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► **To cite this version:**

Hadrien Diakonoff, G. Khalil, Sébastien Jungo, Jean-Marc Treluyer, Hélène Fron Chabouis, et al.. Nonpublication and Selective Outcome Reporting of Oral Health Trials. *Journal of Dental Research*, 2023, 102 (6), pp.599-607. 10.1177/00220345231158544 . hal-04136668

**HAL Id: hal-04136668**

**<https://hal.science/hal-04136668>**

Submitted on 21 Jun 2023

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# Nonpublication and Selective Outcome Reporting of Oral Health Trials

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## Abstract

Less than one-quarter of oral health trials are registered in a public registry. However, no study has assessed the extent of study publication and selective outcome reporting bias in the field of oral health. We identified oral health trials registered between 2006 and 2016 in ClinicalTrials.gov. We assessed whether results of early discontinued trials, trials having an unknown status, and completed trials had been published and, among published trials, whether outcomes differed between the registered record and the corresponding publication. We included 1,399 trials, of which 81 (5.8%) were discontinued, 247 (17.7%) had an unknown status, and 1,071 (76.6%) were completed. The registration was prospective for 719 (51.9%) trials. Over half the registered trials were unpublished ( $n=793$ , 56.7%). To explore the association between trials publication and characteristics of trials, we performed a multivariate logistic regression analysis. Trials conducted in the United States ( $P=0.003$ ) or Brazil ( $P<0.001$ ) were associated with increased odds of publication, whereas trials registered prospectively ( $P=0.001$ ) and industry-sponsored trials ( $P=0.02$ ) were associated with decreased odds. Among the 479 published trials with completed status, the primary outcomes of 215 (44.9%) articles differed from that registered. Major discrepancies consisted of the introduction of a new primary outcome in the published article (196 [91.2%]) and the transformation of a registered secondary outcome into a primary outcome (112 [52.1%]). In the remaining 264 (55.1%) trials, primary outcomes did not differ from that registered, but 141 (53.4%) had been registered retrospectively. Our study highlights the high rate of nonpublication and selective outcome reporting in the field of oral health. These results could alert sponsors, funders, authors of systematic reviews, and the oral health research community at large to combat the nondisclosure of trial results.

**Keywords:** clinical protocols, randomized controlled trial, publication bias, humans, registries, bias

## Introduction

Meta-analyses of randomized controlled trials (RCTs) are considered the gold standard for making informed decisions about which treatment is best. They combine the findings of several RCTs and may overcome the limitations of individual RCTs (Egger et al. 2003). However, a vast number of RCTs remain unpublished, making the conclusions of a meta-analysis misleading (Song et al. 2010). Indeed, investigators, sponsors, or editors tend not to publish results of either full registered RCTs or specific outcomes only because of the direction, magnitude, or statistical significance of the results (Montori et al. 2008). Reporting bias, including nonpublication and selective outcome reporting (SOR), is a recognized cause of waste in biomedical research (Macleod et al. 2014). SOR is defined as the selection of a subset of the original variables recorded, on the basis of the results, for inclusion in publication of trials (Williamson et al. 2005). SOR often favors statistically significant results (Chan et al. 2004). Thus, SOR should compromise the validity of a trial and subsequent meta-analysis. Prospective registration of RCTs represents the best solution to reporting bias if journals or reviewers check registers before publication (Sim et al. 2006). Although trial registration does not ensure that all trial results will be published, it is a key factor in reducing reporting bias (Ioannidis et al. 2014). Thus, the International

Committee of Medical Journal Editors (ICMJE) required registration of all RCTs before enrollment of the first patient in September 2004 and asked for detailed information about trial design in 2005 (Trofimova and Bluemke 2022).

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A supplemental appendix to this article is available online.

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In a previous study, we found that only 23% of a sample of 317 RCTs with results published in oral health journals were registered in a public register, and among those, 91% were registered retrospectively (Smaïl-Faugeron et al. 2015). Moreover, studies in specific dental areas such as endodontics, orthodontics, and implantology found high rates of SOR (Koufatzidou et al. 2019; Sendyk et al. 2019; Tzanetakakis and Koletsi 2021). These results suggest that the risk of reporting bias is high in the field of oral health in general. However, no study has assessed the extent of study publication bias and SOR bias in the field of oral health in general.

