An Assessment of the Risk of Bias in Randomized Controlled Trial Reports Published in Prosthodontic and Implant Dentistry Journals

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ABSTRACT

Purpose: The objective of this study was to assess the risk of bias of randomized controlled trials (RCTs) published in prosthodontic and implantology journals. ***Materials and Methods:*** The last 30 issues of 9 journals in the field of prosthodontic and implant dentistry (Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Implant Dentistry, International Journal of Oral & Maxillofacial Implants, International Journal of Periodontics and Restorative Dentistry, International Journal of Prosthodontics, Journal of Dentistry, Journal of Oral Rehabilitation and Journal of Prosthetic Dentistry) were hand-searched for RCTs. Risk of bias was assessed using the Cochrane Collaboration risk of bias tool and analyzed descriptively. ***Results:*** From the 3667 articles screened a total147 RCTs were identified and included. The number of published RCTs increased with time. The overall distribution of a high risk of bias assessment varied across the domains of the Cochrane risk of bias tool: 8% for random sequence generation, 18% for allocation concealment, 41% for masking, 47% for blinding of outcome assessment, 7% for incomplete outcome data, 12% for selective reporting, and 41% for other biases. ***Conclusions:*** The distribution of high risk of bias of RCTs published in the selected prosthodontic and implant dental journals varied among journals and ranged from 8%-47% and can be considered as substantial.

Key words: randomized controlled trial, implant dentistry, prosthodontics, risk of bias, Cochrane

Introduction

Randomized controlled trials (RCTs) are considered the gold standard to study the effectiveness of medical interventions,[1] but despite their status, RCTs are still susceptible to bias.[2] Bias is defined as the systematic deviation from the actual treatment effect and can have serious implications for clinical practice. A common classification of the types of bias that can be encountered in RCTs is the one proposed by the Cochrane Collaboration.[3] This classification scheme includes selection, performance, detection, attrition, and reporting biases, which are applicable to different trial stages. The extent to which these biases operate in a given trial may yield inaccuracies of varying magnitude and direction in the estimates of a treatment effect.

The Cochrane Collaboration has developed a tool to assess potential bias in trials by examining 7 relevant domains (sequence generation, allocation concealment, masking, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and "other sources of bias").[3] This tool is used in all Cochrane reviews and is supported by empirical evidence.[2,4-7]

In recent years the number of published RCTs in the biomedical field has increased exponentially, however, there is evidence that the quality in terms of methods and reporting is often suboptimal.[8-17] Although several reports have assessed the reporting quality of RCTs in various dental fields,[8-11,13-14,16] reporting quality is not directly associated with risk of bias. To the best of our knowledge, the risk of bias as a proxy to internal validity of RCTs has not been assessed previously in any field of dentistry, including prosthodontics and implant dentistry. Therefore, the objective of this study was to assess the risk of bias in RCTs published in prosthodontic and implant dentistry journals and to explore possible associations between risk of bias and report characteristics.

Materials and Methods

The contents of the last 30 issues of the following nine prosthodontic and implant dentistry journals were hand-searched from March 2012 backwards by 2 authors (S.N.P. and D.K.): *Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Implant Dentistry, International Journal of Oral & Maxillofacial Implants, International Journal of Periodontics and Restorative Dentistry, International Journal of Prosthodontics, Journal of Dentistry, Journal of Oral Rehabilitation and Journal of Prosthetic Dentistry*. Studies were included, if it was stated in the title, abstract or the text that it was an RCT. Non-randomized and all non-clinical studies were excluded.

From the included articles two authors (S.N.P. and D.K.) extracted information on journal, year of publication, continent of origin (based on the corresponding author), ethical approval, statistical significance of the main outcome, number of authors, statistician/methodologist involvement (affiliations or explicit statement) and number of involved centers.

The Cochrane Collaboration's risk of bias tool was used to assess the internal validity of the included RCTs.[18] The risk of bias tools examines the following 7 domains:

1. Random sequence generation: adequate, if the method is stated and is considered truly random (eg, computer-generated sequence, random number table, or coin toss). This domain is associated with selection bias.
2. Allocation concealment: adequate, if an appropriate method to prevent knowing or predicting the allocation sequence in advance is stated to have been used (eg, central randomization or sequentially-numbered opaque envelopes). This domain is associated with selection bias.
3. Masking (blinding of participants and personnel): adequate, if the use of any form of blinding of participants, outcome assessor, investigator, or care givers is reported. This domain is associated with performance bias.

4. Blinding outcome assessment: adequate, if outcome assessment is blinded or it is judged that the outcome and the outcome measurement are not likely to be influenced by lack of blinding. This domain is associated with detection bias.
5. Incomplete outcome data: adequate, if any one of the following is true: no missing outcome data; reasons for missing outcome data unlikely to be related to true outcome; missing outcome data balanced in numbers across groups; similar reasons for missing data across groups. This domain is associated with attrition bias.
6. Reporting bias: adequate, if the study protocol is available and all of the study's pre-specified outcomes have been reported or if the study protocol is not available, but it is clear that the published reports included all pre-specified outcomes. This domain is associated with reporting bias.
7. Other bias: adequate, if the study appears to be free of other sources of bias (stopped early due to some data-dependent process; or extreme baseline imbalance; or claimed to have been fraudulent).

