

# Efficacy of Treatment and Prevention of Radiation-Induced Oral Mucositis

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## ABSTRACT

Radiation-induced oral mucositis (RIOM) is a common and debilitating complication of radiotherapy for head and neck cancers (HNC), significantly affecting patients' quality of life and treatment continuity. Despite extensive research and clinical trials, no single intervention has emerged as a universally accepted standard of care. This literature review identified a wide range of preventative and therapeutic strategies including optimized oral care, radiotherapy techniques, pharmacologic agents, and newer modalities such as laser therapy and cryotherapy. Evidence suggests that multiple approaches show promise in reducing the severity and impact of RIOM, further studies are necessary to establish consistent treatment guidelines.

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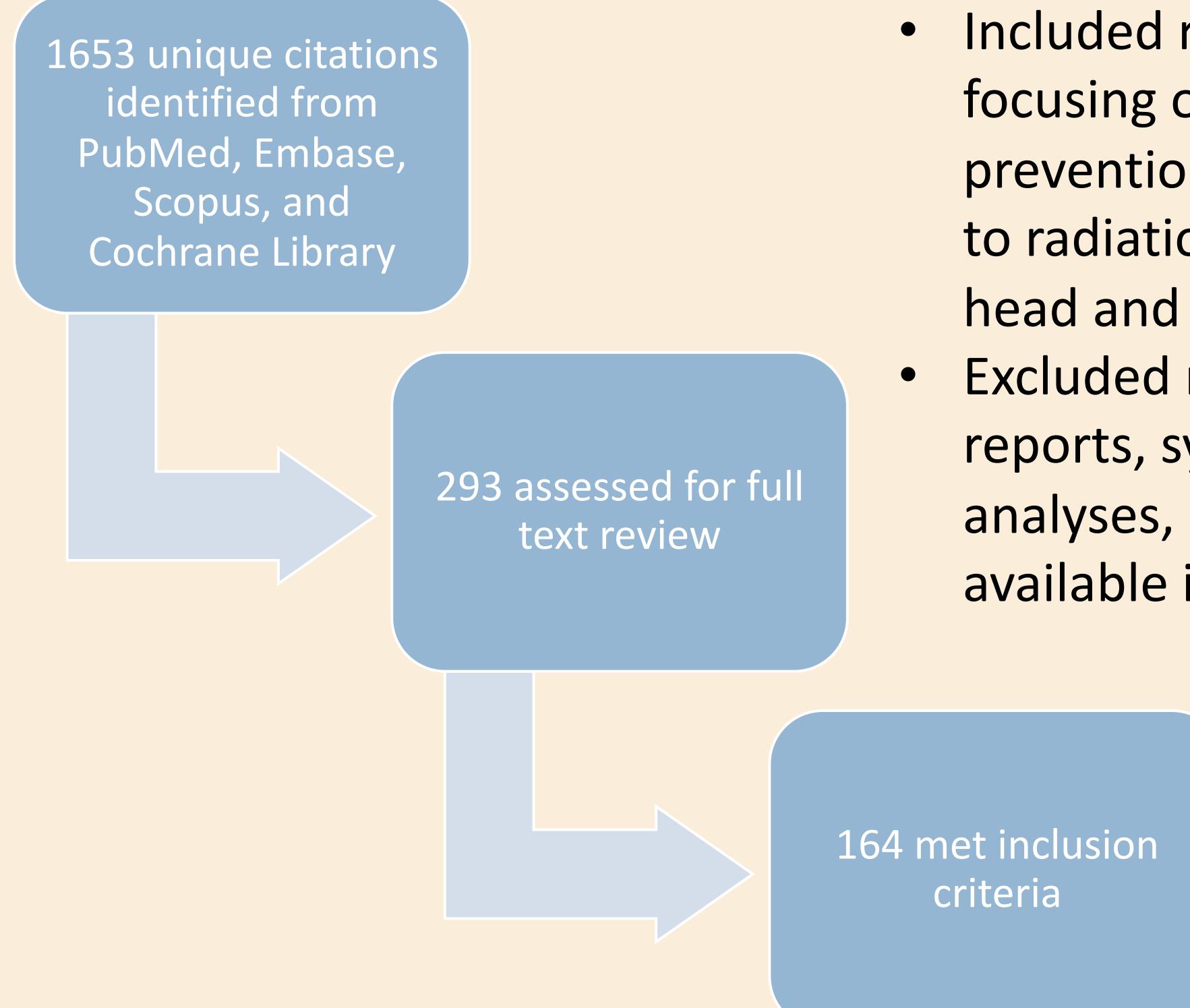
## INTRODUCTION

