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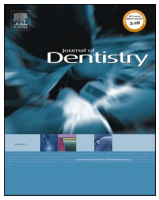

Review article

Oral adverse event reporting in smoking cessation trials using non-combustible nicotine products: A quality assessment

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ABSTRACT

Objectives: To assess the completeness and quality of reporting of oral adverse events (OAEs) in randomized controlled trials (RCTs) that evaluated non-combustible nicotine products (NCNPs) and whether reporting practices have improved over time.

Data sources and study selection: This secondary data analysis was based on 36 RCTs included in a previous systematic review. Trials involved adult smokers and included nicotine replacement therapy, electronic cigarettes, heated tobacco, and smokeless tobacco. The OAE reporting was evaluated using an adapted CONSORT Harms checklist. An Adjusted Checklist Score (ACS), representing the proportion of criteria met, was calculated. Univariate linear regressions explored the association between ACS and study-level variables (publication year, country, funding, blinding and product type).

Results: OAE reporting was fragmented, with a mean ACS of 0.52 (0.11–0.74). Over 80 % of studies (n=30) provided some quantitative data, but only 53 % (n=19) presented results in a tabulated, arm-specific format. Definitions of OAEs and severity measurement were rarely reported (n=5, 14 % and n=6, 17 % respectively). The method of OAEs collection was described in 50 % of the studies (n=18). OAEs were rarely mentioned in titles (n=4, 11 %) and conclusions (n=13, 36 %). Less than half of the studies reported the reasons for participant withdrawal due to AEs (n=16, 44 %). Only 28 % (n=10) and 44 % (n=16) of the studies reported the analysis approach and statistical methods for AEs, respectively. A weak, non-significant positive correlation was found between ACS and year of publication ($r = 0.288$, $p = 0.09$). No study-level variable showed a statistically significant association with ACS.

Conclusions: Reporting of OAEs in clinical trials of NCNPs remains limited and inconsistent, often lacking clear definitions, standardized severity assessments, detailed data collection methods, and predefined statistical plans.

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Clinical significance: Standardized OAE reporting is critical for tolerability data interpretation. We propose practical recommendations to guide researchers in improving the reporting of OAE and strengthening the role of dental professionals in supporting patients through smoking cessation strategies.

1. Introduction

Non-combustible nicotine products (NCNPs) - including nicotine replacement therapies (NRTs) such as gums, lozenges, mouth sprays, and inhalers [1], as well as smokeless tobacco (e.g., snus) [2] and electronic nicotine delivery systems (ENDS) like e-cigarettes (e-cigs) and heated tobacco products (HTPs) [3,4] - have emerged as key tools in smoking cessation strategies. These products offer the potential to reduce harm by eliminating combustion-related toxicants; however, because they are administered via the oral route, the oral cavity is the first site exposed to their chemical constituents [5]. As such, oral adverse events (OAEs) such as dry mouth, aphthous ulcers, gingival irritation, and other mucosal reactions are particularly relevant when assessing the tolerability and safety of NCNPs [6,7].

Despite the growing clinical and public health interest in OAEs associated with NCNPs, much of the existing evidence derives from observational studies, which are inherently prone to confounding and reporting biases [8]. Randomized controlled trials (RCTs) remain the gold standard for evaluating the efficacy and safety of medical interventions [9,10], but the reliability of OAE data emerging from RCTs depends critically on the quality and completeness of harms reporting.

Historically, RCTs have prioritized efficacy endpoints, often relegating safety data, particularly for adverse events not deemed serious or life-threatening, to secondary status. In response to widespread concerns over underreporting and inconsistent harm data, the Consolidated Standards of Reporting Trials (CONSORT) group issued a dedicated Harms extension in 2004, providing detailed guidance on how adverse events should be reported in RCTs [11]. This extension has since undergone a recent update in 2022 to further strengthen and clarify recommendations [12]. These efforts have contributed to improved safety reporting practices across clinical research domains. However, as previously highlighted in oncology and other fields, adverse event reporting remains heterogeneous and often incomplete, especially for events of moderate severity or uncertain causality [13,14]. In particular, oral symptoms - although not life-threatening - can significantly affect adherence, user satisfaction, and long-term effectiveness of NCNP-based cessation strategies [15–17].

