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**Luiza Ribeiro Vargas**

**Efeitos dos exercícios de amplitude de movimento mandibular e terapia de  
deglutição na qualidade de vida dos pacientes em tratamento de câncer de  
cabeça e pescoço: uma revisão sistemática**

Governador Valadares

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Dissertação apresentada ao Programa de Pós-Graduação em Ciências Aplicadas à Saúde, da Universidade Federal de Juiz de Fora, Campus Governador Valadares, como requisito à obtenção do título de Mestre em Ciências Aplicadas à Saúde, área de concentração Biociências.

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## RESUMO

O tratamento do câncer de cabeça e pescoço (CCP) pode ocasionar sequelas funcionais, como trismo e disfagia, comprometendo a qualidade de vida (QV) relacionada à saúde dos pacientes. Embora os exercícios de amplitude de movimento mandibular (EAMM) e a terapia de deglutição sejam amplamente utilizados na reabilitação dessas complicações, seu impacto sobre a QV ainda permanece incerto. Nesse contexto, esta revisão sistemática teve como objetivo avaliar os efeitos dessas intervenções sobre a QV de pacientes com trismo e/ou disfagia decorrentes do tratamento do CCP. A revisão foi conduzida de acordo com as recomendações do *Cochrane Handbook*, registrada no PROSPERO e reportada conforme a declaração PRISMA 2020. As buscas foram realizadas nas bases de dados PubMed, EMBASE, Cochrane Library, LILACS, Scopus e Web of Science, e complementadas na literatura cinzenta, sem restrição de idioma ou data de publicação. O risco de viés foi avaliado pela ferramenta RoB 2 e a certeza da evidência pelo sistema GRADE. Ao todo, foram incluídos 8 ensaios clínicos randomizados (ECRs) que compararam EAMM e/ou terapia de deglutição aos cuidados habituais. De modo geral, os resultados demonstraram benefícios em desfechos funcionais específicos, especialmente relacionados ao aumento da abertura bucal, à melhora da deglutição e à redução do sofrimento emocional. Por outro lado, não foi observada melhora consistente da QV global nem dos domínios de bem-estar físico, social e funcional. Além disso, a elevada heterogeneidade clínica e metodológica entre os estudos, associada ao pequeno tamanho amostral e ao risco de viés, impossibilitou a realização de metanálise e levou à classificação da evidência como de muito baixa certeza para o desfecho QV. Em síntese, os EAMM e a terapia de deglutição apresentam potencial para melhorar aspectos funcionais da reabilitação de pacientes com trismo e/ou disfagia após o tratamento do CCP. No entanto, as evidências atuais ainda são insuficientes para demonstrar benefícios consistentes sobre a QV global. Assim, futuros estudos com maior rigor metodológico, protocolos padronizados e amostras mais representativas são necessários para produzir evidências mais robustas e subsidiar a prática clínica.

**Palavras-chave:** Câncer de cabeça e pescoço; Trismo; Disfagia; Exercícios terapêuticos; Qualidade de vida; Revisão sistemática.

## ABSTRACT

Head and neck cancer (HNC) treatment can lead to functional sequelae, such as trismus and dysphagia, compromising patients' quality of life (QoL). Although mandibular range-of-motion exercises (MROME) and swallowing therapy are widely used to rehabilitate these complications, their impact on QoL remains uncertain. In this context, this systematic review aimed to evaluate the effects of these interventions on the QoL of patients with trismus and/or dysphagia resulting from HNC treatment. The review was conducted according to Cochrane Handbook recommendations, registered in PROSPERO, and reported in compliance with the PRISMA 2020 statement. Searches were performed in the PubMed, EMBASE, Cochrane Library, LILACS, Scopus, and Web of Science databases and supplemented by a search of grey literature, with no language or publication date restrictions. Risk of bias was assessed using the RoB 2 tool, and the certainty of evidence was evaluated using the GRADE. A total of eight randomized controlled trials (RCTs) comparing MROME and/or swallowing therapy with usual care were included. Overall, the results demonstrated benefits regarding specific functional outcomes, particularly increased mouth opening, improved swallowing, and reduced emotional distress. Conversely, no consistent improvement was observed in global QoL or in the physical, social, and functional well-being domains. Furthermore, high clinical and methodological heterogeneity among the studies, combined with small sample sizes and risk of bias, precluded a meta-analysis and resulted in the evidence for the QoL outcome being classified as very low certainty. In summary, MROME and swallowing therapy show potential for improving functional aspects of rehabilitation for patients with trismus and/or dysphagia following HNC treatment. However, current evidence remains insufficient to demonstrate consistent benefits regarding global QoL. Thus, future studies with greater methodological rigor, standardized protocols, and more representative samples are needed to generate more robust evidence and inform clinical practice.

**Keywords:** Head and neck cancer; Trismus; Dysphagia; Therapeutic exercises; Quality of life; Systematic review.

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## LISTA DE ABREVIATURAS E SIGLAS

| <b>SIGLA</b>    | <b>Descrição</b>                                                                                                    |
|-----------------|---------------------------------------------------------------------------------------------------------------------|
| CCP             | Câncer de Cabeça e Pescoço                                                                                          |
| QV              | Qualidade de Vida                                                                                                   |
| EAMM            | Exercícios de Amplitude de Movimento Mandibular                                                                     |
| EEC             | Exercício de Elevação de Cabeça                                                                                     |
| PEED            | Programa Educativo de Exercícios para a Disfagia                                                                    |
| RPD             | Reabilitação Personalizada de Disfagia                                                                              |
| ECRs            | Ensaio Clínicos Randomizados                                                                                        |
| EES             | Esfíncter Esofágico Superior                                                                                        |
| GTQ             | Gothenburg Trismus Questionnaire                                                                                    |
| DHI             | Dysphagia Handicap Index                                                                                            |
| FOIS            | Functional Oral Intake Scale                                                                                        |
| MDADI           | MD Anderson Dysphagia Inventory                                                                                     |
| EORTC QLQ-C30   | European Organization for Research and Treatment for Cancer Quality of Life Questionnaire (Core 30)                 |
| EORTC QLQ-H&N35 | European Organization for Research and Treatment for Cancer Quality of Life Questionnaire (Head and Neck - Core 35) |

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## 1 INTRODUÇÃO

Câncer é um distúrbio em que células de uma região do corpo se multiplicam amplamente, podendo se disseminar para outras partes do corpo <sup>1</sup>. Entre os tipos mais comuns estão o câncer de mama, de pulmão e o de cabeça e pescoço (CCP) <sup>1</sup>. O CCP, que inclui o câncer de boca (CB), é o sétimo mais comum no mundo, com incidência estimada em mais de 660.000 novos casos e 325.000 mortes por ano <sup>1</sup>. O CB é um tumor maligno que pode afetar qualquer tecido da cavidade oral — mucosa, músculos, nervos, dentes, ossos, vasos sanguíneos e/ou glândulas salivares <sup>3</sup>. Devido à sua malignidade, os pacientes com CCP têm expectativa de vida média de 10 a 13 anos <sup>5</sup>.

Considerando essa gravidade, e embora haja várias intervenções de autoridades e agências não-governamentais com o intuito de minimizar os casos, observa-se tendência crescente na frequência do CB globalmente <sup>1</sup>. Na Ásia, é um dos tipos mais comuns, sobretudo na região sul, associado ao uso de tabaco, nozes de betel e álcool <sup>1</sup>. Em Taiwan, em 2015, foram registrados 5.039 novos casos, sendo o CB a quarta causa de morte no país <sup>3</sup>. Cerca de 55% dos casos são diagnosticados tardiamente, com sobrevida de 38% em 5 anos, variando conforme raça e localização do tumor <sup>2</sup>. Na Europa, em 2013, o Reino Unido registrou cerca de 7.600 diagnósticos de câncer de lábio, cavidade oral ou orofaringe <sup>1, 11</sup>. Nas Américas, o CB é o 11º, 12º e 13º câncer mais comum nos EUA, Canadá e México, respectivamente <sup>1</sup>, com cerca de 30.000 novos casos anuais nos EUA <sup>3</sup>.

Diante desse cenário epidemiológico, foram desenvolvidos alguns tratamentos com o objetivo de impedir o crescimento tumoral e aumentar a sobrevida <sup>1, 5</sup>. Estes tratamentos, geralmente, envolvem cirurgia de grande porte com ressecção e reconstrução, associada a quimioterapia e/ou radioterapia adjuvantes <sup>1, 5</sup>. Contudo, a própria terapia para o CCP pode causar morbidade pós-operatória, redução da qualidade de vida (QV) e efeitos de longo prazo, como caquexia e desnutrição, prejudicando a recuperação do paciente <sup>8</sup>.