- RIOM occurs due to damage to adjacent tissue during radiotherapy, and is associated with complications such as susceptibility to infection, discontinuation or delay of treatment, and poor nutritional status.
- RIOM can be assessed clinically with severity scales from the WHO, RTOG, or NCI (Table 1).
- A recent meta-analysis reported a prevalence of RIOM in HNC patients at 94%, with severe RIOM occurring in 37%.
- Treatment strategies are generally targeted towards pain management, reducing mucosal ulceration and inflammation, and minimizing microbial infections.

SCALE	GRADE 0	GRADE I	GRADE II	GRADE III	GRADE IV	GRADE V
WHO	No findings	Erythema & soreness	Erythema & ulcers; solid diet tolerated	Ulcers; liquid diet only	Unable to tolerate liquid or solid diet	-
RTOG	No findings	Painless ulcers, erythema, or mild soreness	Painful erythema, edema, or ulcers, but can eat	Painful erythema, edema, or ulcers but cannot eat	Requires enteral or parenteral support	-
NCI-CTCAE	-	Asymptomatic or mild; no intervention required	Moderate pain or ulcer not affecting oral intake; modified diet indicated	Severe pain interfering with oral intake	Life-threatening consequences; urgent intervention indicated	Patient death

Table 1. Grading scales used for RIOM. WHO=World Health Organization; RTOG=Radiation Oncology Treatment Group; NCI-CTCAE=National Cancer Institute Common Terminology Criteria for Adverse Events.

## METHODS AND MATERIALS



## RESULTS

- Interventions included in the review varied widely, however 1/4 of studies implored the use of natural or herbal products such as honey, turmeric, and aloe vera (Figure 2).
- Topically applied products were by far the most commonly studied, with 62 (37.8%) of the studies focusing on mouthwashes and oral rinses.
  - A targeted review was performed, focusing on trials that used medicated mouthwashes and assessed RIOM using the WHO or RTOG severity scales (Table 2).
  - Benzydamine (n=7), sucralfate (n=6), chlorhexidine (n=5), and GM-CSF (n=4) were the most commonly studied mouthwashes (Table 2).
  - Laser therapy was the most frequently assessed intervention, with 31 studies focusing on its use in both the prevention and treatment of RIOM.

AGENT	STUDY FINDINGS
Benzydamine	<ul style="list-style-type: none"> <li>Incidence of severe (grade <math>\geq 3</math>) mucositis generally decreased compared to control, ranging from 29-43%.</li> <li>Delayed onset or progression compared to controls/placebos in multiple studies.</li> <li>Decreased pain scores, especially in later stages (<math>\geq 4</math> weeks) of treatment.</li> </ul>
Sucralfate	<ul style="list-style-type: none"> <li>All studies reported decreased use of analgesics compared to controls.</li> <li>Did not delay onset or prevent incidence of severe mucositis.</li> </ul>
Chlorhexidine	<ul style="list-style-type: none"> <li>Did not show improvement in patients undergoing RT alone, but some improvement in patients undergoing CT.</li> <li>Significant reports of adverse effects such as discomfort, burning pain, and taste alteration caused termination of multiple studies.</li> </ul>
GM-CSF	<ul style="list-style-type: none"> <li>Significant decreases in severity of mucositis with improvement observed during ongoing RT, suggested better efficacy when RIOM is already present.</li> <li>No adverse effects seen, compared to nausea, vomiting, headache, fever seen when given as an injection.</li> </ul>

Table 2. Grouped findings of studies performed on medicated mouthwashes. CT=chemotherapy; RT=radiation therapy; GM-CSF=granulocyte-macrophage colony-stimulating factor.