This compromises both the evaluation of product tolerability and the ability to inform clinical guidelines and user decision-making. To address this, we aimed to assess the completeness and quality of OAE reporting in RCTs evaluating oral adverse effects linked to NCNP use by using an adapted 19-item checklist based on the CONSORT Harms extension [12]. This tool allows the evaluation of individual reporting components and the generation of an Adjusted Checklist Score (ACS), a continuous summary index ranging from 0 to 1. Similar scoring approaches have been used in prior meta-research on harm reporting [13], but have not yet been applied to the context of NCNPs. Through a comprehensive analysis of the quality of OAE reporting in current RCTs, we aimed to propose a set of practical recommendations to improve reporting in future trials. We also examined whether reporting quality has improved over time.

2. Methods

2.1. Search and study selection

Rather than conducting a new independent search, this analysis drew upon RCTs previously identified in a recent systematic review and network meta-analysis [7], which investigated the oral tolerability of NCNPs for smoking cessation. That review included RCTs published in English and retrieved through a systematic search of PubMed, Scopus, and the Cochrane Library, updated to February 2025.

Eligible trials included adult participants and investigated a wide range of NCNPs, specifically: NRTs administered via local delivery systems (including gum, mouth spray, tablet, lozenge and inhaler); ENDS, including both e-cigs and HTPs; and SMT such as snus.

For detailed information regarding the original eligibility criteria, search terms, and study selection procedures, readers are referred to the methods section of the primary review [7].

2.2. Data extraction

For each included study, we extracted basic study characteristics including first author, year of publication, type of intervention in each arm, blinding status, geographic region where the RCT was conducted, and target population. We also documented whether OAEs were reported and, if so, whether they were presented in tabular or narrative form, and whether the information appeared in the main article or in the supplementary material.

2.3. Quality reporting assessment

In this study, OAEs were broadly defined as any oral symptoms potentially attributable to the investigational product or its administration. Based on the data reported in the included RCTs, five main categories of OAEs were identified: aphthous ulcers, dry mouth, mouth irritation, periodontal/dental issues, and temporomandibular disorders (TMDs).

To assess the completeness and quality of OAE reporting, we employed a tailored version of the CONSORT Harms extension checklist [12]. Our approach was initially inspired by the structured framework proposed by Xie et al. [13] in their evaluation of immune-related adverse events in oncology trials. While Xie's model was itself based on the CONSORT Harms recommendations, we further adapted it to better reflect the specificity of oral adverse events in trials investigating NCNPs. The adapted checklist (Table 1) includes 10 core items, each corresponding to a specific domain of harms reporting. Each core item was subdivided into one or more specific subitems, resulting in a total of 19 items.

The domains covered are the following: mention of adverse events (AEs) in the title or abstract; statement of harms in the introduction; definition and severity of AEs; methods and timing of data collection; plans for harms analysis; reporting of harm-related withdrawals; availability of denominators; quantitative and tabulated data presentation; specification of statistical methods for AEs; and integration of AEs in the discussion and conclusions.

Each item was scored as 1 (Yes) if the criterion was adequately met, and 0 (No) if the information was absent or unclear. Scores were then summed and used to calculate the ACS for each study as the number of items adequately reported divided by the total number of applicable items in the adapted checklist. It ranges from 0 to 1, where 0 indicates that none of the checklist items were met and 1 indicates full adherence to all predefined reporting criteria. The checklist was independently applied by two reviewers (GRMLR and RP). In cases of disagreement, discrepancies were discussed until consensus was reached.

2.4. Statistical analysis

General characteristics of the included studies were summarized as frequencies and percentages. Inter-rater agreement between the two

Table 1
Adapted harms extension of CONSORT checklist for oral adverse events (OAE) assessment.

Core	Core description	Item	Items description
1	**If the study collected data on harms and benefits, the title or abstract should so state**	1a	AEs mentioned in title.
		1b	AEs mentioned in abstract.
2	**If the study collected data on harms and benefits, the introduction should so state**	2a	AEs addressed in introduction.
3	**List addressed AEs with definitions of each**	3a	Does the methods section specify that AEs have been assessed?
		3b	Does the methods section provide a definition of the AEs?
		3c	Was the severity of AEs assessed?
		3d	Was the method for assessing AEs severity clearly described?
4	**Clarify how harms-related information was collected**	4a	Is there a description of the method of collection of OAEs data?
		4b	Are the OAEs reported with a clear indication of the corresponding time point?
5	**Describe plans for presenting and analyzing information on harms**	5a	Does the methods section provide a description of the methods for analysis of AEs (i.e., ITT or per protocol)?
6	**Describe for each arm the participant withdrawals that are a result of harms and their experiences with the allocated treatment**	6a	Does the study report whether any participant withdrawals were due to potential OAEs?
7	**Provide the denominators for analyses of harm**	7a	Does the study report the number at baseline for each arm?
		7b	Does the study report the number included in any analysis of OAEs?
8	**Present the absolute risk per arm and per OAE type, and present appropriate metrics**	8a	Does the study present quantitative data for OAEs?
		8b	Does the study tabulate results for OAEs?
		8c	Does the study report the number of participants experiencing each OAE in each treatment arm?
9	**Describe statistical analysis**	9a	Was a statistical analysis method specified for AEs?
10	**Provide a balanced discussion of benefits and harms**	10a	Are AEs addressed in the discussion?
		10b	Do the study conclusions explicitly refer to the AEs findings?

