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SYSTEMATIC REVIEW

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Reporting and handling of incomplete outcome data in implant dentistry: A survey of randomized clinical trials

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Abstract

Aim: To assess the reporting and handling of incomplete outcome data in randomized clinical trials (RCTs) published in implant dentistry.

Materials and methods: We included RCTs on interventions related to the treatment with dental implants and presented any form of missing data. PubMed, SCOPUS and Cochrane databases were searched for studies published between May 2015 and May 2018. Reporting and handling of missing data at the study level were evaluated using a series of relevant questions. Descriptive data were reported, and univariable analyses were performed to evaluate the association of study variables with quality of reporting and data handling.

Results: One-hundred and thirty-seven RCT reports were included from the 7,116 initially retrieved publications. The reporting of incomplete outcome data varied greatly among the trials and for the different questions. The range of adequately reported questions was between 3.64% (question: comparison of baseline characteristics of all randomised participants) and 100% (question: explicit reporting of missing data). The complete case analysis was the most used (45.3%) approach for incomplete outcome data handling.

Conclusions: Randomized studies in implant dentistry have room for improvement in both the reporting and the handling of incomplete outcome data.

KEYWORDS

bias, methodological study, methods, randomized controlled trial, systematic reviews

1 | INTRODUCTION

Missing data are a common problem in clinical trials, especially with long follow-up. Patients may leave the study for several reasons related or not related to the therapeutic interventions and/or outcomes (Little et al., 2012), but the consequences for this loss to follow-up (LTFU) might be important.

Missing data can introduce attrition bias (Lewin, Brondeel, Benmarhnia, Thomas, & Chaix, 2018; Little et al., 2012) and may have an impact on the direction and size of the effect (Raboud, Montaner, Thorne, Singer, & Schechter, 1996). It is important to clarify that it is not necessarily the size of the losses that introduces bias but more importantly the missingness mechanism (Little et al., 2012). Losses related to the intervention and/or outcome may introduce post-randomization bias as treatment arms may not be similar anymore as they were right after randomization potentially leading to an "unfair" comparison. Therefore, it is important during the analysis to consider losses and possible reasons for losses to follow-up as complete case analysis results may differ substantially from the results using an intention-to-treat approach. An intention-to-treat analysis

requires a complete dataset which in the presence of missing data is not possible unless a complete dataset is reconstructed. Various imputations methods exist with multiple imputations being among the more appropriate methods as they generate multiple complete datasets based on a predictive distribution for the outcome variable and they account for the uncertainty due to the missing data (Fleming, 2011; Little et al., 2012, 2010; Little & Rubin, 2002; May et al., 1981; Robins, Rotnitzky, & Zhao, 1995; Seaman & White, 2013). Potential bias elimination via multiple imputation requires that the missingness in the outcome does not depend on its true value other than through measured variables included in the imputation model and that the model is correctly specified (Rubin, 1987; Sterne et al., 2009).

Therefore, when interpreting trial results with losses to follow it is important to understand the missingness mechanism. This missingness mechanism may belong into one of the following categories (Little & Rubin, 1987): missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR). To be able to better recognize the missingness mechanism, it is necessary that all relevant information is included in the publication accurately and transparently (Hollis & Campbell, 1999).

To show potential differences between only complete cases (PP) and ITT analyses, we have simulated data for a relevant clinical comparison taken from a recently published study (Donati, Ekestubbe, Lindhe, & Wennström, 2018). In this trial, the marginal bone loss was compared between non-modified turned and modified and roughened dental implant surfaces. We used the reported per treatment arm means (taken as positive value) and standard deviations for marginal bone loss for the 5-year time point in order to produce the simulated full dataset (ITT dataset). For simplification purposes, a normal distribution of the data was assumed and for the analysis purposes one implant per patient. We simulated 5 complete case only datasets (PP dataset) with 10%, 20%, 30%, 40% and 50% losses to follow-up. In the PP datasets for all % missing scenarios the largest values from one treatment arm were removed and the lowest values from the other treatment arm. This MNAR approach created a best-case scenario (all losses had a positive outcome) for one treatment arm and a worst-case scenario (all losses had a negative outcome) for the other treatment arm. We fitted univariable linear regression models for the full and the complete case only datasets simulating the intention-to-treat (ITT) and the per-protocol (PP) analyses, respectively. Table 1 and Figure 1 show clearly how the estimates for ITT and PP analyses per simulated % data loss diverge. We can see that as the % of losses increase the treatment effects for PP become larger on an absolute basis and that from 20% losses and on the PP results are significant as the 95% confidence intervals do not include zero. This is expected given the MNAR nature of the simulated losses as explained earlier. Obviously, the adopted scenario is an extreme scenario and it is applied to show the potential problems with ignoring missing data; however, this is only one scenario among several. It is of interest to note that in the Donati et al paper used for this simulation from the 148 originally placed implants, 137 (92.6%), 112 (75.7%), 62 (40.5%) and 64 (43.2%) were assessed at the 5, 8, 12 and 20-year intervals, respectively. This simulation indicates the need to decrease losses to follow-up during the trial conduct as much as possible and also the importance of fully reporting losses to follow-up and handling of missing data.