Custom data collection forms were prepared and the two authors were calibrated before the start of the study. Inter-rater reliability was assessed using the kappa statistic on eighty randomly chosen reports from the overall sample.

The characteristics of the included trials and the distribution of the risk of bias assessments (low, unclear, high) overall and per trial characteristic were tabulated. Due to the relatively small number of RCTs and the large number of variables only descriptive statistics were carried out using the Stata 13 statistical software package (Stata Corp, College Station, TX, USA).

Results

In total 3667 articles were examined; 3520 were excluded for not adhering to the pre-determined inclusion criteria, leaving 147 RCTs for detailed assessment (Figure 1). Inter-

rater agreement was found to be excellent (kappa 0.88, 95% CI: 0.87-0.89). The included articles reported on a wide selection of topics ranging from surgical implant procedures and techniques, survival of implants and prostheses, biological responses, clinician's perspective of esthetics and patient satisfaction. The characteristics of the included trials are shown in Table 1. The journals that had published the greatest number of RCTs in descending order were: *Clinical Oral Implants Research* (n = 46), followed by *International Journal of Oral & Maxillofacial Implants* (n = 24), *Journal of Dentistry* (n = 21) and *International Journal of Periodontics and Restorative Dentistry* (n = 20). The number of published RCTs increased as a function of the publication year and the geographic region contributing the most was Europe (59%), followed by Asia/other regions (21%), and North/South America (20%). Fifty nine percent of the identified RCTs reported statistically significant results, while 71% of the identified RCTs were multicenter.

The overall risk of bias assessment of the included RCTs per domain is given in Table 2 and Figure 2. High risk of bias for the included trials was found in 8% for random sequence generation, in 18% for allocation concealment, in 41% for masking, in 47% for blinding of outcome assessment, in 7% for incomplete outcome data, in 12% for selective reporting and in 41% for other biases.

The risk of bias assessment of the included trials per domain and trial characteristics is shown in Table 3.

Discussion

This cross-sectional study assessed the risk of bias of recently published RCTs published in prosthodontic and implant dentistry journals using the Cochrane risk of bias tool. The percentage of RCTs with low risk of bias varied considerably (15% to 84%) among the 7 domains of the Cochrane tool. Considerable differences were also found in the present study in the percentage of RCTs with low risk of bias for each of the 7 domains compared to

similar studies in medicine:[12,19-21] random sequence generation - 58% in the present study (32%-59% in medicine); allocation concealment - 27% in the present study (25%-50% in medicine); masking - 16% in the present study (31%-89% in medicine); blinding of outcome assessment - 32% in the present study (20%-60% in medicine); incomplete outcome data - 74% in the present study (33%-89% in medicine); reporting bias - 84% in the present study (79%-98% in medicine); and other bias - 15% in the present study (39%-98% in medicine). However, different types of interventions might be prone to different kinds of bias[2,22-23] and, therefore, comparisons across fields should be exercised with caution.

Studies in the biomedical literature have reported that, often, the terms ‘‘randomization’’ and ‘‘randomly assigned to groups’’ are used incorrectly or are not completely reported.[13,16,24-29] Empirical evidence has shown that inadequate or unclear randomization is associated with effect exaggeration by 11%, which is accentuated in RCTs with subjective outcomes.[2]

Masking (blinding of participants or personnel) or blinding of outcome assessors was also assessed to be inadequate in the included RCTs. Although masking might not be always feasible in RCTs of oral implantology or prosthodontics, the blinding of the outcome assessors or data analysts is almost always feasible. Similar inadequacies have been reported in other fields of dentistry[16] and are indicative of the low emphasis given to blinding. Empirical evidence indicates that inadequate blinding is associated with a 13% exaggeration of intervention effects[2] in RCTs with subjective outcomes. The effect of lack of blinding appeared to be greater than the effect of inadequate or unclear random sequence generation or allocation concealment.[2]

Attrition and selective outcome reporting are also a source of bias for RCTs.[4-7] Among the RCTs included in the present study both types of bias were not overly present, with low risk of bias found in 74% and 82% trials respectively.

A number of characteristics were collected from each RCT (Table 1) and used to tabulate the risk of bias (Table 3). However, due to the limited number of RCTs and the high data

dispersion, no inferential statistics were performed to formally test significant associations and the characteristics were analyzed descriptively.

Considerable variability was found in all domains of the Cochrane tool among the 9 selected journals. This may be related to the fact that journals with higher visibility and impact may attract trials of better quality. The assessment of the included trials was based only on their published reports and it is possible that incomplete reporting of trials might have influenced their risk of bias assessment.

The assessed risk of bias of the RCTs did not seem to be associated with publication year in this study. However, the varying number of issues-per-year for each journal and the inclusion of the last 30 issues meant that different years were covered for each journal. Therefore, a direct comparison among publication years cannot be made.