Além desses efeitos, outras complicações comuns da terapia contra o câncer são o trismo e a disfagia. O trismo refere-se à dificuldade de abertura bucal ou

mobilidade mandibular e pode comprometer a fala, a mastigação, a higiene oral e a interação social <sup>5, 7</sup>. A disfagia, consiste em uma disfunção de deglutição com prevalência de 50% a 60%, podendo causar desnutrição, perda de peso e sofrimento emocional, e exigindo modificação da consistência alimentar e estratégias específicas de manejo <sup>3</sup>. O impacto do CCP no equilíbrio funcional do sistema estomatognático — deglutição, mastigação e nutrição — gera sério prejuízo à QV dos pacientes <sup>12</sup>.

Frente à redução do bem-estar e ao isolamento social causados por essas complicações, é importante investigar formas de prevenir e reabilitar tais sequelas. Exercícios mandibulares podem melhorar a abertura bucal e prevenir o trismo <sup>5, 11</sup>. Para a disfagia, programas de fortalecimento muscular podem melhorar a força lingual e a deglutição, inclusive em populações saudáveis, jovens e idosos <sup>7, 8</sup>, com benefícios adicionais como redução de ansiedade, depressão e fadiga <sup>8</sup>. A terapia de deglutição, baseada no paradigma "use ou perca", busca manter a ingestão oral e evitar o desuso muscular, que agrava o edema e a fibrose induzidos pela radiação <sup>23</sup>; pacientes que a realizaram tiveram melhor desempenho faríngeo que os demais <sup>23</sup>.

Apesar desses achados promissores, ainda são escassas as pesquisas sobre os efeitos dos exercícios mandibulares no período pós-cirúrgico e pós-quimiorradioterápico <sup>8, 9</sup>, bem como sobre o impacto da terapia de deglutição na QV de pacientes tratados com quimiorradioterapia primária <sup>5, 24</sup>, o que evidencia a necessidade de estudos rigorosos e controlados sobre os benefícios desses exercícios para a QV de pacientes com CCP <sup>11</sup>. Como ainda não há síntese que agrupe essas intervenções, e considerando a hipótese de que esses exercícios podem influenciar a QV de pacientes pós-tratamento do CCP, o presente estudo consiste em uma revisão sistemática de ensaios clínicos randomizados que busca investigar seu efeito na QV e no bem-estar físico, social, emocional e funcional desses pacientes.

## 2 ARTIGO CIENTÍFICO

### **Effects of Mandibular Range-of-Motion Exercises and Swallowing Therapy on Quality of Life in Patients Undergoing Head and Neck Cancer Treatment: A Systematic Review**

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The authors declare no conflicts of interest.

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#### **Data Availability Statement**

The data supporting the findings of this study are available within the article and its supplementary information files. Additional data may be obtained from the corresponding author upon reasonable request.

#### **AI Statement**

During the preparation of this manuscript, the authors used NotebookLM (Google), ChatGPT (OpenAI), and Claude (Anthropic) as writing assistance tools to help refine language, improve readability, and support text organization and section structuring. All content generated or suggested by these tools was critically reviewed, verified, and edited by the authors, who take full responsibility for the accuracy, integrity, and scientific content of the final work.

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Mandibular Exercises and Quality of Life in Head and Neck Cancer

## **ABSTRACT**

**Background:** Head and neck cancer (HNC) treatment can cause trismus and dysphagia, compromising patients' quality of life (QoL). This systematic review evaluated the effects of mandibular range-of-motion exercises and swallowing therapy on QoL in patients with these complications. **Methods:** The review followed the Cochrane Handbook, was registered in PROSPERO, and was reported according to PRISMA 2020. Risk of bias was assessed using RoB 2, and the certainty of the evidence was evaluated using GRADE. **Results:** Eight randomized controlled trials were included. Although improvements were observed in mouth opening, swallowing function, and emotional distress, no consistent benefit was found for overall QoL. Heterogeneity, small sample sizes, and risk of bias resulted in very low-certainty evidence. **Conclusion:** These interventions may improve functional outcomes, but their effects on overall QoL remain uncertain.

**Keywords:** Head and neck cancer; Trismus; Dysphagia; Therapeutic exercises; Quality of life; Systematic review.

## 2.1 INTRODUCTION

Head and neck cancer (HNC) is the seventh most common cancer worldwide, accounting for more than 660,000 new cases and 325,000 deaths annually <sup>1, 2</sup>. Oral cavity and oropharyngeal cancers represent a substantial proportion of HNC cases, with the tongue among the most frequently affected sites <sup>2, 3, 4</sup>. Diagnosis occurs predominantly after age 50 and, in most cases, at advanced stages (III and IV), worsening prognosis and typically requiring more aggressive treatment, which directly impacts health-related quality of life (HRQoL) <sup>2, 3, 5</sup>.

Medical treatments have been developed and implemented to halt tumor growth and/or eliminate residual tumor tissue, generally involving surgery and reconstruction combined with adjuvant chemotherapy and/or radiotherapy, although the latter may also serve as primary treatment <sup>1, 4, 5, 6, 7</sup>. Despite improving survival rates, these approaches frequently cause postoperative morbidity and functional and psychosocial sequelae that substantially impair quality of life (QoL) <sup>3, 5, 8, 9</sup>. Therapeutic success therefore depends not only on tumor control but also on preserving functional abilities such as eating, communication, social interaction, and daily autonomy, posing a considerable rehabilitation challenge for multidisciplinary teams <sup>2, 4, 6, 9, 10, 11</sup>.

HNC treatment compromises the biomechanics of swallowing and mouth opening, predisposing patients to dysphagia and trismus, complications frequently reported as co-occurring <sup>2, 6, 10, 11</sup>. Trismus, characterized by restricted mouth opening and mandibular mobility (maximum incisal opening under 35 mm; prevalence 5%–38%), can impair speech intelligibility, mastication, swallowing, oral hygiene, and social interaction <sup>5, 6, 7, 10, 11</sup>. Dysphagia, impaired bolus transport from mouth to stomach, can lead to malnutrition, weight loss, emotional distress, hospitalization, enteral feeding needs, aspiration-related infections, and higher healthcare costs <sup>2, 3, 4, 9, 10</sup>. The two conditions are closely related, since restricted mouth opening hinders bolus manipulation during swallowing's oral phases <sup>7, 10, 11</sup>.

Given this substantial impact on the stomatognathic system, targeted management strategies are essential <sup>3, 12</sup>. Since mandibular hypomobility can cause

muscle atrophy and degenerative TMJ changes, stretching exercises for the elevator muscles and TMJ are critical, often facilitated by devices such as the TheraBite® and EZBite systems, and based on progressive stretching of fibrotic tissue to restore mobility <sup>4, 6, 10</sup>. Protocol adherence is essential, as regular stretching helps preserve muscle elasticity and prevent trismus progression <sup>3, 7, 10</sup>.

Swallowing rehabilitation encompasses tongue-strengthening and head-lift exercises (HLE) to strengthen the suprahyoid and pharyngeal musculature, improving laryngeal elevation, upper esophageal sphincter (UES) opening, and neuromuscular coordination <sup>2, 3, 4, 7</sup>. When initiated early, this therapy may preserve swallowing function, reduce reliance on alternative feeding routes, and improve long-term outcomes, typically under the care of trained nurses, physiatrists, and speech-language pathologists <sup>2, 3, 4, 7</sup>. Effectiveness is commonly assessed using validated instruments such as the EORTC QLQ-C30 and QLQ-H&N35, MDADI, DHI, and GTQ <sup>2, 3, 6, 9, 10</sup>, along with Patient-Reported Outcome Measures (PROMs) like the EQ-5D-3L, which capture emotional, physical, functional, and social domains relevant to clinical decision-making <sup>2, 4, 10</sup>.

Despite growing interest in HNC rehabilitation, evidence on the effectiveness of mandibular exercises and swallowing therapy remains limited, with no consensus on their overall impact on QoL. This systematic review of RCTs therefore aimed to evaluate the effects of mandibular range-of-motion (MROM) exercises and swallowing therapy on QoL and on the physical, social, emotional, and functional well-being of patients with trismus and/or dysphagia following HNC treatment.