Our objective was to assess 1) how many RCTs registered in ClinicalTrials.gov were discontinued early (i.e., before all intended participants were enrolled or before the study was completed), 2) how many RCTs registered in ClinicalTrials.gov were unpublished, and 3) among published results, how many RCTs showed discrepancies in the analyzed primary outcomes between registered records and published articles.

## Methods

### *Selection of RCTs*

We searched ClinicalTrials.gov because it is the largest register and comprises most oral health trial protocols (71%) (Zarin et al. 2011; Smaïl-Faugeron et al. 2015). We did not consider trials registered after 2016 to allow an elapsed time of at least 5 y for trial completion and publication (Ioannidis 1998). Trials recruiting patients before 2006 were excluded because the 2004 ICMJE statement had defined July 1, 2005, as a key date for prospective trial registration (Waldman et al. 2008). Two independent authors selected RCTs registered in the category “Mouth and Tooth Diseases” on ClinicalTrials.gov (searched on January 7, 2022). We read all records, included registered RCTs with a closed recruitment status, and excluded any ongoing RCTs. We selected trials if the “allocation” was “randomized” in the field “study design” of the register. Any disagreements were resolved by discussion.

### *Characteristics of RCTs*

For each RCT, 2 authors independently and in duplicate assessed the following characteristics. First, we recorded the unique trial identifying number assigned by the register. Second, we assessed the dental specialty and the study design (i.e., parallel arm, cluster, crossover, or split mouth). Third, we assessed whether the registration was prospective or retrospective, that is, before or after the date of first enrollment. Prospective registration was defined as registration occurring before the date of first enrollment. We distinguished trials registered within 6 mo of the first enrollment from those registered afterward. Fourth, we assessed changes in the protocol by listing initial and current primary outcomes registered. Initial outcomes were outcomes registered on the date of trial registration. Current outcomes were the last outcomes accessible on the registry (modified from initial outcomes); for those, we

retrieved the date of modification. We also listed secondary outcomes registered. Fifth, we assessed the availability of outcome results on ClinicalTrials.gov.

Finally, we reported the planned sample size, included the date on which data collection was completed for all primary outcome measures, the type of investigator (investigator-initiated trial vs. industry-sponsored trial), and listed location countries where research was conducted.

### *Assessment of Early Discontinued RCTs*

We defined a discontinued RCT in ClinicalTrials.gov if the current recruitment status was “terminated,” “suspended,” or “withdrawn.” We tried to contact investigators by email to inquire about the reason for a discontinued status—when there was no explanation on clinicaltrials.gov—and when the recruitment status was unknown. An email reminder was sent after 10 d.

### *Assessment of Unpublished RCTs*

We assessed whether the results of early discontinued trials, trials having an unknown status, and completed trials had been published. We considered an RCT as published when a journal had published a peer-reviewed manuscript, either online or in print. To identify the publication of results, we checked each trial record on ClinicalTrials.gov for links to publications. Second, for register entries that did not include a link to the publication, we searched PubMed, Google Scholar, and Embase using trial registration numbers (Zarin et al. 2005). Third, for RCTs for which no published results were identified, we searched PubMed, Google Scholar, and Embase by using relevant keywords based on the title, authors’ names or participants, experimental intervention, and comparator (Grobler et al. 2008). If more than 1 publication corresponded to a trial, we selected the publication whose primary outcome matched the 1 recorded. When no publication was identified using the described search strategy, we attempted to contact investigators by email (with a reminder after 10 d). If the investigator indicated that the results were unpublished, we asked for the reason.

### *Assessment of SOR*

Among published RCTs, we compared the number and the definition of primary outcomes between the registered record and the corresponding publication. We defined discrepancies according to the modified classification of Chan et al. (2004) (Appendix Table 1).

Primary outcomes were those that were explicitly reported as such in the published article. If none was explicitly reported, we used the outcome stated in the sample size estimation. If none was explicitly identified in the text or the sample size calculation, we used the first outcome reported in the results section. Two review authors independently collected the data in a data extraction form that had been pilot-tested with 50 articles and modified accordingly. Disagreements were resolved by discussion.

