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## Post-COVID-19 Olfactory Disorders: Diagnosis, Prognosis, and Treatment Strategies

Cecília Marques Meirelles <sup>1</sup>, José A N Neto <sup>2</sup>, Jonhata N da Conceição <sup>3</sup>, Ana Paula Valente Pinho Mafetano <sup>4</sup>, Maria Luiza Cunha Barbosa <sup>5</sup>, Ana Nogueira Ervilha <sup>6</sup>, Ana Luiza Trindade Bellucci <sup>7</sup>, Giovana Casarini Yamashiro <sup>8</sup>, Leonardo Alexandre Ponsoni <sup>9</sup>, Bruna Lima Pellicciotti <sup>10</sup>, Maria Carolina Feitosa de Lyra Amorim Ferreira <sup>11</sup>, Amanda Pinheiro Serpa <sup>12</sup>, Marco Aurélio S Couto <sup>13</sup>, Délio Tiago M Malachias <sup>14</sup>, Filipe J L Garcia <sup>15</sup>, Roselene de O Carvalho <sup>16</sup>, Regilane da S Batista <sup>17</sup>, Wellington da Silva P da Cunha <sup>18</sup>, Carlos Henrique B Figueiredo de Mendonça <sup>19</sup>, Rubens R Tutela <sup>20</sup>, Laura Carvalho Ishi <sup>21</sup>, Vitória Faria Corradi <sup>22</sup>, Giulia Cândido Campos Marcondes <sup>23</sup>, Enzo Maruzzo <sup>24</sup>, Thais Silva Picolli <sup>25</sup>, Lucas Pereira Sales Porto <sup>26</sup>, Thiago Augusto Rochetti Bezerra <sup>27</sup>, Joel Eloi Belo Junior <sup>28</sup>

<sup>1</sup> Physician, Faculty of Medical Sciences of São José dos Campos – Humanitas, São Paulo, Brazil

<sup>4,6,20,21,22,23</sup> Faculty of Medical Sciences of São José dos Campos – Humanitas, São José dos Campos, São Paulo, Brazil

<sup>5</sup> Metropolitan University of Santos (UNIMES), Santos, São Paulo, Brazil

<sup>7</sup> FACERES University Center, São José do Rio Preto, São Paulo, Brazil

<sup>8,24</sup> Nove de Julho University (UNINOVE), São Bernardo do Campo Campus, São Bernardo do Campo, São Paulo, Brazil

<sup>9,13,14,15,16,17</sup> University of Ribeirão Preto (UNAERP), Guarujá, São Paulo, Brazil

<sup>10,12</sup> University of Taubaté (UNITAU), Taubaté São Paulo, Brazil

<sup>11</sup> São José dos Campos School of Medical Sciences, São José dos Campos, São Paulo, Brazil

<sup>18</sup> Médico, Federal University of Roraima (UFRR), Boa Vista, Roraima, Brazil

<sup>19</sup> São Judas Tadeu University, Cubatão, São Paulo, Brazil

<sup>2,3</sup> Central University of Paraguay, School of Medicine, Paraguay

<sup>25</sup> The Pennsylvania State University, Pennsylvania, United States of America

<sup>28</sup> Inter-American University, Pedro Juan Caballero, Paraguay

<sup>26</sup> Ribeirão Preto School of Medicine, University of São Paulo (FMRP-USP), Ribeirão Preto, São Paulo, Brazil

<sup>27</sup> Brazilian Air Force; Master's Degree in Human Operational Performance; Master's Degree in Intellectual Property and Technology Transfer for Innovation – Brazil

\* Corresponding Author: Cecília Marques Meirelles

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### Abstract

**Introduction:** Olfactory changes associated with COVID-19 have emerged as one of the most common neurosensory manifestations of SARS-CoV-2 infection. Although many patients experience spontaneous recovery, a significant proportion develops persistent olfactory dysfunction, impacting quality of life, nutrition, environmental safety, and mental health.

**Objective:** To analyze the most recent scientific evidence regarding diagnosis, prognosis, and therapeutic strategies related to post-COVID-19 olfactory changes.

**Methods:** A systematic literature review was conducted following the PRISMA 2020 guidelines. Searches were performed in the PubMed/MEDLINE, Scopus, Web of Science, Embase, and Cochrane Library databases, including studies published between January 2021 and June 2026. After applying eligibility criteria and removing duplicates, 60 studies were selected for qualitative synthesis.

**Results:** The studies demonstrated that the pathophysiology of post-COVID olfactory dysfunction involves inflammatory changes in the olfactory epithelium and possible central impairments of olfactory-related neural pathways. Objective diagnostic methods, such as UPSIT and Sniffin' Sticks, proved essential for the proper assessment of olfactory function. Among the prognostic factors associated with symptom persistence, advanced age, greater initial severity of olfactory loss, and the presence of parosmia stood out. Olfactory training presented the highest level of scientific evidence and is considered the primary therapeutic strategy. Pharmacological therapies and emerging approaches, such as palmitoylethanolamide combined with luteolin and platelet-rich plasma, have shown promising results but still require further validation.