Legend: AEs: Adverse Event; ITT: Intention to Treat; OAEs: Oral Adverse Events.

reviewers was assessed for each checklist-item using both raw percentage agreement and Cohen's kappa coefficient. The quality of OAE reporting was quantified using the ACS. Mean, standard deviation, minimum, and maximum values of ACS were calculated. For each item, the frequency and percentage of studies that met the item were also reported. To explore changes in OAE reporting quality over time, we generated a scatter plot illustrating the distribution of ACS scores across publication years. We calculated the Spearman's correlation coefficient to assess the correlation between the ACS and the study publication year. Univariate linear regression analyses were conducted to examine the association between ACS and each of the following study-level covariates, adopted from Xie et al. [13]: year of publication, funding source, geographic region, blinding status and product type. Statistical significance was set at $p < 0.05$. All analyses were performed using Stata Statistical Software: Release 17 (StataCorp LLC, College Station, TX, USA).

3. Results

3.1. General characteristics

The flow of study selection has been previously reported [7]. A total of 36 RCTs, involving 12,454 participants, were included in the present analysis [18–53]. General characteristics and descriptive statistics of the included studies are presented in Table 2 and **Appendix 1** and further detailed in the previous publication [7]. Eight types of NCNPs were included: e-cigs ($n = 6$, 17 %), HTPs ($n = 1$, 3 %), snus ($n = 4$, 11 %), and various forms of NRTs, including gum ($n = 19$, 53 %), mouth spray ($n = 3$, 8 %), tablet ($n = 3$, 8 %), lozenge ($n = 1$, 3 %), and inhaler ($n = 4$, 11 %). The years of publication ranged from 1982 to 2024. Sixteen studies (44 %) were funded by pharmaceutical or tobacco companies, while 13 (36 %) received funding from non-profit organizations or institutional sources. One study (3 %) reported no funding, and the remaining six (17 %) did not provide any information about funding. The most frequently reported oral adverse events were mouth irritation ($n = 23$, 64 %), aphthous ulcers ($n = 13$, 36 %), dry mouth ($n = 10$, 28 %), and temporomandibular joint disorders ($n = 10$, 28 %). Periodontal or dental issues were documented in 7 studies (19 %).

3.2. Assessment of the reporting of OAEs

The two reviewers demonstrated substantial agreement in the application of the checklist, with raw agreement exceeding 90 % across

Table 2
Descriptive summary of general characteristics of the included studies.

Characteristics	RCTs ($n = 36$) No. (%)
Year of publication	
1980–1990	12 (33)
1991–2000	6 (17)
2001–2010	4 (11)
2011–2020	12 (33)
≥2021	2 (6)
Country	
Africa	1 (3)
Asia	2 (6)
Europe	15 (42)
North America	17 (47)
South America	1 (3)
Intervention	
NRT	27 (75)
ENDS	7 (19)
SMT (i.e., snus)	4 (11)
Sample size	
<100	3 (8)
100–500	27 (75)
500–1000	3 (8)
>1000	3 (8)
Blindness	
Open-label	12 (33)
Double or triple blind	24 (66)
No. intervention arms	
Single	27 (75)
Multiple (dosage)	4 (11)
Multiple (type)	5 (14)
Funding	
Industry	16 (44)
Academy/foundation	13 (36)
None	1 (3)
Not reported	6 (17)

Legend. NRT: nicotine replacement therapy; ENDS: electronic nicotine delivery systems; RCT: randomized controlled trial; SMT: smokeless tobacco.

all items. The mean Cohen's kappa coefficient was 0.938 (SD = 0.166), indicating very high inter-rater agreement across checklist items. Item-specific agreement data are shown in **Appendix 2**.