The risk of bias in this study was not consistently influenced by the trial's country of origin in this study. According to empirical evidence,[30] RCTs from developing countries tend to show more favorable treatment effects than RCTs originating from developed countries. This could arise from biases in study conduct / reporting or could mirror genuine differences in baseline risks or differences in treatment modalities. This can be supported in part from this study by the lower prevalence of low risk for RCTs from Asia/other continents in the masking and blind outcome assessment compared to RCTs from Europe or America.

The importance of a statistician/methodologist in improved study quality has been previously documented.[31] Research without methodological assistance has been reported to be more susceptible to rejection without review and/or publication.[32] In this study, RCTs with involvement of a methodologist were more likely to have low risk of bias in the random sequence allocation and the allocation concealment domains, which could be attributed to their methodological input in the design of the trial.

The number of trials centers influenced almost all of assessed domains, as multicenter RCTs were more likely to have low risk of bias in the random sequence, allocation concealment, masking and blinding, reporting bias and other bias domain than single-center RCTs, which is consistent with the medical literature.[33] In a recent cross-sectional study in

oral implantology the reporting quality of mutlicenter RCTs' abstracts was higher than that of single-center RCTs.[14] The same was observed for the full reports of RCTs in orthodontics.[34]

The limitations of this study included the absence of duplicate data extraction on the entire sample of articles. The inter-rater agreement of the Cochrane tool has been reported to be problematic in some cases.[18] In this study, the inter-rater agreement was fairly good, due to the calibration of the two authors, but still discussion was needed in some instances until a consensus was reached. Also, classification of RCTs was based on reporting only; however, lack of information on the published article does not necessarily mean that correct procedures were not implemented.[35,36] Such domains without adequate description are judged as "unclear" in the Cochrane tool and differ from domains with "low risk". Also, one must bear in mind that some trials labeled from the authors as RCTs probably aren't RCTs.[27-28] Finally, the sample of journals assessed in this study was limited to prosthetic or implant dentistry and the findings may not be generalizable to other fields.

The CONSORT reporting guidelines were formally adopted by only 5 [CIDRR, COIR, JD, JOR and JPD] out of the 9 included journals. Although the adoption of the CONSORT criteria by many journals seems to have improved the reporting of RCTs,[37-39] poor reporting is still a common problem, especially in countries with a limited experience in conducting RCTs. A recent report indicated that reporting quality in public health dentistry has not significantly improved since the publication of the CONSORT statement.[40] Journal editors and peer reviewers have an important role in ensuring optimal reporting of RCTs. This has driven some to suggest the need to better regulate the peer-review process including enforcement of good practice guidelines.[41] Others recommend that more journals should adopt the CONSORT criteria, and that those who endorse it should do more to ensure adherence of submitted trials.[42,43] In this direction, an active implementation strategy of CONSORT adherence adopted by an orthodontic journal[44] improved the reporting quality of RCTs and might be more effective than passive adoption of guidelines. More emphasis in clinical trial methodology in education and better adherence to existing guidelines on

randomized trials may help facilitate improvements in the quality of RCTs in prosthodontics and implant dentistry.

Conclusions

The analysis of the selected prosthodontic and implant dental literature indicated that the risk of bias in RCTs of these fields might be considerable. The percentage of RCTs in high risk of bias ranged from 8% to 47% in the various domains of the Cochrane risk of bias tool. Adherence to existing guidelines can improve the internal validity of RCTs.

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Conflicts of Interest

The authors reported no conflicts of interest related to this study.

References

1. Schulz KF, Grimes DA. Generation of allocation sequences in randomized trials: chance, not choice. Lancet 2002;359:515–519.
2. Savović J, Jones H, Altman D, et al. Influence of reported study design characteristics on intervention effect estimates from randomised controlled trials: combined analysis of meta-epidemiological studies. Health Technol Assess 2012;16:1–82.
3. Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions [version 5.1.0, updated March 2011]. The Cochrane Collaboration; 2011. Available at: www.cochrane-handbook.org.
4. Dwan K, Altman DG, Arnaiz JA, et al. Systematic review of the empirical evidence of study publication bias and outcome reporting bias. PLoS One 2008;3:e3081.
5. Kirkham JJ, Dwan KM, Altman DG, et al. The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews. BMJ 2010;340:c365.
6. Nuesch E, Trelle S, Reichenbach S, et al. The effects of excluding patients from the analysis in randomised controlled trials: meta-epidemiological study. BMJ 2009;339:b3244.
7. Vestbo J, Anderson JA, Calverley PMA, et al. Bias due to withdrawal in long-term randomised trials in COPD: evidence from the TORCH study. Clin Respir J 2011;5:44–9.
8. Antczak AA, Tang J, Chalmers TC. Quality assessment of randomized control trials in dental research. II. Results: periodontal research. J Periodontal Res 1986;21:315–21.
9. Esposito M, Coulthard P, Worthington HV, Jokstad A. Quality assessment of randomized controlled trials of oral implants. Int J Oral Maxillofac Implants 2001;16:783–92.
10. Faggion CMJr, Giannakopoulos NN. Quality of reporting in abstracts of randomized controlled trials published in leading journals of peri-odontology and dental implantology: a survey. J Periodontol 2012;83:1251–6.