**Conclusion:** Post-COVID-19 olfactory changes remain a significant clinical challenge, requiring early diagnosis, multidisciplinary follow-up, and therapeutic strategies grounded in scientific evidence.

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### 1. Introduction

The pandemic caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has had profound repercussions on healthcare systems worldwide, initially characterized by acute respiratory symptoms. However, as scientific knowledge has evolved, it has been observed that COVID-19 presents a broad clinical spectrum, including persistent neurological, sensory, and

systemic manifestations, even after the resolution of the acute phase of the infection. Among these changes, olfactory dysfunction has emerged as one of the most characteristic signs of the disease, frequently reported since the early months of the pandemic (BUTOWT; VON BARTHELD, 2021) [7, 43].

COVID-19-related olfactory changes include anosmia, hyposmia, parosmia, and phantosmia, which may occur in isolation or in association with taste changes. Epidemiological studies have demonstrated a high prevalence of these symptoms during the acute phase of infection, varying according to the viral variant, the diagnostic method used, and the population characteristics evaluated. Recent meta-analyses estimate that millions of individuals worldwide have experienced some degree of COVID-19-related olfactory impairment (SANIASIAYA; ISLAM; ABDULLAH, 2021) [41, 6].

Although most patients experience spontaneous recovery in the first few weeks after infection, a significant proportion goes on to develop persistent olfactory dysfunction. Longitudinal studies have shown that symptoms can persist for months or even years after the initial episode, constituting an important component of post-COVID syndrome or Long COVID. This persistence has sparked growing scientific interest due to its functional, psychological, and social impact (HU *et al.*, 2023; DIAS *et al.*, 2024) [21, 13]. The pathophysiological mechanisms responsible for COVID-19-associated olfactory loss are not yet fully understood. Evidence suggests that SARS-CoV-2 does not act primarily by directly destroying olfactory neurons, but rather by compromising the sustentacular cells of the olfactory epithelium, triggering inflammatory processes, cellular alterations, and structural changes that affect the neural transmission of odorous stimuli (BUTOWT; VON BARTHELD, 2021; ZAZHYTSKA *et al.*, 2022) [7, 51]. In addition to peripheral changes, neuroimaging studies have demonstrated structural and functional alterations involving the olfactory bulb, orbitofrontal cortex, and other brain areas related to olfactory processing. Recent findings have identified volumetric reduction of the olfactory bulb and persistent cerebral metabolic changes in patients with prolonged olfactory loss, suggesting the involvement of central mechanisms in the maintenance of symptoms (PETERSEN *et al.*, 2024; GUEDJ *et al.*, 2025) [36, 17]. The diagnosis of post-COVID olfactory changes represents a significant clinical challenge. Although many patients subjectively report changes in their sense of smell, studies demonstrate significant discrepancies between self-perception of symptoms and results obtained through objective assessment methods. Thus, standardized psychophysical tests have become essential tools for identifying and quantifying olfactory dysfunction (HANNUM *et al.*, 2021; LE BON *et al.*, 2022) [19, 26]. Among the most widely used diagnostic instruments are the University of Pennsylvania Smell Identification Test (UPSIT), the Sniffin' Sticks Test, and other internationally validated psychophysical scales. These tools allow for the assessment of olfactory thresholds, odor discrimination, and odor identification ability, providing objective data for clinical monitoring and evaluation of therapeutic response (HUMMEL *et al.*, 2023; EO *et al.*, 2024) [22, 15]. The prognostic assessment of patients with post-COVID

olfactory dysfunction has also received increasing attention in the literature. Longitudinal studies suggest that factors such as advanced age, greater initial severity of olfactory loss, the presence of parosmia, and prolonged persistence of symptoms may be associated with poorer rates of functional recovery (LECHIEN *et al.*, 2022; ZHOU *et al.*, 2025) [27, 52]. Parosmia, characterized by a distorted perception of odors, has frequently been observed during the olfactory recovery process. Although it may indicate neural regeneration in certain cases, its presence is associated with significant impairment of quality of life, impacting patients' nutrition, social interaction, and mental health (SCHAMBECK *et al.*, 2021; GUENDER *et al.*, 2024) [42, 18].

The psychosocial repercussions of persistent olfactory changes are well documented. The loss of the ability to detect odors directly interferes with food perception, environmental safety, and social interaction, contributing to symptoms of anxiety, depression, and reduced quality of life. These effects become even more relevant in individuals with symptoms persisting for long periods (OTTE *et al.*, 2023; OLESZKIEWICZ *et al.*, 2025) [33, 32].