## Data Synthesis and Analysis

Characteristics of trials were described using frequencies (percentages) for qualitative variables and median (interquartile range, minimum–maximum) for quantitative variables. When appropriate, the Mann–Whitney  $U$  test or Kruskal–Wallis test was used for quantitative variables and Fisher exact test for binary variables, to compare differences between published and unpublished trials registered in ClinicalTrials.gov. To explore the association between trial publication and trial characteristics, on the one hand, and SOR and trial characteristics, on the other hand, univariate and multivariate logistic regression analyses were performed. Variables with  $P \leq 0.2$  in the univariate analysis were introduced into the multivariate logistic regression analysis. Then, backward stepwise procedures based on the Akaike Information Criterion (AIC) were performed to create reduced multivariate models. For each model, regression diagnostics plots are provided in Appendix Figures 1 to 4. Kaplan–Meier curves for the length of time after the completion date until modification of the initial primary outcome were presented for published and unpublished trials. Analyses involved the use of the R software (R Foundation for Statistical Computing).

## Results

### Characteristics of Included Studies

The initial search identified 2,046 trials, of which 1,399 were included in the final analysis ( $\kappa=0.997$ ) (Fig. 1). Among the 1,399 included trials, 1,071 (76.6%) were completed, 81 (5.8%) were discontinued, and 247 (17.7%) had an unknown status. Details of characteristics are given in Table 1.

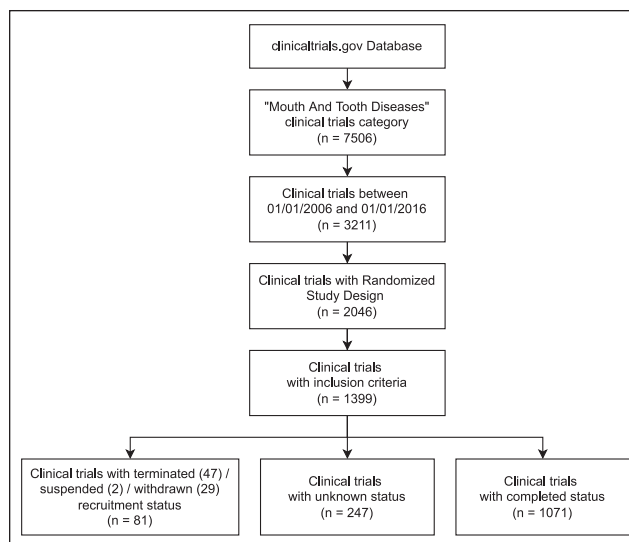
### Early Discontinuation

Among the 81 discontinued trials, 48 (59.3%) were terminated, 31 (38.3%) were withdrawn, and 2 (2.5%) were suspended. The most common reasons for discontinuation were poor recruitment ( $n=26$ , 32.1%), lack of funding or sponsor issues ( $n=17$ , 20.9%), and termination due to negative interim results ( $n=10$ , 12.3%). Sixteen (19.8%) trials had team or protocol concerns, and 3 (3.7%) had not started.

Among the 247 trials with an unknown status, we identified contact email addresses for 161 (65.2%) and received replies from 42. The most common reason for this status was poor recruitment ( $n=15$ , 35.7%). Three (7.1%) trials had not started, 3 (7.1%) were completed but not published (without any reason given), and 6 (14.4%) had team or business concerns. In addition, 15 (35.7%) responded that they had published the results anyway.

### Nonpublication

Of 81 discontinued trials and 247 trials with an unknown status, we identified 0 and 125 (50.6%), respectively, as published following searches on electronic databases. Combining



**Figure 1.** Flowchart of included clinical trials registered in ClinicalTrials.gov.

responses of contacted authors, 201 (61.3%) discontinued trials and trials with an unknown status were unpublished.

Of 1,071 completed trials, we initially identified 472 (44.1%) as published following searches on electronic databases: 162 (34.3%) were found by using the link to the publication provided on ClinicalTrials.gov, 212 (44.9%) by using trial registration numbers provided on ClinicalTrials.gov, and 240 (50.8%) by using relevant keywords. We sought contact email addresses for the remaining 599 (55.9%) unpublished trials, for which 358 email addresses were identified and contacted. Twenty-one (5.9%) replies were received, of which 8 (38%) gave the article reference. The responses identified a further 7 (33.3%) trials as unpublished, with reasons given by the authors. Last, 1 industrial promoter refused to give us the reasons for the nonpublication of 2 clinical trials. Combining these results with published studies found by manual search, we found a total of 592 (55.3%) unpublished completed trials.