The mean ACS was 0.52 (SD = 0.19), with values ranging from 0.11 -reported by one study [46] - to 0.74, reported by seven studies [20,29,31,45,47,51,52]. Item-by-item evaluations and overall ACS scores for all studies can be found in **Appendix 3**. All included RCTs reported the baseline number of participants per arm (item 7a) and 86 % of trials (n = 31) explicitly mentioned OAEs in the methods section (item 3a) (Fig. 1). Sixty-seven percent of the studies (n = 24) specified the number of participants included in the analysis of adverse events (7b). Quantitative data on OAEs (item 8a) and tabulated results (8b) were provided in 83 % (n = 30) and 53 % (n = 19) of the studies, respectively. OAEs were reported separately for each trial arm (8c) in 61 % of the studies (n = 22). Only 14 % of the studies (n = 5) provided a definition of adverse events (3b), and just 17 % (n = 6) of the 22 studies (61 %) that cited severity of AEs (3c) explained how severity was assessed (3d). The method and timing of data collection (items 4a and 4b) were clearly specified in 50 % (n = 18) and 58 % (n = 21) of trials, respectively. Sixteen studies (44 %) specified the reasons for participant withdrawal due to AEs (item 6a). OAEs were mentioned in the discussion and conclusion sections in 64 % (n = 23) and 36 % (n = 13) of the studies, respectively (items 10a and 10b). Less than half of the studies (n = 16, 44 %) mentioned OAEs in the introduction (2a), while 11 % (n = 4) and 67 % (n = 24) did so in the title (1a) and abstract (1b), respectively. Finally, items related to the analysis plan (5a) - such as intention-to-treat (ITT) or per-protocol approaches - and the use of statistical analysis for AEs (9a) were reported in only 28 % (n = 10) and 44 % (n = 16) of the studies, respectively.

3.3. Changes in ACS over time and predictive covariates

Changes in ACS values over time are presented in Fig. 2. A weak, non-significant positive correlation was found between ACS and year of publication (r = 0.288, p = 0.09). We did not find any significant association between each study-variable and the ACS (Table 3).

4. Discussion

This study offers the first structured evaluation of OAE reporting in NCNP trials, highlighting persistent shortcomings. Across 36 RCTs, the mean ACS was 0.52, indicating that only half of the recommended reporting criteria were met. Key gaps included missing definitions of OAEs, limited information on severity assessment, and scarce reporting

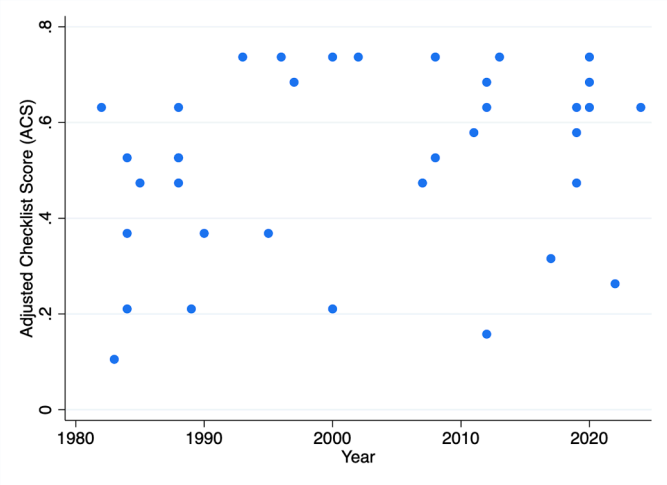

Fig. 2. Variation in adjusted checklist score (ACS) by year of publication.

Table 3
Findings from univariate linear regression analysis.

Univariate linear regression analysis Covariate	Regression coefficient	Standard Error	p value
Year of publication (continuous)	.004	.002	0.115
Country (Ref. North America)			
Europe	0.055	.070	0.431
Asia	0.166	.146	0.265
Africa	−0.018	.200	0.927
South America	−0.124	.200	0.542
Funding (Ref. No funded)			
Academy/foundation	−0.092	.088	0.303
Industry	0.028	.085	0.746
Blinding (Ref. Yes)			
No	−0.073	.066	0.274
Product (Ref. NRT)			
ENDS	.08	.089	0.374
SMT	.028	.120	0.820
NRT+ENDS/SMT	.107	.143	0.464

Legend. ENDS: electronic nicotine delivery systems; NRT: nicotine replacement therapy; SMT: smokeless tobacco; Ref.: Reference.