Clinical Relevance

Scientific rationale for the study: There is so far no information on how authors of randomized studies in implant dentistry report and handle incomplete outcome. Bias in estimates may occur when different types of analyses are performed in the presence of missing data.
Principal findings: The findings demonstrate that the report of incomplete outcome data can be improved. Some information was poorly addressed in the included trials, such as the baseline characteristics of participants lost to follow-up (LTFU) compared to those who remained in the study, or the implications of LTFU in the context of trials findings. Furthermore, complete case analysis was the most common approach used in this sample of RCTs.
Practical implications: Transparent and accurate reporting of missing data may contribute to a more accurate and less biased assessment of trial results. The present findings may increase awareness in the problem of missing data and guide the planning and conduct of more robust trials.

The objectives of the present study were twofold: (a) to assess the reporting and handling of missing outcome data in RCTs published in implant dentistry and (b) to examine trial characteristics that may be associated with LTFU.

2 | MATERIALS AND METHODS

2.1 | Eligibility criteria

We included reports of RCTs published in implant dentistry adhering to the following criteria:

- Any intervention related to dental implants, any clinical outcome, a sample size of at least 10 patients, and in the English language. When articles reported different follow-ups of the same study, we included the article reporting the longest follow-up.

We excluded the following documents:

- Reports of RCTs without interventional purposes (e.g. no therapy-related outcome).
- RCTs reporting only on non-clinical endpoints (e.g. microbiological findings) or not having any missing data in the form of patient dropout.
- In vitro studies, animal studies and non-RCTs studies.
- Studies with only missing data on dental implants, but without patient dropout.