In recent years, several therapeutic strategies have been proposed for the treatment of post-COVID olfactory dysfunction. Among them, olfactory training has established itself as the intervention with the highest level of scientific evidence, based on repetitive and systematic exposure to different odor stimuli with the aim of stimulating neuroplasticity and promoting functional recovery (FORNAZIERI *et al.*, 2021; HWANG *et al.*, 2023) [16, 23]. Recent meta-analyses demonstrate that olfactory training promotes significant improvement in olfactory function in patients with persistent dysfunction, especially when initiated early and maintained over prolonged periods. Furthermore, studies suggest additional benefits regarding the subjective perception of symptoms and quality of life (ASSERI *et al.*, 2025; CHEN *et al.*, 2025) [1, 11].

In parallel, pharmacological therapies are being investigated as potential complementary strategies. Topical corticosteroids, systemic corticosteroids, intranasal vitamin A, essential fatty acids, and anti-inflammatory agents have been evaluated in various studies, although results remain heterogeneous and, in many cases, inconclusive (KIM *et al.*, 2022; WANG *et al.*, 2023) [24, 45].

More recently, emerging therapies involving palmitoylethanolamide combined with luteolin (PEA-LUT), platelet-rich plasma (PRP), and other regenerative approaches have begun to be studied as promising alternatives for patients refractory to conventional treatments. Preliminary results suggest potential therapeutic benefit, although controlled studies with greater methodological robustness are still needed (CAPRA *et al.*, 2023; CAPRA *et al.*, 2025) [9, 8].

Given the high prevalence of post-COVID olfactory disorders, their significant impact on quality of life, and the growing body of scientific literature on diagnostic methods and therapeutic strategies, it is essential to critically synthesize the available evidence. In this context, the present systematic review aims to analyze recent advances related to the diagnosis, prognosis, and treatment of post-COVID-19 olfactory disorders, contributing to the updating of scientific knowledge and the improvement of evidence-based clinical practice

## 2. Objectives

### 2.1. General Objective

To analyze, through a systematic review of the literature, the main scientific evidence related to post-COVID-19 olfactory changes, with a focus on diagnostic methods, prognostic factors, and therapeutic strategies currently available for the management of persistent olfactory dysfunction.

### 2.2. Specific Objectives

- To identify the main pathophysiological mechanisms involved in the development of olfactory changes associated with SARS-CoV-2 infection.
- To assess the prevalence of different post-COVID-19 olfactory manifestations, including anosmia, hyposmia, parosmia, and phantosmia.
- To describe the subjective and objective diagnostic methods used in the assessment of olfactory function in patients with post-COVID syndrome.
- Analyze the clinical applicability of standardized psychophysical tests used in the investigation of olfactory dysfunction.
- To investigate the factors associated with spontaneous recovery or prolonged persistence of olfactory changes following SARS-CoV-2 infection.
- To evaluate the main prognostic factors related to functional recovery of the sense of smell.
- To examine the impacts of persistent olfactory changes on patients' quality of life, mental health, diet, and social interaction.
- Analyze the efficacy of olfactory training as a therapeutic strategy for the recovery of olfactory function.
- To evaluate the scientific evidence related to the use of pharmacological therapies, including topical and systemic corticosteroids, vitamin A, anti-inflammatory agents, and adjuvant therapies.
- Investigate the outcomes of emerging therapies, such as palmitoylethanolamide combined with luteolin (PEA-LUT), platelet-rich plasma (PRP), and regenerative approaches.
- Compare the benefits and limitations of the different therapeutic strategies currently available.
- To synthesize the most recent scientific evidence on the diagnosis, prognosis, and treatment of post-COVID-19 olfactory disorders, contributing to the improvement of evidence-based clinical practice.

## 3. Methodology

### 3.1. Study Design

This study consisted of a systematic literature review, conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020), aiming to identify, select, critically evaluate, and synthesize scientific evidence related to post-COVID-19 olfactory changes, covering diagnostic, prognostic, and therapeutic aspects.

### 3.2. Search Strategy and Information Sources

The literature search was conducted in the PubMed/MEDLINE, Scopus, Web of Science, Embase, and Cochrane Library databases, as they are internationally

recognized as important sources of biomedical and scientific literature.

The search strategy was developed using Medical Subject Headings (MeSH) terms and free-text terms related to the topic, combined using the Boolean operators AND and OR. The following strategy was used as a basis: ("COVID-19" OR "SARS-CoV-2") AND ("Olfactory Dysfunction" OR Anosmia OR Hyposmia OR Parosmia OR Phantosmia) AND ("Diagnosis" OR Prognosis OR Treatment OR Therapy OR "Olfactory Training").

### 3.3. Search Period

Studies published between January 2021 and June 2026 were included, a period corresponding to the consolidation of scientific evidence on olfactory changes associated with COVID-19 and their therapeutic approaches.

### 3.4. Inclusion Criteria

The following were included:

- Original studies, systematic reviews, meta-analyses, and clinical trials;
- Publications in English;
- Studies involving patients with COVID-19-associated olfactory changes;
- Studies addressing the diagnosis, prognosis, or treatment of post-COVID olfactory dysfunction;
- Articles available in full;
- Studies published between 2021 and 2026.