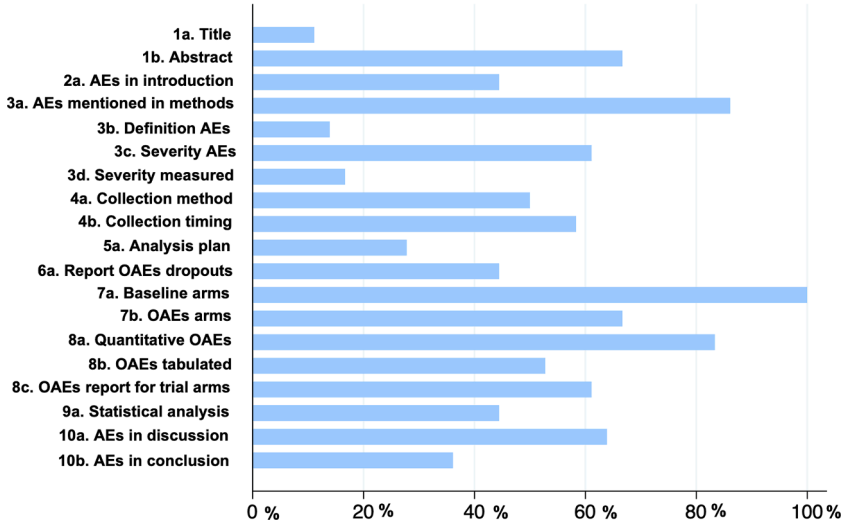

Fig. 1. Proportion of randomized controlled trials (RCTs) reporting oral adverse events (OAEs) in compliance with the adapted CONSORT Harms checklist. Bar chart showing the percentage of included trials (N = 36) meeting each of the 19 items of the adapted reporting checklist for OAEs.

of statistical analysis plans. No significant improvements were observed over time, nor associations with study-level characteristics. These widespread inconsistencies compromise the ability to synthesize evidence on product tolerability, a critical factor for both user adherence and clinical decision-making.

As the first site of exposure to NCNPs, the oral cavity is central to assessing tolerability. Commonly reported OAEs, such as mouth irritation and aphthous ulcers, are frequently under-reported, possibly due to limited attention from non-dental trialists. Yet, these symptoms can compromise key oral functions like chewing and swallowing, affecting nutritional intake and quality of life [54–56]. In the context of smoking cessation, tolerability issues may compromise adherence and perceptions of safety. From a public health perspective, consistent OAE reporting is essential for evaluating the risk-benefit profile of NCNPs and supporting personalized counselling. This study assessed the quality of OAE reporting in RCTs and proposed recommendations to improve future reporting practices.

Nearly 90 % of the included trials did not mention OAEs or related terms in the title. In addition, only 14 % of studies provided an explicit definition of adverse events (i.e., oral or otherwise) and <20 % described how severity was measured. In the context of clinical trials, standardized classification systems for adverse events, such as the Common Terminology Criteria for Adverse Events (CTCAE) [57], Medical Dictionary for Regulatory Activities (MedDRA) [58] or the World Health Organization Adverse Reaction Terminology (WHO-ART) [59] have been used to ensure the reliability and reproducibility of reported outcomes. However, most of the studies relied on subjective, self-reported assessments of oral symptoms without clarifying what constituted an adverse event, nor how such events were explained to participants. This lack of clarity affects the interpretability of findings and may compromise data reliability. In addition, existing adverse event classification systems are often generic and fail to capture the specific clinical nuances of oral adverse events. This limitation may lead to inconsistent reporting or underestimation of their relevance. Notably, there is currently no standardized, dental-specific classification system for OAEs, highlighting the need for tailored frameworks that can better support accurate identification, grading, and communication of these outcomes in smoking cessation research.

Half of the studies reported how oral adverse events were collected. Yet, this information remains highly relevant, as data collection may rely on subjective methods (e.g., self-report questionnaires) or objective assessments (e.g., clinical examination). Beyond the issue of measurement reliability - which has already been addressed in previous bias assessments [7] - transparent reporting of data collection methods is important for interpreting results and understanding their validity. Given the complexity of oral outcomes, involving dental professionals in trial design may help ensure that OAEs are properly identified and consistently reported, enhancing the quality of safety data without shifting the trial's focus. Similarly, reporting the timing of assessment is frequently overlooked, with only 58 % of studies specifying when OAEs were evaluated. In smoking cessation trials, adverse events are typically monitored throughout the study, but this can span an active intervention phase and a longer maintenance phase in which product use may continue ad libitum. A clear indication of when symptoms occur is essential to distinguish between reactions triggered by initial exposure and those that persist or emerge over time. This distinction is not only critical for evaluating the long-term safety profile of the product, but also for assessing the plausibility of a causal relationship between the intervention and the reported event [14]. Without precise temporal information, attributing symptoms to the product -rather than to withdrawal effects, comorbidities, or unrelated causes -becomes inherently uncertain [60,61].