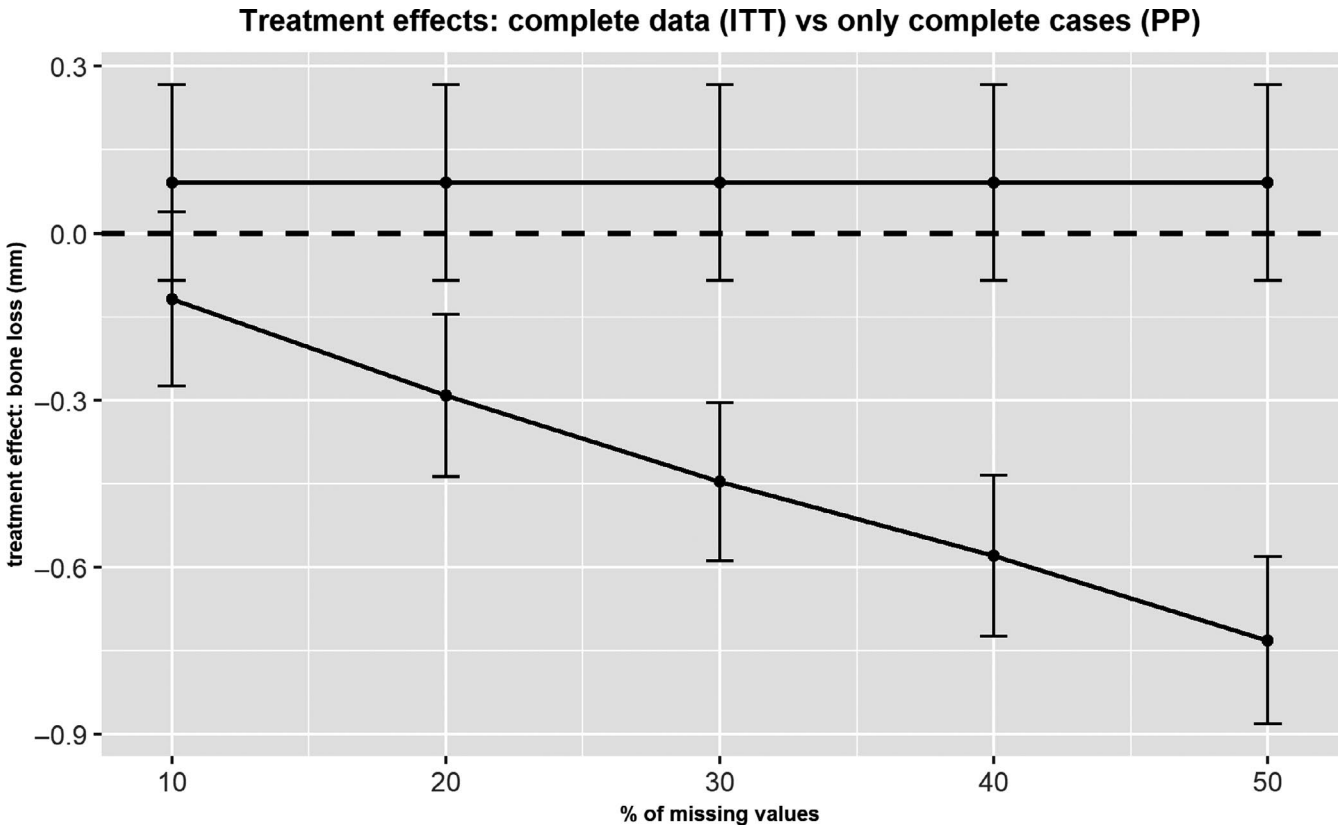

FIGURE 1 Treatment estimates with 95% confidence intervals for intention-to-treat (ITT-upper horizontal line) and per-protocol (PP-lower decreasing line) analyses across 10%-50% simulated losses to follow-up

2.2 | Literature search and selection of RCT reports

Two authors (RL and CMF) searched for RCTs published from May 2015 to May 2018 in MEDLINE (via PubMed), SCOPUS and in the Cochrane Central Register of Controlled Trials (CENTRAL) databases. All terms used in the searches were combined with the Boolean logic operators "OR" and "AND." Full search strategies in the electronic databases are reported in the supplementary file (Table S1). Additionally, the authors manually searched reference lists of selected publications to identify relevant articles. The selection process followed the eligibility criteria and started from the title and the abstract. Excluded papers with reasons for exclusion were recorded. Full-text publications were retrieved for the studies that passed the title and abstract screening stage. After full-text assessment, papers not meeting eligibility criteria were excluded and reasons for exclusion noted.

All searches and the selection of RCTs fulfilling the eligibility criteria were conducted independently and in duplicate by two authors (RL and CMF). Disagreements regarding study selection were resolved by consensus among all authors.

2.3 | Data extraction

Information from the selected RCTs was retrieved and recorded on standardised forms. As suggested by AMSTAR-2 (Shea et al., 2017), the two reviewers initially extracted data from a sample of eligible studies and once they achieved good agreement (at least 80%), the remaining

TABLE 1 Simulated estimates for marginal bone loss (in mm) between treatment groups using complete case only and ITT analyses with different percentages of losses

Percentage of missing values for marginal bone loss	Full (ITT)	95% confidence intervals	Complete case (PP)	95% confidence intervals
10%	0.09	−0.08, 0.26	−0.12	−0.27, 0.04
20%	0.09	−0.08, 0.26	−0.29	−0.44, −0.14
30%	0.09	−0.08, 0.26	−0.45	−0.59, −0.30
40%	0.09	−0.08, 0.26	−0.58	−0.72, −0.43
50%	0.09	−0.08, 0.26	−0.73	−0.88, −0.58

Abbreviation: ITT, intention-to-treat; PP, per protocol.

data extraction was completed by one reviewer. The data extraction forms contained the following information: RCT design (parallel, split-mouth, non-inferiority, factorial, adaptive and other), RCT analysis (ITT and PP),number of arms, sample size, title of the study, year of publication, number of citations in Google Scholar, country of affiliation of the first author, number of participants/implants, type of intervention (non-surgical, surgical, prosthetic and pharmacologic), outcome measure (continuous or categorical), impact factor (IF) and type of sponsorship. In order to maximize the efficiency of the analysis, we used the number of citations reported one year after the date of the literature search. The second reviewer (CMF) checked items at random for accuracy, and when disagreements were found, they were resolved by discussion and consensus.