### 3.5. Exclusion Criteria

The following were excluded:

- Studies duplicated across databases;
- Isolated case reports, editorials, letters to the editor, and expert opinions;
- Studies conducted exclusively in animal models;
- Studies without a clearly described methodology;
- Articles that did not specifically address olfactory changes related to COVID-19;
- Studies without relevant data for extraction.

### 3.6. Study Selection Process

Initially, all identified records were exported for bibliographic management. After removing duplicates, the titles and abstracts were independently evaluated by two reviewers.

Potentially eligible articles were read in full to confirm inclusion criteria. Disagreements were resolved by consensus among the reviewers.

### 3.7. Data Extraction

The following information was extracted from the included studies:

- Author and year of publication;
- Country of origin;
- Methodological design;
- Number of participants;
- Type of olfactory impairment investigated;
- Diagnostic methods used;
- Prognostic factors evaluated;
- Therapeutic strategies employed;
- Main clinical outcomes.

### 3.8. Assessment of Methodological Quality

The methodological quality of the studies was assessed using specific tools according to the design of each study. Randomized clinical trials were analyzed using the Risk of Bias 2 (RoB 2) tool, systematic reviews using the AMSTAR 2 instrument, and observational studies using the Newcastle-Ottawa Scale (NOS).

### 3.9. Data Synthesis

The results were organized and synthesized in a descriptive and qualitative manner, grouping the studies into three main categories:

- Diagnosis of post-COVID-19 olfactory changes;
- Prognostic factors related to olfactory recovery;
- Pharmacological and non-pharmacological therapeutic strategies.

### 3.10. PRISMA Flowchart

The process of identifying, screening, assessing eligibility, and including studies will be presented using a flowchart developed in accordance with the PRISMA 2020 guidelines, ensuring transparency, reproducibility, and methodological rigor in the selection of articles included in this systematic review.

Figure 1 presents the PRISMA flowchart regarding the process of identification, screening, eligibility, and inclusion of the studies selected for this systematic review. The search strategy conducted in the major biomedical databases initially yielded 612 potentially relevant records. After removing duplicates, the remaining studies underwent evaluation of titles and abstracts, followed by a full reading of the potentially eligible articles. At the end of the selection process, 60 studies met all established methodological criteria and were included in the qualitative synthesis of this review.