For instance, aphthous ulcers have been frequently reported after smoking cessation and may be influenced by physiological changes induced by tobacco withdrawal [62]. Several mechanisms have been proposed to explain this phenomenon: tobacco smoke may promote keratinization of the oral mucosa, which could provide mechanical protection [63,64]; some of its components might exert antibacterial effects [65]; and smoking cessation itself may lead to immunological alterations, possibly related to withdrawal-induced stress or broader immune dysregulation [66]. Given this complexity, it would be valuable for future trials to stratify participants by abstinence status and dependence level, and to investigate the timing and persistence of ulcers in relation to product use and cessation outcomes. In the current literature, OAEs are often attributed generically to product exposure without considering their potential interaction with smoking cessation itself, a limitation that warrants further exploration.

The choice of analytical approach (i.e., ITT or per-protocol) plays an important role in shaping the interpretation of safety data [67,68]. While ITT remains the gold standard for evaluating efficacy, per-protocol analysis can provide clearer insight into adverse event rates among participants who actually used the product [69]. However, per-protocol analysis is also subject to bias, as it may fail to fully capture the incidence of adverse events - particularly when participants discontinue treatment due to adverse effects. In such cases, excluding these individuals can lead to an underestimation of harms and appropriate adjustment techniques are required to estimate the effect of treatment [70]. Many of the included studies did not clearly specify the statistical methods used to analyze oral adverse events, making it difficult to interpret the robustness of their findings. In some cases, the number of participants per treatment arm was reported in a way that allowed indirect inference of the analytical approach, although this information was often incomplete. Additionally, the reasons for participant withdrawal due to adverse events were documented clearly in less than half of the included trials, limiting insights into the safety profile of the tested products.

While most studies provided some form of quantitative data on OAEs, the absence of structured and tabulated reporting formats in several trials compromised the clarity and reproducibility of the results. This lack of standardized presentation also impaired the potential for meaningful secondary data analyses and evidence synthesis. When such information is missing, it becomes more difficult to assess the comparative burden of AEs across interventions. This aspect is particularly important in the context of smoking cessation trials, where placebo comparators are not necessarily inert [27,71,72]. For example, gums, inhalers, or sprays, even when nicotine-free, may independently contribute to oral symptoms through mechanical or chemical irritation. As noted in the previously published network meta-analysis [7], the highest odds of mouth irritation associated with specific delivery formats including e-cigs and NRT gum were observed when compared to standard care (but not to placebo). This finding suggests that the mode of administration itself, rather than the presence of nicotine alone, may play a more influential role in the onset of local adverse effects. Furthermore, reporting the number of participants experiencing a given adverse event rather than simply listing the total number of occurrences is critical to avoid overestimation. When multiple events are reported by a single participant and not clearly disaggregated, the overall burden of AEs may appear artificially inflated. Furthermore, a common practice in adverse event reporting is to indicate only the number of participants who experienced at least one event, without providing information on the frequency or duration of repeated occurrences. While this simplifies presentation, it obscures important distinctions relevant to both patient experience and health economic evaluations [14]. For instance, a single report of oral irritation is not equivalent to persistent or recurring symptoms over time; yet such differences cannot be discerned when events are simply reported as "at least one occurrence" [73].

In several trials where quantitative data on oral adverse events were not clearly presented, safety was summarized using generic statements such as "the product was well tolerated" or "no major side effects were observed." These assertions are often based on post hoc comparisons or on the absence of statistically significant differences between arms [14]. However, such interpretations can be misleading, as a non-significant

result does not imply the absence of harm, and multiple unadjusted comparisons increase the likelihood of spurious findings due to chance [14]. Statistical methods for adverse event analysis were frequently underreported, reducing the transparency and robustness of safety claims. Moreover, safety outcomes were not consistently reflected in the discussion and conclusion sections of the trials, suggesting that oral adverse events are often not fully integrated into the overall interpretation of findings. A more balanced appraisal of efficacy and safety, tailored to patient characteristics, could improve the clinical relevance of future trials. The involvement of dental professionals in the OAE interpretation may offer a practical way to enhance reporting accuracy and consistency, supporting more personalized and evidence-based cessation strategies [74].

