUTEN-RICH DIETS ON THE INTESTINAL AND MENTAL HEALTH OF THE ELDERLY POPULATION: AN INTEGRATIVE REVIEW**

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### **ABSTRACT**

During natural aging, a variety of complex degenerative processes occur, particularly in the gastrointestinal tract, affecting both its morphology and function. These modifications in the elderly threaten nutrient absorption and intestinal permeability, promoting a pro-inflammatory environment in the aging gut, which can lead to constipation, gastroparesis and dysbiosis. Chronic inflammation can reach the brain because the gastrointestinal tract integrates signals from the gut-brain axis and induces neuroinflammation-compromising mechanisms that contribute to depression, anxiety, and progressive cognitive decline. Modern diets high in gluten may represent an underestimated factor contributing to intestinal disturbances and to the worsening of neuropsychiatric conditions, which are more severe in older adults than in younger individuals. The purpose of this integrative review was to investigate the effects of a gluten-rich diet on the vulnerabilities generated by aging in intestinal and mental health. A comprehensive search that was conducted in the PubMed and SciELO databases covering publications from 2015 to 2025. Eight studies met the exclusion and inclusion criteria and were selected for the integrative review analysis. The findings of these studies suggest that gluten may exacerbate age-related vulnerabilities and that following a gluten-free diet could potentially improve both intestinal and mental health disorders. However, further research is needed, particularly among non-celiac elderly individuals, to fully understand the impact of gluten on both intestinal and mental health.

### **KEY WORDS**

Celiac disease; Clinical care; Diagnosis; Age-generated vulnerabilities; Non-celiac gluten sensitivity

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## INTRODUCTION

Natural aging causes a series of systemic changes in the human body, which is a gradual and complex process influenced by DNA damage, cellular metabolic alterations, chronic inflammation and intestinal microbiota imbalance, ultimately leading to the functional decline of multiple organs (JING, Y. et al., 2025). In the gastrointestinal tract, aging is primarily associated with progressive impairment of both morphology and function. This process alters intestinal motility, reduces enteric neuron density, weakens the epithelial barrier and causes thinning of the mucosa (PATEJDL, R., 2024; DEJONG et al., 2020; BOSCO, N.; NOTI, M., 2021). As a result, these modifications in the elderly compromise nutrient absorption and increase intestinal permeability, creating a pro-inflammatory environment in the aging gut. This environment is the underlying concept of inflammaging (ZHANG, L. et al., 2023) and predisposes this group to conditions such as constipation, gastroparesis and dysbiosis.

The gastrointestinal tract is increasingly being recognized as a dynamic neuroimmune interface that integrates signals from the Gut-Brain Axis, a complex communications network involving the enteric and central nervous systems, immune mediators, endocrine pathways and microbial metabolites via the vagus nerve and other conduits (PARK, J. C., et al., 2025; FUNG, T. C., et al 2020). Chronic intestinal inflammation can reach the brain and induce neuroinflammation, thereby compromising synaptic plasticity and reducing serotonin availability. These mechanisms further contribute to depression, anxiety and progressive cognitive decline (MAYER et al., 2023; PARK et al., 2025). This information suggests that elderly individuals are particularly susceptible to this cascade of alterations, which amplifies their risk of neuropsychiatric and cognitive disorders (MAYER et al., 2023; PARK et al., 2025).

Beyond the intrinsic mechanisms of aging, external factors such as modern dietary habits significantly impact intestinal health and cognitive outcomes in the elderly due to their predisposition to Celiac Disease (CD) and Non-Celiac Gluten Sensitivity (NCGS) (ARANBURU et al., 2021; CATASSI et al., 2024). The advancement of agriculture, food production and global distribution has led to a profound modification of dietary patterns, often driven more by financial, political or cultural factors rather than health considerations (POPKIN et al., 2020; MONTEIRO et al., 2019). Contemporary gluten-rich diets may contribute to intestinal complications and to neuropsychiatric symptoms, which appear to be more prevalent or severe in the elderly compared to younger individuals (DEJONG et al., 2020; BEAS et al., 2024; CATASSI et al., 2017). This study aims to investigate the effects of a gluten-rich diet on vulnerabilities generated by aging in intestinal and mental health. It also seeks to explore the possible benefits of a gluten-free or reduced diet in the elderly population.