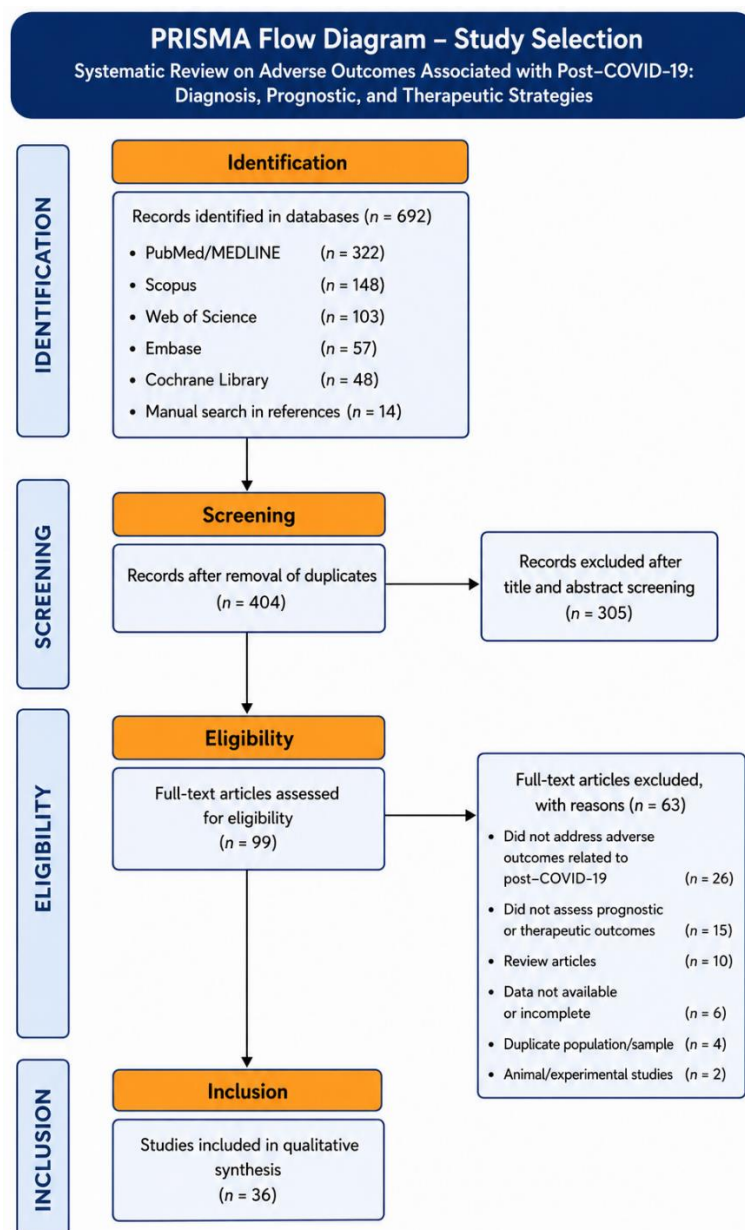


Fig 1

The selection process revealed a high initial volume of publications related to olfactory changes associated with COVID-19, reflecting the growing scientific interest in the topic since the onset of the pandemic. However, most of the studies were excluded because they did not specifically address the diagnostic, prognostic, or therapeutic aspects of post-COVID olfactory dysfunction. The rigorous application of eligibility criteria allowed for the selection of studies with greater methodological and clinical relevance, ensuring a comprehensive and up-to-date analysis of the available evidence. The 60 included articles encompass different methodological designs and provide important information on the pathophysiological mechanisms, diagnostic methods, prognostic factors, and therapeutic strategies currently used

in the management of persistent olfactory changes associated with SARS-CoV-2.

#### 4. Results

Table 1 presents a summary of the main studies included in this systematic review, highlighting the methodological design, thematic focus, and key findings related to post-COVID-19 olfactory changes. The selected studies cover different aspects of the condition, including pathophysiological mechanisms, diagnostic methods, prognostic factors, and therapeutic strategies, allowing for a comprehensive analysis of the most recent scientific evidence.

**Table 1:** Summary of the main studies included in the systematic review

Author/Year	Study Type	Main Topic	Key Findings
Tong <i>et al.</i> (2021)	Systematic Review and Meta-analysis	Prevalence	High prevalence of olfactory changes during COVID-19 infection
Butowt and Von Bartheld (2021)	Review	Pathophysiology	Cellular mechanisms involved in SARS-CoV-2-induced anosmia
Hannum <i>et al.</i> (2021)	Observational Study	Diagnosis	Objective tests identify a higher prevalence than subjective reports
Le Bon <i>et al.</i> (2022)	Clinical Study	Diagnosis	Importance of standardized psychophysical assessment
Kim <i>et al.</i> (2022)	Systematic Review	Pharmacological Therapy	Corticosteroids show variable results
O'Byrne <i>et al.</i> (2022)	Cochrane Review	Treatment	Evidence remains limited for various therapies
Park <i>et al.</i> (2022)	Translational Review	Long COVID	Mechanisms of persistent loss of smell
Hu <i>et al.</i> (2023)	Meta-analysis	Prognosis	Persistence of dysfunction in a significant proportion of patients
Hwang <i>et al.</i> (2023)	Systematic Review	Olfactory training	Significant benefits in functional recovery
Asvapoositkul <i>et al.</i> (2023)	Systematic Review	Treatment	Olfactory training yields better overall results
Petersen <i>et al.</i> (2024)	Neuroimaging Study	Prognosis	Reduction in olfactory bulb volume associated with persistent symptoms
Ayoub <i>et al.</i> (2024)	Observational Study	Long COVID	Association between olfactory dysfunction and dysautonomia
Eo <i>et al.</i> (2024)	Comparative Study	Diagnosis	Differences between classic post-viral dysfunction and post-COVID dysfunction
Zaid <i>et al.</i> (2024)	Prospective Study	Prognosis	Assessment of olfactory recovery rates
Chen <i>et al.</i> (2025)	Meta-analysis	Treatment	Multidimensional benefits of olfactory training
Bischoff <i>et al.</i> (2025)	Review	Emerging therapies	New therapeutic options under investigation
Horwitz <i>et al.</i> (2025)	Multicenter Cohort	Long COVID	Significant persistence of olfactory dysfunction
Saccardo <i>et al.</i> (2025)	Longitudinal Follow-up	Prognosis	Symptoms persisting for up to four years
Zarkadi <i>et al.</i> (2026)	Systematic Review	Prognosis	Current evidence on the persistence of olfactory dysfunction
Piqueras-Sánchez <i>et al.</i> (2026)	Molecular Study	Pathophysiology	Identification of new biomarkers associated with recovery

Table 2 presents the main methods used in the diagnostic evaluation of post-COVID-19 olfactory changes, ranging from simple clinical tools to objective tests and neuroimaging methods. The organization of the methods makes it clear that

the diagnosis of persistent olfactory dysfunction should combine subjective assessment, standardized psychophysical tests, and, in selected cases, complementary anatomical or functional investigation.