2.4 | Missing data reporting and handling

Several questions related to missing data were addressed. In a first stage, we assessed how authors reported follow-up information. The checklists for reporting (Akl et al., 2009) of missing outcome data handling (Wood, White, & Thompson, 2004) are shown in Table 2. A two-level scoring was used depending on the reporting of an item or not.

TABLE 2 Items related to the missing data reporting and handling

Items related to the missing data reporting (Akl et al. 2009)
1. The proportion of RCTs that explicitly reported whether loss to follow-up (LTFU) occurred or not
2. The proportion of RCTs that reported a CONSORT flow diagram with LTFU provided
3. The proportion of RCTs that reported loss to follow-up separately for the 2 comparison groups (3.a patients; 3.b dental implants)
4. The proportion of RCTs that reported loss to follow-up at each planned outcome assessment;
5. The proportion of RCTs that compared the baseline characteristics of participants LTFU to those not LTFU and the proportion that compared the baseline characteristics of those LTFU in intervention and control groups
6. The proportion of trials that discussed the implications of loss to follow-up in the context of their findings.
Items related to missing data handling (Wood et al., 2004)
1. Complete case: excludes subjects with missing outcome
2. Last observation carried forward (LOCF): imputes missing values with the individual's last observation
3. Worst-case imputation: imputes all missing values with the worst-case value
4. Regression imputation: missing outcomes are predicted from the individual's observed data, using a model based on observed individuals
5. Repeated measures: all observed outcomes are modelled, allowing for correlation between the individual's observations
6. Sensitivity analysis: analysis which directly assess the assumptions made in primary analysis

Items adequately reported received a YES score. If the information was not reported, a score of NO was noted. For missing data handling, the statistical approach used by the authors of the RCTs to handle missing data was recorded (Table 2). Disagreements were resolved by discussion until consensus was achieved. An experienced statistician (NP) checked the assessment of missing data for accuracy.

Before the assessments, we independently underwent three rounds of calibration by evaluating 6 RCTs not included in the present review. We selected these RCTs by using an online randomisation software (http://www.randomizer.org) from the MEDLINE (via PubMed) database.

2.5 | Statistical analysis

We summarised the results of missing data reporting and handling in tables. We calculated frequencies per RCT reporting characteristic in different-year time periods to assess the changes in trends based on the assessment criteria and reported medians interquartile ranges (IQR) for citation counts and impact factor. We used Fisher's exact test to assess possible associations between RCT characteristics and missing data handling (Yes: study performed missing data handling; No: study did not report any form of missing data handling). In order to examine potential associations between the ordinal score on the quality of reporting of missing data (outcome) and the predictors type of analysis (ITT, PP and both), type of treatment, COI, sponsorship, IF or geographic location median regression was implemented. A Poisson model was fitted to assess any associations between the number of citations (outcome) and the quality of reporting of missing data score (predictor). The coefficients are presented as risk ratios (RR) with their respective confidence intervals (CI). Statistical significance was set at alpha = 0.05, and all analyses were conducted using Stata 15.1 (Stata Corp).

3 | RESULTS

3.1 | Studies included

The initial search retrieved 2,710 documents in PubMed, 2,123 in Cochrane and 2,283 in SCOPUS databases. After removing duplicates among different databases and journals (n = 6,113), 1,003 documents had their titles/abstracts assessed. After assessment of titles and abstracts, 589 documents were excluded. After full-text analysis, 137 articles were included in this study. The search and selection processes are described in detail in Figure 2. A full list of publication retrieved with reasons for exclusions are reported in the supplementary file.

3.2 | Characteristics of the RCTs

The most prevalent RCT design was the parallel design (N = 119, 86.9%) with most studies (N = 50, 36.5%) being published in 2017. The total