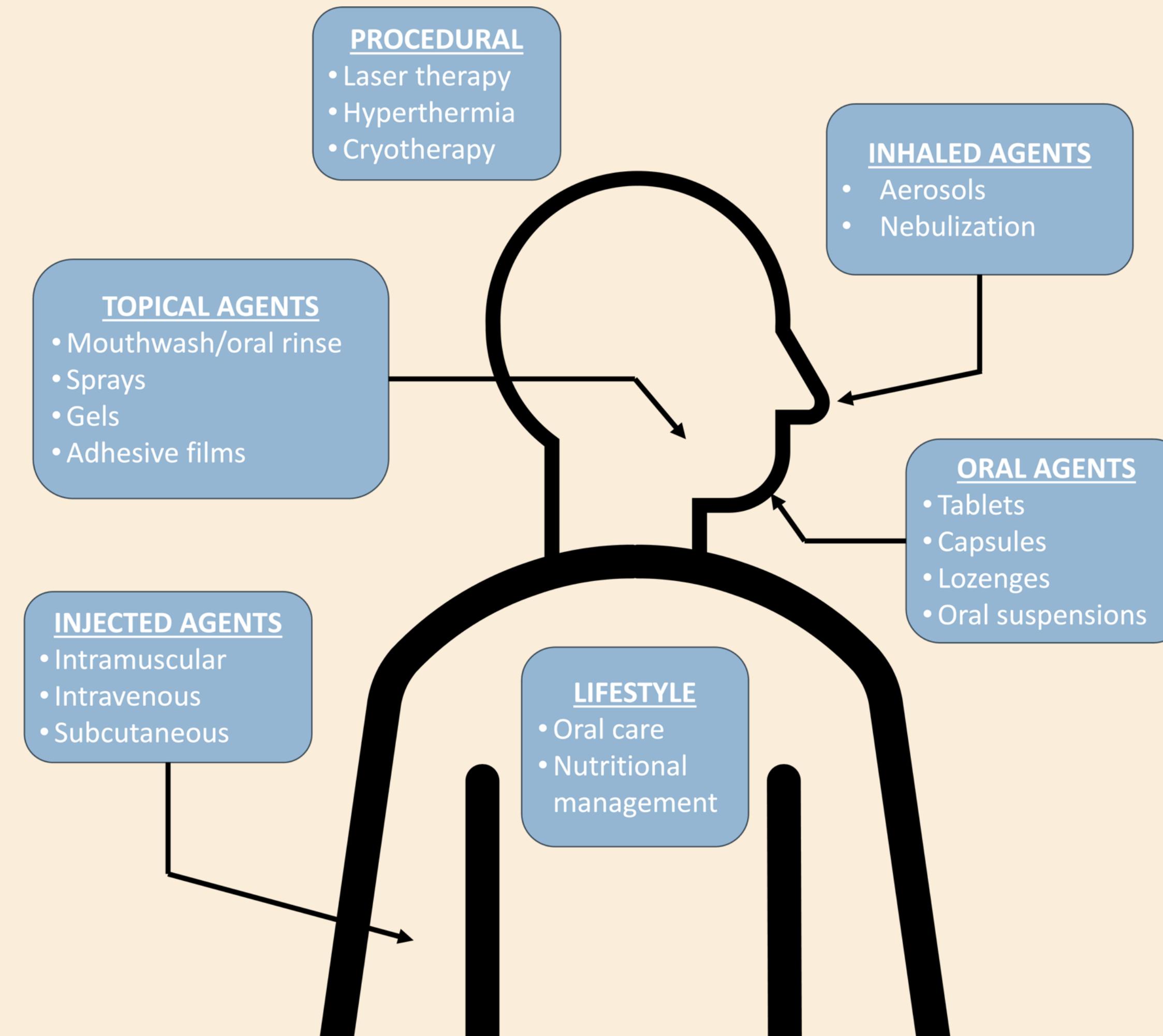


Figure 1. Treatment routes identified in literature review.

## DISCUSSION

- A wide range of pharmacologic, procedural, and supportive strategies have been evaluated, but their efficacy varies significantly depending on the agent, timing, and route of administration.
- Treatment selection is also influenced by cost, accessibility, and physician familiarity.
  - Availability of newer agents such as immunomodulators and biologics may be limited to clinical trials.
  - The large percentage of herbal products, vitamins, and supplements reflects their ease of use and accessibility, though most have limited evidence from single small studies.
  - 2020 guidelines from Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC/ISO) noted laser therapy to be a promising field in OM treatment, likely contributing to the growing number of recent clinical trials.