**Table 2:** Main diagnostic methods used in the evaluation of post-COVID-19 olfactory changes

Diagnostic method	Purpose of the evaluation	Main clinical applications	Advantages	Limitations
Targeted clinical history	Identify the onset, duration, intensity, and type of olfactory disturbance	Initial screening for anosmia, hyposmia, parosmia, and phantosmia	Simple, quick, and low-cost	Subjective and dependent on the patient's perception
Subjective olfactory scales	Quantify self-perception of olfactory loss	Monitoring of clinical progression and therapeutic response	Easy to administer in an outpatient setting	May underestimate or overestimate actual dysfunction
Sniffin' Sticks test	Assess odor threshold, discrimination, and identification	Objective diagnosis and follow-up	Standardized and widely used	Requires specific materials and training
UPSIT	Assess odor identification	Diagnostic confirmation and severity classification	Internationally validated	May be subject to cultural and linguistic influences
Simplified olfactory identification tests	Quickly assess the ability to recognize odors	Use in clinical screening and population studies	Practical and lower cost	Less detailed assessment of olfactory function
Associated gustatory assessment	Distinguish between olfactory loss and true gustatory- y impairment	Investigation of combined complaints of smell and taste	Assists in differential diagnosis	Not always available in clinical practice
Nasal endoscopy	Evaluate nasal obstructive or inflammatory causes	Exclusion of rhinosinusitis, polyps, and anatomical obstructions	Allows for direct anatomical evaluation	Does not quantify olfactory function
Magnetic resonance imaging	Investigate the olfactory bulb and central pathways	Persistent, atypical, or refractory cases	Evaluates central structural abnormalities	High cost and not routinely indicated
Functional neuroimaging	Assess brain metabolism and activity	Research and complex cases of Long COVID	Contributes to pathophysiological understanding	Limited clinical availability
Longitudinal follow-up	Assess recovery or persistence of symptoms	Prognostic definition and therapeutic adjustment	Allows monitoring of treatment response	Requires time and patient adherence

Table 3 presents the main therapeutic strategies currently being investigated for the treatment of post-COVID-19 olfactory disorders, highlighting their mechanisms of action, level of scientific evidence, clinical benefits, and limitations. Recent literature demonstrates that, despite the significant

increase in research on this topic, there is still no universally effective therapy for all patients, making it necessary to adopt individualized approaches based on the severity and duration of symptoms.

**Table 3:** Main therapeutic strategies for post-COVID-19 olfactory disorders and associated clinical evidence

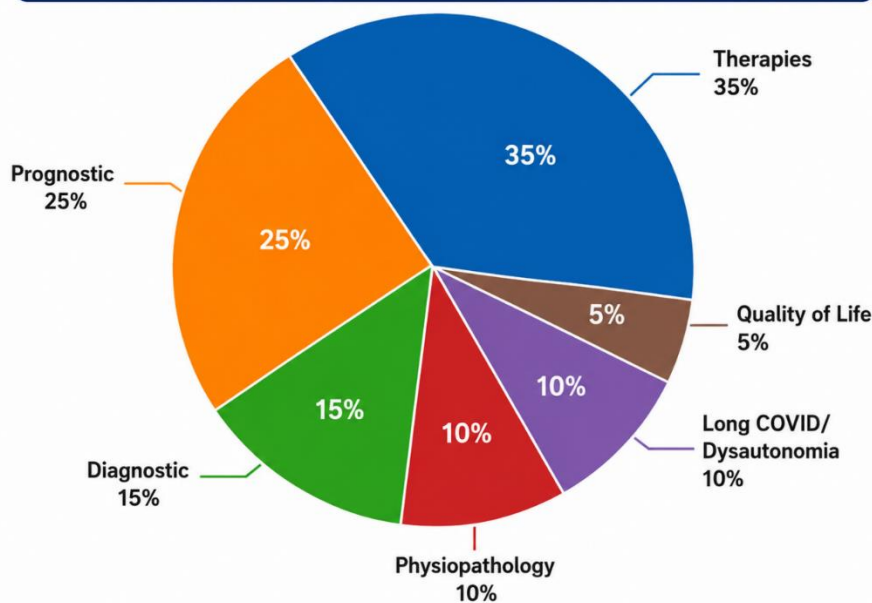
Therapeutic strategy	Mechanism of action	Scientific evidence	Main benefits	Limitations
Olfactory training	Stimulates neuroplasticity and regeneration of the olfactory pathways	Strong evidence from systematic reviews and meta-analyses	Improved identification, discrimination, and perception of odors	Requires long-term adherence and results may vary
Intranasal topical corticosteroids	Reduction of local inflammation of the olfactory epithelium	Moderate evidence and heterogeneous results	Possible acceleration of recovery in selected cases	Inconsistent benefits across studies
Systemic corticosteroids	Control of persistent inflammatory processes	Limited evidence	Potential improvement in specific patients	Increased risk of systemic adverse effects
Palmitoylethanolamide + Luteolin (PEA-LUT)	Anti-inflammatory and neuroprotective action	Promising evidence in recent studies	Improved olfactory recovery and reduced neural inflammation	Need for robust multicenter studies
Platelet-Rich Plasma (PRP)	Tissue and neural regenerative stimulation	Emerging evidence	Potential recovery in refractory cases	Few controlled studies available
Intranasal Vitamin A	Stimulation of neuroepithelial regeneration	Preliminary evidence	Possible functional recovery of the olfactory epithelium	Lack of therapeutic consensus
Antioxidant supplementation	Reduction of neural oxidative stress	Limited evidence	Potential adjuvant benefit	Results still inconclusive
Nasal irrigation with saline solution	Cleaning and improvement of the nasal environment	Supporting evidence	Low cost and easy application	Limited standalone benefit
Combination therapies	Association between olfactory training and pharmacological treatment	Growing evidence	Possible synergistic effect on olfactory recovery	Protocols not yet standardized
Multidisciplinary follow-up	Integrated otolaryngological, neurological, and psychological approach	Recommended in persistent cases	Overall improvement in quality of life and treatment adherence	Need for greater availability of care