11. Fleming PS, Buckley N, Seehra J, Polychronopoulou A, Pandis N. Re-porting quality of abstracts of randomized controlled trials published in leading orthodontic journals from 2006 to 2011. Am J Orthod Dentofacial Orthop 2012;142:451–8.
12. Hopewell S, Dutton S, Yu LM, et al. The quality of reports of randomised trials in 2000 and 2006: comparative study of articles indexed in PubMed. BMJ 2010;340:c723.
13. Jokstad A, Esposito M, Coulthard P, Worthington HV. The reporting of randomized controlled trials in prosthodontics. Int J Prosthodont 2002;15:230–42.
14. Kiriakou J, Pandis N, Madianos P, Polychronopoulou A. Assessing the reporting quality in abstracts of randomized controlled trials in leading journals of oral implantology. J Evid Based Dent Pract 2014;14:9–15.
15. Moher D, Jadad AR, Nichol G, Penman M, Tugwell P, Walsh S. Assessing the quality of randomized controlled trials: an annotated bibliography of scales and checklists. Control Clin Trials 1995;16:62–73.
16. Pandis N, Polychronopoulou A, Eliades T. An assessment of quality characteristics of randomised control trials published in dental journals. J Dent 2010;38:713–21.
17. Patel DR, O'Brien T, Petrie A, Petridis H. A Systematic Review of Outcome Measurements and Quality of Studies Evaluating Fixed Tooth-Supported Restorations. J Prosthodont 2014;26:421–33.
18. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011;343:d5928.
19. Ahmed Ali U, van der Sluis PC, Issa Y, et al. Trends in worldwide volume and methodological quality of surgical randomized controlled trials. Ann Surg 2013;258:199–207.
20. Crocetti MT, Amin DD, Scherer R. Assessment of risk of bias among pediatric randomized controlled trials. Pediatrics 2010;126:298–305.
21. Hartling L, Ospina M, Liang Y, et al. Risk of bias versus quality assessment of randomised controlled trials: cross sectional study. BMJ 2009;339:b4012.

22. Papageorgiou SN, Antonoglou GN, Tsiranidou E, Jepsen S, Jäger A. Bias and small-study effects influence treatment effect estimates: a meta-epidemiological study in oral medicine. J Clin Epidemiol 2014;67:984–992.
23. Wood L, Egger M, Gluud LL, et al. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. BMJ 2008;336:601–5.
24. Adetugbo K, Williams H. How well are randomized controlled trials reported in the dermatology literature? Arch Dermatol 2000;136:381–5.
25. Altman DG, Dore CJ. Randomisation and baseline comparisons in clinical trials. Lancet 1990;335:149–53.
26. Dumbrigue HB, Jones JS, Esquivel JF. Control of bias in randomized controlled trials published in prosthodontic journals. J Prosthet Dent 2001;86:592–6.
27. Koletsi D, Pandis N, Polychronopoulou A, Eliades T. Mislabeling controlled clinical trials (CCTs) as "randomized clinical trials (RCTs)" in dental specialty journals. J Evid Based Dent Pract 2012;12:124–30.
28. Koletsi D, Pandis N, Polychronopoulou A, Eliades T. What's in a title? An assessment of whether randomized controlled trial in a title means that it is one. Am J Orthod Dentofacial Orthop 2012;141:679–85.
29. Montenegro R, Needleman I, Moles D, Tonetti M. Quality of RCTs in periodontology. A systematic review. J Dent Res 2002;81:866–70.
30. Panagiotou OA, Contopoulos-Ioannidis DG, Ioannidis JP. Comparative effect sizes in randomised trials from less developed and more developed countries: meta-epidemiological assessment. BMJ 2013;346:f707.
31. Delgado-Rodriguez M, Ruiz-Canela M, De Irala-Estevez J, Llorca J, Martinez-Gonzalez A. Participation of epidemiologists and/or biostatisticians and methodological quality of published controlled clinical trials. J Epidemiol Community Health 2001;55:569–72.
32. Altman DG, Goodman SN, Schroter S. How statistical expertise is used in medical research. JAMA 2002;287:2817–20.

33. Cho HJ, Chung JH, Jo JK, et al. Assessments of the quality of randomized controlled trials published in International Journal of Urology from 1994 to 2011. Int J Urol 2013;20:1212–9.
34. Lempesi E, Koletsi D, Fleming PS, Pandis N. The reporting quality of randomized controlled trials in orthodontics. J Evid Based Dent Pract 2014;14:46–52.
35. Chan AW, Hróbjartsson A, Haahr MT, Gøtzsche PC, Altman DG. Empirical evidence for selective reporting of outcomes in randomized trials: comparison of protocols to published articles. JAMA 2004;291:2457–65.
36. Dwan K, Altman DG, Cresswell L, Blundell M, Gamble CL, Williamson PR. Comparison of protocols and registry entries to published reports for randomized controlled trials. Cochrane Database Syst Rev 2011;1:MR000031.
37. Kane RL, Wang J, Garrard J. Reporting in randomized clinical trials improved after adoption of the CONSORT statement. J Clin Epidemiol 2007;60:241–249.
38. Moher D, Jones A, Lepage L. Use of the CONSORT statement and quality of reports of randomized trials: a comparative before-and-after evaluation. JAMA 2001;285:1992–1995.
39. Plint AC, Moher D, Morrison A, et al. Does the CONSORT checklist improve the quality of reports of randomised controlled trials? A systematic review. Med J Aust 2006;185:263–267.
40. Savithra P, Nagesh LS. Have CONSORT guidelines improved the quality of reporting of randomised controlled trials published in public health dentistry journals? Oral Health Prev Dent 2013;11:95–103.
41. Wu T, Li Y, Bian Z, et al. Randomized trials published in some Chinese journals: how many are randomized? Trials 2009;10:46.
42. Altman DG. Endorsement of the CONSORT statement by high impact medical journals: survey of instructions for authors. BMJ 2005;330:1056–1057.