In the multivariate analysis, trials conducted in the United States or Brazil were associated with increased odds of publication (1.89 [1.28–2.80] and 2.14 [1.44–3.19], respectively), whereas trials registered prospectively (0.66 [0.52–0.85]) and industry-sponsored trials (0.24 [0.07–0.74]) were associated with decreased odds (Table 2).

The median time from study completion to publication date was 27 mo (interquartile range, 17–44; minimum–maximum, 1–132).

Figure 2 shows that there was no significant difference in the probability of including the initial registered primary outcome between published and unpublished trials.

### SOR

Among the 479 published RCTs with completed status, the primary outcomes of 215 articles (44.9%) differed from those

**Table 1.** Characteristics of Discontinued Trials, Completed Trials, and Trials with an Unknown Status Registered in ClinicalTrials.gov.

Characteristic	Overall Status (n = 1,399)	Discontinued Status (n = 81)	Completed Status (n = 1,071)	Unknown Status (n = 247)	P Value
<b>Dental specialty</b>					
Dental caries	271 (19.4)	11 (13.6)	206 (19.2)	54 (21.9)	<0.001 <sup>a</sup>
Oral diseases and surgery	214 (15.3)	18 (22.2)	156 (14.6)	40 (16.2)	
Oral pain	205 (14.7)	17 (21.0)	159 (14.8)	29 (11.7)	
Orthodontics	56 (4.0)	4 (4.9)	39 (3.6)	13 (5.3)	
Periodontal diseases	507 (36.2)	17 (21.0)	413 (38.6)	77 (31.2)	
Prosthetics	146 (10.4)	14 (17.3)	98 (9.2)	34 (13.8)	
<b>Number of countries</b>					
One country	1,313 (93.9)	81 (100)	1,002 (93.6)	230 (93.1)	0.03 <sup>b</sup>
More than 1 country	86 (6.2)		69 (6.4)	17 (6.9)	
<b>Country</b>					
United States (alone or not)	339 (24.2)	31 (38.3)	289 (27.0)	19 (7.7)	<0.001 <sup>a</sup>
Brazil (alone or not)	181 (12.9)	3 (3.7)	131 (12.2)	47 (19.0)	
Other countries	600 (42.9)	26 (32.1)	442 (41.3)	132 (53.4)	
Not provided	279 (19.9)	21 (25.9)	209 (19.5)	49 (19.8)	
<b>Study design</b>					
Crossover	146 (10.5)	11 (13.9)	113 (10.6)	22 (8.9)	<0.001 <sup>b</sup>
Factorial	33 (2.4)		25 (2.3)	8 (3.3)	
Parallel	1,162 (83.2)	63 (79.7)	893 (83.4)	206 (83.7)	
Single group	15 (1.1)	5 (6.3)		10 (4.1)	
Split mouth	40 (2.9)		40 (3.7)		
<b>Investigator type</b>					
Federal	2 (0.1)		1 (0.1)	1 (0.4)	<0.001 <sup>b</sup>
Individual	2 (0.1)		1 (0.1)	1 (0.4)	
Industry	326 (23.3)	24 (29.6)	281 (26.2)	21 (8.5)	
Network	6 (0.4)		5 (0.5)	1 (0.4)	
National Institutes of Health	3 (0.21)	2 (2.5)	1 (0.1)		
Universities, community-based organizations	1,043 (74.5)	52 (64.2)	773 (72.2)	218 (88.3)	
Government	17 (1.2)	3 (3.7)	9 (0.8)	5 (2.0)	
<b>Enrollment</b>					
>50 participants	641 (47.0)	13 (16.0)	512 (49.4)	116 (47.2)	<0.001 <sup>a</sup>
<50 participants	723 (53.0)	68 (84.0)	525 (50.6)	130 (52.8)	
<b>Results available on ClinicalTrials.gov</b>					
No/not provided	1,097 (78.4)	81 (100)	769 (71.8)	247 (100)	<0.001 <sup>b</sup>
Yes	302 (21.6)		302 (28.2)		
<b>Registration</b>					
Prospectively	720 (51.9)	52 (72.2)	507 (47.3)	161 (66.3)	<0.001 <sup>a</sup>
Retrospectively	666 (48.1)	20 (27.8)	564 (52.7)	82 (33.7)	
<b>Original primary outcome</b>					
Not modified	926 (66.2)	47 (58)	660 (62)	219 (89)	<0.001 <sup>a</sup>
Modified	473 (33.8)	34 (42)	411 (38)	28 (11)	