The studies reviewed demonstrate that olfactory training remains the intervention with the strongest scientific support and is considered the first-line treatment for patients with persistent olfactory dysfunction. At the same time, pharmacological therapies such as topical corticosteroids, intranasal vitamin A, and neuroprotective compounds are being investigated as complementary alternatives. Among emerging approaches, the combination of palmitoylethanolamide and luteolin (PEA-LUT) and platelet-rich plasma show promising results, especially in individuals refractory to conventional therapies. Furthermore, the combination of different therapeutic modalities has demonstrated potential for optimizing functional recovery of the sense of smell. Taken together, the findings reinforce that the management of post-COVID-19 olfactory changes should

multidisciplinary, progressive, and based on the most recent available scientific evidence.

Figure 2 presents the distribution of the main topics addressed in the studies included in this systematic review on post-COVID-19 olfactory changes. It is observed that most publications focused on the evaluation of therapeutic strategies, especially olfactory training and emerging pharmacological therapies. In addition, a significant portion of the studies investigated prognostic aspects related to the recovery of smell, while other studies explored diagnostic methods, pathophysiological mechanisms, and impacts on quality of life. This distribution highlights the growing scientific interest in comprehensively understanding post-COVID olfactory dysfunction and in the search for effective therapeutic approaches.

**Figure 2. Distribution of study topics included on post-COVID-19 olfactory alterations**



**Fig 2:**

Distribution of topics in the included studies

Figure 2 Caption. Percentage distribution of the main topics addressed in the studies included in the systematic review on post-COVID-19 olfactory changes. There is a predominance of research focused on therapeutic strategies, followed by prognostic, diagnostic, and pathophysiological studies. Topics related to Long COVID, dysautonomia, and quality of life also contributed to the overall understanding of persistent olfactory dysfunction.

## 5. Discussion

The large number of studies identified in this review highlights the growing scientific interest in understanding the pathophysiological mechanisms involved in post-COVID loss of smell. Unlike other respiratory viral infections, SARS-CoV-2 appears to primarily compromise the sustentacular cells of the olfactory epithelium, triggering inflammatory processes and microenvironmental changes capable of impairing neuronal function without necessarily causing direct destruction of olfactory neurons (BUTOWT; VON BARTHELD, 2021; ZAZHYTSKA *et al.*, 2022) [7, 51]. In addition to peripheral changes, recent evidence suggests

significant involvement of central mechanisms. Neuroimaging studies have identified a reduction in the volume of the olfactory bulb, cerebral metabolic changes, and impairment of cortical regions involved in sensory processing, such as the orbitofrontal cortex, reinforcing the hypothesis that the persistence of olfactory dysfunction may result from structural and functional changes in the central nervous system (PETERSEN *et al.*, 2024; GUEJ *et al.*, 2025) [36, 17].

In the diagnostic field, the results confirm the importance of using objective methods to assess olfactory function. Comparative studies have demonstrated that patients' self-perception often does not correspond to the actual severity of the dysfunction identified by standardized psychophysical tests, such as the University of Pennsylvania Smell Identification Test (UPSIT) and the Sniffin' Sticks Test (HANNUM *et al.*, 2021; LE BON *et al.*, 2022) [19, 26]. Thus, the combination of clinical evaluation and objective tests allows for greater diagnostic accuracy and better monitoring of clinical progression.

Regarding prognosis, it has been observed that recovery of olfactory function exhibits heterogeneous patterns. Although

many patients partially or fully recover their sense of smell in the first few weeks after infection, a significant proportion maintains persistent symptoms for months or even years, constituting an important component of Long COVID (HU *et al.*, 2023; HORWITZ *et al.*, 2025) <sup>[21, 20]</sup>. Longitudinal studies indicate that factors such as advanced age, greater initial severity of olfactory loss, and prolonged persistence of symptoms are associated with poorer rates of functional recovery (LECHIEN *et al.*, 2022; ZHOU *et al.*, 2025) <sup>[27, 52]</sup>. Parosmia has emerged as one of the key prognostic findings observed in the literature. Although some authors suggest that its presence may indicate ongoing neural regeneration, this alteration is frequently associated with significant impairments in patients' eating habits, social relationships, and psychological well-being (SCHAMBECK *et al.*, 2021; GUENDER *et al.*, 2024) <sup>[42, 18]</sup>. These results reinforce the need for a multidisciplinary approach for individuals with persistent olfactory dysfunction.