43. Hopewell S, Altman DG, Moher D, et al. Endorsement of the CONSORT statement by high impact factor medical journals: a survey of journal editors and journal “instructions to authors.” Trials 2008;9:20.

44. Pandis N, Shamseer L, Kokich VG, Fleming PS, Moher D. Active implementation strategy of CONSORT adherence by a dental specialty journal improved randomized clinical trial reporting. J Clin Epidemiol 2014;67:1044–8.

Tables

Table 1 Characteristics of the 147 Included Randomized Controlled Trials

		n (%)
Journal	CIDRR	13 (9%)
	COIR	46 (31%)
	ID	4 (3%)
	IJOMI	24 (16%)
	IJPRD	15 (10%)
	IJP	20 (14%)
	JD	21 (14%)
	JOR	2 (1%)
	JPD	2 (1%)
Publication year	2007	4 (3%)
	2008	12 (8%)
	2009	13 (9%)
	2010	41 (28%)
	2011	42 (29%)
	2012	35 (24%)
Continent	Europe	86 (59%)
	Americas	30 (20%)
	Asia/other	31 (21%)
Ethics	No	41 (28%)
	Yes	106 (72%)
Significant results	No	60 (41%)
	Yes	87 (59%)
Number of authors	1-3	35 (24%)
	4-5	60 (41%)
	≥6	52 (35%)
Statistician/methodologist involvement	No	92 (63%)
	Yes	55 (37%)
Number of centers	Single-center	42 (29%)
	Multicenter	105 (71%)

CIDRR = Clin Implant Dent Relat Res; COIR = Clin Oral Implants Res; ID = Implant Dent; IJOMI = Int J Oral Maxillofac Implants; IJPRD = Int J Periodontics Restorative Dent; IJP = Int J Prosth; JD = J Dent; JOR = J Oral Rehab; JPD = J Prosthet Dent.

Table 2 Overall Risk of Bias Assessment of the 147 Included Randomized Controlled Trials

Risk of bias	Low - n (%)	Unclear - n (%)	High - n (%)
Random sequence generation	85 (58%)	50 (34%)	12 (8%)
Allocation concealment	40 (27%)	80 (54%)	27 (18%)
Masking	23 (16%)	63 (43%)	61 (41%)
Blinding of outcome assessment	47 (32%)	31 (21%)	69 (47%)
Incomplete outcome data	109 (74%)	28 (19%)	10 (7%)
Reporting bias	123 (84%)	6 (4%)	18 (12%)
Other bias	22 (15%)	65 (44%)	60 (41%)

Table 3 Risk of Bias of Included Randomized Controlled Trials Tabulated by Trial Characteristics