Data are n (%).

<sup>a</sup>P values comparing status are from  $\chi^2$  test.

<sup>b</sup>P values comparing status are from Fisher's exact test.

registered. Of these articles, 161 (74.9%) had 2 or more reasons for differences in primary outcomes (Appendix Table 2). The discrepancies consisted of the introduction of a new primary outcome in the publication (i.e., a secondary outcome or an absent outcome in the registry that becomes a primary outcome; 196 [91.2%]), omission of the registered primary outcome in the publication (76 [35.3%]), published primary outcome registered as a secondary outcome (112 [52.1%]), a registered primary outcome reported as a secondary outcome in the publication (48 [22.3%]), and timing of assessment that differed between publication and registration (83 [17%]). The sample size differed from that registered for 102 articles (21%). The median number of primary outcomes did not differ from

that registered (median number, 1; minimum–maximum, 0–68 for those registered and 1–11 for those published). The number of published primary outcomes was the same as those registered for 388 RCTs (81%); it was higher for 75 (15.7%) RCTs and smaller for 16 (3.3%) RCTs. There were more discrepancies in outcomes when the initial primary outcome was not modified than when it was (143 [49%] vs. 72 [39%]). Details are given in Table 3. Ninety-two (19%) of published RCTs were prospectively registered and used the initial registered primary outcome as such in the final publication. Outcome modification was more frequent with prospective registration than with retrospective registration (115 [62%] vs. 71 [38%]) (Appendix Table 3).