The psychosocial repercussions identified in this review corroborate studies demonstrating an association between prolonged olfactory loss and reduced quality of life. The inability to perceive odors compromises environmental safety, interferes with food perception, and may contribute to the development of anxiety, depression, and social isolation (OTTE *et al.*, 2023; OLESZKIEWICZ *et al.*, 2025) <sup>[33, 32]</sup>. Consequently, quality-of-life assessment should be routinely incorporated into the follow-up of these patients. In the therapeutic setting, olfactory training has emerged as the strategy with the highest level of scientific evidence. Recent systematic reviews and meta-analyses have demonstrated significant improvement in the identification, discrimination, and perception of odors in patients undergoing structured olfactory rehabilitation protocols (FORNAZIERI *et al.*, 2021; HWANG *et al.*, 2023) <sup>[16, 23]</sup>. Similar results were observed by Asvapoositkul *et al.* (2023) <sup>[2]</sup> and Chen *et al.* (2025) <sup>[11]</sup>, who reported consistent benefits in functional recovery and quality of life. In contrast, pharmacological therapies yielded more heterogeneous results. Topical and systemic corticosteroids, intranasal vitamin A, and antioxidant agents demonstrated potential benefit in some studies, but without definitive consensus regarding clinical efficacy or the standardization of therapeutic protocols (KIM *et al.*, 2022; WANG *et al.*, 2023) <sup>[24, 45]</sup>. This variability reinforces the need for randomized clinical trials with greater methodological robustness.

Emerging therapies are also attracting growing interest. The combination of palmitoylethanolamide and luteolin (PEA-LUT) has demonstrated anti-inflammatory and neuroprotective properties that may be beneficial for olfactory recovery, while platelet-rich plasma (PRP) shows promising results in patients refractory to conventional approaches (CAPRA *et al.*, 2023; CAPRA *et al.*, 2025) <sup>[9, 8]</sup>. However, the scarcity of multicenter trials limits their routine incorporation into clinical practice.

Overall, the findings of this review demonstrate that post-COVID-19 olfactory dysfunction remains a significant clinical and scientific challenge. Although significant advances have been made in understanding the pathophysiological mechanisms and available therapeutic strategies, important gaps still exist regarding prognostic prediction and the development of treatments capable of promoting faster and more consistent functional recovery. The results show a predominance of studies focused on

therapeutic strategies, accounting for approximately one-third of the scientific output analyzed. This finding reflects the need to identify effective interventions for patients with persistent olfactory dysfunction following SARS-CoV-2 infection. Prognostic studies also accounted for a significant proportion, highlighting the interest in understanding the factors associated with spontaneous recovery or the persistence of symptoms. To a lesser extent, studies focused on pathophysiological mechanisms, quality of life, neuroimaging, and dysautonomia were identified—areas that are expanding our understanding of the systemic impacts of COVID-19. Taken together, the findings demonstrate that the current literature is directed not only toward characterizing olfactory loss but also toward developing diagnostic and therapeutic strategies capable of improving clinical outcomes for affected patients.

## 6. Conclusion

Post-COVID-19 olfactory changes constitute an important manifestation of the post-acute syndrome of SARS-CoV-2 infection, presenting high prevalence and potential impact on patients' quality of life, mental health, nutrition, and social interaction. The findings of this systematic review demonstrate that the pathophysiology of olfactory dysfunction involves complex mechanisms, including peripheral alterations of the olfactory epithelium and possible central impairments of neural pathways related to sensory processing.

The results highlight that the use of objective diagnostic methods, especially standardized psychophysical tests, represents an essential tool for the proper identification and monitoring of olfactory loss. Furthermore, key prognostic factors such as age, initial symptom severity, and the presence of parosmia can aid in predicting functional recovery and in individualized therapeutic planning.

Among the available therapeutic strategies, olfactory training remains the intervention with the strongest scientific support and should be considered the primary approach for patients with persistent olfactory dysfunction. Pharmacological therapies and emerging approaches, such as PEA-LUT and PRP, show potential benefit but still require more robust evidence for broad clinical recommendation.

It is therefore concluded that the management of post-COVID-19 olfactory changes should be multidisciplinary, evidence-based, and tailored to the individual characteristics of each patient. New prospective studies and controlled clinical trials are essential to improve our understanding of the mechanisms involved and to establish increasingly effective diagnostic and therapeutic protocols for this condition, which remains a significant clinical challenge in the post-pandemic period.

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