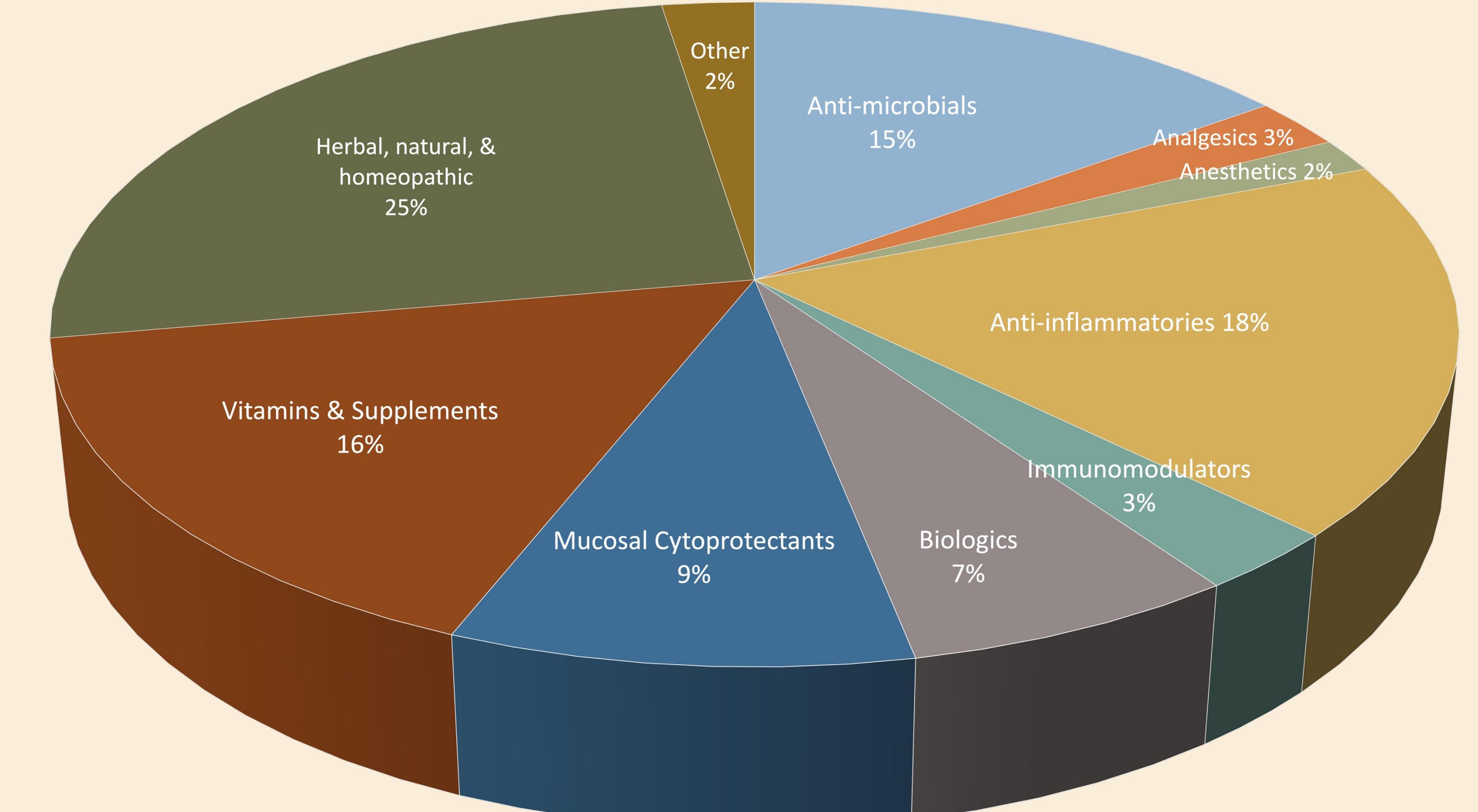


Figure 2. Breakdown of drug categories identified in literature review.

## CONCLUSIONS

- This review is limited by the diversity of study designs, sample sizes, patient characteristics, and outcome measures.
- Preliminary results of this review show promise with multiple therapies, though overall evidence suggests that effective management will likely require a multimodal approach.

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