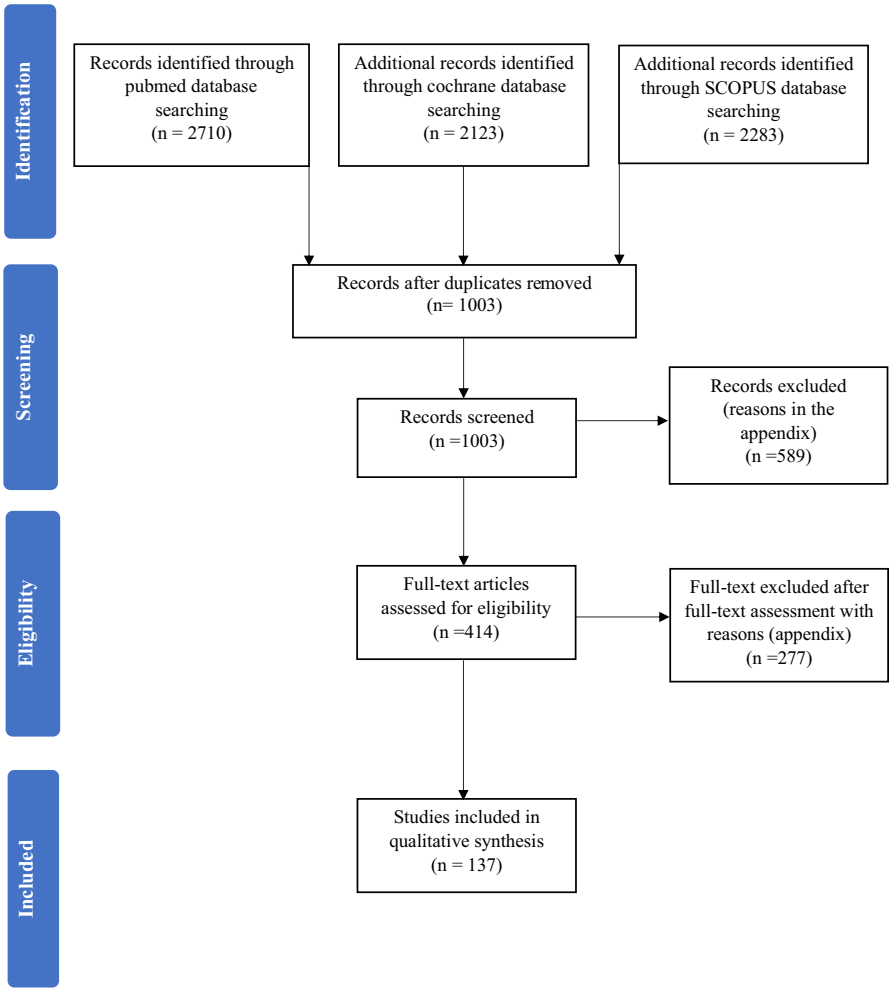

FIGURE 2 Flow of the searching and selection process

number of patients treated in the included RCTs was 8,049 with most (*N* = 122, 89.1%) trials having two treatment arms. Most (*N* = 117, 85.4%) RCTs did not clearly report the type of analysis (ITT vs. per protocol) used. Italy was the most prevalent country according to first author affiliation (*N* = 33, 24%). Ninety-seven (70.8%) of the articles reported continuous variables as primary outcomes. Most (*N* = 97, 70.8%) of the interventions reported in the articles were a combination of surgical and prosthetic treatments and were published in implant dentistry (*N* = 82, 59.9%) journals. The median IF of the journals in this sample was 3.097 (IQR = 1.699), and the median number of citations of the included articles was 9 (IQR = 14.5). The detailed information about the RCTs characteristics are reported in Table 3.

3.3 | Missing data reporting

A flow diagram describing LTFU was reported in 65 (47.5%) of the RCTs. The LTFU at patient level was separately reported for test and control groups in 135 (98.5%) of the RCTs. The LTFU at implant level was separately reported for test and control groups in 92 (67.2%) of the RCTs. The comparison of baseline characteristics of participants LTFU to those not LTFU was reported in 5 (3.6%) of the trials. Twenty (14.6%) of the RCTs discussed the implications of LTFU. Seventy-six (55.5%) RCTs reported LTFU in their abstracts. One-hundred seventeen (85.4%) of the articles reported the reasons for dropout. The complete information on missing data reporting is described in Table 4.

3.4 | Missing data handling

In the present sample of 137 RCTs, 62 (45.3%) of the studies reported a complete case analysis. One (0.7%) trial applied the LOCF approach, two (1.5%) trials used the worst-case scenario imputation and one (0.7%) trial applied the baseline-observation-carried-forward (BOCF) approach. For 71 (51.8%) of the studies, there was no description of the approach used to address missing data handling. Fisher's exact test indicated no association between missing data handling and trial characteristics (Table 5).