## 2.2 METHODS

### 2.2.1 Study design

This systematic review followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions (v6.4) <sup>17</sup>. A pilot search in MEDLINE (via PubMed) assessed feasibility using the FINER criteria (Feasible,

Interesting, Novel, Ethical, Relevant). The search strategy was designed by the reviewers (L.R.V. and L.F.D.) and peer-reviewed using the PRESS 2015 Evidence-Based Checklist <sup>18</sup>. The protocol was developed following PRISMA-P recommendations <sup>19</sup> and prospectively registered in PROSPERO (CRD420251075865; Supplementary Material, Sections S1 and S2). Conduct and reporting adhered to the PRISMA 2020 statement <sup>15</sup>.

### **2.2.2 Eligibility criteria**

Eligibility criteria followed the PICOS framework (Participants, Intervention, Comparator, Outcomes, Study design) (Table S3, Supplementary Material). Eligible studies were RCTs evaluating adult HNC patients with trismus and/or dysphagia resulting from the disease or its treatment, using jaw-opening exercises and/or swallowing therapy, alone or combined with other interventions, provided their effects could be assessed independently, and reporting QoL as an outcome.

Excluded were systematic reviews, observational studies, case reports, non-randomized trials, and other non-RCT designs, as well as studies involving benign tumors or other head and neck conditions, trials not assessing QoL, and studies using exercises targeting body regions other than the head and neck.

### **2.2.3 Search strategy**

The search strategy was developed using the PICOS framework: (1) population, patients with trismus or dysphagia from HNC treatment; (2) intervention, mandibular range-of-motion exercises and/or swallowing therapy; (3) comparator, usual care or standard treatment; (4) outcome, quality of life; and (5) study design, RCTs (Table S4, Supplementary Material). To construct the search strategy, MeSH descriptors were used, including Head and Neck Neoplasms, Exercise or Exercise Therapy, and Quality of Life, supplemented by relevant synonyms (e.g., Oral Cancer/Oral Cavity Cancer, Oropharyngeal Cancer, Life Quality, Health-Related

Quality of Life) to increase sensitivity (full strategy in Table S5, Supplementary Material).

Electronic searches were conducted on April 24, 2025, and updated on May 13, 2025, across PubMed, EMBASE, Cochrane Library, LILACS, Scopus, and Web of Science. Gray literature searches (ReBEC, ClinicalTrials.gov, OpenGrey, ICTRP/WHO, CAPES) were performed on July 17 and 18, 2025, to minimize publication bias (Table S6, Supplementary Material), along with cross-reference checks of prior review articles. No language or date restrictions were applied.

#### **2.2.4 Study selection**

Studies from the selected databases were exported in ".ris" or ".txt" format and imported into Rayyan Reference Manager. Duplicates were identified using the platform's automated tool and verified manually by two independent, blinded reviewers (L.R.V. and D.N.F.N.) based on titles, authors, year, and abstracts.

The same reviewers independently and blindly screened titles and abstracts for eligibility, classifying studies as "included," "excluded" (categorized by reason: ineligible study design, population, outcome(s), or intervention), or "maybe" when eligibility could not be determined. Potentially eligible studies were then retrieved and independently assessed in full text by the same reviewers, with disagreements resolved by consensus or, if needed, arbitration by a third reviewer (L.F.D.). Inter-rater agreement was assessed using Cohen's kappa coefficient <sup>20</sup>.

#### **2.2.5 Data extraction**

Two reviewers (L.R.V. and D.N.F.N.) independently and blindly extracted data from included studies into a structured Google Sheets spreadsheet, categorized as: (1) study characteristics (author, year, journal, study groups); (2) participant characteristics (sample size, age, sex, cancer type, disease stage, clinical intervention); (3) intervention characteristics (exercise type, frequency, duration,

device, comparator group); and (4) outcome data (measurement instrument, mean values, and standard deviation at baseline and post-intervention).

A pilot test of the extraction spreadsheet was conducted to minimize errors, with discrepancies resolved by consensus or, when necessary, by a third reviewer (L.F.D.). For studies with incomplete or graphically reported data, original data were requested from corresponding authors via email or ResearchGate, with two contact attempts seven days apart, per Cochrane Handbook recommendations <sup>17</sup>.

### **2.2.6 Risk of bias and certainty of evidence**

Risk of bias for the primary outcome (QoL) was assessed using the Cochrane RoB 2 tool <sup>17</sup>, classifying studies as "low risk of bias," "some concerns," or "high risk of bias" across five domains: (1) randomization process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported result. No studies were excluded based on this assessment. The certainty of evidence for the QoL outcome was evaluated using GRADE <sup>13</sup>.

### **2.2.7 Data synthesis**

Meta-analyses, along with sensitivity and subgroup analyses accounting for risk of bias and exercise protocol characteristics, were initially planned. However, due to substantial clinical and methodological heterogeneity among included studies, particularly regarding participant characteristics, intervention protocols, devices, treatment duration, follow-up period, and QoL assessment instruments, a narrative synthesis was performed instead (Table 2).

This approach followed Cochrane Handbook recommendations <sup>17</sup> (Chapter 10), which indicate quantitative pooling only when sufficient similarity exists among participants, interventions, comparators, and outcomes; given the lack of methodological uniformity across studies, narrative synthesis was deemed the most appropriate approach.

## 2.3 RESULTS

### 2.3.1 Study selection

A total of 2,163 records were identified through searches of the indexed databases. After manual removal of 411 duplicates, 1,752 studies remained for title and abstract screening. Of these, 1,733 were excluded for failing to meet the eligibility criteria defined by the PICOS framework. Of the 19 potentially eligible studies, 11 were excluded for not meeting the inclusion criteria: 10 for methodological reasons, such as inappropriate study design or ineligible intervention, and one because it corresponded to a study protocol (Table S7, Supplementary Material). Ultimately, 8 studies <sup>2, 3, 4, 6, 7, 9, 10, 11</sup> were assessed in full text and included in the systematic review.

A total of 2,163 records were identified, and after removing 411 duplicates, 1,752 studies underwent title and abstract screening; 1,733 were excluded per PICOS criteria. Of 19 potentially eligible studies, 11 were excluded (10 for methodological reasons; 1 was a study protocol) (Table S7, Supplementary Material), leaving 8 studies <sup>2, 3, 4, 6, 7, 9, 10, 11</sup> included in the review. Authors of two studies were contacted (Table S8, Supplementary Material): no response was received from the authors Şahan & Gökçe (2023) <sup>6</sup>, but the study was included based on published data; Massonet et al. (2022) <sup>16</sup> responded but could not provide the full manuscript (only the protocol had been published), so this record was excluded as unretrievable.

The gray literature search yielded 162 records; 120 from ClinicalTrials.gov were screened via Rayyan (112 excluded), and the remaining 42 were screened using individual tables (Table S9, Supplementary Material). Combined with 8 retained records, 50 records were assessed and all excluded, owing to ineligible study design (n=22), population (n=11), intervention (n=15), or duplication (n=2); as all corresponded to study protocols, none were included (Figure 1).

Cohen's kappa for inter-rater agreement during screening was  $\kappa = 0.36$  ("fair" agreement <sup>21</sup>; Table S10, Supplementary Material), despite high observed agreement ( $P_o = 97.35\%$ ) versus high chance-expected agreement ( $P_e = 95.89\%$ ). This likely

reflects the "kappa paradox" <sup>22</sup>, a known effect in screening processes with a strong predominance of exclusions (1,896 of 2,163 records classified as "exclude"), which artificially inflates chance agreement and lowers kappa.

### 2.3.2 Study characteristics

The eight included studies were published between 2014 and 2023, all in English, representing international output from Brazil <sup>2</sup>, Turkey <sup>6</sup>, Taiwan <sup>3, 11</sup>, the United States <sup>7</sup>, the United Kingdom <sup>10</sup>, Sweden <sup>9</sup>, and China <sup>4</sup>. All employed a prospective randomized design: six studies <sup>2, 3, 4, 7, 9, 11</sup> used two-group designs (intervention vs. control), while two <sup>6, 10</sup> used three-group designs (comparing devices or including healthy/conventional control groups). Interventions targeted mouth-opening recovery via mechanical devices and swallowing rehabilitation via muscle-strengthening exercises, assessed through clinical indicators (MIO <sup>6, 10</sup>; OPSE <sup>7</sup>; FEES <sup>2, 9</sup>) and self-reported PROMs <sup>3, 4, 11</sup>.

