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Corresponding author:

Adriana Assunta De Stefano

aadestefano@hotmail.com

Author Affiliation:

Sapienza University of Rome.

"Can clear aligners release microplastics that impact the patient's overall health? a systematic review"

De Stefano, AA; Horodynski, M; Galluccio, G.

ADMINISTRATIVE INFORMATION

Support - The authors received no financial support for the research, authorship and/or publication of this article.

Review Stage at time of this submission - This systematic review was originally developed as part of a broader research initiative aimed at exploring the environmental and health implications of microplastic release in orthodontic treatment, particularly with clear aligners. At the time of its inception, the study was conceived primarily as an exploratory investigation within our research group, without an immediate intention to publish the results in the form of a systematic review. Only later, after a thorough evaluation of the preliminary findings and the methodological rigor applied, did we recognize the relevance and potential impact of the topic, which justified its formalization as a systematic review in accordance with PRISMA guidelines. By that point, most of the initial steps—such as the protocol definition, search strategy, and inclusion/exclusion criteria—had already been developed and consistently followed. In light of the above, we kindly ask for your consideration in allowing the retrospective registration of this systematic review.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 May 2025 and was last updated on 5 May 2025.

INTRODUCTION

Review question / Objective Research question for this systematic review was "Can clear aligners release microplastics that impact the patient's overall health?" and the aim of the research was to deepen current knowledge on the release of microplastics from clear aligners, identifying potential implications for human health and providing a basis for further research and the development of alternative materials. **Rationale** Microplastics have been linked to several human health risks. Recent studies indicate that once inside the body, these particles can induce inflammatory responses and oxidative stress. Such processes are linked to chronic diseases such as cardiovascular disease, respiratory disorders and, even some types of cancer. In addition, the release of toxic chemicals from microplastics can exacerbate cellular damage by contributing to increased production of free radicals, unstable molecules that compromise cells in the human body, with potential impacts on cellular function and survival.

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The effects of microplastics derived from orthodontic aligners are still being studied, and there are currently no specific guidelines to quantify safe exposure levels. However, evidence of inflammatory and toxic risks makes it urgent to better understand the effect of these particles on human health to inform both consumers and health professionals.

Condition being studied Release of microplastics from clear aligners orthodontic appliance.

METHODS

Search strategy The search strategy used for this systematic review was the keywords ("Clear aligner" OR "orthodontic aligner" OR "transparent aligners" OR "Invisalign") AND (microplastic OR micro plastic OR nanoplastic OR nano plastic OR "surface morphology" OR surface roughness). The studies that are accessible in English were selected.

Participant or population All studies (in vivo or in vitro) investigating any thermoplastic CA material.

Intervention Any type of orthodontic CA, any brand, material and thickness, used or not used.

Comparator A group of untreated patients used as a comparison group, or a control group compared to the experimental groups.

Study designs to be included All studies (in vivo or in vitro).

Eligibility criteria Potentially relevant articles were selected based on these eligibility criteria: published in the period 2000-2024, written in English language, abstract and full text available. The population, intervention, comparison and outcome (PICO) approach was used to establish the inclusion criteria.

Information sources A literature search to find all peer-reviewed citations relevant to the review topic was conducted in the following databases: PubMed, Scopus, Web of Science and Cochrane Library on 31 December 2024. A manual search of grey literature was also performed.

Main outcome(s) Changes in the surface morphology of clear aligners, release of microplastics, and adverse effects on the patient's overall health.

Data management To identify the list of variables to be extracted, two researchers (DAA and HM)

collaborated to execute data extraction. The following data were extracted and organized in Microsoft Excel spreadsheets: title, authors, publication year, study design, sample size, observation period, outcome measures, assessment method, and results. The authors then conducted a consensus analysis of these findings so that they could be discussed in this review.

Quality assessment / Risk of bias analysis As clinical trials were not included in the review, a quality evaluation, such as CASP (Critical Appraisal Skills Program) or a similar tool, could not be conducted. The CONSORT (Consolidated Standards of Reporting Trials) checklist adapted to in vitro studies of dental materials by Faggion et al. [22] was used to assess the quality of the articles. The authors of the present systematic review use this checklist for the evaluation of the quality of the in vitro studies; items from 5 to 9 were eliminated from the checklist due to selected studies are in vitro, so there is a low risk of bias, no need for randomization and sample size is not so determining.

Strategy of data synthesis The narrative synthesis of data from the included studies will concentrate on two primary outcomes: (1) changes to the clear aligners' surfaces that may indicate material degradation, and (2) the measurement of microplastics release during clinical usage. Methodologies, detection strategies, and published results will be compared using a structured thematic analysis with the goal of identifying recurring themes, methodological variations, and evidence gaps pertaining to the clinical behavior and environmental effects of aligners. Due to heterogeneity in study designs, detection methods, and outcome reporting, a meta-analysis was not feasible.

Subgroup analysis Roughness surface of clear aligner; Microplastic release.

Sensitivity analysis Not Applicable.

Language restriction English.

Country(ies) involved Italy.

Keywords Microplastics; dental materials; clear aligner appliances; Invisalign; health; systematic review.

Contributions of each author

Author 1 - Adriana Assunta De Stefano - coordinated the research, developed and executed the review protocol, and contributed substantially

to all stages of the review process and manuscript preparation.

Email: aadestefano@hotmail.com

Author 2 - Martina Horodysnki - contributed to the development of the search strategy, performed study selection and data extraction, and participated in drafting and revising the manuscript.

Email: martina.horodynski@uniroma1.it

Author 3 - Gabriella Galluccio - conceived the original idea for the review, provided overall supervision throughout the study, and critically reviewed the manuscript for intellectual content. Email: gabriella.galluccio@uniroma1.it