**Table 2.** Characteristics of Published and Unpublished Trials Registered with ClinicalTrials.gov.

Characteristic	Overall Status (n = 1,399), n (%)	Nonpublication (n = 795), n (%)	Publication (n = 604), n (%)	P Value	Multivariate OR (95% CI, P Value)	Multivariate OR (95% CI, P Value) <sup>a</sup>
<b>Status</b>						
Discontinued	81 (5.8)	81 (10.2)	0	<0.001	2.76E-08 (0–∞, P=0.97)	0.00 (0–0.25, P=0.97)
Completed	1,071 (76.6)	592 (74.5)	479 (79.3)		0.88 (0.65–1.18, P=0.40)	0.84 (0.62–1.14, P=0.27)
Unknown	247 (17.7)	122 (15.3)	125 (20.7)		—	—
<b>Dental specialty</b>						
Dental caries	271 (19.4)	153 (19.2)	118 (19.5)	0.1	0.82 (0.53–1.27, P=0.37)	
Oral diseases and surgery	214 (15.3)	109 (13.7)	105 (17.4)		1.31 (0.83–2.09, P=0.24)	
Oral pain	205 (14.7)	134 (16.9)	71 (11.8)		0.83 (0.52–1.33, P=0.45)	
Orthodontics	56 (4)	31 (3.9)	25 (4.1)		0.91 (0.47–1.77, P=0.80)	
Periodontal diseases	507 (36.2)	287 (36.1)	220 (36.4)		0.84 (0.56–1.25, P=0.39)	
Prosthetics	146 (10.4)	81 (10.2)	65 (10.8)		—	
<b>Study design</b>						
Crossover	146 (10.5)	94 (11.9)	52 (8.6)	0.36		
Factorial	33 (2.4)	19 (2.4)	14 (2.3)			
Parallel	1,162 (83.2)	647 (81.7)	515 (85.3)			
Single group	15 (1.1)	8 (1.0)	7 (1.2)			
Split mouth	40 (2.9)	24 (3.0)	16 (2.7)			
<b>Registration</b>						
Prospectively	720 (51.5)	447 (57.1)	272 (45.1)	<0.001	0.67 (0.53–0.86, P=0.001)	0.66 (0.52–0.85, P=0.001)
Retrospectively	666 (47.6)	335 (42.8)	331 (54.9)		—	—
<b>Investigator type</b>						
Federal	2 (0.1)	2 (0.3)	0	<0.001	1.40E-08 (0–∞, P=0.99)	0.00 (0–∞, P=0.99)
Individual	2 (0.1)	1 (0.1)	1 (0.2)		0.69 (0.03–13.84, P=0.81)	0.61 (0.02–17.80, P=0.74)
Industry	326 (23.3)	239 (30.1)	87 (14.4)		0.26 (0.08–0.84, P=0.02)	0.24 (0.07–0.74, P=0.02)
Network	6 (0.4)	3 (0.4)	3 (0.5)		0.62 (0.09–4.54, P=0.64)	0.59 (0.08–4.38, P=0.60)
National Institutes of Health	3 (0.2)	3 (0.4)	0 (0)		8.57E-08 (0–∞, P=0.99)	0.00-08 (0–∞, P=0.99)
Universities, community-based organizations	1,043 (74.6)	539 (67.8)	504 (83.4)		0.67 (0.22–2.05, P=0.48)	0.60 (0.18–1.79, P=0.38)
Government	17 (1.2)	8 (1.0)	9 (1.5)		—	—
<b>Enrollment</b>						
>50 participants	641 (47)	360 (46.1)	281 (48.2)	0.44		
<50 participants	723 (53.0)	421 (53.9)	302 (51.8)			
<b>Results available on ClinicalTrials.gov</b>						
No/not provided	1,097 (78.4)	623 (78.4)	474 (78.5)	1		
Yes	302 (21.6)	172 (21.6)	130 (21.5)			
<b>Country</b>						
United States (alone or not)	339 (24.2)	221 (27.8)	118 (19.5)	<0.001	1.82 (1.23–2.70, P=0.003)	1.89 (1.28–2.80, P=0.001)
Brazil (alone or not)	181 (12.9)	80 (10.1)	101 (16.7)		2.17 (1.45–3.24, P<0.001)	2.14 (1.44–3.19, P<0.001)
Other countries	600 (42.9)	315 (39.6)	285 (47.2)		1.87 (1.37–2.57, P<0.0001)	1.92 (1.40–2.63, P<0.0001)
Not provided	279 (19.9)	179 (22.5)	100 (16.6)		—	—
AIC					1,757.928	1,756.780

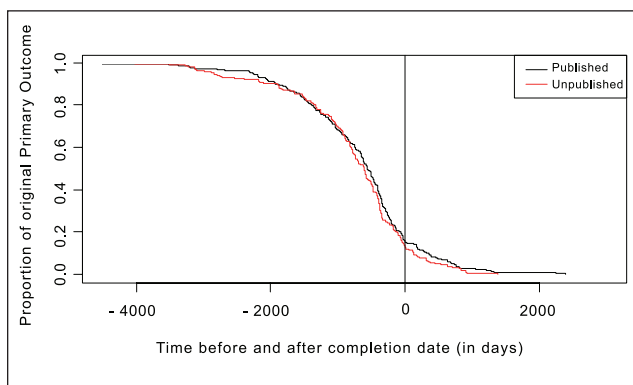
AIC, XXX; CI, confidence interval; OR, odds ratio; —, reference group.

<sup>a</sup>Variable selection after backward stepwise procedure based on AIC criteria.

**Table 3.** Discrepancies between Primary Outcomes in Trial Registration and in Published Article According to Modification of Original Primary Outcome.