#### 2.3.2.1 Participant characteristics

The eight included studies comprised 430 participants total (individual samples: 23 to 76). Most studies showed a predominance of male participants, with mean age ranging from 51 to 63 years (unreported in one study). Intervention and control groups were generally comparable in size, except in two studies <sup>6, 10</sup> with unequal groups (Table 1).

Clinically, studies predominantly enrolled patients with oral cavity cancer (OCC), with others evaluating oral and oropharyngeal cancer or specifically tongue cancer. Surgery (alone or combined with adjuvant radiotherapy/radiochemotherapy) was the most common oncological treatment, followed by exclusive chemoradiotherapy. Five studies evaluated interventions in patients with trismus, and three in patients with dysphagia following HNC treatment. Detailed demographic, clinical, and treatment characteristics are presented in Table 1.

### 2.3.2.2 Interventions and outcomes characteristics

Interventions were grouped into two categories: mandibular range-of-motion (MROM) exercises for trismus and swallowing therapy for functional rehabilitation (Table S11, Supplementary Material). Swallowing therapy was most frequently employed, encompassing oropharyngeal muscle exercises, tongue-strengthening exercises, head-lift exercises, speech therapy, and structured education programs, often implemented multimodally with dietary modification, compensatory maneuvers, and professional monitoring. Trismus management predominantly used MROM exercises, frequently with devices such as TheraBite®, EZBite®, and wooden tongue depressors, aiming for progressive improvement in mouth opening (Table S12, Supplementary Material).

Considerable heterogeneity was observed across protocols regarding duration, session frequency, repetitions, execution time, rest intervals, and positioning. Program duration ranged from 10 days to six months, with regimens from two daily sessions to multiple daily sessions, delivered in-person, remotely, or via home-based protocols (Table 2; and Table S13, Supplementary Material).

QoL was the primary outcome, assessed using varied instruments: HNC-specific questionnaires (EORTC QLQ-C30, QLQ-H&N35), a generic measure (EQ-5D-3L), dysphagia-specific instruments (MDADI, DHI), a trismus-specific measure (GTQ), and a swallowing-related QoL instrument (UW-QOLv4), reflecting diverse approaches to capturing functional, physical, and psychosocial impact (Table 2; and Table S14, Supplementary Material).

### 2.3.3 Risk of bias and certainty of evidence

Six of the eight included studies <sup>2, 3, 6, 7, 10, 11</sup> evaluated global QoL and were assessed using RoB 2: two were classified as low risk and four as high risk of bias. High-risk classifications were mainly attributable to concerns regarding randomization (Domain 1; item 1.3) <sup>1</sup>, outcome measurement due to insufficient assessor blinding

information (Domain 4; item 4.3) <sup>6</sup>, and potential selective reporting given multiple eligible outcome measures (Domain 5; item 5.2) <sup>3, 5</sup>. Deviations from intended interventions (Domain 2) and missing outcome data (Domain 3) showed low risk in most studies (Figure 2).

The certainty of evidence for global QoL, assessed via GRADE <sup>13</sup> based on the six contributing studies, was rated very low. Downgrading reflected: (1) serious risk of bias (four high-risk trials, mainly due to allocation, lack of blinding, and multiple outcome measures); (2) very serious inconsistency from substantial clinical and methodological heterogeneity (protocols and instruments); and (3) very serious imprecision due to limited sample size, with effect estimates spanning clinically important benefit, little or no effect, and potential harm. Indirectness and publication bias were not downgraded, as studies directly addressed the PICO question and no consistent evidence of publication bias was found. Confidence in the effect estimate thus remains limited, so larger sample sizes and well-designed studies are likely to influence current conclusions (Figure 3).

#### **2.3.4 Participant and intervention timing characteristics**

Mean ages across the eight studies ranged from 51 to 63 years, predominantly middle-aged and elderly individuals <sup>2, 3, 4, 6, 7, 9, 10, 11</sup>; one study <sup>11</sup> reported only comparable mean ages across groups without disaggregated values. Advanced-stage tumors (III-IV) predominated, though some studies included early-stage disease (I-II) <sup>6, 10</sup>; Şahan et al. (2023) <sup>6</sup> reported only that groups had comparable staging without detailed distribution. Considerable heterogeneity was observed in the treatment phase at intervention onset (Table S15, Supplementary Material).

Regarding timing, four trials initiated exercises during the post-radiotherapy or post-chemoradiotherapy period (3-4 weeks to 36 months post-treatment) <sup>3, 6, 7, 9</sup>. The remaining four enrolled surgical patients, with interventions starting perioperatively (1-3 weeks before radiotherapy through 3 weeks post-surgery) <sup>4</sup>, in the early postoperative period (postoperative day 6 after reconstructive surgery) <sup>11</sup>, in the late

postoperative period (median 7 months post-surgery) <sup>2</sup>, or following trismus onset postsurgically <sup>10</sup>.

Adherence was reported variably: two studies reported high adherence (around 89% or described as high), attributed to motivation, goal setting, and professional monitoring <sup>6, 9</sup>, while others reported reduced adherence linked to mucositis, pain, anxiety, lack of defined goals, and depressive symptoms <sup>7, 10</sup>. One study used app-based and specialist nurse supervision to promote compliance <sup>4</sup>, while another did not formally assess adherence, noting this as a limitation <sup>3</sup>.

### **2.3.5 Effects of Exercise on QoL**

To evaluate the effects of exercise interventions on QoL, studies were organized by domain: (1) overall QoL, (2) swallowing function, (3) mouth opening, (4) physical, (5) social, (6) emotional, and (7) functional well-being.

#### **2.3.5.1 Overall QoL**

Eight between-group comparisons showed substantial heterogeneity in instruments (DHI, FOIS, MDADI, UW-QOLv4, EORTC QLQ-C30/H&N35, EQ-5D-3L), protocols, and effect magnitude. Four comparisons in three studies <sup>3, 4, 9</sup> favored the intervention group and two <sup>2, 10</sup> favored the control group; notably, Balbinot et al. (2022) <sup>2</sup> used the DHI, where lower scores indicate benefit, so the lower intervention-group score reflected clinical improvement. Only this study and Zhang et al. (2022) <sup>4</sup> reached statistical significance, indicating inconsistent benefits overall. Remaining studies showed only within-group or domain-specific improvements, with TheraBite® showing no superiority over wooden tongue depressors, suggesting functional gains don't necessarily translate to overall QoL perception, likely due to heterogeneity, small samples, and differing scoring directions (Table 3).

### 2.3.5.2 Swallowing

Three studies (eight comparisons) used EORTC QLQ-H&N35 and UW-QOLv4. Two studies showed higher control-group scores for swallowing, sticky saliva, and dry mouth domains, indicating rehabilitative benefit in the intervention group, once perceived salivary insufficiency, altered saliva viscosity, and effort required to swallow foods were more pronounced in the control group. Zhang et al. (2022) <sup>4</sup> similarly favored intervention for saliva-related outcomes, with salivary function variables trending favorably overall. Zhang et al. (2022) <sup>4</sup> also showed significant improvement in DHI, FOIS, and dysphagia severity; Chen et al. (2018) <sup>3</sup> showed significant swallowing function improvement, but without overall QoL change; Petersson et al. (2023) <sup>9</sup> showed only transient improvement; Şahan et al. (2022) <sup>6</sup> showed no significant differences. Overall, exercise programs may aid functional swallowing recovery without consistently changing overall QoL.

### 2.3.5.3 Mouth Opening

Seven comparisons evaluated mouth opening using the EORTC QLQ-C30, QLQ-H&N35, and GTQ, showing no relevant differences in two comparisons. GTQ trismus variables showed lower (better) scores in the intervention group, as less jaw spasm, limitation, and mucosal stiffness, suggesting favorable jaw function effects, though magnitude varied. Li et al. (2019) <sup>11</sup> showed significant improvement in maximum mouth opening and reduced trismus symptoms across all GTQ domains; TheraBite® studies showed no consistent superiority over wooden depressors, suggesting protocol-dependent responses influenced by intensity, timing, and adherence (Table 6).

### 2.3.5.4 Physical, social, emotional, and functional well-being

Considerable heterogeneity was observed across instruments, scales, and effect sizes. Four studies <sup>3, 4, 6, 9</sup> evaluated physical well-being: only one comparison <sup>4</sup>

showed significantly higher mean scores for intervention group (UW-QOLv4 activity domain,  $p=0.026$ ); others showed no differences, suggesting limited effect on overall physical well-being perception, with benefits confined to discrete functions like swallowing and mouth opening (Table S16, Supplementary Material).