	Random Sequence Generation			Allocation Concealment			Masking			Blind Outcome Assessment			Attrition Bias			Reporting Bias			Other Bias			
	Low	Unclear	High	Low	Unclear	High	Low	Unclear	High	Low	Unclear	High	Low	Unclear	High	Low	Unclear	High	Low	Unclear	High	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N(%)
Journal																						
CIDRR	6 (46)	7 (54)	0 (0)	0 (0)	10 (77)	3 (23)	1 (8)	7 (54)	5 (38)	2 (15)	6 (46)	5 (38)	6 (46)	3 (23)	4 (31)	12 (92)	0 (0)	1 (8)	0 (0)	4 (31)	9 (69)	13 (9)
COIR	33 (72)	12 (26)	1 (2)	12 (37)	29 (63)	0 (0)	5 (11)	27 (59)	14 (30)	20 (43)	11 (24)	15 (33)	41 (89)	4 (9)	1 (2)	40 (87)	0 (0)	6 (13)	9 (20)	21 (46)	16 (35)	46 (31)
ID	3 (75)	1 (25)	0 (0)	2 (50)	1 (25)	1 (25)	0 (0)	1 (25)	3 (75)	0 (0)	2 (50)	2 (50)	4 (100)	0 (0)	0 (0)	4 (100)	0 (0)	0 (0)	0 (0)	3 (75)	1 (25)	4 (3)
IJOMI	13 (54)	11 (46)	0 (0)	7 (29)	17 (71)	0 (0)	3 (13)	12 (50)	9 (38)	11 (46)	3 (13)	10 (42)	16 (67)	8 (33)	0 (0)	20 (83)	1 (4)	3 (13)	3 (13)	13 (54)	8 (33)	24 (16)
IJPRD	10 (67)	2 (13)	3 (20)	3 (20)	3 (20)	9 (60)	5 (33)	0 (0)	10 (67)	3 (20)	1 (7)	11 (73)	7 (47)	7 (47)	1 (7)	9 (60)	4 (27)	2 (13)	4 (27)	1 (7)	10 (67)	15 (10)
IJP	10 (50)	3 (15)	7 (35)	3 (15)	5 (25)	12 (60)	3 (15)	4 (20)	13 (65)	2 (10)	2 (10)	16 (80)	16 (80)	2 (10)	2 (10)	20 (100)	0 (0)	0 (0)	5 (25)	5 (25)	10 (50)	20 (14)
JD	9 (43)	12 (57)	0 (0)	8 (38)	13 (62)	0 (0)	6 (29)	10 (48)	5 (24)	9 (43)	4 (19)	8 (38)	16 (76)	4 (19)	1 (5)	15 (71)	1 (5)	5 (24)	0 (0)	18 (86)	3 (14)	21 (14)
JOR	1 (50)	1 (50)	0 (0)	0 (0)	1 (50)	1 (50)	0 (0)	1 (50)	1 (50)	0 (0)	1 (50)	1 (50)	1 (50)	0 (0)	1 (50)	2 (100)	0 (0)	0 (0)	1 (50)	0 (0)	1 (50)	2 (1)
JPD	0 (0)	1 (50)	1 (50)	0 (0)	1 (50)	1 (50)	0 (0)	1 (50)	1 (50)	0 (0)	1 (50)	1 (50)	2 (100)	0 (0)	0 (0)	1 (50)	0 (0)	1 (50)	0 (0)	0 (0)	2 (100)	2 (1)
Year																						
2007	1 (25)	2 (50)	1 (25)	1 (25)	1 (25)	2 (50)	0 (0)	2 (50)	2 (50)	0 (0)	2 (50)	2 (50)	1 (25)	2 (50)	1 (25)	4 (100)	0 (0)	0 (0)	0 (0)	2 (50)	2 (50)	4 (3)
2008	7 (58)	4 (33)	1 (8)	2 (17)	7 (58)	3 (25)	1 (8)	4 (33)	7 (58)	3 (25)	2 (17)	7 (58)	7 (58)	5 (42)	0 (0)	9 (75)	1 (8)	2 (17)	1 (8)	4 (33)	7 (58)	12 (8)
2009	8 (62)	4 (31)	1 (8)	4 (31)	5 (38)	4 (31)	3 (23)	2 (15)	8 (62)	2 (15)	1 (8)	10 (77)	11 (85)	2 (15)	0 (0)	9 (69)	3 (23)	1 (8)	2 (15)	6 (46)	5 (38)	13 (9)
2010	24 (59)	13 (32)	4 (10)	14 (34)	21 (51)	6 (15)	5 (12)	19 (46)	17 (41)	16 (39)	6 (15)	19 (46)	32 (78)	6 (15)	3 (7)	37 (90)	0 (0)	4 (10)	6 (15)	15 (37)	20 (49)	41 (28)
2011	23 (55)	19 (45)	0 (0)	12 (29)	25 (60)	5 (12)	7 (17)	19 (45)	16 (38)	13 (31)	9 (21)	20 (48)	34 (81)	6 (14)	2 (5)	32 (76)	2 (5)	8 (19)	8 (19)	19 (45)	15 (36)	42 (29)
2012	22 (63)	8 (23)	5 (14)	7 (20)	21 (60)	7 (20)	7 (20)	17 (49)	11 (31)	13 (37)	11 (31)	11 (31)	24 (69)	7 (20)	4 (11)	32 (91)	0 (0)	3 (9)	5 (14)	19 (54)	11 (31)	35 (24)
Continent																						
Europe	50 (58)	28 (33)	8 (9)	24 (28)	46 (53)	16 (19)	12 (14)	40 (47)	34 (40)	31 (36)	15 (17)	40 (47)	65 (76)	16 (19)	5 (6)	70 (81)	4 (5)	5 (12)	12 (14)	39 (45)	35 (41)	86 (59)
Americas	20 (67)	8 (27)	2 (7)	8 (27)	20 (67)	2 (7)	8 (27)	11 (37)	11 (37)	11 (37)	6 (20)	13 (43)	20 (67)	7 (23)	3 (10)	25 (83)	1 (3)	3 (4)	4 (13)	15 (50)	11 (37)	30 (20)
Asia/other	15	14	2	8	14	9	3	12	16	5	10	16	24	5	2	28	1	3 (2)	6	11	14	31