Characteristic	Overall (n=479)	Original Primary Outcome Not Modified (n=293)	Original Primary Outcome Modified (Current Outcome) (n=186)	P Value
Discrepancies in outcomes				
No	264 (55)	150 (51)	114 (61)	0.03
Yes	215 (45)	143 (49)	72 (39)	
Introduction of a new primary outcome				
No	283 (59)	161 (55)	122 (66)	0.021
Yes	196 (41)	132 (45)	64 (34)	
Registered primary outcome reported as a secondary outcome				
No	431 (90)	263 (90)	168 (90)	0.84
Yes	48 (10)	30 (10)	18 (10)	
Omission of the registered primary outcome				
No	403 (84)	245 (84)	158 (85)	0.70
Yes	76 (13)	48 (16)	28 (15)	
Published primary outcome registered as a secondary outcome				
No	367 (77)	218 (74)	149 (80)	0.015
Yes	112 (23)	75 (26)	37 (20)	
Absent outcome in the register as primary outcome in the article				
No	307 (64)	173 (59)	134 (72)	0.004
Yes	172 (36)	120 (41)	52 (28)	
Timing of assessment differs				
No	396 (83)	240 (82)	156 (84)	0.58
Yes	83 (17)	53 (18)	30 (16)	
Enrollment size differs				
No	377 (79)	226 (77)	151 (81)	0.29
Yes	102 (21)	67 (23)	35 (19)	

Data are n (%). P values comparing status are from the  $\chi^2$  test.



**Figure 2.** Kaplan–Meier estimate of cumulative original primary outcome percentage by time elapsed from trial completion to modification of original primary outcome among published and unpublished trials.

In the multivariate analysis, industry-sponsored trials were associated with decreased odds of SOR (0.38 [0.22–0.66]) (Appendix Table 4).

## Discussion

Our large study assessed nonpublication and SOR of all 1,399 oral health RCTs registered in ClinicalTrials.gov.

### Discontinuation

Out of 1,399 registered oral health trials, 5.8% were discontinued. In medicine, trial discontinuation reached 30%. In both specialties, poor recruitment was the main discontinuation cause. The higher the sample size, the harder the recruitment. In this aspect, lesser trial discontinuation in oral health may be explained by smaller sample sizes (median 53 in our oral health registered RCTs and 250 in medical RCTs) (Speich et al. 2022).

### Nonpublication

Trials registered prospectively had decreased odds of publication (odds ratio [OR], 0.67 [0.53–0.86]). A possible explanation is an increased risk of early discontinuation for prospectively registered trials, which is consistent with Table 1 showing that 72.2% of early discontinued trials were registered prospectively.

Over half of the registered oral health RCTs were unpublished. Nonpublication in dentistry seems to be higher than in medicine. It seems 20% to 50% of medical trials remain unpublished (Jones et al. 2013; Speich et al. 2022). Small and nonpharmaceutical medical trials seem to convey a higher risk for nonpublication, which could partly explain the high nonpublication rate observed in oral health. The other reasons could be searched, as more publications would help in enhancing research results dissemination.

**Nonpublication and country.** We found that trials conducted in the United States or Brazil were associated with increased odds of publication. These results are consistent with those of recent bibliometric analyses evaluating the publications in the field of dentistry, which indicate that the United States is the most productive country, followed by Brazil (Yahya Asiri et al. 2020; Jiang et al. 2021). These results are also consistent with other bibliometric analyses of general biomedical publications (Bornmann et al. 2018; Web of Science Group 2019).

**Nonpublication and industry funding.** We found that nonpublication is more common among trials that received industry funding. See Appendix Table 5.

**Nonpublication and registration.** In our previous study published in 2014, we found that 77% of published oral health RCTs were not registered in a public registry (Smaïl-Faugeron and Esposito 2014), compared to 6% to 7% in medicine (Loder et al. 2018; Speich et al. 2022). Since 2014, trial registration has hopefully improved in oral health.

In medicine, only 2% of published randomized trials were not registered, while 21% of nonpublished trials were not registered (Speich et al. 2022). This means nonpublication is more frequent in unregistered trials, and our high rate of nonpublication in oral health (56.7%) is probably underestimated.

**Publication and retrospective registration.** In medicine, retrospective registration of RCTs published in 2013 could be as high as 67%, mostly before publication submission (Harriman and Patel 2016). Of the RCTs submitted for publication in the *BMJ* in the period 2013–2017, 89 were retrospectively registered and rejected as such but subsequently published in another journal (Loder et al. 2018). ICMJE guidelines paid off as 41.7% of RCTs published in 2018 complied with prospective registration (Al-Durra et al. 2020).

We found a 57% rate of retrospective registration among oral health published RCTs registered between 2006 and 2016. This is consistent with the rates observed in other medical specialties and hopefully a sign of progress in prospective registration of trials, although we could not find any publication in the oral health field to check if there was a trend toward prospective registration.