Five studies <sup>4, 6, 7, 9, 11</sup> evaluated outcomes related to social well-being, yielding seven comparisons: four <sup>6, 7, 9, 11</sup> numerically favored control group, three <sup>4, 6, 9</sup> favored intervention. Given inverted scoring on EORTC "social contact" <sup>6</sup> and GTQ "social activity" <sup>11</sup>, higher control scores actually indicated less intervention-group discomfort, as well as less embarrassment during social interactions and fewer restrictions on participation in leisure activities. Significant differences ( $p<0.001$ ) occurred only for recreation and social activity domains in two studies <sup>4, 11</sup>, suggesting personalized protocols or trismus-specific devices may improve social participation and functional gains related to eating and mouth opening may positively influence patients' social participation, though evidence on social dimension of QoL remains complex (Table S17, Supplementary Material).

Nine comparisons were conducted for emotional well-being across four studies <sup>3, 4, 6, 9</sup>: six favored intervention, three favored control; positive effects concentrated in MDADI emotional domain and UW-QOLv4 appearance, mood and anxiety items, suggesting a favorable trend for the interventions with respect to the emotional dimension of QoL, although instrument heterogeneity limits the consistency of this evidence. Significant benefit was seen only in Chen et al. <sup>3</sup> (structured swallowing program), showing improved MDADI emotional domain and reduced depressive symptoms, suggesting functional gains may reduce psychosocial burden, though inconsistently across instruments (Table S18, Supplementary Material).

Three studies <sup>3, 6, 9</sup> evaluated functional well-being, yielding six comparisons covered practical/logistical eating aspects (MDADI), social/occupational functioning (EORTC Function), and cognitive functioning (EORTC Cognitive). Most comparisons favored control with no significant between-group differences, though structured programs showed within-group functional improvement in swallowing capacity and specific MDADI domains at follow-up, however this benefits were not consistently sustained long-term or confirmed between groups, suggesting dependence on

training intensity, adherence, and follow-up duration (Table S19, Supplementary Material).

### 2.3.6 Weighting by sample size and risk of bias

All included studies had relatively small sample sizes, and several were rated as high risk of bias, reducing the precision of effect estimates and limiting generalizability. Although studies demonstrating significant effects<sup>2, 4, 9, 11</sup> included only 15, 25, 34, and 37 participants, respectively, these results warrant cautious interpretation, as small samples increase the likelihood of effect overestimation and reduce statistical power. A detailed comparison of exercise effects on QoL is presented in Table 5.

## 2.4 DISCUSSION

This systematic review evaluated the effects of MROM exercises and swallowing therapy on QoL in patients with trismus and/or dysphagia from HNC treatment. Although interventions showed benefits in specific domains, such as swallowing, mouth opening, and emotional well-being, no consistent evidence of improvement in overall QoL versus usual care. Furthermore, the certainty of the evidence was rated as very low due to the high risk of bias, substantial heterogeneity among the studies, and imprecision of the estimates.

In light of these findings, the lack of consistent improvement in global QoL is likely attributable to the multidimensional nature of this outcome<sup>6, 7</sup>. Although exercise interventions promote recovery of specific functions, such as swallowing and mandibular mobility, overall health perception is also shaped by a range of persistent treatment-related sequelae, including xerostomia, mucositis, chronic pain, alterations in taste and smell, fatigue, tissue fibrosis, communication difficulties, and aesthetic limitations<sup>4, 6, 7</sup>. These factors directly affect patients' autonomy, social participation, and psychological well-being, potentially attenuating the impact of

functional gains on global QoL <sup>2, 3, 7, 11</sup>. Thus, isolated improvement in a single physiological function is not always sufficient to alter the overall health-related perception associated with HNC <sup>7, 9</sup>.

Among the interventions evaluated, swallowing therapy programs showed favorable eating-related functional outcomes <sup>2, 4</sup>, including reduced dysphagia severity, improved oral intake, and reduced emotional distress <sup>2, 3, 4</sup>. From a clinical standpoint, these findings are clinically meaningful, as recovery of swallowing function reduces aspiration risk, facilitates earlier discontinuation of alternative feeding methods, and promotes greater functional independence <sup>2, 4</sup>. Consequently, potentially improving eating-related confidence and social meal participation <sup>4, 7, 9</sup>. Nevertheless, these benefits remained domain-specific rather than reflected in overall QoL <sup>2, 3, 4</sup>.

Similarly, MROM exercises also produced significant functional benefits, improving mouth opening and reducing trismus symptoms <sup>6, 10</sup>, with protocols incorporating active mandibular opening and lateral excursion movements, and including devices as TheraBite® and EZBite®, supporting mandibular mobility recovery and downstream benefits for eating, hygiene, and communication <sup>6, 10</sup>. These effects are likely related to the prevention of muscle fibrosis and scar tissue maturation resulting from cancer treatment, reinforcing the role of these interventions in promoting progressive mouth opening and, consequently, mitigating trismus <sup>6, 10</sup>. However, as observed with swallowing therapy, these functional gains were insufficient to produce consistent improvement in overall QoL, underscoring the multifactorial nature of this outcome <sup>10, 11</sup>.

Beyond these functional benefits, effects varied across QoL domains <sup>2, 3</sup>: emotional outcomes showed the most consistent benefit, especially when combined with education and multidisciplinary support, reducing psychological distress and increasing self-confidence <sup>2, 3</sup>. Physical, social, and functional domains remained inconsistent, suggesting persistent sequelae (fibrosis, neuropathies, chronic pain, speech impairment) continue to influence QoL regardless of functional gains <sup>7, 9</sup>.

Considerable variability was observed with respect to participant characteristics (as tumor location and therapeutic modality), protocols, equipment,

session frequency, duration, adherence, timing, and follow-up <sup>2, 3, 4, 7</sup>. In addition, differing instruments were employed to assess QoL, each targeting distinct domains, which hindered cross-study comparison and likely explains the observed heterogeneity and inconsistency of the findings (Tables S18 and S1). These findings must be interpreted alongside methodological limitations <sup>14</sup>: small samples and risk-of-bias concerns (randomization, allocation concealment, blinding of outcome, selective outcome reporting) resulted in very low GRADE certainty <sup>13</sup>, limiting confidence in pooled estimates <sup>2, 6, 9</sup>. Future research may substantially alter current conclusions <sup>2, 6, 9</sup>.

Clinically, while evidence does not yet support a universal exercise protocol, functional benefits support individualized rehabilitation tailored to clinical limitations, cancer treatment characteristics, and patient needs <sup>6, 9, 10</sup>. To strengthen the evidence base, future RCTs should prioritize methodological rigor (adequate randomization, blinding of outcome assessors, sufficient powered sample sizes, standardized protocols and QoL instruments) <sup>4, 10, 13</sup>. Besides, there is also a need for studies stratified by treatment modality, tumor stage, and severity of trismus and dysphagia, with long-term follow-up combining objective functional measures and patient-reported outcomes; such studies would help identify which interventions yield the most consistent and durable clinical benefits <sup>3, 4, 7</sup>.

## 2.5 CONCLUSION

In summary, MROM exercises and swallowing therapy provide functional benefits for HNC patients with trismus and/or dysphagia, as particularly improved mouth opening, swallowing function, and emotional/functional QoL domains, however these benefits did not consistently translate into overall QoL improvement versus usual care, reflecting QoL's multifactorial nature and study heterogeneity. Given the very low certainty of evidence and high risk of bias, rigorous RCTs with adequate sample sizes, standardized protocols, and uniform QoL instruments are needed to generate robust evidence for clinical practice and individualized rehabilitation strategies.

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### **3 CONCLUSÃO**

De modo geral, esta revisão sistemática demonstrou que os exercícios de amplitude de movimento mandibular e a terapia de deglutição promovem benefícios em desfechos funcionais específicos de pacientes com trismo e/ou disfagia decorrentes do tratamento do câncer de cabeça e pescoço, especialmente relacionados à abertura bucal, à deglutição e ao bem-estar emocional. Entretanto, esses benefícios não se refletiram de forma consistente na qualidade de vida global nem nos domínios de bem-estar físico, social e funcional. A ampla heterogeneidade clínica e metodológica entre os estudos, associada ao pequeno tamanho amostral e ao risco de viés, resultou em evidência de muito baixa certeza, limitando a confiança nos achados. Assim, futuros ensaios clínicos randomizados, com maior rigor metodológico, amostras mais representativas, protocolos padronizados e instrumentos uniformes de avaliação da qualidade de vida, são necessários para produzir evidências mais robustas e orientar a prática clínica na reabilitação desses pacientes.