3.5 | Regression analysis

Median regression indicated an association between the score on the quality of reporting of missing data and the type of analysis (p = .04, Wald test), type of treatment (p < .001, Wald test). No associations

TABLE 3 Characteristics of 137 included articles

Article characteristics	Frequency (%)
Year of publication	
2015	26 (18.9)
2016	39 (28.5)
2017	50 (36.5)
2018	22 (16.1)
Continent of first author	
America	18 (13)
Asia	25 (18)
Europe	94 (69)
Country of first author	
Argentina	1 (0.7)
Austria	2 (1.5)
Belgium	1 (0.7)
Brazil	4 (2.9)
China	1 (0.7)
Egypt	3 (2.2)
Germany	15 (10.9)
Greece	1 (0.7)
India	3 (2.2)
Iran	3 (2.2)
Ireland	1 (0.7)
Israel	1 (0.7)
Italy	33 (24)
Korea	6 (4.4)
Netherland	11 (8)
New Zealand	2 (1.5)
Norway	1 (0.7)
Poland	1 (0.7)
Saudi Arabia	2 (1.5)
Serbia	1 (0.7)
Spain	7 (5.1)
Sweden	11 (8)
Switzerland	7 (5.1)
Taiwan	1 (0.7)
Turkey	3 (2.2)
UK	2 (1.5)
USA	13 (9.8)
Study design	
Parallel	119 (86.9)
Split-mouth	14 (10.2)
Cross-over	2 (1.5)
Parallel + split-mouth	1 (0.7)
Unclear	1 (0.7)
Superiority	43 (31.4)
Equivalence	6 (4.4)
Non-inferiority	3 (2.2)
Not stated	85 (62)
RCT analysis	
Intention-to-treat	8 (5.8)
Per protocol	8 (5.8)
Intention-to-treat and per protocol	4 (2.9)
Unclear	117 (85.4)
Number of treatment arms	
2	122 (89.1)
3	10 (7.3)
4	5 (3.6)
Type of journal	
Periodontology journal	22 (16.1)
General dentistry journal	29 (21.1)
Medical journal	1 (0.7)
Dental implantology journal	82 (59.9)
Prosthodontic journal	1 (0.7)
Periodontology and implantology journal	2 (1.5)
Type of primary outcome	
Continous	97 (70.8)
Binary	38 (27.7)
Both	2 (1.5)
Type of intervention	
Non-surgical	5 (3.6)
Surgical	23 (16.9)
Surgical & prosthetic	97 (70.8)
Non-surgical & pharmacological	5 (3.6)
Surgical & pharmacological	6 (4.4)
Surgical & pharmacological & prosthetic	1 (0.7)
Impact factor	
Median (IQR)	3.097 (1.699)
Google citations	
Median (IQR)	9 (14.5)

Abbreviation: IQR, interquartile range.

were found between the score on the quality of reporting of missing data and COI, sponsorship, impact factor or geographic location (Table S2, supplementary file). Studies better reporting LTFU were associated with a greater number of citations (RR: 1.056, CI: 1.017, 1.102, $p = .006$).

4 | DISCUSSION

4.1 | Key findings

Our study attempted to examine how RCTs published in implant dentistry report and handle missing data. The present findings

suggest that there is room for improvement in the quality of reporting of missing data in these trials. Furthermore, the strategies for handling missing data were not reported in half of these trials, with the "complete cases analysis" being the most frequent approach for missing data handling. Our findings provide comprehensive information on the current status on handling and reporting of missing data and may help to guide more robust future trials.

4.2 | Interpretation and implications

The lack of information on handling of LTFU might have important implications on the results of RCTs, mainly on those which have greater patient losses or where data are not missing at random. Some studies lost almost 50% of the originally randomized patients. Therefore, incomplete outcome data in these studies might be an important source of attrition bias that can possibly interfere with treatment estimates (Yao et al., 2017) and their precision given the lower than planned sample size (Spineli, Fleming, & Pandis, 2015). Again, it is important to emphasize that incomplete data may not lead to baseline imbalances in the evaluated primary outcome as this depends on the missingness mechanism (Hewitt, Kumaravel, Dumville, & Torgerson, 2010).