## METHODOLOGY

This study consists of an integrative review. A comprehensive search was conducted in PubMed and SciELO databases covering publications from 2015 to 2025. The search strategy combined standard descriptors (MeSH/DeCS) and free-text keywords, including “Aging”, “Elderly”, “Intestine”, “Gut”, “Gluten”, “Gluten Sensitivity”, “Celiac Disease”, “Diet”, and “Mental Health”. The search was then limited by exclusion criteria, which included studies that did not involve children or adults with stratified analysis, non peer-reviewed articles and duplicates. Articles were screened through title and abstract reading to eliminate those with no

relevance to the review theme. Finally, the remaining articles were subjected to eligibility analysis through full text reading, selecting the articles that were included in the review.

The inclusion criteria consisted of original research articles and meta-analyses that examined the inflammatory properties of gluten, the effects of a gluten-rich diet, and the development of celiac disease and Non-Celiac Gluten Sensitivity in adult and elderly populations. These studies also looked at gastrointestinal, immunological and neurological changes associated with aging, as well as the connection between gluten sensitivity and mental health outcomes such as depression, anxiety, idiopathic fatigue and cognitive decline. The Exclusion criteria consisted of non-peer-reviewed studies and articles that lacked relevance to adults or elderly individuals (Table 1).

**Table 1** - Eligibility criteria for study inclusion and exclusion in the integrative review

Category:	Inclusion Criteria:	Exclusion Criteria:
Study Type	Original research articles, meta-analyses and reviews.	Non-peer reviewed studies, opinion papers and editorials.
Type of studies	Adults and elderly populations ( $\geq 18$ years), with stratified analysis when applicable.	Studies limited exclusively to children or non-stratified adult populations.
Focus	Inflammatory effects of gluten; Impact of gluten-rich diets; development of Celiac Disease or Non-Celiac Gluten sensitivity; Gastrointestinal tract, immune and neural aging.	Studies lacking translational relevance to adults or elderly.
Outcomes	Relation between gluten and Gastrointestinal, immunological and neurological alterations, as well as impacts on Mental Health.	No relevant clinical, physiological, or neuroimmune outcomes.
Language	Articles published in English or Portuguese.	Articles published in languages not accessible for translation/review.
Timeframe	Published between 2015 and 2025.	Publication outside this time frame.