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## APÊNDICE

### Figures:

Figure 1. Flow diagram of study selection according to PRISMA guidelines.

Figure 2. Risk-of-bias assessment of individual included studies.

Figure 3. GRADE assessment of the certainty of evidence across the included studies.

### Legends:

Figure 1. \*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/register). \*\*If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. This work is licensed under CC BY 4.0. To view a copy of this license, visit <https://creativecommons.org/licenses/by/4.0/> Note: Adapted from the PRISMA 2020 statement.<sup>15</sup>

Figure 2. Note: Prepared by the authors (2026).

Figure 3. CI: confidence interval Explanations: a. Some studies raised concerns regarding the randomization process (Domain 1; Item 1.3)<sup>1</sup>, the blinding of outcome assessors (Domain 4; Item 4.3)<sup>6</sup>, and the selection of the reported results due to the presence of multiple eligible outcome measurements (Domain 5; Item 5.2).<sup>3, 5</sup> b. High and statistically significant heterogeneity ( $I^2 = 94.4\%$ ;  $p < 0.0001$ ). Most 95% confidence intervals crossed the line of no effect, with only one study entirely favoring the intervention. Point estimates varied substantially across studies. The inconsistency was likely due to variability in exercise protocols and quality-of-life assessment instruments. c. The total sample size was below the optimal information size (<400 participants; downgraded one level). In addition, the effect estimate crossed the line of no effect, indicating imprecision (downgraded one additional level).

### Tables:

Table 1. Baseline characteristics of participants in the included studies.

Table 2. Characteristics of interventions, exercise protocols, and quality-of-life assessment instruments.

Table 3. Between-group comparison of overall quality-of-life responses to the exercise interventions.

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Table 5. Between-group comparison of mouth opening responses to the exercise interventions.

### Legends:

Table 1. I, intervention; C, control; N, number; W, woman; M, man; HNC, head and neck cancer; RT, radiotherapy; CRT, chemoradiotherapy, CT, chemotherapy; SEEP, swallowing educational exercise program; PSR, personalized swallowing rehabilitation; HLE, Head-lift exercise.

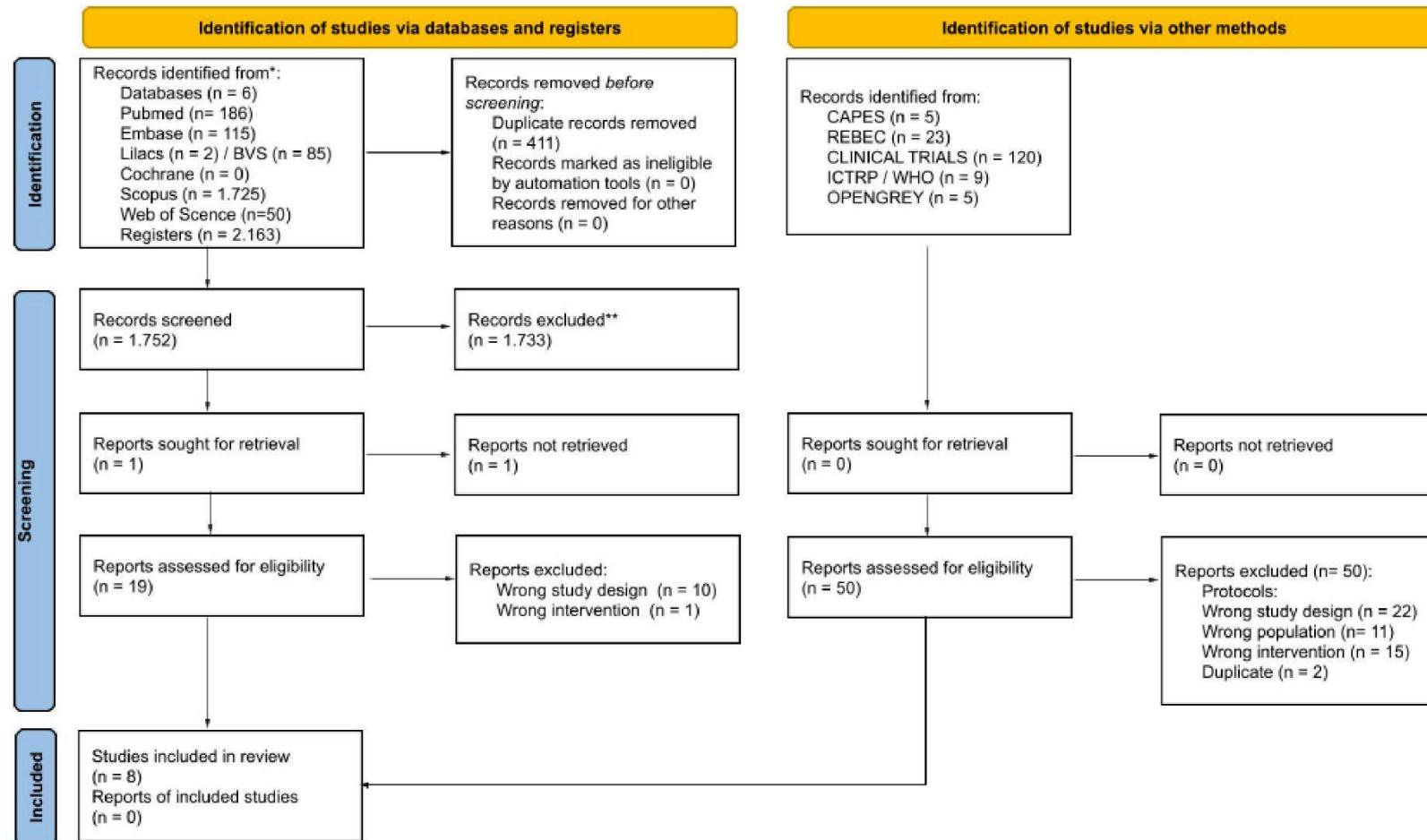
Table 2. ROM, Range-of-motion exercise; SEEP, Swallowing exercise education program; NR, Not reported; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (Core 30); EORTC H&N35, Head and Neck (Core 35); MDADI, MD Anderson Dysphagia Inventory; DHI, Dysphagia Handicap Index; GTQ, Gothenburg Trismus Questionnaire; UWQOLv4, University of Washington Quality of Life (version 4); HNCL, Head and Neck Cancer Inventory; EQ-5D-3L (EuroQol): European Quality of Life – 5 Dimensions – 3 Levels.

Table 3. n, number; I, intervention; C, control; M, mean; SD, standard deviation; \*\*EORTC QLQ-C30, \*MDADI, "DHI, "FOIS.

Table 4. n, number; I, intervention; C, control; M, mean; SD, standard deviation; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (Core 30); UWQOLv4, University of Washington Quality of Life (version 4).

Table 5. n, number; I, intervention; C, control; M, mean; SD, standard deviation; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (Core 30); GTQ, Gothenburg Trismus Questionnaire.

Figure 1. Flow diagram of study selection according to PRISMA guidelines.



\*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

\*\*If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

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Note: Adapted from the PRISMA 2020 statement.<sup>15</sup>