The temporal analysis did not yield statistically significant results, possibly due to the inconsistent adoption of the CONSORT extension for harms over time. The development and dissemination of standardized tools are expected to promote more consistent and comprehensive reporting of adverse events [12]; however, their use may remain limited unless explicitly required by journals. Of note, almost all trials evaluated products already approved and commercially available at the time of publication, with a primary focus on confirming efficacy rather than systematically assessing safety. This likely contributed to the limited attention given to OAEs in trial reporting.

We did not analyze the association between reporting quality (ACS) and journal impact factor, due to inconsistencies in indexation timelines across journals, especially those published before 2000. Applying current metrics retrospectively could also introduce bias, as impact factors may have changed significantly over time. However, it is plausible that journals with higher impact factors - often enforcing stricter editorial standards - are more likely to ensure adherence to international reporting guidelines such as CONSORT.

The high inter-rater agreement observed in this study supports the clarity and reproducibility of the adapted checklist. Discrepancies were rare and typically due to unclear reporting rather than checklist ambiguity. Consensus was always reached through discussion, reinforcing the tool's reliability.

As previously noted [7], the absence of trials on widely used products like nicotine pouches reflects the lack of eligible RCTs. Our analysis was limited to studies published up to February 2025; future trials are expected to improve reporting quality through better adherence to standardized guidelines.

Most included studies assessed short-term local tolerability (e.g., dryness, irritation, ulcers), with no reports of mucosal lesions or long-term outcomes, likely due to limited follow-up (≤12 months). Therefore, reporting quality reflects the scope and design of these trials. Future research with extended follow-up and dedicated endpoints is needed to evaluate long-term oral effects.

4.1. Recommendations for improving OAE reporting in smoking cessation RCTs

Our study contributes by adapting the CONSORT Harms extension checklist to evaluate the completeness of OAE reporting in smoking cessation trials. Rather than judging the validity of study procedures - which is the focus of risk of bias tools - this checklist provides practical guidance on the essential safety information that should be disclosed to ensure transparent, reproducible reporting.

Fig. 3 summarizes a set of recommendations to enhance the reporting of OAEs in RCTs of smoking cessation by a practical and user-friendly framework for future research. Organized according to each manuscript section, the scheme outlines key elements such as explicitly mentioning safety in the title and abstract, defining OAEs and severity assessment methods, specifying timing and statistical approaches in the methods, disaggregating results by treatment arm, and reflecting on safety implications in the discussion and conclusions. This structured guidance aims to promote transparent, consistent, and clinically informative reporting of OAEs. Greater researcher awareness is essential to ensure systematic reporting of oral adverse events, which supports both ongoing safety surveillance and the integration of dental professionals into smoking cessation care. Accurate and transparent reporting enhances understanding of product tolerability and enables clinicians to deliver personalized, evidence-based guidance to individuals aiming to quit smoking.

5. Conclusions

This study highlights the fragmented, inconsistent and often insufficient reporting of OAEs in RCTs evaluating NCNPs for smoking cessation. Critical areas include the absence of standardized definitions, inconsistent reporting of severity assessment, and unclear timing and methods of data collection. Furthermore, OAEs were often not reported by treatment arm, nor adequately discussed in the interpretation of