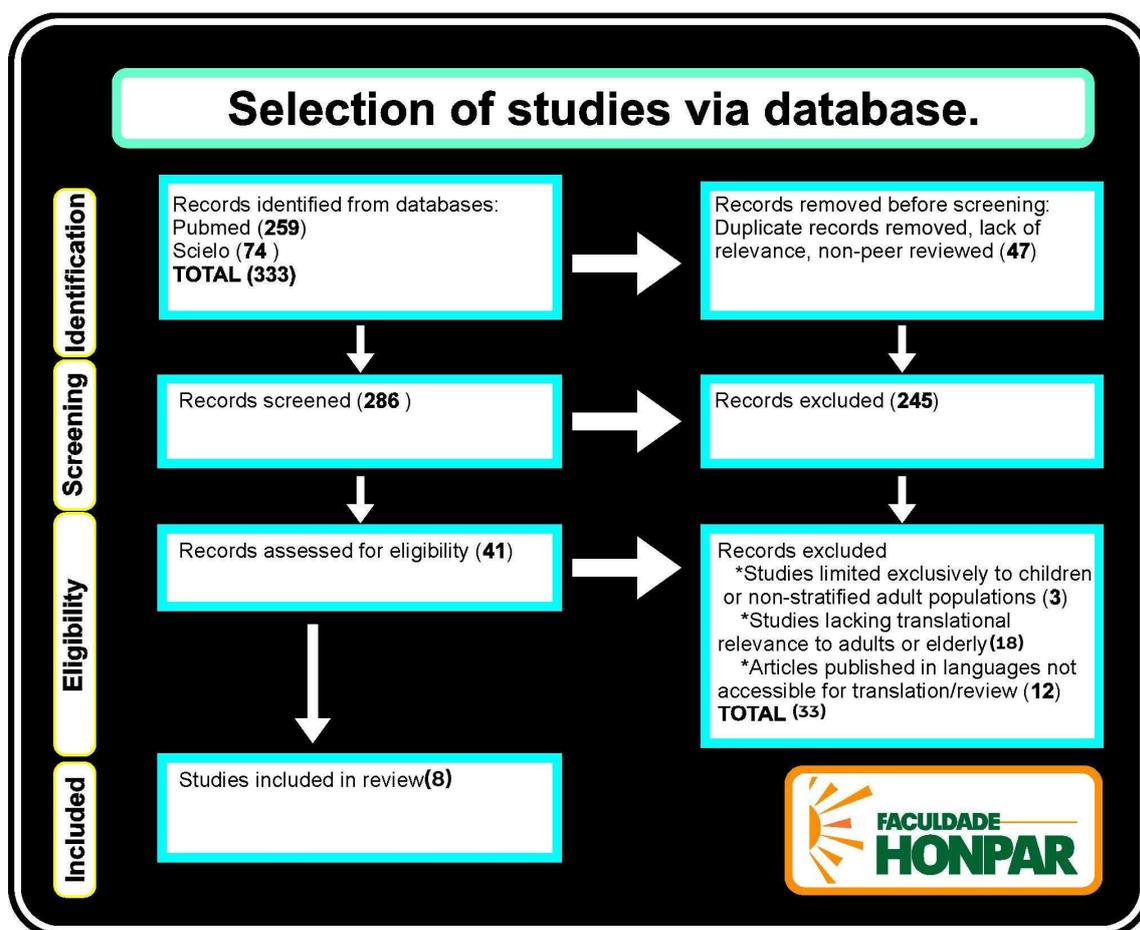
Two independent reviewers (Marson, A. C. F. and Consalter, F. S.) screened the titles, abstracts, and full texts according to the eligibility criteria. Disagreements were resolved through discussion until consensus was reached.

The flow of information through the different phases of the review was summarized using an adapted PRISMA 2020 flow diagram. The process followed principles of scientific relevance, multidisciplinary integration and identification of knowledge gaps, aiming to critically synthesize the available evidence and highlight the lack of targeted studies in elderly populations. Details of the selection process and reasons for exclusion are provided in Table 2 and image 1.

## RESULTS

After applying predefined inclusion and exclusion criteria to publications from 2015 to 2025, eight peer-reviewed studies focusing on frailty, villous atrophy, dietary intake in non-celiac gluten sensitivity, microbiome changes and psychological outcomes in celiac disease were selected for full analysis. These studies comprised cohort analyses, cross-sectional surveys and a randomized crossover trial, providing a diverse yet complementary dataset on the interplay between gluten consumption, aging and health outcomes in the elderly (Table 2) (Table 3) (Image 1).

Image 1 - PRISMA adapted diagram of the selection process of studies via database.



**Table 2** - Studies main authors and year, with study design/population.

<b>Study (year):</b>	<b>Study Design/Population:</b>
Zylberberg et al. (2024).	Nationwide Swedish cohort; 4,646 adults $\geq 60$ years with incident celiac disease between 2004–2017, matched to 21,944 controls.
Mahadev et al. (2017).	Nested cross-sectional; 1.345 symptomatic celiacs on gluten-free diet.
Ching & Lebwahl. (2022).	Narrative review, focusing on elderly patients with celiac disease ( $\geq 60$ years old).
Skodje et al. (2019).	Cross-sectional; 65 adults with self reported non-celiac gluten sensitivity following a gluten-free diet ( $\geq 6$ months).
Hansen et al. (2018).	Randomised, controlled, cross-over trial; 60 healthy adults (low- vs high-gluten).
Rato & Veríssimo (2021).	Narrative review on celiac disease in elderly.
Beas et al., (2024).	Systematic review and meta-analysis; 259 celiac patients (insomnia studies) and 179 celiac patients (cognitive impairment studies).
Boutahar et al. (2023).	Cross-sectional; 103 coeliac adults vs 101 controls during COVID-19.