**Figure 2. Risk-of-bias assessment of individual included studies.**

| Intention-to-treat | Unique ID | Study ID                | Experimental             | Comparator | Outcome                | Weight | D1 | D2 | D3 | D4 | D5 | Overall |    |                                            |  |  |
|--------------------|-----------|-------------------------|--------------------------|------------|------------------------|--------|----|----|----|----|----|---------|----|--------------------------------------------|--|--|
|                    | 1         | Şahan, M.H., Gökçe      | jaw range of motion exer | usual care | global quality of life | 1      | ⊖  | !  | +  | +  | +  | ⊖       | +  | Low risk                                   |  |  |
|                    | 2         | Balbinot, J. et al. (20 | jaw range of motion exer | usual care | global quality of life | 1      | +  | +  | +  | +  | +  | +       | !  | Some concerns                              |  |  |
|                    | 3         | Chen, S-C. et al. (20   | jaw range of motion exer | usual care | global quality of life | 1      | +  | +  | +  | !  | ⊖  | ⊖       | ⊖  | High risk                                  |  |  |
|                    | 4         | Lee, R. et al. (2018)   | jaw range of motion exer | usual care | global quality of life | 1      | +  | +  | +  | +  | +  | +       |    |                                            |  |  |
|                    | 5         | Petersson, K. et al. (  | jaw range of motion exer | usual care | global quality of life | 1      | +  | +  | +  | +  | ⊖  | ⊖       | D1 | Randomisation process                      |  |  |
|                    | 6         | Zhang, J. et al. (202   | jaw range of motion exer | usual care | global quality of life | 1      | +  | +  | +  | ⊖  | +  | ⊖       | D2 | Deviations from the intended interventions |  |  |
|                    |           |                         |                          |            |                        |        |    |    |    |    |    |         | D3 | Missing outcome data                       |  |  |
|                    |           |                         |                          |            |                        |        |    |    |    |    |    |         | D4 | Measurement of the outcome                 |  |  |
|                    |           |                         |                          |            |                        |        |    |    |    |    |    |         | D5 | Selection of the reported result           |  |  |
|                    |           |                         |                          |            |                        |        |    |    |    |    |    |         |    |                                            |  |  |
|                    |           |                         |                          |            |                        |        |    |    |    |    |    |         |    |                                            |  |  |
|                    |           |                         |                          |            |                        |        |    |    |    |    |    |         |    |                                            |  |  |
|                    |           |                         |                          |            |                        |        |    |    |    |    |    |         |    |                                            |  |  |

Note: Prepared by the authors (2026).

### Figure 3. GRADE assessment of the certainty of evidence across the included studies.

**Author(s):** Şahan & Gökçe, 2023<sup>1</sup>; Balbinot et. al., 2022<sup>2</sup>; Chen et. al., 2018<sup>3</sup>; Lee et. al., 2018<sup>4</sup>; Petersson et. al, 2023<sup>5</sup>; Zhang et al., 2022<sup>6</sup>

**Question:** Mandibular range-of-motion exercises and swallowing therapy compared to routine care and standard exercises for patients with trismus and/or dysphagia following head and neck cancer treatment

**Setting:** Rehabilitation of patients with head and neck cancer

**Bibliography:** BRASIL. Ministério da Saúde. Secretaria de Ciência, Tecnologia, Inovação e Insumos Estratégicos em Saúde. Departamento de Gestão e Incorporação de Tecnologias em Saúde. Diretrizes metodológicas: elaboração de revisão sistemática e meta-análise de ensaios clínicos randomizados. Brasília: Ministério da Saúde, 2021. 93 p. HIGGINS, Julian P. T. et al. (ed.). Ferramenta de risco de viés Cochrane revisada para estudos randomizados (RoB 2). [Tradução para o português]. [S. l.]: Cochrane, 2019. 72 p. REIS, Alessandra; LOGUERCIO, Alessandro. Capítulo 5: Análise do risco de viés em Ensaios Clínicos Randomizados (ECR) com a Ferramenta da Colaboração Cochrane RoB 2.0. In: RISCO de viés em revisões sistemáticas: guia prático (COBE/UFSC). Florianópolis: UFSC, 2024.

| Certainty assessment |              |              |               |              |             |                      | № of patients                                               |                                     | Effect            |                   | Certainty | Importance |
|----------------------|--------------|--------------|---------------|--------------|-------------|----------------------|-------------------------------------------------------------|-------------------------------------|-------------------|-------------------|-----------|------------|
| № of studies         | Study design | Risk of bias | Inconsistency | Indirectness | Imprecision | Other considerations | mandibular range-of-motion exercises and swallowing therapy | routine care and standard exercises | Relative (95% CI) | Absolute (95% CI) |           |            |

Global quality of life (assessed with: Quality of life assessments)

|   |                   |                      |                           |             |                           |      |                 |                 |                                    |                                        |                                   |          |
|---|-------------------|----------------------|---------------------------|-------------|---------------------------|------|-----------------|-----------------|------------------------------------|----------------------------------------|-----------------------------------|----------|
| 6 | randomised trials | serious <sup>a</sup> | very serious <sup>b</sup> | not serious | very serious <sup>c</sup> | none | 169/400 (42.3%) | 180/400 (45.0%) | <b>SMD 0.30</b><br>(-3.86 to 4.47) | <b>-- per 1.000</b><br>(from -- to --) | ⊕○○○<br>Very low <sup>a,b,c</sup> | CRITICAL |
|---|-------------------|----------------------|---------------------------|-------------|---------------------------|------|-----------------|-----------------|------------------------------------|----------------------------------------|-----------------------------------|----------|

**CI:** confidence interval

#### Explanations

a. Some studies raised concerns regarding the randomization process (Domain 1; Item 1.3)<sup>1</sup>, the blinding of outcome assessors (Domain 4; Item 4.3)<sup>6</sup>, and the selection of the reported results due to the presence of multiple eligible outcome measurements (Domain 5; Item 5.2).<sup>3,5</sup>

b. High and statistically significant heterogeneity ( $I^2 = 94.4\%$ ;  $p < 0.0001$ ). Most 95% confidence intervals crossed the line of no effect, with only one study entirely favoring the intervention. Point estimates varied substantially across studies. The inconsistency was likely due to variability in exercise protocols and quality-of-life assessment instruments.

c. The total sample size was below the optimal information size (<400 participants; downgraded one level). In addition, the effect estimate crossed the line of no effect, indicating imprecision (downgraded one additional level).

**Table 1. Baseline characteristics of participants in the included studies.**

| Authors (Year)   | Groups                         | Sample Size |    |    | N (groups) |    | Age          |              | Type of Cancer           | Cancer stage                                    | Therapy       |
|------------------|--------------------------------|-------------|----|----|------------|----|--------------|--------------|--------------------------|-------------------------------------------------|---------------|
|                  |                                | N           | W  | M  | I          | C  | I            | C            |                          |                                                 |               |
| Şahan (2023)     | Therabite                      | 50          | 22 | 28 | 20         | 5  | 56           | 56           | Oral cavity cancer (OCC) | Primary HNC                                     | surgery + RT  |
| Şahan (2023)     | Wooden tongue spatula          | 50          | 22 | 28 | 20         | 5  | 56           | 56           | OCC                      | Primary HNC                                     | surgery + RT  |
| Chen (2018)      | SEEP                           | 76          | 3  | 73 | 38         | 38 | 53.03 ± 8.67 | 51.13 ± 7.99 | OCC                      | I (5), II (7), III (13), IV (51)                | surgery + CRT |
| Li (2019)        | EZBite                         | 60          | 19 | 41 | 20         | 10 | 56.4 (37–75) | 55.8 (30–72) | OCC                      | I (7), II (8), III (16), IV (17)                | surgery + CRT |
| Li (2019)        | Wooden tongue spatula          | 60          | 19 | 41 | 20         | 10 | 54.2 (30–67) | 55.8 (30–72) | OCC                      | I (7), II (8), III (16), IV (17)                | surgery + CRT |
| Zhang (2022)     | PSR                            | 68          | 23 | 45 | 34         | 34 | 51.00 ±13.12 | 54.32±12.04  | OCC                      | I (3), II (21), III (18), IV (19), Unclear (7)  | surgery       |
| Balbinot (2022)  | Speech Therapy                 | 30          | 5  | 25 | 15         | 15 | 60.3 ± 6.7   | 59.4 ± 10.1  | Tongue cancer            | II (7), III (13), IV (10)                       | surgery + CT  |
| Lazarus (2014)   | Tongue strengthening exercises | 23          | 1  | 22 | 12         | 11 | 62.3 +- 8.06 | 61.7 +- 7.27 | Oral and Oropharyngeal   | AJCC II (1), III (3), IVA (16), IVB (3)         | CRT           |
| Lee (2018)       | Therabite                      | 71          | 22 | 49 | 37         | 34 | NI           | NI           | Oral and Oropharyngeal   | T1/2 N+ M0 (30), T3/4 N0 M0 (9) T3/4 N+ M0 (32) | surgery + CRT |
| Petersson (2023) | HLE                            | 52          | 13 | 39 | 25         | 27 | 63 ± 8.4     | 63 ± 6.7     | Oral and Oropharyngeal   | I (3), II (6), III (3), IV (40)                 | CRT           |

Legend: I, intervention; C, control; N, number; W, woman; M, man; HNC, head and neck cancer; RT, radiotherapy; CRT, chemoradiotherapy, CT, chemotherapy; SEEP, swallowing educational exercise program; PSR, personalized swallowing rehabilitation; HLE, Head-lift exercise.