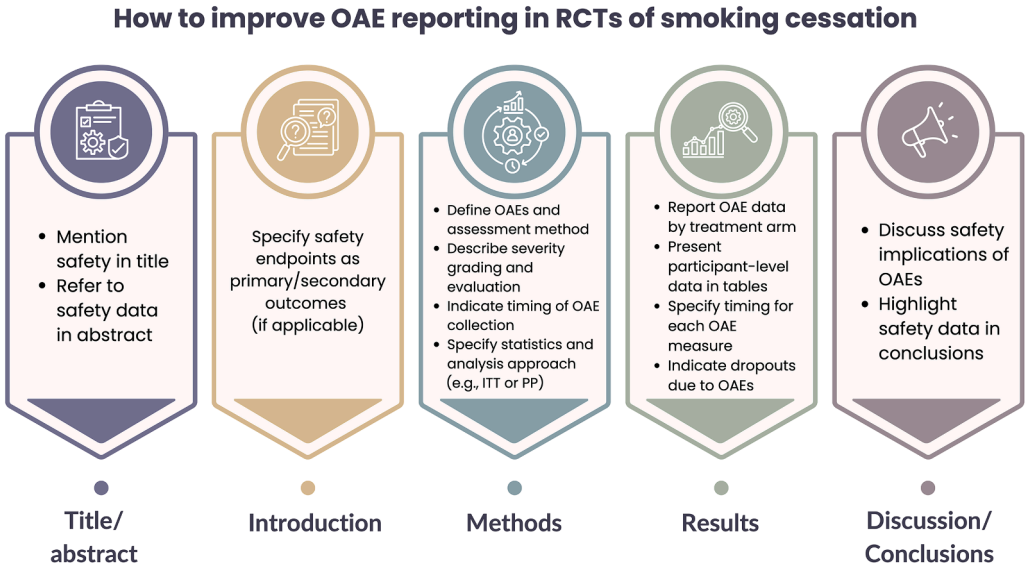

Fig. 3. Graphical summary of practical recommendations for improving OAE reporting, organized according to the typical structure of a scientific manuscript (title/abstract, introduction, methods, results, discussion/conclusions).
Legend. ITT: intention-to-treat; OAE: oral adverse event; PP: per protocol; RCT: randomized controlled trial.

study findings. No significant association was found between year of publication and reporting quality, likely due to the inconsistent implementation of the CONSORT extension for harms.

In light of these findings, we propose a set of practical recommendations aimed at enhancing the reporting of OAEs in smoking cessation trials. The improvement of completeness and consistency in safety reporting is essential not only to support evidence-based clinical decisions, but also to empower oral health professionals to play an active role in advising patients and tailoring cessation strategies based on tolerability profiles.

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CRediT authorship contribution statement

Giusy Rita Maria La Rosa: Writing – review & editing, Writing – original draft, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Cinzia Del Giovane:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Silvia Minozzi:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Jan Kowalski:** Writing – review & editing, Validation. **Iain Chapple:** Writing – review & editing, Visualization. **Amaliya Amaliya:** Writing – review & editing, Visualization. **Dewi Zakiawati:** Writing – review & editing, Visualization. **Francesco Saverio Ludovichetti:** Writing – review & editing, Data curation. **Baek Il Kim:** Writing – review & editing, Validation, Supervision. **Wanninayake Mudiyanselage Tilakaratne:** Writing – review & editing, Validation, Supervision. **Konstantinos Farsalinos:** Writing – review & editing, Visualization, Supervision. **Riccardo Polosa:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Conceptualization.

Declaration of competing interest

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RP is full tenured professor of Internal Medicine at the University of Catania (Italy) and Medical Director of the Institute for Internal Medicine and Clinical Immunology at the same University. He has received grants from U-BIOPRED and AIR-PROM, Integral Rheumatology & Immunology Specialists Network (IRIS), Global Action to End Smoking (formerly known as Foundation for Smoke-Free World), Pfizer, GlaxoSmithKline, CV Therapeutics, NeuroSearch A/S, Sandoz, Merk Sharp & Dohme, Boehringer Ingelheim, Novartis, Arbi Group Srl., Duska Therapeutics, Forest Laboratories, Ministero dell Universita' e della Ricerca (MUR) Bando PNRR 3277/2021 (CUP E63C22000900006) and 341/2022 (CUP E63C22002080006), funded by NextGenerationEU of the European Union (EU), and the ministerial grant PON REACT-EU 2021 GREEN- Bando 3411/2021 by Ministero dell Universita' e (MUR) – PNRR EU Community. He is founder of the Center for Tobacco Prevention and Treatment (CPCT) at the University of Catania and of the Center of Excellence for the Acceleration of Harm Reduction at the same university. He receives consultancy fees from Pfizer, Boehringer Ingelheim, Duska Therapeutics, Forest Laboratories, CV Therapeutics, Sermo Inc., GRG Health, Clarivate Analytics, Guidepoint Expert Network, and GLG Group. He receives textbooks royalties from Elsevier. He is also involved in a patent application for ECLAT Srl. He is a pro bono scientific advisor for Lega Italiana Anti Fumo (LIAF) and the International Network of Nicotine Consumers Organizations (INNCO); and he is Chair of the European Technical Committee for Standardization on "Requirements and test methods for emissions of electronic cigarettes" (CEN/TC 437; WG4).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jdent.2025.106057.

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