**Table 3** - Research findings study design, intestinal outcomes.

<b>Study (year):</b>	<b>Key Intestinal Outcomes:</b>
Zylberberg et al. (2024).	Baseline frailty: 54.4% in celiac patients vs 29.7% in controls ( $p < 0.001$ ); Among those without baseline frailty, celiac patients had a 61% higher risk of developing frailty within 5 years (odds ratio 1.61; 95% CI 1.46–1.78)
Mahadev et al. (2017).	Older age was linked with risk of persistent villus atrophy, ranging from 25% among 18–29 year olds up to 45,7% among 60–69 years old and 62% among those aged $\geq 70$ after the adherence to a gluten-free diet.

<b>Study (year):</b>	<b>Key Intestinal Outcomes:</b>
Ching & Lebwohl. (2022).	Healing of mucosal lesions after a gluten-free diet was often incomplete: up to 56% of patients $\geq 70$ y had persistent villous atrophy despite adherence to a gluten-free diet. Age was identified as a major predictor of poor mucosal recovery, compounding malabsorption, inflammation, and frailty..
Skodje et al. (2019).	Persistent gastrointestinal symptoms despite gluten-free diet. (bloating, abdominal pain, diarrhea, gas). Although patients followed a gluten-free diet, it was not nutritionally balanced, high fat intake (with 43% of energy coming from fat) and suboptimal vitamin D, folic acid, calcium, iodine and iron intake.
Hansen et al. (2018).	Low-gluten diet reduced bloating and breath hydrogen; however, changes in postprandial well-being were unexpectedly driven mainly by the high-gluten diet, suggesting roles for wheat components such as FODMAPs or dietary fiber rather than gluten alone.
Rato & Veríssimo (2021).	25 % of celiac disease diagnoses are in patients $\geq 60$ years old; common symptoms in the elderly: anemia, osteoporosis, neuropathy; 60–80 % anemia; 67–70 % osteoporosis.
Beas et al., (2024).	Showed that chronic intestinal inflammation in celiac patients is associated with higher risk of insomnia and cognitive decline, potentially mediated by intestinal barrier dysfunction and pro-inflammatory cytokines.

**Table 4 -** Research findings study design, mental outcomes.

<b>Study (year):</b>	<b>Key Mental Outcomes:</b>
Skodje et al. (2019).	Extra-intestinal complaints included fatigue, reduced concentration, and “brain fog,” associated with poorer self-reported quality of life; Mild depression in 19% of participants vs. 11% in the general Norwegian population

Study (year):	Key Mental Outcomes:
Boutahar et al. (2023).	During COVID-19 confinement, state anxiety was significantly higher in celiac patients (65.3%) than in controls (41.6%), while adherence to a gluten-free diet was associated with greater improvement in trait anxiety (41.5% vs. 26.7% in non-adherent patients).
Rato & Veríssimo (2021).	Depression, anxiety and irritability are common; peripheral neuropathy and ataxia frequent; cognitive performance is often worse in those diagnosed > 65 y, with controversial but possible links to vascular dementia.
Beas et al., (2024).	Celiac patients had a significantly increased risk of insomnia (OR 1.83), more frequent use of hypnotics and descriptive evidence of cognitive impairment (“brain fog”, attention deficits, slower reaction times) in celiac patients; pooled OR not computed due to insufficient controls. These effects may be mediated by anti-gliadin antibodies and pro-inflammatory cytokines.
Ching & Lebowhl. (2022)	In case-control studies of patients >65 years with celiac disease, deficits were observed mainly in attention and speech, while memory was largely preserved. These neurocognitive changes may be influenced both by microvascular changes (linking to vascular dementia) and by underlying depression, which is more common in celiac patients

## DISCUSSION

The integrative review found that age-related changes, such as increased intestinal permeability, chronic low-grade inflammation and alterations in the gut microbiota, create a physiological environment in which gluten may act as an additional stressor, even in otherwise healthy elderly individuals. Reducing gluten intake may therefore help preserve mucosal function, mitigate frailty and protect mental health (CATASSI et al., 2023; HANSEN et al., 2018).