As pointed out earlier, assumptions on the relationship between incomplete data due to dropouts and influence on the treatment effects based on the quantity and the pattern of dropouts may be misleading (Bell, Kenward, Fairclough, & Horton, 2013). The keys for evaluating attrition bias are the reasons for dropouts and the approach used to deal with missing data (Bell et al., 2013; Rubin, 1976; Spineli et al., 2015). When data are MCAR (Little et al., 2012; Spineli et al., 2015): missing data are completely unrelated to the study variables. In this scenario patients leaving the study constitute a random sample of the study participants with similar event probability of having the outcome with those remaining in the study (Bell et al., 2013). MAR dropouts can be explained by the observed characteristic such as baseline characteristics. The response of the dropouts can be inferred from the response of those who remain in the study (Carpenter & Kenward, 2013). Methods such as direct likelihood would be valid but not generalized estimating equations (GEE) unless appropriate adjustments are implemented (Fitzmaurice, Molenberghs, & Lipsitz, 1995; Molenberghs & Kenward, 2007).

MNAR dropouts are directly associated with the outcome or outcome related side-effects. Missing data depends on the unobserved data, even after taking into account all the information in the observed data as in MAR. Under MNAR, inference is harder than MCAR or MAR because both the response of interest and the missingness mechanism must be considered (Carpenter & Kenward, 2013).

In our sample, the most common approach was the "complete case analysis" (N = 62, 45.3%), and this is in agreement with other studies (Fiero, Huang, Oren, & Bell, 2016; Powney, Williamson, Kirkham, & Kolamunnage-Dona, 2014). This method can be misleading in many occasions, because it considers that all data were MCAR, most likely an unrealistic assumption. One potential strategy would be to try to impute missing data and perform sensitivity analyses under various and plausible scenarios. If the sensitivity analyses do not change the study's conclusions, it is likely that missing data are not a threat to the study's validity (Bankhead, Aronson, Nunan, 2017). The number of trials using sensitivity analysis to evaluate the robustness of results when missing data are present seems to be low (Fiero et al., 2016). In half of the included trials in our study the method used to handle missing information was unclear. This is higher than a previously published review of RCTs published in five major medical journals which concluded that 19% of the trials did not report the method for handle LTFU (Akl et al., 2012).

In implant dentistry two levels of missing data may occur: at patient and at dental implant level. We may consider two different outcomes for implant loss: the first outcome is that resulting from the intervention applied or any disease involved (e.g. peri-implantitis) with the therapy. Therefore, this type of implant loss is not considered missing data, but it is an outcome. However, when the implants are lost in a very early stage (before occlusal load was applied), then we may consider missing values when this loss is not accounted for in the statistical analysis.

Interestingly, the intervention type was associated with more losses to follow-up. Trials including surgical and prosthetic phases (i.e. placement of dental implants plus dental prostheses) had greater losses compared to surgery alone. These results might be explained by the potentially longer follow-up periods in these studies. Similarly, inclusion of both ITT and PP analysis in the RCTs was associated with greater losses to follow-up than in trials with other types of analysis. However, such a finding is difficult to interpret but could be related with just better reporting and authors being more aware of the missing data consequences.

Many studies reported baseline characteristics of the patients included, but only a few reported the baseline characteristics of patients who dropped out of the study. Reporting of baseline characteristics should be detailed enough to allow the reader to understand whether any difference on patient's characteristics might have an influence on the reason for the dropout and may be associated with the outcome. Item 4 ("The proportion of RCTs that compared the baseline characteristics of participants LTFU to those not LTFU and the proportion that compared the baseline characteristics of those LTFU in intervention and control groups") was considered inadequately reported in 50% of the trials.

4.3 | Strength and limitations

This study included a sample of RCTs (N = 137) published mostly (N = 132) in IF journals. We feel that this sample is representative of the best evidence available in the field of implant dentistry. Due to the lack of good reporting, regarding the approaches used to handle missing data, it was not possible to adequately examine statistically potential associations between articles' characteristics and missing data handling. In many occasions, there was absolutely no report on the missing data handling or it was necessary to interpret which

TABLE 4 Missing data reporting

Question	Yes (%)	No/Unclear (%)
1. Did the randomized controlled trial (RCT) explicitly report whether lost to follow-up (LTFU) occurred or not?	137 (100)	0 (0)
2. Did the RCT report a CONSORT flow diagram with LTFU provided?	CONSORT: 32 (23.4) Non-CONSORT: 33 (24.1)	72 (52.5)
3a. Did the RCT report loss to follow-up separately for the 2 comparison groups? (Patients)	135 (98.5)	2 (1.5)
3b. Did the RCT report loss to follow-up separately for the 2 comparison groups? (Implants only)	92 (67.2)	45 (32.8)
4. Did the RCT report loss to follow-up at each planned outcome assessment?	68 (49.6)	69 (50.4)
5. Did the RCT compare the baseline characteristics of participants LTFU to those not LTFU and the proportion that compared the baseline characteristics of those LTFU to in intervention and control groups?	5 (3.6)	132 (96.4)
6. Did the RCT discuss the implications of the LTFU in the context of their findings?	20 (14.6)	117 (85.4)
7. Did the abstract report any information about missing data?	76* (55.5)	61 (44.5)

*Four abstracts only reported missing data on dental implants.