	(48)	(45)	(6)	(26)	(45)	(29)	(10)	(39)	(52)	(16)	(32)	(52)	(77)	(16)	(6)	(90)	(3)		(19)	(35)	(45)	(21)
Ethics																						
No	26 (63)	11 (27)	4 (10)	12 (29)	16 (39)	13 (32)	8 (20)	14 (34)	19 (46)	11 (27)	8 (20)	22 (54)	28 (68)	9 (22)	4 (10)	34 (83)	3 (7)	4 (10)	4 (10)	17 (41)	20 (49)	41 (28)
Yes	59 (56)	39 (37)	8 (8)	28 (26)	64 (60)	14 (13)	15 (14)	49 (46)	42 (40)	36 (34)	23 (22)	47 (44)	81 (76)	19 (18)	6 (6)	89 (84)	3 (3)	14 (13)	18 (17)	48 (45)	40 (38)	106 (72)
Significant results																						
No	39 (65)	14 (23)	7 (12)	15 (25)	31 (52)	14 (23)	6 (10)	27 (45)	27 (45)	18 (30)	15 (25)	27 (45)	39 (65)	12 (20)	9 (15)	51 (85)	0 (0)	9 (15)	11 (18)	20 (33)	29 (48)	60 (41)
Yes	46 (53)	36 (41)	5 (6)	25 (29)	49 (56)	13 (15)	17 (20)	36 (41)	34 (39)	29 (33)	16 (18)	42 (48)	70 (80)	16 (18)	1 (1)	72 (83)	6 (7)	9 (10)	11 (13)	45 (52)	31 (36)	87 (59)
No of authors																						
1-3	24 (69)	9 (26)	2 (6)	11 (31)	17 (49)	7 (20)	8 (23)	16 (46)	11 (31)	13 (37)	11 (31)	11 (31)	24 (69)	7 (20)	4 (11)	29 (83)	1 (3)	5 (14)	5 (14)	13 (37)	17 (49)	35 (24)
4-5	31 (52)	23 (38)	6 (10)	15 (25)	32 (53)	13 (22)	5 (8)	22 (37)	33 (55)	12 (20)	11 (18)	37 (62)	46 (77)	11 (18)	3 (5)	50 (83)	4 (7)	6 (10)	9 (15)	23 (38)	28 (47)	60 (41)
≥6	30 (58)	18 (35)	4 (8)	14 (27)	31 (60)	7 (13)	10 (19)	25 (48)	17 (37)	22 (42)	9 (17)	21 (40)	39 (75)	10 (19)	3 (6)	44 (85)	1 (2)	7 (13)	8 (15)	29 (56)	15 (29)	52 (35)
Statistician/methodologist involvement																						
No	47 (51)	38 (41)	7 (8)	20 (22)	56 (61)	16 (17)	15 (16)	43 (47)	34 (37)	33 (36)	20 (22)	39 (42)	66 (72)	18 (20)	8 (9)	78 (85)	2 (2)	12 (13)	9 (10)	46 (50)	37 (40)	92 (63)
Yes	38 (69)	12 (22)	5 (9)	20 (36)	24 (44)	11 (20)	8 (15)	20 (36)	27 (49)	14 (25)	11 (20)	30 (55)	43 (78)	10 (18)	2 (4)	45 (82)	4 (7)	6 (11)	13 (24)	19 (35)	23 (42)	55 (37)
Number of centers																						
Single-center	21 (50)	16 (38)	5 (12)	10 (24)	25 (60)	7 (17)	5 (12)	19 (45)	18 (43)	12 (29)	12 (29)	18 (43)	33 (79)	6 (14)	3 (7)	33 (79)	1 (2)	8 (19)	3 (7)	20 (48)	19 (45)	42 (29)
Multicenter	64 (61)	34 (32)	7 (7)	30 (29)	55 (52)	20 (19)	18 (17)	44 (42)	43 (41)	35 (33)	19 (18)	51 (49)	76 (72)	22 (21)	7 (7)	90 (86)	5 (5)	10 (10)	19 (18)	45 (43)	41 (39)	105 (71)
Total	85 (58)	50 (34)	12 (8)	40 (27)	80 (54)	27 (18)	23 (16)	63 (43)	61 (41)	47 (32)	31 (21)	69 (47)	109 (74)	28 (19)	10 (7)	123 (84)	6 (4)	18 (12)	22 (15)	65 (44)	60 (41)	147 (100)

CIDRR = Clin Implant Dent Relat Res; COIR = Clin Oral Implants Res; ID = Implant Dent; IJOMI = Int J Oral Maxillofac Implants; IJPRD = Int J Periodontics Restorative Dent; IJP = Int J Prosth; JD = J Dent; JOR = J Oral Rehab; JPD = J Prosthet Dent.