Gluten is a heat-stable protein that serves two purposes in food processing: it acts as a binding agent and an extending agent. This dual functionality explains its widespread use in processed foods. On average, individuals in Western populations consume approximately 5–20 grams of gluten daily, an amount that has been linked with various disruptions in gastrointestinal physiology. From a biochemical perspective, gluten represents the main storage protein of wheat

grains and is also present in rye and barley. Gluten is a complex mixture of hundreds of distinct proteins, primarily consisting of gliadin and glutenin (BIESIEKIERSKI, J. R.; 2017; CATASSI, C. et al., 2017).

Gliadin is particularly relevant due to its high resistance to proteolytic enzymes. This resistance results in the production of digestion-resistant peptides that remain in the lumen and can cross the intestinal barrier (HERRERA et al., 2021; MAMONE et al., 2022). This process can trigger immune responses, leading to inflammation in individuals with celiac disease or non-celiac gluten sensitivity (CATASSI et al., 2017). Additionally, even in individuals without these conditions, the digestion of gluten is more complex compared to other dietary proteins, such as those found in meat, eggs and milk (YE et al., 2023; FREITAS et al., 2022; BIESIEKIERSKI et al., 2017).

The elderly are already more susceptible to developing pathologies, and a modern diet rich in gluten could contribute to intestinal and neuropsychiatric disruption in vulnerable aging populations (MUTTALIB et al., 2025; ARANBURU et al., 2021). Aging also increases the susceptibility to celiac disease and non-celiac gluten sensitivity (ARANBURU et al., 2021; CATASSI et al., 2024). In cases where this sensitivity develops, the negative impacts on intestinal inflammation, gut-brain axis disruption, and mental health decline may be more pronounced in the elderly compared to those outside this age group (DEJONG et al., 2020; CATASSI et al., 2017).

Elderly individuals with celiac disease experience disproportionately high rates of frailty and persistent villous atrophy, primarily due to cumulative malabsorption and chronic inflammation (ZYLBERBERG et al., 2024; MAHADEV et al., 2017). Aging itself is associated with impaired digestion, reduced gastric acid secretion and increased intestinal permeability, contributing to the phenomenon known as “inflammaging”. In celiac disease, repeated exposure to gluten leads to villous atrophy and crypt hyperplasia, further reducing absorptive efficiency and setting the stage to frailty due to nutrient deficiency (CHING; LEBWOHL., 2022).

In contrast to celiac disease, where villous atrophy is a hallmark, individuals with non-celiac gluten sensitivity often adopt unbalanced diets that are deficient in essential nutrients such as vitamin D, folate, calcium, iodine and iron. This nutritional imbalance compromises musculoskeletal health and may predispose these individuals to frailty in a manner similar to the malabsorption-driven deficits observed in celiac disease (ZYLBERBERG et al., 2024; MAHADEV et al., 2017).

Beyond nutritional factors, non-celiac gluten sensitivity is associated with persistent gastrointestinal complaints, such as bloating and gas accumulation and mild cognitive dysfunctions, including fatigue and difficulty concentrating. These manifestations suggest that gluten or wheat components may disrupt the gut–brain axis, even in the absence of structural intestinal lesions. For elderly individuals, whose intestinal barrier is naturally more fragile, these mechanisms may further amplify both frailty and cognitive decline (SKODJE et al., 2019).

While non-celiac gluten sensitivity illustrates how gluten-related mechanisms can impair intestinal and cognitive health in the absence of structural lesions, celiac disease in the elderly presents an additional challenge: mucosal healing remains incomplete in up to 56% of patients even after strict adherence to a gluten-free diet (MAHADEV et al., 2017; CHING; LEBWOHL., 2022). This incomplete recovery exacerbates the effects of aging-associated intestinal decline, leading to amplified malabsorption, systemic inflammation and nutrient deficiencies. The

findings suggest that standard dietary approaches may not be sufficient for older adults, emphasizing the need for intensified nutritional counseling and strict monitoring to prevent frailty and osteoporosis. Furthermore, stricter gluten restriction may also help to reduce inflammatory signaling and gut–brain axis disturbances, thereby supporting both physical and mental resilience in aging (MAHADEV et al., 2017; CHING; LEBWOHL., 2022).