**Table 2. Characteristics of interventions, exercise protocols, and quality-of-life assessment instruments.**

| Authors (Year)              | Intervention       |                       | Exercise Protocol |                         |                          |                  |                  |                    | QOL Assessment                  |
|-----------------------------|--------------------|-----------------------|-------------------|-------------------------|--------------------------|------------------|------------------|--------------------|---------------------------------|
|                             | Type               | Device or Program     | Position          | Sessions                | Repetitions              | Duration         | Interval or Rest | Daily Applications |                                 |
| Şahan, M.H. et al. (2023) a | ROM                | Therabite             | Upright           | 3-week program          | 7                        | 7s               | 7s               | 7                  | (1) EORTC QLC-C30,<br>(2) H&N35 |
| Şahan, M.H. et al. (2023) b | ROM                | Wooden tongue spatula | Upright           | 3-week program          | 5                        | 30s              | 30s              | 5                  | (1) EORTC QLC-C30,<br>(2) H&N35 |
| Lee et al (2018)            | ROM                | Therabite             | NR                | 5 per day for 6 months  | 5                        | 30s              | 30s              | 5                  | (1) EQ-5D-3L                    |
| Li et al (2018) a           | ROM                | EZBite Device         | Upright           | 12-week program         | 5x passive and 5x active | 30s              | Yes              | 9                  | (1) GTQ                         |
| Li et al (2018) b           | ROM                | Wooden tongue spatula | Upright           | 12-week program         | 5x passive and 5x active | 30s              | Yes              | 9                  | (1) GTQ                         |
| Balbinot et al (2022)       | Swallowing Therapy | Speech therapy        | NR                | 1 per week for 1 month  | 5                        | 30 min           | NR               | 3                  | (1) DHI                         |
| Chen et al (2018)           | Swallowing Therapy | SEEP                  | NR                | 2 per week for 6 months | NR                       | 15-20 min        | NR               | 3                  | (1) MDADI                       |
| Lazarus et al (2014)        | Swallowing Therapy | Tongue strengthening  | NR                | 5 per day for 6 months  | 10                       | 2s per direction | NR               | 5                  | (1) HNCI                        |

|                        |                    |                          |                       |                                              |      |       |       |                   |                                         |
|------------------------|--------------------|--------------------------|-----------------------|----------------------------------------------|------|-------|-------|-------------------|-----------------------------------------|
| Petersson et al (2023) | Swallowing Therapy | Elevação de cabeça       | Supine                | 3 times every 8 weeks, then 1/day or 3/week. | 3    | 60s   | 60s   | 30 (consecutives) | (1) EORTC QLC-C30, (2) H&N35, (3) MDADI |
| Zhang et al (2022)     | Swallowing Therapy | Exercícios de Deglutição | Seated or semi-supine | 10 days                                      | 5-10 | 2 min | 2 min | 2                 | (1) UW-QOLv4                            |

Legend: ROM, Range-of-motion exercise; SEEP, Swallowing exercise education program; NR, Not reported; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (Core 30); EORTC H&N35, Head and Neck (Core 35); MDADI, MD Anderson Dysphagia Inventory; DHI, Dysphagia Handicap Index; GTQ, Gothenburg Trismus Questionnaire; UWQOLv4, University of Washington Quality of Life (version 4); HNCl, Head and Neck Cancer Inventory; EQ-5D-3L (EuroQol): European Quality of Life – 5 Dimensions – 3 Levels.

**Table 3. Between-group comparison of overall quality-of-life responses to the exercise interventions.**

| Studies                       | Instruments   | n_I | M_I    | SD_I   | n_C | M_C    | SD_C   | p-value |
|-------------------------------|---------------|-----|--------|--------|-----|--------|--------|---------|
| Şahan, M.H. et al. (2023)     | EORTC QLQ-C30 | 20  | 82.22  | 18.13  | 10  | 84.88  | 9.58   | 0.967   |
| Zhang, J. et al. (2022)       | UW-QOLv4      | 34  | 996.39 | 75.67  | 34  | 809.62 | 152.12 | <0.001  |
| Lee, R. et al. (2018)         | EQ-5D-3L      | 37  | 0.6935 | 0.2523 | 34  | 0.7481 | 0.1844 | 0.39    |
| Petersson, K. et al. (2023)*  | EORTC QLQ-C30 | 25  | 82.5   | 20.4   | 27  | 78.5   | 19.2   | > 0.05  |
| Balbinot, J. et al. (2022)''  | DHI           | 15  | 21.6   | 3.8    | 15  | 61.8   | 4.8    | < 0.001 |
| Balbinot, J. et al. (2022)''' | FOIS          | 15  | 6.4    | 0.1    | 15  | 4.1    | 0.3    | < 0.001 |
| Chen, S-C. et al. (2018)*     | MDADI         | 38  | 3.66   | 0.82   | 38  | 3.50   | 0.86   | 0.619   |
| Petersson, K. et al. (2023)** | MDADI         | 25  | 83.2   | 24.3   | 27  | 81.7   | 22.8   | > 0.05  |

Legend: n, number; I, intervention; C, control; M, mean; SD, standard deviation; \*\*EORTC QLQ-C30, \*MDADI, ''DHI, '''FOIS.

**Table 4. Between-group comparison of swallowing responses to the exercise interventions.**

| Studies                     | Variable      | n_I | M_I   | SD_I  | n_C | M_C   | SD_C  | p-value |
|-----------------------------|---------------|-----|-------|-------|-----|-------|-------|---------|
| Şahan, M.H. et al. (2023)   | Dry Mouth     | 20  | 46.66 | 17.6  | 10  | 50    | 17.09 | 0.541   |
| Şahan, M.H. et al. (2023)   | Sticky Saliva | 20  | 65    | 31.48 | 10  | 73.33 | 29.81 | 0.403   |
| Şahan, M.H. et al. (2023)   | Swallowing    | 20  | 57.91 | 38.84 | 5   | 73.33 | 33.28 | 0.171   |
| Petersson, K. et al. (2023) | Dry Mouth     | 25  | 47.4  | 33.9  | 27  | 51.4  | 38    | > 0.05  |
| Petersson, K. et al. (2023) | Sticky Saliva | 25  | 40.4  | 39.4  | 27  | 47.2  | 28.7  | > 0.05  |
| Petersson, K. et al. (2023) | Swallowing    | 25  | 23.5  | 29.6  | 27  | 23.3  | 15.3  | > 0.05  |
| Zhang, J. et al. (2022)     | Swallowing    | 34  | 83.33 | 15.34 | 34  | 57.69 | 26.28 | 0.001   |
| Zhang, J. et al. (2022)     | Saliva        | 34  | 93.33 | 12.83 | 34  | 78.85 | 25.35 | 0.031   |

Legend: n, number; I, intervention; C, control; M, mean; SD, standard deviation; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (Core 30); UWQOLv4, University of Washington Quality of Life (version 4).

**Table 5. Between-group comparison of mouth opening responses to the exercise interventions.**

| Studies                       | Variable                       | n_I | M_I   | SD_I  | n_C | M_C   | SD_C  | p-value |
|-------------------------------|--------------------------------|-----|-------|-------|-----|-------|-------|---------|
| Şahan, M.H., Gökçe, B. (2023) | Fatigue                        | 20  | 30    | 21.05 | 10  | 27.22 | 11.66 | 0.736   |
| Şahan, M.H., Gökçe, B. (2023) | Mouth opening                  | 20  | 88.33 | 19.57 | 10  | 90    | 15.67 | 0.919   |
| Petersson, K. et al. (2023)   | Mouth opening                  | 25  | 15.8  | 28    | 27  | 13.9  | 25.9  | > 0.05  |
| Li Y-H. et al. (2019)         | Jaw spasm                      | 20  | 33.6  | 6.8   | 10  | 64.7  | 6.8   | <0.001  |
| Li Y-H. et al. (2019)         | Clenching                      | 20  | 22.5  | 5.8   | 10  | 59.5  | 9.3   | <0.001  |
| Li Y-H. et al. (2019)         | Rigid texture of buccal mucosa | 20  | 30.6  | 7.9   | 10  | 63.5  | 9     | <0.001  |
| Li Y-H. et al. (2019)         | Jaw limitation                 | 20  | 28.2  | 9.5   | 10  | 63.9  | 9     | <0.001  |

Legend: n, number; I, intervention; C, control; M, mean; SD, standard deviation; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (Core 30); GTQ, Gothenburg Trismus Questionnaire.

## **MATERIAL SUPLEMENTAR**

Disponível no link abaixo:

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