Figures

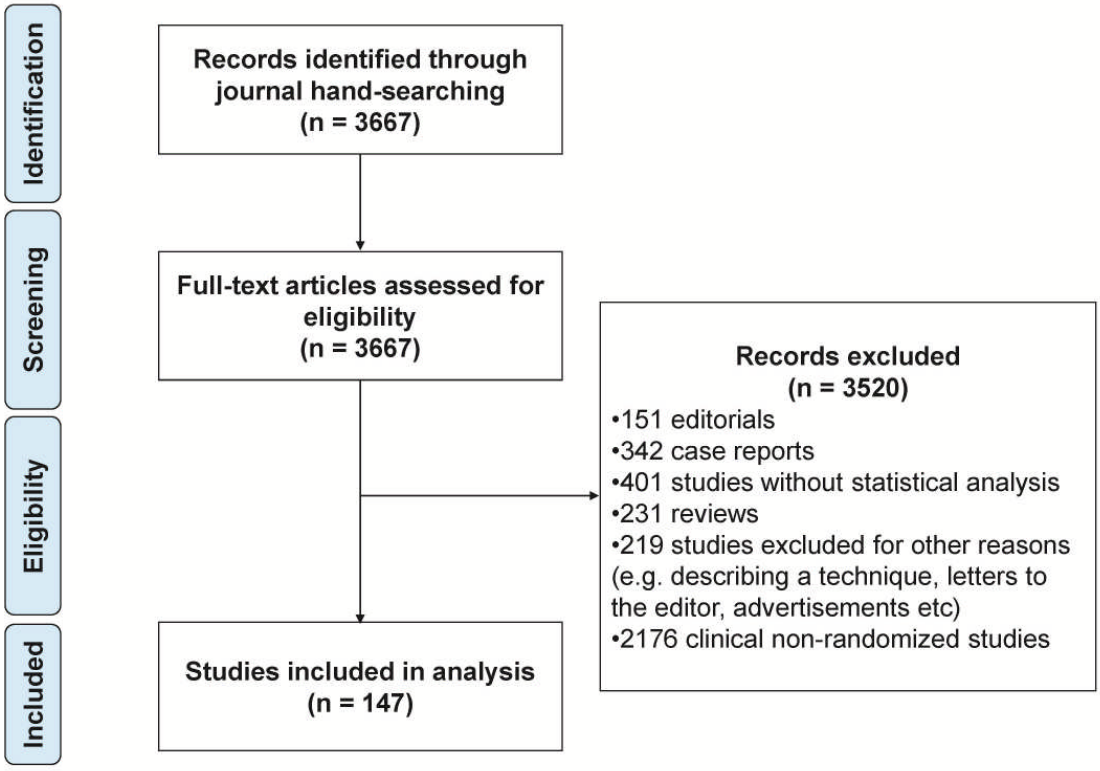

Fig 1 Flow diagram of study selection.

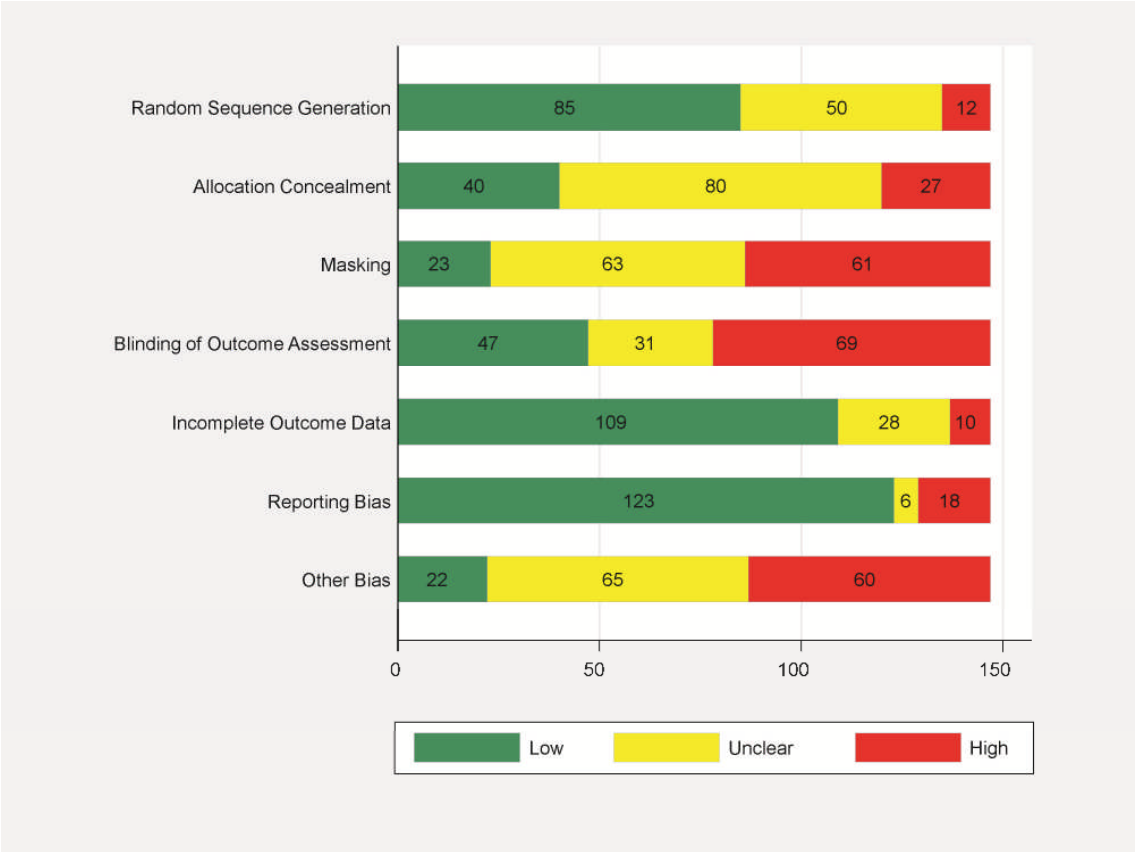

Fig 2 Overall risk of bias in the included randomized controlled trials.