Data indicates that celiac disease in the elderly often presents with extraintestinal symptoms such as anemia, osteoporosis/osteopenia and neuropathies. These symptoms are frequently mistaken for natural aging, when in fact they are indicative of an underlying gluten-driven pathology (RATO; VERÍSSIMO., 2021). Furthermore, the negative effects of gluten-rich diets in the elderly without celiac disease may also go unnoticed, suggesting that intestinal and neuropsychiatric disruptions are being underestimated and undertreated in this population. This misattribution to aging highlights the need for heightened clinical suspicion and dietary assessment in elderly patients presenting with such symptoms.

Although gastrointestinal symptom relief is often reported with low-gluten diets, controlled studies suggest that these benefits may not be directly attributable to gluten itself. A crossover trial found that reducing gluten intake from 18 grams/day to 2 grams/day improved bloating, decreased hydrogen exhalation and altered the microbiome profile (HANSEN et al., 2018). However, controlled challenge studies indicate that purified gluten does not exacerbate symptoms compared with a placebo in most individuals. Instead, Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols (FODMAPs) and wheat

amylase-trypsin inhibitors were identified as the main triggers of abdominal discomfort (CATASSI et al., 2023). These findings provide a more nuanced interpretation of “gluten

sensitivity,” suggesting that symptom relief may often result from reduced exposure to non-gluten wheat components rather than gluten itself. This is particularly relevant when evaluating dietary interventions in older adults.

Building upon these findings, it is relevant to consider that while some evidence suggests symptom relief in low-gluten diets may be due to reduced FODMAPs rather than gluten itself, the consistent improvements in microbiota composition, gas production and bloating emphasize the potential of dietary modulation to support intestinal function in aging individuals (HANSEN et al., 2018; CATASSI et al., 2023). For older adults, reducing gluten-containing foods may not only alleviate gastrointestinal discomfort but also help reduce inflammation and gut–brain signaling that can exacerbate frailty, fatigue and mood disturbances, reinforcing the importance of exploring gluten mitigation as a strategy to protect both intestinal and mental health in this population.

The consequences of gluten exposure extend beyond gastrointestinal outcomes to the central nervous system. Research on the mental health impacts of gluten exposure reveals a complex interplay of factors, including intestinal inflammation, nutrient status and psychosocial relationships. Studies have found that celiac patients are nearly twice as likely to develop insomnia compared to non-celiac individuals, with associated symptoms including poor sleep quality, frequent use of sleep aids and cognitive impairment (BEAS et al., 2024). The mechanism behind these observations may involve anti-gliadin antibodies crossing the blood–brain barrier and reacting with neuronal antigens, as well as pro-inflammatory cytokines from the gut inducing neuroinflammation and altering neurotransmitter synthesis (BEAS et al., 2024). This bidirectional

immunological response could explain the increased risk of cognitive and sleep dysfunction in individuals with gluten sensitivity.

In the elderly, coeliac disease and insomnia take on particular significance due to poor sleep quality and cognitive impairment. Aging is already associated with increased neuroinflammation, reduced neuroplasticity and a greater vulnerability to sleep-wake dysregulation. This vulnerability can be exacerbated by gluten-related immune responses (BEAS et al., 2024). In this context, reducing dietary gluten emerges not merely as a gastrointestinal intervention but also as a potential strategy to mitigate neuroinflammatory burden, protect cognitive resilience and preserve sleep quality in older adults.

In addition, anxiety and depression affect approximately 25% of celiac patients, with symptomatic improvement often reported after two years of adherence to a gluten-free diet. However, brain fog and fatigue persist in nearly half of cases (THERRIEN et al., 2021). During the COVID-19 pandemic, anxiety was present in 65.3% in celiac patients compared with 41.6% in controls (BOUTAHAR et al., 2023). These findings highlight how external stressors can amplify psychological vulnerabilities and emphasize that dietary adherence not only reduces inflammatory burden but also provides a subjective sense of self-care (BOUTAHAR et al., 2023).