Among all registered RCTs, we found 47.6% were retrospectively registered, which means there is more retrospective registration in published trials than in unpublished ones. This confirms Harriman and Patel's (2016) findings: many RCTs are registered retrospectively, before publication, to conform with journals' guidelines for submission. More precisely, most RCTs are registered retrospectively within a year of submission for publication (Al-Durra et al. 2020).

The Indian register has been insisting on prospective registration since 2018 (Birajdar et al. 2019). In Australia and New Zealand, prospective registration increased from 48% in 2006 to 63% in 2012 and plateaued afterward, with investigators citing a lack of awareness as a reason for not registering their study prospectively (Hunter et al. 2018). To enforce prospective registration, ethics committees could require registration

for final trial approval. Journals publishing retrospectively registered trials could require that the authors give a transparent rationale as to why their study was not registered (Gray and Mackay 2020).

## SOR

Most trials had only 1 primary outcome (median number, 1; minimum–maximum, 0–68), which means most investigators now conform with this CONSORT recommendation in oral health. Among oral health published RCTs, we found that almost half had primary outcomes differing from that registered (44.9%). This rate is consistent with SOR rates in endodontics (36.4%) (Tzanetakis and Koletsi 2021), implantology (55%) (Sendyk et al. 2019), and orthodontics (47%) (Koufatzidou et al. 2019). Similar SOR rates were found in medicine (Dwan et al. 2011) and when authors compared systematic reviews to protocols (45.4%) (Pandis et al. 2015).

This rate is probably underestimated, as 57% of published trials were registered retrospectively and change in outcomes is less probable in the latter cases. After correction for retrospective registration, the “real” rate of SOR could be as high as 74.3% ( $n=356$ ). In medicine, SOR rates seem lower: 12% in oncology, 14% in psychopharmacotherapy, 8% to 18% in the leading journals in 2012–2015, 37% in obesity, 39% in anesthesia and pain, and 76% in neuro-otology.

Despite the fact that SOR often favors statistically significant results (Fleming et al. 2015; Raghav et al. 2015; Bonnot et al. 2016; Rankin et al. 2017; Zhang et al. 2017; van Beurden et al. 2021; Lancee et al. 2022), our results did not show this trend. However, industry-sponsored trials were associated with decreased odds of SOR; such a trend has been reported in other medical specialties (Lancee et al. 2022), but an opposite trend has been observed for dental implants (Sendyk et al. 2019) and in medicine (Rankin et al. 2017).

## Limitations

First, our search strategy may have failed to identify some trials, either due to unidentified registers or publication further delayed after registration. Second, our study had difficulties in tracing trial investigators: contact information on registration records is often scarce, and investigators can change their surnames, email addresses, or institution. Finally, we chose to focus on primary outcomes and did not address the problem of unreported secondary outcomes.

In conclusion, our study highlights the high rate of nonpublication and SOR in the field of oral health. These results could alert the oral health research community at large. Transparency in oral health research is the responsibility of researchers as well as journal editors and ethics committees. Ethics committees could condition approval to trial registration; this would theoretically enforce prospective registration. Moreover, any changes to the protocol should be submitted to an ethics committee and explained in the trial report. Journal editors or reviewers should systematically assess reporting bias; they should check that the registration identification number is



mentioned, check that registration was prospective, and compare reported to registered outcomes. Editors should not reject nonsignificant results and maybe hide numbers in the manuscript to prevent reviewer bias. Trial results publication, at least in the registry, should be mandatory. We need to combat the nondisclosure of trial results to prevent the waste of biomedical research.

### Author Contributions

H. Diakonoff, contributed to conception, data acquisition, analysis, and interpretation, drafted the manuscript; G. Khalil, contributed to acquisition and data interpretation, critically revised the manuscript; S. Jungo, contributed to design, data acquisition, analysis, and interpretation, critically revised the manuscript; J.M. Treluyer, H. Fron-Chabouis, contributed to data interpretation, drafted and critically revised the manuscript; V. Smail-Faugeron, contributed to conception and design, data acquisition and interpretation, edited and critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of the work.

### Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

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

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