TABLE 5 Distribution of trial characteristics in the presence or absence of statistical approach for missing data handling at the trial level

Characteristic	No (%)	Yes (%)	Total (%)	Fisher Exact test
RCT analysis				
Unclear	62 (53)	55 (47)	117 (85.4)	0.075
Intention-to-treat	3 (37.5)	5 (62.5)	8 (5.8)	
Per protocol	6 (75)	2 (25)	8 (5.8)	
Intention-to-treat and per protocol	0 (0)	4 (100)	4 (3)	
COI				
No Report of COI	70 (52.2)	64 (47.8)	134 (97.8)	0.609
Report of COI	1 (23.3)	2 (66.7)	3 (2.2)	
Sponsorship				
Unclear/no funding	21 (67.7)	10 (22.3)	31 (22.6)	0.136
Non-profit	16 (47.1)	18 (52.9)	34 (24.8)	
Industry	34 (47.2)	38 (52.8)	72 (52.6)	
Intervention				
Non-surgical	7 (70)	3 (30)	10 (7.3)	0.405
Surgical	13 (48.5)	16 (61.5)	29 (21.2)	
Surgical & prosthetic	51 (52)	47 (48)	98 (71.5)	
Continent				
Africa	2 (50)	2 (50)	4 (2.9)	
Americas	14 (77.8)	4 (22.8)	18 (13.1)	0.110
Asia	10 (44.5)	12 (54.5)	22 (16.1)	
Europe	45 (48.4)	48 (51.6)	93 (67.9)	

approach was used (e.g. in the case of "complete case" analysis, when authors did not explicitly report the approach, but the text suggested that the missing variables were removed from the analysis).

The regression analysis indicated a positive association between better LTFU reporting and a higher number of citations. Although it is difficult to determine a clear reason for this association, these

findings may suggest that researchers may be more interested in trials with a more comprehensive reporting of all trial aspects including missing data. Furthermore, the inclusion of only articles in English might have introduced some sort of language bias. Finally, it was challenging to determine the sample of studies. It would be challenging to include studies representative from all time periods. We would need to include a larger number of RCTs that would make the study not feasible. Therefore, we decided to focus on the most recent publications in a 3-year time frame. However, we understand that by selecting the most recent published RCTs our findings may be more optimistic due to the expected increased awareness over time of the importance of methodological principles in research. Finally, we included only clinical outcomes, because they might be considered the most important outcomes for decision-making and are more in line to patient-important outcomes and the COMET initiative (Wolters et al., 2016).

4.4 | Further research

The analysis of missing data reporting and handling should be further performed in other dental fields to understand how authors of the other dental disciplines address this issue. It is also evident that there is a need to increase awareness among investigators in dentistry about the perils of ignoring or mishandling missing data. Furthermore, it would be also important to evaluate how the results of published trials in dentistry with incomplete data could change under different missingness assumptions. However, it would be necessary to have access to raw datasets in order for this to be accomplished. Authors of RCTs should also consider efficient strategies for retaining study participants (Robinson, Dennison, Wayman, Pronovost, & Needham, 2007). This would potentially contribute to the reduction of missing data, a problem especially in studies with long observation periods.

5 | CONCLUSIONS

The present study found that the majority of RCTs in implant dentistry do not report any information on how authors handled missing data. The most used approach to deal with missing data was the "complete case analysis" which can be problematic in terms of bias and precision. Authors of RCTs in implant dentistry should focus on a more comprehensive report of reasons for dropouts in order to choose the best approach for dealing with missing information. Analysis of missing data involving imputations requires knowledge of relevant statistical methodology. We understand that our results have important research and clinical implications. Authors of future trials will likely be more aware on the adequate reporting and handling of missing data. Clinicians reviewing implant dentistry publications will be better informed about the potential limitations due to missing data in the decision-making process.

CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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