The high prevalence of anxiety and depression among celiac patients, highlights the complex relationship between intestinal health, neuroinflammation and psychosocial stressors (THERRIEN et al., 2021). External factors, such as the COVID-19 pandemic, can exacerbate these vulnerabilities, emphasizing the interplay between biological and psychosocial factors in shaping mental health in celiac disease (BOUTAHAR et al., 2023). For older adults, reducing or eliminating gluten intake may provide both physiological benefits and a sense of self-care and control, which can support emotional stability and help protect against the cumulative burden of aging-related mental health decline, as noted by THERRIEN et al. (2021) and BOUTAHAR et al. (2023).

Although most research focuses on celiac patients, emerging evidence suggests that gluten-rich diets may also exacerbate age-related intestinal vulnerabilities in non-celiac elders. Studies on non-celiac gluten sensitivity have reported that patients often experience symptoms similar to those of Irritable Bowel Syndrome (IBS), including bloating, abdominal pain, diarrhoea, as well as extra-intestinal complaints such as headache, chronic fatigue and “brain fog” (CATASSI et al., 2023). Randomised challenges have shown that purified gluten alone does not worsen symptoms compared with a placebo, whereas wheat fructans and amylase–trypsin inhibitors increase intestinal water influx, gas production and innate immune activation (CATASSI et al., 2023). In the elderly, underlying “inflammaging” - characterised by increased intestinal permeability, immune dysregulation and microbiota shifts - may amplify these responses (DEJONG et al., 2020). Taken together, this suggests that moderating gluten and wheat component intake could help preserve intestinal integrity and reduce frailty risks, even in non-celiac aging populations, a group often overlooked in current research (HANSEN et al., 2018).

The overlap of Irritable Bowel Syndrome-like symptoms and extra-intestinal complaints such as fatigue and brain fog in non-celiac gluten sensitivity demonstrates how wheat components, including Fermentable Oligosaccharides, Disaccharides, Monosaccharides and Polyols (FODMAPs) as well as amylase–trypsin inhibitors, may exacerbate inflammaging processes in the elderly. This underscores the fact that even in the absence of structural intestinal lesions, functional and extra-intestinal manifestations can converge to compromise quality of life.

In this context, moderating gluten intake may help reduce mucosal inflammation and dysbiosis, thereby preserving intestinal integrity and supporting healthier aging trajectories (CATASSI et al., 2023; HANSEN et al., 2018).

Even with current evidence showing the negative effects of gluten on intestinal and mental health in elderly individuals diagnosed with celiac disease or non-celiac gluten sensitivity, the impact on otherwise healthy older adults remains largely unexplored. Given that aging is associated with increased intestinal permeability, low-grade chronic inflammation and changes in the gut microbiota, it is plausible that gluten intake could act as an additional stressor, aggravating mucosal vulnerability, nutrient malabsorption and gut–brain axis dysregulation even in non-celiac elders. Therefore, controlled studies specifically targeting healthy elderly populations are needed to clarify whether adopting a gluten-free or reduced-gluten diet can provide benefits in maintaining intestinal health, preventing frailty and supporting mental health in this age group.

## CONCLUSION

The integrative review research results showed evidence of the negative effects of gluten and/or wheat-rich diets on the already vulnerable elderly intestine. This was also found to potentially exacerbate mental health disorders commonly observed in the elderly population. Furthermore, the review revealed a lack of focused research on the effects of gluten on the intestinal and mental health of vulnerable individuals, such as the elderly, who may benefit from adopting a gluten-free or reduced diet.

Additionally, the review highlighted the need for further research on gluten-free or reduced diets in individuals with mental health disorders, such as anxiety, depression, reduced focus and cognitive decline, who do not have a sensitivity to gluten. This is particularly important for elderly patients, as the cause of such disorders may be incorrectly attributed to natural aging, leading to inadequate care for this portion of the population.

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